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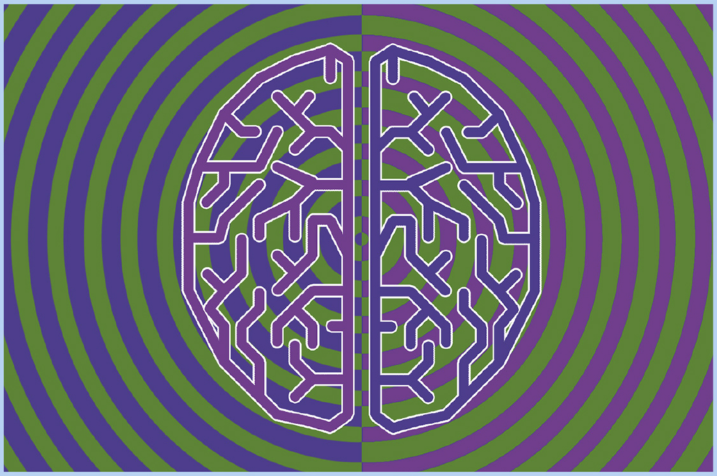
Cerebral Lateralization and Cognition: Evolutionary and Developmental Investigations of Behavioral Biases



EDITED BY

Gillian S. Forrester, William D. Hopkins
Kristelle Hudry and Annukka Lindell

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Volume 238

Cerebral Lateralization and Cognition: Evolutionary and Developmental Investigations of Behavioral Biases

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Volume 238

Cerebral Lateralization and Cognition: Evolutionary and Developmental Investigations of Behavioral Biases

Edited by

Gillian S. Forrester
Department of Psychological Sciences, Birkbeck, University of London, London, United Kingdom

William D. Hopkins
Neuroscience Institute, Georgia State University; Division of Developmental and Cognitive Neuroscience, Yerkes National Primate Research Center, Atlanta, GA; Ape Cognition and Conservation Initiative, Des Moines, IA, United States

Kristelle Hudry
Victorian Autism Specific Early Learning and Care Centre and Olga Tennison Autism Research Centre, School of Psychology and Public Health, La Trobe University, Melbourne, VIC, Australia

Annukka Lindell
Department of Psychology and Counselling, La Trobe University, Melbourne, VIC, Australia

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Production Project Manager: Abdulla Sait
Cover Designer: Alan Studholme

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Contributors

Rodrigo Alonso-Alcalde
Museo de la Evolución Humana, Burgos, Spain

Iryna Babik
Department of Physical Therapy, University of Delaware, Newark, DE, United States

Emiliano Bruner
Centro Nacional de Investigación sobre la Evolución Humana, Burgos, Spain

Julie M. Campbell
Psychology Department, Illinois State University, Normal, IL, United States

Annapaola Fedato
Centro Nacional de Investigación sobre la Evolución Humana, Burgos, Spain

María Ángeles Fernández-Durantes
Sociograph Marketing Science Consulting, Valladolid, Spain

Dorothea L. Floris
Department of Child and Adolescent Psychiatry, Hassenfeld Children's Hospital at NYU Langone Health, Child Study Center, New York, NY, United States

Gillian S. Forrester
Department of Psychological Sciences, Birkbeck, University of London, London, United Kingdom

Elisa Frasnelli
School of Life Sciences, University of Lincoln, Lincoln, United Kingdom

Robbin L. Gibb
Department of Neuroscience, Canadian Centre for Behavioral Neuroscience, University of Lethbridge, Lethbridge, AB, Canada

Andrey Giljov
Department of Vertebrate Zoology, Faculty of Biology, Saint Petersburg State University, Saint Petersburg, Russia

Claudia L.R. Gonzalez
The Brain in Action Laboratory, Department of Kinesiology; Department of Neuroscience, Canadian Centre for Behavioral Neuroscience, University of Lethbridge, Lethbridge, AB, Canada

Jessica C. Hodgson
School of Psychology, University of Lincoln, Lincoln, United Kingdom

William D. Hopkins
Neuroscience Institute, Georgia State University; Division of Developmental and Cognitive Neuroscience, Yerkes National Primate Research Center, Atlanta, GA; Ape Cognition and Conservation Initiative, Des Moines, IA, United States

Henrietta Howells
Laboratory of Motor Control, Department of Medical Biotechnologies and Translational Medicine, Humanitas Research Hospital, University of Milan, Milan, Italy

John M. Hudson
School of Psychology, University of Lincoln, Lincoln, United Kingdom

Karina Karenina
Department of Vertebrate Zoology, Faculty of Biology, Saint Petersburg State University, Saint Petersburg, Russia

Annukka Lindell
Department of Psychology and Counselling, La Trobe University, Melbourne, VIC, Australia

Emily C. Marcinowski
Department of Physical Therapy, Virginia Commonwealth University, Richmond, VA, United States

Elena Martín-Guerra
Sociograph Marketing Science Consulting, Valladolid, Spain

George F. Michel
Psychology Department, University of North Carolina Greensboro, Greensboro, NC, United States

Eliza L. Nelson
Psychology Department, Florida International University, Miami, FL, United States

Jeremy E. Niven
School of Life Sciences, University of Sussex, Falmer, United Kingdom

Marietta Papadatou-Pastou
Department of Primary Education, School of Education, National and Kapodistrian University of Athens, Athens, Greece

Giulia Prete
Department of Psychological, Health and Territorial Sciences, ‘G. d’Annunzio’ University of Chieti and Pescara, Chieti, Italy

Lesley J. Rogers
School of Science and Technology, University of New England, Armidale, NSW, Australia

Lana Ruck
Cognitive Science Program; Department of Anthropology, Indiana University, Bloomington, IN, United States

María Silva-Gago
Centro Nacional de Investigación sobre la Evolución Humana, Burgos, Spain

Valeria Anna Sovrano
Center for Mind/Brain Sciences; Department of Psychology and Cognitive Sciences, University of Trento, Rovereto, Italy

Gionata Stancher
Rovereto Civic Museum Foundation; Center for Mind/Brain Sciences, University of Trento, Rovereto, Italy

Marcos Terradillos-Bernal
Universidad Internacional Isabel I de Castilla, Burgos, Spain

Brenda K. Todd
Psychology Department, City, University of London, London, United Kingdom

Luca Tommasi
Department of Psychological, Health and Territorial Sciences, ‘G. d’Annunzio’ University of Chieti and Pescara, Chieti, Italy

Natalie T. Uomini
Department of Linguistic and Cultural Evolution, Max Planck Institute for the Science of Human History, Jena, Germany

Giorgio Vallortigara
Center for Mind/Brain Sciences, University of Trento, Rovereto, Italy

Nicole A. van Rootselaar
The Brain in Action Laboratory, Department of Kinesiology; Department of Neuroscience, Canadian Centre for Behavioral Neuroscience, University of Lethbridge, Lethbridge, AB, Canada

Contents

SECTION 1 BEHAVIORAL BIASES IN ANIMALS

SECTION 2 BEHAVIORAL BIASES IN HUMANS

CHAPTER 8 Atypical Structural and Functional Motor Networks in Autism 207

Dorothea L. Floris, Henrietta Howells

CHAPTER 9 Lateralization of the Expression of Facial Emotion in Humans 249

Annukka Lindell

CHAPTER 10 Split-Brain Patients: Visual Biases for Faces 271

Giulia Prete, Luca Tommasi

SECTION 3 METHODOLOGICAL CONSIDERATIONS

SECTION 4 CEREBRAL LATERALIZATION AND BEHAVIORAL BIASES AS A FOUNDATION FOR HIGHER COGNITIVE FUNCTION

Introduction

Gillian S. Forrester[*], **William D. Hopkins**[‡,§,¶], **Kristelle Hudry**[‖], **Annukka Lindell**[†]
[*] *Department of Psychological Sciences, Birkbeck, University of London, London, United Kingdom*
[†] *Department of Psychology and Counselling, La Trobe University, Melbourne, VIC, Australia*
[‡] *Neuroscience Institute, Georgia State University, Atlanta, GA, United States*
[§] *Division of Developmental and Cognitive Neuroscience, Yerkes National Primate Research Center, Atlanta, GA, United States*
[¶] *Ape Cognition and Conservation Initiative, Des Moines, IA, United States*
[‖] *Victorian Autism Specific Early Learning and Care Centre and Olga Tennison Autism Research Centre, School of Psychology and Public Health, La Trobe University, Melbourne, VIC, Australia*

1 BEHAVIORAL BIASES IN EVOLUTION

Cerebral lateralization, the asymmetric and dominant control of different behaviors by the left and right hemispheres, was historically believed to be uniquely human. Today, it is clear that this characteristic of the brain is present in many animal species, suggesting a long evolutionary lineage. By allowing different functions to operate in parallel across the hemispheres, cerebral lateralization increases neural efficiency. In addition, hemispheric dominance reduces duplication of functioning and, as a result, minimizes the generation of simultaneous and incompatible responses from the two hemispheres, offering an adaptive advantage (Rogers et al., 2013).

The study of nonhuman animals has led to the discovery of basic patterns of cerebral functional asymmetry common to a wide range of vertebrate species. The right hemisphere dominates the ability to attend to novelty and threat in the environment, preparing organisms for fight or flight responses. The left hemisphere, by contrast, dominates the ability to carry out goal-oriented motor action sequences, often associated with feeding and other well-practiced behaviors. In its simplest form the two hemispheres of the brain work in tandem to provide an "*eat and not be eaten*" parallel processor. Animal studies indicate that strong cerebral lateralization of function increases the survival rate of the individual organism (Vallortigara and Rogers, 2005). Thus, it is likely that cerebral lateralization was preserved throughout evolution because it affords adaptive outcomes (MacNeilage et al., 2009), and may be a feature of central nervous systems that precede the emergence of vertebrates (Frasnelli et al., 2012).

2 BEHAVIORAL BIASES IN DEVELOPMENT

In humans, behavioral biases are associated with anatomical and functional cerebral dominances. For example, right-handedness for object manipulation is linked to left hemisphere specialization for language ability (Hervé et al., 2006), and a left visual field dominance for face identity and emotional expressions is associated with right hemisphere dominance for social–emotional processing (Demaree et al., 2005). Although the causal relationships are unclear, behavioral biases are argued to reflect the strength of functional cerebral lateralization. During development, early and strong behavioral biases are associated with early and typical cognitive development (Nelson et al., 2013) and thought to reflect successful delineation of dominance between the two hemispheres (Toga and Thompson, 2003). Reciprocally, based on these robust associations, behavioral biases can serve as markers of brain organization and cognitive ability.

The strong associations between behavioral biases and cognitive ability during development should not be underestimated. As in nonhuman animals, the presence and strength of behavioral biases in humans may represent a level of *fitness* related to the development of cerebral lateralization and cognitive function. By proxy, behavioral biases can act as markers and potential predictors of cognitive ability. As a result, behavioral biases offer the possibility of earlier and more sensitive screening of individuals at risk for neurodevelopmental disorders and pave the way for the development new diagnostic criteria and therapeutic interventions.

3 BEHAVIORAL BIASES AS A FOUNDATION FOR COGNITION

In the literal sense, ontogeny (the development of the individual) does not recapitulate phylogeny (the evolution of the species) (Ehrlich et al., 1974). However, during both human evolution and development, higher cognitive abilities are argued to build upon early sensorimotor behaviors, which are governed by cerebral lateralization of function. Here we broach the major impetus for this special volume—to consider the relationships between cerebral lateralization, behavioral biases, and cognition.

Evolutionary investigations report advantages of the lateralized brain with respect to the *fitness* of the organism. Similarly, from a "neoconstructivist" perspective (Karmiloff-Smith, 2009), it is argued that during development, every single cognitive domain (e.g., language, social–emotional, executive function, etc.) scaffolds on top of early motor experiences (Pezzulo, 2011), such that early experiences have cascading consequences for the acquisition of all higher cognitive function.

With this knowledge in mind, it is important to not only consider humans within an evolutionary framework but also view early sensorimotor behavior as part of a dynamic system required for the emergence and development of subsequent cognitive abilities (Whyatt and Craig, 2012). Moreover, the integrity of the sensorimotor system has consequences for the cognitive outcomes. In this manner, cognitive outcomes may represent a measure of the developmental *fitness* of the individual.

4 IN THIS VOLUME

This special volume of *Progress in Brain Research* presents the most up-to-date research examining associations between cerebral lateralization, behavioral biases, and cognition. Through 15 chapters divided into 4 sections, we consider how these linked features manifest through both evolution and development, drawing on evidence from species as disparate as the honeybee, the Indian flying fox, and the human. The varying theories and methodologies presented within this volume reveal different relationships between cerebral lateralization, behavioral biases, and cognition, advancing our understanding of evolutionary and developmental processes, and making a significant contribution to this rapidly expanding field. Importantly, we provide convincing evidence that behavioral biases comprised of sensorimotor actions are not distinct from cognition, but rather represent foundational components of a single system that supports cognition.

Section 1 (Chapters 1–5) focuses on behavioral biases across a range of animal species including insects (Chapter 1: Niven and Frasnelli); fish, amphibians, and reptiles (Chapter 2: Stancher, Sovrano, and Vallortigara); and primates (Chapter 3: Hopkins). While Chapter 4 (Rogers) focuses on a specific motor bias (manual), personality, and cognition in marmosets and other primates, Chapter 5 (Karenina and Giljov) evidences a consistency in motor biases associated with social behavior, specifically in mother–offspring dyads, across a vast range of animal species. These chapters document the different types of motor biases associated with cerebral lateralization of function, and their associations with fitness, performance, and/or cognitive ability.

Section 2 (Chapters 6–10) then examines behavioral biases in humans. Specifically, these chapters investigate the relationships between structural and functional brain asymmetries and behavioral biases in both typical and atypical populations. Chapter 6 (Hodgson and Hudson) examines issues relating to the organization, development, and measurement of motor control and speech representation in typically developing adults and children. Chapter 7 (Papadatou-Pastou) presents findings from meta-analyses that evaluate the associations between hand dominance and cognitive ability. Chapter 8 (Floris and Howells) focuses on the atypical structure and function of motor networks in the brains in individuals with autism. Chapter 9 (Lindell) explores the right hemisphere's emotion processing superiority and the resulting manifestation of hemifacial asymmetries. Finally, Chapter 10 (Prete and Tommasi) reveals how the study of split-brain patients can inform us about cerebral lateralization and visual biases for faces.

Section 3 (Chapters 11–13) introduces disparate methodological approaches that have the scope to expand our understanding of the links between cerebral lateralization, associated behavioral biases, and cognition. Chapter 11 (Uomini and Ruck) takes an archaeological perspective to manual biases and the evolution of human cognition. Chapter 12 (Bruner, Fedato, Silva-Gago, Alonso-Alcalde, Terradillos-Bernal, Fernández-Durantes, and Martín-Guerra) explores indirect evidence of cognitive processes that rely sensory experience, feedback, and recognition of one's own body and associations with cerebral lateralization in fossils via paleoneurological analyses. Chapter 13 (Michel, Babik, Nelson, Campbell, and Marcinowski) presents a synthesized evolutionary-developmental methodological approach to the study of cerebral lateralization, behavioral biases, and cognition, offering the capability to reveal variations and consistencies in developmental trajectories of hand dominance that considers genetic and environmental factors.

Finally, Section 4 (Chapters 14 and 15) attempts to draw causal relationships between cerebral lateralization, behavioral biases, and cognition, arguing that cerebral dominances manifest as behavioral biases; it is these behaviors that support the emergence of cognition in both evolution and development. Chapter 14 (Forrester and Todd) argues that through evolution, behavioral biases associated with domain specific cerebral lateralization laid a foundation for the development cognition in modern human development. This chapter takes a comparative approach and focuses specifically on social behavior. Finally, Chapter 15 (Gonzalez, van Rootselaar, and Gibb) reviews hemispheric differences for behavioral biases across a range of cognitive abilities and proposes that sensorimotor abilities serve as a supporting framework from which cognition emerges during infant and child development.

The presence of behavioral biases in humans and other animals provides a unique opportunity to investigate human cognition under the common framework of a shared evolutionary history. Behavioral biases are likely to reflect an early evolutionary division of primary survival functions of the brain's left and right hemispheres. In modern humans, these features may provide a foundational platform for the development of higher cognitive functions, inextricably cementing the ties between the evolution and development of cognition.

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Short Biographies

Gillian S. Forrester is a Senior Lecturer in Psychology at Birkbeck, University of London's Department of Psychological Sciences. Her research focuses on the evolution and development of cognition with a specialization in cerebral lateralization and motor biases in great apes and in neurotypical and nonneurotyopical human populations.

William D. Hopkins is a Professor of Neuroscience at Georgia State University. He has published over 330 research articles focusing on individual and phylogenetic differences in cognition and the brain of primates. Many of his research endeavors have considered the evolution and heritability of cerebral lateralization of function.

Kristelle Hudry is a Senior Lecturer in Developmental Psychology and Senior Research Fellow at the Olga Tennison Autism Research Centre, La Trobe University, Melbourne. Her research focuses on the natural course of development of young children with autism spectrum disorder and developmental plasticity through experience, including early intervention.

Annukka Lindell is a Senior Lecturer in Experimental Neuropsychology at La Trobe University, Melbourne, specializing in the consequences of cerebral lateralization for human perception.

SECTION

1

Behavioral biases in animals

CHAPTER

Insights into the evolution of lateralization from the insects

1

Jeremy E. Niven*,[1], **Elisa Frasnelli**†

*School of Life Sciences, University of Sussex, Falmer, United Kingdom
†School of Life Sciences, University of Lincoln, Lincoln, United Kingdom
[1]Corresponding author: Tel.: +44-1273-678632; Fax: +44-1273-877586,
e-mail address: j.e.niven@sussex.ac.uk

Abstract

Behavioral lateralization is widespread across the animals, being found in numerous vertebrate species as well as in species from across many invertebrate phyla. Numerous recent studies have focused on lateralization in the insects, exploring the behaviors themselves as well as their neural basis and the possible selective pressures that led to their evolution. Lateralization in the insects can occur in any sensory modality and may be generated by peripheral or central neural asymmetries. The lateralization of particular insect behaviors can show either population-level or individual-level lateralization but which of these types of lateralization is present is strongly influenced by their social environment. Different behaviors from the same species show population-level or individual-level lateralization depending on whether these behaviors are used in social interactions or not. This has broad implications for our understanding of how lateralization and handedness evolves not just in insects but also in vertebrates.

Keywords

Lateralization, Handedness, Insect, Invertebrate, Population, Individual, Social, Honey bee, *Apis*, Locust, Fly, *Drosophila*

1 INTRODUCTION

In recent years there has been a revolution in our understanding of all aspects of lateralization in animals—morphological, anatomical, physiological, and behavioral (for a review, see Rogers et al., 2013b). Since the prevailing view that humans were unique in possessing lateralization was first overturned by studies that demonstrated domestic chicks possessed lateralization (Rogers and Anson, 1979), numerous studies have demonstrated that other animals from across the subphylum Vertebrata such as teleost fish (e.g., Cantalupo et al., 1995), amphibians (e.g., Bisazza et al., 1996),

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and reptiles (e.g., Deckel, 1995) show behavioral asymmetries. In some cases, brain asymmetries and neural substrates have also been identified in macroscopic anatomy (e.g., the lateral sulcus in humans: Heilbroner and Holloway, 1988; Rubens et al., 1976; Yeni-Komshian and Benson, 1976), in the different size of the fibers connecting sensory inputs to motor outputs (e.g., the Mauthner cells responsible for the lateralization in the C–start bending reaction to danger in fishes; Heuts, 1999), or in the distribution of molecular components (e.g., the glutamate *N*-methyl-D-aspartate (NMDA) receptor, in rodents; Kawakami et al., 2003).

More recently, investigations of a wide range of invertebrate species have reinforced the view that lateralized behavior is widespread among animals, being found in numerous phyla including representatives of both Arthropoda and Mollusca (for a review, see Frasnelli, 2013; Frasnelli et al., 2012b). These studies have identified asymmetries within sensory perception (e.g., Alves et al., 2007; Jozet-Alves et al., 2012; Pierce-Shimomura et al., 2001), motor outputs (e.g., Cooper et al., 2011; Kight et al., 2008), and in central brain regions several synapses removed from both (e.g., Buchanan et al., 2015; Pascual et al., 2004). The direction and the strength of these asymmetries in invertebrates may differ from individual to individual, which is known as individual-level lateralization (e.g., Bell and Niven, 2014; Byrne et al., 2002, 2004) or the majority of individuals within a population may have a consistent bias, known as population-level lateralization (e.g., Alves et al., 2007; Kight et al., 2008). Some invertebrates show forelimb preferences though these are typically context-dependent and not equivalent to true handedness (e.g., Bell and Niven, 2014), a population-level behavioral lateralization in the same direction across many different manual tasks.

Many demonstrations of behavioral lateralization within invertebrate phyla have come from studies of one particular class of arthropod, Insecta. The emergence of the insects as the major invertebrate phylum investigated in terms of lateralization is not surprising because they possess many features that make them highly amenable to these studies. The insects are the most species rich class of animals and contain enormous diversity in terms of life history, physiology, and morphology. Moreover, many species are easy to maintain in laboratory conditions. These features combine to make insects ideal to studies at the behavioral, neural, comparative, and ecological levels of analysis.

Insects may be particularly useful for studying the factors that promote the evolution of lateralization because their lineage has been separated from that of vertebrates for several hundred million years (Grimaldi and Engel, 2005; Parfrey et al., 2011). The ancestor of both insects and vertebrates is likely to have possessed a vermiform *Bauplan*, and unlikely to have possessed the behavioral and cognitive repertoire of vertebrates and insects. Lateralization, if present in such an ancestor, would most likely be restricted to behaviors like turning preference. Consequently, behavioral lateralization and the neural lateralization that underpins it most likely evolved separated in the insects and vertebrates, and so is analogous rather than homologous. So insects provide a lineage separate from that of the vertebrates in which to assess the evolutionary pressures that produce lateralization. A general framework for understanding the evolution of lateralization in vertebrate cognition, then, should also explain the evolution of behavior in the insects. Here, we review lateralization in the insects, combining the diverse set of studies in which lateralization has been documented and characterized to draw out common themes and establish a general framework in which existing and new studies can be placed.

2 LATERALIZATION IN THE INSECTS

Lateralization within insects can occur in various aspects of behavior and the neural circuits that underpin it from sensory inputs to motor outputs. Lateralization may be observed in individuals even when they are tested alone in highly controlled laboratory environments, such as “Y” or “T” mazes. In other cases, however, it is observed only in behaviors involving interactions with conspecifics. Later, we discuss many examples showing how lateralized behavior can be clustered by the behavior in which lateralization is observed. The advantages that are conferred by lateralization are discussed later (see Section 3), as are the scenarios that have been proposed to explain its evolution (see Section 4).

2.1 BEHAVIORAL AND MOTOR LATERALIZATION

Asymmetries have been documented in the behavior of many insect species; however, it can be challenging to determine the mechanistic bases of these biases because behavioral assays necessarily require some motor activity. Here, we discuss those behaviors in which the cause of a bias is unknown, can be attributed to central brain regions within insects (e.g., central complex, a series of central neuropiles implicated in sensorimotor integration and orientation), or to motor circuits.

Studies performed using Y- or T-maze apparatus have revealed motor biases in a variety of insects. Individual ladybirds (*Coccinella septempunctata*) have a persistent bias toward a particular arm of a Y-maze in almost half of those tested, indicative of individual-level lateralization in turning (Girling et al., 2007). Conversely, American cockroaches (*Periplaneta americana*) tested in a T-maze present a population-level rightwards bias, even after ablation of antennal inputs (Cooper et al., 2011). Giant water bugs (*Belostoma flumineum*) also have a significant population-level turning bias within a T-maze, though in this case it is to the left (Kight et al., 2008).

Biases have been investigated also in fruit flies, looking at a variety of behaviors including Y-maze paradigms. Perelle et al. (1978) observed individual-level asymmetries in *Drosophila melanogaster* and *Drosophila paulistorum* in their circling behavior, tapping, and wing extension, but not for wing folding side and Y-maze choice preference. More recently, Buchanan et al. (2015) confirmed the presence of individual biases in circling behavior in *D. melanogaster*, but also found then in Y-maze choices with many flies being strongly left or right biased consistently over time. Interestingly, this individual-level locomotor bias was not correlated with asymmetries such as the laterality of gut twisting, leg length asymmetry, or wing-folding preference, and was observed in all genotypes examined, including wild-derived populations and inbred isogenic laboratory strains (Buchanan et al., 2015). This locomotor side bias seems to be generated centrally: when neurons of the central complex are silenced, exploratory laterality increases, with more extreme left and right biases (Buchanan et al., 2015).

A consistent leftward bias in exploring unknown nest sites was recently observed in *Temnothorax albipennis* ants by using a binary tree paradigm, where individuals need to repeatedly choose between a right and a left arm (Hunt et al., 2014). Anatomical differences in the number of ommatidia on the right and left eyes were also documented, but without a clear correlation with the turning behavior (Hunt et al., 2018). The same species was also found to rely more on using the right than the left eye to recognize landmarks for navigation (Basari et al., 2014), suggesting that the different number of ommatidia may play a role in motor tasks. Further studies are needed to understand whether those behavioral biases are driven by an asymmetry in the brain or are mainly sensory-driven.

Motor biases have been reported for other species of ants during their foraging trips. Twelve ant species belonging to the genus *Lasius* were found to keep mainly to the right side of their foraging "streets," and only one species to the left (Heuts et al., 2003). Black-meadow ant workers (*Formica pratensis*) also move to the left side to avoid encountering other workers on their trails in the field (Hönicke et al., 2015). Interestingly, this bias seems to be context dependent as ants present it only when they walk toward the nest with the food, but not when they leave it in search for food (Hönicke et al., 2015).

Asymmetries in motor patterns and in the nervous system have been studied for decades in locusts. Rowell (1964) reported pronounced individual handedness for response by either the left or the right leg to stimulation in adult desert locusts (*Schistocerca gregaria*) (Rowell, 1964). Desert locusts also exhibit consistent individual asymmetries in their rolling behavior with some individuals preferentially rolling clockwise and other counter-clockwise, accompanied by asymmetries in electrical activity of the muscles (Wilson, 1968). More recently, Bell and Niven (2014) provided further evidence of individual lateralization in *S. gregaria* in the forelimb used to reach across a gap. Many individuals showed a side bias in the use of the first forelimb, but the strength and direction of this bias differed among individuals, with strongly biased locusts performing better than weakly biased ones and overall no alignment within the population (Bell and Niven, 2014, 2016).

Further evidence supporting the hypothesis that brain lateralization enhances brain function also in insects comes for the larvae of the antlion (*Myrmeleon bore*) (Miler et al., 2017). Only some antlion larvae possessed an asymmetry in righting from a supine to normal position, but those that did outperformed other larvae in a subsequent learning task.

Thus, lateralized behavior is widespread in the insects being found in numerous behaviors and species from many different orders. This lateralization can be found at the individual-level and, primarily in social species, at the population-level (see Section 3.1).

2.2 SENSORY LATERALIZATION

In some species, asymmetries can be attributed to peripheral sensory receptors or to the early stages of central sensory processing rather than to biases within motor outputs or central brain regions that may be many synapses removed from motor output and/or sensory input. Such biases have been reported within sensory modalities including olfaction, mechanoreception, audition, and vision. These sensory asymmetries, which occur at the population-level, have been identified through various methods including electrophysiology and/or imaging of early sensory circuitry. Consistent lateralization in early sensory processing among distantly related species suggests that some behaviors may benefit from a specific bias when pairs of sense organs, such as compound eyes or antennae, are used.

Asymmetries are present in at different levels in the auditory system of various insects. In the water bug (*Corixa punctate*) there are asymmetries in the tuning of the tympana in the periphery (Prager and Larsen, 1981). However, electrophysiological measurements have also shown asymmetries in the responses of auditory interneurons in the bush cricket (*Tettigonia viridissima*) (Rheinlaender and Römer, 1980).

Lateralization has also been documented in response to chemosensory stimuli. Fruit flies (*D. melanogaster*) show a consistent asymmetry in antenna-mediated flight control, in which the sensory signals coming from the left antenna contribute more to odor tracking than do sensory signals coming from the right antenna (Duistermars et al., 2009). Larval fruit flies show the opposite chemosensory asymmetry, when larvae possess only a functional olfactory sensory neuron on their right they display significantly better chemotaxis than those with the sensory neuron on the left (Louis et al., 2007).

Honeybee (*Apis mellifera*) workers have left–right differences in the number of antennal olfactory sensilla (Frasnelli et al., 2010a). Although asymmetry in antenna-mediated flight control has not been investigated, a bias in the recall of olfactory memories has been documented (see Section 2.5). The morphological difference in the periphery is supported by functional asymmetries within the antennal lobes themselves (Rigosi et al., 2015); differences in odor representations exist between the right and left antennal lobes although they are broadly anatomically symmetrical (Rigosi et al., 2011). This suggests that lateralization may be present centrally, in the functional specialization of the two sides of the brain to respond to specific stimuli or tasks, but is not necessarily related to marked anatomical differences in those brain regions.

Conversely, in cockroaches (*Nauphoeta cinerea*) the sensory asymmetry at the level of the antennae is accompanied by anatomical asymmetry within the antennal lobes (Sreng, 2003). Females of this species but not males possess more glomeruli in the right than in the left antennal lobe (Sreng, 2003). This lateralization may improve females' ability to locate males using the sex pheromones that they produce. Such lateralization of antennal function may also occur in the American cockroach (*P. americana*), in which an asymmetry in antennal grooming is observed (Zhukovskaya and Lychakov, 2016). However, such evidence is circumstantial and could equally be interpreted to suggest a motor asymmetry in grooming.

Lateralization within insect sensory systems appears within several different modalities including olfaction, vision, and audition. In contrast to behavioral and motor lateralization, sensory asymmetries have mainly been identified at the population-level, though this may reflect a bias toward assessing sensory systems in cases where a pronounced population-level bias exists in behavior.

2.3 LATERALIZATION IN FEEDING BEHAVIOR

In activities related to feeding and foraging, vertebrates share the same bias to use the right side of their body, i.e., the left cerebral hemisphere (for a review, see Rogers et al., 2013b). This specialization of the right part of the body may derive from the anatomical and functional asymmetry of the mouth, which is documented in species ancestral to Chordata, similar to modern Branchiostoma (Rogers, 2002). Investigating right–left asymmetries in feeding in insects is, hence, particularly interesting from an evolutionary and comparative perspective.

Bumblebees (*Bombus lapidarius*, *Bombus lucorum*, and *Bombus pascuorum*) show preferred directions of circling as they visit florets arranged in circles around a vertical inflorescence (Kells and Goulson, 2001). Most individuals circled in the same direction (two species circled counter-clockwise and one clockwise), whereas no lateralization was observed in *Bombus terrestris* for this behavior. This type of lateralized behavior could result from learning; bumblebees copy the behavior of others with regard to floral choices (Kawaguchi et al., 2007) and can learn to make nectar-robbing holes in flowers as a result of encountering them (Leadbeater and Chittka, 2008). Goulson et al. (2013) investigated handedness in nectar-robbing bumblebees *Bombus wurflenii* and *B. lucorum* feeding on *Rhinanthus minor*, a flower that can be robbed from either the right-hand or the left-hand side. Several patches of *R. minor* were robbed on either the right or the left side, with the intensity of the side bias being the strongest in the most heavily robbed patches. Goulson et al. (2013) suggested that bees within patches learn robbing strategies (including handedness) from one another, either by direct observation or from experience with the location of holes, leading to rapid frequency-dependent selection for a common strategy, i.e., adopting the same handedness within particular flower patches.

The social behavior linked to foraging present population-level asymmetries in the Hymenoptera. Leaf-cutting ants (*Acromyrmex echinatior*) preferentially use the right mandibles in the leading position when cutting leaves (Jasmin and Devaux, 2015). Red wood ants (*Formica rufa*) mainly use their right antenna during “feeding” contacts where a “donor” ant exchanges food with a “receiver” ant through trophallaxis (Frasnelli et al., 2012a). Honeybees from the same colony also seem to rely on their right antenna in feeding interactions (Rogers et al., 2013a). Dyads of bees tested using only their right antennae contacted after shorter latency and were significantly more likely to interact positively (PER) than were dyads of bees using only their left antennae, suggesting that the right antenna motivates bees to approach and contact each other probably because it is involved in exchange of odoriferous information between same-colony worker bees.

Thus, lateralization in feeding is present at the population-level (see Section 3.1) irrespective of whether feeding occurs by individuals locating food sources in isolation, or in cases where food is transferred from one individual to another in social insects. It is worth considering that lateralization in feeding has only been reported from eusocial hymenopterans, so whether it is found in other insect orders remains unclear. As with other insect behaviors, it is unclear whether lateralized feeding confers any proximate advantages. There are potential fitness benefits from eliciting feeding from conspecifics who act as donors but why these donors should prefer lateralized movements from the receiver is unclear.

2.4 LATERALIZATION IN INTERACTIONS

In addition to the lateralized interactions that occur during feeding in some species (see Section 2.3), interactions occur in many insect species in the context of aggression or mating. Here, we review the evidence for lateralized interactions within these two contexts.

2.4.1 Aggressive interactions

Although there is still limited evidence documenting lateralization in aggressive behavior in insects, it is already clear that the direction of the asymmetry is not as consistent as it is among vertebrates. In bees, both eusocial and solitary species appear to control aggressive responses toward agonistic individuals by means of the left antenna (Rogers et al., 2013a, 2016). When honeybees interact with individuals of the same colony, dyads with only the left antenna in use engage in aggressive interactions more often than the dyads with only the right antenna (Rogers et al., 2013a). Conversely, dyads in which bees come from different hives show more aggression when they have only their right antennae than only their left antennae (Rogers et al., 2013a). Overall, this suggests that in honeybees the left and the right antenna affect aggressive responses between different-colony and same-colony workers, respectively.

A similar study on solitary mason bees (*Osmia bicornis*) (Rogers et al., 2016), in which all females are fertile, make their own nest and compete for nest sites (Nepi et al., 2005), showed that the number of aggressive interactions is higher in dyads of females having only their left antenna than in those with only their right antenna. A weaker effect was found in male–male dyads suggesting that the left antenna leads to aggressive behavior in mason bees, as in honeybees from the same hive. More evidence of the use of the left antenna in aggressive approaches and avoidance behavior comes from Australian stingless bees (*Tetragonula carbonaria*) (Rogers and Frasnelli, 2016). Dyads of bees with left antennae made significantly fewer contacts than dyads of bees with right antennae. In dyads of one left and one right antennae, the bee with a left antenna approached the bee with the right antenna more often that the opposite scenario, and the bee with the left antenna often aggressively attacked (by biting) its hive mate (Rogers and Frasnelli, 2016). Hence, the low number of contacts in dyads of bees using their left antennae appears to be due to mutual avoidance, indicating that, the left antenna stimulates avoidance or attack.

Several examples of lateralization have also been documented from the flies. For instance, two species of tephritid flies (*Ceratitis capitate, Bactrocera oleae*) show a left-biased population-level lateralization of aggressive displays in both female–female and male–male dyads (Benelli et al., 2015a,b). Male blowflies (*Calliphora vomitoria*) also show a consistent preferential use of their right legs in boxing behavior (Romano et al., 2015).

In the Asian tiger mosquito (*Aedes albopictus*) a right bias in kicking behavior is found, when mosquito females display aggressive responses against undesired males (Benelli et al., 2015c). Interestingly, when the mosquitos did use their left legs, the mean number of kicks per rejection event was not different from that performed with right legs, and both left and right kicking behavior led to successful displacement of undesired partners (Benelli et al., 2015c).

Population-level biases exist in cases in which there are dyadic aggressive interactions between members of the same sex or of different sexes in insects. Such asymmetries occur in antennal or in leg movements but in no case is it clear why such lateralization exists.

2.4.2 Mating

When analyzing asymmetries in mating displays, it is important to consider the connection between anatomical and behavioral asymmetries. In insects, asymmetric genitalia evolved multiple times and in association with changes in mating positions, suggesting that the behavioral asymmetry preceded and drove morphological asymmetry (Huber, 2010). A good example is the asymmetrical mating display reported in the earwig (*Labidura riparia*) males, which have two intromittent organs (analogous to the vertebrate penis) but nearly 90% of them hold them in the “right-ready” state (Kamimura, 2006). Interestingly, male earwigs seem to have evolved from a primitive state in which both penises were held in the “not-ready” orientation to a stage in which they always held one penis (either the right or left at random) in the “ready” orientation. The next evolutionary stage was represented by males that still possessed two morphologically indistinguishable penises, but which preferentially held the right penis in the “ready” orientation. Finally, the less-preferred (left) penis disappeared altogether, leaving only traces of a closed, nonfunctional ejaculatory duct (Kamimura, 2006). Thus, a purely behavioral asymmetry might have facilitated the evolution of a complete morphological asymmetry.

Females of bedbugs (*Cimex hemipterus*, *Cimex lectularius*) normally develop a single spermalege (an organ on the abdomen linked to traumatic insemination; Siva-Jothy, 2006) on the right side of the abdomen but spermalege duplication sometimes occurs (Kamimura et al., 2014). During mating, males pierce the female abdomen to inject sperm using their needle-like genitalia. By analyzing the piercing sites on the body of females with spermalege duplication, Kamimura et al. (2014) observed a highly biased distribution toward the right side of the female body. Moreover, mating experiments showed that when the normal insemination site (i.e., the right-side spermalege) was artificially covered, females remained unfertilized even though they had a spermalege on the left side. Interestingly, histological examination did not reveal any differences between the right and left-side spermaleges and artificial insemination experiment confirmed that spermatozoa injected into the left-side spermalege show apparently normal migration behavior to the female reproductive organs, indicating that the bias was not due to a lack of functionality (Kamimura et al., 2014).

The fruit fly (*Drosophila pachea*) exhibits strong asymmetry in male genitalia external lobes, with the left lobe significantly longer and thinner than the right. Interestingly, when mutants with fully symmetric lobes were tested, they adopted a right-sided mating posture in successful copulations (Lang and Orgogozo, 2012). A recent study by Rhebergen et al. (2016) suggests that the asymmetric lobes are part of a grasping device and stabilize one-side mating.

Population-level biases in approaching the mate on the left side seem a common characteristic in insects that often leads to a higher mating success (Benelli et al., 2015a,b,c, 2017a,b; Romano et al., 2016b, 2017). Copulation approaches are biased in the rice weevil (*Sitophilus oryzae*) and in the flour beetle (*Tribolium confusum*) with most males approaching potential mates from the left side and having a higher mating success over right-biased males (Benelli et al., 2017b). Geographical origin and rearing media do not seem to effect male mating success and lateralization in three strains of *S. oryzae* (Romano et al., 2016b). Indeed, male weevils have the same right-biased head-wagging behavior and left-biased copulation attempts with higher mating success in males performing left-biased copulation attempts followed by right-biased head wagging behavior.

The khapra beetle (*Trogoderma granarium*) presents biases in different mating-related behaviors; a left bias in male recognition and mounting, as well as the female postcopulation kicks, and a right bias in male foreleg tapping acts (Benelli et al., 2017a). Also in this case there are benefits associated with lateralization as left biases in the recognition approach led to significant differences in recognition duration, number of head wagging acts, whole mating duration and, most importantly, male mating success (Benelli et al., 2017a). Olive fruit fly (*B. oleae*) males approached females mainly from the left rather than the right, front or back, but male mating success was independent the side of approaching the female (Benelli et al., 2015b).

During courtship, males of the parasitic wasp (*Leptomastidea abnormis*) exhibit a right-biased antennal tapping on the female's head (Romano et al., 2016a). However, these right-biased male courtship acts were not characterized by higher tapping frequencies or mating success (Romano et al., 2016a). Interestingly, in another parasitic wasp (*Angyrus* sp.) both sexes use the right antenna predominantly to start antennal tapping (Romano et al., 2017). As with *L. abnormis* lateralization had no impact on the frequency of the antennal tapping, but a right antenna in start to the tapping led to a higher mating success (Romano et al., 2017).

The interactions involved in mating in many insect species, like those of aggression, appear to show population-level lateralization, though many studies have not explicitly assessed this. Again, the specific role of the asymmetric contacts of antennae or legs is unknown. However, the observation of lateralization during mating comes closest to evidence that it confers an ultimate benefit (see Section 3.2).

2.5 LEARNING, MEMORY, AND LATERALIZATION

Lateralization is hypothesized to increase brain efficiency and cognitive performance, and some evidence in support of this comes from work in vertebrates (for a review, see Rogers et al., 2013b). However, the relationship between brain and behavioral asymmetries and cognition remains uncertain. In insects, one case in which brain lateralization and behavioral performance has been correlated is the fruit fly (*D. melanogaster*) (Pascual et al., 2004). The majority of fruit flies contain a neuropile region, the asymmetric body (AB), in only their right hemisphere but in a small proportion of wild flies there are a pair of ABs, one in each hemisphere. Those flies in which the AB is found in both hemispheres have impaired long-term but not short-term memory (Pascual et al., 2004), providing clear evidence of the importance of population-level lateralized neural circuits in behavioral performance.

Honeybees have provided evidence of lateralization in olfactory and visual memory. Letzkus et al. (2006) showed that *A. mellifera* displays laterality in learning to associate an odor with a sugar reward. Three groups of bees with only the right antenna, only the left antenna, or with both antennae were conditioned to extend their proboscis when perceiving a particular odor associated with a food reward. Bees with only the left antenna in use learned less well than those with only their right or with both. Peripheral (Frasnelli et al., 2010a) and central (Rigosi et al., 2015) asymmetries have been identified also at the morphological and functional level (see Section 2.1). Using a similar conditioning paradigm in which honeybees were trained to associate a colored visual stimulus with a reward, Letzkus et al. (2007) showed that there was a bias in right eye use to learn the association.

In the studies by Letzkus et al. (2006, 2007) the bees were trained and tested with only one antenna (or one eye) making it difficult to assess whether their test performance was a measurement of how well they learned the association or how well they could recall the memory of the association. To overcome this problem, Rogers and Vallortigara (2008) trained the bees with both antennae, subsequently testing them with only one antenna. One to two hours after training using both antennae, the recall of short-term memory occurred only with the right antenna, whereas 23–24 h after training, long-term memory was recalled only using the left antenna (Rogers and Vallortigara, 2008). However, the asymmetric olfactory memory recall seems affected by previous experience of the test odor because multiple memory traces can lead to response competition and a lack of specificity in longer-term olfactory memory (Frasnelli et al., 2010b). Different tested odors may also lead to different asymmetries of short-term olfactory memory recall, suggesting that scents that play a key role as stimuli to route pollinator visits are processed in a lateralized way, whereas unspecific and ubiquitous scents with limited importance for bee pollinators are not (Rigosi et al., 2011).

The above research conducted on eusocial honeybees found an olfactory asymmetry in learning and recall of memory that manifests itself as population-level bias. The same is not true for the solitary mason bee (*Osmia cornuta*), which do not show any asymmetry in the PER paradigm (Anfora et al., 2010). Comparative electroantennographic assays testing the antennal sensitivity to a floral volatile compound and an alarm pheromone showed overall stronger responses in the right over the left antennae in *A. mellifera* but not in *O. cornuta*, which instead showed asymmetries at the individual level (Anfora et al., 2010).

Lateralized recall of olfactory memory at 1 h after training was also tested in bumblebees (Anfora et al., 2011). Like *A. mellifera* (Anfora et al., 2010; Frasnelli et al., 2010b; Letzkus et al., 2006; Rogers and Vallortigara, 2008), bumblebees with only the right antenna performed similarly to those with both antennae; but those with only the left antenna had impaired performance (Anfora et al., 2011). However, no differences were observed in electroantennographic assays conducted on the or left and right antennae of *B. terrestris* stimulated by an alarm pheromone or a floral scent, but a higher number of olfactory sensilla trichodea type A on the right antennal surface compared to the left one was detected (Anfora et al., 2011).

Antennal asymmetry in the recall of long- and short-term olfactory memories in honeybees (Rogers and Vallortigara, 2008) also occurs in three species of primitive social Australian native stingless bees (*Trigona carbonaria*, *Trigona hockingsi*, and *Austroplebeia australis*) (Frasnelli et al., 2011). Memory recall 1 h after training was better when odors were presented to the bee's right side than on the left side, whereas after 5 h it was better when the odor was presented to the left than to the right side of the stingless bees (Frasnelli et al., 2011). In honeybees and bumblebees, the behavioral asymmetry in the recall of olfactory memories was suggested to be partially related to an asymmetrical distribution of the olfactory antennal sensilla (Anfora et al., 2011; Frasnelli et al., 2010a). However, this is not the case for *T. carbonaria* and *A. australis* stingless bees, which have a symmetrical sensilla distribution on their right and left antennae (Frasnelli and Vallortigara, 2017; Rogers and Frasnelli, 2016). These results suggest that the asymmetries in the recall of memories are more likely to be centrally driven and be related with a functional asymmetry in the brain rather than a simple asymmetry in terms of sensory receptors.

3 WHAT ADVANTAGES DOES LATERALIZATION CONFER?

The widespread occurrence of behavioral lateralization suggests that it is adaptive, though this is not the sole explanation; lateralized behavioral character traits could arise for nonadaptive reasons (for a review, see Gould and Lewontin, 1979). One possible explanation for lateralization is that constraints on the developmental mechanisms that produce brain and body inevitably produce biases in behavior. This emphasizes that the adaptive function of traits cannot be assumed by default and must be proven. Here, we consider the advantages that lateralization has been shown to confer upon insects, emphasizing that there is remarkably little experimental evidence to support an adaptive function for lateralization at present.

3.1 THE EVOLUTION OF INDIVIDUAL AND POPULATION-LEVEL LATERALIZATION

A broadly accepted hypothesis for the evolution of lateralization suggests that it evolved in individuals. There may be many possible benefits of such individual-level lateralization, which apply to insects just as they do to vertebrates, and indeed to all other animals. Introducing a bias, for instance, may promote efficient decision-making by preventing a deadlock in selecting between two equivalent alternatives. Alternatively, there may be an advantage to avoiding the duplication of neural circuitry on both sides of the brain; devoting neural resources to different tasks on either side of the brain may save on information processing, time, space, and energy (Rogers et al., 2013b; Vallortigara, 2006; Vallortigara and Rogers, 2005). Indeed, such efficient resource allocation may be particularly important in insects, which are relatively small and have limited resources to expend on neural computation (Chittka and Niven, 2009; Niven and Farris, 2012). The ultimate benefit must be to increase the survival and/or reproduction of lateralized individuals. Assuming that there is a heritable component to the trait laterality, this could then spread throughout the population.

There are potential costs to individuals being lateralized. The most obvious may be that their behavior will become more predictable to other animals, which may lead to exploitation by conspecifics as well as by other species (Vallortigara, 2006; Vallortigara and Rogers, 2005). For instance, a predator may be able to predict the orientation of a strongly lateralized prey's escape response gaining an advantage. The possibility of such exploitation will increase with the strength of the lateralization displayed by individuals. Interactions among conspecifics may, in certain circumstances, be beneficial. For those animals that live in social groupings, beneficial interactions may be commonplace and may require coordinated activity of both individuals. Such cases, promoting the coordination of movements between individuals within a social grouping may result in individuals benefitting from being coordinated with one another. This can lead to the evolution of population-level lateralization in which one side is favored throughout the population. The most familiar example of this is handedness in humans, in which ~90% of the population are right-handed (Papadatou-Pastou et al., 2008). In insects, population-level lateralization is less extreme but is found in the antennal movements of social bees and ants (Frasnelli et al., 2012a; Rogers et al., 2013a).

Game theoretic models suggest that population-level lateralization may arise as evolutionarily stable strategy (ESS) when asymmetric individuals need to coordinate their behavior with other asymmetrical individuals (Ghirlanda et al., 2009; Ghirlanda and Vallortigara, 2004). In vertebrates, this can be seen in terms of the coordinated movements of individuals in herds, shoals, flocks, or packs. Coordination may promote cohesive movements within insect groups, such as swarms or bands, though it is equally relevant to dyadic interactions sharing food or information, as occur during trophallaxis. However, this does not imply that all behaviors in all social species are lateralized at the population-level. Moreover, the evolutionary history of species must also be considered; species that are now solitary may be derived from those that were social (Wcislo and Danforth, 1997), complicating the relationship between social environment and population-level lateralization. Later in this section, we will see that recent evidence (e.g., Rogers et al., 2016) supports the idea that the important factor is whether individuals engage in interactions where their asymmetry influences that of others.

3.2 EVIDENCE FOR THE BENEFITS AND COSTS OF LATERALIZATION IN INSECTS

Determining whether an insect shows individual- or population-level lateralization does not in itself demonstrate how it confers a proximate advantage or that such an advantage impacts upon ultimate success. Even when a proximate advantage is identified through improved performance on a particular behavioral task within a laboratory environment, this is not necessarily the task or the situation in which the advantage of lateralization manifests itself within more naturalistic environment (but one would sure hope so). In insects, the proximate advantages of lateralization have not, to our knowledge been related to ultimate success in most cases.

Experiments carried out in laboratories investigating the role of the asymmetrical use of the antennae in social interactions suggest that lateralization plays a role in effective communication among conspecifics. Wood ants (*F. rufa*) are biased at the population-level in antennal use to stimulate a donor ant carrying food during trophallaxis behavior, i.e., the exchange of food between members of the colony (Frasnelli et al., 2012a). There is also an antennal bias also in honeybees that plays an important role in regulating their behavior depending on the context. Dyads of bees from the same colony with only the right antenna interacted positively, whereas those from different colonies displayed an aggressive behavior (Rogers et al., 2013a). A proximate benefit has also been shown for conspecific aggressive interactions. In tephritid flies (*C. capitate*, *B. oleae*), a left-biased population-level lateralization of aggressive displays leads to a proximate advantage because aggressive behaviors performed with left body parts produced to greater success during fights than did right body parts (Benelli et al., 2015a,b). A higher fighting success has been documented also in male blowflies (*C. vomitoria*) related to a consistent preferential use of their right legs in boxing behavior (Romano et al., 2015).

An advantage for individual-level lateralized behavior has been demonstrated in the forelimb movements made by desert locusts while crossing gaps in the substrate upon which they are walking (Bell and Niven, 2016). Individuals differed in both the strength and direction of lateralization of these targeted forelimb movements (Bell and Niven, 2014), and individuals that produced more strongly lateralized forelimb movements were less likely to make errors while performing targeted movements with their preferred forelimb. This suggests that lateralization improves motor control, though how it does so remains unclear. It may permit specialization of neural circuits controlling forelimb movements, which could be beneficial if limited neural resources are available (Niven and Bell, 2018).

A relationship between the strength of individual-level lateralization and an improvement in learning ability has also been demonstrated recently in larval antlions (*Myrmeleon bore*) (Miler et al., 2017). A small proportion of individual antlions showed lateralized righting behavior, which was correlated with their ability to associate a vibrational cue with prey removal. Miler et al. (2017) suggest that behavioral lateralization is a reflection of general brain asymmetry, though this need not be the case; asymmetries in the central neural circuitry governing righting behavior need not be correlated with the central circuits governing other behaviors. It is unclear from the current understanding of neural circuitry within the insect brain and ventral nerve cord, how lateralized righting behavior is related to learning. Nevertheless, the improved performance of strongly lateralized larvae is pronounced, suggesting a substantial advantage.

Ong et al. (2017) have shown that honeybees, like locusts, demonstrate individual-level lateralization in some behaviors. They provided workers with a pair of identical apertures through which they had to fly on multiple trials. Some, though not all, workers showed a preference for particular apertures. Ong et al. (2017) used a computational model to suggest that this individual-level strategy may be advantageous by allowing bees to move rapidly through environments that may contain dense foliage. This is because the flow of worker "traffic" through cluttered environments is more efficient when individual bees have different preferences because it prevents congestion. Ong et al. (2017) also suggest that a definite preference may reduce indecision and, therefore, transit times.

Some studies of mating have provided links between lateralized behavior and benefits in terms of mating success (see Section 2.4.2). In numerous species, the approach of the male to the female is lateralized, and males that approach females from a particular side are more likely to secure mating opportunities (Benelli et al., 2015b, 2017a,b; Romano et al., 2016b, 2017). These studies come closest to linking behavioral lateralization to ultimate benefits, though even in these cases there are no established links to life time reproductive success.

Together these studies emphasize that even when potential proximate advantages of lateralized behavior within individuals can be identified through experimental or modeling approaches (Bell and Niven, 2016; Frasnelli et al., 2012a; Miler et al., 2017; Ong et al., 2017; Rogers et al., 2013a, 2016), the ultimate benefits are unknown. Even when feeding or aggression is being studied, the ultimate benefits to lateralization remain unclear. In most studies, the costs of lateralization are usually overlooked at both the proximate and ultimate levels of explanation. It is, of course, possible to form hypotheses to explain how proximate advantages/disadvantages can relate to ultimate benefits/costs; however, it is not necessarily the case that all lateralized behaviors are adaptive and have ultimate implications, and each case must be proven.

Understanding both the costs and benefits of lateralization is important for explaining the patterns of individual-level lateralization observed in insects. Assuming that at least some lateralized behaviors observed at the proximate level are ultimately beneficial and can be inherited, then laterality will spread throughout the population. Without any cost to laterality, it would be expected to become increasing strong. Yet within bees, locusts, and antlions, individuals differ in the strength and direction of their lateralized behavior (Bell and Niven, 2014, 2016; Buchanan et al., 2015; Frasnelli et al., 2012a; Miler et al., 2017; Ong et al., 2017; Rogers et al., 2013a, 2016). Indeed, some individuals may be strongly lateralized, whereas others show no obvious laterality within the limited repetitions possible in these experiments (Bell and Niven, 2014, 2016; Buchanan et al., 2015; Miler et al., 2017; Ong et al., 2017). These patterns could be explained if there are costs that penalize strong behavioral lateralization in laterality. For instance, individuals that are too strongly lateralized could be penalized because they are more predictable than less lateralized individuals. One example of cost to strong lateralization has been documented in leaf-cutting ants (*A. echinatior*) in which workers preferentially used their right mandible to lead when cutting leaves (Jasmin and Devaux, 2015). The most lateralized foragers are the slowest and harvest the smallest leaf area per second, suggesting a cost to extreme lateralization.

Another possibility is that in some cases individual-level lateralization is nonheritable. Buchanan et al. (2015) have demonstrated that fruit flies (*D. melanogaster*) show individual-level lateralization in their preferred turning direction within a Y-maze. Flies are lateralized with some individuals showing a strong bias to right or leftward turns but this lateralization is nonheritable and is present in even inbred lines (Buchanan et al., 2015). Instead, variation in neural circuits within the central brain may be sufficient to generate variation in the strength and direction of laterality of flies. This may be a potential explanation for individual-level lateralization within many insects, including bees and locusts (e.g., Bell and Niven, 2016; Ong et al., 2017), and could also explain why large numbers of individuals lack strong lateralization in these species.

Establishing whether behavioral lateralization is both heritable and confers ultimate advantages is clearly important. Indeed, the hypothesis that population-level lateralization is derived from individual-level lateralization depends upon these two key factors. This emphasizes that while recent studies of laterality have improved our knowledge of the types of behavioral lateralization insects produce, and our understanding of the proximate advantages it confers, there is less clarity about its heritability, genetic basis, and the ultimate advantages it confers.

4 SOCIAL INTERACTIONS, BEHAVIORAL MODULARITY, AND THE EVOLUTION OF LATERALIZATION

A model for the evolution of population-level lateralization based upon game theoretic analysis suggests that social interactions may produce a selective environment that favors the coordination of lateralized behaviors among individuals of the same species (Ghirlanda and Vallortigara, 2004; Ghirlanda et al., 2009). The range of levels of social organization within insects, from solitary to eusocial (Andersson, 1984), make them ideally suited to comparisons of species that differ in their social organization. An explicit experimental test of this hypothesis has come from comparisons of lateralized behaviors performed by social and solitary insect species (Anfora et al., 2010; Frasnelli et al., 2011, 2012a). While initial studies supported the view that social environments select for population-level lateralization (Anfora et al., 2010; Frasnelli et al., 2011, 2012a), more recent studies have emphasized that the impact of social interactions may be highly restricted to specific behaviors and that it is the asymmetry of the interaction itself that is important (Ong et al., 2017; Rogers et al., 2016; Romano et al., 2017). Indeed, even simple behaviors such as aggressive interactions or courtship displays (Benelli et al., 2015b; Rogers et al., 2016) can provide the selection pressures needed to align individual-level asymmetries to the same direction within the group. For the ESS theory, the individual-level and the population-level asymmetry are parts of the same continuum: The stability can be obtained with the individual-level or with the population-level asymmetry depending on the context (Ghirlanda and Vallortigara, 2004; Ghirlanda et al., 2009; Vallortigara, 2006).

4.1 SOCIAL ENVIRONMENTS PROMOTE POPULATION-LEVEL BEHAVIORAL LATERALIZATION

An experimental test of whether social interactions promote the evolution of population-level lateralization requires the identification of a homologous behavior in both a social and a solitary species. Using bees for such a comparison makes sense because both social and solitary species have been identified (Wcislo and Danforth, 1997). Honeybees (*A. mellifera*), which are eusocial, were known to be lateralized in their antennal use while responding to and learning about odors (Letzkus et al., 2006) and to visual stimuli (Letzkus et al., 2007). Initial studies compared honeybees to a solitary mason bee species (*O. cornuta*), using the recall of an olfactory memory for behavioral tests (Anfora et al., 2010). In honeybees odor memories evoked by stimulating only the right antenna produce a higher level of recall than those of the left, whereas in mason bees no such population-level lateralization is apparent. This evidence suggests that social environments do indeed select for population-level lateralization (Anfora et al., 2010).

Although the original study compared just two species, the conclusions were reinforced by subsequent studies demonstrating the population-level lateralization of olfactory learning in primitively social bumblebees (*B. terrestris*) (Anfora et al., 2011) and primitively social stingless bees (*Trigonia* and *Austroplebeia* sp.) (Frasnelli et al., 2011), which, being much older than honeybees from an evolutionary point of view, suggests that lateralization in bees evolved prior to the evolutionary divergence of these species. Further support for the linkage between social interactions and population-level lateralization comes from studies directly examining antennal interactions among pairs of individuals in two species of social Hymenoptera; wood ants and honeybees (Frasnelli et al., 2012a; Rogers et al., 2013a). In both species, beneficial social interactions are associated with lateralized antennal contacts.

The association of social pressures with population-level lateralization was further reinforced by studies on cockroaches and locusts (Bell and Niven, 2014; Cooper et al., 2011), neither of which is eusocial. Cockroaches (*P. americana*) are gregarious, aggregating during the day but foraging independently at night (Lihoreau et al., 2012). Cooper et al. (2011) showed that cockroaches in a Y-maze show a consistent turning bias to the right. Desert locusts are gregarious but not social, and antagonistic interactions between individuals are common (Pener and Simpson, 2009). Consequently, lateralization if present in desert locusts would be expected to be individual-level, which is indeed what Bell and Niven (2014) found in their forelimb movements while crossing a gap in the substrate they are walking upon. Thus, social environments and interactions do appear to be associated with lateralization supporting the predictions of game theoretic models (Ghirlanda and Vallortigara, 2004; Ghirlanda et al., 2009).

4.2 SPECIFICITY OF LATERALIZED BEHAVIORS

Recent studies have continued to explore the role of social interactions in producing population-level lateralization (Ong et al., 2017; Rogers et al., 2016; Romano et al., 2017). Taken together, these studies suggest that population-level lateralization is restricted to just a subset of behaviors, regardless the social structure of the species itself. Indeed, individual-level lateralization is present for some tasks even in eusocial insects such as honeybees. This emphasizes the specificity with which selective pressures can act on individual behavioral modules and suggests that individual-level and population-level lateralization are “two sides of the same coin.”

Rogers et al. (2016) assessed antagonistic interaction between pairs of solitary red mason bees because antagonistic interactions can occur between conspecifics even in solitary species. They found that between pairs of bees engaged in antagonistic interactions, significantly more aggression occurred when only the left antenna was used in comparison to those in which only the right antenna was used (Rogers et al., 2016). Other, nonaggressive interactions showed no such bias, suggesting that interactions among conspecifics can select for population-level lateralization, even in solitary species.

Conversely, Ong et al. (2017) have shown that individual-level lateralization occurs in some behaviors in honeybees. They provided honeybee workers with a pair of identical apertures through which they had to fly on multiple trials. Overall, the population of honeybees chose the left and right apertures equally often, although they could see both apertures (Ong et al., 2017). When the individual preferences of the bees were examined, some had a clear preference for the left or the right aperture, whereas others showed no preference. Whether there really are three distinct categories of bees, those with left, right, and no bias or whether there is a continuum of bias is unclear. Nevertheless, this demonstrates that even in a social species in which population-level lateralization occurs in some behaviors, others show individual-level lateralization.

A third recent study by Romano et al. (2017) has shown that migratory locusts (*Locusta migratoria*) can express both individual-level and population-level lateralization. Migratory locusts form large swarms that contain millions of individuals that interact with one another, however, these swarms lack any obvious social structure (Pener and Simpson, 2009). Romano et al. (2017) observed that there was population-level lateralization in the eye with which locusts observed a guinea fowl-mimicking robot predator. In contrast, locusts showed individual-level lateralization in the direction they jumped to escape a predator.

The presence of both individual-level and population-level lateralization in both solitary and social species suggests that individuals can express a mixture of traits irrespective of social organization (Anfora et al., 2010; Bell and Niven, 2014; Buchanan et al., 2015; Cooper et al., 2011; Frasnelli et al., 2011; Letzkus et al., 2006, 2007; Ong et al., 2017; Rogers et al., 2016; Romano et al., 2017). This can be explained by the specificity with which selective pressures can act on behaviors provided that they are independent of one another. This specificity is remarkable because even behaviors involving the same appendages being used in different circumstances can show different levels of lateralization. Indeed, this context-dependency extends not just to whether behaviors are lateralized at the individual or population-level; desert locusts show individual-level lateralization in visually targeted limb movements at gaps but are unbiased in other forelimb movements immediately before or afterward (Bell and Niven, 2014).

Such a mix of both individual- and population-level lateralization also occur in vertebrates. For example, common marmosets (*Callithrix jacchus*) have an individual-level preference in the hand they use for reaching, approximately half preferring to use their right hand and half their left (Hook and Rogers, 2000). They do, however, have a population-level bias in terms of the eye with which they view food through a peephole, though this shows context-dependency changing when the marmosets view a threatening stimulus (Hook-Costigan and Rogers, 1998). Together these observations emphasize that, in insects and vertebrates alike, behavioral modules can be independent even when they involve similar sets of sensory inputs and motor outputs so that selection can act to produce individual-level or population-level lateralization.

4.3 ARE THERE ALTERNATIVE EXPLANATIONS FOR THE EVOLUTION OF LATERALIZATION?

Although social environments are an attractive explanation for the evolution of population-level lateralization receiving support from both theory (Ghirlanda and Vallortigara, 2004; Ghirlanda et al., 2009) and experiment (e.g., Anfora et al., 2010; Rogers et al., 2016), they do not explain all examples of population-level lateralization among the insects (e.g., Kight et al., 2008; Romano et al., 2017). Kight et al. (2008) observed a consistent leftward bias in giant water bugs (*B. flumineum*) within a T-maze. Though male giant water bugs provide parental care to eggs cemented to their back by females (Smith, 1997), they do not form social groups as adults.

Consequently, the social environment cannot explain the presence of population-level lateralization of turning within the giant water bugs. Likewise, migratory locusts show a consistent bias in the eye with which they view a predator while stationary (Romano et al., 2017), which cannot be explained by their social environment (Niven and Bell, 2018).

One factor that has been suggested to be important in the evolution of population-level lateralization is posture and gait (Giljov et al., 2015; MacNeilage et al., 1987). Specifically, Giljov et al. (2015) suggest that bipedality is a key factor in promoting handedness in marsupial and placental mammals alike. A similar suggestion was made earlier by MacNeilage et al. (1987) for handedness in primates in relation to their arboreal lifestyle. Could posture, gait, or arboreal habitats be important factors promoting the evolution of population-level lateralization in insect species? Many studies of insect lateralization have focused on antennal movements. These antennae are not involved in supporting the body while standing or during locomotion, so like the forelimbs of bipedal mammals the antennae of insects can be used to gather information from the environment and adopt lateralized functions. There are some insect species that have modified their stance sufficiently to enable their forelimbs to be used for reaching or for raptorial movements (e.g., Niven et al., 2012; Prete et al., 1999), though whether this influences forelimb lateralization is unknown.

5 COMMON ORIGIN OR INDEPENDENT EVOLUTION?

The presence of lateralization in insect species spread across several insect orders, in addition to lateralization other invertebrate phyla, raises several questions about its evolution and origins: Is there a single common origin of lateralization within the insects? Are the lateralized behaviors observed in insects derived from a common mechanism or have they evolved independently? Is there an even deeper homology with the origin of lateralization in the vertebrates?

5.1 ORIGINS OF LATERALIZATION IN THE INSECTS

Lateralization can only evolve where there is differentiation of left and right, which requires specification of the left/right body axis. Within the insects, details of the molecular basis of left/right axis specification within the embryo are known from studies of the fruit fly *D. melanogaster* (reviewed in Coutelis et al., 2008). Although *D. melanogaster* is highly derived and possesses left/right asymmetries lacking in basal species within the insect phylogeny, such as that of the gut (Hayashi and Murakami, 2001), it seems reasonable to assume a common origin for left/axis specification within the insects: Developmental specification of anterior–posterior (AP) and dorsal–ventral (DV) axes has a common origin within the insects even when some aspects, such as long and short germ band segmentation may differ and there may be specific adaptations to ecological niches (reviewed in; Kalinka and Tomancak, 2012; Liu and Kaufman, 2005; Raff and Kaufman, 1991).

A common origin of left/right axis determination within the insects does not necessarily imply that behavior lateralization has a common origin. Behavioral lateralization within the insects encompasses sensory perception, motor control, learning, and memory (see Section 2). Yet the extent and direction of lateralization within one behavior do not necessarily correlate with that of any other behavior or with morphological asymmetries (e.g., Buchanan et al., 2015). Indeed, even when different behaviors involve similar sets of morphological structures, lateralization does not necessarily show similar direction or strength, suggesting that these may be independent behavioral modules subject to different selective pressures (see Section 4). This suggests that some of the neural substrates generating lateralized behaviors are independent of one another both in producing the lateralization and in their susceptibility to selective pressures.

One means of reconciling these observations is that a conserved developmental mechanism specifies the left/right axis in the insects that can be used by the developing nervous system to produce asymmetries in neural circuits within the brain, ventral nerve cord, and periphery. Circuits involved in the generation of one behavior need not be lateralized in the same direction or to the same extent as those producing another independent behavior. Biases within neural circuits that occur either at the sensory input or the common motor output will influence many behaviors, while those occurring in interneurons may affect only one or a restricted set of behaviors. For example, asymmetries within the central brain regions, such as the central complex, may produce lateralization of behaviors such as turning or orientation but leave targeted antennal or forelimb movements unaffected.

Although behavioral and neural modularity suggests the independent evolution of lateralization in different behaviors, this does not necessarily preclude a common origin for the lateralization of particular behaviors. Yet even behaviors such as lateralized turning do not necessarily have common origins within the insects. Many insects including cockroaches, water bugs, ants, and flies show lateralization of turning within test mazes (e.g., Buchanan et al., 2015; Cooper et al., 2011; Hunt et al., 2014; Kight et al., 2008). The direction and strength of the turning lateralization differs among these insects. In some cases, individuals within a population differ in their preferred turning direction, whereas in other cases the majority of members of a population show a preference for a particular side (e.g., Buchanan et al., 2015; Kight et al., 2008). Population-level turning preferences are unlikely to have a common origin because they are found in only a few species but the individual-level turning preferences, from which they are thought to derive and that are widespread in insects, may have a common origin. It is possible that these individual-level turning biases were present in the apterygote insects, which are the most ancient of the insect lineages (Grimaldi and Engel, 2005). However, a reporting bias may exist because failing to observe a turning preference in an insect species may be less likely to be published. Other lateralized behaviors, such as antennal or forelimb lateralization (e.g., Bell and Niven, 2014; Frasnelli et al., 2012a), have been only sparsely reported precluding any conclusion from being drawn.

Like behavioral lateralization, morphological asymmetries are also likely to depend upon early developmental specification of the left/right axis but again may be produced independently. Indeed, it may also be that the same directional bias in the behavior may arise from individuals having brains that are asymmetrical in opposite directions. For example, the nematode (*Caenorhabditis elegans*) shows a distinct motor handedness preference: at the population-level, males show a pronounced right-hand turning bias during mating. Interestingly, this motor preference is also observed in worms with mirror-reversed anatomical handedness, suggesting that it is independent from overall anatomical asymmetry and it may be driven by epigenetic factors rather than by genetic variation (Downes et al., 2012). This would explain the lack of correlation between the extent and direction of lateralization in different behaviors, and the lack of correlation with morphological asymmetries.

5.2 IS THERE A COMMON ORIGIN OF INSECT AND VERTEBRATE LATERALIZATION?

Many features of axes during development are conserved among insects and vertebrates during development (Gilbert and Barresi, 2016), however, left/right axis specification may not be as conserved as is anterior–posterior and dorsoventral axis formation (Levin, 2005). Nevertheless, at least one of the molecular components involved in the specification of the left/right axis in *Drosophila*, Myosin 1D, is conserved in vertebrates (Juan et al., 2018). Orthologues (i.e., homologous gene sequences in different species) of the Nodal family in the evolution of body plans and left–right specification are involved in both vertebrates (Boorman and Shimeld, 2002) and in Bilateria (Grande and Patel, 2009), suggesting that Nodal was present in the common ancestor of bilaterians. This raises the possibility that some aspects of the mechanisms specifying the left/right axis are evolutionarily conserved across large phylogenetic distances, though it cannot exclude the possibility that the same molecular components have been recruited independently.

Even if left/right axis specification is conserved between insects and vertebrates, this does not imply that lateralized behavior must have a common origin. As suggested earlier (see Section 5.2), specifying a left/right axis merely provides a ground plan which can be used to produce asymmetries in neural circuits that are the basis for behavioral lateralization. The presence of a bilateral ancestor (an urbilaterian) of both insects and vertebrates has been hypothesized but the exact form of this ancestor remains highly debated (for a review, see Northcutt, 2012). This urbilaterian need not have possessed behavioral or morphological lateralization though, given the prevalence of turning biases among invertebrate taxa (see Section 2), such a bias may be the best candidate for a lateralized behavior present in an urbilaterian. Biases in sensory perception, as well as learning and memory, may also have been present, though again there is no evidence of this. The vermiform *Bauplan* of the hypothetical urbilaterian means that lateralized control of specialized appendages almost certainly evolved independently in insect and vertebrate lineages.

6 CONCLUSION

In this chapter, we have reviewed recent work on lateralized behavior in insects, the majority of which has been published with the last 10 years. Understandably, for such a young field of scientific enquiry, these studies have focused on relatively few species, particularly focusing on bees and other hymenopteran insects (bees, ants, and wasps) (e.g., Anfora et al., 2010; Frasnelli et al., 2011, 2012a; Hönicke et al., 2015; Hunt et al., 2014; Rogers et al., 2013a, 2016). While this concentration has yielded valuable insights into the mechanistic basis and utility of lateralization (Frasnelli et al., 2014), it has ignored the vast majority of the ~5.5 million insect species (Stork et al., 2015). Broadening the range of insect species studied will likely provide new, surprising insights into the occurrence, mechanistic basis, and evolution of lateralization. Even so, published work has already demonstrated that lateralized behavior occurs in species from a many insect orders, is found in sensory perception, motor output, and central processing, and can occur at the individual or population-level.

Studies of insect lateralization are valuable because they afford an opportunity to assess the selective pressures that drive the evolution of lateralization in a lineage distinct from that of the vertebrates, providing independent tests of evolutionary scenarios. In this respect, two aspects of lateralization have been most thoroughly tested within the insects: the role of the social environment in selecting for lateralization through intraspecific interactions, and the occurrence of individual and population-level lateralization among different species. A range of levels of social organization occur within insect species, and studies have shown that social interactions are an important factor in promoting lateralization, particularly population-level lateralization. Recently, these studies have also emphasized that the influence of social interactions is likely restricted to very specific behavioral modules rather than being more generalized.

Yet even in these cases relatively few insect species have been tested, comparisons are often restricted to just two species, or use different behavioral paradigms to assess lateralization making interspecific comparisons difficult. Harnessing the power of studying insect species will require studies that use many species the phylogenetic relationships of which are clearly understood. The impact of other selective environments on lateralization, such as living in arboreal environments and/or food handling, remains to be tested explicitly within the insects. However, there are certainly species and behaviors that would permit explicit tests of such a scenario (e.g., Niven et al., 2010, 2012).

A further advantage of studying laterality within the insects is that it affords an opportunity to perform comparative neurobiological studies. Within vertebrates comparative neurobiological studies are often unfeasible because of ethical or logistical/financial considerations. This is not the case in insects, which are relatively easy to maintain in laboratory culture and are not subject to the same ethical considerations. Moreover, insects typically have much smaller nervous systems with fewer neurons than do vertebrates making behaviorally relevant circuit-level analysis possible. Until now, neurobiological studies of the circuits generating lateralization have rarely been attempted, though there are exceptions (e.g., Anfora et al., 2010; Buchanan et al., 2015; Rigosi et al., 2015).

Taken together, these considerations suggest that the study of insect lateralization can make substantial contributions to the broader study of lateralization within the animals. Indeed, they are likely to be most powerful when explicitly addressing and testing hypotheses that arise not just from other insect studies but also from work on vertebrates. This complementarity between insect and vertebrate studies of lateralization offers great possibilities for future research that, we envisage, will produce substantial insights for understanding the function and evolution of animal lateralization.

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CHAPTER

Motor asymmetries in fishes, amphibians, and reptiles

2

Gionata Stancher[*,†], **Valeria Anna Sovrano**[†,‡], **Giorgio Vallortigara**[†,1]
**Rovereto Civic Museum Foundation, Rovereto, Italy*
†Center for Mind/Brain Sciences, University of Trento, Rovereto, Italy
‡Department of Psychology and Cognitive Sciences, University of Trento, Rovereto, Italy
1Corresponding author: Tel.: +39-464808676; Fax: +39-464808654,
e-mail address: giorgio.vallortigara@unitn.it

Abstract

The study of brain and behavioral lateralization in so-called "lower vertebrates" (fish, amphibians, and reptiles) has received increasing attention in the last years, in an attempt to understand its phylogenetic origins and evolutionary significance. Observations on the earliest tetrapods, the amphibians, have helped us to understand the evolution of limb preference and suggest that laterality could have appeared even prior to the evolution of tetrapods. Insights into lateralized behaviors in fish—such as the turning behavior—have had an important role in uncovering proximate and ultimate causes of motor lateralization in the vertebrate subphylum. Additionally, investigations on the alignment of behavioral preferences in fish populations have helped do develop formal models to explain the unequal distribution of left- and right-lateralized individuals as the result of evolutionarily stable strategies among lateralized asymmetric individuals that interact cooperatively or competitively.

Keywords

Asymmetry, Lateralization, Limb preferences, Eye preferences, Handedness, Fish, Amphibians, Reptiles

1 THE OCCURRENCE OF MOTOR ASYMMETRIES IN LOWER VERTEBRATES

The term "motor lateralization" refers to the presence of behavioral biases at one of the two sides of the body, linked to functional and/or structural asymmetries between the two sides of the nervous system. Some examples include turning preferences in fish and biases in limb usage in tetrapods (four-limbed vertebrates)

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(see for general reviews, Bisazza et al., 1998; Güntürkün and Ocklenburg, 2017; Rogers et al., 2013; Vallortigara et al., 1999; Vallortigara and Bisazza, 2002; Vallortigara and Versace, 2017).

The best known example of motor lateralization is human handedness, a trait formerly and for a long time deemed as related to strictly human cognitive functions, such as language and tool use (Corballis, 1991). This view has been challenged however by the observation of a variety of motoric asymmetries in nonhuman vertebrate species (review in Rogers et al., 2013), including the so-called "lower vertebrates." As we will explain in this chapter, studies on fishes, amphibians, and reptiles may play a key role in the understanding of the evolutionary origins of this behavioral trait also in human beings.

The term "lower vertebrates" refers here to a group of species (fish, amphibians, and reptiles) that could have diversified early from the vertebrate lineage. We have included reptiles in the "lower vertebrates" group for our purposes, although the usual definition would include only the so-called anamniotes (fish and amphibians). Of course, the term "lower" merely indicates a time reference related to the earlier emergence of the ancestors of living fish, amphibians, and reptiles.

Unfortunately, lateralization data for the Class Agnata (jawless fish) are lacking, except for anatomical asymmetries in the habenular nuclei (Braitenberg and Kemali, 1970), and this is a remarkable gap in our knowledge, as jawless fish are believed to be the most ancient group of living vertebrates (Ströckens et al., 2013). However, current-living bone fish could be regarded as the descendants of those animals for which we have extensive knowledge more strictly related to the first vertebrates. Alternatively, modern amphibians (frogs, toads, and salamanders) could be regarded as the living animals more strictly related to the first tetrapods. One of the aims of this chapter will be to show how extensive studies of the living species belonging to the classes of fish, amphibians, and reptiles may help to unravel some crucial aspects of motor lateralization, including its phylogenetic origins and evolutionary significance.

1.1 LIMB PREFERENCES IN FISHES, AMPHIBIANS, AND REPTILES

Population-level human handedness shows some distinctive characteristics, such as being mostly task-invariant and relatively stable over time (Ströckens et al., 2013). Such features do not seem, at first glance, to have strict correspondence with nonhuman animal species, since in nonhuman animals lateralization appears to be more variant, especially at the population level (Versace and Vallortigara, 2015); moreover, lateralization seems to be modulated by external factors to some extent, such as the subject's stress levels and the experimental paradigm, as well as by individual predispositions (Rogers, 2000; Ströckens et al., 2013).

The inclusion of lower vertebrates in studies of population-level laterality has revealed that limb preferences are widespread among tetrapods and most likely they appeared in ancient times, rather than being confined to humans and other primates. In this regard, understanding the evolution of limb preference would be incomplete without examination of the earliest tetrapods, the amphibians (Bisazza et al., 1998). The common European toad (*Bufo bufo*) has been shown to exhibit a significant population-level preference for the use of the right forepaw to remove both a paper strip (snout-wiping test) and a plastic balloon from the head (59% and 55%, respectively, Bisazza and Vallortigara, 1996; Bisazza et al., 1997a). Similar results have been obtained with *Bufo marinus* (Robins and Rogers, 2002) but not with *Bombina orientalis* (Goree and Wassersug, 2001), as this latter species did not show any significant forelimb preference. Motor lateralization seems clear when specifically associated with feeding behavior: European green toads (*Bufotes viridis*) preferentially use their left forelimb to help themselves in the ingestion of living larvae (when pushing food into the mouth) (Sovrano, 2007).

Three different species of toads (*B. marinus*, *B. bufo*, and *B. viridis*) have been tested for righting responses, observing their turning behavior when overturned on a horizontal surface. Results demonstrated that footedness in toads is species specific: *B. marinus* and *B. bufo* preferentially used the right hindlimb (by pushing it against the substrate in order to perform the righting), while *B. viridis* showed preferential left hindlimb use. Green tree frogs (*Litoria caerulea*) have been investigated for their forelimb preferences during climbing (Robins and Rogers, 2006) and results showed a significant right forelimb preference as the leading limb. Overall, the available data suggest that while possessing lateralized limb preferences is a common trait in anuran amphibians (frogs and toads), the direction of lateralization can vary between species.

Asymmetries have been observed also in the reproductive behavior of urodelan amphibians (newts and salamanders, Marzona and Giacoma, 2002). While the alpine newt (*Ichthyosaura alpestris*) showed no lateral bias at the population level, male *Lissotriton vulgaris* displayed a marked bias for turning left after spermatophore deposition. Differences in lateralization between the two species have been interpreted according to the more complex courtship sequence of *L. vulgaris* compared to *I. alpestris*.

Malashichev (2002) tried to document a relationship between morphological and behavioral asymmetry in amphibians. With regard to behavioral asymmetry, preferences in forelimb use and turning behavior were measured. With regard to morphological asymmetry, the shoulder girdle (epicoracoid asymmetries), the position of spiracles, and the order of forelimb emergence in tadpoles were considered. With the possible exception of forelimb use and forelimb emergence (Malashichev and Nikitina, 2002), no direct cause-and-effect relationship between these traits was found. For example, the lateral bias in forelimb use in *B. marinus* showed no relationship with either the epicoracoid overlap asymmetry or the asymmetry in the spiracle position (Robins and Rogers, 2002); *B. bombina* tadpoles showed a preference in turning behavior but their spiracle was single and symmetrically placed, thus these traits lacked of any clear or significant relationship (Goree and Wassersug, 2001).

Among anurans some species appear to be more asymmetric than others at the population level (Malashichev, 2002). For example, *Bombina* spp. and *Xenopus* spp.

are extremely symmetric both in their morphology and behavior (i.e., there is less asymmetry than in other anurans in the shoulder girdle, in the spiracle position, in the forelimb emergence, in the turning behavior of tadpoles, and in the legs use). Since both genera are considered to be archaic anuran taxa (Suborder: Archaeobatrachian), Malashichev hypothesized that motor asymmetry in anurans could be in general a less primitive state than symmetry. However, in contrast to this view, eye preference has been supposed to predate the origin of the Order Anura since it has been observed both in archaic and derived families (Bisazza et al., 2002). It is interesting to consider visual motor asymmetries in tadpoles of the amphibian species *B. bufo* while approaching a conspecific. The propensity to move to make social aggregation appeared after several minutes following placement in a novel environment and this corresponded with the appearance of lateralization, when tadpoles showed a higher probability of approaching a conspecific appearing in their left rather than on their right hemifield (Dadda et al., 2003).

Observations of 11 species of amphibians have shown a connection between the degree of lateralization in motor responses (wiping an object off the snout and the righting response) and the type of locomotion used by a species. In particular, seven species characterized by using alternating-limb locomotion (*L. caerulea*, *Litoria latopalmata*, *Ceratophrys ornata*, *B. bufo*, *B. marinus*, *B. viridis*, *Pelobates fuscus*) have been found to be lateralized at the population level, whereas four species with synchronous jumping and/or swimming (*Rana temporaria*, *Rana lessonae*, *Bombina*, *B. orientalis*) were not lateralized when tested under the same experimental paradigm (Bisazza et al., 1996, 1997a; Goree and Wassersug, 2001; Malashichev, 2006; Malashichev and Nikitina, 2002; Robins et al., 1998; Rogers, 2002). Malashichev (2006) suggested that the quadruped locomotion could have required differential neural control and therefore a higher degree of asymmetry in the neural system.

When considering reptiles, only a handful of species have been investigated so far for presence of motor asymmetries. Seligmann (2002) reported individual-level preferences for hindlimb first releasing off the ground in gekos (*Hoplodactylus duvaucelii*). The leatherback turtle (*Dermochelys coriacea*) showed a spontaneous preference for the right hindlimb use in covering the chamber during egg laying (Sieg et al., 2010). However, the authors pointed out that only very few of the observed females showed a significant preference at individual level.

A strong lateralization has been found in the terrestrial tortoise (*Testudo hermanni*). Stancher et al. (2006) investigated the righting response in Hermann's tortoise, a species particularly suitable for this test because of its rigid body structure, allowing researchers to block the subjects in a perfectly horizontal supine position during testing. Results revealed consistent individual preferences and a population-level bias for turning on the right side. Interestingly, individual preferences were consistent over time, as two-thirds of the animals retested 10 months later retained the same preferred righting direction. A possible reason for the lack of individual preferences in *D. coriacea*, but not in *T. hermanni*, is that while the covering of eggs requires mostly symmetrical movements, the righting response on the contrary needs to be properly performed without repeated changes in the sides. Consistent with the right bias dominance in righting preference, *T. hermanni* also showed a significant preference for right paw use in starting movements from a resting position (while investigating the lateralized social behavior during mirror-images inspection; Sovrano et al., 2017).

The role of locomotion in affecting the strength of laterality in righting response has been investigated in sea turtles (Malashichev, 2016). These authors found individual lateralization only in the Green turtle (*Chelonia mydas*), while another species (Olive Ridley turtle—*Lepidochelys olivacea*) failed to show individual preferences. Since both species use synchronous locomotion (i.e., all four limbs are used in scratching), while terrestrial species—like *T. hermanni*—are asynchronous (i.e., they alternate limbs during locomotion), these authors suggest that, as for amphibians (Malashichev, 2006), in chelons, the more inherent asynchronous locomotion is prevalent, the greater the strength of laterality is for righting.

As to fish species, one study focused on the blue gournami (*Trichogaster trichopterus*), a fish equipped with a pair of ventral filamentous fins with gustatory and tactile functions (Bisazza et al., 2001a). When exposed to a series of novel objects in a test, it showed a preferential use of the left fin during the initial contacts. Such observation has suggested that "handedness" could have appeared even prior the evolution of tetrapods. This is an important point because, as we will see later on, one of the main questions about lateralization concerns whether it emerged independently in different lineages of vertebrates or if it was inherited by a common ancestor.

1.2 TURNING IN FISH AS A MODEL BEHAVIOR IN THE STUDY OF LATERALIZATION

Turning behavior in fish has been investigated in order to test the hypothesis that lateralized trunk/tail use predates the evolution of lateralized limb use. The study of this very simple behavior has largely helped to uncover the nature and origin of lateralization in the vertebrate subphylum. According to Rogers (2000), since fish seemed to diverge early from the main vertebrate lineage, it is possible to speculate that turning biases represented the first evolutionary step for lateralization present at the population level, thus predating handedness by millions of years. Furthermore, teleosts lateral preferences have been hypothesized (Ghirlanda et al., 2009; Ghirlanda and Vallortigara, 2004) to have evolved in response to the pressure of group aggregation and/or interactive/cooperative vs competitive behavior (Vallortigara, 2006). Hence, we will first describe some research on turning behaviors in fish and tadpoles and we will subsequently show how these have been used to better understand lateralization in vertebrates.

The escape responses in fish are mediated by the Mauthner cells (M-cells), a pair of giant reticulospinal neurons that decussate and synapse upon motor neurons innervating the contralateral body musculature. Such neurons, which ensure short response latencies (10–20 ms, Eaton et al., 2001), are at the origin of the so-called

C-shaped contraction visible in the turning behavior of fish (Zottoli, 1977). The typical response consists of a unilateral muscle contraction, followed by a flip of the tail (Wakeling, 2005). Dadda et al. (2010) found that behavioral lateralization affects the escape performance in the shiner perch (*Cymatogaster aggregata*): specifically, fish strongly lateralized in the escape response had shorter latencies, thus a higher escape reactivity. In particular, 92% of the highly lateralized individuals showed latencies shorter than 50 ms, a value that is well within the typical Mauthner cell response range. The predator–escape response has been tested also in the teleost fish (*Jenynsia lineata*) by Bisazza et al. (1997b). The stimulus was presented as the fish swam across the middle of the experimental tank and the direction of the subject's turning was recorded. Results showed that individual subjects were significantly lateralized, but no population-level lateralization was found. However, the individual direction of turning was maintained by subjects at retest, 1 month later.

Lateralization of predator–escape response in the teleost fish *Girardinus falcatus* revealed that when placed in front of a simulated predator, both juveniles and adult fish revealed a population-level rightward escape bias during the initial presentation of the stimulus, and a progressive reversal of the direction of turning after repeated presentations, ending with a population-level leftward escape bias (Cantalupo et al., 1995). Bisazza et al. (1998) tried to explain this shift from right to left as the result of repeated presentation of the same stimulus: as the recurring appearance of the predator was not followed by attacks or injuries, it might be categorized by fish as relatively innocuous, with a shift toward control by the left side of the brain. An alternative explanation involved the control of neural structures located in the left sides of the nervous system for fast motor responses, i.e., before any precise recognition of the stimulus, followed by a leftward bias due to a preferential right eye use to monitor the stimulus. It is apparent that in any natural situation both the motor and sensory component are, to varying degrees, involved in the production of asymmetrical behavior.

Zebrafish (*Danio rerio*) and goldfish (*Carassius auratus*) (Heuts, 1999) showed right-biased fast swimming turns and left-biased slow turns during an undisturbed situation. Such differences could be explained by an asymmetry at the neural and muscular level, as suggested by Heuts (1999) rather than being related to the categorization of a stimulus. In particular, fast swimming and slow swimming recruit different types of muscles (white muscles and red muscles), that might be differently distributed at the two sides of fish and used in different responses. In zebrafish, for example, the right side of the trunk has a larger white-muscle mass than the left side (Heuts, 1999). Turning choices in a T-maze and rotational swimming preferences have been investigated in sharks (*Heterodontus portusjacksoni*) with the purpose to examine for laterality during exploration of a novel environment (Byrnes et al., 2016). The tested sharks showed lateralization only at the individual level in both the tasks and a link between the strength of lateralization and individual stress reactivity emerged in rotational swimming (i.e., more strongly lateralized subjects were more reactive to stress).

Turning biases have been studied in tadpoles (Wassersug et al., 1999). A typical tadpole's behavior consists of descending the surface of the water by turning to the left or to the right after surfacing to breathe air. Tadpoles of the bullfrog (*Rana catesbeiana*) showed a turning preference to the left side, whereas tadpoles of the clawed frog (*Xenopus laevis*) failed to show population-level lateralization. Gross anatomical differences in the external morphology have been proposed to explain the differences in the observed behaviors: in particular, ranid ("true frogs," family Ranidae) tadpoles have a single left spiracle (it allows the water to be expelled to the body), whereas pipid ("tongueless frogs," family Pipidae) tadpoles, such as *X. laevis*, have in contrast one spiracle on each side of their body. The discovery of a left turning bias in the startle response of *Microhyla ornata* tadpoles (Yamashita et al., 2000) helped to rule out the external asymmetries as the cause of the behavioral bias. In fact, *Microhyla* tadpoles are externally symmetrical like *Xenopus*, but they are more closely related to *Rana*: it seems therefore that the explanation of the asymmetry has more plausibly to be searched in the phylogenetic relationships between different species rather than in their external features. Such observations and comparisons are important in that they show that functional lateralization cannot be easily explained as a mere byproduct of gross anatomical asymmetries (i.e., external asymmetries).

The startle response has been investigated by Briggs-Gonzalez and Gonzalez (2016) in tadpoles of *Agalychnis callidryas* and *Leptodactylus melanonotus*. They found a right side preference in tadpoles of *L. melanonotus* and a left-side bias in *A. callidryas* tadpoles. A correlation between behavioral lateralization in larvae and adults of species belonging to the same Superfamily (Neobatrachian vs Archaeobatrachian) has also been found. On the basis of such observations and correlations, the authors, in agreement with Malashichev (2002) and Malashichev and Wassersug (2004), suggested that lateralized behavior in anurans may be a highly conservated feature acquired at the base of the neobatrachian group, rather than due to external (larval or adult) morphological asymmetries, thus reflecting their phylogenetic relationship. It has been further suggested (Briggs-Gonzalez and Gonzalez, 2016; Malashichev, 2006) that behavioral lateralization may be linked to locomotor strategies of different species (see Section 1.1).

Asymmetrical turning has been observed also in urodelan amphibians: during mating behavior and in order to transfer the spermatophore sac to the female, in which adult males of the newt *Triturus vulgaris* showed a population bias to turn leftward, folding their tails along the flank (Green, 1997). In an attempt to categorize it either as sensory or motor lateralization, Green argued that the sexual behavior of newts appears to be mainly driven by internal programming, therefore visual lateralization is unlikely to have affected asymmetry in this context. In fact, if the female was removed before the male started to turn, this had no influence on the observed behavior and on the subject orientation.

Spontaneous swimming preferences were tested in mosquitofish (*Gambusia holbrooki*) by Bisazza and Vallortigara (1996, 1997). It was found that females tended to switch the direction of swimming according to the time of the day: they rotated in a clockwise direction in the morning and in a counterclockwise direction at night, whereas males did not show any population preference (i.e., only individual rotational preferences were observed). Since the bias disappeared when females were tested under diffuse lighting conditions and when using naïve subjects, the authors suggested that fish were using a sun-compass orientation mechanism. Interestingly enough, when males were faced with a predator placed at the center of the tank, they showed a significant bias to rotate in an anticlockwise direction, irrespective of the time of day, whereas no bias was observed in the absence of a predator (Bisazza et al., 1997d). These results are consistent with those observed in a detour test performed on the same species: when males were required to move around an obstacle to approach a target (either a group of females or a dummy predator), they showed a bias to detour to the left side (Vallortigara and Bisazza, 2002). However, it should be noted that, just because the lateralization disappeared when males were tested in the absence of any target, it seems likely that the biases reflected preferences in eye use rather than true motor asymmetries (Vallortigara and Bisazza, 2002).

Some studies have demonstrated a high degree of plasticity in fish lateralization and associated it with the role of predation in prey's turning behavior, such that the strength of lateralization is correlated with escape performance (Dadda et al., 2010). Chivers et al. (2016) observed a significant decrease in the strength of lateralization (turning bias behavior) in wild–caught coral reefs shooling fish (*Caesio teres*) after the predation pressure was experimentally elevated or relaxed: in particular, fish of low-risk groups were not strongly lateralized after experiencing an absence of risk for 5 days, while in high-risk groups all fish were individually lateralized. Ferrari et al. (2015) manipulated the predation pressure in captive breeding juvenile damselfish (*Pomacentrus* spp.) in order to evaluate their influence in the turning bias tendencies. In one experiment, they exposed juvenile whitetail damsels (*Pomacentrus chrysurus*) to injured conspecifics cues for 4 days ("injured conspecific cues" or "alarm cues" are chemicals that are able to elicit an antipredator response when detected by conspecifics). At test, fish exposed to high-risk conditions displayed both behavioral and physiological alterations that were maintained for at least 2 weeks. Among these, an increased behavioral lateralization was observed to compare the low-risk condition fish. In another study (Ferrari et al., 2015), juvenile Ambon damselfish (*Pomacentrus amboinensis*) were trained to recognize different patterns of risk throughout the day: fish were exposed to one of two pattern of risk for 9 days, with a peak of the risk either at mid-day or in the evening. Being that the fish were subsequentially tested both at the noon and in the evening, authors found stronger turning bias tendencies at the time of the day that was perceived by each individual as the more risky on the basis of its previous experience during training sessions. In a different experiment (Ferrari et al., 2017), fish were exposed to the cortisol stress hormone for 48 h before test, as the only factor differing between the two experimental groups. Fish exposed to cortisol exhibited a higher degree of turning bias compared to fish of the control condition. On the opposite side, the exposure of Siamese fighting fish (*Betta splendens*) to the antidepressant drug fluoxetine (Prozac) caused both a decrease in the aggressive displays and a switch in the preferential eye use during aggressive encounters, from the right to the left eye (HedayatiRad et al., 2017). Overall, these results provide evidence that lateralization is a highly variable trait, whose expression can be modulated within days or even hours. Moreover, a link between stress and lateralization expression seems to be apparent.

In the present day quickly changing environment due to, for example, anthropic factors, have raised concerns that the exposure of fish (*Neopomacentrus azysron* and *Atherina presbyter*) to elevated CO_2 concentrations might disrupt individual lateralization, by directly affecting brain functions in larval fish (Domenici et al., 2011; Lopes et al., 2016). A similar impairment in brain lateralization has been found in larval coral reef fish (*Acanthurus triostegus*) exposed to agricultural pesticide (e.g., chlorpyrifos) (Besson et al., 2017). Since lateralization is associated with performance in a variety of behavioral responses, including antipredatory ones (e.g., influencing group cohesion), ocean acidification can increase the vulnerability of larval fishes to predation. The opposite effect has been observed in sharks (*Scyliorhinus canicula*): subjects exposed to elevated CO_2 showed an increased lateralization (Green and Jutfelt, 2014) together with some other behavioral effects, such as a change in the nocturnal swimming pattern. Overall observations suggest that fish neurophysiology is affected by CO_2 concentrations.

2 EVOLUTIONARY PERSPECTIVES ON MOTOR ASYMMETRIES: PROXIMATE AND ULTIMATE CAUSES OF MOTORIC LATERALIZATION

Asymmetries in brain anatomy are common in lower vertebrates and, unlike anatomical differences in the external morphology, associated with behavioral asymmetries. The habenular nuclei are conserved, bilateral structures acting as a regulator of central nervous system neurotransmitters, with a key role in encoding of aversive and rewarding stimuli, influencing motivational states and also involved in the regulation of biological rhythms (Bianco and Wilson, 2009; Fakhoury and Domíniguez López, 2014). In both amphibians and reptiles, habenulae are located in the anterior dorsal diencephalon and are asymmetrical in size in hagfish, teleost fish, and cartilaginous fish (Brandshaw and Rogers, 1993). In lower vertebrates, the dorsal habenulae receive innervation from multiple sensory regions (Krishnan et al., 2014) working as an essential integrating center; interestingly, they show striking left–right differences in their size, neuronal connections, and also gene expression (Roberson and Halpern, 2017). For example, the left dorsal habenula, but not the right one, has been found necessary for input-dependent light-preference behavior in zebrafish larvae (Zhang et al., 2017), displaying also a functional specialization in attenuating the fear responses, by promoting the recovery following an aversive stimulus or event (Duboué et al., 2017). Within the Class of amphibians, the left habenula was found to be more lobate than the right one in *Triturus cristatus*, *Rana esculenta* (Braitenberg and Kemali, 1970), and *R. temporaria* adults and larvae (Morgan et al., 1973). In *R. temporaria*, both spontaneous and light-evoked activity in the left habenula is less marked than in the right; in lizards (*Uta stansburiana*), fibers arising from ganglion cells of the parietal eye project unilaterally to the left medial habenular nucleus. This suggests that the habenular lateralization may be associated with asymmetries in peripheral organs such as the pineal gland, therefore with its functions and derived behaviors. Since they have been found also in the most primitive living vertebrates, jawless fish, habenular asymmetries are probably very ancient (Jansen, 1930; Shanklin, 1935).

Turning preferences in fish has been linked to asymmetries in the nervous system as well. The Mauthner cells are a pair of giant reticulospinal neurons that decussates and synapses upon motor neurones innervating the contralateral body musculature (Fetcho, 1991, 1992). Found in teleost fish and some amphibians (Will, 1991; Zottoli, 1978), such cells are supposed to be correlated with the C-start turning reaction (Eaton and Emberley, 1991; Zottoli, 1977). Moulton and Barron (1967) reported a marked asymmetry in several goldfish (*C. auratus*) and in caudate and anuran tadpoles. In the *C. auratus* species, the left Mauthner cell was approximately three times the size of the right one. Thus, motor neurons asymmetries can easily account for behavioral asymmetries both in fish and amphibians larvae. Nevertheless, in spite of the fact that C-start reaction does not rely on sensory information once the movement begins, it seems obvious that sensory information is necessary to coordinate the C-start. Information about the nature and location of the stimulus and about the fish own position are projected from the optic tectum to the Mauthner's cells so that the behavioral asymmetry may be generate also at the level of the tecta, preceding the C-start escape sequence (Bisazza et al., 1998).

Although it is unclear how genes influence the phenotype, results suggest that genetic factors may play a major role in the determination of the direction of lateralization (Concha et al., 2012; Doboué and Halpern, 2017). Evidence of hereditability of the direction of behavioral asymmetries in fish was found in the poeciliid *G. falcatus* (Bisazza et al., 2000b). Males and females that scored a similar eye preference for inspecting a potential predator in a detour test were mated together. As a result, researchers found a highly significant correlation in the strength and the direction of the asymmetries between parents and offspring. Moreover, direction of lateralization as found in selected lines of fish, was maintained in other behavioral responses (Bisazza et al., 2001b), namely: turning direction in a T-maze, direction of rotation in a circular arena, and preferential eye use during shoaling behavior (females), sexual behavior, and agonistic behavior (males).

Although such observations provide reliable physiological and genetic explanations for the turning preferences in the tested subjects, they fail to address several important questions regarding the biological relevance of motor asymmetries, namely (i) trying to identify the evolutionary pressures that led to physiological and behavioral asymmetries in bilaterally symmetrical organisms; (ii) explaining the preferences distribution in the population, often deviating from the predictable

50:50, as observed in several species (included humans); (iii) answering the question of why some species show lateralization only at the individual level and others at the population level.

Any evolutionary and adaptive explanation of the lateralization in vertebrates has to take into account two issues. The first issue is pertinent to the explanation of lateralization at the individual level: why does an organism, which evolves with a bilaterally symmetrical distribution of sensory and motor organs, show asymmetrical behaviors and asymmetrically process sensory inputs? The second issue concerns population- or group-level asymmetry. That is, what is the reason for an uneven distribution of preferences or biases within a population: the expected distribution in a population of individually lateralized individuals, with all conditions being equal, should be 50:50. While some species seem to display only individual lateralization for some behaviors (see, e.g., Bisazza et al., 1997c; Cantalupo et al., 1996) several vertebrate species show a significant alignment of the direction of motor asymmetries at the population level (e.g., Ströckens et al., 2013 reported that about 51% out of 119 vertebrate species show population-level limb asymmetries).

First of all, with regard to individual lateralization, one question is whether motor lateralization is a by-product of so-called fluctuating asymmetries. Fluctuating asymmetries are random deviations from bilateral asymmetries of individuals, often associated with environmental stress and supposed to be related to the incapacity of individuals to achieve identical development of both sides of the body (Leary and Allendorf, 1989). Since fluctuating asymmetries have been described for a number of different animal species, including fish (Bisazza et al., 1998), it potential role in developing behavioral asymmetries has been hypothesized. In a study by Bisazza et al. (1997b) an index of fluctuating asymmetries was calculated in specimens belonging to *J. lineata* in order to investigate for any relationship between morphological (i.e., the number of: rays of the pectoral fin, scales, supraorbital pores, postotic, and preopercular pores) and behavioral (escape–behavior directions) asymmetries. Results show that none of the four measures of fluctuating asymmetries correlated with the behavioral asymmetry.

Evidence suggest that having lateralized brain functions could increase individual neural capacity, therefore enhancing cognitive performances (e.g. by carrying out simultaneous processing in which the two hemispheres are specialized for different functions, Levy, 1977) or preventing the simultaneous initiation of incompatible responses (Vallortigara et al., 1999; Vallortigara and Rogers, 2005). For example, fruit flies (*Drosophila melanogaster*) with an asymmetrical brain were found to form better long-term memories than those who were more symmetrical (Pasqual et al., 2004). In a dual task (Rogers et al., 2004), in which chicks (*Gallus gallus*) had to monitor overhead to detect a model predator and, at the same time, to discriminate between grains and pebbles, the more lateralized subjects performed the task better. Strongly lateralized chicks detected a model predator sooner, and learned to avoid pecking at pebbles better than did weakly lateralized chicks. Therefore, if the brain needs to be lateralized in order to function efficiently, it may be irrelevant which side is used to support a specific set of functions. On the other hand, clear disadvantages may be associated with the possession of sensory and motor asymmetries (Vallortigara and Rogers, 2005). Bilateral asymmetries would have evolved together with the differentiation of the head region and the development of unidirectional movement in animals. For this reason, any lateralized sensory deficit in an individual might leave it vulnerable to attack on one side or unable to hunt a prey on one side. Similarly, directional motor asymmetries may convey evident disadvantages in species living in groups, namely predictability of behavior: any bias in the population can be exploited by a predator by learning the most frequent direction of turning and taking advantage of it. Apparently, advantages of laterality extend to populations, within a quite complex prey–predator or more generally interindividual dynamic.

Frequency-dependent selection (Poulton, 1884) is a particular type of selection in which the fitness of an individual depends on the frequency of its phenotype relative to other phenotypes in a given population. Frequency-dependent selection is well known in evolutionary biology for leading to polymorphic equilibria in the populations and is often assumed to be the result of the interaction between species, particularly in relation to antipredator responses. The scale-eater fish of the lake Tanganika (genus *Perissodus*), for example, is renowned for exhibiting an asymmetry in the opening side of the mouth, either to the left or to the right as the result of an asymmetrical joint of the jaw to the sospensorium. The trait has been found to be inherited and determined by a simple Mendelian one locus, two allele system, with the right side dominant over the left side (Hori, 1993). Since the less frequent phenotype enjoys an advantage because it can attack prey on the unexpected side, the proportion of the right and left phenotype deviate from 50:50 but it does not stay at an equilibrium level: it varies with about a 5-year periodicity instead, as the result of a frequency-dependent selection acting in this species (Hori, 1993). Thus, not only the dominant direction of the asymmetry varies between different populations of the same species but also among each population it oscillates around an equilibrium level with a well-defined periodicity.

The alignment of the behavioral preferences in animal populations (therefore the deviation from 50:50) was explained by Ghirlanda and Vallortigara (2004) as the result of interactions, either between different species (as in the case of prey–predator interactions) or conspecifics (“social” interactions). In both cases, individuals showing the less common phenotype benefit from an immediate, generic advantage due to the unpredictability of their behavior. In a typical scenario, a predator could learn the more frequent turning direction in fish, yielding an advantage to the individuals departing from the mass. However, the “favored” phenotype cannot spread his genes in the population by increasing its representation, as would be expected in a more typical evolutionary scenario, because the advantage is strictly associated to its rarity, that is, it is frequency dependent. In other words, as the uncommon phenotype increase in number, its fitness will decrease as a consequence. Negative frequency-dependent selection acting on lateralized behaviors explains the alignment of the preferences in animal populations accounting, at the same time, for the presence of a small percentage of individuals (variable from 10% to 35%) that do not conform to the pattern of the majority (Vallortigara and Rogers, 2005). This is the case of many species, including handedness in humans (McManus, 2002). Ghirlanda et al. (2009) demonstrated that the unequal distribution of left- and right-lateralized individuals into a population can be explained as the result of intraspecific interactions among individuals. In particular, the model predicts that with a predominance of antagonistic interactions, we expect the minority phenotype to be more common. On the other side, when synergistic interactions are more important, the minority phenotype will decrease in number.

Fish differ widely in their lifestyles and their interactions, as some species are mainly solitary while other species tend to move in large groups. Since, as argued by Ghirlanda and Vallortigara (2004) laterality is supposed to be strongly linked to and influenced by the type of individual interactions, we will expect that these two very different lifestyles affect in opposite ways the resulting pattern of behavioral lateralization in fish. "Shoaling" species, in particular, take advantage of the so called "dilution effect" (Burger and Gochfeld, 2001), namely, the fact that the likelihood of being preyed is lower in larger groups. Thus, for each individual of such species it is advantageous to show the same turning preferences of the other individuals in the group. In contrast, solitary species do not have the need to align their behavior to that of the others: thus, researchers predicted that shoaling fish species will be lateralized at the population level, while solitary species will be lateralized at the individual level only. This prediction was tested for turning biases in fish (Bisazza et al., 2000a). First, the social tendency of 16 species was determined in terms of propensity to school: 6 of them were found to be gregarious and 10 were found nongregarious. Then, the turning direction when faced with a dummy predator was quantified. Results showed a nonperfect correlation, nevertheless the data fit the hypothesis quite well: all 6 shoaling species were lateralized at the population level; 6 out 10 of the solitary species were found lateralized only at the individual level.

It is important to stress, however, that the theory cannot be equated to the very simplistic idea that directional lateralization emerges in "social" species. The original version of the theory (Ghirlanda and Vallortigara, 2004; Vallortigara, 2006; Vallortigara and Rogers, 2005) explained that the issue of the presence of interaction between individually asymmetric individual referred to the evolutionary first appearance of direction lateralization, because for current-living animals the distinction between "social" and "nonsocial" species is largely meaningless. What is crucial instead is whether the types of tasks animals are engaged with do involve interaction. Some species have limited social behavior (Anfora et al., 2010) but they do exhibit directional laterality when they engage in interactive behavior (e.g., aggression; see Rogers et al., 2016).

According to this idea, lateralization at the individual level and at the population level are both examples of a general Evolutionarily Stable Strategy, a concept developed in Game Theory (Vallortigara, 2000, 2006). For example, Kurvers et al. (2016) used a combined behavioral and morphological approach to investigate the presence of lateralization during sailfish's (*Istiophorus platypterus*) attacking of schooling sardines in the wild. The aim of their research was to test whether the increase capture success because of specialization in a lateralized attack was affected by the cost of an increased predictability to the prey, with the latter eventually counterbalanced by the benefit of group hunting. Results provided evidence for individual-level (but not population-level) lateralization in sailfish's attacks and a higher capture success in the more strongly lateralized individuals. Moreover, Kurvers et al. found that the predictability of the attacks by single sailfish rapidly declines with increasing group size. Results demonstrate also that individual-level lateralization can evolve by alternating attacks in a hunting group, in the absence of population-level lateralization. The benefit of the group overtakes the negative consequences of individual-level predictability as predicted by theoretical models such as those of Ghirlanda and Vallortigara (2004).

2.1 THE OCCURRENCE OF LATERALIZED BEHAVIORS IN LOWER VERTEBRATES AND THE TRICKY PHYLOGENY OF MOTORIC LATERALIZATION

Research on genes involved in asymmetry is at the beginning but a continuity of gene expression from invertebrates to vertebrates has been speculated to exist (Rogers and Vallortigara, 2015). The signaling molecules Nodal and Pitx2 have been identified in the development of structural asymmetry in vertebrates, being such genes expressed on the left side of all the studied vertebrate embryos and nonvertebrate chordata, such as amphioxus and ascidians (Boorman and Shimeld, 2002). Nodal signaling pathway is involved in embryogenesis and development of visceral and neural asymmetry in zebrafish (*D. rerio*), it also plays a role in the development of later embryogenesis asymmetries of sea urchin and determines the structural axis in *Hydra*, a radially symmetrical cnidarian. Overall, these studies suggest that asymmetry is regulated by a pathway shared by all vertebrates and all chordates: a conserved molecular mechanism evolved before the separation of the lineages of living chordates.

In an attempt to reconstruct the evolutionary origin of lateralization and to understand the possible homology or homoplasy of asymmetry among vertebrate taxonomic groups, researchers need to evaluate the pattern of variation of this trait among species in order to assess if it was either inherited by a common ancestor or it has emerged more than once in the vertebrate phylogenetic tree (see Fig. 1 and Table 1). In fact, while structural asymmetry is supposed to have evolved more than once in animals, the frequent occurrence of transitions between symmetric and asymmetric states suggest a conserved molecular mechanism. Moreover, the application of parsimony criteria on the wide distribution of structural asymmetries among bilaterians (i.e., animals with bilateral symmetry) indicate a possible homology of this trait (Boorman and Shimeld, 2002).

Research on lower vertebrates can help to untie the knot about the phylogeny of laterality and motoric lateralization, at least for the vertebrate subphylum. Recent studies (Hori et al., 2017) have revealed that functional laterality is steadily associated with morphological asymmetry in fishes and aquatic invertebrates, whereas a weakened of morphological laterality, but on the other hand a retain of functional laterality, has been observed in terrestrial vertebrates. Unlike terrestrial

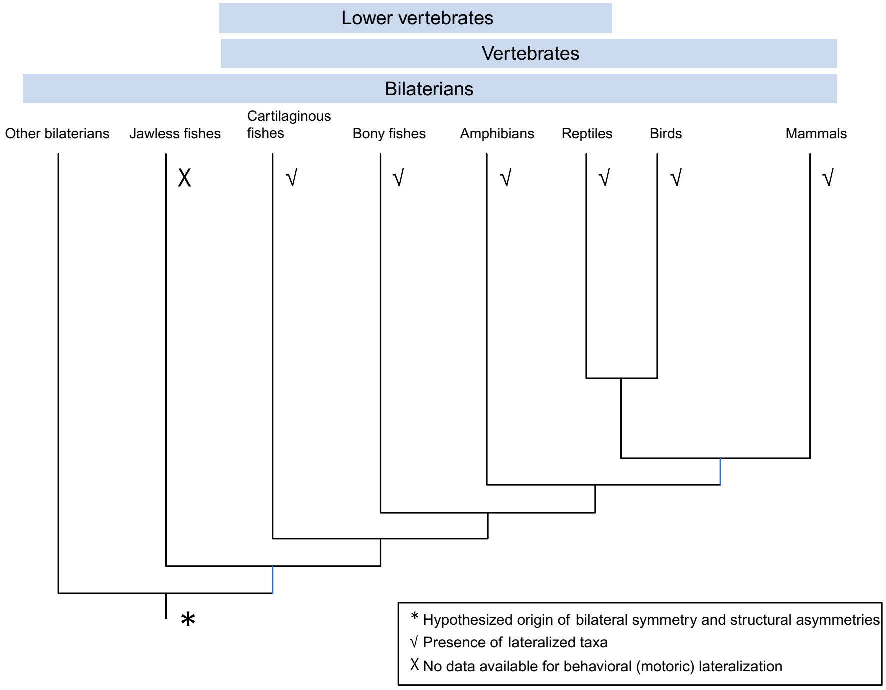

FIG. 1

Phylogenetic tree of vertebrates and bilaterians. *The chart* shows the hypothesized origin of both bilateral symmetry and structural asymmetries, and the occurrence of behavioral lateralization in living taxa.

Table 1 Occurrence of Behavioral Lateralization in the Species Cited in the Text

	Behavioral Lateralization	No Behavioral Lateralization Observed	
Fish			
Acanthurus triostegus	X[a]		Besson et al. (2017)
Ancistrus sp.	X		Bisazza et al. (2000a)
Atherina presbyter	X[a]		Domenici et al. (2011) and Lopes et al. (2016)
Barbus conchonius	X		Bisazza et al. (2000a)
Betta splendens	X[a]		Bisazza et al. (2000a) and Cantalupo et al. (1996)

Continued

Table 1 Occurrence of Behavioral Lateralization in the Species Cited in the Text—cont'd

	Behavioral Lateralization	No Behavioral Lateralization Observed	
Caesio teres	X[a]		Chivers et al. (2016)
Carassius auratus	X		Heuts (1999)
Channa obscura	X[a]		Bisazza et al. (2000a)
Corydoras aeneus	X		Bisazza et al. (2000a)
Danio rerio	X		Heuts (1999) and Bisazza et al. (2000a)
Gambusia holbrooki	X		Bisazza and Vallortigara (1996) and Bisazza et al. (1997d, 1998)
Girardinus falcatus	X		Cantalupo et al. (1995) and Bisazza et al. (1998)
Gyrinocheilus aymonieri	X[a]		Bisazza et al. (2000a)
Heterodontus portusjacksoni	X[a]		Byrnes et al. (2016)
Istiophorus platypterus	X[a]		Kurvers et al. (2016)
Jenynsia lineata	X[a]		Bisazza et al. (1997b)
Knipowitschia punctatissima	X		Bisazza et al. (2000a)
Lepomis gibbosus	X		Bisazza et al. (2000a)
Neopomacentrus azysron	X[a]		Domenici et al. (2011) and Lopes et al. (2016)
Pomacentrus chrysurus	X[a]		Ferrari et al. (2015)
Pomacentrus amboinensis	X[a]		Ferrari et al. (2015)
Pterophyllum scalare	X		Bisazza et al. (2000a)
Scyliorhinus canicula	X[a]		Green and Jutfelt (2014)
Syngnathus pulchellus	X[a]		Bisazza et al. (2000a)
Trichogaster trichopterus	X		Bisazza et al. (2001a)
Xenotoca eiseni	X[a]		Bisazza et al. (2000a)
Amphibians			
Agalychnis callidryas	X		Briggs-Gonzalez and Gonzalez (2016)

Table 1 Occurrence of Behavioral Lateralization in the Species Cited in the Text—cont'd

	Behavioral Lateralization	**No Behavioral Lateralization Observed**	
Bombina orientalis		X	Goree and Wassersug (2001)
Bombina		X	Malashichev and Nikitina (2002)
Bufo	X		Bisazza et al. (1996, 1997a)
Bufo marinus	X		Bisazza et al. (1996, 1997a) and Robins and Rogers (2004)
Bufotes viridis	X		Bisazza et al. (1997a)
Ceratophrys ornata	X		Malashichev (2006)
Hyla regilla	X		Dill (1977)
Ichthyosaura alpestris	X[a]		Marzona and Giacoma (2002)
Leptodactylus melanonotus	X		Briggs-Gonzalez and Gonzalez (2016)
Lissotriton vulgaris	X		Green (1997)
Litoria caerulea	X		Malashichev (2006)
Litoria latopalmata	X		Rogers (2002)
Microhyla ornata	X		Yamashita et al. (1999)
Pelobates fuscus	X		Malashichev (2006)
Rana catesbeiana	X		Wassersug et al. (1999)
Rana lessonae		X	Malashichev (2006)
Rana temporaria		X	Malashichev (2006)
Xenopus laevis		X	Wassersug et al. (1999)
Reptiles			
Chelonia mydas	X[a]		Malashichev (2016)
Dermochelys coriacea	X[a]		Sieg et al. (2010)
Hoplodactylus duvaucelii	X[a]		Seligmann (2002)
Lepidochelys olivacea		X	Malashichev (2016)
Testudo hermanni	X		Stancher et al. (2006) and Sovrano et al. (2017)

[a] *Cases in which only individual-level asymmetries were observed.*

animals, species moving in aquatic environment suffer minimal effects from gravity and this could have allowed them to develop bodies asymmetry; in a terrestrial environment, by contrast, the gravity forces to develop a laterally symmetric body supported by limbs. Behavioral asymmetry seems to have existed already in Cambrian trilobites (Babcock, 1993) and since fish appeared only at the end of Cambrian, it is possible that laterality appeared first in Arthropoda. Most animal phyla developed new eye sight during Cambrian in response to the worsening of predator–prey interactions, which may have led to the development of the asymmetrical bodies of bilaterians (Hori et al., 2017). Moreover, since laterality has been found also in lobe-finned fishes (coelacants and lungfish, which show a strong similarity to the expected ancestral form of tetrapods, i.e., amphibians, reptiles, birds, and mammals), it has been suggested that the trait was inherited by tetrapods from fish (Hori et al., 2017; Rogers et al., 2013).

The overall available data on functional asymmetries in vertebrates clearly suggest a shared rightward bias for foraging responses (review in MacNeilage et al., 2009), especially when animals have to visually discriminate food from similar targets (e.g., toad show a rightward preference for catching a prey that has to be recognized precisely and dealt with care, such as crickets, but not for simplified prey models; Robins and Rogers, 2004). Thus, the left hemisphere would be involved in considered responses, while the right hemisphere in rapid responses, such as antipredatory reactions. As the left hemisphere controls, in humans, the right hand use for fine manipulation and the motor planning for the execution of actions by both the left and right hand (Janssen et al., 2011), it has been suggested (Vallortigara and Rogers, 2005) that handedness may have arisen from a more general ancient specialization of the left side of the vertebrate brain for pondered motor responses. Note also that actions by the left and right hand are controlled by the left hemisphere. This is consistent with the notion of "pondered" action. Furthermore, this suggests that motor and sensory lateralization may be linked to each other by the sharing of the same general pattern of functions' distribution in the two hemispheres.

Nevertheless, it seems that there are exceptions to the rule: for example, when tested on the side preferences in monitoring a predator, 10 fish species out of 16 showed a population-level turning preference, 6 of them a rightward bias and four an opposite leftward bias (Bisazza et al., 2000a). Because all species were presented to the same situation (and stimulus) it seems to be arduous to account for these results with a similar mechanism of lateralization among species. However, a possibility suggested by Vallortigara and Rogers (2005) is that the observed variations in the direction of laterality may reflect differences in the species-specific behavioral strategies rather than differences in the laterality per se. For example, if two species experience significant differences in the degree of emotionality within the same context, a difference in processing of the stimuli could be expected, and animals may show opposite directions of lateralization as a consequence. The overall available data suggest that, while between-species differences in the expression of lateralization may occur, the existence of a common pattern of lateralization (at least for visual lateralization) among vertebrates is well supported.

Ströckens et al. (2013) analyzed limb preferences in 119 different vertebrate species by employing cladographic comparisons. Results revealed that 51.26% of the species showed evidence for population-level asymmetries, 16.81% individual level only asymmetries, and 31.93% no evidence for asymmetry. Overall, these results support the claim that population-level limb preferences represent a common vertebrate feature. However, application of phylogenetic comparative methods was not possible due to the lack of data for some critical orders, some of them belonging to lower vertebrates. Strockens et al. highlight how studies on the Classes Agnata (jawless fish) and Chondrichtyes (Cartilaginous fish) would be necessary to derive a proper evolutionary interpretation of limb asymmetries in vertebrates. Data on behavioral asymmetries in cartilaginuous fish are scarce (Byrnes et al., 2016; Green and Jutfelt, 2014) and these animals are, as well as jawless fish, certainly regarded as key taxonomical groups for the understanding of the phylogeny of motor lateralization in general. Data on Crocodylia are also not available: this is an unfortunate absence as Crocodylia are the closest living relatives of birds, on which most of the studies on lateralization has been focused on. At the same time, Crocodylia represents the closest living link between birds and mammals, confirming a key role of this taxonomic group. The overall lack of data for several orders of vertebrates makes difficult to use at present phylogenetic comparative methods (Ströckens et al., 2013).

Even though there is little doubt that population-level motoric asymmetries are not unique to *Homo sapiens*, being widespread among vertebrates, the application of a phylogenetic approach in the study of lateralization in vertebrates, and particularly for motoric lateralization, could benefit of a deepening of the studies on the earlier taxonomical groups of living vertebrates.

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CHAPTER

3

A review of performance asymmetries in hand skill in nonhuman primates with a special emphasis on chimpanzees

William D. Hopkins[1]
Neuroscience Institute, Georgia State University, Atlanta, GA, United States
Division of Developmental and Cognitive Neuroscience, Yerkes National Primate Research Center, Atlanta, GA, United States
Ape Cognition and Conservation Initiative, Des Moines, IA, United States
[1]Corresponding author: Tel.: +1-404-413-5812; Fax: +1-404-413-5856, e-mail address: whopkins4@gsu.edu; whopkin@emory.edu

Abstract

Most humans report preferring the right hand for a variety of manual actions. Additionally, most humans perform motor tasks better with their right hand, particularly among right-handed individuals, but less so among left-handed people. Some have suggested that asymmetries in performance rather than hand preference may better reflect left hemisphere specializations in motor functions. In contrast to humans, research on performance asymmetries in manual tasks by nonhuman primates has received far less empirical investigation. In this chapter, I review the evidence presented to date on individual- and population-level asymmetries in motor tasks in nonhuman primates. Broadly speaking, studies on motor asymmetries have focused on (1) intermanual differences in grasping morphology and (2) intermanual differences in performance on a variety of different motor tasks. The results suggest that some species show population-level left–right differences in motor skill. Moreover, performance differences between the left and right hands appear to be mediated by preferred hand use but not in a dissociative manner. The collective data suggest that measures of performance asymmetries in different primate species may provide additional insight into theories on the evolution of hemispheric specialization in motor control.

Keywords

Motor asymmetries, Nonhuman primates, Hand preference, Evolution of hemispheric specialization, Laterality

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ABBREVIATIONS

DNA	did not analyze
DNP	data not reported
HI	handedness index
QHP	quantification of hand preference

1 INTRODUCTION

Right-handedness is a universal trait of the human species (Perelle and Ehrman, 1994; Porac and Coren, 1981). Cross-cultural studies, including data from non-Westernized societies, clearly show that a majority of individuals prefer to use their right hand for several manual activities such as writing, drawing, and throwing (Marchant et al., 1995; Raymond and Pontier, 2004). Archaeological evidence indicates that right-handedness can be traced back at least 2 million years, suggesting that it was an early adaptation among hominids and therefore likely had some adaptive value (Uomini, 2009). When, in evolutionary time, population-level right-handedness (or any population-level handedness) emerged in more distantly related primate species remains a topic of considerable theoretical and empirical debate (Cashmore et al., 2008; Corballis et al., 2012; Crow, 2004; Fagot and Vauclair, 1991; Forrester et al., 2013; Hopkins, 2006; MacNeilage et al., 2009; Marchant and McGrew, 1991; McGrew and Marchant, 1993, 1996; Rogers and Andrew, 2002; Vallortigara and Bisazza, 2002; Warren, 1980; Wiper, 2017).

As a means of determining what evolutionary factors may have contributed to the emergence of right-handedness, there have been a number of comparative studies of hand preference with nonhuman primates and, to date, the interpretation of the findings is difficult and conflicting. Several recent papers summarizing the evidence of hand preferences in nonhuman primates have shown that some species show population-level left- or right-handedness, while other species fail to show a consistent bias in one direction or another (Fagot and Vauclair, 1991; Hopkins, 2006; Marchant and McGrew, 1991; McGrew and Marchant, 1996; Warren, 1980). It is also clear that hand preferences in nonhuman primates are influenced by the type of task used to assess hand use, and this has been hypothesized as being one possible explanation for the within-species discrepancies in findings (Fagot and Vauclair, 1991). Other factors thought to influence hand preferences within and between species are sample size, age, sex, and the rearing history of the animals (Hook-Costigan and Rogers, 1997; Hopkins, 2013c; Hopkins and Cantalupo, 2005; MacNeilage et al., 1987; Marchant and McGrew, 1991). Indeed, even in instances in which the same task has been used to measure handedness in different species, no clear results have emerged that directly supports any specific theory. For instance, at least 20 different species representing ~30 million years of primate evolution have been tested on the "tube" task, a measure of hand use that requires subjects to engage in coordinated bimanual actions to extract food from a small cylinder or a pipe (see Fig. 1)

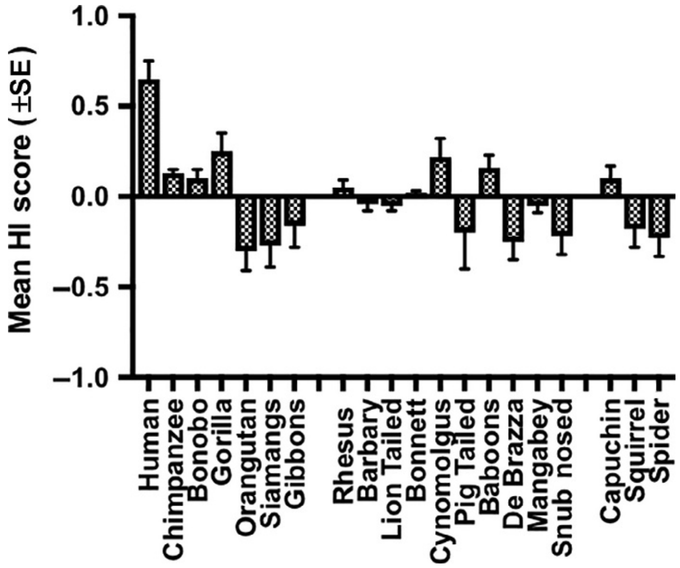

FIG. 1

Mean handedness indexes (HI) scores ± standard error in each species.

(Bennett et al., 2008; Chapelain and Hogervorst, 2009; Fan et al., 2017; Hopkins et al., 2011; Llorente et al., 2009, 2010; Maille et al., 2013b; Mangalam et al., 2015; Meguerditchian et al., 2012, 2013; Meunier and Vauclair, 2007; Morino et al., 2017; Nelson et al., 2015; Salmi et al., 2016; Spinozzi et al., 1998; Zhao et al., 2010, 2012). Measures of coordinated bimanual actions, such as the "tube" task, are particularly sensitive measures of hand preference because the hands have to be used in a coordinated manner, with one hand assuming the subordinate actions of the holding the device, while the opposite hand performs the skilled action (which is the one coded as dominant). Shown in Fig. 1 are the mean handedness indices (HIs) for each species. In this case, HI scores were computed following the formula (#R − #L)/(#L + #R), where L and R reflected the number of responses by the left and right hand. HI scores range from −1.0 to 1.0 and reflect the direction and strength of hand preference on a continuous scale of measurement. In Fig. 1, positive HI scores reflect right-hand biases and negative values reflect left-hand biases in hand use. As can be seen, some species exhibit a population-level bias and some do not. Additionally, of those species that show a significant bias, some prefer the left hand and others prefer the right hand. The lack of consistent results between species has been interpreted by some as evidence that the expression and potential mechanisms that underlie nonhuman and human primate handedness are fundamentally different (Cashmore et al., 2008; Crow, 1998; Warren, 1980; Williams et al., 2006).

Besides preferring their right hand, most humans also perform simple and complex motor actions better with their preferred compared to nonpreferred hand. In light of the fact that most individuals prefer to use their right hand, not surprisingly, all things being equal, the right hand performs better than the left on tasks that assess motor skill and strength; however, and critically, the degree of and pattern of asymmetry observed in manual skill performance are fundamentally different from hand preference data (Annett, 2002; Elliott and Roy, 1996; Kimura, 1993). For instance, on measures like the Annett Pegboard task, the distribution of asymmetries in motor skill is normally distributed but shifted rightward and away from a hypothetical value of zero. In contrast, the distribution for HI scores based on self-reported measures of hand use for different actions assumes a J-shaped distribution. That is, many subjects will report using their right hand for all actions (100% right-hand use) with the remaining, smaller proportion of individuals reporting percentages in right-hand use less than 100%. Additionally, in many studies that have examined correlations between self-reported handedness and intermanual differences in motor skill, the associations are far from perfect (Brown et al., 2004; Bryden et al., 2016; Corey et al., 2001; Dellatos et al., 2003; Doyen et al., 2008; Nelson et al., 2017; Peters and Ivanoff, 1999; Steenhuis and Bryden, 1999; Tapley and Bryden, 1985). Thus, being strongly right- or left-handed as defined from self-report does not necessarily predict that the same individual will show larger or smaller differences in intermanual skill (i.e., how well the right or left hand performs on a specific task). Further, intermanual differences in motor skill have sometimes been reported to be mediated by hand preference but not in an entirely dissociative manner. For example, Gonzalez et al. (2006) examined hand use when grasping for large and small objects in sample of right- and left-handed individuals. Among right-handed individuals, a significantly higher proportion of individuals used a precision grip when grasping small subjects with their right compared to their left hand. In contrast, among left-handed participants, approximately 50% of subjects produced more precision grasping responses by the right compared to the left hand, while the remaining 50% showed the opposite pattern. Thus, the relation between grasping morphology and preferred hand use was mediated by the subjects' preferred hand.

As noted earlier, the majority of studies on manual specialization in nonhuman primates have focused on measures of hand preference rather than skill or performance measures. This is unfortunate for several reasons. First, it has been well documented that some measures of hand use are strongly influenced by situational factors (see Lehman, 1993). Thus, situational noise (e.g., the position of the food relative to subject midline) can be introduced in quantifying hand preferences, particularly when measured in unstructured circumstances. A similar argument has been made with respect to the measurement of hand preference and hand skill in humans with some suggesting that social and cultural factors (e.g., taboos against the use of the left hand, or formal schooling) likely mask inherent differences in hemispheric specialization for motor skill (e.g., Geuze et al., 2012). Second, the underlying assumption in the measurement of hand use is that preferences underlie the inherent functional specialization of the contralateral hemisphere, but this is rarely quantified and there is at least some evidence that this is not the case for all tasks (see Chapter "Speech lateralization and motor control" by Hodgson and Hudson, this volume). Third, in a number of studies of behavioral lateralization in more distantly related species, the outcome measures often directly compare performance between bilateral traits. For instance, studies in many vertebrate species focus on performance differences between sensory systems, like the eyes, as a means of assessing which hemisphere is specialized for this function (reviewed in Rogers et al., 2013). With respect to motor manual skill, this would suggest that more direct measures comparing the left or right hands on specific motor tasks would more directly assess the specialization of each hemisphere. Finally, in humans, the evidence of a genetic basis for population-level handedness is not terribly robust based on genome-wide association studies (Armour et al., 2014; Brandler and Paracchini, 2014; Brandler et al., 2013; Medland et al., 2009). Indeed, the more compelling evidence that genes influence manual specialization come from studies in which manual skill was assessed rather than self-reported hand preference (e.g., Brandler et al., 2013). This suggests that nongenetic factors such as situational factors, social learning, culture, reward-based learning, or other experiential factors may have a stronger influence on hand preferences, while intermanual differences in hand skill may be more strongly influenced by biological mechanisms and therefore more likely to have been under evolutionary selection.

To this end, in this chapter, I review the existing literature on intermanual differences in performance on a variety of motor tasks that have been used in nonhuman primates. Basically, there have been two approaches to characterizing asymmetries in motor skill in nonhuman primates including (1) measuring grip morphology in relation to hand use and (2) direct comparison in performance between the left and right hands on different motor tasks. Existing data from nonhuman primates for each of these approaches are summarized and followed by suggestions for future research.

2 GRASPING MORPHOLOGY AND HAND USE

Several studies have considered hand use in relation to grip morphology. Specifically, what distinguishes primates from other mammals is an opposable thumb and many have hypothesized that this played a critical role in the evolution of increasingly sophisticated manipulatory propensities in primate species (Fragaszy and Crast, 2012; Marzke, 1997; Napier, 1980; Neufuss et al., 2017; Pouydebat et al., 2008, 2009). For example, Napier (1980) described the opposability index, which quantifies the variation in length of the thumb relative to the index finger and indirectly indicates the degree of prehensile grasping skills of primates (see also Almecija et al., 2015). Many have hypothesized that the evolution of grasping morphology, and in particular prehensile grasping, was an important preadaptation that led to changes in aspects of brain size and complexity as well as more sophisticated motor functions, such as language and speech (Gonzalez and Goodale, 2009; Heldstab et al., 2016).

With respect to hand preference, nonhuman primates show considerable individual differences in grasping morphology and, within this context, several investigators have quantified between-species and intermanual differences in grasping techniques (Boesch, 1991; Christel, 1994; Christel et al., 1998; Costello and Fragaszy, 1988; Fragaszy, 1998; Hopkins et al., 2002, 2005b; Pouydebat et al., 2008, 2009, 2011; Rigamonti et al., 1998; Tonooka and Matsuzawa, 1995; Welles, 1976). In these studies, hand use and grip morphology are typically characterized during unimanual grasping of small food items. Different ethograms have been used to characterize the digit use during different grasping responses but, for the sake of simplicity, I have characterized them fairly broadly between power (use of all fingers engaged in simultaneously movements during grasping), precision (use of the thumb and index finger to grasp an object), and imprecise (use of thumb with other fingers or the use of fingers other than the thumb) grasping responses. A summary of the published data on hand use and grip morphology is provided in Table 1. At the most general level, Costello and Fragaszy (1988) examined hand use and grasping morphology in squirrel and capuchin monkeys. In this study, they distinguished broadly between power and precision grips and found that capuchins engaged in significantly more precision grips compared to squirrel monkeys. Indeed, squirrel monkeys were rarely observed to use a precision grasp and almost exclusively used a power grip. They also noted that the ratio of right- to left-handed use was greater in the capuchins compared to squirrel monkeys, which they implied might be attributable to their increased use of prehensile grips.

Table 1 Grasping Morphology and Hand Use in Great Apes and Monkeys

Species (Common Name)	#L	#A	#R	HI (SE)
Squirrel (Costello and Fragaszy, 1988)				
Precision	4	0	2	DNP
Power	—	—	—	DNP
Total	4	0	2	DNP
Capuchin (Costello and Fragaszy, 1988)				
Precision	2	0	4	DNP
Power	—	—	—	DNP
Total	2	1	5	DNP
Capuchin (Spinozzi et al., 2004)				
Precision	6	4	6	−0.095 (0.198)
Power	7	1	6	−0.100 (0.193)
Overall	9	3	8	−0.057 (0.176)
Orangutan (Meguerditchian et al., 2015)				
Precision	7	7	14	0.137 (0.104)
Imprecise	7	6	15	0.182 (0.110)
Total	12	17	20	0.073 (0.057)
Orangutan (Christel, 1994)				
Precision	3	2	2	−0.093 (0.141)
Imprecise	4	0	4	−0.275 (0.327)
Total	4	1	3	−0.003 (0.131)

Table 1 Grasping Morphology and Hand Use in Great Apes and Monkeys—cont'd

Species (Common Name)	#L	#A	#R	HI (SE)
Gorilla (Pouydebat et al., 2010)				
Precision	0	0	3	0.800 (0.040)
Power	0	0	3	0.867 (0.037)
Gorilla (Meguerditchian et al., 2015)				
Precision	12	15	27	0.104 (0.075)
Imprecise	17	7	14	−0.002 (0.094)
Total	10	28	28	0.140 (0.050)[a]
Gorilla (Christel, 1994)				
Precision	2	1	3	−0.057 (0.194)
Imprecise	1	1	4	0.397 (0.231)
Total	1	1	4	0.331 (0.178)
Chimpanzee (Jones-Engel and Bard, 1996)				
Precision	3	9	1	DNP
Power	4	8	0	DNP
Total	5	4	5	DNP
Chimpanzee (Meguerditchian et al., 2015)				
Precision	106	61	153	0.082 (0.031)[a]
Imprecise	112	71	125	0.017 (0.033)
Total	96	129	129	0.044 (0.021)[a]
Chimpanzee (Llorente et al., 2009)				
Precision	0	4	9	0.611 (0.067)[a]
Imprecise	3	3	4	0.222 (0.140)
Total	3	2	9	0.221 (0.133)
Chimpanzee (Tonooka and Matsuzawa, 1995)				
Precision	19	28	22	0.010 (0.054)
Imprecise	28	16	13	−0.224 (0.076)[a]
Total	23	28	22	−0.034 (0.042)
Chimpanzee (Pouydebat et al., 2011)				
Precision	1	9	8	0.149 (0.047)[a]
Imprecise	6	5	7	0.029 (0.075)
Total	0	10	8	0.129 (0.039)[a]
Bonobo (Meguerditchian et al., 2015)				
Precision	11	17	18	0.055 (0.081)
Imprecise	16	10	11	−0.107 (0.096)
Total	23	33	39	0.058 (0.041)

References for the data are presented in the table.
DNP, *data not reported. Values in* parentheses *are standard errors*
[a] *Indicates a significant left–right difference at* $P < 0.05$.

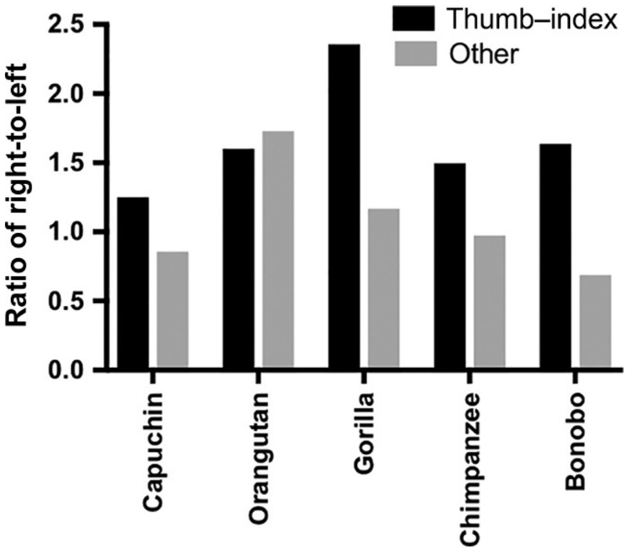

FIG. 2

Ratio of right-to-left handed subjects for precision and nonprecision grasping in different primate species.

When considering hand use in relation to grip type or digit use, within a species, the results, at least in great apes, suggest increased preferential use of the right hand for thumb–index precision grasping (see Table 1 and Fig. 2). In this summary of the existing data, the number of left-, ambiguously, and right-handed individuals is presented as a function of grip type. Note that the data points are not necessarily independent of each other within a grip type because some individuals exhibit variability in their grasping morphology. In other words, there are individual subjects that produced more than one type of grip when reaching for the same food items within and between test sessions. When between-species comparisons are made, the ratio of right-to-left handed subjects is greater when hand preferences are classified on the basis of their frequencies in left- and right-hand precision grips compared to nonprecision grasping responses in bonobos, chimpanzees, and gorillas (Meguerditchian et al., 2015; see Fig. 2). Indeed, in chimpanzees, three separate studies reported a similar observation of increased use of the right hand for precision compared to imprecise grips, suggesting that these observations are consistent and repeatable across laboratories and samples (see Table 1). Spinozzi et al. (2004) also examined hand use in relation to grip morphology in capuchin monkeys. These authors found considerable individual variation in grip morphology but failed to find increased left- or right-hand use for precision compared to imprecise grasping. Finally, the aye-aye is a prosimian species with a very unique hand feature that includes an extenuated third digit that is used for extractive foraging. Feistner et al. (1994) measured hand use for food holding, wood tapping, and digit use when feeding in 11 aye-ayes. With respect to digit use, though no overall bias was found for digit use, 8 of the 11 individuals preferred to forage with the middle digit of their left hand, a finding consistent with preferred hand preferences for simple reaching reported in other prosimian species (Lehman, 1993; Ward et al., 1998).

In summary, all four great ape species appear to exhibit increased preferential use of the right hand when producing precision compared to nonprecision grasping responses. Evidence of performance asymmetries in grasping skill in capuchin monkeys did not show this same pattern of results, albeit these data are from a single study. The aye-aye did not show consistent biases in hand use but did exhibit a trend toward increased left-hand use.

3 INTERMANUAL DIFFERENCES IN MOTOR SKILL OR PERFORMANCE

Less prevalent in the literature are studies that have attempted to directly contrast the left and right hand on performance measures that assess motor skill in some manner. In these approaches, rather than solely assess hand preference for tasks with different motor demands, a finite number of observations in hand use are assessed for the left and right hands and they are subsequently compared to determine whether intermanual differences in performance are evident. A summary of these published studies and the type of measure used to evaluate hand skill is shown in Table 3.

3.1 GRASPING PERFORMANCE

In terms of errors made when grasping small food items, Hopkins et al. (2002) tested 132 chimpanzees on the number of errors made when grasping small food items by the left and right hands and found a right-hand advantage. In a follow-up study, in which we controlled for the type of grip used by the chimpanzees when picking up the food item with the left and right hands, Hopkins and Russell (2004) also found a right-hand advantage. More recently, our laboratory has also collected grasping error data in smaller samples of bonobos, gorillas, and orangutans. The percentage of trials (out of 20 possible) in which the subjects made a grasping error (failed to successfully grasp the food item) for each hand and species is shown in Table 3. When considering the data from all great apes, a significant right-hand bias is found with all four species, making fewer errors when grasping food items with the right compared to the left hand. When analyzing the data separately for each species, significant differences were only found in chimpanzees and gorillas.

As a means of further evaluating the influence of hand preference on grasping skill, we performed some additional analyses on our existing data from chimpanzees. Specifically, we had grasping error and hand preference data for simple reaching in 297 chimpanzees (Hopkins et al., 2005b). Within the sample, there were 84 left-, 101 ambiguously, and 112 right-handed individuals based on z-scores computed on the frequency of left- and right-hand reaching responses. We computed HI scores for the

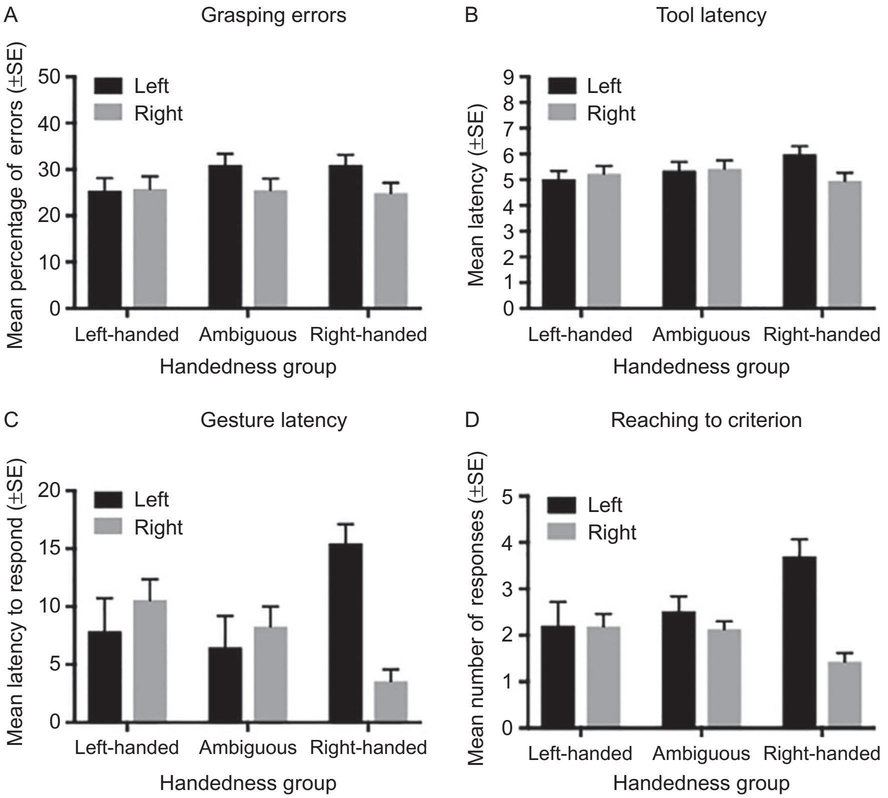

FIG. 3

(A) Mean percentage of errors (±SE) by the left and right hands in grasping small food items in left-, ambiguously, and right-handed chimpanzees. (B) Mean dipping latency (±SE) by the left and right hands in a tool use task in left-, ambiguously, and right-handed chimpanzees. (C) Mean latency (±SE) to elicit a ipsilateral manual gesture by the left and right hands in left-, ambiguously, and right-handed chimpanzees. (D) Mean number of reaching responses (±SE) made by the left and right hands in left-, ambiguously, and right-handed chimpanzees.

grasping error data and compared them using an analysis of variance with sex and hand preference classification serving as between-group factors. A significant main effect for hand preference classification was found $F(1, 278) = 4.70$, $P < 0.02$. The mean number of errors for the left and right hands among left-, ambiguously, and right-handed chimpanzees is shown in Fig. 3A. Within left- and ambiguously handed chimpanzees, no significant differences in grasping errors between the left and right hands were found; however, for right-handed chimpanzees, fewer grasping errors were made for the right compared to left hand. Thus, intermanual differences in grasping errors were more pronounced in right-handed chimpanzees.

Christel (1994) measured hand use and grasping morphology in a variety of different primate species but did not report specific patterns of hand use in relation to different types of grips. In one study, Christel and Fragaszy (2000) measured the regularity in reach-to-grasp movements in five capuchin monkeys for three different tasks including grasping a food item from (1) a shallow well, (2) a flat board, and (3) a grooved board. The five monkeys generally preferred the left hand for grasping food items from the well and flat surface, but three of the five switched to the right hand for grasping food items from a grooved board. In terms of the regularity in reach-to-grasp movements, the right hand performed significantly better than the left, particularly for the grooved board task, while no intermanual differences were evident for the well and flat surface measures. In another study, Christel et al. (1998) similarly measured regularity in reach-to-grasp movements in three bonobos when picking up small food items. All three bonobos showed a right-hand bias for the reach-to-grasp regularity movements compared to the left hand.

To summarize, when directly comparing grasping performance between the left and right hands, representatives of all four great ape species tested to date show a right-hand performance advantage. Evidence of performance differences in capuchin monkeys was less clear, particularly across the different tasks. For chimpanzees, performance asymmetries in grasping skill were mediated by their hand preferences for simple reaching. Intermanual differences in grasping skill were more pronounced in right- compared to ambiguously and left-handed apes.

3.2 TOOL USE

Save humans, chimpanzees are the most sophisticated users of tools in the animal kingdom. Studies have shown that chimpanzees exhibit a wide range of different forms of tool use across a variety of habitats ranging from east to west Africa (Whiten et al., 2001). As noted earlier, there have been some studies that have quantified hand preference for different types of tool use in various chimpanzee communities (reviewed in Hopkins, 2013a). However, there is only one study that has examined asymmetries in hand skill for tool use in wild chimpanzees. Sanz et al. (2016) measured hand preference and latency to successfully insert a stick into a termite mound in 89 chimpanzees living in the Goualougo Triangle. With respect to hand preference, Sanz et al. found a borderline significant sex difference with a higher proportion of females showing a left-hand preference compared to males. For latency in dipping responses, Sanz et al. found that right-handed chimpanzees, on average, showed significantly faster dipping responses than left-handed individuals and this was consistent across both males and females. A minority of chimpanzees ($n = 22$) used both the left and right hands for the termite fishing observed by Sanz et al. Within this subsample of chimpanzees, the authors did find a borderline significant effect of hand preference on intermanual differences in dipping latency. Left- and right-handed chimpanzees had significantly faster dipping responses for their dominant compared to nondominant hands.

In captivity, there have been two related studies on performance asymmetries in chimpanzee tool use. In one study, Hopkins et al. (2009) used a device that was designed to simulate termite fishing, in which the chimpanzees had to insert a small stick (e.g., a lollipop stick) into a hole to extract food. Hopkins et al. (2009) measured hand preference and dipping latencies in 251 captive chimpanzees and found (1) no evidence of population-level hand preferences for the task, (2) no population-level bias in intermanual differences in dipping latency, and (3) no significant hand preference effects on mean latency in dipping responses. Similar to Sanz et al. (2016) among chimpanzees that exhibited dipping responses by both hands, Hopkins et al. (2009) found that right- and left-handed chimpanzees performed significantly better with their dominant compared to nondominant hand. In a follow-up study, quantitative genetic analyses showed that both hand preferences and mean dipping latency were significantly heritable in the chimpanzees (Hopkins et al., 2015).

One limitation of the previous studies by both Sanz et al. and Hopkins et al. is that, because the focus was on quantifying hand preferences, the number of dipping responses produced by the left and right hands was not balanced or equal across subjects. Thus, as a follow-up study, Hopkins et al. (2018) have retested 187 chimpanzees on the same simulated termite-fishing task but positioned the device in the subject's home cage in such a manner to encourage the use of either the left or right hand. Instead of focusing on hand preference, latency for 30 dipping responses was recorded for both the left and right hands in each subject, which allowed us to compute a measure of asymmetry in dipping skill based on an equal number of responses for each hand. The findings are shown in Table 2 and Fig. 3B. In this study, we found an overall significant right-hand bias in dipping latency $t(186)=2.114$, $P<0.03$. Further, we compared the left- and right-hand latency scores in this task between left-, ambiguously, and right-handed subjects from the original Hopkins et al. (2009) paper. This analysis revealed a significant two-way interaction between hand

Table 2 Performance Asymmetries for Different Measures of Motor Skill in Nonhuman Primates

			Significantly
	Left	**Right**	**Different?**
Grasping			
Chimpanzee ($n=194$) (Hopkins and Russell, 2004; Hopkins et al., 2002)	29.10 (1.70)	25.00 (1.40)	Yes
Bonobo ($n=31$) (W.D. Hopkins, E. Lonsdorf, S. Ross, and A. Bania, unpublished data)	34.40 (4.02)	27.41 (3.60)	No
Gorilla ($n=40$) (Hopkins et al., unpublished data)	36.52 (3.70)	28.30 (3.20)	Yes
Orangutan ($n=14$) (Hopkins et al., unpublished data)	51.43 (6.20)	40.00 (5.40)	No
Overall ($n=279$)	37.80 (2.10)	30.10 (1.80)	Yes

Table 2 Performance Asymmetries for Different Measures of Motor Skill in Nonhuman Primates—cont'd

	Significantly		
	Left	**Right**	**Different?**
Capuchins (*n* = 8) (Spinozzi et al., 2004) Precision	230 ms	415 ms	Yes
Capuchins (*n* = 11) (Spinozzi et al., 2004) Power	512 ms	326 ms	No
Capuchins (*n* = 20) (Spinozzi et al., 2004) Total	412 ms	377 ms	No
Bonobo (*n* = 3) (Christel et al., 1998) Precision	873 ms	667 ms	No
Food retrieval			
Capuchins (Spinozzi et al., 2007)			
Left (*n* = 5)	997 ms	1964 ms	No
Right (*n* = 4)	1315 ms	940 ms	No
Ambiguous (*n* = 5)	1104 ms	864 ms	No
Overall (*n* = 20)	1110 ms	1203 ms	No
Bonnet monkeys (Mangalam et al., 2015)			
Left (*n* = 6)	2.83 s	3.79 s	No
Right (*n* = 4)	3.85 s	2.55 s	No
Overall (*n* = 10)	3.23 s	3.30 s	No
Brinkman board			
Cynomolgus monkeys (*n* = 9) (Chatagny et al., 2013)	27.00	27.68	No
Pig-tailed macaque (Rigamonti et al., 1998)			
Right (*n* = 6)	327.50 (50.14)	345.83 (48.43)	No
Left (*n* = 3)	195.00 (17.55)	350.00 (35.12)	DNA
Overall (*n* = 9)	283.33 (39.51)	347.22 (32.87)	No
Bent wire task			
Chimpanzee (Lacreuse et al., 2014)			
Right (*n* = 29)	3.22 (0.266)	2.87 (0.218)	No
Ambidextrous (*n* = 19)	3.42 (0.335)	3.26 (0.276)	No
Left (*n* = 9)	3.09 (0.456)	3.26 (0.375)	No
Overall (*n* = 57)	3.24 (0.208)	3.13 (0.171)	No
Rhesus monkeys			
Overall (*n* = 10) (Lacreuse and Herndon, 2003; Lacreuse et al., 2005)	DNP	DNP	Yes
Right (*n* = 9) (Lacreuse et al., 2005, Lacreuse and Herndon, 2003)	4.48 (0.656)	4.07 (0.580)	No
Ambiguous (*n* = 2) (Lacreuse and Herndon, 2003; Lacreuse et al., 2005)	4.11 (0.401)	5.29 (0.373)	No

Continued

Table 2 Performance Asymmetries for Different Measures of Motor Skill in Nonhuman Primates—cont'd

	Significantly		
	Left	**Right**	**Different?**
Left (*n* = 17) (Lacreuse and Herndon, 2003; Lacreuse et al., 2005)	5.94 (0.755)	7.46 (1.952)	No
Overall (*n* = 28) (Lacreuse and Herndon, 2003; Lacreuse et al., 2005)	5.31 (0.484)	6.18 (1.141)	No
Tool use probing			
Chimpanzee (Sanz et al., 2016)			
Right (*n* = 46)	3.46 (0.22)	3.31 (0.25)	
Ambiguous (*n* = 4)	DNA	DNA	
Left (*n* = 39)	3.50 (0.20)	3.53 (0.24)	
Overall	3.48 (0.15)	3.37 (0.15)	
Chimpanzee (Hopkins et al., 2017b)			
Right (*n* = 80)	9.21 (0.640)	6.34 (0.649)	Yes
Ambiguous (*n* = 76)	6.04 (0.573)	6.47 (0.582)	No
Left (*n* = 80)	7.03 (0.554)	9.78 (0.562)	Yes
Overall (*n* = 236)	7.42 (0.341)	7.53 (0.346)	No
Chimpanzee (Hopkins et al., 2018)			
Right (*n* = 71)	6.00 (0.297)	4.96 (0.292)	Yes
Ambiguous (*n* = 53)	5.36 (0.318)	5.40 (0.312)	No
Left (*n* = 63)	5.07 (0.296)	5.33 (0.291)	No
Overall (*n* = 187)	5.41 (0.164)	5.14 (0.159)	Yes

DNA, *did not analyze because too few subjects;* DNP, *data not reported. Values in* parentheses *are standard errors.*

preference for tool use and intermanual differences in dipping latency $F(2, 175) = 6.636$, $P < 0.003$. Post hoc analysis indicated no significant difference in latency between the left and right hands for left- and ambiguously handed chimpanzees; however, right-handed chimpanzees performed significantly faster with their right hand compared to their left hand (see Fig. 3B).

3.3 BRINKMAN BOARD TASK

Cynomolgus and pig-tailed monkeys have been tested on different versions of the Brinkman Board (BB) task, a device designed to measure motor skill. In the BB task, small food items (pellets) are placed in shallow wells in a board and the subjects typically use a precision grip to grasp the pellets. Rigamonti et al. (1998) tested nine monkeys (pig-tailed macaques) on the BB task and recorded hand use and the latency in successfully obtaining each food item. Note that the monkeys had a free choice on which hand to use. Thus, the number of attempted grasping responses was not controlled for within each subject. Notwithstanding, Rigamonti et al. found that six monkeys preferred the right hand and three preferred the left for the BB task. When comparing the latencies between hands, no significant differences were found though the left hand appeared to successfully grasp the food items more quickly than the right, even among subjects that preferred to use their right hand. Chatagny et al. (2013) used a modified version of the BB task and independently measured both hand preference and intermanual differences in grasping skill in a sample of nine cynomolgus monkeys. These authors found no significant differences in the number of errors made in grasping the food items or in the latency to retrieve the foods between the left and right hands. Two monkeys retrieved the food significantly faster with their left hand, two with their right hand, and three showed no significant differences in latency.

3.4 BENT WIRE OR LIFESAVER TASK

The bent wire (BW) task was originally designed to assess problem-solving abilities in different primate species (Davis et al., 1957) but more recently has been used to measure motor skill, particularly in the context of quantifying sex-dependent and age-related changes in motor function (e.g., Mahovetz and Stoinski, 2015). In the BW task, a wire that has been bent into different shapes, such as an “S,” is presented to the subject. A life saver (a small, round candy with a hole in the center) is threaded onto the wire and placed at the base of one end. The device is then presented to the subject and they must manipulate the life saver off the wire to obtain the reward. Latency to successful removal of the lifesaver and the number of errors (i.e., drops of the food) are the most common outcome measures recorded by the experimenters.

In rhesus monkeys, Lacreuse and Herndon (2003) measured performance on three versions (i.e., different shaped wires) of the BW task in 10 female monkeys. Though the mean latency data for the left and right hands were not presented in this chapter, these authors did report that overall the monkeys performed significantly faster with their left compared to right hand. Lacreuse and Herndon (2003) also reported that among the 10 monkeys tested during a free choice task, 7 preferred to perform the BW task with the left hand and 3 preferred their right. Interestingly, five of the seven that preferred the left hand performed better with their left hand, while two of the three monkeys that preferred their right hand performed better with their left hand. In a second study, Lacreuse et al. (2005) tested 28 monkeys on three versions of the BW task and reported no overall significant intermanual differences in latency. Within this sample, 17 monkeys preferred to perform the task with the left hand, 9 with the right hand, and 2 had no hand preference. When combining the data between studies, 24 monkeys preferred their left hand and 12 preferred the right and 2 had no preference on the BW task. A binomial z-score shows the number of subjects that prefer the left compared to right hand is significantly higher ($z = 2.00$, $P < 0.05$). On a task not unlike the BW task, Moore et al. (2010) tested 16 rhesus monkeys for their hand use and latency to retrieve foods placed on an “L” shape wire. Though no individual data were reported in this chapter, the authors reported that all 16 monkeys preferred their left hand for this task. Furthermore, the average latency to retrieve the food, particularly early in training, was found to be significantly higher for the dominant hand (presumed to be the left) compared to nondominant hand.

In our laboratory, we have tested 57 chimpanzees on 3 different versions of the BW task using methods not unlike those employed by Lacreuse et al. (2014). In the chimpanzees, there was no significant intermanual differences in the BW task (Lacreuse et al., 2014) (see Table 2). Further, when intermanual differences were compared in right-, ambiguously, or left-handed chimpanzees (based on their hand use for tool use), no significant intermanual differences were found within any hand preference group. Thus, unlike rhesus monkeys, chimpanzees did not perform significantly better with their preferred compared to nonpreferred hand nor were there any overall significant intermanual differences in performance.

3.5 JOYSTICK MANIPULATION

Beginning in the late 1980s, automated test systems were developed for assessing cognitive functions and motor skills in different primate species. One such automated system uses a joystick that controls the movements of cursor projected on a computer screen (Hopkins, 1991; Rumbaugh et al., 1989; Washburn and Rumbaugh, 1992). Isomorphic movements of the cursor are controlled by the subjects manipulating the joystick and most develop a consistent hand preference. Though the number of subjects tested on these systems has been relatively small, there are some reports of data on hand use. Hopkins et al. (1989) reported that two rhesus monkeys and three chimpanzees all preferred their right hand for manipulation of the joystick and, moreover, we found that all five subjects performed a psychomotor task better with their right compared to left hand. In a follow-up study, Hopkins et al. (1992) examined the hand preference and acquisition of two psychomotor tasks (SIDE and CHASE) involving the manipulation of a joystick in a sample of 35 rhesus monkeys (all males except one female). There were two phases to the study. In Phase I, hand preference in joystick use was quantified in all 35 monkeys and 21 were found to prefer the right hand and 14 the left hand for manipulating the joystick on each trial. In Phase II, the acquisition in learning the two psychomotor tasks was compared in 18 monkeys that were trained using the exact same training criteria. Hopkins et al. then compared the acquisition data between those that preferred to use their right or left hand. Hopkins et al. found that right-handed individuals reached the asymptotic training criteria performance on both the SIDE and CHASE task in significantly fewer trials than left-handed individuals. Using a slightly different method, Andrews and Rosenblum (2001) similarly measured the number of trials needed to reach criterion on the joystick manipulation task in eight bonnet macaques living in social groups. Microchips were placed in the left and right wrists of the monkeys, and when they went to manipulate the joystick with one hand or the other, a computer would record the hand used and their performance on that specific trial. Across increasing levels of visuomotor difficulty, a right-hand preference for joystick manipulation emerged in six monkeys and a left-hand bias in two monkeys. When the joystick manipulation hand preference data from the macaques in the Hopkins et al. (1992) and Andrews and Rosenblum (2001) study are combined, a significantly higher proportion of right- compared to left-handed monkeys is found ($z = 2.25$, $P < 0.05$).

Fagot and Vauclair (1993) trained eight baboons on a similar type of joystick testing apparatus, though their system used a digital rather than analog interface between the movements of the joystick and the cursor on the screen. Fagot and Vauclair (1993) initially trained four monkeys on the device with their left hand and four with their right hand. After reaching the training criteria with the initial hand, transfer of learning was tested for the opposite hand in each group. For the initial training, the number of trials needed to reach criterion did not differ significantly between the baboons initially trained on the right (mean = 1014.5, SD = 261.5) compared to left (mean = 1099.5, SD = 298.5) hands. When testing for transfer of learning, baboons tested on their right hand (after being trained on the left) needed fewer trials to reach criterion (mean = 310.2, SD = 84) compared to individuals tested on left hand (mean = 633.2, SD = 173.4) (after initially being trained with the right), though the differences were not significant. Fagot and Vauclair (1993) also tested for differences in latency and found no significant differences but did find that the baboons used a shorter path between the cursor and target in the computer screen when performing with their left (mean = 431.5, SD = 40.1) compared to right hand (mean = 623.3, SD = 107.4).

3.6 BIMANUAL FEEDING

Two studies have quantified latencies when monkeys were engaged in bimanual feeding. In bimanual feeding tasks, typically one hand assumes the subordinate role by holding the object, while the opposite hand is used for the manipulation. Spinozzi et al. (2007) measured the average latency for the insertion and extraction of food in the "tube" task in a sample of eight right-handed, seven left-handed, and five ambiguously handed capuchin monkeys. They reported no differences in the mean latencies between the different handedness groups, but they found a trend for subjects to extract the food more quickly with their preferred hand compared to their nonpreferred hand. Within the five ambiguously handed monkeys, the mean latency was shorter for the right compared to left hands. Mangalam et al. (2015) also measured latency in performance for solving a bimanual task in a sample of six left-handed and four right-handed bonnet macaques. Though no significant overall differences in latency were found between the left and right hands, Mangalam et al. reported that the monkeys performed the task more quickly with their dominant compared to nondominant hand. In short, in both of these studies, latency in extracting food from inside the pipe in the "tube" task did not differ significantly between monkeys that preferred their right or left hand for the task.

3.7 QUANTIFYING HANDEDNESS PREFERENCE (THE QHP TASK)

Finally, in an attempt to characterize strength in laterality in relation to hand use, several studies have examined the degree to which monkeys and apes will prefer one hand or another in producing motor actions directed toward objects in their ipsilateral or contralateral hemispace. As noted earlier, it has been suggested that hand preferences are subject to situational or positional factors, but whether the sensitivity to situational factors extends to all measures of hand use has remained relatively unexplored. The studies in nonhuman primates have been developed to model the quantification of hand preference (QHP) task originally developed by Bishop et al. (1996) in human subjects. In the QHP, hand preference is quantified in relation to the position of objects. In this task, subjects grasp objects placed central to and lateral of their midline. Of particular interest in the QHP task is the extent to which the left or right hand will cross the midline to grasp an object in their contralateral space, which presumably reflects the inherent strength of biases in cerebral lateralization.

Adapting the QHP for testing in 42 baboons, Meunier et al. (2011) sequentially placed food items on a flat board at seven different spatial locations that varied from extreme left (LL), moderately left (ML), central (C), moderately right (MR), and extreme right (RR) with respect to the subject's egocentric reference space. During each trial, the authors recorded the hand used to grasp the food item. To compare hand use across the different spatial locations, an HI score was computed at each location. To evaluate hand preference, *z*-scores based on the frequency of right- and left-hand use were derived for the reaching responses at the central location. First, when considering handedness when reaching for food items in the central location, there were 12, 20, and 10 right-, ambiguously, and left-handed baboons, respectively. Additionally, when considering the HI scores between the different locations, the baboons showed a bimodal distribution in hand use such that displacement of the food to the left or right hemispace induced a significant ipsilateral hand preference (see Table 3).

Chapelain et al. (2012) also used the QHP to assess hand use for grasping in 12 red-capped mangabeys and 11 Campbell monkeys. In this study, the authors placed items at 5 spatial locations and recorded their hand use to grasp the food item for 12 trials at each location. The mean HI scores at each position and for each species are shown in Table 3. One sample *t*-tests on the HI scores for the central responses showed a significant right-hand bias in the Campbell monkeys and no significant bias in the mangabeys. Further, as was the case in the baboons for grasping, the HI scores for the laterally placed food items were bimodally distributed based on ipsilateral hand use responses. Chapelain et al. also examined the HI scores at each of the five spatial locations as a function of the hand preference for their sample of monkeys. Left-handed monkeys showed significant left-hand biases for reaching across all five spatial locations, while right-handed monkeys showed right-hand biases in four of the five spatial locations, the exception being the extremely left position. Monkeys with no hand preference showed left-hand biases for the extremely left position and significant right-hand biases for the moderate and extreme right positions.

In another study with a smaller cohort of 12 baboons and 10 human infants between 14 and 20 months of age, Meunier et al. (2012) used the same QHP paradigm and measured hand use for both reaching and "pointing" (i.e., gesturing to an out of reach food) as a means of evaluating whether lateralization for communicative

Table 3 Summary of Results Using the QHP Task

	Egocentric Position of Stimulus							
	LLL	**LL**	**L**	**C**	**R**	**RR**	**RRR**	**Task**
Baboons (Meunier et al., 2011)	−0.82	−0.79	−0.64	0.06	0.77	0.90	0.86	Grasping
Mangabeys (Chapelain et al., 2012)	−0.64	−0.40		−0.10		0.19	0.19	Grasping
Campbell monkeys (Chapelain et al., 2012)	−0.32	−0.06		0.41		0.39	0.50	Grasping
Baboons (Bourjade et al., 2013)	−0.94	−0.61		−0.16		0.87	0.98	Grasping
Baboons (Bourjade et al., 2013)	−0.02	0.02		0.09		0.31	0.09	Pointing
Baboons (Meunier et al., 2012)	1	5		50		90	99	Grasping
Baboons (Meunier et al., 2012)	62	42		70		82	78	Pointing
Humans (Meunier et al., 2012)	10	22		65		95	96	Grasping
Humans (Meunier et al., 2012)	40	73		80		83	95	Pointing
Chimpanzees (Hopkins and Wesley, 2002)		49		67		87		Pointing

signals differs from manual grasping. As in the previous Meunier et al. (2012) paper, for grasping, the baboons showed a bimodal distribution in hand use depending on the location of the food. In contrast, for "pointing," the baboons were significantly more likely to use their right hand to gesture into their left hemisphere but not vice versa. It should be noted that previous studies in baboons have reported a significant population-level right-hand bias for a specific-typical manual gesture called hand slapping (Meguerditchian and Vauclair, 2006); thus, these results suggest that lateralization, and particularly the degree of right-handedness, is more robust in communication than for hand use in simple reaching actions. The pattern of results for the developing human infants was similar and did not differ from those reported in the adult baboons.

We know of no studies that have explicitly used the QHP paradigm with great apes. However, our laboratory has performed several studies in which we examined hand preference while attempting to control for positional factors. For instance, Hopkins and Wesley (2002) tested 127 chimpanzees for hand use in manual gestures on three trials with the experimenter positioned either centrally to the subject or on their extreme left or right side. The percentage of subjects that gestured with their right hand as a function of the experimenter being positioned to the left, center, or right of the subject were 35%, 65%, and 91%, respectively. Similarly, we performed an additional study in a sample of 123 chimpanzees in which we recorded the latency to elicit a manual gesture in response to a human offering a food when positioned to the subjects left or right at an angle of ~45 degrees. We recorded the latency between the initial presentation of the food and the production of a manual request gesture by the ipsilateral hand. No encouragement was displayed by the human experimenter and they simply waited until the subject produced a manual gesture with the ipsilateral hand. Each subject got two trials with the order of the testing for the right and left hand counterbalanced across subjects. When we compared the latency data for the left and right hands as a function of the chimpanzees preferred hand for manual gestures, we found a significant two-way interaction $F(2, 110)=10.884$, $P<0.001$. The intermanual differences to elicit ipsilateral or contralateral gestural responses were almost entirely explained by right-handed subjects. Chimpanzees that preferred to gesture with their left hand $t(22)=-0.860$, $P=0.399$, or were ambiguously handed $t(28)=-1.121$, $P=0.272$ did not show significant differences in latencies for the left and right hands. However, in right-handed chimpanzees $t(70)=6.375$, $P<0.001$, it took significantly longer to elicit a left-hand manual gesture when the experimenter was positioned to the subject's left side compared to eliciting a right-hand gesture when the experimenter was positioned to the subject's right side (see Fig. 3C).

In a similar vein, our laboratory has measured persistence in hand use for simple reaching in a sample of 178 chimpanzees. In this unpublished study, there were two test sessions, designated right and left, which were counterbalanced across subjects. During each session, single food items were sequentially placed in the subject's outdoor enclosure in a manner that required they locomote at least 3 m between reaching responses. On either the left or right test session, the observer recorded how many reaching responses were made before producing the designated "left"- or "right"-hand response. We then compared the number of trials needed to produce a left- and right-hand response between left- ($n=36$), ambiguously ($n=81$), and right-handed ($n=61$) chimpanzees based on their hand use for simple reaching. We found a significant two-way interaction between hand preference and the number of trials needed to elicit a left- or a right-hand response $F(2, 171)=5.442$, $P=0.005$ (see Fig. 3D). The number of trials needed to elicit a left- and right-hand response did not differ between left- $t(35)=0.174$, $P=0.863$ and ambiguously handed $t(80)=1.432$, $P=0.150$ chimpanzees; however, right-handed chimpanzees needed significantly more trials to elicit a left- compared to a right-hand reaching response $t(60)=3.715$, $P<0.001$.

4 DISCUSSION

Based on the relatively few studies that have reported on asymmetries in manual skill in nonhuman primates, several tentative conclusions can be drawn, albeit cautiously. First, for grasping preference and skill, though the effect sizes are relatively small, great apes appear to show a left hemisphere specialization. Whether more distantly related monkeys show this pattern of results is unclear and definitive conclusions cannot be made based on limited number of subjects that have been tested to date.

When considering other measures in hand skill, the data from monkeys and apes reveal some consistencies, but clearly additional studies are needed. In macaque monkeys, in unbiased testing circumstances in the BW and BB tasks, subjects show a strong trend or significant left-hand bias and this asymmetry seemed to be evident even among individuals who preferred to perform the task with their right hand. Thus, there is a dissociation between which hand is preferred to perform the task and which performs the task better (defined as faster or producing fewer errors). For the BB task, one limitation in the monkeys tested by Rigamonti et al. (1998) is that the number of trials that each hand performed on their grasping task was not balanced. This was also a limitation in the tool use performance measures reported by Sanz et al. (2016) and Hopkins et al. (2009). Ideally, on measures of performance asymmetry, equal numbers of responses should be obtained from each hand so that an equal sampling of variability is obtained. It is also worth noting that for the BW task, overall the average latency was much lower for monkeys that preferred their right hand (mean = 4.275 s) compared to monkeys with no hand preference (mean = 4.70 s) or a left-hand preference (mean = 6.70 s).

In contrast to the BB and BW tasks, macaque monkeys appear to show rightward biases in the development of hand-eye coordination as manifest by the data obtained from the joystick testing systems. Specifically, when the data were combined across species, macaque monkeys (1) preferred to use their right hand for joystick manipulation and (2) those that preferred their right hand to manipulate the joystick learned the task more quickly than left-handed individuals and this difference remained evident when the monkeys were tested on a novel, psychomotor task. In the few monkeys and apes that were tested on intermanual differences in psychomotor performance, all performed better with the right compared to left hand; however, these data should be interpreted with caution as the observed differences may have simply reflected practice effects because the data were obtained after the subjects had learned and used the test system for an extended period of time. The one exception is the report in baboons by Fagot and Vauclair (1993) which controlled for pretraining experience prior to testing for transfer of learning.

In macaques, one might view the evidence for left-hand biases in performance and preference on the BW and BB tasks as being inconsistent with the evidence for right-hand performance advantages in the acquisition and use of the tasks requiring hand–eye coordination associated with the manipulation of the joystick. This is a valid and legitimate concern, but I think some further evaluation of the sensory and motor demands of these tasks may offer some explanation for the differences in functional lateralization. In my view, the motor demands of the BB and, particularly the BW tasks are not as demanding as those associated with the use of the joystick. Based on our observation of performance on the BW in the chimpanzees, the subjects appear to slide the object or lifesaver candy along the edge of the metal wire rather than grasp the item and manipulate it through the various bends of the wire. Indeed, one might envision the subjects grasping the food with the thumb and index finger and manipulating the food off the wire. This is not the impression we have on the performance of the chimpanzees on this task and thus it raises some question regarding the exact motor demands of the task. In contrast, the joystick manipulation task has a strong visuomotor demand that requires significant integration of motor response with visual feedback based on the temporal and spatial location of the cursor controlled by the joystick. Ideally, data on both the joystick and BW task within the same subjects would provide invaluable information on these discrepancies.

With respect to the performance asymmetry data for tool use from chimpanzees, the results are interesting for two reasons. First, for both captive and wild chimpanzees, there seems to be a dissociation between performance asymmetries and hand preferences. Notably, in both populations, no population-level preferences were found yet performance asymmetries were evident. Second, within the captive population, performance advantages were particularly evident in right- but not left- or ambiguously handed apes.

Indeed, when considering intermanual differences in grasping skill and the tool use probing task in chimpanzees, the left–right differences were mediated by hand preferences but not in a double dissociative manner. For both measures, intermanual differences between the left and right hands were evident only in right-handed individuals and not in ambiguously and left-handed apes. For the ambiguously handed apes, one would predict no differences in performance between the left and right hands. However, if performance asymmetries strictly conformed to hand preference, then the left-handed chimpanzees should have showed leftward performance asymmetries. We did not find this result and, importantly, this does not appear to be due to a lack of power within the different handedness groups. Notably, for both simple reaching and tool use, there were no significant differences in the number of left- and right-handed individuals and the sample sizes within each handedness group were sufficient to detect intermanual differences in performance. These results lead to two conclusions. First, the observed differences in intermanual skill are likely not attributed to practice effects. Presumably chimpanzees that show significant left- or right-hand preferences would have comparable degrees of practice with their dominant hand. Second, these findings further suggest that the magnitude of lateralization within right-handed chimpanzees is greater than ambiguously and left-handed individuals, a finding that is often reported in studies of handedness in humans. That is to say, the absolute difference in performance between the left and right hands is greater within right- compared to left-handed individuals. Why this is the case is not clear but I would offer the following speculative hypothesis. If we assume that the left hemisphere is dominant for motor control and skill, then the compliance between preferred hand use and the inherent left hemisphere specialization for motor control manifestly expresses itself by larger intermanual performance asymmetries. Essentially this would reflect the additive effect of the inherent left hemisphere specialization combined with practice effects. In contrast, for ambiguously and particularly left-handed apes, the influence of practice by the left compared to right hand essentially blunts the expression of the intrinsic left hemisphere dominance for motor skill resulting in a more balanced expression in skill.

There are at least two limitations of the existing data and the approach used in this chapter. First, we used a very broad classification schema for characterizing precision and nonprecision grips. Basically, any use of the thumb and index finger was classified as precision grasping, while the use of other digits in grasping was characterized as nonprecision grasping. We did not attempt to distinguish between contacts between the thumb and different portions of the index finger (i.e., tip or lateral portion) which some have argued distinguishes human grasping from more distantly related primates. Second, we did not attempt to characterize independent digit control when quantifying grasping in the great apes and we did not summarize any hand preference data based on single digit use. For instance, in the tube task described earlier, a number of investigators have reported digit use when extracting the food from the device and there is some evidence that single-digit use results in an increased expression of strength and direction of handedness (Hopkins, 1995; Maille et al., 2013a; Morino et al., 2017; Nelson and Boeving, 2015; Vauclair et al., 2005). It is possible that variation in digit use may, in fact, alter hand use and this warrants further investigation.

Finally, the recent papers using the adopted QHP task reveal interesting results. Indeed, the collective efforts to record hand use while explicitly controlling for positional and situational factors reveal two patterns of results. In baboons and developing children, it seems that the distribution of hand use across the differing spatial positions elicits different patterns of hand use based on simple reaching compared to manual gestures. Specifically, hand use was more strongly right handed for manual gestures compared to simple reaching. These results are also consistent with previous findings in children, great apes, and baboons tested in different experimental and observational conditions (Harrison and Nystrom, 2008, 2010; Hobaiter and Byrne, 2013; Hopkins et al., 2005a; Meguerditchian and Vauclair, 2006; Prieur et al., 2016a,b; Shafer, 1993, 1997). Though the QHP does not necessarily measure hand skill per se, it does seem to be sensitive to (1) strength of handedness and (2) task variation in hand use. Thus, the QHP appears to be an amalgamated measure of both hand preference and performance and also merits further use and investigation in nonhuman primates.

In sum, though there are far fewer studies that have examined asymmetries in motor performance compared to hand preference, the evidence to date certainly suggest that this may be a promising avenue of future investigation. As noted earlier, there are some conceptual and empirical advantages to directly testing for functional asymmetries in motor performance rather than assessing solely hand preference. Notably, many investigators interested in the evolution of hemispheric specialization have relied on measures of hand preference, with the underlying assumption that preferred hand use reflects an inherent specialization in the contralateral hemisphere. The data presented here are not entirely consistent with this view and suggest that nonhuman primates may show asymmetries in motor function that are either independent of or mediated by their hand preferences but not in a reversed manner. In short, I believe that direct intermanual comparisons in motor skill or performance may reveal more consistent results with respect to asymmetries in motor control rather than measuring hand preferences alone. A number of years ago, Hamilton and Vermeire (1988) argued that cognition, not hand preference, is lateralized at the population level in macaque monkeys and the argument presented here simply extends this view to potentially include performance measures in motor functions.

Though not discussed in this chapter, a fruitful area of future investigation is to consider lateralization in motor planning rather than motor execution, as manifest by the hand preferred to perform a task. In humans, several imaging studies have demonstrated that the left hemisphere controls the planning of the execution of motor actions by both the left and right hands (Martin et al., 2011). From an evolutionary perspective, primates have adapted to many environments and use their hands in ways that reflect these ecological adaptations. For example, as noted earlier, chimpanzees use tools in a variety of ecological settings; thus, the type of tool use they use reflects the availability of different foods that require extractive foraging. What is common across ecological niches is the potential need to *plan* motor actions, particularly for complex, bimanual, or sequential actions. Thus, whether consistency in asymmetries for motor planning rather than hand preference is evident across different types of tool use would be of interest. Importantly, there are now ways of quantifying lateralization in motor planning using either observational or experimental methods. For example, in the reach-to-grasp study by Christel et al. (1998), they recorded the preshaping of the hand and digit when picking up food items, which presumably reflects their motor planning. Experimentally, recent studies have measured end-state comfort in grasping movements in primates (Chapman et al., 2010; Frey and Povinelli, 2012; Nelson et al., 2011; Weiss et al., 2007; Zander and Judge, 2015), which is also a measure of motor planning and has been shown by some to be left lateralized in humans (Coelho et al., 2014; Janssen et al., 2011).

Finally, based on the evidence presented here, rightward or leftward shifts in performance asymmetries, within different species and tasks, resemble the distribution of performance data from human participants. In other words, the data appear to be normally distributed but shifted in either a leftward or a rightward direction. This pattern of results differs from the distribution of hand preference data between human and nonhuman primates. Indeed, evidence of extreme right-handedness, as measured by preference, seems to be a very recently evolved trait among primates and appears to be unique to humans. To be clear, evidence of population-level hand preference is evident in some nonhuman primate species for some tasks but none of the evidence shows that degree of extreme right (or left) handedness found in humans (i.e., 8 to 9:1 ratio in right-to-left-handedness). If we assume that chimpanzees (Hopkins et al., 2017a,b), and perhaps other nonhuman primates, show a left hemisphere asymmetry in motor control and performance, then it is fair to ask why they do not show extreme population-level right-handedness, particularly for tasks such as tool use. One possibility is that hand preference, as measured by self-report in humans, does not accurately assess inherent functional specializations in manual motor function. In the same manner that some measures of hand preference in nonhuman primates are sensitive to situational factors, the same limitation may apply to self-report measures of hand preference in humans, but in this case, the data are subject to cultural or social factors that potentially mask the biological expression of motor asymmetries. Alternatively, as I have argued elsewhere (Hopkins, 2013b), comparing human (particularly adults) and nonhuman primates on measures of hand preference is nearly impossible given the current methods and approaches. Human handedness relies heavily on self-report and rarely uses objective measures of hand use (except in children), which is the primary means of measurement in nonhuman primates. Furthermore, there are many challenges to the analytic approaches used to characterize hand preference groups (i.e., the use of z-scores compared to arbitrary thresholds/boundaries?). Many of these comparative challenges can be overcome by assessing asymmetries in performance rather than solely hand preference. Thus, I would advocate that there be an increasing effort to quantify performance asymmetries between primate species as a means of advancing evolutionary theory on the origins of hemispheric specialization in motor functions.

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CHAPTER

Manual bias, behavior, and cognition in common marmosets and other primates

4

Lesley J. Rogers[1]
School of Science and Technology, University of New England, Armidale, NSW, Australia
[1]Corresponding author: Tel.: +61-266-515-006, e-mail address: lrogers@une.edu.au

Abstract

This chapter examines the importance of studying hand preference together with different expressions of behavior. Cognitive differences between left- and right-handed primates are discussed. As shown in several species of primate, eye preference, but not hand preference, is biased at the level of the population and reflects hemispheric asymmetry of processing. Hand preference, determined from simple grasping of pieces of food and taking them to the mouth, is consistent for individuals but it is not population biased. It is a measure of an individual's preference to use a particular hemisphere, and hence which cognitive processes are characteristic of the individual. Compared to left-handed subjects, right-handed subjects are more active in exploring novel objects, show more social facilitation of behavior, have a positive cognitive bias, and express lower levels of fear and stress responses. In marmosets, learning of food searching tasks is not associated with hand preference. Strength of hand preference, rather than its direction, is linked to the ability to perform two tasks at once, viz., detection of a predator while searching for food. Marmosets with strong hand preferences are able to perform these two tasks at once but those with weak or no hand preference are unable to do so.

Keywords

Hand preference, Exploration, Social behavior, Cognitive bias, Fear, Stress, Personality, Primates, Marmosets

1 INTRODUCTION

Much effort has gone into comparing the performance of left- and right-handed human subjects, with variable results and, at best, showing weak although significant associations between hand preference and several different patterns of behavior (summarized recently by Kushner, 2017; but see Beratis et al., 2013, for significant

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differences in higher cognitive function between left- and right-handed humans and also Somers et al., 2015). More recently, the behavior of right-handed subjects has been compared to that of a collective group of left-handed and mixed (or inconsistent)-handed subjects (the latter includes use of a preferred hand to perform some tasks but not others). This approach affords researchers with a larger group to compare with a group of right-handed subjects, and it has revealed significant differences in cognitive performance between the two groups (Prichard et al., 2013). However, it confounds significant left-handed with weak-handed subjects. This is probably a mistaken approach, since comparison of strong vs weak handed groups, regardless of the direction of asymmetry, has revealed significant differences in behavior in both human and nonhuman species (discussed further by Hardie and Wright, 2014; Rogers, 2017; also discussed later in this chapter). In brief, comparison of three groups, consistent-left, consistent-right, and mixed-handed, now seems to be the best approach.

Since hand preferences in humans are influenced by a wide range of factors (Llaurens et al., 2009), including social pressures (by negative attitudes to left-handedness in most cultures: Kushner, 2017), revealing differences in cognition and general behavior between left- and right-handed subjects might be more readily determined in nonhuman primates than in humans in order to eliminate, or at least reduce, the influence of social norms or culture as potential factors influencing handedness.

Common marmosets, *Callithrix jacchus*, are an excellent primate species for examining potential differences in behavior between left- and right-handed subjects because approximately half of any group or colony is left-handed and the other half right-handed (Hook and Rogers, 2008; see also de Sousa et al., 2001). After marmosets reach the age of approximately 12 months, this distribution of hand preferences is particularly clear, as determined by repeated scoring of the hand used to pick up pieces of food from the floor or a dish and take them to the mouth, referred to as simple visuospatial reaching (Hook and Rogers, 2000; see Fig. 1). In a study of 21 common marmosets reaching for food in several different tasks, by far the majority was found to be either left- or right-hand preferring, and only 7% were ambi-preferent (i.e., with no significant preference for repeated use of the left or right hand) (Hook and Rogers, 2008). Some marmosets show a shift in hand preference when the task is changed to one requiring more visuospatial demands (Hook and Rogers, 2008) or when a different body posture has to be adopted in order to reach for and grasp a food reward (Hashimoto et al., 2013) but most individuals keep the same preferred hand use across tasks (Hook and Rogers, 2008). Furthermore, the strength of preference in left- and right-handers is the same and does not differ significantly (approximately 80% left or right, as seen in figure 1 of Rogers, 2009). As yet, there has been no detailed investigation of ambi-preferent marmosets, largely because they are a small minority in the adult population. Here it must be noted that ambi-preference in primates refers to no significant preference to use either the left or the right hand on a given task. It differs from the terminology used in studies of

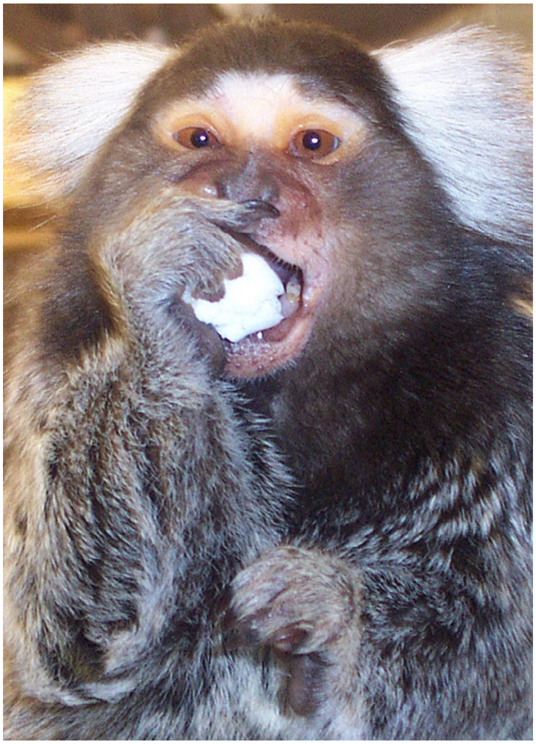

FIG. 1

A marmoset holding a piece of food to its mouth. This would be scored as one event of right-hand use.

humans, in which mixed or inconsistent hand preference usually refers to using a different hand on different tasks (Hopkins et al., 2013).

Focusing on simple visuospatial reaching in common marmosets (picking up pieces of food and taking them to the mouth), repeated testing of individuals annually from year 1 through to 13 years of age has shown that each individual retains its left- or right-hand preference throughout adulthood (Rogers, 2009). Hence, this measure of hand preference is a characteristic that might be associated with other aspects of behavior. The research discussed to follow has compared left- vs right-handed marmosets and other primate species on various tasks or in the expression of various types of behavior.

It is important to note that hand preferences of marmosets have no relationship to eye preferences for viewing different stimuli, as found by testing the eye preferences of 21 marmosets of known hand-preference repeatedly at four different ages between 3 and 22 months of age (Hook-Costigan and Rogers, 1995, 1998). Eye preferences were measured by scoring the eye used to look through a peephole. All but one of the subjects used their right eye to look at familiar stimuli (banana, beetle, a watch, or a mirror), which interested them but caused no obvious arousal. For these stimuli, the strong population bias of right-eye preference was expressed quite independently of hand preference. The right-eye preference suggests that the left hemisphere is used when the marmoset looks at these nonarousing stimuli, as shown previously in tests of eye preference in young chicks (summarized in MacNeilage et al., 2009; Rogers et al., 2013). When the stimulus was changed to one that resembled rearing snakes, the eye preference shifted to either no preference or a left-eye preference, and "tsik" (loud, short sounds beginning with ascending frequency and followed by descending frequency, ranging from 8 to about 20 kHz), "egg" and "ock" calls (the latter two commonly associated with tsik calls, of low intensity and with a fundamental frequency below 2 kHz, and with harmonics: Agamaite et al., 2015; Epple, 1968) emitted by the marmosets showed that their arousal levels had increased markedly in response to seeing the model snakes (Hook-Costigan and Rogers, 1998). Preferred use of the right hemisphere in responding to potential predators, as shown in other species (e.g., Lippolis et al., 2002, 2005), could be the explanation for this result. In other words, the hemisphere specialized to process a visual stimulus and to control the behavioral response to it is strongly linked to eye preference. This is not associated with hand preference in any way (e.g., Spearman rank correlation between eye and hand preferences at 22 months of age was $r_s = 0.01$, $P = 0.96$; see Hook-Costigan and Rogers, 1998). Bushbabies, *Otolemur garnettii*, also display a group bias for using a preferred eye and, in this species too, eye preference is not associated with hand preference (Rogers et al., 1994).

Testing eye preferences of chimpanzees, also using a peephole to look at different stimuli, Braccini et al. (2012) found a result very similar to that of the marmosets. The chimpanzees had right eye preferences for viewing bananas and left-eye preferences for viewing a model snake, particularly when they first saw it. These authors interpreted the results as reflecting hemispheric differences in emotional responses, the left hemisphere (right eye) for positive emotions and the right hemisphere (left eye) for negative emotions (consistent with the Valence Model of Davidson, 1992). Alternatively, the differences between eyes could stem from specialization of the left hemisphere to categorize stimuli and attend to a subset of key features vs specialization of the right hemisphere to attend to details of a stimulus and detect novelty (Rogers, 2009; Vallortigara and Rogers, 2005).

Regardless of these considerations, here I want to emphasize the discrepancy between specialization of the hemispheres (and eyes) and motor output manifested in use of a preferred hand. Based on their studies of brain-lesioned macaques, Hamilton and Vermeire (1988) reached a similar conclusion. In the majority of individuals, the left hemisphere carries out processing of information in a way distinctly different from the processing performed in the right hemisphere, and these hemispheric specializations have been shown in a wide range of species (Rogers et al., 2013; Vallortigara and Rogers, 2005). Hand preference for simple reaching in primates might reflect, or even determine, which hemisphere an individual has a propensity to use. If this is so, it can be predicted that left- vs right-handed marmosets would process inputs in different ways and respond in different ways to the same stimulus or context. For example, left-handed marmosets may show avoidance of novel stimuli and express stronger emotions, especially negative ones, than do right-handed marmosets, because the right hemisphere controls the left hand and is specialized for these particular functions. Experiments testing this hypothesis will now be discussed.

2 PERFORMANCE DIFFERENCES BETWEEN LEFT- AND RIGHT-HANDED PRIMATES

2.1 EXPLORATION

A convincing number of different experiments has shown that right-handed primates are more likely than left-handed ones to explore novel objects by touching them and by examining them visually. To my knowledge, the first evidence for this was obtained by presenting novel objects to chimpanzees. In a sample of 49 chimpanzees, Hopkins and Bennett (1994) found that right-handed chimpanzees approached novel objects sooner and touched them more times than did left-handed ones, a finding that they attributed to positive affect in right-handers and negative affect in left-handers. An alternative explanation arises from research by Forrester et al. (2012), who found that chimpanzees (number of subjects, $N=9$) display a right-hand preference to touch inanimate objects, whereas no significant hand preference is seen for touching animate targets. The same result was also obtained for gorillas (Forrester et al., 2011). Accordingly, it could be hypothesized that the right-handed chimpanzees in the Hopkins and Bennett (1994) study might have interacted with the novel objects more than the left-handed ones because they had a greater propensity to manipulate inanimate objects.

Turning now to hand preferences and behavior in New World primates, there have been a number of studies reporting differences in exploration of novel objects between left- and right-handed individuals. The first experiment examining this in common marmosets scored approach and interaction with novel objects placed in an unfamiliar setting, a room considerably larger than their home cage (Cameron and Rogers, 1999). The strength of hand preference of each marmoset had been determined 1 month prior to this test by scoring the hand used to pick up pieces of food and take them to the mouth, and this act was repeated 100 times over at least 10 days (Fig. 1). It is important to emphasize that the marmosets were in a relaxed state when their hand preferences were scored. There were 12 left-handed and 8 right-handed subjects (aged 21–68 months).

The marmosets were tested alone. At the time of testing, a marmoset was carried to the novel room in its own nesting box, which was placed on a table in the room and the door of the box was opened. Latency to leave the nesting box was scored. All of these latency scores were quite short, showing that the marmosets were not obviously fearful of the novel setting, but right-handers moved out of the nesting box significantly sooner than the left-handers. Once the marmoset had left the nesting box, the following variables were scored for 1 h: number of objects touched, total number of touches made, number of parallax movements, and number of leaps. The right-handed marmosets had significantly higher scores on all of these measures. Collectively, the findings demonstrate increased exploration of the novel objects by the right-handed marmosets. This deduction is a straight-forward interpretation of the touching scores. The parallax movements are most likely part of visual examination of the objects, used to determine depth and distance. Leaping could be an independent measure of activity level with no direct association with exploration but, since it correlated positively with scores of touching the objects, it may also reflect exploration.

Both males and females were tested and no significant effects of sex were found on any of the measures. In fact, an absence of significant sex differences was found in the experiments to be discussed later, and this result is consistent with a more recent study examining the reaction of common marmosets to novel objects, referred to as "boldness" by the researchers (Koski and Burkart, 2015).

Exploration has also been assessed by presenting novel stimuli in the home cage to same-sex groups of 2–4 common marmosets (Rogers, 1999). Hand preference varied independently of group. The stimuli were presented one at a time in random order. The following were presented, each inside a glass Petri dish placed on a small platform above ground level: plastic models of insects, live cockroaches, and a mirror. There were two additional stimuli presented by placing them on the platform and these were a coiled model snake and a model resembling two rearing snakes. Although the number of times the subjects stood on the platform to examine the stimuli varied for each stimulus, for every stimulus, inspection scores were higher for the right-handed marmosets ($N=8$) than for the left-handed marmosets ($N=10$). This trend was clear for all stimuli except the coiled snake, although subadults ($N=8$) were more interested in the coiled snake than were adults ($N=10$) and right-handed subadults spent significantly more time on the platform with the snake than their age-matched left-handed group. Also, the differences between the left- and right-handed groups were more marked in subadults than in adults, for all of the stimuli. In summary, in both age groups the left- vs right hand difference was manifested for both potential food items (insects) and fear-inducing stimuli (coiled and rearing snakes). Only the snakes elicited fear or mobbing vocalizations (tsik, egg, and ock calls), the latter believed to recruiting conspecifics to assist in driving a predator away.

A subsequent study investigating responses of common marmosets to stimuli known to induce fear found significantly more head-cocking and parallax movements, as in the above studies, and also more tsik calling in right-handed ($N=10$) than in left-handed marmosets ($N=10$) (Gordon and Rogers, 2010). Head cocking and parallax movements are indicative of visual examination of the stimulus, and tsik calls are emitted as an aspect of mobbing behavior (Clara et al., 2008). This higher production of vocalizations in response to stimuli was also shown by presenting marmosets with crickets, which were unfamiliar prey items (Gordon and Rogers, 2010). On seeing the crickets, more tsik, crackle, whistle, and cough calls were emitted by right- compared to left-handed marmosets. These calls replaced phee calls, which were made less frequently when the crickets were presented. By contrast, on seeing the crickets, left-handed marmosets did not change their various vocalizations, apart from an initial decrease in the number of phee calls. Phee calls are used in long-distance social communication (Bezzera and Souto, 2008), and the other calls produced are part of the mobbing response. It seems that the right-handed subjects were aroused by seeing the crickets and produced calls that might solicit group members to join them, whereas the left-handed subjects not only made no such intraspecific communication but also reduced long-distance contact calling. This suggests that social facilitation is characteristic of right-handers but not of left-handers (discussed further below).

Taking all of these studies into consideration, one can conclude that right-handed common marmosets are more inquisitive and reactive than left-handed ones regardless of whether they are tested in their social group, in their home cages or alone in an unfamiliar setting. This difference between left- and right-handed subjects applies to a wide range of unfamiliar stimuli (live and inanimate food and potential predators).

A similar result has been reported for another marmoset species of the same genus, *Callithrix geoffroyi*, tested with novel foods (vegetables and nuts that they had not seen previously) and on hearing the territorial calls of their major predators, hawks and the Harpy eagle. These calls were not entirely unfamiliar to the marmosets. Braccini and Caine (2009) found that right-handed subjects sniffed and tasted novel foods sooner than left-handed ones (total $N = 18$), and on hearing the calls of the predators, they froze for half as long as did the left-handers. These results indicate that left-handers are less likely to explore novel foods and are more fearful than right-handers.

The Braccini and Caine (2009) study included some subjects with no significant hand preference ($N = 6$), determined as no significant bias of the Handedness Index calculated as (left − right)/(left + right) with a total of 50 scores per subject. This group behaved similarly to the left-handed group on some scores (time spent freezing on hearing the calls and time before tasting the novel foods), but on other scores (e.g., latency to sniff the novel foods) they were similar to the right-handed group. Overall, therefore, the responses of the monkeys without significant hand preferences were intermediate between those of the left- and right-handed groups. To reiterate an earlier point cautioning about lumping together left-handers and mixed-handers in studies on humans, as the results of Braccini and Caine (2009) show, it would clearly be erroneous to lump together the left-handed monkeys and those without a significant hand preference as a single group to compare with the group of right-handers.

In all of these studies it was important to ascertain that the effects of hand preference were not confounded with the age, sex, or social grouping of the marmosets, and all of them eliminated this possibility. Although, in some cases, age was associated with reaction to novelty, it could be clearly distinguished from the association between hand preference and response to novel stimuli and predators.

In summary, all of these studies demonstrate that right-handed primates are more likely than left-handed members of their species to approach and interact with novel stimuli. This result is consistent with a study of humans by Wright et al. (2013) in which, compared to right-handers, left-handers were found to delay responding to novelty.

2.2 SOCIAL BEHAVIOR

From the change in vocalizations produced by right-handed marmosets when they see a model predator or crickets and the absence of any such change in left-handed marmosets (see above), one could deduce that right-handed marmosets have more influence on the behavior of group members than do left-handed marmosets. Right-handed marmosets might also be more influenced by members of their social group. This deduction was investigated by Gordon and Rogers (2010). Right-handed ($N = 9$) and left-handed ($N = 6$) common marmosets were presented with live crickets when they were in their social groups, and their responses were compared to those obtained when they were tested in social isolation (see above). When tested alone both left- and right-handers delayed for the same time before they captured the first cricket but, in their social groups, right-handers delayed for a significantly shorter time than did left-handers (right-handers were more than four times faster than left-handers). In fact, the latency to the first capture made by the left-handed marmosets was the same regardless of whether they were alone or in a group. This fits with evidence presented in the previous section, suggesting that left-handed marmosets are not only more reluctant to approach relatively unfamiliar stimuli but also less influenced by the presence of conspecifics. Over the 15 min of testing, both groups caught the same number of crickets, and did so more when in a group than when alone. From this result, it can be concluded that both groups were equally motivated to feed, and the only difference between them was in the initial latency to commence capturing the crickets when they were in their social group. In other words, the right-handed marmosets showed social facilitation of initial approach and capture, whereas this did not occur in left-handed marmosets.

A relationship between hand preference and another aspect of social behavior has been observed in free-ranging rhesus macaques, *Macaca mulatta* (Westergaard et al., 2003, 2004). Right-handed males were groomed more than left-handed males, and they adopted fewer bouts of submissive behavior than did left-handed males (total $N = 24$), whereas the opposite was the case in females (total $N = 41$). Hence, in rhesus macaques, hand preference is associated with social status but oppositely so in males and females. Although this sex-difference contrasts to the absence of any sex-effect in the research on marmosets discussed earlier, it does highlight the need for larger sample sizes and more examination of potential sex-differences in relation to behavior associated with hand preference.

In the same studies, Westergaard et al. (2003, 2004) found that right-handed male rhesus macaques received less aggression from conspecifics than did left-handed males and, again, the opposite was the case for females. Consistent with this effect in male rhesus monkeys, retrospective examination of long-term colony records of 39 male and female common marmosets housed at the University of New England, Australia, revealed that right-handers were subjected to less aggression from conspecifics than were left-handers: left-handers were recorded to be subjected to aggressive attacks twice as often as were right-handers (Gordon and Rogers, 2015). Differing from the study of rhesus macaques, no sex difference was evident in the data for common marmosets.

2.3 COGNITIVE BIAS

The concept of cognitive bias was used first to describe the behavior of humans in response to an ambiguous stimulus, one that could be interpreted as either negative or positive (see Haselton and Nettle, 2006). It is now applied to nonhuman species, typically tested following training the animals to distinguish between a stimulus associated with a reward and another not associated with a reward or with punishment (Paul and Mendl, 2004; Paul et al., 2005). Testing involves presenting the trained subjects with a stimulus intermediate between the positive and negative stimuli and scoring whether the animal treats it as negative or positive. For example, if the positive stimulus is a black key and the negative stimulus is a white key, the ambiguous stimulus is a gray key. The animal's response to the gray stimulus indicated the individual's perceived cognitive bias.

For example, in an experiment designed to test cognitive bias in common marmosets, Gordon and Rogers (2015) first trained the subjects ($N = 12$) individually to obtain a reward by removing a black card covering a bowl containing a mealworm and to abstain from removing a white card covering an empty bowl. The bowls were presented in random order one at a time. To avoid any bias related to shade of the negative and of the positive keys, some of the marmosets were trained with the white card as positive and the black card as negative. After training, each marmoset was presented with a bowl covered with a gray card as a nonrewarded probe trial placed randomly between trials with the black and white stimuli as used in training. Using this procedure, Gordon and Rogers (2015) found that right-handed marmosets were more likely to respond to bowls covered with gray cards as if they were positive (i.e., they would approach and remove the cover to look for mealworms), whereas left-handed marmosets were more likely to consider the gray card to be equivalent to the negative stimulus, most often not removing it from the bowl or even approaching it (Fig. 2). Thus, right-handed marmosets were said to express a more positive cognitive bias than were left-handed marmosets.

In recent years, cognitive bias has been used as a measure of animal welfare in a range of species, including primates (e.g., rhesus macaques, Bethell et al., 2012; capuchins, Pomerantz et al., 2012; also see Rogers, 2010). Animals less able to judge ambiguous stimuli as positive are more prone to stress, as shown in rats (Rygula et al., 2013). In humans also, negative cognitive bias is associated with reactivity to stress and vulnerability to depression (Dearing and Gotlib, 2009). Furthermore, setting aside the problems of collapsing left-handers and ambidextrous or mixed

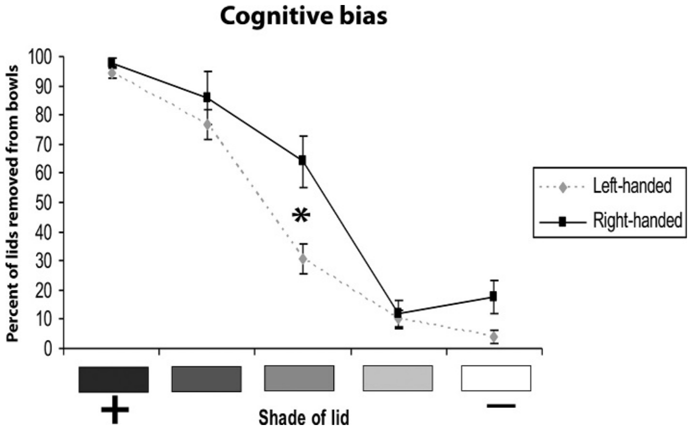

FIG. 2

Results of the cognitive bias test reported in Gordon and Rogers (2015). Mean scores of the percent of lids removed from dishes are plotted with standard error bars. The results are represented as though all of the marmosets had been trained with *black cards* covering the dishes baited with mealworms (positive) and *white cards* covering the bowls with no rewards (negative). However, some of the marmosets were trained with the opposite combination. Note that both left- and right-handed marmosets have learnt to discriminate between the positive and negative cards. The *gray card* in the middle was ambiguous, and scores for the left-handed group were significantly lower than those of the right-handed group (indicated by the *asterisk*). The experiment also included covering bowls with two other shades of *gray*, one closer to the positive stimulus and the other closer to the negative stimulus. These cards were not ambiguous, as the results show. The contribution of D.J. Gordon to this figure is gratefully acknowledged.

handers into one group (see above), it is worth noting that nonright-handed people are more prone to depression than are right-handers (Denny, 2009). This leads to the next topic of fear and stress responses that might be associated with hand preference in primates.

2.4 FEAR AND STRESS RESPONSES

Of course, it can be argued that the reluctance of left-handed primates to interact with novel stimuli reflects higher levels of fear in left-handed primates than in right-handed ones. However, it is difficult to separate fear responses from reduced attention to novelty. Therefore, a measurement of stress hormone levels might be a beneficial approach to addressing the issue of differences in fear between left- and right-handed subjects. Westergaard et al. (2003) assayed plasma samples taken from male rhesus macaques ($N = 24$) for stress hormone levels (viz., cortisol), among other metabolites. The plasma samples were collected after trapping the monkeys in a corral and, therefore, in a stressful situation. The researchers found a significant positive correlation between Handedness Index scores [$(R - L)/(R + L)$, where R = frequency of right-hand use and L = frequency of left-hand use] and plasma cortisol levels, meaning that cortisol levels were higher as right-hand preference increased in strength. However, a simple comparison of cortisol levels in left-hand ($N = 10$) vs right-hand ($N = 8$) groups revealed no significant difference in cortisol levels.

Samples were also taken from female macaques ($N = 41$) in the same conditions as for the males (Westergaard et al., 2004) and the researchers obtained the same positive correlation between the Handedness Index and plasma cortisol level. In this case, a comparison of left- vs right-handed animals was not possible since too few females had a right-hand preference. Nevertheless, as a general trend, one can say that plasma cortisol levels were lowest in the left-handed males and females (summarized in Howell et al., 2007). This is opposite to the prediction made above that left-handed primates might be more fearful and show stronger reactions to stress. In fact, Kalin et al. (1998) found that, in rhesus macaques, plasma cortisol levels correlated positively with levels of activity in the right frontal cortex, and the right bias in frontal asymmetry was associated with higher levels of defensive and fear behavior (see also Kalin et al., 2000). Although these researchers did not measure the hand preferences of these monkeys, neural activity should be greater in the hemisphere opposite the preferred hand, in which case one can deduce that cortisol levels may have been higher in the left-handed than right-handed monkeys.

One study of cortisol levels in common marmosets supports this deduction. It found that left-handed ($N = 9$) subjects compared to right-handed subjects ($N = 8$) showed more prolonged elevation of cortisol levels in plasma collected in the morning (i.e., controlling for the diurnal cycle in cortisol levels) following time spent in an unfamiliar environment (Rogers, 2009). This fits with other evidence of heightened fear and higher activity of the hypothalamic–pituitary–adrenal (HPA) axis in left-handed primates. However, further research is needed and vocalizations need to be taken into account since, in common marmosets, it has been shown that production of mobbing calls, or simply hearing mobbing calls, lowers cortisol levels (Clara et al., 2008; Cross and Rogers, 2006). In other words, vocal behavior of the individual or the social group interacts with hormonal responses to fear.

In summary, and as Koolhaas et al. (2010) have pointed out, the relationship between coping style and activity of the HPA axis is rather complicated, and although there is empirical support for reactive individuals showing the highest HPA response (as seen above in marmosets), variation between species has been reported.

2.5 LEARNING

Some studies, but not others, have found a difference in learning performance between left- and right-handed primates. Here those studies reporting significant associations between learning and hand preference are discussed. Those not showing such association are covered under the next heading.

Horster and Ettlinger (1985) found that left- and right-handed rhesus macaques differed in rate of acquisition of a tactile discrimination task. The left-handed monkeys ($N = 78$) learnt the task faster than the right-handed ones ($N = 77$). Ambidextrous monkeys ($N = 82$) were faster than both of these groups. Although there was an overlap between the scores for each group, these differences were significant. Following on from this significant finding, Hopkins and Washburn (1994) investigated learning performance in rhesus macaques trained to use a joystick and use it to guide images on a computer screen: hand preference was determined from the hand used to operate the joystick ($N = 12$ left- and 14 right-handed). The monkeys were tested on six different match-to-sample tasks, including maze tasks and matching-to-sample tasks with and without delays between presentation of the sample and test cues. The cues in the latter tasks were either shape/form or spatial cues. Significant differences were found between the left- and right-handed monkeys in scores to reach criterion of performance, and performance of the left-handed monkeys was superior on the delayed spatial-matching task, whereas the opposite was true on the delayed form-matching task. In fact, whereas performance of the right-handed subjects was the same on both of these tasks, performance of the left-handed subjects was markedly better on the delayed spatial task than on the delayed form task. This finding of poorer spatial learning in the left-handed monkeys is consistent with the known specialization of the right hemisphere for processing spatial cues (e.g., Shulman et al., 2010; Tommasi and Vallortigara, 2004; Vallortigara and Versace, 2017).

3 ABSENCE OF DIFFERENCES BETWEEN LEFT- AND RIGHT-HANDED PRIMATES

Hand preference was found to have no association with problem solving ability in common marmosets presented with a transparent cylinder containing a mealworm that they could obtain only by sliding across a small sheet of clear plastic (Cameron and Rogers, 1999; Fig. 3). The latter had a hole through which the worm would fall to the bottom of the cylinder, and from there it could be accessed by the marmoset. There were two obstacles to obtaining the mealworm: the first was to slide the sheet across so that the hole aligned with the inside of the cylinder and the second was finding the hole at the bottom of the cylinder through which the marmoset could reach in order to grasp the mealworm. The latter step was surprisingly difficult for some of the marmosets: many reached around the base of the cylinder with both hands until they felt were the hole was. A number of measures were collected over 100 trials per subject, including the number of successful manipulations of the sliding sheet, time attending to the apparatus, and number of mealworms retrieved. A total of 19 left- and right-handed marmosets were tested. Older marmosets were better at solving this task than were younger ones but neither hand preference nor sex was associated with any of the measures of success in solving the task.

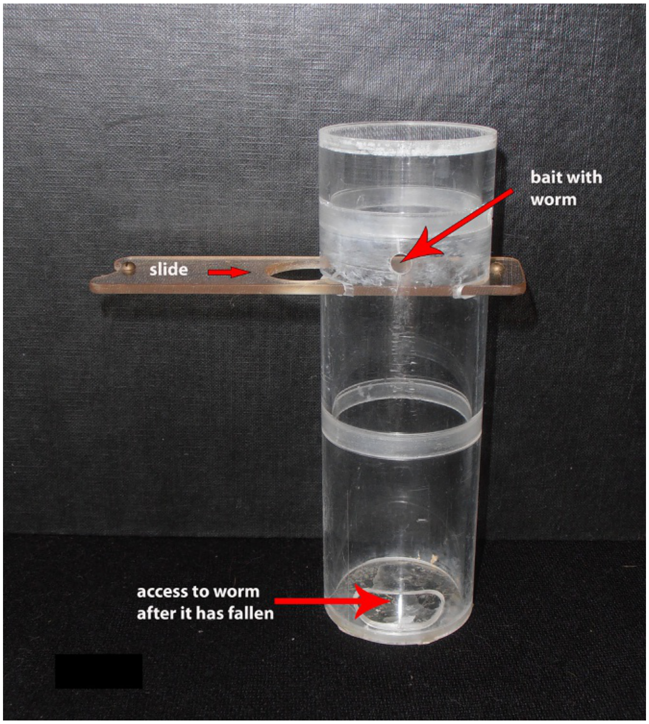

FIG. 3

The problem-solving task on which no differences were found between left- and right-handed common marmosets (Cameron and Rogers, 1999). A mealworm is inserted through the small hole at the top of the cylinder and on to the plastic sheet positioned as shown in the figure. The marmoset has to slide the sheet across so that the hole in it is *centered* in the tube and the mealworm falls to the *bottom*, from where the marmoset can grasp it via the hole at the bottom of the cylinder.

Before testing the common marmosets for cognitive bias (see above) they had to be trained on the positive bowls with white (or black) cards covering a bowl containing a mealworm and negative bowls with black (or white) cards covering an empty bowl. On the first two or three trials the marmosets removed the cards from both bowls but thereafter they began to inhibit removing the card from the negative bowl. The data collected on the number of negative bowls inspected each day over the first 10 days of training were analyzed by ANOVA with day as a repeated measure (unpublished results of D.J. Gordon, University of New England). This revealed a significant effect of day ($F_{9,90} = 3.72$, $P = 0.001$), no effect of hand preference ($F_{1,10} = 0.007$, $P = 0.94$) or interaction between day and hand preference ($F_{9,90} = 1.06$, $P = 0.40$). Also, there was no effect of hand preference on the number of days of training needed to reach criterion before the cognitive bias tests were applied (Gordon and Rogers, 2015). Hence, there was no association between hand preference and rate of learning this task.

In a task of food searching, Piddington and Rogers (2013) presented marmosets (left-handed, $N = 5$; right-handed, $N = 5$) with pairs of small bowls, one blue containing a mealworm and the other green and empty, secured to branches, each pair at a different height in a room much larger than the marmosets' home cages. There were eight blue bowls and eight green bowls in total. To search efficiently, once a marmoset had eaten the mealworm from a blue bowl, it had to move on to the next pair of bowls (i.e., adopt a win-shift strategy). On each of 10 days, learning was scored as number of visits to the empty green bowls (errors) and time taken to retrieve all of the mealworms. Left- and right-handed marmosets did not differ significantly in learning this task. Small sample size could have precluded detecting any effect of hand preference but there was no indication of any trend toward a difference.

At least on these three tasks (problem solving, conditioned learning, and win-shift food-search) left- and right-handed marmosets did not differ. It is noted that the marmosets were not stressed or fearful in any of these tests. Two of the tasks were performed in the home cage with other marmosets in nearby cages, and the other test was carried out in isolation in a familiar room. It remains to be seen whether rate of learning and problem solving would differ between left- and right-handed subjects if fear levels were increased.

4 STRENGTH OF HAND PREFERENCE

The results reported so far have focused on differences between left- and right-handed subjects. Other tasks might show that strength, rather than direction, of hand preference is an important variable. Indeed, Piddington and Rogers (2013) reported that strength but not direction of hand preference is associated with the ability of common marmosets to perform two tasks at once, one task requiring use of the left hemisphere and the other task requiring use of the right hemisphere.

The design of this experiment was based on a prior study in which performance of chicks with strong lateralization for processing visual information had been compared to that of chicks with no lateralization of this function (Rogers et al., 2004). Chicks are known to use the right eye and left hemisphere in search for grains of food scattered among small pebbles (Rogers and Anson, 1979) and to use the left eye and right hemisphere to detect and respond to a predator (Rogers, 2000). Strength of brain asymmetry had no bearing on the ability of the chicks to perform either one of these tasks separately, but when they had to perform both tasks at once, those without lateralization for processing visual information were not only unable to learn to avoid pecking at the pebbles but they were also slower in detecting the model predator moving overhead. In fact, they were so confused by having to perform the two tasks simultaneously that their performance of pecking at food grains and discriminating them from the pebbles deteriorated as the task progressed. By contrast, the chicks with lateralization were able to learn to discriminate the grain from the pebbles and they detected the predator readily. They were not disturbed by having to perform both tasks at the same time, which suggests they would survive better in the natural environment where being exposed to predators while searching for food is a common experience.

Piddington and Rogers (2013) adapted this procedure to test common marmosets ($N = 10$). First, they trained the marmosets to search for mealworms in blue bowls and avoid looking into or reaching into empty green bowls (as described earlier, left- and right-handers learnt at the same rate). The task with two demands consisted of allowing the marmosets, tested singly, to commence searching for mealworms and then a model predator was presented. The predators were a taxidermic specimen of a predatory bird moved across the ceiling of the testing room using pulleys, a snake pulled across the floor, and a wooden carving resembling rearing snakes pulled across the floor. Each stimulus was presented in a different trial and in random order. The marmoset's latency to detect the model predator was scored, as indicated by freezing, fleeing, approaching, or mobbing. Vocalizations were also recorded and analyzed.

Significant negative correlations between time to detect the predator and strength of hand preference were found in trials with presentation of the bird, in particular, and the rearing-snakes (note that there was no difference between the range of strengths of hand preference in the left- and right-handed groups). Direction of hand preference had no significant effect on this performance. Marmosets with weaker hand preferences were slower to detect the predator. When the trials with the predators were repeated without the need to search for mealworms, no effect of strength of hand preference was found; all of the marmosets detected the predator after very short delays. Hence, consistent with the finding in the chicks, only when they had to perform the two tasks at once did the animals with weaker laterality (weaker hand preferences) have difficulty, presumably because they had weaker brain asymmetry and so were less able to separate the different types of processing needed to perform the two tasks at once. As suggested by Vallortigara et al. (1999) the advantage of being lateralized may depend on the ability to perform separately different computational functions on each side of the brain. This hemispheric separation of functions and parallel processing ability appears to an evolutionarily ancient trait common to, at least, vertebrates (Rogers et al., 2013).

The marmosets with stronger hand preferences also responded to the model predators by emitting tsik and phee calls more than did those with weaker hand preferences (the number of both vocalizations correlated positively with hand preference), although in the case of the bird stimulus the mobbing followed an initial period of silent freezing behavior. Such vocalizations would communicate the presence of the predator to other group members and solicit their help in mobbing the predator. Thus, being strongly lateralized seems to have a clear advantage in survival and also in group interaction (discussed further by Vallortigara and Rogers, 2005).

5 ASSOCIATIONS BETWEEN HAND PREFERENCE AND NEUROANATOMY

So far, this chapter has discussed hand preferences as a propensity to use the hemisphere contralateral to the preferred hand, thus reflecting an individual's sensorimotor engagement with the social and physical environment. Michel et al. (2016) considered the possibility that sensorimotor engagement in early life may influence both the structure and the function of the brain, and hypothesized that human infants with consistent hand preferences in early life might follow a differing trajectory of cognitive development compared to those with inconsistent hand preferences in early life (Michel, 2018). Some evidence supports this concept: for example, consistent hand preference (left or right) in infancy facilitates the acquisition of language (Nelson et al., 2014) and tool-using behavior (Fraz et al., 2014).

In this context, it is relevant to note that structural differences in the brain have been found in left- compared to right-handed common marmosets (Gorrie et al., 2008). Postmortem brains of adult marmosets ($N = 11$) of known hand preference were examined for asymmetries in surface measurements, cortical thickness, and thickness of the corpus callosum. A strong, positive correlation was found between the length of the right lateral sulcus, adjusted for brain weight, and strength of right-hand preference (Fig. 4). Right-hand preference also correlated positively with the

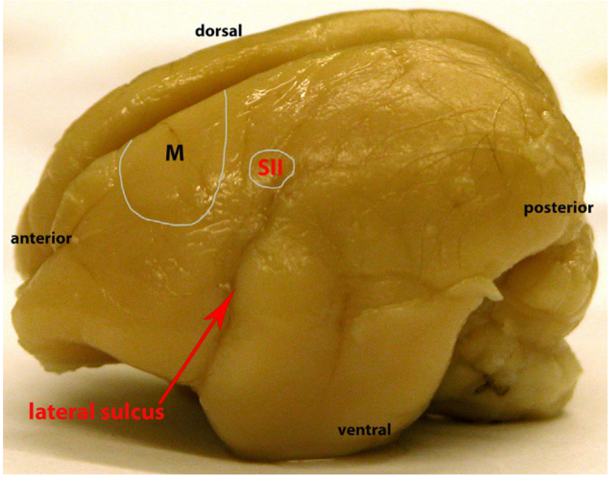

FIG. 4

A lateral view of the brain of the common marmoset, showing the locations of the lateral sulcus, secondary somatosensory area (SII), and the motor area (M) in the left hemisphere. The right hand is controlled by the motor area in the left hemisphere, and the left hand is controlled by the equivalent area in the right hemisphere. The primary somatosensory areas lie between M and SII but they are not indicated in the figure. See text for details of lateralization.

thickness of the secondary somatosensory (SII) cortex, a region involved in processing tactile information from the hands and fingers and in somatosensory discrimination (Kaas, 2004; Krubitzer and Kaas, 1990; Qi et al., 2002). The significant positive correlation between SII and strength of right-hand preference was found for the SII region in both hemispheres. No relationship between hand preference and thickness of the corpus callosum was found, despite the fact that SII has strong callosal connections to SII in the contralateral hemisphere. The authors speculated from their results that increasing strength of right-hand preference might be associated with increasing ability to process somatosensory information. If this also applies across species, it might have implications for the evolution of right-handedness. Of more relevance to this chapter is the likely difference in sensory processing between left- and right-handed marmosets and the effect this has on behavior. These differences in brain structure could develop as a consequence of preferential use of the left or right hand during early life, as Michel et al. (2016) suggest, or the difference in brain structure could be a determinant of hand preference.

Structural differences between the hemispheres have also been found in chimpanzees. Hopkins et al. (2017) found that chimpanzees who performed a tool using task better with their right than with their left hand had greater leftward asymmetry in their homologue of Broca's area and in the hand-motor area of the precentral gyrus. The converse was also true for those that performed the task better with their left hand but in this case the effect was not as marked.

6 GENERAL DISCUSSION

Previously researchers have broadly assigned animals to one of two types of coping style, proactive and reactive, or active and passive (Keay and Bandler, 2001; Koolhaas et al., 1999). An individual may express its particular style of coping consistently throughout its life, although it may be not expressed in all contexts. Research on nonprimate species has shown consistency in individuals of level of aggression, activity, risk taking, fearfulness, and exploration (e.g., Boissy, 1995; Dingemanse et al., 2002; Sih et al., 2004). There is some evidence that clustering of behavior types occurs in individuals and hence may be referred to as personality (e.g., Øverli et al., 2004, for association of coping style and aggression; see also Koolhaas and de Boer, 2008).

From the experiments discussed in this chapter, we can conclude that right-handed marmosets, also chimpanzees and male macaques, are positive and actively interact with novel stimuli, whereas left-handed ones are negative and withdrawn (see Bateson and Matheson, 2007; Burman et al., 2008, for such polarization of types in other species). This polarization fits with the differing cognitive styles of left- and right-handers. Right-handed primates might also be described as proactive and left-handed as reactive. A recent study of common marmosets ($N = 21$) has found that individuals display consistent differences over time on four major dimensions considered to constitute personality: viz., boldness vs shyness both in foraging and in response to a predator (e.g., a snake), stress vs activity, and exploration vs avoidance (Šlipogor et al., 2016). The last dichotomy (exploration or approach vs avoidance) is most relevant to the experiments that I have discussed in relation to hand preference but hand preference was not measured in the study by Šlipogor et al. (2016).

Since the behaviors of marmosets discussed in this chapter are consistently related to hand preference and expressed when the animals are tested alone or in their social groups, they could be considered as personality traits. However, and despite attempts to allocate a constellation of the behavior of marmosets under the general term "personality" (e.g., Iwanicki and Lehmann, 2015; Koski and Burkart, 2015; Koski et al., 2017), I am not convinced that this terminology is useful at this time since using generalized terminology could obfuscate understanding and cloud future research. It is the case that different types of behavior are associated with left-hand preference and other types with right-hand preference but collapsing them under the single label of personality would not be advantageous at this stage of knowledge, although it might have value in application to issues of welfare (see Rogers, 2010, for more discussion of the implications of lateralization to animal welfare).

A convincing body of evidence shows that the right hemisphere of a wide range of vertebrate species is specialized to process social information, and this is manifested as a population bias to keep conspecifics on the left side (e.g., Gilov et al., 2018; Karenina et al., 2017; Quaresmini et al., 2014). Therefore, one could deduce that left-handed individuals might have a stronger propensity for social behavior. On this account, however, the data reported above for associations between hand preference and social behavior, in common marmosets and rhesus macaques, are equivocal. Nevertheless, one could predict that there might be differences in parenting style between left- and right-handed primates, and that should be possible to ascertain.

Future research on limb preferences and behavior in primate and nonprimate species should be able to broaden research on the links between limb/hand preferences and cognitive behavior and thus provide models for investigating both genetic and experiential influences on these behavioral expressions (Strökens et al., 2013; Versace and Vallortigara, 2015).

There is growing evidence that handedness may contribute to individual differences in cognitive/executive function of humans (Capizzi et al., 2017; Hardie and Wright, 2014). Indeed, as Sainburg (2014) has demonstrated, limb choice in humans depends on interaction between brain lateralization and specific sensorimotor demands of a task or context. In fact, Sainburg has shown that motor control of the left and right limbs matches the functional specializations of the right and left hemispheres, respectively, which broadens limb control from simple motor output to more general specializations of the controlling hemisphere. This generalization could embrace other hemispheric specializations typically associated with limb/hand preference (e.g., those patterns of behavior discussed in this chapter and associated with hand preference).

Some of the questions raised about potential association between behavior and hand preference in humans might be addressed in model species, at least in the first instance. The common marmoset is being used increasingly as a model for research in visual neuroscience (Mitchell and Leopold, 2015), auditory neuroscience, and vocal communication (Takahashi et al., 2013). As I hope this chapter illustrates, the marmoset is also a valuable model for understanding lateralization of the brain and behavior associated with hand preference in primates.

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CHAPTER

Mother and offspring lateralized social behavior across mammalian species

5

Karina Karenina[1], **Andrey Giljov**

Department of Vertebrate Zoology, Faculty of Biology, Saint Petersburg State University,
Saint Petersburg, Russia

[1]*Corresponding author: Tel.: +7-812-328-9689, e-mail address: zoology.gilev@gmail.com*

Abstract

Findings on nonprimate mammals place the issue of mother–infant lateralized relations in a broader context, demonstrating that humans are one of many species showing this feature. The remarkable interspecies consistency in the direction of lateralization points to a continuity between lateralized mother–infant interactions in primates and nonprimate mammals and suggests ancient evolutionary roots of human cradling bias. The results from species which, in contrast to primates, have no direct involvement of forelimbs in mother–infant spatial interactions clearly support the perceptual origin of this type of lateralization. A right hemisphere advantage for social functions relevant to mother–infant interactions is the most probable background for the left-sided biases in the behavior of mothers and infants. Recent findings suggest the contribution of lateralized mother–infant interactions to biological fitness. Mother and infant both can gain advantage from keeping the other on the left side.

Keywords

Cradling bias, Mother–child relations, Maternal monitoring of infant state, Lateralization in wild mammals, Hemispheric asymmetry, Holding bias, Nipple preference, Left eye bias

1 INTRODUCTION

Asymmetrical functioning of the nervous system and associated behavioral lateralization is pervasive in vertebrate and invertebrate animals (Rogers et al., 2013; Vallortigara and Versace, 2017). Current knowledge suggests that this phylogenetically ancient feature significantly contributes to biological fitness (MacNeilage et al., 2009; Vallortigara and Bisazza, 2002; Vallortigara and Rogers, 2005). The emergence of behavioral lateralization has long been theorized to be underpinned by selective advantages (Ghirlanda and Vallortigara, 2004; Ghirlanda et al., 2009; Rogers, 2000), and there is now an increasing amount of empirical evidence demonstrating that lateralized perception and reactions can confer fitness benefits.

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Results from diverse animal species, ranging from insects to fish to birds to mammals, demonstrate that stronger lateralized individuals outperform weakly lateralized individuals for cognitive and motor abilities in various tasks (e.g., Bell and Niven, 2016; Dadda et al., 2010; Gunturkun et al., 2000; Kurvers et al., 2017; Magat and Brown, 2009; Marchant and McGrew, 1996; Miler et al., 2017; Rogers et al., 2004). Furthermore, in fish, lateralized behavior is linked with improved cooperative activity in social interactions (Bisazza and Dadda, 2005; Chivers et al., 2016). In the context of this knowledge, it is now reasonable to consider any pronounced and stable lateral bias in behavior as a significant adaptation rather than a curious but incidental trait. Infant left-cradling/holding bias in humans has been regarded as a possible by-product of right handedness, greater detectability of the heartbeat on the left side or care-giving traditions for decades (Harris, 2010). However, the issue of lateralized relations between mother and infant has been placed in a broad context since it has become clear that humans are one of many species showing this feature (Karenina et al., 2017). Currently, lateralization of spatial positioning is considered to be an important mechanism supporting mother–infant bonding and interactions.

1.1 INFANT CRADLING/HOLDING BIAS IN HUMANS AND NONHUMAN PRIMATES

Left-cradling bias, viz., an infant, is preferentially positioned on the mother's left side, has been a reported for at least 350 years (Harris, 2010), while the first scientific study of this bias in humans was published in 1960 (Salk, 1960). The last five decades of focused investigation have proven this bias to be intriguingly universal. The preference to cradle, hold, or carry an infant on the left rather than right side of the body has been found in different cultures and periods of history (e.g., Finger, 1975; Harris, 2007; Harris et al., 2007). Left-cradling bias exists not only in mothers but in nulliparous female adults (Saling and Tyson, 1981) and even in female children from 6 years old (De Château and Andersson, 1976), indicating that the emergence of this lateralized behavior is not dependent upon motherhood or sexual maturity. In male children and adult nonfathers, the cradling bias is generally less pronounced than in females (Harris, 2010). At the same time, the majority of fathers do hold their infants on the left side (Harris et al., 2007; Scola and Vauclair, 2010).

In humans, one-sided bias in cradling is remarkably consistent across contexts. A life-like doll served as the "infant" in numerous studies of cradling bias, with consistent results obtained in the studies using a doll and a real infant (e.g., De Château and Andersson, 1976; Saling and Tyson, 1981; Vauclair and Donnot, 2005). Left-cradling bias is evident in adults even when they imagine holding an infant, but actually are holding an inanimate object like a ball or a pillow (Sperber and Weiland, 1973; Weiland and Sperber, 1970), or in the absence of any physical object (Nakamichi and Takeda, 1995). Furthermore, left-side cradling can be elicited in female, but not male, adults by noninfant animate objects, such as a dog (Abel, 2010). In general, cradling bias in females appears to be particularly stable and robust.

Studies on nonhuman primates have demonstrated that cradling preference is not unique to humans. Captive female gorillas (*Gorilla gorilla gorilla*) and chimpanzees (*Pan troglodytes*) prefer to cradle their infants on the left side (Manning et al., 1994). However, to the best of our knowledge, this bias has not been replicated in any other primate species. The studied species of nonhominid primates show individual, but no population-level preferences for maternal cradling (Hopkins, 2004). In common marmosets (*Callithrix jacchus jacchus*), population-level lateral bias for infant carrying has been found neither in mothers nor in fathers (Rogers and Kaplan, 1998).

In addition to parental cradling/carrying, infant preferences for one of the mother's nipples have been reported in nonhuman primates. Left nipple preference is evident in wild and captive chimpanzees, and captive bonobos (*Pan paniscus*) (Hopkins and De Lathouwers, 2006; Nishida, 1993). In addition, less clear preference for the left nipple disappearing after the first 3 weeks of life has been found in captive rhesus macaques (*Macaca mulatta*) (Tomaszycki et al., 1998). Other primate species studied show only individual nipple preferences, with no lateral bias at the population level (Hopkins, 2004; Zhao et al., 2008). It is suggested that nipple preferences are associated with maternal lateralization (Nishida, 1993) since there are significant positive correlations between carrying bias in mother and nipple preference (Rogers and Kaplan, 1998).

1.2 WHEN LEFT IS RIGHT: LATERAL PREFERENCES IN MOTHER AND INFANT IN RELATION TO BRAIN LATERALIZATION

Human studies have shown that cradling bias is associated with mother–infant attachment and, more generally, with basic socioemotional processes. Preference to cradle on the left is reduced in individuals that are stressed, depressed, or deficient in empathy (Fleva and Khan, 2015; Pileggi et al., 2015; Reissland et al., 2009; Suter et al., 2007; Weatherill et al., 2004). For example, both children and adults high on autistic traits show a reduced left-cradling bias (Fleva and Khan, 2015; Pileggi et al., 2015). These recent findings provide support for a long-standing hypothesis that leftward bias in infant positioning results from right hemisphere advantage for social processing (Manning et al., 1994; Sieratzki and Woll, 1996). When an infant's face is to the left of its mother's body midline, the visual and auditory information about the infant is predominantly transferred to, and processed by, the mother's right hemisphere. The right hemisphere plays a crucial role in social processing and is more accurate and faster than the left in performing a variety of social cognition tasks (Brancucci et al., 2009; Lindell, 2013). Furthermore, human maternal behavior is assumed to be predominantly mediated by the right hemisphere (e.g., Bourne and Todd, 2004; Huggenberger et al., 2009; Lorberbaum et al., 2002; Minagawa-Kawai et al., 2009). The left-sided position of the infant may facilitate maternal monitoring of infant's well-being and her responding to the signs of distress expressed by the infant (Manning et al., 1994). Indeed, the preferred cradling side is contralateral to the hemisphere dominant for face and emotion processing (the right hemisphere in the majority of individuals) (Bourne and Todd, 2004; Vauclair and Donnot, 2005). Females who preferably cradle on the left more successfully recognize infant facial expressions presented to their left visual field (Huggenberger et al., 2009).

The left-sided position relative to mother has been suggested to be beneficial for the infant itself, since the most expressive, left side of mother's face is more visible to the infant (Vauclair and Donnot, 2005). This could enhance infant's perception of its mother's emotional state and, consequently, facilitate face-processing development. An experimental study, where mothers were asked to pick up an "infant" doll with an inbuilt camera in its face, showed that less of the mother's face was visible when the "infant" was held on their right than when it was held on their left (Hendriks et al., 2011). This result is a plausible explanation of a reduced "normal" left visual bias for recognizing faces in adults whose mothers had had a right-side preference for holding them as infants (Vervloed et al., 2011). Thus, left-side cradling provides the infant with optimal face exposure and, presumably, optimal development of face and emotion processing.

To conclude, cradling bias reflects socioemotional processes and is relevant to mother–infant relationships. It appears that the left side is the right side in terms of infant cradling\holding since it characterizes efficient communication and bonding between mother and her infant (Sieratzki and Woll, 2002).

1.3 AN EVOLUTIONARY PERSPECTIVE ON LATERALIZED MOTHER–INFANT RELATIONSHIPS IN PRIMATES

A variety of studies demonstrate that lateralized mother–infant relationships are associated and, likely, originate from lateralization of basic brain functions, such as social processing and cognition. That is, this behavioral bias reflects a more general division of functions between hemispheres, rather than a distinct specialization. The right hemisphere advantage for socioemotional processes is argued to arise from an ancient evolutionary ability of the right hemisphere for recognition of identity or familiarity (MacNeilage et al., 2009). The ancient evolutionary origin of lateralized social behavior is corroborated by the diversity of species showing a common pattern of asymmetrical implementation of social functions. In a variety of vertebrates, the right hemisphere plays a crucial role in a number of social cognition tasks ranging from face and emotion recognition (Lindell, 2013) to spatial coordination (Nagy et al., 2010) and social learning (Daisley et al., 2009). Within this context, one can expect lateralized mother–infant relationships not to be a new, primate-unique characteristic, but to emerge well before the primates in the course of evolution. Taking into account that lateralized positioning may be beneficial for both mother and infant, it is reasonable to suggest a prevalence of lateralization of mother–infant spatial interactions across other mammalian groups. The rapid expansion of knowledge during the last decade has confirmed this assumption. Here, we highlight the recent advances in our understanding of behavioral lateralization in mothers and offspring across nonprimate mammals and discuss their consistency with primate studies.

2 LATERALIZATION OF INFANTS' PERCEPTION OF MOTHER

The leftward bias in cradling is thought to reflect the maternal rather than infant's preference, although the potential influence of infant's behavior on mother's cradling side cannot be excluded (Scola et al., 2013). For example, it is hypothesized that in chimpanzees, the left-sided position of the infant may arise from not only mother's preference but also from the infant's motor bias (Hopkins, 2004). The greater strength and postural development of the right forelimbs shown for infant chimpanzees may lead to infants positioning themselves more so on mother's left side when clinging the mother's chest (Hopkins, 2004). Studies in human and nonhuman primates typically record the mothers' side preference when picking up the infant (e.g., Todd and Banerjee, 2016) or the resulting position of mother–infant dyad (e.g., in photographs; reviewed in Harris, 2010). Nonprimate mammals, with much less involvement of limbs in mother–infant spatial relations, offer an opportunity to trace the impact of mother and infant on lateralization separately. In mammal species, those infants are significantly more spatially independent from their mothers than are primate infants, lateral preferences in the positioning relative to mother have been investigated.

2.1 APPROACHES TO INVESTIGATING LATERALIZED INFANTS' BEHAVIOR

To date, a range of phylogenetically and ecologically diverse species has been studied in terms of infants' preferred lateral position near the mother (Fig. 1). Lateralization has been assessed in various infants' behaviors ranging from slow traveling and fleeing to suckling and resting. A wide variety of methods are applied for investigation of lateralized infant's behavior. For example, domestic sheep (*Ovis aries*) lambs have been tested in an experimental task in which they faced a transparent obstacle and should avoid it on either the right or left side to rejoin their mothers (Versace et al., 2007). Since the mothers were visible during the obstacle avoidance, the choice of the side determined the visual field (left or right) in which lambs kept their mothers. An unusual approach has been applied in beluga (*Delphinapterus leucas*) and southern right whales (*Eubalaena australis*)—the preferable calves' position near the mother has been estimated based on the analysis of aerial photographs of traveling mother–calf pairs (Karenina et al., 2013a, 2017). Other mammal species have been studied using observational approach, with the particular method varying according to the species. In humpback whales (*Megaptera novaeangliae*) (Zoidis and Lomac-MacNair, 2017) and belugas (Karenina et al., 2010), mother–calf spatial interactions have been recorded using underwater video documentation techniques. Boat-based observations have been used for orcas (*Orcinus orca*) (Karenina et al., 2013b), while the behavior of Pacific walrus (*Odobenus rosmarus divergens*) has been observed from a cliff top, with the observer remaining unnoticed by the animals (Karenina et al., 2017). Observations of terrestrial species, such as, for example, Siberian tundra reindeers (*Rangifer tarandus sibiricus*) and argali sheep (*Ovis ammon*), have been conducted on foot by the

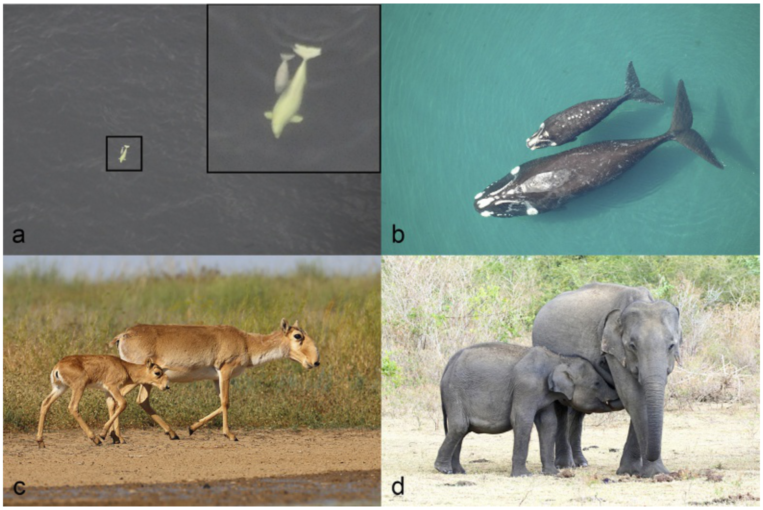

FIG. 1

Infant in a lateral position relative to the mother. (A) Beluga whale (*Delphinapterus leucas*; aerial photograph). (B) Southern right whale (*Eubalaena australis*; aerial photograph). (C) Saiga antelope (*Saiga tatarica tatarica*). (D) Asian elephant (*Elephas maximus*).

Panels (A)–(C): Reprinted from Karenina, K., Giljov, A., Ingram, J., Rowntree, V.J., Malashichev, Y., 2017. Lateralization of mother–infant interactions in a diverse range of mammal species. Nat. Ecol. Evol. 1, 0030. Panel (D): Reprinted from Karenina, K., Giljov, A., De Silva, S., Malashichev, Y., 2018. Social lateralization in wild Asian elephants: visual preferences of young and mothers. Behav. Ecol. Sociobiol. 72, 21.

observers in camouflage clothing which minimized disturbance approaching animals by crawling and using features in the landscape to hide (Karenina et al., 2017).

The numbers of data points obtained per individual infant also vary according to the species and type of behavior. Multiple observations of lateral position choice per infant have been used for estimation of individual preferences and population-level analyses based on scores from an individual laterality index (LI) (e.g., Forrester et al., 2014; Karenina et al., 2013b, 2017). A LI was calculated for each individual using a formula: $LI = (L - R)/(L + R)$, where L and R are the number of times the infant chose to keep the mother on the left or right side, respectively. LI scores range on a continuum from -1.0 to $+1.0$, with negative values indicating the right-side bias and positive values indicating the left-side bias.

When the collection of multiple data points was not possible, single observations have been used for estimation of population-level bias only. In case of simple dichotomy into right- vs left-sided response (or choice), single observations per individual have repeatedly proven to be an adequate method for estimation of population-level biases (e.g., Bourne and Todd, 2004; Chapelain et al., 2015; Coren, 1993; Giljov et al., 2017; Hill et al., 2017; Siniscalchi et al., 2012). Furthermore, recent studies of lateralized mother–infant interactions in a variety of mammal species showed that the results of population-level analyses based on multiple and single observations (on the same behavior and/or population) were consistent, indicating the similar lateral bias (Hill et al., 2017; Karenina et al., 2010, 2013a,b, 2017, 2018a,b). The robustness of the lateral biases in the behavior of mothers and infants appears to improve comparability between studies and approaches.

2.2 INFANTS' LATERAL POSITION PREFERENCES

In the majority of mammal species studied, infants prefer to keep their mothers in the left hemispace, i.e., in the left visual field (Giljov et al., 2018; Karenina et al., 2017, 2018a,b). This bias has been revealed using different types of analysis across various behaviors. A left-sided preference in infants is evident not only in routine behaviors such as traveling, resting, and approaching the mother for suckling, but also in fleeing associated with potentially dangerous and stressful situations, as shown in feral horses (*Equus ferus caballus*), muskoxen (*Ovibos moschatus*), gray (*Macropus giganteus*), and red kangaroo (*Macropus rufus*; Karenina et al., 2017). A comparative study summarizing the data on 10 species in which LI scores (based on multiple data points per individual infant) have been calculated has shown a consistent left visual field bias (Fig. 2A).

A greater number of species (Fig. 2B) have been investigated to date based on single observation per individual infant. A meta-analytic approach to interspecies analysis revealed a consistent prevalence of left-sided bias in infants across 14 species, as indicated in the forest plot (Fig. 2B). The lateralization in nonprimate mammals corresponds with lateralized spatial positioning within proximity of adults in human children. Natural and spontaneous lateral navigational routes of children around adults have been observed unobtrusively in a naturalistic environment within a public play area and a school playground (Forrester et al., 2014). In both locations, a rightward navigational path favoring the left visual field use was preferred by children. This study showed a lateral bias in human children comparable to that found in nonprimate infants (Karenina et al., 2017). In both studies, immature individuals prefer to keep an adult conspecific in the left visual field when actively approaching it. The human study, though, does not specify whether an adult was a mother of the child or not (this was not possible owing to the method applied), but most likely the left visual bias would be evident if mother–child interactions are specifically investigated.

2.3 LATERALIZED SUCKLING POSITION

The results of studies investigating lateralization of suckling in mammal infants appear to be not as straightforward as those of studies examining other types of infant behavior. In cetaceans, the lateral biases in suckling position of the calf have been reported in sperm (*Physeter macrocephalus*) (Gero and Whitehead, 2007) and humpback whales (Zoidis and Lomac-MacNair, 2017). Peduncle dives (calves' dives underneath the mother's rear portion of the torso assumed to be indicative of suckling) occur predominantly on the left side of the mother in sperm whale. In contrast, humpback whale study (Zoidis and Lomac-MacNair, 2017) shows that, within a

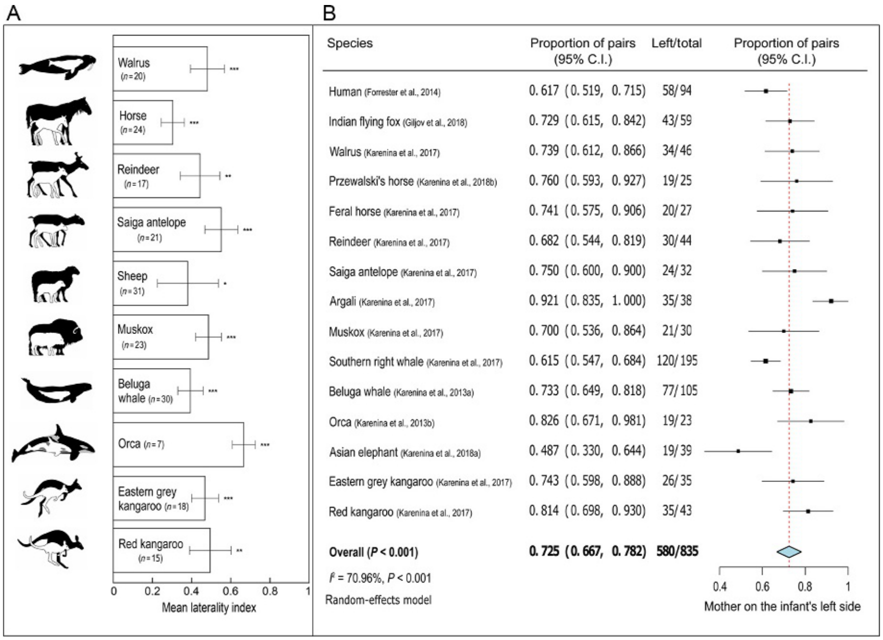

FIG. 2

Consistent lateralization of infants' active choice of spatial position near the mother/adult. (A) Mean laterality index scores based on multiple choices of lateral position from each individual infant indicate a population-level preference for keeping the mother on the *left side* in 10 species of mammals. The score for domestic sheep was calculated on experimental data for 3- to 6-month-old lambs approaching their mothers from Versace et al. (2007). For all other species, the data on slowly traveling pairs observed unobtrusively in the wild were used. Significantly positive values indicate left-side bias. *Error bars* indicate the SEM. Population-level bias was tested using a one-sample Wilcoxon signed-rank test in all species, except orca in which one-sample *t* test was used. $*P<0.5$, $**P<0.01$, $***P<0.001$. (B) Consistent lateralization of active choice of spatial position near the adult. Forest plot for random-effects meta-analysis of proportions of lateral position choice by infants demonstrates the general consistency of lateralization in 14 nonprimate mammal infants and human children. Analysis is based on the single choice of lateral position per individual. For human children (4–11 years old) data on approaching adults within a school playground (M-Population from Forrester et al., 2014) were used. For each species, the proportion of infants/children, who chose to keep the mother/adult on the *left side*, is presented. *Horizontal lines* indicate individual 95% confidence intervals and *rectangles* reflect the point estimate of individual species. The *diamond* reflects the pooled overall estimate (95% C.I.) across all species. *C.I.*, confidence interval.

Modified and reprinted from Karenina, K., Giljov, A., Ingram, J., Rowntree, V.J., Malashichev, Y., 2017. Lateralization of mother–infant interactions in a diverse range of mammal species. Nat. Ecol. Evol. 1, 0030.

small sample studied, calves positioned itself on the right side of the mother when suckling. Both these reports (Gero and Whitehead, 2007; Zoidis and Lomac-MacNair, 2017) analyze only the stationary position of the calf, while the majority of other studies of lateralized infant behavior in nonprimate mammals examine mother–infant joint traveling or the infant's active approaches to the mother (Karenina et al., 2013b, 2017, 2018a,b). When only the position during suckling is recorded, it remains unknown whether the mother moved toward the calf and, consequently, influenced the suckling position or the calf itself approached the mother and chose the position. Therefore, further investigation is needed to gain a better understanding of lateralized suckling in cetaceans.

The assessment of lateralization based solely on the suckling position of the infant has many limitations also in terrestrial mammals. The foals' preferences for suckling side have been examined in domestic horses (*Equus caballus*) and zoo populations of three zebra species (*Equus* spp.), with no population-level bias revealed (Komárková and Bartosová, 2013; Pluháček et al., 2013). In these works, the side of suckling was the only analyzed category. More recent studies, in contrast, consider the behavior of foals prior to suckling. The foals' approaches to the mare for suckling are strongly lateralized in both feral (Karenina et al., 2017) and Przewalski's horses (*E. ferus przewalskii*) (Karenina et al., 2018b). Importantly, two types of approaches have been distinguished and separately analyzed (Fig. 3). First, preference to keep the mother on the left has been revealed in approaching for suckling without a detour. In this type of behavior, the foal approached the standing mother from behind, stopped on one side of her, and then turned to the mother's udder for suckling. Second, left-sided visual preferences have been observed in foals'

FIG. 3

Two types of foal's approaches to mother for suckling in Przewalski's horses (*E. ferus przewalskii*). The sequence of foal's movements is presented from the *left* to the *right*. *Top line*: approaching for suckling without a detour. *Bottom line*: approaching for suckling with a detour. The side on which the foal kept its mother initially (second frame in each line) was recorded to assess visual lateralization. The results showed that foals preferentially keep the mother on the *left side* when approaching her regardless of the side of her body they reach for suckling.

Reprinted from Karenina, K., Giljov, A., Malashichev, Y., 2018b. Lateralization of mother-infant interactions in wild horses. Behav. Processes 148, 49–55.

approaches for suckling with a detour. In these cases, the foal made a detour around its traveling mother, presumably, to stop her and to be able to suckle. In this type of approach, the foal first approached the mother from behind and then took a lateral position near her. Next, the foal continued to move around the mother's front in order to reach the opposite side of her body and started suckling. Thus, foals preferentially keep the mother on the left side when approaching her regardless of the side of her body they reach for suckling. The different types of approaches resulting in different side positions of the foal during suckling may explain the absence of population-level biases in the earlier studies that considered only the final positioning of the foal (Komárková and Bartosová, 2013; Pluháček et al., 2013). To conclude, lateral bias may not be pronounced in the infants' suckling positioning, but be evident in infants' movements prior to suckling. The suckling position itself appears to be not informative enough for estimation of lateral preferences infants' behavior toward the mother.

Another confounding factor in the assessment of lateralized suckling may be the asymmetry of milk production. In lactating red deer (*Cervus elaphus* spp.) hinds, lateral differences have been recently found for daily yield, being greater in the left teats than in the right ones (Ceacero et al., 2016). The authors hypothesized that differences in the milk production between the teats can result in suckling preferences in infants. The left-sided milk production could potentially be present in other mammals and explain left mammary gland preference in chimpanzees (Nishida, 1993), bonobos (Hopkins and De Lathouwers, 2006), and sperm whales (Gero and Whitehead, 2007), but not the absence of suckling side preference in domestic horses (Komárková and Bartosová, 2013) and zebras (Pluháček et al., 2013).

Lateralized suckling becomes even more difficult to interpret when considering suckling and nipple attachment separately. Suckling is usually defined as a contact of infant's mouth with the mother's teat/udder (Karenina et al., 2017; Komárková and Bartosová, 2013), although nipple contact may be just comfort for the infant and does not necessarily include suckling. In Indian flying foxes (*Pteropus giganteus*), pups have no lateral bias in the frequency of the use of the left and right nipples; however, episodes in which pups are attached to the left nipple are longer than the episodes attached to the right nipple (Giljov et al., 2018). Attachment to the left nipple favors keeping the mother in the left visual field, which is supposed to be a more comfortable position for the infant. Overall, lateralization of suckling requires a multifaceted analysis, which is not always possible in the natural setting. The lateral preferences in infants' positioning prior to suckling may be more informative for estimation of lateralization of an infant's perception of their mother. For example, in Przewalski's horse (Karenina et al., 2018b) and Pacific walrus (Giljov et al., 2018), infants' lateral preferences prior to suckling are consistent with those in other types of behavior.

2.4 POTENTIAL CONFOUNDING FACTORS

A variety of intrinsic and environmental factors can significantly influence the manifestation of behavioral lateralization. For example, lateral biases in particular behavioral responses have been reported to be modified by space availability

(Zucca et al., 2011), predation risk (e.g., Brown et al., 2007; Ferrari et al., 2017; Lucon-Xiccato et al., 2016), stress (reviewed in Rogers, 2010), and social environment (Bennett et al., 2008; Quaresmini et al., 2014). General consistency between the majority of species and majority of behaviors suggests the stability of a manifestation of lateralization in infant's perception of the mother in mammals. Indeed, calves' lateralized spatial position relative to mother in beluga whales is preserved in different environmental conditions and populations (Hill et al., 2017; Karenina et al., 2013a). Considering terrestrial mammals, lateral preferences in foals' behavior toward the mother in an island population of feral horses have been confirmed in the study on a wild equid—Przewalski's horse (Karenina et al., 2018b). This finding implies that lateralized social behavior of foals is a robust trait of equine behavior, not elicited by domestication or specific environmental conditions of the studied population. Intriguingly, Przewalski's horse foals show even stronger preference for the use of the left eye for monitoring the mother when traveling than feral horse foals (Karenina et al., 2018b).

Intrinsic factors appear to be more influential in the manifestation of lateralized perception of the mother in mammal infants. The ontogenesis of lateralized positioning relative to the mother has not been studied longitudinally using the same individuals at different developmental stages. Nevertheless, the comparison of lateralization in different age classes (cross-sectional approach) has been employed in six species of nonprimate mammals (Giljov et al., 2018; Karenina et al., 2013a,b, 2017, 2018a). The only significant effect on lateralization found was in beluga whales. A significant preference to keep the mother on the left was evident in all age classes, but 2- to 6-month-old belugas were more strongly lateralized than the newborns and 7- to 18-month-old calves. The differences in the strength of lateralized behavior have been suggested to be associated with general developmental changes in calves' behavior (Karenina et al., 2013a). In primates, the changes in the expression of nipple preferences have been traced for the first 6 weeks of life in captive rhesus macaques, with left nipple preference for the first 3 weeks, and no preference after 3 weeks (Tomaszycki et al., 1998). Sex-related differences in offsprings' lateralized behavior have been tested in five nonprimate mammal species (Karenina et al., 2017, 2018a,b). Except for one species, there was no significant effect of sex. In Asian elephants (*Elephas maximus*), young daughters and sons showed strikingly different lateralized behavior toward the mother that may have resulted from distinct social strategies of the two sexes (Karenina et al., 2018a; discussed in detail in Section 4.3).

2.5 RIGHT HEMISPHERE ADVANTAGE FOR AN INFANT'S PERCEPTION OF THEIR MOTHER

The overall evidence indicates that lateral biases in infants' spatial positioning near the mother, at least when the infant actively chooses the position, reflect a preference to keep the mother in their left hemispace. The specificity of lateralization has been tested in children (Forrester et al., 2014) and feral horse foals (Karenina et al., 2017).

In both species, no population-level bias was found in the control condition—choosing a position relative to stationary inanimate objects. Furthermore, the preference for a particular side of the mother's body (e.g., owing to the asymmetrical lactation) cannot explain the lateralized infants' behavior. Feral horse foals and saiga antelope (*Saiga tatarica tatarica*) calves preferentially keep the mother on the left side when approaching her for suckling from different sides of her body. Similarly, Pacific walrus calves prefer to keep mother on the left side when resting both in a codirected position and in a counter-directed position relative to the mother (Karenina et al., 2017). Thus, infants preferentially position the mother in the left hemispace regardless of which side of the mother's body is exposed to them.

As supported by a wide range of vertebrate studies (Rogers et al., 2013), one-sided preferences in spatial positioning, relative to a stimulus, arise from the asymmetrical use of the lateral visual fields of the left and right eye underpinned by hemispheric lateralization. This interpretation of one-sided behavioral biases is straightforward in species with laterally positioned eyes and little binocular vision (Rogers, 2017b). The majority of nonprimate mammals investigated for lateralized mother–infant interactions have this type of visual system. When the mother is on the left side of the infant, the visual information about her is primarily transferred to and processed by the infant's right hemisphere.

In humans, the right hemisphere controls many aspects of social perception (Brancucci et al., 2009, but see, e.g., Prete et al., 2015 for the valence-dependent involvement of both hemispheres). The right hemisphere plays an important role in the recognition of conspecific faces, which is one of the key functions in human social cognition (Lindell, 2013). Based on a growing body of evidence, the right hemisphere advantage for face perception is assumed to evolve from more basic abilities of early vertebrates to recognize the visual appearance of conspecifics (MacNeilage et al., 2009). Lateralization of infants' social behavior supports the continuity in lateralized social cognition in humans and other mammals. Typically developing human infants show a left visual field (right hemisphere) superiority for adult face perception (reviewed in Dundas et al., 2012). In infants of nonprimate mammals, the right hemisphere advantage for the perception of adult conspecifics elicits predictable lateralized positioning already evident in newborns (e.g., Karenina et al., 2013a). In human infants who are significantly less spatially independent, the comparable positional lateralization can be observed at a later age (Forrester et al., 2014). Overall, the findings in humans and nonhuman mammal species are strikingly congruent implying an ancient evolutionary origin of infants' lateralized social behavior, and its underlying brain specialization.

The empirical evidence suggests that the left-sided visual preferences in infants are a part of a more general lateralization than a specific response to the mother. Human children prefer to keep a peer on the left when choosing a navigational path around it (Forrester et al., 2014). A preference to keep age-mates to the left rather than the right side has been also found in nonhuman mammals, such as muskox, saiga antelope, feral horse (Karenina et al., 2017), beluga whale (Karenina et al., 2010), and orca (Karenina et al., 2013b). The similar lateralized positioning relive to social stimuli during naturalistic encounters has been reported for in great apes (Quaresmini et al., 2014). Much like infants of nonprimate mammals, captive gorillas and chimpanzees tended to keep social partners on the left compared to the right side. The general left-side bias of infant's social perception may be underpinned by the attentional bias for the left visual hemifield, implicating the right hemisphere. The dominance of the right hemisphere for visuospatial attention has been reported in both human infants (Fogel et al., 1990) and human adults (De Schotten et al., 2011), as well as in nonhuman vertebrates (Rogers, 2002).

3 LATERALIZATION OF MOTHERS' PERCEPTION OF INFANT

In human and nonhuman primates, mothers can regulate infant's physical positioning according to their lateral preferences when cradling. In contrast, in many nonprimate mammals, mothers cannot easily move their infants and have to move themselves instead to keep the infant on the preferred side of the body. Despite these differences in mother–infant spatial interactions, studies of primates and nonprimates have shown that mothers can actively choose to keep their offspring predominantly in one hemispace.

3.1 MATERNAL PREFERENCES FOR THE LATERAL POSITION FAVORING RIGHT HEMISPHERE PROCESSING

Among nonprimate mammals, the preference to keep the infant predominantly on the left side was first reported for orca mothers (Karenina et al., 2013b). Boat-based observations on mother–calf pairs showed that at close distance to a research boat, i.e., in a potentially dangerous and stressful situation, the calves were more likely observed on the mother's left rather than right side. However, in this study, it was not possible to record an active choice of lateral position in mothers, and maternal preferences were interpreted based on indirect behavioral cues only. Further investigations on terrestrial mammals have allowed for a straightforward assessment of lateralized behavior in mothers. In feral horses and wild eastern gray kangaroos, maternal lateral preferences appear to be behavior-type-specific. Mothers of these species show no lateralization at the individual or population levels when choosing a position relative to their infants during routine slow traveling (Karenina et al., 2017). Conversely, stressful situations, such as fleeing caused by a disturbance, elicited, in mothers, pronounced preferences for keeping their young on the left side, i.e., for positioning the young predominantly in the visual field of the left eye. These findings suggest that the manifestation of a left visual preference in mothers of these species is associated with the increased need to monitor the infant in an unsafe environment. This resembles the results of human mothers showing a left-cradling bias that is most pronounced during the first weeks of an infants' life when the monitoring of infant's state is most critical (Todd and Banerjee, 2016).

In two nonprimate mammals, however, maternal preference to keep the infant on the left has been found even in routine behaviors. In contrast to feral horse mares displaying lateralized positioning relative to the foal only when fleeing (usually caused by agonistic interactions between nearby conspecifics), Przewalski's horse mares preferentially keep their offspring in the visual field of their left eye during slow traveling (Karenina et al., 2018b). This inconsistency between closely related subspecies may be linked to the different environmental conditions of the studied horse populations, such as different levels of predation pressure. There is strikingly higher risk of predation on foals in the Przewalski's horse population (Dorj and Namkhai, 2013) compared with the feral horse population studied (Karenina et al., 2017). The enhanced need to control the foal's state in Przewalski's horses may explain the manifestation of maternal lateralization even in routine behavior such as when traveling slowly during grazing. This is consistent with the studies reporting stronger lateralization in high predation risk individuals/situations as compared to low-risk individuals/situations (e.g., Brown et al., 2007; Ferrari et al., 2017; Lucon-Xiccato et al., 2016).

Maternal lateralization in routine behaviors has been also reported for Asian elephants studied in Uda Walawe National Park, Sri Lanka (Karenina et al., 2018a), with significant preference to keep calves in the left visual field found in mothers during slow traveling. No other populations of elephants have been studied to date to compare with Uda Walawe elephants. It is possible that maternal lateralization during routine behaviors may be associated with increased stress in mothers from this population. Uda Walawe is one of the most visited national parks in the country, and the local elephant population is exposed to significant tourism-induced disturbance (Ranaweerage et al., 2015). It has been suggested that, in mammals, stress is associated with increased activity of the right brain hemisphere which responds to unexpected stimuli and controls emergency responses (Rogers, 2010). Thus, one could suggest that left eye (right hemisphere) preferences are pronounced in elephant mothers even in routine circumstances owing to the chronically elevated stress level. Alternatively, robust maternal lateralization may be a characteristic of Asian elephants not elicited by the specific characteristics of habitat (Karenina et al., 2018a).

In conclusion, evidence suggests that the preference of mothers of nonprimate mammals to keep their infants on the left side is elicited by particular behaviors associated with disturbance and stress, but also can be manifested in routine activities. Potentially, the differences in the manifestation of maternal lateralization are associated with environmental factors, e.g., predator pressure or anthropogenic disturbance. The results from nonprimate mammals are generally in line with the findings in primates. A great number of studies demonstrate the left-sided preference in infant cradling, holding, and carrying in human mothers (e.g., Finger, 1975; Harris, 2007; Harris et al., 2007). For example, when mothers are asked to pick up their infant and to sit holding him/her in any way that they feel comfortable, the left-side holding bias is preserved across repeated trials (Todd and Banerjee, 2016). The preference to cradle infants on the left side is also evident in great apes

(Manning et al., 1994). Initial explanations of left-cradling bias such as handedness (i.e., keeping the dominant right hand free for manipulations) and heartbeat (which is more detectible for an infant on the left side of the mother's chest) have been called into question by the revealing of left-sided bias in left-handed mothers (Salk, 1960; reviewed in Harris, 2010) and a mother with dextrocardia (the heart positioned on the right side of the body (Todd and Butterworth, 1998), respectively. Moreover, role of visual monitoring in the emergence of maternal lateralization has been demonstrated experimentally (Manning and Chamberlain, 1991). The covering of the left eye of the mother with an opaque patch significantly reduced left-cradling bias, which was evident when both eyes were open. In contrast, occluding the right eye had no effect on left-cradling bias. This finding implies that the preference to position an infant on the left is underpinned by left visual field use in mothers.

Recent studies further support the explanations of left-sided infant positioning that focus on improved maternal monitoring of infant's state (Todd and Banerjee, 2016) and, more generally, improved mother–infant bonding (Sieratzki and Woll, 1996, 2002). These explanations fit in a more general theory according to which the right hemisphere plays a dominant role in social attachment (e.g., Hecht, 2014; Lorberbaum et al., 2002; Nagasawa et al., 2013), broader emotional interactions (e.g., Packheiser et al., 2018), and maternal bonding toward infants (Bourne and Todd, 2004; Huggenberger et al., 2009; Minagawa-Kawai et al., 2009). Indeed, in adult humans, images of infants are prioritized by the attention system as strong emotionally positive stimuli with high biological significance when presented in the left visual field (Brosch et al., 2007). In contrast, images of infants of other mammal species (puppies and kittens) do not capture attention under the same experimental conditions. These findings imply an adjustment of the human right brain hemisphere to the perception of conspecifics' infants. The consistent lateral preferences in mothers of phylogenetically diverse mammals (e.g., Proboscidea, Primates, Perissodactyla, Diprotodontia) suggest that the dominant role of the right hemisphere in the perception of the offspring is a fundamental characteristic of mammalian maternal behavior.

3.2 FACTORS AFFECTING LATERALIZATION IN MOTHERS

The type of behavior can determine the expression of maternal lateralization in nonprimate mammals, as discussed earlier. Other factors potentially affecting the lateralized behavior of mothers toward their infants have not been studied in-depth. In three species studied to date, it was possible to record the infant's sex in relation to maternal lateral preferences. In Asian elephants (Karenina et al., 2018a), feral horse, and gray kangaroo (Karenina, 2016), mothers preferentially kept their young in the visual field of the left eye regardless of the young's sex. In contrast, some primate studies report the effect of infant's sex on lateralization in mothers. In one study, left-holding bias in women was found to be stronger for male infants than for female infants (Lockard et al., 1979). The same trend has been shown in gorillas, with more male than female offspring held on the mother's left side

(Manning et al., 1994). In addition to sex, the age of the infant appears to influence the magnitude of the left bias in humans. The cumulative body of evidence indicates [edits query]the maternal preference to hold on the left peaks for newborns and infants less than 1 year old, and then declines as infants mature (reviewed in Harris, 2010; Todd and Banerjee, 2016). Among nonprimate mammals, the lateralization in mothers with offspring of different age classes has been compared in feral horse. In contrast to humans, no effect of infant's age on the manifestation of left-side preference in mothers has been found (Karenina, 2016). Further research is clearly needed to estimate whether maternal lateralization is influenced by infants' age and sex and whether the individual characteristics of the mother itself (such as, e.g., age, maternal experience, and social status) can determine the degree of the left visual bias.

4 COSTS AND BENEFITS OF LATERALIZED MOTHER–INFANT INTERACTIONS

Current theories consider lateralization as a behavioral trait having fitness consequences in intra- and interspecific interactions with other organisms (Ghirlanda and Vallortigara, 2004; Ghirlanda et al., 2009; MacNeilage et al., 2009; Vallortigara and Rogers, 2005; Vallortigara and Versace, 2017). That is, the manifestation of one-sided biases in the animals' behavior is determined by costs and benefits associated with lateralized responses. The robustness and consistency of lateralization in mother–infant interactions in mammals suggest that its benefits significantly outweigh its costs. The right hemispheric advantage for many aspects of social processing appears to be a pervasive and ancient feature of vertebrates (reviewed in Brancucci et al., 2009; Lindell, 2013; MacNeilage et al., 2009). Assuming that, in mammals, the right hemisphere is specialized for social functions relevant for mother–infant interactions, keeping the mother in the left visual field is beneficial for the infant, and, at the same time, keeping the infant in the left visual field is beneficial for the mother (a potential spatial conflict between mother and infant is discussed in Section 4.2).

The overall evidence demonstrates significant advantages of the greater involvement of the left eye—right hemisphere system in the communication between mother and infant (discussed in Section 4.1). The potential costs of left-sided bias for infants and mothers may be associated with the limited use of the left visual field for perception of other types of stimuli. For a large range of vertebrate species, the right side of the brain is more responsive to threatening and alarming stimuli (Rogers, 2010). Besides the social processing, the right hemisphere controls the visual perception of danger (predators and conspecifics during agonistic interactions) and novelty (unexpected stimuli) (e.g., MacNeilage et al., 2009; Rogers, 2017a; Siniscalchi et al., 2010). The positioning of the other pair member on the left side may reduce the success of rapid recognition of threatening and alarming stimuli by distraction and partial obstruction of the left visual field. That is, the processing of the competing stimuli (nonsocial) may be disadvantaged when the social partner is in the left visual field. This may play a more significant role for mothers, since infants can rely on the recognition of dangerous situations by its mother. The paucity of studies makes the negative contribution of behavioral lateralization to biological fitness speculative, while the benefits conferred by the enhanced right hemispheric social processing are empirically confirmed.

4.1 ADVANTAGES OF GREATER RIGHT HEMISPHERE INVOLVEMENT FOR MOTHER AND INFANT

A crucial role of the right hemisphere in the encoding of socially significant visual information in the appearance of conspecifics can be manifested in form of lateralized processing of social stimuli in the visual periphery. For example, discrimination between emotional (babies, erotica, human attack, etc.) and neutral scenes in humans is more accurate and faster when the emotional scene appears in the left than in the right visual field (Calvo et al., 2015). This suggests that when an infant's face is in the mother's left peripheral visual field during left-sided cradling/carrying, she may gain improved performance extracting affective significance from the visual information about the infant. Based on this concept, the position of the infant on the mother's left side signifies closer maternal attention and care as a consequence of predominant right hemisphere activation (Manning et al., 1994). This is consistent with the lack of left-cradling bias in people who are deficient in empathy (Fleva and Khan, 2015; Pileggi et al., 2015).

In nonhuman mammals, mothers also may gain improved infant's state recognition by keeping the infant on the left side. Right hemisphere advantage for emotion recognition evolved well before humans (Lindell, 2013; MacNeilage et al., 2009). For example, nonhuman primates prefer the position favoring the left visual field (right hemisphere) involvement in the monitoring of conspecifics in both agonistic (Casperd and Dunbar, 1996) and affiliative (Boeving et al., 2017) interactions. Additionally, in sheep, the right hemisphere has been shown to play the pivotal role in discriminating between images of the same individual's face when calm and stressed (Kendrick, 2006). Thus, the left-sided rather than right-sided position of the infant can provide enhanced control of infant's well-being, and, consequently, benefit the mother by improving the chances of her offspring's survival.

Pronounced lateralization of infant's active choice of a position near the mother found in nonprimate mammals implies that infants also gain an advantage from keeping the mother on the left. Empirical evidence supports the hypothesis that lateralization in infants is associated with fitness benefits. In their study, Karenina et al. (2017) aimed to compare the behavior of infants when the mother was in their left and right visual fields. In order to exclude the influence of the infant's preference for one of the lateral positions, the equal time intervals infants spent keeping mother on the left and right side were analyzed. In feral horse foals, the frequency of initiation of bonding behavior easily recognizable by the observer (such as grooming and rubbing with the head or lips) was compared. Within equal time intervals, foals initiated more bonding behavior when they kept the mother in the left compared with the right visual field. That is, keeping the mother on the left favored the infant's bonding with the mother that, in turn, may have a positive impact on infant's survival.

Further evidence of advantages associated with keeping the mother on the left comes from the analysis of the frequency of spontaneous mother–infant spatial separations in feral horses and Pacific walruses (Karenina et al., 2017). Situations were investigated where, after traveling beside the mother, the infant was left behind (at an approximate distance of 10m or more). The separation was included in the analysis only if the infant appeared alarmed just after being left behind and tried to rejoin the mother, i.e., the separation was seemingly unintentional on its part. In both species studied, the frequency of separations was lower when the infant kept its mother in the left visual field. Hence, perceiving the mother predominantly via the left eye—right hemisphere system, allowed infants to maintain close spatial proximity with the mother more successfully than when perceiving her via the right eye—left hemisphere system (Fig. 4).

Additional advantages for keeping the mother on the left, besides those found to date, could be hypothesized. Left-sided position favors the flow of social information (from the mother) to the infant's right hemisphere, which is assumed to play a key role in the development of social perception (e.g., Tsur et al., 1995). By facilitating the right hemisphere involvement, infants may benefit, for example, from improved learning of the mother's appearance (which is important for recognition of mother among other group members), and social learning conferred by optimal processing of mother's behavioral patterns and visual cues. However, the existing evidence is enough to argue that, from the point of view of selective pressures, lateralization can bear significant advantages for an infant.

4.2 SPATIAL CONFLICT BETWEEN MOTHER AN INFANT

The codirected side-by-side position of mother and infant is more or less typical for many mammal species. When both, mother and infant, prefer to keep one another on the left side, only one of the pair members can take the preferable position when moving side by side. From the point of view of spatial coordination, this creates a potential conflict between mother and infant. The results from nonprimate mammals demonstrate that the relative positioning of the pair members depends on who is choosing the lateral position. In primates, this conflict can be solved when the infant is facing its mother since in this position left-sided bias favors the right hemisphere involvement in both mother and infant (Sieratzki and Woll, 1996, 2002).

A recent study has demonstrated that primates are not the only mammals employing dyad positioning in a way that may provide optimal social processing to both pair members. In two phylogenetically and ecologically distant species, Pacific walrus and Indian flying fox, face-to-face interactions between mother and infant were investigated unobtrusively in the wild (Giljov et al., 2018). A significant population-level preference for the position which facilitates the use of the left visual

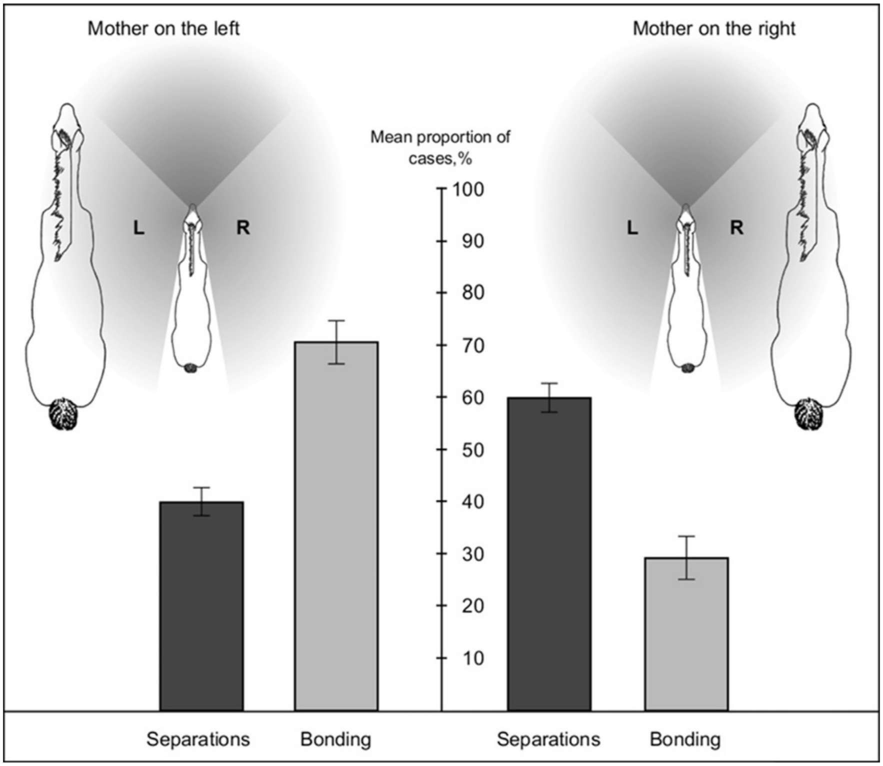

FIG. 4

Advantages for keeping the mother in the *left visual field* for feral horse foals. The frequencies of spatial separations and bonding behavior are illustrated in different lateral positions of the foal relative to the mother. Only the separations, which were seemingly unintentional on foal's part, were analyzed. Bonding behavior was defined as positive tactile contacts initiated by the foal. When keeping the mother in the *left visual field* foals displayed more efficient maintenance of spatial proximity and a higher frequency of bonding behavior than when keeping her in the *right visual field*. *Error bars* indicate the SEM. Horse visual fields are depicted according to Waring (2003).

Reprinted from Karenina, K., Giljov, A., Ingram, J., Rowntree, V.J., Malashichev, Y., 2017. Lateralization of mother–infant interactions in a diverse range of mammal species. Nat. Ecol. Evol. 1, 0030.

field in both mother and infant was found (Fig. 5). In face-to-face interactions, the left-sided positional bias is likely mutually beneficial for mother and infant, providing both of them an optimal perception of each other by the improved flow of information between their right hemispheres. This finding demonstrates that marine and terrestrial nonprimate mammals can show left-sided positional bias in face-to-face mother–infant interactions resembling left-cradling bias in primates. Are there any other ways to solve a spatial conflict between mother's and infant's lateralization besides face-to-face positioning?

FIG. 5

The position facilitating the use of the *left visual field* in both mother and infant when resting. (A) Pacific walrus (*Odobenus rosmarus divergens*). (B) Indian flying fox (*Pteropus giganteus*).

Reprinted from Giljov, A., Karenina, K., Malashichev, Y., 2018. Facing each other: mammal mothers and infants prefer the position favouring right hemisphere processing. Biol. Lett. 14, 201820170707.

4.3 DIFFERENTIAL LATERALIZATION IN SONS AND DAUGHTERS

Presumably, an alternative way to solve the potential conflict in lateralized spatial interactions between mother and infant is a behavioral alignment of one pair member to another. Lateralization of mother–son interactions in Asian elephants may represent an example of such alignment (Karenina et al., 2017). Elephant mothers preferentially keep their young on the left side when approaching them during traveling. Unlike the infants of other mammals studied, male elephant young prefers to approach their mothers on the right. That is, in Asian elephant mother–son pairs the preferential position choice of both pair members results in the same relative positioning (the young is on the left of the mother). Notably, male young prefers to keep nonmother companions on the left, which is in line with social lateralization typically observed in mammal infants (Karenina et al., 2017). Thus, males showed differential lateralized behavior toward mother and nonmother companions. It can be suggested that sons align their lateral preferences to the mother's lateralization by taking the position preferable for the mother. Such alignment may be elicited by benefits conferred by the mother's better perception and/or faster recognition of the son and, consequently, her more anticipated and appropriate reaction. Similarly, in gray-cheeked mangabeys (*Lophocebus albigena*), nondominant individuals prefer to approach a dominant group member on its left, which is assumed to be beneficial for an approaching individual by improving the dominant individual's perception and recognition (Baraud et al., 2009).

In contrast to sons, Asian elephant daughters preferentially keep both mother and nonmother companion on the left side (Karenina et al., 2017). This bias can be explained by a right hemisphere advantage for social functions relevant to the infant's interactions with her mother (see Section 4.1). The positioning to the left and to the right of the mother may have its own benefits, and we hypothesize that in elephants these benefits have differential significance for sons and daughters. For daughters, it may be more important to facilitate its own perception of the mother by keeping her in the left visual field, while for sons it may be more beneficial to be on the mothers' left to optimize her perception and responses to him. This difference may be associated with distinctive social strategies of the two sexes in elephants (de Silva et al., 2011; Lee and Moss, 2011; Sukumar, 2003). When reaching adulthood, daughters remain within their natal family unit and maintain tight and prolonged affiliative relationships with the mother. On the other hand, males disperse and are characterized by more solitary lifestyle. The differences in the degree of sociality between adult males and females may underlie differential emotional and/or motivational bases of relationships with the mother in young sons and daughters that in turn may be reflected in their lateralized behavior. The results on Asian elephants suggest that, in mammals with different social strategies of the two sexes, male and female infants can follow distinct patterns of lateralized behavior toward mother. The results on Asian elephants suggest that social strategies of the two sexes may elicit lateralized social behavior in mammal infants. Whether this is the exception or the rule requires further investigation. It seems, however, that sex-specific lateralization in infants is rare, since in other species investigated from this aspect, the infants' preferences to keep mother on the left were manifested regardless of the sex.

5 CONCLUSION

The findings presented in this chapter demonstrate that lateralization is an important component of mother–offspring interactions in many mammals, both primate and nonprimate. While there is still much to learn about lateralized behavior in mothers and infants, current knowledge suggests that this feature has an impact on mother–infant bonding and infant's survival. This makes it an important topic for further research. Directions for future studies may include investigation of effects of lateralization in infants' relations with their mother, on their social behavior at adulthood and testing effects of maternal lateralization (toward the infant) on infant's survival success. Such studies would shed light on the evolutionary background of the emergence of this lateralization, and its prevalence across the taxa. A greater understanding of maternal lateralization stability may be gained by longitudinal studies of individual mothers with different infants throughout her life. Investigations on populations of the same species existing in strikingly different conditions (e.g., with and without predators) may also improve our understanding of the impact of ecological factors on lateralization in mother–infant interactions.

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SECTION

Behavioral biases in humans

2

CHAPTER

Speech lateralization and motor control

6

Jessica C. Hodgson, John M. Hudson[1]
School of Psychology, University of Lincoln, Lincoln, United Kingdom
[1]Corresponding author: Tel.: +44-1522-886782; Fax: +44-1522-886026,
e-mail address: jhudson@lincoln.ac.uk

Abstract

A relationship between motor control and speech lateralization has long been postulated by researchers and clinicians with an interest in the functional organization of the human brain. Exactly *how* motor control might be related to speech representation, however, is rarely examined. This chapter examines current issues relating to the organization, development, and measurement of motor control and speech representation. We further consider from neuropsychological, developmental, neurological, and genetic perspectives that speech and fine motor control involve planning and sequencing processes, which are mediated by an integrated neural network localized to the left hemisphere. Specifically, we discuss studies from our laboratory using functional transcranial Doppler ultrasonography to determine speech laterality, correlating this with hand preference and pegboard measures of motor laterality. Our findings show that handedness, as measured by a motor skill task, can be predictive of speech laterality, both in typically developing adults and children. We have also shown that individuals with developmental motor coordination impairments also show atypical speech lateralization, providing further evidence that neurological motor and speech systems are intrinsically connected. We consider these results in the context of a left-lateralized speech–praxis center model, which could account for the relationship shown between sequence-based motor and speech tasks.

Keywords

Speech production, Lateralization, Transcranial Doppler, Motor control, Speech–praxis model

1 INTRODUCTION

The cortical organization of speech and language processes has been the subject of much research in cognitive neuroscience and neuropsychology, and yet it is still not completely understood. Historically, speech production has been seen solely as a left-hemisphere function, due to early evidence from patients with brain injury

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and their subsequent language impairments. However, modern neuroimaging techniques have revealed a more intricate set of cortical networks underlying speech processing, which integrate associated sensory input and output modalities, such as motor control, and result in a distributed and complex pattern of cerebral lateralization of function (e.g., Hickok and Poeppel, 2007). The neural relationship between speech production and motor action underlie the long-established links language lateralization research has with hand preference research, which was driven initially by accounts of patients displaying co-occurring deficits in motor control and language following focal left-hemisphere lesions (Goldenberg, 2013). However, evidence for a clear causal relationship between handedness and speech laterality has proven inconsistent, due to the wide variation in measurement and classification approaches used to measure both functions (Bishop, 2013; Knecht et al., 2000a). A suggestion by Flowers and Hudson (2013) is that motor and speech laterality are related where they involve a common feature of motor output, namely the coordination of sequences of movements or utterances to execute a plan or intention so as to achieve a goal, either limb movement or articulation of an idea (e.g., Greenfield, 1991; Grimme et al., 2011; Tettamanti and Weniger, 2006). This chapter sets out to investigate cerebral lateralization from this perspective, specifically exploring the hypothesis that sequencing-based motor skill and speech production share common neural networks and are lateralized to the same hemisphere.

2 SPEECH LATERALIZATION

Speech production is one of the most studied aspects of functional cortical asymmetry and hemispheric lateralization. Converging evidence from decades of lesion studies and functional neuroimaging demonstrates a clear left-hemispheric specialization for language processing, and in particular that cortical regions in the inferior frontal gyrus (pars opercularis (PO)) are crucial for speech production (Costafreda et al., 2006; Geschwind and Levitsky, 1968; Hickok and Poeppel, 2007; Price, 2000; Stephan et al., 2003).

Research using neuroimaging techniques has attempted to localize specific aspects of language to distinct areas within the dominant hemisphere. Evidence suggests that semantic processing aspects of speech production are localized primarily to areas of the left hemisphere, including the PO and pars triangularis (PT), regions of the inferior frontal gyrus, also known as Broca's area (Brodmann areas 44 and 45; Binder et al., 2000; Price, 2000). Lesions to these regions result in behavioral deficits in word generation and difficulty with naming and articulation (Binder et al., 1997). In contrast, language comprehension (the understanding of spoken words) is supported by the posterior temporal–parietal region, including Wernicke's area (Brodmann areas (BAs) 39 and 40, and posterior 21 and 22; Hickok and Poeppel, 2007).

Neuroimaging evidence has also extended our view of the cortical organization of speech and language by providing data indicating that the right hemisphere has an important role to play in speech production processes. Examples of this include the utilization of contextual cues to inform speech production and the insertion of emotive inflection into speech (e.g., Gardner et al., 1983). Although language-related activation in healthy right-handed participants is predominantly left hemispheric, almost all participants activate right-hemisphere areas to some extent during functional imaging studies (Buckner et al., 1995; Pujol et al., 1999; Springer et al., 1999; Tzourio et al., 1998). Furthermore, evidence suggests that the right hemisphere may even be the dominant hemisphere for speech in a minor proportion of the population (e.g., Hertz-Pannier et al., 2002; Knecht et al., 2000a; Möddel et al., 2009; Szaflarski et al., 2002; Vingerhoets et al., 2013).

Predominant neural models of speech processing suggest a differential contribution of the two hemispheres, which may be task dependent. One such account is the dual-stream model (Hickok and Poeppel, 2004, 2007), which proposes that a distinction should be made between the dorsal and ventral streams of language processing and production. This model indicates that the specialization of the left hemisphere can be associated with particular aspects of language production, characterized by the dorsal processing route. The dorsal stream is said to involve the posterior and dorsal-most aspect of the temporal lobe and parietal operculum, as well as the posterior frontal lobe, to convert sensory input into motor information. Conversely the ventral stream, involving structures in the superior and middle portions of the temporal lobe, processes verbal input for comprehension. Hickok and Poeppel (2007) suggest that the dorsal stream is left-lateralized, while the ventral stream is organized bilaterally, a suggestion which has recently been supported by studies using diffusion tensor imaging (Rilling et al., 2012) and fMRI (Häberling et al., 2016).

The idea that speech production processes may rely on a different set of neural structures and networks than those used for language comprehension is perhaps unsurprising, given the differing sensory processing requirements of each function. Indeed, evidence from patients with focal lesions allows the dissociation of component processes of the language system, due to specific deficits being associated with damage in particular areas (Wise and Geranmayeh, 2016). For example, lesions to Broca's area affect the ability to produce fluent and coherent speech, as well as sometimes producing difficulties in naming and word finding. This damage, however, does not affect comprehension abilities, indicating that different brain regions or networks must be involved in that process (see Price, 2000 for review).

The hypothesis that networks supporting language function may be distributed across the hemispheres has important implications for the experimental approaches used to elicit speech activation. Studies using a verbal fluency or word generation paradigm dominate the literature on speech lateralization (e.g., Bishop et al., 2009; Knecht et al., 1998, 2000a,b; Somers et al., 2011). This paradigm requires participants to produce corresponding words when shown a letter or category stimulus and tends to produce a clear left-hemisphere activation pattern which is highly reproducible within individuals (Knecht et al., 1998). However, paradigms that rely more upon receptive language skills, such as matching pictures and words, semantic decision making, reading, or listening to spoken words, have been shown to produce increased bilateral or right-hemisphere activation (e.g., Badcock et al., 2012; Bishop et al., 2009; Haag et al., 2010; Hodgson et al., 2014; Stroobant et al., 2009).

2.1 SEX DIFFERENCES IN SPEECH LATERALIZATION

One factor which is frequently raised in research on cerebral lateralization of speech is whether differences in brain organization occur on the basis of sex. Previous research indicates that sex differences exist generally in brain structure and function (see Cosgrove et al., 2007 for review); however, the literature on the influence of sex on language laterality is inconsistent. A highly cited study using fMRI to explore hemispheric dominance during a phonological rhyme task indicated that left-sided lateralization patterns were clear in males, but not in females (Shaywitz et al., 1995), a finding that is supported by subsequent studies (e.g., Baxter et al., 2003; Gur et al., 2000). However, a recent meta-analysis of the fMRI data from 26 studies found no overall effect of sex on the direction of language lateralization (Sommer, 2010). Sommer (2010) also analyzed data from dichotic listening tasks designed to determine hemispheric dominance for language based upon auditory processing. These data from 3822 participants revealed no significant sex effects, with both males and females displaying a right ear advantage, regardless of their hand preference. Furthermore, a recent study by Hudson and Hodgson (2016) indicated via functional transcranial Doppler (fTCD) ultrasound, a direct measure of speech laterality, and digit ratio, a method of estimating prenatal testosterone exposure, that effects of sex difference on laterality of speech were not discernible. Inconsistent findings related to the effect of sex on language lateralization suggest that the differences in the functional organization of language processes, if any exist, are small.

2.2 DEVELOPMENTAL PATTERNS OF SPEECH LATERALIZATION

Researchers have focussed on understanding whether the left hemisphere is predisposed to support speech function, and if so, whether left-hemispheric dominance for language is present at birth or if it develops during childhood and early adolescence. It has been shown that left-hemisphere language specialization can be observed even in very young babies who display adult-like left-lateralized activation in perisylvian areas when listening to sentences in their native language (Dehaene-Lambertz and Houston, 1998) as well as left inferior frontal lobe (e.g., Broca's area) activation during speech processing (Dehaene-Lambertz et al., 2002; Imada et al., 2006). Furthermore, studies have shown that the behavioral repertoire of infants with regard to language includes abilities in categorical perception of phonemes (Eimas et al., 1971) and early involvement of Broca's area in verbal memory (Dehaene-Lambertz et al., 2006). This evidence supports the notion that the brain is predisposed to support speech function several months before the onset of speech production or even prespeech babbling.

School-aged children and adolescents typically show a predominant left-hemisphere activation for silent word generation tasks (Norrelgen et al., 2012; Szaflarski et al., 2012; Wood et al., 2004), silent reading (Gaillard et al., 2003), and an auditory categorization task (Balsamo et al., 2006) in areas of the frontal and temporal gyri as well as fusiform and supplementary motor area. In addition, a number of these studies have indicated a positive correlation between left-hemisphere activation and task proficiency (Balsamo et al., 2006; Wood et al., 2004).

Magnetoencephalography studies with children and adolescents aged 5–19 years have also shown a predominant left lateralization to word generation tasks but, unlike in fMRI studies, one that increases in prominence with age between around 5–7 years and mid-late adolescence (Balsamo et al., 2006; Kadis et al., 2011; Wood et al., 2004).

Typically, developing children have also been shown to vary in the degree of language lateralization compared to adults (Holland et al., 2001). In Holland et al.'s (2001) study, although most tested participants at all ages showed left-hemisphere dominance for the language task, the degree of lateralization increased with age. This study demonstrates that fMRI can reveal developmental shifts in the pattern of brain activation associated with semantic language function. The idea that strengthening of lateralization increases with age has also been supported by a recent fTCD study in children aged 1–5 years (Kohler et al., 2015). These data showed that although most children displayed the typical left-hemisphere dominant pattern during speech, the variability of the response changed as a function of age, with younger children producing a more variable lateralization index.

One suggestion to explain left-hemispheric dominance is that during language development functional clustering in one hemisphere allows for faster linguistic processing because transmission times between brain regions within one hemisphere are shorter than when signals have to cross the corpus callosum (Nowicka and Tacikowski, 2011). Increased connectivity in left-hemispheric language regions is also reflected by the increase in white matter integrity in crucial language structures such as the arcuate fasciculus. Evidence suggests that most people demonstrate a greater proportion of white matter tracts in the left hemisphere in this region (Hickok, 2014).

Developmental neuropsychological research into functional localization of speech has predominantly focussed on children with acquired language impairments (e.g., Ballantyne et al., 2008; Liégeois and Morgan, 2012). Evidence shows that children's brains have a greater propensity toward cortical plasticity: the ability of the brain to rewire and establish new connections following injury (e.g., Duffau, 2006); and studies have shown that children with brain injuries affecting speech and language have better and faster recovery than adults with the same pathologies (Beharelle et al., 2010). Furthermore, it has been shown that children exhibit superior capacity to trans-hemispherically compensate for impaired language functions compared to older children and adults (Ballantyne et al., 2008; Lohmann et al., 2004). This therefore suggests that there are fundamental differences between the way in which the developing brain and the developed brain process and produce speech and language.

3 MOTOR LATERALIZATION

The most obvious behavioral asymmetry displayed in humans is hand dominance, the fact that in most people one hand is preferred over the other for skilled work and fine motor control (Papadatou-Pastou, 2011). Handedness presumably reflects an asymmetry of cortical processing and neurological organization, as opposed to morphological asymmetry of the hands themselves (Corballis, 2010). Traditionally, handedness was considered a uniquely human trait; however, recent comparative work has shown that other species in fact also display hand preferences (see Corballis, 2003 for review), although the population level bias to the right-hand side is considerably marked in humans (around 90%). Multiple factors are thought to affect the determination of handedness including maternal handedness and family history of left-handedness (Annett, 1998), sex (Gilbert and Wysocki, 1992), age (Ellis et al., 1998), testosterone level (Tan, 1991), and history of early brain injury (Rasmussen and Milner, 1975). The persistence of the dominant right-hand preference observed throughout history and across populations distributed in different geographical locations suggests the involvement of some evolutionary mechanisms. However, for selection of this trait to take place, hand laterality should also be heritable (Llaurens et al., 2009).

3.1 DEVELOPMENTAL PATTERNS OF MOTOR LATERALIZATION

Human hand preference emerges very early in an infant's life, where genetics and environmental influences are believed to play a key role in development (Scharoun and Bryden, 2014). Some evidence suggests hand preference in adulthood can be predicted from lateralized motor behavior observed in early gestation (for review, see Scharoun and Bryden, 2014), for example, through ultrasound observation of thumb sucking preference behaviors (Hepper et al., 1991), and grasp reflex strength measured in neonatal infants (Tan and Tan, 1999). Researchers have also studied infant postural preferences with a view that these behaviors in fact guide the development of handedness (e.g., Coryell and Michel, 1978; Michel, 1981). These observational studies showed significant correlations between hand preference in infancy for reaching (Marschik et al., 2008) and grasping objects (Michel et al., 2002, 2006) and hand-use distributions among adults. Research has also indicated that hand preference can be detected from 6 months onward (see Butterworth and Hopkins, 1993 for review of handedness in infants). Evidence from cross-sectional (Hawn and Harris, 1983; Morange and Bloch, 1996; Peters, 1983) and longitudinal studies (Carlson and Harris, 1985; Coryell and Michel, 1978; McCormick and Maurer, 1988; Michel and Harkins, 1986; Ramsay, 1985; Ramsay et al., 1979) indicates that some degree of hand preference can be observed at the point at which the infant is developing grasping skills. Although these findings indicate that hand preference can be observed very early in life, there is also evidence which suggests that handedness is a highly malleable trait (Corbetta et al., 2006). Different patterns of hand preference development have been observed in young children, including frequent shifting from right- to left-hand use during fine motor tasks (e.g., Corbetta et al., 2006; Michel et al., 2006). Studies measuring hand preference from early childhood to adolescence (i.e., ages 3–12) provide no general consensus regarding the age at which adult-like handedness is actually attained (Scharoun and Bryden, 2014). Some researchers (Archer et al., 1988; Longoni and Orsini, 1988;

McManus et al., 1988) suggest that direction of hand preference is fixed at age three, further explaining that degree increases between the ages of three and seven. Based on this idea, an individual's hand preference cannot be reliably assessed until at least 4 years of age (McManus, 2002), although some studies have noted that children 3–4 years of age do not reliably select a preferred hand when performing unimanual tasks, and that it is not until the age of six that a clear preference can be observed (e.g., Bryden et al., 2000a,b). The equivocal findings may be due to the different ways of quantifying hand preference and performance abilities in the research (Scharoun and Bryden, 2014).

3.2 MEASUREMENT AND CLASSIFICATION

An important factor for the effective examination of the development of hand preference is the exact definition of handedness itself. There are various elements that make up motor skill, such as grip strength, dexterity, sequencing ability, and coordination, all of which can be revealed in different functional tasks (Bishop, 1990). However, most studies allude to handedness as a unitary phenomenon and seek to measure and classify across a simple dichotomy of right vs left. Individuals are generally classified as being left- or right-handed based on their preferred use of one hand over the other, although a handedness classification does not rule out the use of the nondominant hand (Annett, 2002). While the majority of people self-report using their right hand for most tasks, many will also use their left hand to some extent more than others (Annett, 1996, 1998, 2002). A common issue arises from the fact that handedness is actually classified differently between studies, with particular variation when it comes to classifying ambiguous or mixed handedness. These can either be treated as distinct categories or as a continuum of handedness as determined by a laterality quotient (see Marchant and McGrew, 2013, or Forrester, 2017 for review). Laterality quotients are used to provide a standardized measurement of handedness direction from responses on a handedness inventory or performance task (e.g., the Edinburgh Handedness Inventory, Oldfield, 1971). However, their use as a way of quantifying inventory responses has been criticized for disguising the variance in hand usage across different tasks (because responses are simply converted to a numerical value); indeed, such nuances may actually be very informative when it comes to assessing and classifying an individual's hand preference (Annett, 2002).

There is debate over how handedness should be categorized. One perspective is that handedness should be divided into two populations, those who are strongly right-handed (i.e., those who use the right hand for almost all activities) and those who are nonright-handed (who may prefer the left hand for some, or the majority, of fine motor activities) (McManus, 2002). However, Annett (2002) has suggested that handedness lies on a continuum with strong left- and right-handedness lying at the two extremes and a mixture of preferences in between. This continuous distribution of hand preference takes the form of a single normal (Gaussian) curve, which for humans is displaced in the dextral direction, the so-called right shift

(RS) (Annett, 1972, 2002; Annett and Alexander, 1996; Annett and Kilshaw, 1983). Using this classification, the proportions of consistent left-, mixed-, and right-handers are approximately 4%, 30%, and 66%, respectively (Annett, 1996; Annett and Turner, 1974; Annett et al., 1979).

3.3 PREFERENCE MEASURES

Alongside classification, another crucial issue with research into handedness is how it is measured across studies. Some studies define hand preference simply on the basis of writing hand (Perelle and Ehrman, 2005; Stellman et al., 1997), as this skill is largely specific to one hand in the majority of people and remains poorly executed in the nonpreferred hand even after considerable training (Perelle and Ehrman, 2005). Furthermore, Perelle and Ehrman (1994) found that only 0.9% of individuals considered themselves to be ambidextrous for writing, meaning that the majority of people will be easily categorized as either right- or left-handed using this approach. However, writing is a skill which has been subject to cultural and societal influence in terms of the hand individuals have been taught to use, normally the right hand. This could result in people over a certain age (as this practice was common up until the mid-20th century) and from different cultures showing a right-hand bias that does not necessarily reflect the actual manual skill or dexterity of their hands.

Other approaches to hand preference measurement include the use of self-report questionnaires or inventories that examine hand preference for everyday tasks, such as throwing, striking a match, using scissors (e.g., Annett, 1970; Oldfield, 1971). One of the most well established of these is the Edinburgh Handedness Inventory (EHI; Oldfield, 1971) which allows for the classification of handedness as both a continuous or categorical variable based on the strength to which the individual uses one hand more than the other. Other self-report tools have been developed such as Annett's hand preference questionnaire (Dragovic and Hammond, 2007) or the Waterloo Handedness questionnaire (Steenhuis and Bryden, 1989). Inventories are the most commonly used indicators of hand preference; however, results are highly malleable and open to variations in interpretation of hand dominance. There is no consensus in the field about how to classify inventory responses, and specifically on how many separate classifications or groups to use, which leads to an unsatisfactory situation where arbitrary cutoffs are used to distinguish groupings (McManus et al., 2016). Preference measures have also been criticized over reliability (McMeekan and Lishman, 1975) and validity (Williams, 1991), with the suggestion that respondents may either avoid extreme responses to the inventory items or select solely extreme responses, thus confounding the measurements (Beaton and Moseley, 1984).

3.4 PERFORMANCE MEASURES

It is possible to assess handedness on the basis of proficiency (so-called performance measures) using tasks designed to assess hand skill, such as Annett's Peg-Placing task (Annett, 1972), the Purdue Pegboard task (Tiffin and Asher, 1948, as cited in Annett, 2002), Tapley–Bryden's dot-filling task (Tapley and Bryden, 1985), and the Wathand Box (Bryden et al., 2000a). Such techniques are based on the premise that manual action and dexterity is best understood in the context of a task, which requires the use of such skills. Performance measures are able to detect subtle differences in the performance of each hand and place handedness on a continuum based on relative skill. Such measures of hand skill are preferred as the J-shaped distribution, which results from handedness questionnaires, is unlikely to reflect the underlying continuous distribution of handedness scores (Tapley and Bryden, 1985).

Steenhuis and Bryden (1989) characterized manual activities as either those that were "skilled" (e.g., writing, throwing darts) or those that were "unskilled" (e.g., picking up large objects, petting a cat or dog). They reported differences in handedness distribution between skilled and unskilled activities, with weaker hand preference scores associated with less-skilled behaviors. In a later study by the same authors (Steenhuis and Bryden, 1999), it was demonstrated that stronger hand performances are dependent on the difficulty level of the task being measured. Participants completed a battery of tasks including self-report hand preference measures and skill-based tasks, which varied in complexity. Results showed that although self-reported hand preference scores correlated well with performance scores (in other words, people can accurately report which hand is their dominant hand), the extent to which the nonpreferred hand was used varied between participants. Left-handers used their nonpreferred hand more frequently than did right-handers, and their relative skill differences were smaller. Similarly the nonpreferred hand of right-handers (i.e., the left hand) was only rarely used in skilled, complex tasks (Bryden, 2015). This pattern of results is supported by recent findings that increasing the task difficulty in a performance measure, such as using a grooved pegboard where pegs only fit the holes when placed in a specific orientation, increases the performance advantages of the preferred hand (Bryden and Roy, 1999; Bryden et al., 2007).

Bishop et al. (1996) tested the agreement between measures of hand preference and hand performance in a sample of right-handed participants. Three handedness groups were identified using the EHI, which relies on a proportional measure of left and right unimanual hand actions (laterality index or quotient $R - L/R + L$): strong right-handers, predominant right-handers, and weak right-handers. Results showed that the groups did not differ on three measures of hand skill of the two hands: peg moving, finger tapping, and dotting. However, there was a difference between the groups on an experimental measure of preference rather than performance. Participants performed a novel reaching task which significantly distinguished the predominant right-handers from the other groups, due to their variation in choosing the left hand when reaching on the ipsilateral side of space. This finding provides support for the idea that hand preference measurements need to be based on empirical data as opposed to self-report. Taken together these results indicate that classifying handedness on a simple dichotomy of right vs left does not provide a comprehensive view of behavior across task and skill conditions.

4 ASSOCIATIONS BETWEEN SPEECH AND MOTOR LATERALITY

Research on the association between handedness and language lateralization spans at least the last four decades and is thought to comprise over 10,000 studies (Sommer, 2010). Evidence consistently shows that there are different patterns of functional language lateralization between right- and left-handers (e.g., Annett and Alexander, 1996; Cabeza and Nyberg, 2000; Cabeza et al., 2004; Corballis, 2003; Deppe et al., 2000; Flöel et al., 2005; Knecht et al., 2001; Pujol et al., 1999). Estimations of variance in hemispheric language dominance across handedness groups suggest that approximately 95% of right-handed individuals display left-hemisphere dominance, whereas this is only true for approximately 76% of left-handed people (Flöel et al., 2005; Knecht et al., 2000a,b; Pujol et al., 1999). This is a robust pattern which has been demonstrated using different methodologies, including the Wada test (Rasmussen and Milner, 1975; Wada et al., 1975; Zatorre, 1989), fMRI (Deppe et al., 2000; Pujol et al., 1999; Szaflarski et al., 2002), and fTCD (Deppe et al., 2000; Flöel et al., 2005; Knecht et al., 2000a, 2001). Evidence from studies involving large participant samples also suggest the existence of a continuum of language lateralization patterns ranging from strongly left dominant to strongly right dominant (Frost et al., 1999; Knecht et al., 2000a; Pujol et al., 1999; Springer et al., 1999; Tzourio et al., 1998).

A series of seminal papers from Knecht et al. (2000a,b), using fTCD ultrasonography, drew interesting observations on the natural distribution of language dominance across the hemispheres in healthy right- and left-handed participants. Their studies indicated that atypical right-hemispheric language dominance increased linearly with the degree of left-handedness from 4% in strong right-handers to 15% in ambidextrous individuals and to 27% in strong left-handers. While these results clearly show a relation between handedness and language dominance, they also illustrated that 73% of strong left-handers showed typical left-hemispheric language dominance, just as most right-handers do. This work was critical in demonstrating that functional localization of language processes is not automatically assigned to the left hemisphere, as some people display right-hemisphere dominant speech networks. This work also suggested that hand dominance and speech lateralization can be seen as independent biases, where lateralization profiles may not be solely reliant on one another.

To investigate this idea further several studies have compared handedness measures and language lateralization profiles. Badzakova-Trajkov et al. (2010) used fMRI to measure brain activation during word generation in a sample of 155 adults and correlated it with the handedness LQ (laterality quotient) obtained from a 12-item questionnaire. The correlation coefficient for the correlation between the laterality index for frontal activation asymmetries during word generation and the handedness LQ was $r = 0.357$, $P < 0.001$ level, indicating that individuals with stronger right-handedness were also more likely to show a strong leftward bias for speech activation. However, the coefficient of determination r^2 for this correlation coefficient is 0.127, indicating that roughly 13% of the variance in language lateralization could be explained by their LQ score (Ocklenburg et al., 2014). More recently, Somers et al. (2015) also examined whether hand preference was related to direction of hemispheric language dominance as measured by the EHI and fTCD. They concluded that degree of hand preference does not predict the degree of language lateralization, but their data showed that increasing strength of left-handedness was associated with increased variation in directionality of cerebral dominance. These studies appear to undermine the functional relationship between speech and handedness; however, it is important to note that in each case, handedness measurements were done via self-report questionnaire. As discussed earlier, these methods are potentially less likely to detect the underlying component processes of motor sequencing and skill that may relate to speech processing.

A similar study by Groen et al. (2013) compared three different handedness tasks with a direct measure of speech lateralization in children aged 6–16 years. Two of the tasks were skill-based: a pegboard task and a reaching task (see Bishop et al., 1996) and the third was a shortened version of the EHI. Correlational analysis showed that the reaching task and the shortened handedness inventory were significantly associated with the speech lateralization indices, but not the peg-moving task. This is initially surprising given the neurophysiological and neuropsychological evidence indicating a link between skilled manual tasks and language. However, closer inspection of the results revealed that the correlations with speech scores only existed at the level of hand preference groupings, and that when the scores in each task were converted into laterality quotients the significant relationships with speech indices disappeared. Performance on the pegboard is measuring hand skill, rather than preference, and so is not equally comparable to the other measures used. In addition, the authors themselves point out that none of the measures were able to explain the variance in speech lateralization by more than 16%, leading to their conclusion that motor performance and language networks are relatively independent of one another. It would appear that weak connections between hand preference and speech lateralization exist when measured as factors in a preference continuum; however, what is not yet clear is how direct measures of relative hand skill (regardless of an individual's hand preference) relate to direct measures of speech lateralization. McManus et al. (2016) argue that measurements of performance, rather than preference, should be relied upon as indicators of cerebral lateralization, because such tasks tap into the mechanisms thought to be common to both functions.

4.1 NEUROPSYCHOLOGICAL EVIDENCE

Even though in the healthy brain the associations between speech and handedness are variable and task dependent, there are clear links between the two functions in the neuropsychological literature. After focal left-sided brain injury aphasia and apraxia often co-occur (e.g., Vingerhoets et al., 2013), suggesting that the region affected by the lesion must be subserving both functions. Patients with apraxia experience difficulties in manual action including gestural ability and tool use, both real and pantomimed, as well as with communicative gestures. Evidence suggests that the incidence and severity of apraxia are reduced in left-handed patients, for example, Kimura (1983) found that the frequency of apraxia in left-handed patients was 9% compared to an incidence of 30% in right-handed patients with left-hemisphere damage. Furthermore, a study of defective hand gestures and imitations in apraxic patients showed that left-handers were defective in approximately 35% of cases, compared to 66% in right-handed patients (Goldenberg, 2013). These data suggest that patients whose hemispheric dominance is more bilaterally dispersed experience milder impairments. However, there is criticism of these figures as they fail to adjust for the incidence of impairments in right-handed patients with right-sided damage (Goldenberg, 2013).

A means of addressing the variability in evidence for the association between handedness and hemispheric language dominance is to examine the predictive power of handedness measures to detect speech representation. Flowers and Hudson (2013) used this approach in the assessment of motor and language laterality in a group of epilepsy patients undergoing the Wada procedure for establishing hemispheric speech dominance prior to surgery. In this study, patients were given a pegboard task and a handedness inventory based upon an amalgamation of several questionnaires (Annett, 1970; Oldfield, 1971), and these handedness results were compared with the eventual classification of speech dominance derived from the Wada results. The data showed that patients whose between-hand difference on the pegboard task was small or inconsistent were likely to have atypical speech representation. Those with a consistently large between-hand difference (mean ≤ 2.2 s) on the motor task all showed clear unilateral speech representation in the hemisphere controlling the better hand. This is an important evidence for arguments supporting an association between cerebral laterality and handedness, and crucially it is derived from a skill-based performance measurement of handedness, rather than a classification according to preference. Indeed, categorizing individuals as either left- or right-handed, or indeed ambilateral, on the basis of self-report questionnaire responses failed to effectively discriminate between the lateralized and anomalous groups.

Flowers and Hudson (2013) contend that handedness and speech involve a common feature of motor output sequencing and timing (Ojemann, 1984) and that pegboard performance constitutes a valid measure of this mechanism. However, in addition to motor sequencing, the pegboard also involves an array of component processes, which are fundamental for the successful execution of the task. These include precision grasp and release, arm movement, finger dexterity, and psychomotor speed. Our laboratory recently deconstructed these factors into separate tasks and then correlated left- and right-hand performance with fTCD speech lateralization indices to examine the relationship between speech representation and hand proficiency on a wider range of motor tasks (pegboard, coin rotation, finger tapping, circle marking, peg sorting, and grip strength; Hodgson, 2016). Results showed that there was good correlation across a number of measures, indicating that preferred and nonpreferred hand performance remained constant across all tasks. Notably, correlations of handedness tasks and speech scores indicated that only two of the handedness tasks significantly correlated with speech laterality indices: namely, the pegboard and the coin rotation task, both of which involve a high degree of motor sequencing.

In a second experiment, we deployed a novel imaging paradigm using fTCD to derive lateralization indices of *motor action* during three of these tasks (pegboard, coin rotation, and finger tapping). We found that the right hand activated the contralateral (left) hemisphere for each of the tasks, whereas the left hand activated the ipsilateral (left) hemisphere during the pegboard task and produced bilateral activation during the coin rotation task. This was compared to a control condition task of finger tapping, with a single digit (index finger), during which both hands activated the contralateral hemisphere. Collectively, these results provide compelling evidence in support of the hypothesis that motor-sequencing tasks are most similar to speech production and that they are represented more strongly in the left hemisphere during activity of either hand. This is in contrast to tasks not reliant on sequencing, such as the control task, which elicited equal strength contralateral activation, and did not show a hemispheric preference. The findings are in line with existing evidence on fine motor control of the left and right hands that demonstrate predominant left-hemisphere activation during such tasks (Serrien et al., 2006; Verstynen et al., 2005) and extend the previous work by indicating an integration of motor control with speech production pathways (Gentilucci, 2003) supporting the assumption that they rely on the same left-hemisphere networks.

4.2 DEVELOPMENTAL EVIDENCE

Task proficiency has been associated with increased laterality (Groen et al., 2012; Sheehan and Mills, 2008), indicating that very young children, who are not yet proficient in speech or motor control, may demonstrate varied patterns of hemispheric lateralization for these functions. Although the direction of language and motor laterality may be biologically determined, complex interactions of environmental and genetic factors modulate the degree of cerebral lateralization during development (e.g., Bishop, 2013). It is important therefore to consider the extent to which an individual's laterality profile modifies through development. If lateralization shifts with age and task proficiency, then the underpinning neural architecture may also alter in this period and potentially be susceptible to factors influencing this developmental trajectory.

Because of methodological difficulties in measuring language performance in preverbal children a limited number of studies have examined speech lateralization in children below age 6. Methodological approaches which are appropriate for adults are not generally suitable for examining speech production in very young children, either due to literacy or due to task difficulty. However, notable exceptions have demonstrated predominantly left hemisphere lateralized speech in typically developing 4-year-old children (Bishop et al., 2014). In another study, no main effect of age in overall laterality profiles was reported in preschool children aged between 1 and 5 years, although the measure of lateralization was found to be less variable as a function of age (Kohler et al., 2015).

More recently, Hodgson et al. (2016) conducted an fTCD cross-sectional study to explore the relationship between motor skill and the development of speech lateralization in 148 children aged 3–10 years. Results demonstrated that mean speech lateralization scores showed a significant leftward bias across all ages tested, providing compelling evidence that speech lateralization is strongly represented in the left hemisphere at least by 3 years of age, in line with the previous research (Bishop et al., 2014; Kohler et al., 2015). These data also revealed that hand preference was similarly well established by age 3, with all the children in this study showing a clear hand dominance effect on both a five-item preference questionnaire and an electronic pegboard task. This concords with previous studies which demonstrate a link between strength of hand dominance and language ability in children (Leask and Crow, 2001; Rodriguez et al., 2010). However, notably, in the data presented by Hodgson et al. (2016) there was an age effect in pegboard times, whereby younger children showed a greater performance difference between their hands compared with older children (see also Roy et al., 2003). Interestingly, these results also showed that, in contrast to the adult data reported by Flowers and Hudson (2013), children with a typical language lateralization showed larger between hand differences in performance on the pegboard. These greater increases in performance differences between the hands were largely due to reduced proficiency in skill of the nonpreferred hand, which improved to near adult-like levels after around 7 years of age.

4.3 NEURODEVELOPMENTAL EVIDENCE

Evidence from neurodevelopmental disorders indicates the profile of cerebral lateralization changes when development does not follow a typical pattern. Stuttering is a motor speech disorder, which has also been associated with bilateral language lateralization (Nil et al., 2000) and reduced planum temporale asymmetry (Foundas et al., 2001). The distribution of hand preference in individuals with neurodevelopmental disorders has been found to deviate from the general population. Left-handedness has been more highly associated with language and motor disorders including dyslexia (Galaburda et al., 1985) and autism (Cornish and McManus, 1996) and developmental coordination disorder (DCD; Goez and Zelnik, 2008). Moreover, atypical lateralization for language has been shown in disorders such as dyslexia (Illingworth and Bishop, 2009) and specific language impairment (SLI; Whitehouse and Bishop, 2008) where higher proportions of these groups display reduced left-hemisphere bias during speech than typically developing controls. It is thus suggested that atypical hemispheric speech activation could be representative of an immature, or impaired, neural speech network. Although atypical cerebral lateralization is not indicative of reduced language ability, and left-handedness is not a prerequisite for neurodevelopment disorders (Bishop, 2013), Flowers and Hudson (2013) posit that individuals with dyspraxia or DCD who demonstrate reduced asymmetry in motor laterality are likely to have an increased chance of atypical speech representation. Hodgson and Hudson (2016) deployed fTCD to directly test this hypothesis in 12 adults with DCD but no other developmental or cognitive impairments (nonverbal reasoning, phonological processing, and speech production). Consistent with the view of Flowers and Hudson (2013), we found participants with DCD demonstrated a reduced leftward asymmetry during speech production and were also disproportionally slower than controls with their nonpreferred hand on an electronic pegboard task. Collectively, the results suggest that DCD patients have impairments in motor sequencing, which not only impacts upon motor coordination per se but also modulates the organization of neural networks controlling speech production. One explanation for the link between the hemispheric control of speech and motor control is that both functions implicate sequencing components that are subserved by a common system localized to the dominant hemisphere. Indeed, Haaland et al. (2004) demonstrated that complex sequencing operations performed with either hand are lateralized to left premotor and parietal areas regardless of handedness. DCD would therefore appear to be associated with both atypical localization of this network and a reduction in the integrity of the ipsilateral pathway that is modulated by the network and necessary for the execution of complex motor action.

4.4 NEUROPHYSIOLOGICAL EVIDENCE

There is converging evidence from neuropsychology and neurophysiology that cortical networks, which support language function, are related to those that support motor control. This includes the following strands of evidence: (1) common brain mechanisms are activated by both language and motor function (Vingerhoets et al., 2013); (2) motor action (especially fine motor skills and hand usage in complex tasks) is located in areas known to be involved in language (Verstynen et al., 2005); (3) speech production also activates areas known to be typically involved in motor tasks (e.g., cerebellum, premotor area, and motor cortex; see Price, 2000 for review); and (4) patterns of breakdown and recovery of language functions are closely linked (for review, see Iverson and Thelen, 1999).

The specialized role of the left hemisphere for controlling performance of skilled complex tasks, such as those underlying praxis and speech, has been suggested through the early work of Steenhuis and Bryden (1989). This theory is supported by evidence that larger performance differences were found favoring the preferred hand (usually the right) for complex, highly skilled manual tasks compared to simple tasks (e.g., Bryden et al., 2011; Flowers, 1975). Evidence suggests sequencing and motor timing are common mechanisms that are supported by a network distributed in key regions of the left hemisphere. Broca's area has been observed to be associated with various nonlanguage motor functions such as planning, recognition, and imitation of actions and tool use (Binkofski and Buccino, 2004; Higuchi et al., 2009;

Nishitani and Hari, 2000) as well as with syntactic operations required for the hierarchical representation of sequential behavior (Ocklenburg et al., 2014). The contribution of each hemisphere to motor control is also modulated by movement complexity. Whereas a simple movement such as unimanual finger tapping is organized by a local neural circuit, more complex actions such as those involving a sequence of finger movements engage distributed (often bilateral) networks (Haaland et al., 2004). Indeed, patients with left-hemisphere parietal lesions are likely to show impairments in producing skilled actions with either hand, whereas comparable right-hemisphere lesions produce deficits that are largely restricted to the contralateral hand (Wyke, 1971).

A significant factor linking speech and motor control neurologically is the association in overlapping cortical regions that are activated during tasks thought to be functionally independent. Neuroimaging studies of speech production have shown that during speech, activation is evident in motor control regions as well as in classic speech production areas (Hickok and Poeppel, 2007). The premotor cortex is known to become active not only during motor tasks but also during action observation and listening to common action-related sounds (Gallese et al., 1996; Kohler et al., 2002). Spoken and written words can also activate the motor system (Sahin et al., 2009) and this activation can even be specific to semantic word types (Hauk and Pulvermuller, 2004; Pulvermüller et al., 2001). Words related to actions involving different body parts, such as *pick* and *kick*, activate motor and premotor cortex in a somatotopic fashion so that, for example, the reading of leg-related words "makes the motor humunculus move its feet" (de Lafuente and Romo, 2004). This demonstrates category-specific links between the core language areas and motor representations in the processing of action words.

Furthermore, there is evidence that manual action with the hands, in the form of communicative gestures, may be beneficial in aphasia recovery (Rose et al., 2013), again indicating a crucial link between these two systems. One dominant hypothesis emphasizes functional connections between the cortical hand motor area and language circuit (Hauk and Pulvermuller, 2004; Pulvermüller et al., 2005) may have been essential for the evolution of language from manual gestures rather than vocal calls (Corballis, 2003), which is supported by the robust use of gestures that typically accompany speech (Iverson and Goldin-Meadow, 1998). People gesture as they speak, and these actions tend to be more frequent with the dominant hand (Kimura, 1973). Evidence from sign language users shows that although both hands are involved in the signing action, one hand tends to be dominant (Corballis, 2003). In addition, evidence for the role of gestures in early language acquisition demonstrates that there is a close link between motor and speech developmental trajectories, with gestural ability at 18 months being shown to predict language ability at 4 years (e.g., Alcock and Krawczyk, 2010). There is some consensus that language may have evolved from manual gestures rather than from indistinct vocalizations (e.g., Arbib, 2005; Corballis, 2003; Pollock and de Waal, 2007; Tomasello, 2008). Supporting evidence for the idea that gesture forms the neural basis of language comes from the observation of the firing patterns of a group of cells in the brain known as "mirror neurons" (Rizzolatti and Craighero, 2004). These cells, identified in macaque monkeys, were shown to activate when the monkey performed a manual action, but also crucially when the monkey observed a manual action being performed. This finding led to the conclusions that motor simulation provides the basis for understanding the actions of others, a necessary component of gestural communication (Rogalsky et al., 2013). What was important about the discovery of mirror neurons, however, was that these cells seemed to cluster specifically in area F5 of the macaque brain, an area which is deemed to be the homologue of Broca's region in the human brain (Hickok, 2014). Neuropsychological evidence suggests a causal link between damage to the mirror neuron system and subsequent impairments in speech and motor control, such as those seen in aphasia and apraxia. Evidence shows that gesture recognition is impaired in apraxic patients and that damage to Broca's area is correlated with poor gesture recognition (Pazzaglia et al., 2008). However, the validity of the mirror neuron theory has been questioned (e.g., Hickok, 2014) by evidence showing that damage to motor speech mechanisms in aphasia does not impair speech recognition (Hickok et al., 2011) and that sign language comprehension is not impaired in deaf individuals despite damage to the mirror system (Rogalsky et al., 2013).

4.5 NEUROBIOLOGICAL EVIDENCE

It has been suggested that the crucial component underlying the relationship between language lateralization and handedness is the extent to which each of these functions relies on sequential processing, for example, through motor phrases or speech utterances (Kimura, 1993). Speech production is a highly complex motor act involving the coordination and synchronization of multiple neural and muscular networks. During speech, a number of component processes occur to support the retrieval of the phonological code, which underlies the lexical representation of word forms (Tremblay et al., 2016). This code consists of segmental information, such as syllables and phonemes, and suprasegmental information, such as emphasis or stress.

This process of retrieval of phonologically encoded material is associated with the preparation of speech motor action, which involves the activation and translation of phonological representations into multiple domain-general mechanisms, such as response selection, response sequencing, and movement initiation. These so-called supramotor functions are not specific to speech but underlie all action preparation (Pulvermüller and Fadiga, 2010). Such models of speech motor planning posit that speech builds on common action control and motor-sequencing mechanisms which support many different cognitive processes (Freund et al., 2005; Tremblay et al., 2016) and therefore suggest that the neural organization of speech production is likely to overlap with motor control regions.

Studies have examined each component process of the speech motor control system and have made considerable progress identifying the associated neural substrates. Response selection processes involve a bilateral network of supporting motor areas, predominately the pre-SMA, which have been shown to activate more strongly during execution of specific stimulus responses tasks requiring selection of appropriate responses from a range of alternatives (Crosson et al., 2001). Speech motor response sequencing, the act of organizing segmental information into words and sentences prior to vocalization, relies more heavily on the motor areas. Indeed, interruption of these regions via transcranial magnetic stimulation (TMS) has been shown to disrupt sequencing performing on a finger-tapping task and impair performance on oral motor gestures (Tremblay and Gracco, 2009), which demonstrate the complementary cortical organization of motor and language networks (Gentilucci, 2003). Finally, the response initiation component of speech production is perhaps the least well documented, although early studies show a clear role for the cerebellum and basal ganglia in translating motor planning into action (Tremblay et al., 2016). Indeed, deficits in cerebellar–parietal networks have been identified in children who have neurodevelopmental motor impairments such as DCD (Zwicker et al., 2011), supporting the suggestion that response initiation involves these regions.

4.6 GENETIC CONSIDERATIONS

The idea that language lateralization and handedness are related is captured by the genetic models put forward by Annett (1972, 2002) and McManus (1985, 2002), which seeks to explain the dominant pattern of left-hemisphere bias and right-handedness at the population level. Both theories suggest that genetic expression affects the hemispheric lateralization of language and motor control (Corballis, 2010). For example, Annett's RS theory suggests that individual differences, in cerebral organization, arise from natural variation associated with the presence or absence of a single gene with two alleles, a right shift allele RS+ and an allele without directional specification RS–. Annett (2002) suggests that in the human population, handedness follows a normal distribution that ranges from strong left-handedness to strong right-handedness. However, the mean of this distribution is located to the right, which she attributes to the influence of a gene for left cerebral advantage (Annett and Alexander, 1996). Thus, the gene does not determine right-handedness, but increases its probability by displacing a random distribution in a dextral direction (Annett, 2002).

Attempts to localize and identify candidate genes driving cerebral lateralization and handedness have had mixed results. A recent meta-analysis of handedness genome-wide association studies (McManus et al., 2013) estimated the number of genetic loci involved in determining handedness to be at least 40, but possibly up to 100, thus also providing evidence against single gene accounts of handedness. Heritability estimates for handedness are in the range of 0.23–0.45 (Annett, 1985; McManus and Bryden, 1992; Medland et al., 2002; Porac and Coren, 1981; Risch and Pringle, 1985; Warren et al., 2006). A higher prevalence of left-handedness has been found in children from right-handed fathers and left-handed mothers (R × L pair) than from left-handed fathers and right-handed mothers (L × R pair) (Annett, 1975; McKeever, 2000; McManus, 1991). McManus (1991) estimated there to be a difference of 0.4% in the frequency of left-handedness in children of R × L pairs, compared with a difference of 2.9% in children of L × R pairs, with higher left-handedness rates reported in male offspring in both sets. However, these studies are confounded, once again, by the variability in classification and measurement of handedness, making it very difficult to infer causal patterns of heritability.

Research into genetic determinants of language dominance has produced several candidate genes (Bishop, 2013). One of the best studied is FOXP2, which has been causally linked to individuals with severe childhood apraxia of speech. Watkins et al. (2002) showed that a mutation in FOXP2 in some members of the KE family had resulted in severe deficits in articulation and speech production. Further studies showed that these mutations were also linked to an absence of Broca's area activation during speech, as well as to atypical hemispheric speech lateralization (Liégeois et al., 2004). However, the role of FOXP2 as an indicator of speech lateralization is not proven; indeed it is likely that it is not the primary source of lateralization determination (Corballis, 2010) as its influence on the brain has been shown to occur bilaterally (Vargha-Khadem et al., 2005).

Furthermore, affected members of the KE family show no deficits in motor control and appear to have typical handedness distributions. Other genes that have been considered to play a role in language include CNTNAP2 (Folia et al., 2011; Kos et al., 2012), DCDC2 (Darki et al., 2012), DYX1C1 (Darki et al., 2012), and KIAA0319 (Darki et al., 2012; Pinel et al., 2012); however, inconsistencies between studies cast doubt on the robustness of the results (Bishop, 2013). Although evidence suggests that genetic variants are involved in the determination of hemispheric dominance to some degree, it is likely that the picture is more complex than being dependent on just one or two genes.

5 A MODEL FOR PRAXIS AND SPEECH

It has been hypothesized that the control of handedness/motor skill is mediated by a "praxis center" in the left hemisphere, responsible for specific control of complex motor-based sequencing tasks undertaken by either hand. First described in the unpublished PhD thesis of Pamela Bryden (1988), as cited in McManus et al. (2016), and subsequently revisited by McManus et al. (2016), this model describes the functional relationship between the left-hemispheric dominance in the control of complex motor output across the hands. It posits that although the contralateral pathways for control of the hands are still activated during handedness tasks, it is in fact a specialized region in the left hemisphere, a so-called praxis center that mediates the control of this system. McManus et al. (2016) argue that the extent of left-hemispheric control of motor output is determined by the complexity of the motor task. Accordingly, low-skill tasks would be performed by the motor control centers in each hemisphere, which are directly connected to the contralateral hand. However, when motor tasks involve complex movements requiring sequential timing, visuomotor control, and accurate integration of visual feedback, the use of a lateralized praxis center is required, which is typically in the left hemisphere. They suggest that the praxis center model can explain why nonpreferred hand performance is usually worse, as it is said to rely on an "inherently nosier" motor center in the right

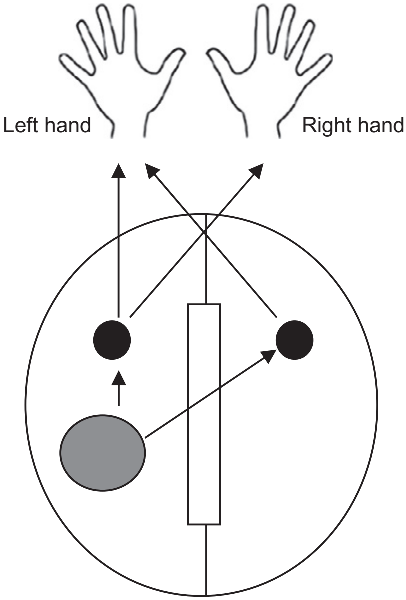

FIG. 1

A Speech-Praxis Centre model depicting ipsilateral and contralateral pathways.

hemisphere, which is dependent on transfer of information via the corpus callosum for control of the left hand. Our research (Flowers and Hudson, 2013; Hodgson and Hudson, 2016; Hodgson et al., 2016) concurs with suggestions about a specialized praxis center in the left hemisphere and extends upon the model by integrating speech production into the network, in order to propose a specialized speech–praxis component (see Fig. 1). Moreover, the model can be further extended by the proposal that this speech–praxis center in the left hemisphere becomes established via a developmental continuum of strengthening connections with increasing age (Hodgson and Hudson, 2016; Hodgson et al., 2016). We suggest that the left-hemisphere "center" activated by speech and motor control functions on a computational network basis of integration between "areas" or "sets" of neural connections involved in the processing of a number of key functions including motor action, visuomotor control, motor planning, phonological and auditory processing, and sequential control of complex "higher order" operations.

Evidence from TMS studies lends support to this notion; for example, it has been shown that the optimal site to elicit motor-evoked potentials (MEPs) for the ipsilateral hand are in areas slightly lateral and ventral to the site of maximal contralateral MEP (Ziemann et al., 1999). This shift in location within the left hemisphere for control of ipsilateral relative to contralateral hand movements has also been shown using neuroimaging (e.g., Cramer et al., 1999). Furthermore, recent evidence demonstrates that even within Broca's area, the region classically thought of as the heart of speech production and, crucially, an area which is confined to a specific part of the left hemisphere, there are spatially and temporally separate processes which occur to support speech (Flinker et al., 2015; Sahin et al., 2009). Therefore, a revised model of speech and praxis argues that the interconnectedness of these functions will determine the efficiency with which the left hemisphere is able to support motor control of both hands as well as speech production processes.

In light of emerging evidence about the structural and functional divisions within Broca's area (e.g., Flinker et al., 2015), it could be argued that strength or efficiency of callosal networks, responsible for transfer of information across between the hemispheres, is less important for the typical person who has left-hemisphere speech and right-hand dominance. For example, the speech–praxis center model comfortably explains the data from a typical participant, who probably displays left-hemisphere speech, left-hemisphere activation during right- and left-hand use on the pegboard task and for whom both hands are able to perform complex sequential tasks relatively similarly (although a hand preference still exists). In such an individual, control of the right hand is excellent due to well-integrated and frequently used contralateral motor pathways (e.g., Verstynen et al., 2005), and ipsilateral control of the left hand is good due to the effective networking of all of the aforementioned processes; put simply, the speech–praxis center in the left hemisphere is better connected to relevant core functions and is integrated with pathways highly strengthened by speech processing which also makes use of them. This therefore allows for good control of complex, sequential motor action in the left hand (e.g., van den Berg et al., 2011), something not seen in the individuals who show greater performance differences between hands. For individuals who display atypical handedness or speech then the callosal pathway/interhemispheric transfer component of the model is more critical. The level of connectivity between the hemispheres becomes more integral to successful functioning, as intrahemispheric networking may be poorer and so less able to operate independently. This would be an interesting area for further research.

One way to probe the concept of a lateralized speech–praxis center is via a dual-task paradigm, designed to produce a performance decrement when two modalities (e.g., speech and motor praxis) that rely on a common network are engaged simultaneously. Data from the unpublished PhD thesis of Hodgson (2016) show that during such a dual-task paradigm, involving a word generation task and a motor sequence praxis task, a decrement in performance is shown on the word generation task before affecting performance of the motor praxis task (see also Gentilucci, 2003). This suggests that in this paradigm the motor task is taking up more of the available network (i.e., demanding more integration from visual processes, sequencing, motor timing, planning) of overlapping processes in the left hemisphere, and less attention is therefore being paid to word production (e.g., Serrien, 2009). This nicely supports an integrated speech–praxis center model as the system appears to function well and is able to maintain low-level activity in both domains, until it is overstretched, when the weights on connections between the component processes have to be diverted to one or other of the tasks. If one assumed a model whereby speech and praxis were relatively independently controlled in the brain, albeit in the same hemisphere perhaps, then the data from this dual-task paradigm would not look like it does—there would be no specific decrement to one task over the other, and there would instead be a greater variance in performance decrements between motor and speech tasks across individuals. It would also be possible to detect a temporal order to the performance decreases, as one area or set of connections would remain functional until the other competing set came online, this does not appear to be the case from the existing data (Hodgson, 2016), although it would be interesting to test such a paradigm using temporally sensitive techniques such as EEG.

One expectation of this model might be that individuals who have atypically lateralized speech, or left-handedness, may be compromised in terms of their ability in these functions. However, there is evidence in the literature that suggests this is not true of most atypically lateralized people (see Bishop, 2013). In fact, this revised model can provide an explanation for the observation that atypically lateralized individuals are not functionally impaired. It is possible to argue that atypical speech or handedness is not indicative of compromised processing or ability, but instead such individuals are making use of differently lateralized neural networks to produce the same behavioral outcomes. It is possible therefore to envisage a continuum of atypical processing which would depend on the interconnectedness of underlying key cognitive processes (as described previously), and the relative computational strength of supporting networks. At one end of this continuum the hemispheric representation of these processes is altered, but the connectedness is still strong, and at the other end the profile of lateralization and connectivity of core components is poorer, which, in the worst cases, would lead to developmental impairments in language processing or motor control, such as DCD or SLI (e.g., Bishop et al., 2014; Hodgson and Hudson, 2016; Hsu and Bishop, 2014). This would explain such idiopathic neurodevelopmental disorders where the impairments arise due to deficits in particular sets of cognitive processes, and where behavioral deficits occur in the absence of impairments to general intelligence or other sensory processes. Hodgson and Hudson (2016) presented a study involving adults with DCD, which showed that despite no speech or language impairments, these individuals displayed atypical hemispheric lateralization for speech. Similarly, the motor performance, while impaired as expected, was worse specifically with the nonpreferred hand. This pattern of data fits with handedness performance profiles of young children (Hodgson et al., 2016) and so lends support to the idea that where one function is developmentally affected, it will have implications for the proficient development of related functions.

6 SUMMARY

This chapter has discussed the relationship between language lateralization and motor praxis, drawing on evidence from neuropsychology, developmental psychology, and cognitive neuroscience. There are a wealth of data demonstrating links between the two functions, both in terms of their neurobiology and in terms of the behavioral characteristics displayed by people across these functions. Our review of the literature indicates that common sequential processing requirements of speech production and fine motor skill are subserved by capabilities specific to the left hemisphere. In light of this converging evidence, we have proposed a unifying cognitive model to explain the variances in performance data in typically developing individuals, as well as to suggest reasons for atypical performance in individuals with developmental speech and motor disorders. Far from being a relic of the 20th century, research into speech and motor lateralization faces a bright future, not least due to exciting increases in technical proficiency abounding in brain imaging methodologies. It seems highly likely that new paradigms, probing the nature of lateralized sequential processing, can be explored in greater detail, across modalities, and across developmental trajectories, as we seek to further understand the neurological complexities of these fundamental human characteristics.

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CHAPTER

7

Handedness and cognitive ability: Using meta-analysis to make sense of the data

Marietta Papadatou-Pastou[1]
Department of Primary Education, School of Education, National and Kapodistrian University of Athens, Athens, Greece
[1]Corresponding author: Tel.: +30-210-3642771,
e-mail address: marietta.papadatou-pastou@seh.oxon.org

Abstract

The literature on the relationship between handedness and cognitive ability is riddled with studies using different conceptualizations of handedness (e.g., hand preference vs hand skill, direction vs degree, consistency vs inconsistency) and different conceptualizations of cognitive ability (intelligence vs distinct abilities), as well as different measurements thereof. Recently the literature was summarized by means of meta-analytic techniques. The findings show quite robustly that when handedness is assessed as hand preference and individuals are classified according to direction (i.e., as left-handers vs right-handers), no differences in cognitive ability emerge between handedness groups. However, other evidence points to the importance of assessing degree rather than direction of handedness and of employing hand skill rather than hand preference measures. A meta-analysis of such studies has not been possible to date, due to their scarcity. It is here suggested that degree of handedness and hand skill measures are employed in future studies exploring the possible relationship between handedness and cognitive ability so as to elaborate whether or not such a relationship exists and if so, what its characteristics are.

Keywords

Handedness, Hand skill, Hand preference, Intelligence, Cognitive ability, Meta-analysis

1 INTRODUCTION

In a recent survey of prospective teachers nearly 35% responded that the statement “Left-handed individuals don’t have a higher IQ than right-handed individuals” is false. Another 40% stated that it is true, while the rest of the surveyed participants reported that they did not know whether this statement is true or false (Papadatou-Pastou et al., 2017). Similar response patterns seem to be the case for acting teachers

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(Papadatou-Pastou et al., 2018). Confusion, when it comes to the relationship between handedness and cognitive ability (oftentimes used interchangeably with the term intelligence or IQ), is therefore present among professionals, at least in education.

This confusion is not surprising, if one takes into account that the media relish every opportunity to report on genius left-handers (e.g., “Left-handed people are more likely to be geniuses,” Sala and Gobet, 2017), while at the same time presenting the cognitive disadvantages of being left-handed (e.g., “Are you left-handed? That’s bad news (unless your mother is also a lefty),” Wright, 2014). When one turns to the scientific literature for more reliable accounts, it is only to realize that the sheer volume of the pertinent literature is challenging to manage. As an illustration, when trying combinations of keywords, such as “handedness,” “hand skill,” “hand preference,” “intelligence,” “IQ,” and “cognitive ability,” in search engines, such as PubMed and PsychInfo, one gets more than 2500 records (May 2018). What is more, these studies report conflicting and often confusing findings. For example, some studies report evidence that left-handedness is linked to cognitive deficits, if only in a subtle way (e.g., Nicholls et al., 2010), other studies have shown elevated cognitive abilities in left-handers (e.g., Ghayas and Adil, 2007), while a number of studies have failed to report any relationship between handedness and intelligence (e.g., Witelson et al., 2006). A large number of studies do not report differences between right- and left-handers in overall IQ scores, but focus on distinct cognitive abilities. Among these studies, some claim that left-handers achieve lower scores on performance IQ (e.g., Bradshaw et al., 1981; Resch et al., 1997), while others argue that left-handers tend to perform better on verbal intelligence (e.g., Johnson and Harley, 1980; Mascie-Taylor, 1980). A few studies have focused on the degree (i.e., strong vs weak) rather than the direction (i.e., left vs right) of handedness and have shown that increasing dominant-hand skill is related to enhanced language abilities (e.g., Leask and Crow, 2001) or, on the contrary, that moderate right-handers—again indexed by hand skill measures—have higher general cognitive ability scores compared with strong left- or strong right-handers (e.g., Nicholls et al., 2010).

2 IMPORTANCE OF UNDERSTANDING WHETHER A RELATIONSHIP BETWEEN HANDEDNESS AND COGNITIVE ABILITY EXISTS

Making sense of the convoluted literature on the relationship between handedness and cognitive ability can have important practical applications. Should handedness be a correlate or even a predictor of cognitive ability, then this information can help channel support to those who need it, such as those at risk of presenting cognitive delays or lower cognitive ability. On the contrary, if evidence on the relationship between handedness and cognitive ability is weak or nonexistent, then parents, teachers, and the medical community at large should refrain from dedicating resources to individuals on the basis of their handedness. Moreover, if no relationship exists, then left-handers (typically, but oftentimes right-handers too, depending on each person's beliefs) should be destigmatized as belonging to a group with lower cognitive abilities.

Understanding the relationship between handedness and cognitive ability is also important in uncovering the neurological underpinnings of individual differences in cognitive ability. Handedness is a behavioral indicator of the lateralization of the nervous system, especially the cerebral laterality for language functions (e.g., Knecht et al., 2000). Indeed, studies using methodologies as varied as the Wada technique (Loring et al., 2012), repetitive transcranial magnetic stimulation (TMS, Khedr et al., 2002), and functional magnetic resonance imaging (fMRI, Pujol et al., 1999, Springer et al., 1999) have repeatedly shown that handedness is a biological proxy—albeit a weak one—for the cerebral lateralization of language. In a seminal study including 326 healthy volunteers, Knecht et al. (2000) showed that the incidence of right-hemispheric dominance increased linearly with the degree of left-handedness, from 4% in strong right-handers, to 15% in ambidextrous individuals, and 27% in strong left-handers.

The lateralization of other functions, such as visuospatial ability (Cai et al., 2013), embodied cognition (e.g., Willems et al., 2010a), and even the function of the visual cortex (Willems et al., 2010b), has also been related to handedness (for a review, see Willems et al., 2014). Anatomical brain asymmetries have similarly been linked to handedness. For example, a larger left planum temporale and a larger right posterior ascending ramus have been observed in right-handers compared to left-handers (Foundas et al., 2002). However, a recent study including 17,141 healthy individuals found no significant associations between brain anatomical asymmetries and handedness (Kong et al., 2018). Lateralization of function may thus not reflect an underlying lateralization of brain anatomy.

In addition to the earlier, should left-handers present with higher cognitive ability compared to other handedness groups—such as mixed- or right-handers—then this finding could possibly inform the question of why there is even such a phenomenon as left-handedness. For example, genetic models, which will be presented later on in this chapter (e.g., Annett, 2002; McManus, 2004), suggest that left-handers exist due to a heterozygote advantage in cognition.

A possible association between handedness and cognitive ability (or lack thereof) is furthermore of interest because cognitive ability has been itself associated with a number of important life outcomes. For example, studies report associations of intelligence with school achievement (e.g., Deary et al., 2007; Johnson et al., 2006), socioeconomic success (e.g., Strenze, 2007), job performance (e.g., Kuncel and Hezlett, 2010), even health and longevity (e.g., Gottfredson and Deary, 2004; Singh-Manoux et al., 2005; Wraw et al., 2015), although findings are not always straight forward (e.g., Mears and Cochran, 2013; Nedelec et al., 2012; Zagorsky, 2007). When it comes to education, teachers who might erroneously believe that some of their pupils—whether left- or right-handed—are more intelligent might implicitly offer them an undue advantage compared to the other students. It has been indeed found that teacher judgments of student intelligence predict life outcomes even 40 years later (Fischbach et al., 2013).

In this chapter, I will discuss the sources of discrepancy in the findings of the pertinent literature, present the theories that have been proposed to explain the putative relationship between handedness and cognitive ability, and argue why meta-analysis is a useful tool for making sense of these findings. I will further discuss the relationship between handedness and cognitive ability by presenting the findings of recently published meta-analyses. I will conclude with the overall picture we have to date and with recommendations for future research.

3 SOURCES OF DISCREPANCY IN THE LITERATURE

The literature on handedness and cognitive ability is not only vast, but it further includes studies reporting contradictory findings. The discrepancy in study findings can be attributed to a number of factors, including the definition of cognitive ability adopted—which is often but not always equated with intelligence—and its measurement, issues pertaining to the conceptualization and measurement of handedness, the sample size of the study, and the characteristics of the populations studied. Each of these factors will be discussed below.

3.1 COGNITIVE ABILITY VS INTELLIGENCE: ISSUES OF DEFINITION AND MEASUREMENT

Studies that address the probable relationship between handedness and cognitive ability oftentimes equate cognitive ability to intelligence (Singh-Manoux et al., 2005), as it will be the case in this chapter. The very definition of intelligence is challenging and, as a result, controversial. It has been even claimed that the notion of intelligence is socially constructed (Sternberg, 2004) not only by current social conditions, but also by contemporary scientific ideas (Sternberg et al., 2005). Nevertheless, regardless of the different approaches and different definitions adopted, there are some basic cognitive functions that are recognized as fundamental to the concept of intelligence; perception, logical/critical thinking, effective adaptation to the environment, abstract thinking, creativity, and understanding (Snyderman and Rothman, 1987). On December 13, 1994, 52 academic researchers in fields associated with intelligence, defined intelligence as follows (Arvey et al., 1994; Gottfredson, 1997):

> *A very general mental capability that, among other things, involves the ability to reason, plan, solve problems, think abstractly, comprehend complex ideas, learn quickly and learn from experience. It is not merely book learning, a narrow academic skill, or test-taking smarts. Rather, it reflects a broader and deeper capability for comprehending our surroundings—"catching on," "making sense" of things, or "figuring out" what to do. (Gottfredson, 1997, p. 13)*

Studies that have assessed intelligence and its relationship with handedness have employed a number of different instruments to do so, possibly resulting in somewhat different findings. Among the tests used have been the Wechsler Scales (e.g., Bradshaw et al., 1981; Fagan-Dubin, 1974), Raven's Progressive Matrices (e.g., Ghayas and Adil, 2007), the California Test of Mental Maturity (e.g., Keller et al., 1973), the Culture Fair Intelligence Test (e.g., Hicks and Beveridge, 1978), and the Lorge–Thorndike Intelligence Test (e.g., Hardyck et al., 1976). In some cases, batteries of IQ tests have been used (e.g., Annett and Turner, 1974; Levander et al., 1989).

Other researchers in the area have opted for the term cognitive ability. For example, Nicholls et al. (2010) used the "Brain Resource Cognition" battery to measure general cognitive ability, including the assessment of sensory motor skills (motor tapping and choice reaction time), attention (digit span, continuous performance task, span of visual memory, and trail making), executive function (verbal interference, switching of attention, and maze tasks), language ability (letter and animal fluency), and memory (verbal list learning). From those tests, they derived a single measure for each participant, which corresponds to the first unrotated component obtained through principle component analysis. Furthermore, a number of studies have investigated the relationship of handedness with distinct cognitive abilities—mainly verbal (e.g., Peters et al., 2006), spatial (e.g., Gregory et al., 1980), or reading ability (e.g., Keller et al., 1973)—while some studies have even used the terms cognitive ability and intelligence interchangeably (e.g., Singh-Manoux et al., 2005).

Overall, intelligence is not only challenging to define; it has been further measured using a number of different tests or batteries. In addition, some studies focus on distinct cognitive abilities, again using a range of tests, while some studies equate the terms intelligence and cognitive ability.

3.2 CONCEPTUALIZATION AND MEASUREMENT OF HANDEDNESS

Handedness seems like an easy concept to grasp and is often understood as one's preferred hand for writing. However, among the experts in the field, handedness is conceptualized, and thus measured, in a number of different ways. The two most important conceptualizations of handedness are those of hand preference, referring to the individual's preference to use one hand predominantly in unimanual tasks, and relative hand skill, referring to the relative efficiency, speed, or strength of one hand compared to the other (Papadatou-Pastou et al., 2008). In the literature investigating the relationship between handedness and cognitive ability, both conceptualizations have been used and have been typically assessed using self-report of handedness (e.g., Inglis and Lawson, 1984), hand preference inventories (e.g., Sherman, 1979), or performance tests (e.g., McManus et al., 1988). The latter two methods can also vary in terms of the number of items comprising each tool. For example, some studies have employed as few as three items (e.g., Calnan and Richardson, 1976), while others have used batteries of between 8 and 14 manual tasks (e.g., Witelson et al., 2006).

In addition to the preference vs relative hand skill dichotomy, handedness can be regarded as a discrete variable in terms of its direction (e.g., Caplan and Kinsbourne, 1981), but can also be treated as continuous if one focuses on the degree (or strength) of handedness (e.g., Resch et al., 1997). Furthermore, handedness classifications can be binary (right or left) or they can include a third category, such as mixed-handedness, ambiguous handedness, or ambidexterity. Individuals with ambiguous handedness use different hands for the same tasks at different times (within tasks variability), while mixed-handers and ambidextrous individuals use different hands for different tasks (across tasks variability). The term ambidexterity further connotes the same level of skill in either hand, when mixed-handedness is typically used in the context of hand preference and not hand skill. The distinction between consistent vs nonconsistent handedness is also found in the literature (Nelson et al., 2014).

The different criteria used to classify participants are another source of discrepancy in the literature. By way of illustration, Newcombe and Ratcliff (1973) assessed hand preference using a 7-item handedness inventory and participants were classified as right- or left-handers only if they showed a uniform pattern for all the seven activities, with the remaining participants classified as mixed-handed. By contrast, Sherman (1979) used a 14-item hand preference questionnaire, with possible scores ranging from 14 to 70, and participants were classified as right-handed if they scored between 14 and 17 or as left-handed if they scored at least 40 (the rest of the participants were excluded from the sample).

Handedness is therefore a convoluted concept, conceptualized as direction vs degree, preference vs skill, and consistency vs inconsistency. Moreover, a number of different measurements have been proposed and used, each with varying numbers of items. In addition, different criteria have been employed for forming handedness groups in different studies.

3.3 SAMPLE SIZE AND PARTICIPANT CHARACTERISTICS

The discrepancy in the literature investigating the relationship between handedness and cognitive ability could be further explained by the fact that any associations between handedness and cognitive ability may be subtle, therefore only detectable using large sample sizes (Nicholls et al., 2010). This could possibly explain why, with a sample of 530 participants, Mayringer and Wimmer (2002) failed to replicate the findings of reduced levels of cognitive ability for mixed-handers reported by Crow et al. (1998) with a sample of 12,770 eleven-year-olds. Peters et al. (2006) arrived at a similar conclusion to Crow et al. (1998) in a study including 255,100 individuals.

Participant characteristics might also moderate findings. In the previous example, Mayringer and Wimmer (2002) had used a boys-only sample. This is not a sample representative of the population, and what is more a large meta-analysis has shown that males are 23% more likely to be left-handed compared to females (Martin et al., 2010; Papadatou-Pastou et al., 2008). In addition, older studies may have misclassified left-handers, as left-handedness was previously considered to be socially unacceptable (Douglas et al., 1967; Hardyck et al., 1976; Wilson and Dolan, 1931).

3.4 SECTION SUMMARY

To summarize, the literature suffers from the fact that both variables—intelligence and handedness—are concepts that are hard to define and measure, which has resulted in different studies using different definitions as well as different measurements thereof. Moreover, there is some evidence that the relationship between the two variables is subtle, therefore requiring large sample sizes to be investigated, possibly to the thousands. Furthermore, differences in the characteristics of the participants assessed in different studies might be further making the findings of different studies not directly comparable.

4 THEORIES LINKING HANDEDNESS WITH COGNITIVE ABILITY

The putative differences in cognitive ability between different handedness groups have been addressed by a number of theoretical accounts. One account builds on the relationship between handedness and the neurobiological substrate for language (Knecht et al., 2000). As left- and mixed-handedness reflect a shift in the typical left-hemispheric dominance for language and hand representation, this could have a knock-on effect on the localization of other cognitive functions as well as the interaction between them. For example, this reorganization could lead to enhanced brain function, as it could result in new anatomical and functional patterns, which could be optimal for supporting cognitive functioning (Benbow, 1986). Another possibility is that the effects of this reorganization would be disadvantageous, as different cognitive functions would compete for the same neural space resulting in "cognitive crowding" and hence reduced cognitive ability (Lidzba et al., 2006).

Other theoretical accounts attempt to explain the cognitive deficits not of left-handers, but of individuals lacking consistent handedness or having weak laterality patterns (e.g., Corballis et al., 2008, Crow et al., 1998, but see also Mayringer and Wimmer (2002) who found no such deficits). Corballis et al. (2008) suggested the possibility that reporting to write with either hand could represent a manifestation of intellectual confusion. For example, a confusion might exist over which hand is which or which hand is the preferred one. A historically much older account was formulated by Orton (1937) stating that ambidexterity could reflect a lack of cerebral dominance and could be associated with learning difficulties. Crow et al. (1998) proposed that individuals with equal skill in the two hands suffer from "hemispheric indecision" (p. 1275), which leads not only to suboptimal academic ability but also renders them more prone to psychotic disorders. Leask and Crow (1997) argued that there is an optimal point of lateralization away from the point of symmetry, regardless of its left- or right-hemispheric dominance.

Developmental accounts attempting to explain the putative relationship between handedness and cognitive ability have been also put forward. Boles et al. (2008) have claimed that laterality-performance correlations in adults are consistent with the developmental history of a particular process. They report data showing that lateralization is relevant to performance, though this relationship varies for different processes, with strong lateralization associated with enhanced performance for processes such as auditory, linguistic, and spatial processes, and with decreased performance for processes such as spatial emergent, spatial quantitative, and visual lexical processes. The direction of the correlation was related to the age at which lateralization for each specific process develops. Early and late lateralizing processes appear to have positive correlations while those in the middle appear to have negative ones. However, the Boles et al. (2008) data are based on a sample of right-handed adults, leaving left-handers unaccounted for.

Nelson et al. (2014) suggested that early hemispheric specialization of motor skills—manifested as consistent infant hand preference—are linked to language development. As Kotwica et al. (2008) showed, infants with consistent hand preference experience the world differently as, for example, they transfer objects to the opposite hands more readily than do infants with inconsistent hand preference. Lifter and Bloom (1989) have also shown that the timing of first words and growth in vocabulary size are linked to changes in object manipulation by infants. In other words, consistency of infant hand preference could be a marker for the efficiency of object manipulation skills, which in turn relates to the rate of language acquisition. Nelson et al. (2014) indeed showed that consistent right-handedness in infancy was associated with advanced language skills at 24 months, whereas children who were not lateralized as infants, but later developed either left or right lateralization, had more normative language scores. Nelson et al. (2014) reported that 25% of variance in language ability at 2 years was explained by handedness consistency trajectories. However, their theory focuses only on language skills, not cognitive ability in general, which is the focus of this chapter.

The cascade theory of handedness (Michel, 1983; Michel et al., 2002) postulates that handedness is the result of a cascade of motor asymmetries beginning in neonatal life and continuing through early childhood. For example, head orientation in the womb might lead to greater control of the preferred side limb, through increased proprioceptive feedback from that side of the body. This greater control could lead to hand preference on the same side, which would result in differences in object manipulation. This theory predicts that stable hand preference affects infant cognition through advantages such as the earlier acquisition of skills for object stacking (Marcinowski et al., 2016), as well as the development of language skills, as shown earlier (Kotwica et al., 2008). Again, this theory emphasizes the *stability* of hand preference, rather than specific left- or rightward *direction*.

Genetic models have also attempted to explain the link between cognitive ability and handedness observed in some studies. While a number of tentative associations of left-handedness with the genes AR, COMT, PCSK6, and LRRTM1 have been recently suggested (Brandler et al., 2013; Francks et al., 2007; Savitz et al., 2007; Scerri et al., 2010), the theoretical models that explain the putative genetic link between handedness and cognitive ability are rather old. The models of Annett (1972, 1985, 1999, 2002) and McManus (1985, 1999, 2004)—which are the most regularly cited—suggest that the very fact of the existence of the phenomenon of left-handedness can be attributed to a heterozygote advantage in cognition.

Specifically, Annett (1985) proposed that two alleles code for hand skill: an allele for right-hand dominance (rs+) and an allele for chance dominance between the two hands (rs−). Heterozygotes (rs+/rs−) will be moderately right-handed with optimal brain organization and enhanced cognitive abilities. Those individuals who are homozygous (rs+/rs+ or rs−/rs−) are the ones who will present with cognitive deficits. At the behavioral level, the latter group may be either strongly left- or strongly right-handed, depending on the allele for which they are homozygous.

McManus et al. (2013) also claimed that heterozygotes could have enhanced cognitive ability. They attributed this advantage to the fact that processing advantages might be conferred when cognitive modules that are typically located in different hemispheres (typically language functions in the left hemisphere and visuospatial functions in the right hemisphere) are organized within one hemisphere. Recent genetic studies have shifted to a multifactorial rather than a monogenic approach (for a review, see Ocklenburg et al., 2013). However, both the models by Annett and McManus et al. refer to hypothetical genes that might correspond not only to a single gene, but also to a group of genes (McManus et al., 2013). Of note, the studies that have been successful in locating genes associated with handedness (e.g., Brandler et al., 2013) have assessed handedness as *hand skill*, as opposed to the left- vs right-hand *preference* categories that give null results in genetic studies (Savitz et al., 2007).

While a 10% population incidence of left-handedness seems to have remained stable in the last centuries (Coren and Porac, 1977) and left-handedness is considered to reflect a normal variation of human behavior, it has been claimed that some cases of left-handedness might be pathological in nature. Satz was the first to propose the term "pathological" left-handedness, suggesting that left-handedness and cognitive deficits could be independent results of brain damage to the left hemisphere prenatally or perinatally (Satz, 1972; Satz et al., 1985). It has been argued that about 1 in 20 cases of left-handedness could fall under the category of "pathological" left-handedness (Bishop, 1990). However, this concept has not been widely accepted (Harris and Carlson, 1988; McManus, 1983), though there is evidence of an increased prevalence of left-handedness among individuals with various neurodevelopmental disorders such as autism spectrum disorder (Markou et al., 2017), individuals who suffered severe childhood bacterial meningitis (Ramadhani et al., 2006), females with early-life brain insult (Miller et al., 2005), and deaf individuals (Papadatou-Pastou and Sáfár, 2016).

Overall, the theories attempting to explain the putative differences in cognitive ability between different handedness groups vary from theories focusing on the cerebral localization of cognitive functions (e.g., Benbow, 1986) to theories suggesting hemispheric indecision for individuals with equal skill in the two hands (e.g., Crow et al., 1998). Other theories take a developmental perspective, such as the cascade theory of handedness (e.g. Michel et al., 2002), while genetic models propose a heterozygote advantage (e.g., Annett, 2002; McManus, 2004). The concept of pathological left-handedness has also been suggested (e.g., Satz et al., 1985).

5 THE META-ANALYTIC METHOD

When an empirical literature is not only large, but also includes inconsistent findings—as in the question of the relationship between handedness and cognitive ability—then reviews of said literature can assist in elucidating the knowledge underpinning the evidence. Traditional qualitative reviews can, for instance, provide a narrative, chronological discourse of findings. However, this method has several inherent drawbacks. First, authors undertaking the task of a narrative review are unable to deal with very large numbers of studies on a given topic, and thus tend to choose to discuss a small subset of the existing literature. This process is subjective and hence prone to bias and error. For example, the selective inclusion of studies that support an author's own point of view is not uncommon practice. Furthermore, a common way to review results is to list and describe conflicting findings, grouping together studies that report similar types of results or outcomes or even tallying the number of studies supporting various perspectives on an issue and advocating the one that gained the larger number of supporters. This procedure is not methodologically rigorous, as it ignores the size of observed effects, the design of each study as well as research quality markers, such as whether randomization or blinding took place.

Meta-analysis—a statistical technique that is gaining increasing popularity—can overcome the issues troubling traditional narrative reviews, while preserving their advantages in summarizing a given literature (see Cooper, 2015; Cuijpers, 2016; Schmidt and Hunter, 2014, for complete theoretical and practical accounts on this method). First, meta-analysis can handle a large number of studies, an overwhelming prospect for traditional literature reviews. Moreover, when performing a meta-analysis, the researcher collects the studies to be included in the analysis in a systematic, transparent, and reproducible manner using clearly defined criteria, and often including unpublished data.

Meta-analysis also represents findings in a more sophisticated manner compared to conventional reviews, by summarizing them in a quantitative manner. The actual effect sizes obtained within individual research studies are collected, coded, and interpreted using statistical methods similar to those used in the primary analysis of data, allowing for an objective appraisal of findings. This synthesis of effect sizes takes into account the accuracy of each study, assigning different weights to the effect sizes reported in each study, according to its sample size. By focusing on effect size rather than on null-hypothesis significance testing, meta-analysis protects against overinterpreting apparent differences across studies. At the same time, as individual study results are statistically integrated into one more precise outcome, even studies of small sample size and reporting nonsignificant effects contribute to the result of the metaanalysis.

One of the contributions of meta-analysis as a scientific tool is that it shows that no single study is adequate in isolation to answer a scientific question (Schmidt and Hunter, 2014). For example, while large-scale studies do exist in the field of handedness and cognitive ability, these have adopted different measures of handedness—as either hand preference (e.g., Peters et al., 2006) or hand skill (e.g., Crow et al., 1998)—and different measures of cognitive ability. Hence, despite their large sample sizes, none alone can account for all of the different manifestations of handedness or cognitive ability, limiting one's ability to generalize based on their findings.

While the inclusive nature of meta-analysis is considered a virtue, the approach has also been criticized for taking into account studies of low quality; this is referred to as the "garbage in and garbage out" problem (Hunt, 1997, p. 42). Sensitivity analysis is thus an essential component of meta-analysis for examining the robustness of the results obtained in an overall analysis of studies' findings. For example, studies of low quality or those whose sample might be deemed unrepresentative of the population can be removed in order to examine changes in the overall effect size or the resulting level of significance.

Comparability between studies that are pooled together for meta-analysis can also be an issue, as sometimes they vary notably in their sampling techniques or other aspects of their methodology. This constitutes the "apples and oranges" problem (Hunt, 1997, p. 61), which applies equally to meta-analysis as to traditional reviews. It can be argued, however, that by synthesizing findings across studies that have employed different measures to assess handedness and/or cognitive ability and which have studied different samples of the population, the outcome of a meta-analysis can be readily generalizable to the population at large. Furthermore, heterogeneity among studies can be estimated through meta-analytic techniques and, should it exist, it indicates the need to investigate potential moderator variables (Egger and Smith, 1997, Rosenthal and DiMatteo, 2001, Walker et al., 2008). Thus, meta-analysis can lead to the detection of relationships across studies that would be obscured in other approaches.

The published literature oftentimes is prone to what is called *publication bias*, which exists when the literature is systematically unrepresentative of the population of completed studies (Rothstein et al., 2006). In other words, publication bias exists when only studies that have found statistically significant results or whose findings are in line with the hypotheses put forward get published. Meta-analytic techniques allow for publication bias to be detected using both statistical tests and graphical procedures. Using only published data can introduce other kinds of biases as well, since the outcome with the most favorable findings is usually reported (Smith and Egger, 1998). Obtaining and including data from unpublished studies seem to be the solution to the problem.

To summarize, meta-analysis can be a fundamentally useful technique for summarizing results, solving ambiguity, and detecting publication bias. Meta-analysis, however, is not a panacea; it should be carried out with methodological rigor. It is only then that confidence in the results of meta-analysis can be justified.

Below I will present the recent application of meta-analytic techniques in the question of the putative relationship between handedness and cognitive ability. The first two meta-analyses (Ntolka and Papadatou-Pastou, 2017; Somers et al., 2015) have used general population samples (healthy individuals) and have compared different handedness groups in terms of their cognitive ability. The third meta-analysis (Papadatou-Pastou and Tomprou, 2015) has compared individuals with intellectual disability to neurotypical ones, as well as gifted individuals to typically developing ones in terms of their odds of presenting atypical hand preference patterns (left-, mixed-, or non-right-handedness). A fourth meta-analysis (Markou et al., 2017) compared the atypical handedness odds of individuals with autism compared to neurotypical individuals.

6 META-ANALYSIS OF GENERAL POPULATION STUDIES ON THE RELATIONSHIP BETWEEN HANDEDNESS AND COGNITIVE ABILITY

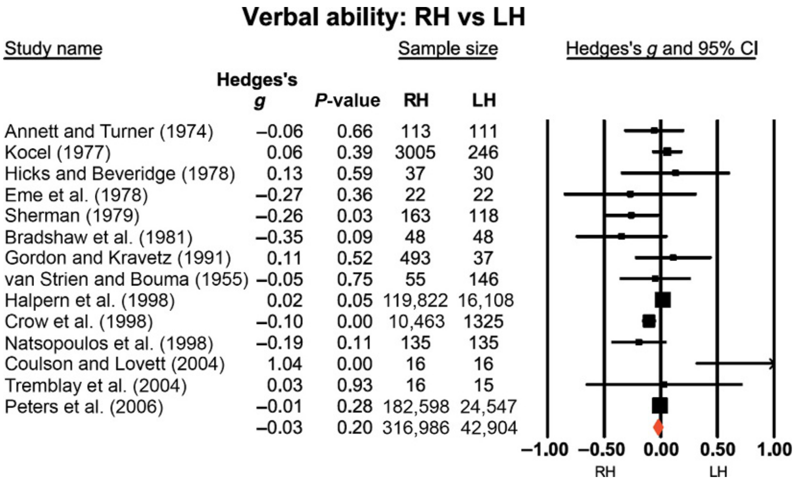
The extensive literature on the relationship between handedness and cognitive ability in the general population has been summarized by two recent meta-analyses. The first investigated the relationship of handedness with verbal and spatial ability (Somers et al., 2015), while the second included studies that measured full-scale IQ using standardized IQ tests (Ntolka and Papadatou-Pastou, 2017).

6.1 HANDEDNESS AND VERBAL AND SPATIAL ABILITY

Somers et al.'s (2015) meta-analysis compared verbal and spatial ability in left- vs right-handers. Studies eligible for inclusion needed to have measured one or more specific aspects of verbal or spatial ability (e.g., tests of vocabulary, verbal comprehension, figure completion, or mental rotation). Studies that reported verbal or performance IQ from the WAIS, but did not report separate results for subscales, were not included. The studies further measured hand preference, and not hand skill, with participants grouped according to direction rather than degree of preference. Participants who did not present a clear preference (e.g., ambidextrous individuals) were not included in the meta-analysis. Eligible studies had to have used healthy participants between 7 and 65 years of age. Out of 191 papers that had assessed hand preference in relation to verbal ability, and/or spatial ability, or cognitive function in general, 14 studies met the inclusion criteria for the verbal ability meta-analysis and 16 studies met the inclusion criteria for the spatial ability meta-analysis. A separate meta-analysis on mental rotation was also performed.

The meta-analysis of verbal ability did not reveal a significant difference in verbal ability between right- and left-handers (see Fig. 1). No sex differences were found. A small effect favoring right-handers was detected for the subsample of studies that had used children samples. However, when the two largest studies were removed (Halpern et al., 1998; Peters et al., 2006), this effect lost significance. As this comparison included only five studies, even before the exclusion of the two largest studies, its findings can only be treated as indicative.

The overall meta-analysis of spatial ability revealed a small but significant difference in favor of right-handers, Hedges' $g = -0.14$, $P = 0.03$ (95% $\mathrm{CI} = -0.26$ to -0.01) (see Fig. 2). However, the largest study (Peters et al., 2006) accounted for 96.6% of the right-handers and 94.1% of the left-handers, as assessed by self-



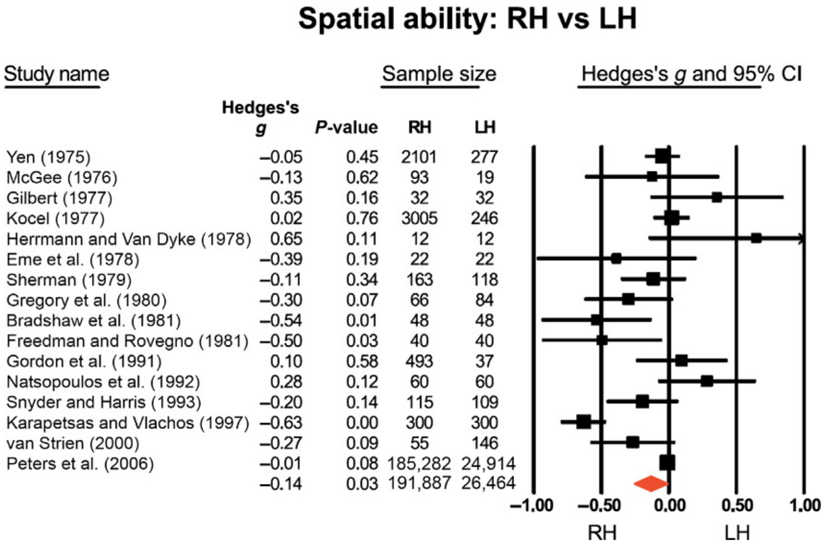
Verbal ability: RH vs LH

Study name	Hedges's *g*	*P*-value	Sample size RH	Sample size LH
Annett and Turner (1974)	−0.06	0.66	113	111
Kocel (1977)	0.06	0.39	3005	246
Hicks and Beveridge (1978)	0.13	0.59	37	30
Eme et al. (1978)	−0.27	0.36	22	22
Sherman (1979)	−0.26	0.03	163	118
Bradshaw et al. (1981)	−0.35	0.09	48	48
Gordon and Kravetz (1991)	0.11	0.52	493	37
van Strien and Bouma (1955)	−0.05	0.75	55	146
Halpern et al. (1998)	0.02	0.05	119,822	16,108
Crow et al. (1998)	−0.10	0.00	10,463	1325
Natsopoulos et al. (1998)	−0.19	0.11	135	135
Coulson and Lovett (2004)	1.04	0.00	16	16
Tremblay et al. (2004)	0.03	0.93	16	15
Peters et al. (2006)	−0.01	0.28	182,598	24,547
	−0.03	0.20	316,986	42,904

FIG. 1

Forest plot of Hedges's *d* for verbal ability between right- and left-handers.

Reprinted with permission from Somers, M., Shields, L.S., Boks, M.P., Kahn, R.S., Sommer, I.E., 2015. Cognitive benefits of right-handedness: a meta-analysis. Neurosci. Biobehav. Rev. 51, 48–63.



Spatial ability: RH vs LH

Study name	Hedges's *g*	*P*-value	Sample size RH	Sample size LH
Yen (1975)	−0.05	0.45	2101	277
McGee (1976)	−0.13	0.62	93	19
Gilbert (1977)	0.35	0.16	32	32
Kocel (1977)	0.02	0.76	3005	246
Herrmann and Van Dyke (1978)	0.65	0.11	12	12
Eme et al. (1978)	−0.39	0.19	22	22
Sherman (1979)	−0.11	0.34	163	118
Gregory et al. (1980)	−0.30	0.07	66	84
Bradshaw et al. (1981)	−0.54	0.01	48	48
Freedman and Rovegno (1981)	−0.50	0.03	40	40
Gordon et al. (1991)	0.10	0.58	493	37
Natsopoulos et al. (1992)	0.28	0.12	60	60
Snyder and Harris (1993)	−0.20	0.14	115	109
Karapetsas and Vlachos (1997)	−0.63	0.00	300	300
van Strien (2000)	−0.27	0.09	55	146
Peters et al. (2006)	−0.01	0.08	185,282	24,914
	−0.14	0.03	191,887	26,464

FIG. 2

Forest plot of Hedges's *d* for spatial ability between right- and left-handers.

Reprinted with permission from Somers, M., Shields, L.S., Boks, M.P., Kahn, R.S., Sommer, I.E., 2015. Cognitive benefits of right-handedness: a meta-analysis. Neurosci. Biobehav. Rev. 51, 48–63.

reported writing hand. When this study was removed, the overall effect size was not only smaller, but it had also lost significance (Hedges' $g = -0.15$, $P = 0.07$; 95% CI $= -0.30$ to 0.01). For both males and females, an effect in favor of right-handers was detected (although the P-value was exactly 0.05 for the males' analysis). However, the same analysis by sex does not appear to have been conducted without the large study by Peters et al. (2006). With regard to the meta-analysis on mental rotation, specifically, Somers et al. (2015) report a small but significant effect favoring right-handers (Hedges' $g = -0.13$, $P = 0.01$; 95% CI $= -0.22$ to -0.03), which remained significant after removing the Peters et al. (2006) study. Effects of sex did not reach significance ($P = 0.06$ for males and $P = 0.10$ for females). No publication bias was detected in any of the analyses. Overall, the Somers et al. (2015) meta-analysis does not provide strong evidence for a difference in either verbal or spatial IQ in favor of either handedness group.

6.2 HANDEDNESS AND INTELLIGENCE MEASURED VIA FULL-SCALE IQ

Ntolka and Papadatou-Pastou (2017) took a different approach to the question of a possible relationship between handedness and cognitive ability and—rather than spatial and verbal ability—examined full-scale IQ scores among left- vs right-handers. They reported a systematic review and meta-analysis of the studies that have measured the handedness of their participants as well as their full-scale IQ scores. Thus, in order to be included in the Ntolka and Papadatou-Pastou (2017) meta-analysis, the studies had to have employed standardized IQ tests (e.g., WISC, WAIS, and Raven's test) and to have measured the handedness of at least two handedness groups, excluding those studies that had reported IQ data only for right-handers or for left-handers. Moreover, participants had to be healthy and unselected for IQ. Through a rigorous search process Ntolka and Papadatou-Pastou located 8725 initial records, of which only 36 studies (totaling 66,108 participants) met the inclusion criteria. Moreover, only 18 studies (totaling 20,442 participants) reported the arithmetic data allowing for them to be included in the meta-analysis (i.e., IQ means and standard deviations for each handedness group or sufficient raw data to calculate these statistics from).

The systematic review of the 36 studies took a vote count approach, whereby 18 studies did not find a significant effect of handedness on IQ scores, nine studies found that right-handers obtained higher IQ scores, five studies found that left-handers obtained higher IQ scores, three studies reported lower IQ scores for mixed-handers, and one study reported higher IQ scores for mixed-handers. These findings did not seem to differ when looking only at the data on children, which comprised 20 out of the 36 studies of the systematic review. In this case, 13 studies found no differences in IQ score for any handedness category, three reported higher IQ scores for right-handers, two reported higher IQ scores for left-handers, while two reported lower IQ for mixed-handedness. Of note, the latter two studies (Crow et al., 1998; Nettle, 2003) had both drawn from the National Child Development Study dataset. Overall, the findings of the systematic review were mixed, with almost half of the studies pointing toward no effects of handedness on IQ scores.

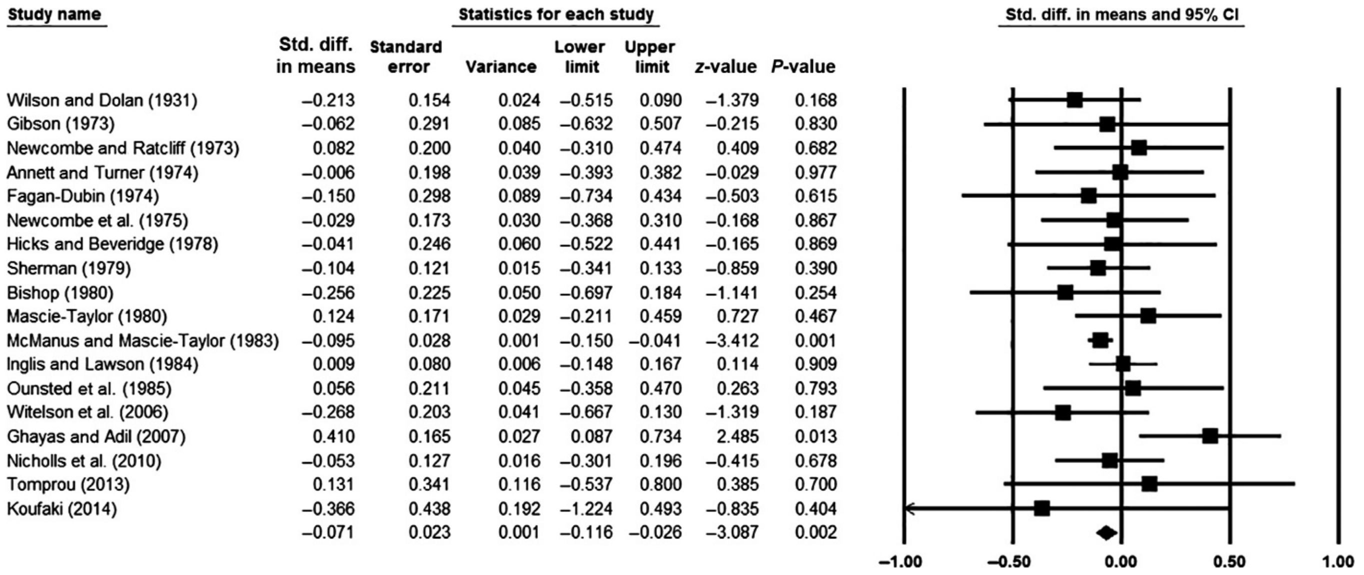
The vote count approach cannot account for factors like individual study sample size, which is an index of the study's precision, nor can it provide quantitative estimates of the relationship under investigation. Therefore, a meta-analysis was further conducted using the 18 studies that provided usable arithmetic data. A major difficulty when performing a meta-analysis of handedness data is the fact that different studies have used different handedness classifications, as described earlier. In order to overcome this issue, the authors performed three separate meta-analyses, investigating possible differences in standardized mean IQ scores between right-handers and each of (i) left-handers, (ii) non-right-handers, and (iii) mixed-handers.

When the IQ scores of right-handers were contrasted with those of left-handers, a very small but statistically significant difference emerged in favor of right-handers, with the overall standardized difference in mean IQ scores being $d = -0.07$ (see Fig. 3). If one translates this difference into full-scale IQ score points, then, if the mean score of a group of left-handers was exactly 100 with a standard deviation of 15, the mean IQ score of a group of right-handers would be 101.05, if the standard deviation was again 15. Thus, this difference is negligible in magnitude even if statistically significant. Moreover, when the authors excluded the largest study from the meta-analysis (McManus and Mascie-Taylor, 1983), the difference became even smaller and lost significance. It was further shown that no sex differences moderate the relationship between left-handedness and intelligence.

With regard to non-right-handedness and mixed handedness, Ntolka and Papadatou-Pastou (2017) found no significant differences in the IQ scores of non-right- and mixed-handers, compared to right-handers. However, only four studies in total provided mean scores and standard deviations for the IQ of mixed-handers, all of which were published on or before 1980, thus this finding should be treated with caution (Annett and Turner, 1974; Mascie-Taylor, 1980; Newcombe et al., 1975; Newcombe and Ratcliff, 1973). Moreover, the individuals who were considered to be non-right-handed were those individuals who were classified as left-handers in addition to the mixed-handers. Thus, the non-right-handedness classification also suffers from the problem of relying on a small sample of old studies.

All studies included in the meta-analysis by Ntolka and Papadatou-Pastou (2017) used direction of handedness and not degree of handedness as the manifestation of handedness. Moreover, only studies assessing hand preference were included, even though a number of studies had measured both hand preference and hand skill. However, in a number of those studies no information was reported on the relationship between hand skill and IQ, while in the remaining studies, the findings were presented inconsistently in such different ways that they could not be synthesized meta-analytically using a uniform effect size. No publication bias was detected using Egger's t statistical test (Egger and Smith, 1997).

Overall, the meta-analyses by Somers et al. (2015) and Ntolka and Papadatou-Pastou (2017) found very subtle effects favoring right-handers for general IQ and for overall spatial ability, but not for verbal ability. However, as discussed earlier, these findings lost significance when sensitivity analysis was performed.



Study name	Std. diff. in means	Standard error	Variance	Lower limit	Upper limit	*z*-value	*P*-value
Wilson and Dolan (1931)	−0.213	0.154	0.024	−0.515	0.090	−1.379	0.168
Gibson (1973)	−0.062	0.291	0.085	−0.632	0.507	−0.215	0.830
Newcombe and Ratcliff (1973)	0.082	0.200	0.040	−0.310	0.474	0.409	0.682
Annett and Turner (1974)	−0.006	0.198	0.039	−0.393	0.382	−0.029	0.977
Fagan-Dubin (1974)	−0.150	0.298	0.089	−0.734	0.434	−0.503	0.615
Newcombe et al. (1975)	−0.029	0.173	0.030	−0.368	0.310	−0.168	0.867
Hicks and Beveridge (1978)	−0.041	0.246	0.060	−0.522	0.441	−0.165	0.869
Sherman (1979)	−0.104	0.121	0.015	−0.341	0.133	−0.859	0.390
Bishop (1980)	−0.256	0.225	0.050	−0.697	0.184	−1.141	0.254
Mascie-Taylor (1980)	0.124	0.171	0.029	−0.211	0.459	0.727	0.467
McManus and Mascie-Taylor (1983)	−0.095	0.028	0.001	−0.150	−0.041	−3.412	0.001
Inglis and Lawson (1984)	0.009	0.080	0.006	−0.148	0.167	0.114	0.909
Ounsted et al. (1985)	0.056	0.211	0.045	−0.358	0.470	0.263	0.793
Witelson et al. (2006)	−0.268	0.203	0.041	−0.667	0.130	−1.319	0.187
Ghayas and Adil (2007)	0.410	0.165	0.027	0.087	0.734	2.485	0.013
Nicholls et al. (2010)	−0.053	0.127	0.016	−0.301	0.196	−0.415	0.678
Tomprou (2013)	0.131	0.341	0.116	−0.537	0.800	0.385	0.700
Koufaki (2014)	−0.366	0.438	0.192	−1.224	0.493	−0.835	0.404
	−0.071	0.023	0.001	−0.116	−0.026	−3.087	0.002

FIG. 3

Forest plot of the standardized differences in mean IQ scores between right- and left-handers. In the plot the 95% confidence interval for each study is represented by a *horizontal line* and the point estimate (Cohen's *d*) is represented by a *square*. The confidence intervals for the overall mean effect size are represented by a *diamond shape* at the bottom of the plot.

Reprinted with permission from Ntolka, E., Papadatou-Pastou, e.M., 2017. Right-handers have negligibly higher IQ scores than left-handers: systematic review and meta-analyses. Neurosci. Biobehav. Rev. 84, 376–393.

7 META-ANALYSIS OF STUDIES WITH SPECIAL POPULATIONS

The meta-analyses of Somers et al. (2015) and Ntolka and Papadatou-Pastou (2017) investigated the relationship between hand preference and cognitive ability in the general, healthy population. In these meta-analyses, participants in the studies included were grouped according to their handedness. Their IQ was subsequently measured and compared between groups. Another way to approach this question would be to investigate possible handedness differences in different intelligence groups. In other words, the participants could be rather grouped according to their IQ scores, with their handedness patterns subsequently measured and compared. Papadatou-Pastou and Tomprou (2015) followed this route and investigated the prevalence of handedness in populations that have very high IQ (who are usually referred to as “gifted” or “talented” individuals) and in populations with intellectual disability, compared to the general population. More recently, Markou et al. (2017) investigated the handedness prevalence of individuals with autism spectrum disorder and comorbid intellectual disability (i.e., excluding high-functioning individuals or those diagnosed with Asperger’s disorder in which intellectual ability is in the normal range).

Papadatou-Pastou and Tomprou (2015) located 12 studies that had compared individuals with intellectual disability with general population samples in terms of handedness and merely six studies that had compared gifted individuals with general population samples. According to the inclusion/exclusion criteria of this meta-analysis, for a study to be considered eligible it was required to include a control group of neurotypical individuals. This way, the handedness assessment was kept the same for both groups and the base rate of handedness in each individual study did not moderate findings. This control procedure is crucial given that the criteria for assessing handedness can differ significantly from study to study, as described in Section 3.2 of this chapter, resulting in large differences in absolute handedness scores. Moreover, intellectual disability needed to be of unknown or idiopathic nature. Thus, studies including participants diagnosed with Down syndrome or attention deficit hyperactivity disorder (ADHD), or participants with low birth weight were excluded. Moreover, studies in which participants were specifically selected on the basis of their handedness (typically to increase the number of left-handers) were excluded.

The findings showed that individuals with intellectual disability present with elevated levels of left-handedness compared to the general population. More specifically, the odds of left-handedness among individuals with intellectual disability compared to neurotypical individuals were 1.98, with a wide 95% confidence interval (95% CI) of 1.24–3.15. In other words, if the left-handedness prevalence in the general population was exactly 10%, then the prevalence of left-handedness for individuals with intellectual disability would be between 12% and 26%, with the best estimate being 18%. Two sensitivity analyses were performed. When the study that reported an odds ratio that was a clear outlier was excluded (Porac et al., 1980), the odds ratio changed to 1.67, with a 95% CI of 1.07–2.62. Most importantly, though, when the largest and historically oldest study (Gordon, 1921) was excluded from the analysis, the odds ratio became 1.73, 95% CI = 0.94–3.18, and was no longer statistically significant. Therefore, even if we take the upper limit of the confidence interval of the most inclusive analysis, then individuals with intellectual disability are still right-handed in their majority. If we choose to exclude the oldest and largest study, then this difference is no longer significant.

When it came to non-right-handedness—a more liberal criterion of atypical handedness—then the odds ratio between individuals with intellectual disability and neurotypical individuals remained significant, even after the study by Gordon (1921) was excluded. The actual values were OR = 2.66, 95% CI = 1.63–4.35 for the inclusive analysis, OR = 2.60, 95% CI = 1.33–5.09 for the analysis without Gordon (1921), and OR = 2.11, 95% CI = 1.49–2.98 for the analysis without Porac et al. (1980). Of note, when official/school records were used to measure handedness, the odds of being non-right-handed were 233% higher for intellectually disabled compared to neurotypical individuals, but only 110% when standardized tests were used, although this difference did not reach statistical significance. Possibly studies that used more rigorous tests to assess intelligence, also used more rigorous handedness measures.

The same meta-analysis showed further that intellectually gifted individuals are 0.76 times less likely to be left-handed compared to the general population. As an illustration, if the prevalence of left-handedness in typically developing individuals was exactly 10%, then 7.79% of intellectually gifted individuals would be left-handed. When it came to nonright-handedness odds, then no difference was to be found between gifted individuals and the general population. A word of caution is in order here: only six published studies have compared the handedness prevalence between intellectually gifted individuals and the general population, so this is a question that calls for further investigation.

Possible developmental effects could not be investigated in Papadatou-Pastou and Tomprou’s (2015) meta-analysis, due to the fact that the age ranges of participants across the various studies were for the most part overlapping. Almost all studies had included participants who were up to 18 years old. Handedness was measured as hand preference—rather than skill—and direction rather than degree of handedness was employed. No publication bias was detected.

A meta-analysis by Markou et al. (2017) found that individuals with autism spectrum disorder and comorbid intellectual disability are 3.48, 2.49, and 2.34 times more likely to be non-right-handed, left-handed, and mixed-handed, compared to neurotypical individuals, respectively. Thus, if neurotypical individuals have exactly 10% left-handedness rates, then the rate for individuals with autism would be 21.67%. The elevated levels of nontypical handedness in individuals with autism should be taken with caution, as they could be explained by the condition per se or by the associated language disability, rather than intellectual disability more generally. In this meta-analysis, the studies included had similarly used hand preference and not hand skill measures, as only two published studies have measured hand skill in individuals with autism (Cornish and McManus, 1996; McManus et al., 1992). Only five studies had further measured the degree of hand preference; these were included in a separate meta-analysis, showing weaker preferences in individuals with autism compared to neurotypical individuals. Still, the very small number of included studies does not allow for firm conclusions to be drawn.

In summary, individuals with intellectual disability were found to have elevated levels of left-handedness compared to the general population, but this findings lost significance when the oldest and largest study (Gordon, 1921) was excluded (Papadatou-Pastou and Tomprou, 2015). However, elevated levels of non-right-handedness were found both in the inclusive analysis, as well as in an analysis excluding Gordon (1921). Increased odds of right-handedness were found in studies comparing gifted individuals with the general population, but in this case the sample of studies was very small to allow for any confidence in this finding (Papadatou-Pastou and Tomprou, 2015). Individuals with autism were found to have elevated odds of being left-, mixed-, and non-right-handed, although this difference could be explained by the condition itself or by the associated language disability and not by the accompanying intellectual disability (Markou et al., 2017).

8 SUMMARY AND CONCLUSIONS

The field of handedness is vast and includes studies on the relationship between handedness and cognitive ability that are not only numerous, but also report convoluted findings due to the many ways in which handedness is conceptualized (e.g., direction vs degree, hand preference vs relative hand skill, consistency vs inconsistency), measured (i.e., via questionnaires, observation, self-report, performance measures), and classified (e.g., using two, three, or even greater numbers of categories with varying cut-off criteria). In addition to the issues pertaining to handedness, cognitive ability is another notoriously complex area of investigation, with different studies measuring different cognitive abilities and using a wide range of tests, while some studies have focused on intelligence alone using standardized intelligence tests.

With regard to the direction of hand preference, the summary of the literature as synthesized via the meta-analyses described in this chapter, allows for the rather robust conclusion that there are no differences in cognitive ability between right- and left-handers. In the cases when such differences were uncovered, they were trivial in magnitude and the analyses lost statistical significance after sensitivity analyses were performed. Specifically, the meta-analysis by Ntolka and Papadatou-Pastou (2017) found a very small difference ($d = -0.07$) in IQ scores between left- and right-handers, which lost significance when the authors excluded the largest study from the meta-analysis (McManus and Mascie-Taylor, 1983). Similarly, when Somers et al. (2015) performed separate meta-analyses for studies measuring verbal and spatial abilities, small effects in favor of right-handers were detected only for spatial abilities, but these again lost significance when the largest study—accounting for nearly 95% of the data (Peters et al., 2006)—was removed from the analysis. Papadatou-Pastou and Tomprou (2015) contrasted individuals with intellectual disability to neurotypical individuals with regard to handedness, similarly finding elevated levels of left-handedness among individuals with intellectual disability, but with this comparison becoming nonsignificant when the oldest and largest study (Gordon, 1921) was removed. With regard to gifted individuals, a small advantage in favor of right-handers was detected, although here the number of included studies was very small to allow for safe conclusions to be drawn, adding up to only six studies.

The fact that the meta-analyses detected effects of very small magnitude in favor of right-handers (before the sensitivity analyses took place) could be attributed to such effects being subtle and only detectable in large samples, as suggested by Nicholls et al. (2010). Another possible explanation could be that no differences exist between right- and left-handers, and that the small effects found in the meta-analyses are due to a misclassification of mixed-handed individuals into left-handers, especially in studies using two-way classifications. Moreover, it could be that the left-handedness of some of the participants could be "pathological" in nature (Satz, 1972).

The finding that the effects in favor of right-handers were lost after performing sensitivity analysis could be explained by the fact that, in all cases, the largest studies were excluded. While one might argue that those are exactly the studies that need to be included under the rationale that effects are subtle, the case is that the study by Gordon (1921) was published almost a century ago, and included the retrieval of intelligence data from official records rather than through the administration of standardized intelligence tests. In the study by McManus and Mascie-Taylor (1983) the measurement of handedness is not reported, while the study by Peters measured handedness by self-report of writing hand—a potential problem given that writing hand has been found to mismatch hand preference inventories in 13.5% of left-handers, but only in 0.4% of right-handers (Papadatou-Pastou et al., 2013).

Overall, when meta-analyses were performed carefully and with proper sensitivity analyses, no differences in cognitive ability were found between right- and left-handers. Notably, this conclusion is only based on studies that have assessed *direction* of handedness using *hand preference* measures. Thus, direction of hand preference does not appear to be related to cognitive ability.

When it comes to degree of handedness, the meta-analyses on general population samples do not lend themselves to answering the question of a possible relationship between degree of handedness and intelligence. In the Somers et al.'s (2015) meta-analysis, mixed-handers were excluded, whereas in the Ntolka and Papadatou-Pastou's (2017) meta-analysis, only four rather old studies provided IQ scores for mixed-handers. Papadatou-Pastou and Tomprou (2015) did find a robust difference in non-right-handedness between individuals with intellectual disability and neurotypical individuals, which did not lose significance when the study by Gordon (1921) was removed. Non-right-handedness is still a category formed on the basis of direction, but it represents a nonspecific definition of atypical handedness, typically including mixed-handers. It is in that sense that it could be relatively informative when it comes to degree of handedness, as mixed-handers are weakly lateralized. Still, direct evidence on the effects of the degree of handedness cannot be retrieved from the meta-analyses conducted to date.

However, a number of individual studies suggest that it is the degree rather than the direction of handedness that relates to cognitive ability (e.g., Corballis et al., 2008; for a review, see Prichard et al. (2013), although other studies do not attest to this conclusion, e.g., Mayringer and Wimmer, 2002). In fact, an fMRI study has shown that direction and degree of hand preference are independent aspects of handedness coded separately in the brain (Dassonville et al., 1997). When it comes to consistent vs inconsistent handedness, studies that have found predictive effects of infant handedness on later intelligence have used consistency of handedness as the criterion (e.g., Nelson et al., 2014).

In addition to the lack of information on degree as opposed to direction of handedness, an important limitation of the meta-analyses presented in this chapter is that they only included studies assessing hand preference. Studies that measured handedness as relative hand skill could not be included in the meta-analyses due to their scarcity. Yet, there is evidence from individual studies that hand skill is a more valuable conceptualization compared to hand preference when examining possible relationships between handedness and cognitive ability. For example, Nicholls et al. (2010) reported an association between cognitive ability and handedness for hand performance data whereby moderate right-handers had higher general cognitive ability scores compared with strong left- or strong right-handers. This association was negligible for the hand preference data. Nicholls et al. (2010) suggested that these findings might be due to the fact that measures of preference group individuals toward the extremes of the handedness distribution. Crow et al. (1998) analyzed data from the National Child Development Study and showed cognitive deficits for children close to the point of equal hand skill in a robust way. However, Mayringer and Wimmer (2002) studied 530 boys aged around 7 years and found no evidence for a dip in performance on tests of reading speed, orthography, or nonverbal intelligence at the point of equality between the hands—whether measured in terms of skill (peg-moving) or preference. However, as Nicholls et al. (2010) suggested, the effects of handedness on cognitive ability might be subtle and only detectable using large sample sizes. Another possibility is that studies that have reported positive findings using hand skill have done so because hand skill is usually regarded as a matter of degree rather than direction. Of note, the studies that have detected candidate genes statistically associated with handedness (e.g., Brandler et al., 2013) have assessed handedness as hand skill.

Overall, no convincing evidence for differences in cognitive ability between right- and left-handers have been shown in meta-analyses of studies that have assessed handedness as *hand preference* and have classified participants according to the *direction* of such. Effects negligible in size lost statistical significance when sensitivity analysis was performed. When it comes to degree of handedness and relative hand skill measurement, there is evidence from individual studies that these could be better predictors of cognitive ability compared to direction of hand preference, although not all findings point to the same direction. It is therefore suggested that future studies investigating the possible relationship between handedness and cognitive ability include measures of both hand preference and hand skill, and further report findings both by direction and degree.

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CHAPTER

Atypical structural and functional motor networks in autism

8

Dorothea L. Floris*[,1], **Henrietta Howells**[†]

**Department of Child and Adolescent Psychiatry, Hassenfeld Children's Hospital at NYU Langone Health, Child Study Center, New York, NY, United States*

[†]*Laboratory of Motor Control, Department of Medical Biotechnologies and Translational Medicine, Humanitas Research Hospital, University of Milan, Milan, Italy*

[1]*Corresponding author: e-mail address: dorothea.floris@nyumc.org*

Abstract

Structural and functional differences between the two cerebral hemispheres constitute one of the most fundamental aspects of brain organization. It is well established that functions related to language and motor behaviors are more strongly represented in the left hemisphere. Individuals with autism spectrum disorder (ASD) show impairments particularly in social communication, language, and a variety of motor-related symptoms, alongside intact or enhanced right hemisphere functions. This pattern of deficits and strengths has given rise to theories, suggesting that the neuropathology of ASD involves atypical hemispheric specialization. Here, we review the literature on atypical hemispheric specialization in the motor domain, which is an understudied field, but one that bears great potential for finding meaningful subgroups within the heterogeneous autism spectrum. It appears that atypical motor lateralization constitutes a candidate neural phenotype of ASD, in being a stable measure across structure, function, and behavior.

Keywords

Autism spectrum disorder, Hemispheric lateralization, Motor deficits, Structural asymmetries, Functional lateralization, Functional MRI, Diffusion tractography, Left hemisphere dysfunction

1 CEREBRAL LATERALIZATION

1.1 INTRODUCTION

Cerebral lateralization is a fundamental aspect of human brain organization and refers to the fact that the two cerebral hemispheres differ from one another in their structural and functional properties (Gazzaniga, 1972; Levy, 1974; Levy-Agresti and Sperry, 1968; Vallortigara and Rogers, 2005). Its study has a long tradition and is tied

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to the origins of cognitive neuroscience itself in the 19th century (Broca, 1864; Wernicke, 1874). Since then, research on hemispheric lateralization has experienced a notable rise in interest in the neurosciences, focusing both on the typical population and neurodevelopmental and psychiatric conditions. Today, with modern in vivo neuroimaging techniques such as functional magnetic resonance imaging (fMRI), it has been possible to pinpoint the location of lesions or regions of interest (ROIs) precisely and relate them to lateralized cognitive and behavioral measures. As a result, the concept of functional segregation in the brain has gained broad acceptance (Deco et al., 2015; Tononi et al., 1998). With the development of diffusion imaging and resting-state functional magnetic resonance imaging (R-fMRI) techniques, it has also become possible to extend the concept of functional specialization to functional integration and hodology, and further, to characterize whole brain structural and functional brain networks and their lateralization patterns (Ffytche and Catani, 2005; Gotts et al., 2013; Sporns et al., 2004).

Autism spectrum disorder (ASD) is a lifelong neurodevelopmental condition characterized by deficits in social interaction and communication alongside unusually stereotyped, repetitive behaviors, and restricted interests and resistance to unexpected change, as well as atypical sensory sensitivity (World Health Organization, 1992). It has been estimated that the prevalence of ASD in the United States is 1 in 59 children (Baio et al., 2018), with signs developing most commonly in the first years of life. Although some children with ASD may be especially dexterous and coordinated, many show profound difficulties in gross and fine motor coordination (Green et al., 2009; Mostofsky et al., 2006; Teitelbaum et al., 1998).

Motor deficits have been linked to those on the spectrum with poorer cognitive skills and low IQ, rather than those with high functioning or Asperger's conditions (Mandelbaum et al., 2006; Mari et al., 2003; Staples and Reid, 2010). Although motor deficits are not included in current diagnostic criteria for ASD, even initial observations by Kanner (1943) detail characteristic motor deficits in his profiled children, in particular in gross motor coordination. As movement disorders may occur ahead of social and communicative abnormalities (Leary and Hill, 1996), research into the neural underpinnings of early motor deficits has increased considerably in recent decades. The intention is to isolate early biomarkers, as early diagnosis makes a significant impact on the individual's quality of life (Moore and Goodson, 2003).

ASD has, more recently, emerged as a condition of atypical connectivity (Geschwind and Levitt, 2007). Theories of disconnectivity in ASD suggest there are increased local connectivity and reduced long-range connectivity (Anderson et al., 2011; Belmonte et al., 2004; Courchesne and Pierce, 2005; Just et al., 2004), and decreased frontoposterior and increased parietooccipital connectivity (Just et al., 2012; Minshew and Keller, 2010). More recent accounts postulate that hypo- and hyperconnectivity vary as a function of the underlying neural network (Di Martino et al., 2014; Picci et al., 2016). Other hypotheses about the neurobiology of ASD surround molecular, regional, or systemic dysfunction (for an overview, see Abrahams and Geschwind, 2008). Among these, the theory of atypical cerebral lateralization has emerged as one of the earliest theories trying to reconcile the complex clinical profile in ASD of both cognitive and behavioral deficits in the social domain alongside strengths and talents in unrelated nonsocial areas. Accordingly, individuals with ASD present deficits in skills mainly ascribed to the left hemisphere, such as language, communication, and motor skills, while appearing relatively unimpaired in right hemisphere functions such as visuospatial abilities (Caron et al., 2004; O'riordan, 2004; Shah and Frith, 1983). Consequently, research has suggested that atypical lateralization of these left hemisphere functions might be one potential neurobiological underpinning of the condition, and theories about atypical cerebral asymmetry and neurobiological disruption to the left hemisphere have received considerable attention in the quest to map the neuropathology of ASD (Fein et al., 1984; Prior and Bradshaw, 1979; Ricks and Wing, 1976).

While there is a large body of research on hemispheric lateralization of language-related measures across cognition, behavior, and brain imaging, other lateralized domains that are key to ASD symptomatology, such as motor aspect, are understudied. Here, we will provide an overview of research into hemispheric specialization in the structural and functional motor domains.

1.2 EVOLUTIONARY PERSPECTIVE

The presence of structural and functional asymmetries at the population level has been linked to a possible evolutionary advantage, ensuring efficient use of neural processing resources (Hirnstein et al., 2008; Nicholls, 1996). Accordingly, the division of labor between the two hemispheres prevents identical cortical representations from being unnecessarily duplicated (Hirnstein et al., 2008; Hugdahl, 2000) and increases processing speed and efficiency, given that transcortical processing and information integration are time-consuming (Ringo et al., 1994; Toga and Thompson, 2003). Also, spatially restricted, unilateral networks allow for increased capacity for parallel processing across hemispheres without information loss or interference between concurrent processes (Bradshaw, 2001; Levy, 1977). Some studies show that functional lateralization does indeed provide a cognitive and behavioral advantage (Barber et al., 2012; Gotts et al., 2013). Similarly, handedness has likely arisen to bestow an evolutionary advantage, as differential specialization of the two hands allows for the development of refined, manipulative skills and complementary bimanual actions (Michel et al., 2013). Nevertheless, results are mixed as to what extent the degree and direction of lateralization are linked to enhanced cognitive abilities (Hardyck et al., 1976); for example, bilateral or rightward language dominance in (mainly left-handed) typical individuals does not pose any cognitive disadvantage (Knecht et al., 2001).

It has been argued that leftward lateralization for language might have evolved as a consequence of gesture, based on already asymmetric motor control systems for handedness which have favored the asymmetric development of motor systems involved in speech and language (Corballis, 2003, 2009). Consistent with this, processing of verbal input also activates motor systems (Meister et al., 2003; Tettamanti et al., 2005) and deaf individuals activate similar networks involved in speech production when using gestural sign language (Emmorey et al., 2002).

The overlap of the mirror neuron system with language processing areas may provide additional support for the possible gestural origin of language (Corballis, 2010).

Thus, while hemispheric lateralization is thought to be adaptive at the population level, it remains unclear how deviations from the "standard leftward pattern" can be related to cognitive or behavioral deficits. This observation has paved the way for research into disorders such as ASD that are characterized by deficits in leftward lateralized functions. The potentially close developmental origins of language- and motor-related systems have important implications for the study of these two core domains of impairment in ASD.

1.3 ORIGINS: GENETIC AND ENVIRONMENTAL FACTORS

Although cerebral lateralization is a widely investigated topic, its underlying biological basis and developmental mechanisms are still not fully understood. There has been long-standing debate about how genetic, epigenetic, and environmental influences differentially contribute to the establishment and origins of laterality in the brain (Annett, 1978a; Bishop, 2001; Laland et al., 1995; Provins, 1997). As most people show the same directional bias in hemispheric specialization (Annett, 1985; Damasio and Geschwind, 1984; Geschwind, 1970; Wada et al., 1975), the idea that nonrandom biological mechanisms are involved in predisposing the cerebral hemispheres for lateralization is well accepted. Other data provide support for this: (a) some structural cerebral differences such as in the temporal lobe and white matter tracts are already present early in maturational development as seen in fetuses (Chi et al., 1977; Kasprian et al., 2011), newborns (Witelson and Pallie, 1973), and infants (Dubois et al., 2009); (b) handedness originates prenatally (Hepper, 2013; Hepper et al., 1998). In ultrasound scans, Hepper et al. (1991) observed fetuses sucking the thumb of one preferred hand by 12 weeks of gestation, which correlated with later hand preference (Hepper et al., 2005); and (c) some studies show familial aggregation of left-handedness (Mcmanus, 1985; Mcmanus and Bryden, 1992). Based on these lines of evidence, genetic theories have been put forward stating that cerebral language lateralization and motor dominance have an innate, biological foundation with genetic determination (Annett, 1978b, 1985; Mcmanus, 1991; Mcmanus and Bryden, 1992).

A prominent theory is the right shift theory (Annett, 1985), suggesting a genetic influence toward right-, but not left-handedness. This theory proposes that one single gene with two alleles (one "right-shift" allele: rs+; one allele without directional specification: rs−) is responsible for cerebral lateralization. If a person features the dominant rs+ allele which codes for leftward cerebral dominance, this causes a bias toward right-handedness, whereas its absence signifies no liability to any side and depending on random environmental factors there can be an equal outcome of either right- or left-handedness. Due to the clear relationship between handedness and language lateralization, Annett (2002) and Mcmanus (2002) argue that they are associated with the same lateralizing gene.

Other single gene models were proposed by Crow (2002), stating that a single laterality gene would be located in homologous regions on the X and Y chromosome, but this has not been confirmed (Francks et al., 2002). Other single genes implicated in handedness and language lateralization are the *LLRTM1* gene, which has been associated with handedness and schizophrenia (Francks et al., 2007), and the *FOXP2* gene, for which disruption has been linked to speech and language impairment (Lai et al., 2001; Zeesman et al., 2006).

On the other hand, Mcmanus et al. (2013) reported the involvement of more than 30 genetic loci in the establishment of hand preference (which might potentially overlap with those for language), lending support to a polygenetic model of the establishment of handedness. In line with Annett's theory, Geschwind et al. (2002) report that the genetic influence on frontal and temporal regions is larger in monozygotic twins who are concordant for right-handedness compared to monozygotic twins who are left-handed or discordant for handedness, implying a greater involvement of environmental factors in left-handers. Annett's model acknowledges the interactive developmental process between genes and environment in the establishment of laterality. However, most single loci models are probably too simplistic to explain such a complex trait as cerebral lateralization. Single gene models explain only low variance in individuals' handedness and are, for example, at odds with the equivalent concordance rates of handedness in monozygotic and dizygotic twins (Laland et al., 1995). Multifactorial models and multigenetic control are therefore much more likely, and genome-wide association studies may help identify genes and advance understanding of the ontogenesis of cerebral lateralization.

Genetics is undoubtedly involved in the origins of laterality. However, several lines of evidence suggest a significant role for environmentally induced plasticity (Schaafsma et al., 2009). There are cases of monozygotic twins with weak concordance for handedness (Rife, 1940; Sicotte et al., 1999), language lateralization (Sommer et al., 2002), and asymmetry of brain regions that are known to be leftward asymmetric and play a key role in language processing such as the planum temporale (Eckert et al., 2002). In line with this, a meta-analysis shows that only 25% of the variability in handedness can be explained by genetic factors (Medland et al., 2006). In addition, Geschwind et al. (2002) report that left frontal and temporal regions are under reduced genetic control compared to the right hemisphere, and more susceptible to environmental influences.

As lateralization differs between the sexes (Shaywitz et al., 1995; Voyer, 1996) and males are exposed to higher androgen levels prenatally (Hines et al., 2015), several theories have been put forward pointing to noninherited in utero factors, such as prenatal testosterone, in contributing to the establishment of functional brain lateralization. Evidence for this includes that (a) males (11.6%) are more often left-handed than are females (8.6%) (Mcmanus, 2002); and (b) males show a more pronounced lateralization of cognitive functions in comparison to females who display greater bilateral representation (Beaton, 1985; Voyer, 1996). This has also been shown in cortical language regions such as the planum temporale and Heschl's gyrus (Good et al., 2001; Shaywitz et al., 1995). Furthermore, (c) girls affected by a medical condition that results in high intrauterine levels of testosterone (congenital adrenal hyperplasia) show a higher incidence of left-handedness (Kelso et al., 2000; Nass et al., 1987); (d) women prenatally exposed to diethylstilbestrol, a synthetic estrogen that is supposed to have a masculinizing effect on the brain, show a higher incidence of left-handedness than neurotypical females (Scheirs and Vingerhoets, 1995); and (e) girls from opposite sex twin pairs exhibit a more masculine pattern of cerebral auditory lateralization than girls from same sex twin pairs (Cohen-Bendahan et al., 2004). Since animal studies confirm that androgenic steroids have organizational effects on both brain and behavior (Phoenix et al., 1959; Schaafsma et al., 2009), three influential theories about the role of prenatal testosterone in the establishment of lateralization have been proposed.

One of the most commonly cited theories about the modulating effect of fetal testosterone on early brain organization is that of Geschwind and Galaburda (1985a,b,c). They stated that exposure to elevated levels of prenatal testosterone during critical periods of fetal brain development alters the "standard dominance pattern" in the hemispheres and leads to an unequal development of the cerebral hemispheres, characterized by an inhibition of maturation of the left hemisphere, with a corresponding enhancement of development of the right hemisphere, resulting in atypical cerebral dominance for language and handedness. This theory may explain why men are more often left-handed than are women, and are more strongly lateralized in visuospatial skills dominated by the right hemisphere. It also provides the best explanation for atypical patterns of lateralization (such as an overrepresentation of left-handedness and a reversal of cortical asymmetries and functional lateralization) associated with neurodevelopmental conditions (Brandler and Paracchini, 2014). However, it cannot account for the fact that men have stronger leftward dominance for language.

In contrast, the callosal hypothesis (Witelson and Nowakowski, 1991) states that prenatal testosterone exposure leads to increased axonal pruning during fetal development, resulting in less interhemispheric connectivity and stronger hemispheric specialization of function in males. This was based on Witelson and Nowakowski's observation that nonright-handed males show increased corpus callosum volume compared to consistently right-handed males. As this association was observed in males only, they hypothesized that elevated levels of prenatal testosterone are related to greater lateralization of cognitive functions and a stronger right-handedness. The sexual differentiation theory put forward by Hines and Shipley (1984) postulates that lateralization is formed as part of sexual differentiation in the brain and prenatal testosterone exposure has a masculinizing effect on both the direction and degree of lateralization. The prediction of this theory would be that higher levels of prenatal testosterone exposure are related to more masculine patterns of handedness (direction: i.e., left-handedness) and a stronger lateralization for cognitive functions (degree).

Neither theory has received full confirmation in either humans or animals (Pfannkuche et al., 2009). In typically developing individuals, Geschwind and Galaburda's (1985a,b,c) theory has been corroborated in one study showing a positive association between fetal testosterone and rightward asymmetry of the isthmus of the corpus callosum (Chura et al., 2010). Most studies seem to find confirmation, however, for the callosal hypothesis, showing a positive relationship between fetal testosterone and leftward language lateralization (Grimshaw et al., 1995; Hollier et al., 2014; Lust et al., 2010) and left-handedness (Lust et al., 2011).

Apart from biological factors acting in the prenatal environment, alternative environmental factors such as perinatal stress (Orlebeke et al., 1996; Soper and Satz, 1984), fetal posture or head position, or asymmetric vestibular stimulation in utero (Michel and Goodwin, 1979; Previc, 1991), cradling by mothers (Donnot, 2007), and social pressure (Porac et al., 1986) have all been suggested to influence the establishment of hemispheric lateralization. A recent R-fMRI study has confirmed that asymmetry is influenced by multiple, independent factors (Liu et al., 2009). The complex interplay of genetic and nongenetic factors poses a challenge for determining the ontogenetic and epigenetic bases of handedness and other forms of cerebral asymmetries. It is still unclear how their differential contribution varies between typical individuals and those with neurodevelopmental conditions involving atypical lateralization.

2 ALTERED MOTOR BEHAVIOR IN AUTISM SPECTRUM DISORDER

2.1 EARLY MOTOR DEVELOPMENT

Many individuals with ASD exhibit characteristic motor impairments that can be present as early as the first few days after birth (Teitelbaum et al., 1998). Delay in major developmental milestones has been reported (Ornitz et al., 1977), but so too have broad differences in motor behavior. Retrospective video analysis has shown that there are altered motor patterns in infants who are later diagnosed with ASD across major developmental motor milestones: in lying, righting from the back to stomach, sitting, crawling, standing, and walking (Adrien et al., 1993; Teitelbaum et al., 1998). At 3 months of age, neurotypical babies commonly start rolling from their back to stomach using a sequential rotational movement starting from pelvis, to trunk then the upper body (Teitelbaum et al., 1998). However, babies later diagnosed with ASD have been reported to be able to perform this movement only between 6 and 9 months, and are unable to coordinate this in a sequential motion (Teitelbaum et al., 1998). Other characteristics of motor behavior include inhibition of motor activity (hypoactivity), repetitive and rhythmic movements (motor stereotypies), and low muscle tone (hypotonia), as well as difficulties in postural adjustment, which may be part of the motor repertoire of individuals with ASD throughout life (Baranek, 1999; Shetreat-Klein et al., 2014).

These motor deficits have been linked to a persistent lack of symmetry in motor actions between the two sides of the body, even in these early stages of life. Babies later diagnosed with ASD exhibit a lower level of symmetry when lying, in contrast with neurotypical babies between 12 and 21 weeks of age (Esposito et al., 2009).

Children with ASD show more visible motor asymmetry when static, visible in a left–right slant when sitting or standing (Esposito et al., 2009). Dynamic motor asymmetry is also present, in that a left–right postural instability is present when crawling (Teitelbaum et al., 2004) and jumping (Paquet et al., 2016). It has been speculated that this lack of symmetry in postural control may be related to differences at the cerebellar level, which influences vestibular control, and this may underlie the gross motor disturbance commonly reported across the life span (Mostofsky et al., 2009).

Both the delay in major motor milestones and disturbance in the form of hypoactivity, motor stereotypies, and hypotonia can be evident in babies and children, well before a diagnosis of ASD is given. Studies also suggest that both static and dynamic motor symmetry during postural control is disrupted in children with ASD. These behaviors may be the precursor to the gross and fine motor disturbance discussed in the following sections.

2.2 GROSS MOTOR DISTURBANCE

2.2.1 Gait

Gross motor disturbance is most visible in the walk of a child with ASD. For this reason, walking is one of the most well-studied motor aspects in ASD (Fournier et al., 2010). Locomotor activity requires highly complex coordination of the body to achieve equilibrium, and impairments may be linked to cerebellar and basal ganglia disturbance (Rinehart et al., 2006). Although “clumsy gait” is commonly reported in children with ASD, studies testing kinematic aspects of gait have shown contrasting results with respect to neurotypical children. The two earliest studies reported a similarity between the walks of children with ASD and adults with Parkinson’s disease (Damasio and Maurer, 1978; Vilensky et al., 1981), characterized by slower gait velocities, shorter step lengths, increased stance time, increased hip flexion at toe-off, decreased knee extension and ankle dorsiflexion at ground contact, and a flexed posture of the limbs and trunk. This similarity was disputed by Hallett et al. (1993) who reported no difference in gait between children with ASD and neurotypical children.

A more recent study analyzed stride duration, mean velocity, frequency, and oscillatory and support phases of gait in six children with ASD and nine neurotypical children, also concluding these to be similar in both groups (Vernazza-Martin et al., 2005). However another study—again with a small sample size—reported inconsistent stride length and difficulties walking in straight lines among children with ASD in contrast with neurotypicals (Rinehart et al., 2007). The discrepancies in these findings may be related to the heterogeneous profile of individuals with ASD and the inclusion criteria, which can vary in IQ level, age range, and kinematic analysis across studies.

Another feature of ASD is an increased prevalence of idiopathic “toe walking,” whereby children walk on the toes with little weight on the heel, which is considered abnormal when it continues past the age of 2 (Ming et al., 2007). In a large sample of children with ASD with an average age of 6 years, toe walking was present in 20% of the group (Barrow et al., 2011). Interestingly, this is a feature long associated with language disorders in children (Accardo et al., 1992), as well as other neurodevelopmental disorders such as attention deficit hyperactivity disorder (ADHD) (Cole et al., 2008), although its neurophysiological basis is still not well known.

In many children with ASD, clumsiness in gait is accompanied by abnormal arm flaying (Loh et al., 2007). One study investigating kinematics of upper limb movement reported that ASD children produce more jerky, horizontal sinusoidal arm movements than neurotypical controls, with greater acceleration and velocity (Cook et al., 2013). Further, intensity of this atypical behavior has been correlated with autism severity, but also with perception of biological motion. One study has shown that children with ASD swing their arms with less symmetry while walking, which may be a compensatory mechanism to resolve problems with postural control (Esposito et al., 2009).

In sum, unusual gait patterns and stereotypies such as toe walking and arm flaying are generally present in ASD and could potentially serve as a behavioral marker of ASD. However, due to the heterogeneity of behavioral presentations of children with ASD, it still remains to define exactly how these patterns are altered.

2.2.2 Posture

Postural stability requires the ability to maintain one's center of gravity within a given base of support to maintain an upright stance (Shumway-Cook and Horak, 1986). This is crucial not just for standing still but also for changing positions and performing many tasks such as riding a bicycle or throwing objects. Appropriate posture requires a high level of sensorimotor integration, between visual, vestibular, and somatosensory inputs and motor output. In ASD, postural control is much less well developed in contrast to neurotypical controls, as measured by postural sway, sway path length or sway velocity (Fournier et al., 2010; Travers et al., 2013). ASD children can have particular difficulties in postural control when somatosensory or perceptual inputs are altered (Kohen-Raz et al., 1992; Minshew et al., 2004; Molloy et al., 2003), although one study has reported that in fact limiting one or both of these sensory inputs can enhance postural control (Kohen-Raz et al., 1992).

Children with ASD may rely more on reactive rather than anticipatory strategies in postural control. Schmitz et al. (2003) recorded kinematic and electromyographic (EMG) activity on both the arms of neurotypical children and children with ASD during bimanual load lifting tasks requiring forearm stabilization during imposed or voluntary unloading. It was reported that although stabilization was good in both groups, delay in the latency of kinematic and muscular activity during unloading indicated the children with ASD were not anticipating the required muscular event, but rather moving as a feedback response. This could be explained by a general impairment in building internal representations, but perhaps underlying this may be a more general problem in the anticipation of motor behavior in ASD, which may pervade other cognitive and emotional domains (Sinha et al., 2014).

Gross motor asymmetry observed in toddlers with ASD is also evident in the direction of postural instability of older children. Typically developing children show postural instability characteristically in an anteroposterior direction, whereas the instability of ASD children follows a left–right lateral sway (Kohen-Raz et al., 1992; Memari et al., 2014). This suggests that some asynchrony may exist in structural and functional brain networks, at a subcortical but also at a cortical level. Although gross deficits are the best-studied aspect of motor behavior in ASD, evidence is building to indicate that more subtle aspects of motor control are also substantially altered, in fine motor control for both manual dexterity and coordination.

2.3 FINE MOTOR DISTURBANCE

Although some individuals with ASD display highly skillful fine motor behaviors, many can show impairments in manual actions, which causes difficulties in the fulfillment of prospective goal-directed actions (Bhat et al., 2011). Theories of embodied cognition indicate that higher cognitive ability crucially requires sensorimotor representations, which is facilitated by exploration of the external environment (Caramazza et al., 2014). Appropriate cognitive development should thus be more dependent on the most complex adaptive behaviors such as those performed by the hands, rather than those performed by the lower limbs.

In early motor development, atypical exploration of objects with the hands is reported in infants that later develop ASD, and both oral and manual motor abilities can distinguish ASD from typical development in children, with high sensitivity and specificity (Gernsbacher et al., 2008; Ozonoff et al., 2008). In childhood, fine motor skill using the Movement-ABC (and ABC-2) batteries has demonstrated a strong correlation between ASD severity and motor impairment (Green et al., 2009; Hilton et al., 2007). These fine motor impairments may also be linked to deficits in other cognitive functions in ASD, such as linguistic ability (Whyatt and Craig, 2012). Differences between individuals with ASD and neurotypicals are also detectable in handwriting, with enlarged letter size evident (macrographia) and a lower speed of production (Kushki et al., 2011).

Kinematic studies of motor planning and execution have shown that while basic movements may be performed with similar reaction times to those in neurotypical individuals, there is higher variability among individuals with ASD (Dowd et al., 2012). More apparent group differences occur for more complex motor tasks, showing specific deficits in motor programming. One study has demonstrated this in adults with ASD and neurotypical controls, using a valid precue to direct the hand to be moved and the distance of the target to grasp, showing longer and more variable movements in ASD (Glazebrook et al., 2008). A follow-up study introduced invalid cues to this setup, requiring an extra planning step for reprogramming, which adversely affected individuals with ASD more than neurotypical individuals (Nazarali et al., 2009). These motor-planning deficits may be related to difficulties in responding to visual information in an appropriate way. Fabbri-Destro et al. (2009) examined this, using a reaching and grasping paradigm for containers of different sizes, and reported that children with ASD did not adjust the temporal characteristics of their movement in accordance with the object in the same way as neurotypical controls. They suggested that this may reflect a tendency for children that later develop ASD to program movements in independent steps rather than in a cohesive pattern.

One evident interpretation of this lack of ability to sequence actions in motor plans may be an impairment in being able to anticipate actions beyond the immediate goal. This may extend beyond fine motor actions with the hands, as reported in a study using EMG analysis of mouth muscles in children diagnosed with ASD and neurotypical children (Cattaneo et al., 2007). In this study, neurotypical children showed anticipatory activity in the muscles of the mouth when reaching to grasp food, whereas children with ASD did not activate mouth muscles until the phase of bringing the food toward the mouth. It was proposed that impairment in muscle action chains may lead to deficits in ASD for goal-directed movements. A similar study in a less naturalistic setting, minimizing environmental distractors, did not find similar results (Pascolo and Cattarinussi, 2012), which may indicate that these differences are subtle and can be detectable only in situations of heightened sensory stimulation. Further investigation is required to confirm this pattern.

What these results do suggest, however, is that the relationship between perception and motor action may be altered in ASD. Being able to chain together sequences of motor actions to achieve a goal crucially requires the ability to appreciate the constantly updating salience of the surrounding environment. This demands both an appreciation of the motion patterns of other living organisms—termed biological motion (Simion et al., 2008)—and an understanding of an object's features that allows the viewer a full appreciation of the possibility of different motor actions, or their affordance (Linkenauger et al., 2012). Further, action observation results in a resonant response in the individual's motor execution network, that is, modulated by attention and perceptual information (Leonetti et al., 2015; Puglisi et al., 2017). It has been proposed that one or both of these abilities are impaired in ASD, and that this may be the underpinning of the wider social and communicative difficulties encountered (Kaiser and Shiffrar, 2009). A number of studies have evaluated perception of biological motion in ASD, concluding this to be unimpaired relative to the case of neurotypical controls, at least in adults (Murphy et al., 2009; Saygin et al., 2010). However, earlier in development, detectable differences have been reported in 2-year olds with ASD, that fail to orient toward biological motion, unlike neurotypical children (Klin et al., 2009). As previously described, individuals with ASD are slower and more prone to making errors during reaching and grasping tasks, suggesting difficulties in determining action capabilities (Linkenauger et al., 2012).

Current research has demonstrated that there may be subtle but detectable differences in fine motor behavior of children with ASD, which may be explained by altered integration of perception with motor actions. Kinematic pattern analysis of reaching and grasping has started to yield putative biomarkers for detecting differences between typically developing individuals and those with ASD in naturalized hand movements (Anzulewicz et al., 2016; Sacrey et al., 2014), which may prove to be a powerful tool in the diagnosis of ASD.

3 HANDEDNESS AND AUTISM SPECTRUM DISORDER

3.1 DEVELOPMENTAL ORIGINS

In humans, reaching and grasping movements are most commonly performed with one preferred hand over the other. In the general population, most people (70%–90%) prefer to use the right hand for specialized everyday tasks, while those who choose to use the left hand, or both hands interchangeably, are the exception in around 10% of individuals (Gilbert and Wysocki, 1992). Non-right-handedness has sparked considerable interest in research due to its overrepresentation in neurodevelopmental conditions such as ASD (Boucher, 1977; Colby and Parkison, 1977), ADHD (Reid and Norvilitis, 2000; Yamamoto and Hatta, 1982), dyslexia (Eglinton and Annett, 1994, Richardson, 1994), epilepsy (Bolin, 1953; Slezicki et al., 2009), and schizophrenia (Dragovic and Hammond, 2005; Lishman and Mcmeekan, 1976).

As previously described, handedness emerges early in infant development with some studies, suggesting that precursors to handedness can be observed in early gestation already. Prenatal thumb sucking—but no other mouth contacts with the hand (de Vries et al., 2001)—is correlated with postnatal handedness at ages 10–12 years old (Hepper et al., 2005). Over the first few years of life, manual skills show a dramatic developmental change with symmetric bimanual movements preceding asymmetric reaching and grasping actions. In the first year of life, fluctuations between right-, left-, and bilateral hand preference for reaching are typically observed (Corbetta and Thelen, 1996; Gesell and Ames, 1947; Mccormick and Maurer, 1988; Thelen et al., 1996). This variable hand use in infancy suggests that handedness is not yet reliable and stable early in development. Despite great variability in the first year of life, however, some suggest that preference for reaching in 7- to 13-month-old infants can serve as an early marker of later hand preference (Michel et al., 2002, 2006).

There is no clear consensus about the age at which handedness is attained. According to Mcmanus (2002), handedness cannot be assessed reliably before the age of 4, whereas others suggest that a clear preference is not established until the age of 6 (Bryden et al., 2000). It has been suggested that the direction of handedness is established around the age of 3, whereas the degree of handedness becomes gradually more refined between the ages of 3 and 9 (Longoni and Orsini, 1988; McManus et al., 1988). Taken together, there is probably a shift from weak, inconsistent hand preference at around age 3–5, to the strongest tendencies toward handedness between the ages of 7 and 10 (Bryden et al., 2000; Scharoun and Bryden, 2014; Singh et al., 2001). Despite the involvement of genetic programming and the emergence of precursors of handedness in early infancy, its establishment is highly malleable (Corbetta et al., 2006) and different pathways for its development exist (Michel et al., 2006), with experience, learning, and practice being major factors influencing the continuous strengthening and maturation of hand preference across development.

Handedness is often used as a general marker of other functional asymmetries such as language lateralization. Although it has been suggested that the two should share a genetic component (Annett, 2002; Mcmanus, 2002), as previously described, recent genetic analysis has indicated the two are ontologically independent phenotypes (Schmitz et al., 2017). Traditional assessment of hemispheric lateralization of language function using WADA testing has indicated around 97% of right-handers have language function lateralized to their left hemisphere (Annett, 1985; Damasio and Geschwind, 1984; Geschwind, 1970; Wada et al., 1975). Language lateralization has been tested more recently using fMRI and has been studied in a large cohort of 297 subjects (153 nonright-handers), with the indication that the incidence is smaller, with 88% of right-handers having strongly left-lateralized processing for language production (and 78% of nonright-handers), 12% of right-handers having bilateral language lateralization (15% of nonright-handers), and only 7% of nonright-handers having strongly right-lateralized language lateralization (Mazoyer et al., 2014). Thus, compared to right-handers, there is an increased association between left-handedness and atypical language lateralization. There is a growing body of evidence that is starting to explore the relationship between handedness, language lateralization, and ASD (Lindell and Hudry, 2013). These studies have indicated that those individuals with ASD with language deficits have a more atypical handedness profile than those individuals with lower language impairment and neurotypical controls (Escalante-Mead et al., 2003; Hauck and Dewey, 2001; Knaus et al., 2010). In the future, this direction of study may yield a useful early biomarker for diagnosis of ASD in infants; for example, Eyler et al. (2012) used fMRI to show that 1-year-old children with ASD showed an atypical lack of left temporal activation in response to speech. It is unknown how this unusual language lateralization relates to patterns of handedness and altered motor lateralization in ASD.

3.2 HANDEDNESS IN AUTISM SPECTRUM DISORDER

Based on the overrepresentation of left-handedness in neuropsychiatric conditions, neuropathological theories for the origins of left-handedness have been put forward stating that its formation might be associated with disruptive events during pregnancy, such as early asymmetric brain insult (Satz, 1972, 1973) and/or perinatal stress (Soper and Satz, 1984), although left-hand preference is also observed in uncomplicated pregnancies (Hepper et al., 1991, 1998).

The left hemisphere dysfunction theory received its earliest confirmation based on the observation that individuals with ASD demonstrate elevated rates of non-right-handedness relative to family members, neurotypical controls, and the wider population, comprising both left-handedness (Colby and Parkison, 1977; Gillberg, 1983; McCann, 1981; Soper et al., 1986; Tsai, 1982, 1983) and mixed handedness (Bryson, 1990; Cornish and Mcmanus, 1996; Fein et al., 1984; Soper et al., 1986). More recent studies confirm elevated rates of non-right-handedness among individuals with ASD (Bonvillian et al., 2001; Dane and Balci, 2007; Escalante-Mead et al., 2003; Lewin et al., 1993). Consistent with this, 30%–40% of children with ASD display inconsistent hand preference, whereas 15%–20% exhibit established left-hand preference, an almost twofold increase compared to the general population (Leboyer et al., 1988). Mixed-handed individuals with ASD score lower on cognitive tasks in comparison to those with consistent hand preference (Dawson et al., 1982; Fein et al., 1984; Soper et al., 1986; Tsai, 1982), which makes handedness a potential measure of future outcome in children with ASD at the age of 5 or 6 (Tsai, 1983).

Apart from left hemisphere dysfunction, several other theories have been suggested to explain this atypical pattern of handedness. As mixed handedness is part of typical development under the age of 4, before the establishment of consistent handedness, Annett (1970) and Fein et al. (1984) suggested that atypical handedness reflects a developmental or immaturity due to early brain insult (Satz et al., 1988). Others suggest that ambiguous handedness might be related to bilateral brain insult, whereas those individuals with ASD who establish consistent handedness are less severely affected (Soper et al., 1986; Tsai, 1983).

Bishop (1990) and Cornish and Mcmanus (1996) argue that increased rates of non-right-handedness in ASD might reflect deficits in motor functioning. Hauck and Dewey (2001) did not find support for a relationship between non-right-handedness in ASD and poor motor functioning or cognitive developmental delays and it is more likely that uni- or bilateral brain alterations may explain the increased prevalence of left-handedness in ASD, which we will now discuss from a structural and functional perspective.

Despite the clearly established notion of increased rates of non-right-handedness in ASD, it remains unclear whether this relates primarily to direction (left vs right), degree (hand preference between tasks; e.g., right hand on task A vs left hand on task B), or consistency (hand preference within tasks, i.e., either hand on same task). As all three measures are altered in individuals with ASD and show some associations with poorer cognitive and behavioral outcome, further research is needed to establish its biological underpinnings in ASD.

4 STRUCTURAL LATERALIZATION AND AUTISM SPECTRUM DISORDER

4.1 DEVELOPMENTAL ORIGINS

Morphological left–right asymmetries are a key property of most biological systems, ranging from single cells to human beings (Geschwind and Galaburda, 1985a,b,c; Kimura, 1973). The higher complexity of humans is characterized by more pronounced and elaborate specialization of biological structure, as expressed in asymmetries of the placement of visceral organs (e.g., the heart) or asymmetries of gross external features (e.g., feet, hands, and the face) (Kimura, 1973; Levy and Levy, 1978; Purves et al., 1994). This pattern also applies to neuroanatomy and cognitive processing, and it is well documented that in both humans and many mammals the two hemispheres differ in anatomy (e.g., in size, location, and shape of some regions) and function (i.e., information processing abilities) from each other (Gazzaniga, 1972; Levy, 1974; Levy-Agresti and Sperry, 1968; Vallortigara and Rogers, 2005).

The left and right hemispheres in 12-week-old fetuses have asymmetric gene expression, which is likely linked to asymmetric cortical development starting in gestation (Sun et al., 2005). Gross left–right asymmetries between the hemispheres are apparent around 20–22 weeks of gestation (Hering-Hanit et al., 2001). The sylvian fissure starts developing at around 21 weeks of gestation (Bernard et al., 1988), and first asymmetries in this region are detectable at around 29–31 weeks of gestation (Chi et al., 1977; Wada et al., 1975). Also, in neonatal brains, left-bigger-than-right hemispheres (Gilmore et al., 2007) and a larger left-sided planum temporale and deeper left superior temporal sulcus (Hill et al., 2010; Witelson and Pallie, 1973) are present. Diffusion imaging studies have reported that neonates show a trend toward leftward corticospinal tract asymmetry at 30 weeks (Liu et al., 2010). Cross-sectional and longitudinal studies confirm that these cortical asymmetries in left frontal, temporal, and parietal regions surrounding the sylvian fissure continue to develop throughout childhood and adolescence up to around age 30 (Sowell et al., 2003, 2004a,b).

Age-related increases in leftward asymmetry have also been found in the sylvian fissure (Sowell et al., 2002). In line with this, Gogtay et al. (2004) showed that the posterior superior temporal gyrus constitutes the last region within the temporal lobe to mature. Cytoarchitectonic asymmetries in Broca’s area are also gradually increasing across age (Amunts et al., 2003). Asymmetry patterns resembling adult-like structures are reached at age 5 for the pars triangularis and at age 11 for the pars opercularis (Amunts et al., 2003). The authors suggest that these developmental changes constitute a structural correlate of language development and increasing language lateralization in childhood.

Cortical asymmetries keep changing across the life span, which is likely due to typical aging effects. Accordingly, Good et al. (2001) report an accelerated decline in gray matter concentration in the left planum temporale and bilateral Heschl’s gyrus, pointing to an age-related decrease in asymmetry. Besides gray matter changes, there are also hemispheric differences in white matter maturation. One- to three-month-old toddlers already exhibit leftward asymmetries in the arcuate fasciculus and corticospinal tract (Dubois et al., 2009). Similar to increases in cortical asymmetries, Paus et al. (1999) report an age-related increase in white matter density in the left arcuate fasciculus.

It is likely that the typical development of gray and white matter asymmetries described may be altered in ASD, thus leading to atypical functional brain asymmetries affecting motor behavior.

4.2 ALTERED STRUCTURAL LATERALIZATION IN AUTISM SPECTRUM DISORDER

In neurotypical individuals, asymmetry in the primary motor cortex (M1) is subtle and characterized by a deeper and more asymmetric left central sulcus (Amunts et al., 1996; Hervé et al., 2006) (particularly in consistently right-handed males; Amunts et al., 2000), increased leftward neuropil (subcortical tissue that is not classified as white matter) in Brodmann area 4 (Amunts et al., 1996), increased space between cell bodies in the M1 (Amunts et al., 1997), increased cortical thickness in the left precentral gyrus (Luders et al., 2004), and an increased left-hand motor area in right-handers (Volkmann et al., 1998). Differences between right- and left-handers have been reported for the primary motor cortex, in particular for morphology of the central sulcus (Sun et al., 2012) and white matter volume (Büchel et al., 2004), although the corticospinal tract is left-lateralized irrespective of hand preference (Howells et al., 2018; Westerhausen et al., 2007). The higher prevalence of left-handers in ASD, and altered functional lateralization in motor execution network in ASD (Floris et al., 2016a), indicates that atypical structural asymmetry in the motor system is likely in ASD.

One study has reported an association between increased white matter volume in the left precentral gyrus and premotor regions and poorer motor skill in ASD, in contrast with associations between increased bilateral white matter and improved motor performance in neurotypical controls (Mostofsky et al., 2007). Notably, increased brain volume in young children with ASD is a well-reproduced finding, although this declines into adolescence (Carper and Courchesne, 2005; Carper et al., 2002; Hazlett et al., 2005). This has been associated with increased white matter, specifically in more superficial regions closer to the cortex (Herbert et al., 2004). Postmortem studies have further demonstrated abnormalities in cortical minicolumns localized in superficial white matter rather than longer fibers connecting cortical and subcortical regions (Casanova et al., 2006).

Ecker et al. (2016) reported that abnormal patterns of gyrification close to the precentral gyrus and postcentral gyrus were present in ASD male adults ($N=51$) in contrast to controls ($N=51$), which corresponded with diffusion measurements of the white matter close to the cortical sheet. This suggests that abnormal patterns of brain development occur closer to the cortex; therefore, structural asymmetries may be likely in the most superficial white matter systems such as the U-shaped tracts (Catani et al., 2012, 2017).

One diffusion tractography study has reported that short-range corticocortical connectivity between the M1 and somatosensory cortex is altered in a large group of individuals with ASD ($N=60$) vs neurotypical controls ($N=60$) (Thompson et al., 2017). Specifically, they reported an association between precision grasping on a pegboard task, and left hemisphere tract measurements in neurotypical controls, whereas this association only existed with right hemisphere tracts in the ASD group, as shown in Fig. 1. The right hemisphere shift in sensorimotor tracts may play a role in the prevalence of left-handedness in autism, although this has not yet been explored.

Motor planning for complex voluntary movements recruits widespread frontal and parietal regions and is supported by the superior longitudinal white matter fasciculi (Budisavljevic et al., 2017; Grafton, 2010; Jeannerod et al., 1995). As previously described, in ASD there may be some disruption in the coupling of perception and action, resulting in behavioral impairments on these tasks. Structural differences exist between individuals with ASD and neurotypical controls in rightward asymmetry of the inferior parietal lobule, a region crucial for integration of grasp-relevant information and preparation of reaching movements (Floris et al., 2016b; Tarantino et al., 2014). Notably, the frontoparietal tract connecting the inferior parietal lobule with ventral premotor regions important for supporting transformations for hand posture in grasping (the ventral branch of the superior

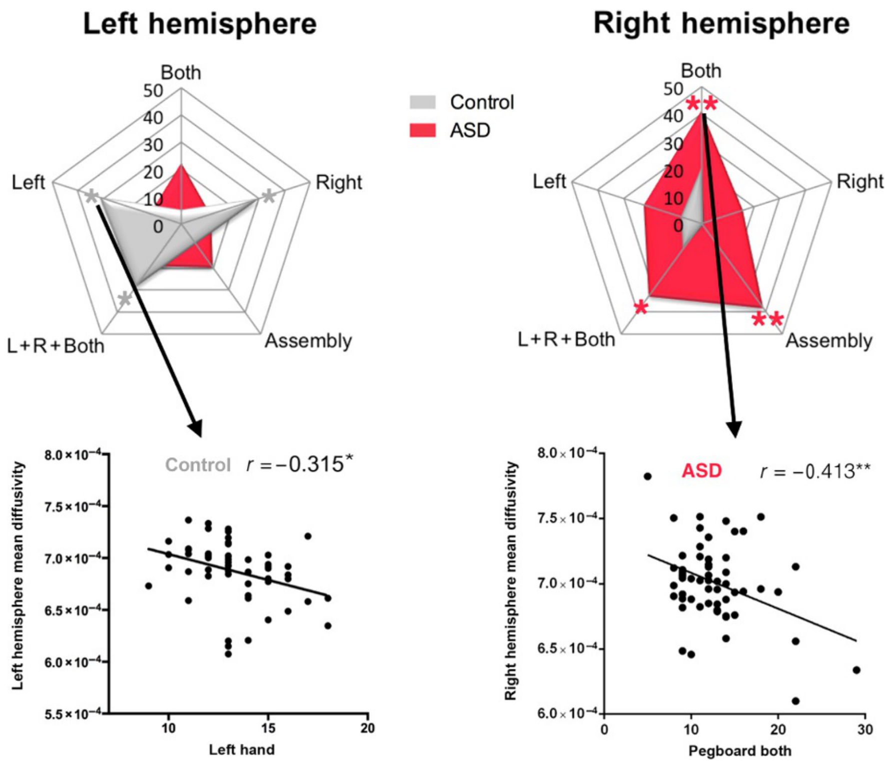

FIG. 1

The radar charts show the relationship between scores on different components (left hand, right hand, both hands, composite score, and assembly) of the Purdue pegboard task in the U-shaped motor-sensory white matter tracts in the left and right hemisphere of ASD male adults ($n=60$) and matched healthy controls ($n=60$). The *asterisks* represent significant association with structural measures, two of which are shown in the scatter graphs. Here, significant correlations are shown between left-hand performance and tractography measurements of tracts in the left hemisphere in controls (*left panel*) and pegboard performance when using both hands together, and tracts in the right hemisphere in the ASD group (*right panel*).

Figure reproduced with permission from Thompson, A., Murphy, D., Dell'acqua, F., Ecker, C., Mcalonan, G., Howells, H., Baron-Cohen, S., Lai, M.C., Lombardo, M.V. & MRC AIMS Consortium, and Marco Catani, 2017. Impaired communication between the motor and somatosensory homunculus is associated with poor manual dexterity in autism spectrum disorder. Biol. Psychiatry 81, 211–219.

longitudinal fasciculus) is more strongly rightward asymmetric in neurotypical left-handers than right-handers (Fornia et al., 2018; Howells et al., 2018). This may again be relevant in exploring the higher incidence of left-handedness in ASD, although no studies have currently evaluated the asymmetry of these tracts in ASD.

The studied structural asymmetries involved in direct sensorimotor integration along U-shaped tracts, and those involved in broader visuomotor transformations along long-range frontoparietal tracts, indicate a structural rightward shift and associated correlations with behavioral measurements of motor skill (Budisavljevic et al., 2017; Howells et al., 2018). This is not unexpected, given the left hemisphere dysfunction theory (Fein et al., 1984), but suggests that the role of right hemisphere in supporting motor actions—possibly bilaterally—in ASD requires further study.

Another important aspect is the role of callosal connectivity in facilitating both fine and gross motor coordination. As previously described, children with ASD have difficulties in coordinating the left and right sides of the body, and this may be linked to the reduced interhemispheric connectivity commonly reported in ASD as compared with neurotypical controls (Anderson et al., 2011; Egaas et al., 1995; Lo et al., 2011; Zhu et al., 2014). In particular, Catani et al. (2016) reported that tract measurements of the genu and anterior body of the corpus callosum show a decreased microstructural organization in ASD adults, which connect the left and right frontal and motor cortices (Fig. 2).

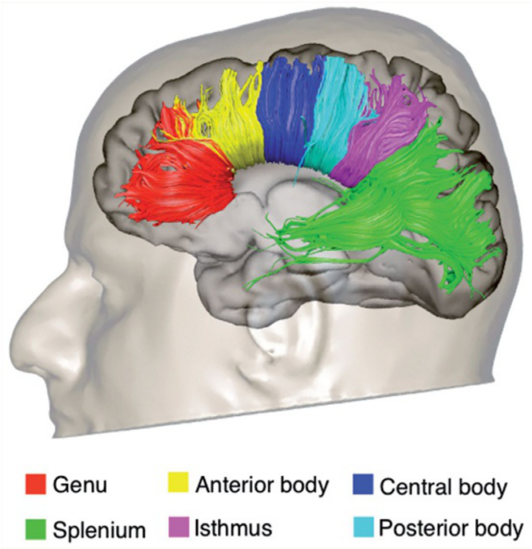

FIG. 2

Tractography reconstruction of the different divisions of the corpus callosum according to Witelson (1989). In this study comparing 61 male adults with ASD with 61 matched healthy controls, a significant increase in fractional anisotropy and radial diffusivity of the genu and anterior body was observed in the ASD group. These regions connect the left and right prefrontal cortices, and premotor regions, respectively.

Figure reproduced with permission from Catani, M., Dell'acqua, F., Budisavljevic, S., Howells, H., Thiebaut De Schotten, M., Froudist-Walsh, S., D'anna, L., Thompson, A., Sandrone, S., Bullmore, E.T., Suckling, J., Baron-Cohen, S., Lombardo, M.V., Wheelwright, S.J., Chakrabarti, B., Lai, M.C., Ruigrok, A.N., Leemans, A., Ecker, C., Consortium, M.A., Craig, M.C., Murphy, D.G., 2016. Frontal networks in adults with autism spectrum disorder. Brain 139, 616–630.

Floris et al. (2013) specifically investigated the structural asymmetry of the corpus callosum in 40 adolescents with ASD and 40 healthy controls, and its relationship to handedness. They showed again a significant rightward asymmetry in the anterior and posterior midbodies of the corpus callosum—subsections carrying connections to sensorimotor and parietal cortices—among males with ASD (across the entire handedness spectrum) compared to typically developing adolescents. This difference was especially present in left-handed individuals with ASD as revealed by a significant interaction between diagnosis and handedness, with left-handed adolescents with ASD exhibiting stronger rightward asymmetry in the posterior midbody. Thus, atypical callosal morphology is present in some, but not all individuals with ASD who also exhibit stronger left-handedness.

Luders et al. (2006) found similar results in right-handed neurotypical males showing stronger rightward lateralization in the anterior callosal section which projects to the motor cortices, concluding that stronger leftward lateralization of motor functions in right-handers reduces left interhemispheric fibers. Thus, atypical callosal asymmetry in ASD findings is consistent with this and reports suggesting that motor transfer is more efficient from the right to the left hemisphere via the corpus callosum (Braun et al., 2003; Saron et al., 2003).

5 FUNCTIONAL LATERALIZATION AND AUTISM SPECTRUM DISORDER

5.1 DEVELOPMENTAL ORIGINS

The developmental ontogenesis of functional lateralization occurs at a very early stage in neurotypical development. Hemispheric asymmetries in auditory evoked signals measured by fetal magnetoencephalography can be seen in fetuses in the third trimester (Schleussner and Schneider, 2004) and newborns (Molfese, 2000). Dehaene-Lambertz et al. (2002) suggest that neural precursors of language processing networks are present before the onset of speech production, demonstrating leftward activation in 0- to 3-month-old infants in the superior temporal gyrus and angular gyrus observed by fMRI while listening to speech during sleep. In toddlers, left hemisphere activation can be observed while babbling (Holowka and Petitto, 2002).

Many studies corroborate a gradual maturation of language-related left hemisphere lateralization with age (Gaillard et al., 2000; Hertz-Pannier et al., 1997; Holland et al., 2001). Szaflarski et al. (2006) show in both cross-sectional and longitudinal studies that language lateralization gradually increases between the ages of 5 and 20 years, plateaus between 20 and 25 years, and then gradually decreases with age thereafter. Increases in lateralization in childhood and adolescence have been explained by age-related maturational processes rather than by an improvement in linguistic skills (Brown et al., 2005; Schlaggar et al., 2002), whereas decreases later in life could be attributed either to ageing effects or a compensatory, functional reorganization as a response to age-related cognitive decline (Cabeza, 2002). The close link between language and motor lateralization is highlighted by a study by Gotts et al. (2013) reporting that left-lateralized hubs of language and motor control networks show a bias toward intrahemispheric interactions operating in a less integrative manner across the hemispheres compared to visuospatial functions.

Motor lateralization has typically been studied in terms of handedness. However, more recent fMRI studies show that networks associated with motor control develop earlier than other brain networks and are already detectable in infants as early as 2 weeks of age (Lin et al., 2008). The developmental nature of lateralization in motor-related networks was confirmed by Agcaoglu et al. (2015) showing age-related decreases in four sensorimotor networks resulting in greater cross-hemispheric balance. Similar patterns have been shown by Zuo et al. (2010) reporting increased voxel-mirrored homotopic connectivity as a marker of interhemispheric integration in sensorimotor regions across age groups in typically developing individuals.

Evidence for motor system lateralization stems from lesion studies showing that apraxia is more often observed after left hemisphere than right hemisphere insult (Poizner et al., 1998). Functional examination of motor circuit connectivity demonstrates that the left motor cortex is more extensively connected with the rest of the brain compared to the right motor cortex (Guye et al., 2003). The planning of complex, sequential movements (Haaland et al., 2004; Schluter et al., 1998; Verstynen et al., 2005), bimanual coordination (Jäncke et al., 2003; Serrien et al., 2003), praxis and tool use (Bohlhalter et al., 2009; Króliczak and Frey, 2009), and response selection (Weissman and Banich, 2000) are more strongly mediated by the left hemisphere.

Taken together, functional lateralization goes beyond the language network and is present also in motor networks—even though in general it is less pronounced. The developmentally early ontogenesis and close interaction with functional language lateralization further underline the importance of motor functions as a target for early intervention.

5.2 ALTERED FUNCTIONAL LATERALIZATION IN AUTISM SPECTRUM DISORDER

Extensive research exists on atypical hemispheric specialization in autism in the language-related domain. For example, atypical rightward responses to linguistic stimuli can be observed in toddlers at risk for ASD as young as 6–12 months as measured by ERPs (Seery et al., 2013) and in young children with ASD as measured by fMRI (Eyler et al., 2012; Redcay and Courchesne, 2008). Flagg et al. (2005) demonstrated that initially bilateral language activation becomes more left-lateralized in typically developing children, whereas children with ASD show a disrupted developmental trajectory becoming increasingly rightward lateralized. In line with this, atypical language lateralization has also been reported in adolescents (Knaus et al., 2010) and adults with ASD (Anderson et al., 2010; Kleinhans et al., 2008).

The neural correlates of disturbances in motor functioning in individuals with ASD have been examined using fMRI. Studies show that adults with ASD recruit regions beyond those typically involved in motor performance (Allen et al., 2004; Müller et al., 2001, 2003) and show overconnectivity between motor regions and regions outside the motor network (Carper et al., 2015). Using both task-fMRI and resting state fMRI analyses, Mostofsky et al. (2009) showed decreased cerebellar activation and increased premotor activation along with overall functional underconnectivity in the motor control network during a finger sequencing task in children with ASD.

Despite increasing exploration of motor network alterations in ASD, hemispheric lateralization of motor functions in ASD has been less extensively examined to date. Specialization in the motor network in ASD has mainly been addressed by (a) examining hemispheric right–left differences or reports of unilateral alterations, (b) reports of the lack of network differentiation, and (c) the computation of laterality indices.

(a) One of the earliest accounts reported reduced leftward regional glucose metabolism in subcortical structures in ASD, such as the putamen (Siegel et al., 1992). This was of particular interest given the association of striatal dysfunction and abnormalities in the basal ganglia with restricted repetitive behaviors in ASD (Kohls et al., 2014; Sears et al., 1999). More recently, Abbott et al. (2018) found decreases in corticostriatal motor connectivity between a seed in the posterior putamen and right motor and premotor areas (along with increases in corticostriatal limbic and frontoparietal connectivity) in individuals with ASD. These reductions in motor connectivity in ASD showed an association with increases in measures of restricted repetitive behaviors. A range of studies report greater involvement of the right hemisphere in individuals with ASD during imitation (Dawson et al., 1983), procedural learning (D'cruz et al., 2009), and sequence learning (Müller et al., 2004), and the latter study showed that greater reliance on the right premotor cortex was required in later stages of sequence learning in ASD (while, in typical individuals, such was more the case at early learning stages).

(b) A range of studies indirectly point to a lack of specialization within the motor network in individuals with ASD. Nebel et al. (2014) applied a clustering technique to establish organizational differentiation in the motor homunculus based on M1 connectivity in children with ASD and neurotypical controls (8–12 years). Discrepancies emerged in the size and functional segregation of M1, with individuals with ASD specifically showing a lack of somatotopic differentiation between regions associated with the lower limb and trunk and upper limb and hands (Fig. 3A). This finding was interpreted as the result of a failure to acquire functional specialization in the motor cortex in children with ASD. In addition, the study addressed the possibility that this was due to a developmental delay, showing a more similar pattern among younger neurotypical children and children with ASD, compared to that for older neurotypical children (Fig. 3B). This may be linked to the reported delays in motor development in ASD we have previously described. Other studies confirm a lack of functional segregation in individuals with ASD in motor networks, such as findings of atypical distribution and scatter of the recruitment of cortical motor regions (Müller et al., 2003) and less atypical patterns of activation during a finger movement task (Müller et al., 2001).

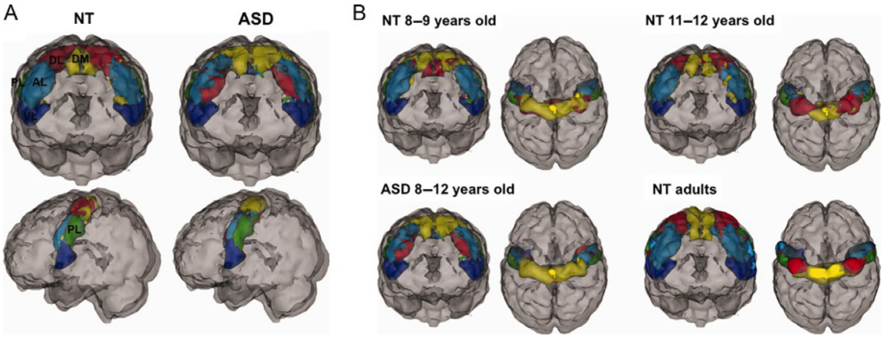

FIG. 3

Both panels show the organization of M1 connectivity in neurotypical (NT) controls vs individuals with autism spectrum disorder (ASD). (A) The connectivity between voxels in the primary motor cortex (M1) and voxels outside of the M1 was established. In a next step, the M1 was subdivided into parcels based on its connectivity pattern using a clustering approach. The illustration shows a five-cluster solution in neurotypical (NT) children and children with ASD. Significant differences emerged in the size of the DM portion. (B) M1 parcellations (subdivisions of functionally related connectivity patterns) derived from a clustering method are depicted in younger and older TD children. Images illustrate the M1 parcellation in 8- to 9-year-old NT children and in 11- to 12-year-old NT children compared with children with ASD and NT adults. *AL*, anterior lateral; *ASD*, autism spectrum disorder; *DL*, dorsolateral; *DM*, dorsomedial; *NT*, neurotypical controls; *PL*, posterior lateral; *VL*, ventrolateral.

Figure adaptive with permission from Nebel, M.B., Joel, S.E., Muschelli, J., Barber, A.D., Caffo, B.S., Pekar, J.J., Mostofsky, S.H., 2014. Disruption of functional organization within the primary motor cortex in children with autism. Hum. Brain Mapp. 35, 567–580.

(c) Rather than comparing the right and the left hemisphere in isolation from each other, hemispheric dominance is generally computed by a measure called the "laterality index" (LI) (Seghier, 2008). The LI is usually based on the following formula: $f*(R-L)/(R+L)$, where R represents the quantities measured for the right hemisphere and LH for the left hemisphere. f is a scaling factor determining the range of laterality values. When computing the LI, resting-state fMRI studies confirm atypical patterns of rightward lateralization in widespread brain networks including both language and motor circuits in individuals with ASD (Cardinale et al., 2013; Nielsen et al., 2014). This suggests that patterns of functional asymmetry may be in accordance with the patterns of right shift of structural connections for motor control reported earlier. Barber et al. (2012) examined the lateralization of functional connectivity between ROIs derived from the activation patterns observed in Mostofsky et al. (2009) in neurotypical children between 8 and 12 years and found that leftward lateralization was associated with enhanced performance on a motor task. Floris et al. (2016a) used the same seed regions (Fig. 4A) to apply laterality analyses of

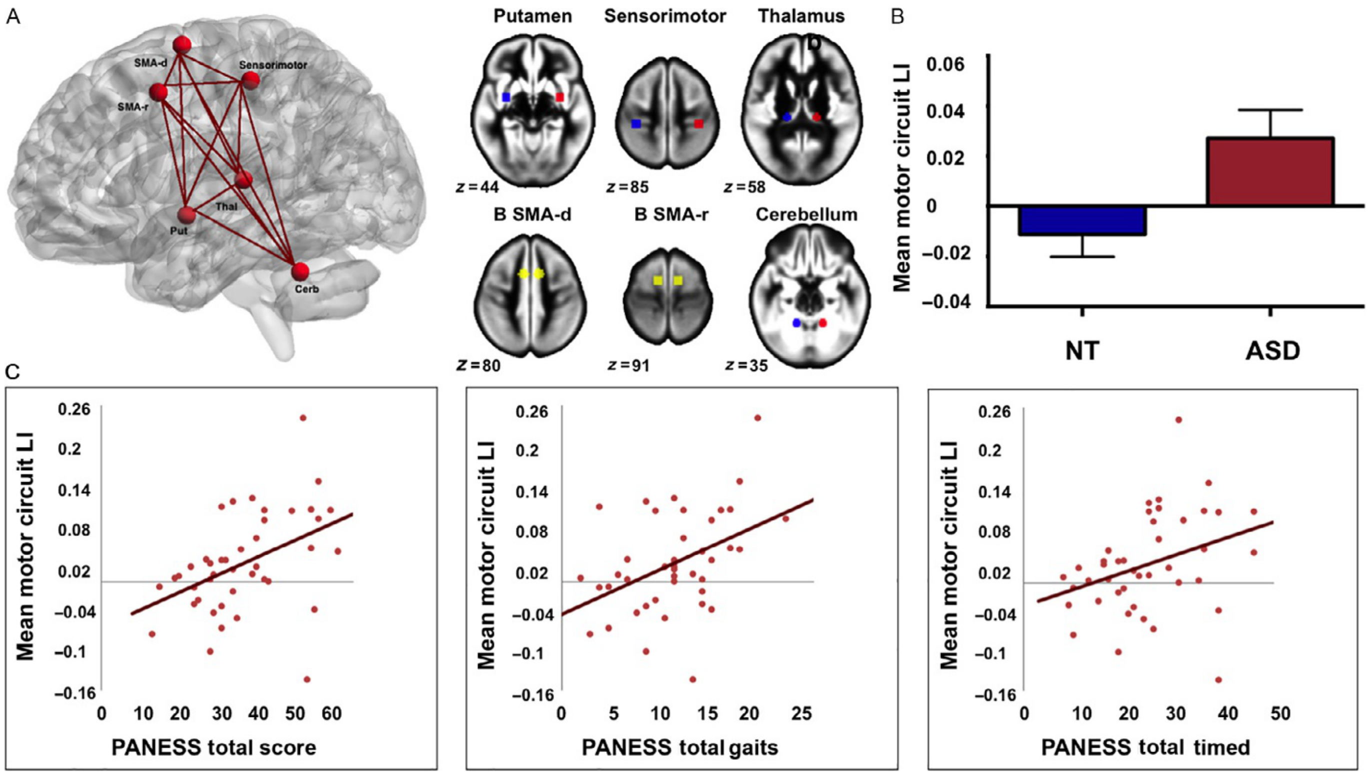

FIG. 4

(A) The brain surface maps and coronal views show the homotopic motor seed ROIs derived from Mostofsky et al. (2009). *Red* shows the left hemisphere seeds, while *blue* shows the right hemisphere seeds. (B) The graph depicts group differences in LIs of mean motor network connectivity. Positive values indicate rightward lateralization, negative values indicate leftward lateralization. Children with ASD show reversed rightward lateralization of mean motor connectivity. (C) Graphs depict the associations between LI of mean motor network connectivity and PANESS total scores, PANESS total gaits scores, and PANESS total timed scores. Across all measures individuals with ASD show an association between reversed rightward lateralization of mean motor connectivity and poorer motor performance. *ASD*, autism spectrum disorder; *B SMA-d*, dorsal bilateral supplementary motor area; *B SMA-r*, rostral bilateral supplementary motor area; *Cerb*, cerebellum; *LI*, laterality index; *NT*, neurotypical controls; *Thal*, thalamus; *PANESS*, Physical and Neurological Examination of Subtle Signs; *Put*, putamen (Denckla, 1985).

Figure adapted with permission from Floris, D.L., Barber, A.D., Nebel, M.B., Martinelli, M., Lai, M.C., Crocetti, D., Baron-Cohen, S., Suckling, J., Pekar, J.J., Mostofsky, S.H. 2016a. Atypical lateralization of motor circuit functional connectivity in children with autism is associated with motor deficits. Mol. Autism 7, 35.

intranetwork motor connectivity using resting-state fMRI data in a representative sample of children with ASD ($N = 42$) and neurotypical control children ($N = 76$). They observed stronger rightward lateralization of the overall mean connectivity in the functional motor execution network in children with ASD compared to neurotypical children (Fig. 4B). Interestingly, this atypical rightward shift in motor lateralization was associated with poorer performance on three different measures of the Physical and Neurological Examination of Subtle Signs (PANESS) (see Fig. 4C) establishing for the first time a link between atypical motor specialization and motor performance in ASD. Similarly, Carper et al. (2015) showed functional overconnectivity of predominantly the right PCG with frontal and parietal association areas and visual cortex. In addition, they calculated hemispheric asymmetry for intra- and interhemispheric connectivity with a left and right PCG seed and observed reduced asymmetry in individuals with ASD compared to controls.

Thus, taken together, the majority of studies points to a greater involvement of the right hemisphere in motor-related functions in ASD which may be the result of delayed or disrupted network segregation/differentiation.

6 CONCLUSION

Our current understanding of the neuropathology of ASD remains limited, with most findings pointing to an early onset and lifelong atypical course of development in behavior, anatomy, function, and connectivity. ASD is still diagnosed on the basis of behavioral observations and clinical interviews assessing symptoms that manifest at around 2 years of age (Charman and Baird, 2002). Given that most dramatic brain maturational changes occur in the first years of postnatal life (Ment et al., 2009), early detection and intervention are of upmost importance.

Atypical hemispheric lateralization can reflect different functions: (a) neuronal compensation in response to altered neuronal networks or atypical changes in anatomy and physiology due to the condition; or (b) neuronal dedifferentiation reflecting a deficiency in specialization and recruitment of specialized neural systems. These two functional accounts have been used to explain an age-related decline in hemispheric specialization, which is a typically occurring phenomenon in neurodevelopment (Cabeza, 2002). Thus, the question arises whether neurodegenerative mechanisms, such as cerebral atrophy and age-related size reductions in the corpus callosum (O'sullivan et al., 2001)—that are likely to induce age-related laterality reductions—might happen prematurely in individuals with ASD or whether other genetic and environmental mechanisms account for reduced hemispheric specialization in ASD.

Both structural and functional lateralization appear to be driven by both leftward volume reductions/underconnectivity and rightward volume increases/overconnectivity. The disturbance in establishing normal patterns of hemispheric specialization is not therefore confined to one hemisphere; rather, alterations of function in both hemispheres contribute to the observed abnormalities. This would explain why it is not just functions that are typically ascribed to the left hemisphere—such as linguistic processing and fine motor control—that are affected in ASD, but also those more strongly represented in the right-hemisphere—such as processing of emotional tone and prosody, and proprioception. In light of these findings, the left hemisphere dysfunction theory, stating that neural deficits are confined to the left hemisphere, is probably too simplistic an explanation for the complexity of atypical lateralization observed in ASD. Both left- and right-sided disturbances seem to contribute depending on the examined structure/function and individual sample characteristics. Thus, an alternative explanation for atypical asymmetry might be a lack of hemispheric specialization, resulting in hemispheric equivalence, both structurally and functionally (Mitchell and Crow, 2005).

Results across studies converge to show the consistent picture that atypical lateralization has the potential of serving as a neural marker of atypical development in ASD. In particular, motor behavior may be a useful tool, as it is measured using more quantifiable and reproducible measurements than complex social behaviors, and therefore may be an important means to investigate and diagnose ASD. Even though this pattern seems to be consistently present across several levels of neural organization, replication in larger samples and with participants including both sexes and different ages is necessary to confirm findings (Preslar et al., 2014; Stanfield et al., 2008). Atypical lateralization seems to have the potential for differentiating individuals with distinct symptom profiles and might thus be an indicator of different subtypes across the autism spectrum. In the context of current neuroimaging approaches yielding inconsistent findings and an incoherent picture of the neurobiology of ASD, atypical cerebral lateralization may be a key and consistent feature characterizing the neuropathology of autism with great potential to delineate certain groups within the autism spectrum at a stage when intervention is likely to have the greatest prospect in helping children with ASD.

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CHAPTER

Lateralization of the expression of facial emotion in humans

9

Annukka Lindell[1]
Department of Psychology and Counselling, La Trobe University, Melbourne, VIC, Australia
[1]Corresponding author: Tel.: +61-3-9479-2708; Fax: +61-3-9479-1956,
e-mail address: a.lindell@latrobe.edu.au

Abstract

Though superficially symmetrical, the human face expresses emotion asymmetrically. Darwin (1872) first noted this phenomenon, conceding to being at a loss to explain why expressions such as smiling and sneering defiance were predominantly one-sided. Emotion lateralization offers a plausible account. Because the lower two-thirds of the face is contralaterally controlled, the emotion-dominant right hemisphere innervates the lower left hemiface, resulting in more intense expressions. Thus whether smiling or sneering, humans show stronger emotion on the left side of the face. This chapter reviews research examining asymmetries in the expression of facial emotion in humans, commencing with discussion of the right hemisphere's dominance for emotion processing. The right hemisphere's emotion-processing superiority results in hemifacial asymmetries in expressivity: the left hemiface is anatomically more expressive, moving more and earlier than the right hemiface. Not surprisingly then, viewers are sensitive to the left cheek's greater physiognomic expressivity, perceiving the left hemiface as more expressive than the right, even when digitally reversed. Critically, human behavior implies an intuitive awareness that the left cheek is more emotionally expressive, influencing behaviors including cradling infants and posing for photographs. Thus despite the absence of conscious awareness, when conveying emotion we intuitively favor the more expressive left cheek.

Keywords

Emotion, Valence, Laterality, Faces, Expression, Perception, Asymmetry

The lateral division of the human brain into two halves is one of its most conspicuous characteristics. This superficial similarity between the left and right hemispheres masks underlying asymmetries in both structure and function across a broad range of motor, sensory, and cognitive processes. However, it was not until the 1860s that the inherent asymmetry of the brain was discovered. Broca (1861) famously proposed that the brain is lateralized, with the left hemisphere playing the dominant role

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in language processing. Initially hemispheric lateralization was argued to be a defining human characteristic, being “the most imposing difference between man and animal” (Pruner-Bey, 1865, p. 558). However, it is increasingly clear that lateralization is a fundamental principle of nervous system organization throughout the animal kingdom (Ocklenburg and Güntürkün, 2012), presumably because lateralization of function enhances processing efficiency (Corballis, 2017; Rogers et al., 2004). While language is the paradigmatic lateralized function, it is not alone: a decade after Broca’s (1861) discovery, Hughlings-Jackson (1874/1915) proposed that emotion is also lateralized but to the *right* rather than left hemisphere.

Emotion plays a fundamental role in adaptive human behavior. As valenced responses to internal or external stimuli that are important to the individual, emotions have three key components: (1) physiological reaction to a stimulus (e.g., increased heart rate); (2) behavioral response (e.g., facial expression); and (3) feeling (e.g., subjective experience of joy; Ocklenburg and Güntürkün, 2017). As such, emotions are critically involved in effective everyday communication and social interaction. Indeed, the ability to efficiently express our own, and to interpret others’, emotional expressions is vital to survival: emotional expressions indicate the likely future behavior of the displaying human (Andrew, 1963) and thus communicate intentions and desires. Ekman and Friesen’s (1971) cross-cultural research initially identified six basic emotional expressions—happiness, sadness, fear, anger, surprise, and disgust. However, recent research suggests that the expression repertoire could be expanded to include up to 22 distinct expressions of facial emotion, including both core and compound expressions (e.g., happily disgusted; see Du et al., 2014).

Regardless of the precise number of categories of emotional expression, research suggests that when humans express emotion we do so asymmetrically. This may appear initially surprising for in everyday life we are rarely conscious of differences in expressivity between the two sides of the face. However, evidence confirms that the left side of the face, predominantly controlled by the emotion-dominant right hemisphere, expresses emotion more intensely than the right side of the face (Lindell, 2013a).

This chapter reviews research examining asymmetries in the expression of facial emotion in humans. Evidence of the right hemisphere’s dominant role in emotion processing is first examined, commencing with Hughlings-Jackson’s (1874/1915) historic observation that emotion is lateralized to the right hemisphere. The consequences of right hemisphere emotion lateralization for the facial expression of emotion are then explored, with the first recorded observation that emotional expressions are asymmetric dating back to Darwin (1872). Following discussion of research examining hemifacial asymmetries in the expression of emotion, the consequences of the left hemiface’s greater expressivity are then discussed, demonstrating that humans appear intuitively aware that the left cheek is more emotionally expressive, and this intuitive knowledge influences a surprisingly broad range of behaviors, from cradling infants to posing for photographs.

Throughout the chapter the term “lateralized” is used to denote a relative difference between the hemispheres rather than absolute lateralization. For example, when emotion is described as being right lateralized, this should not be taken to imply the absence of left hemisphere involvement. Instead, “emotion lateralization” is used to indicate that hemispheric processing of emotion is asymmetric, with the right hemisphere typically playing a more dominant role than the left hemisphere.

1 RIGHT HEMISPHERE EMOTION LATERALIZATION

Following Broca’s (1861) revolutionary proposal that the brain was functionally lateralized, Hughlings-Jackson (1874/1915) suggested that the right hemisphere controlled emotion. Hughlings-Jackson (1874/1915) (Fig. 1) was a prominent neurologist working with patients with aphasia at what is now The National Hospital for Neurology and Neurosurgery, London (known at the time as the National Hospital for the Paralysed and Epileptic; The National Archives, 2018). In his clinical practice, Hughlings-Jackson repeatedly observed that though language ability was generally compromised following left hemisphere damage, the ability to produce emotional speech was retained: “…there is loss of the most (special) voluntary form of language (speech) without loss of the more automatic (emotional manifestations). The patient smiles, laughs, and carries the tone of his voice… As I used to put it, there is a loss of Intellectual Language with conservation of Emotional Language” (p. 41). Observing that even patients with severe motor aphasia (now known as Broca’s aphasia) following left hemisphere insult could still swear fluently and blurt out emotional exclamations (Hughlings-Jackson, 1866; see Finger, 2001), Hughlings-Jackson (1874/1915) concluded that this emotional speech must be controlled by the right hemisphere. As such, Hughlings-Jackson was first to introduce the notion that emotion is controlled by the right hemisphere (now known as *the right hemisphere hypothesis*).

The right hemisphere’s dominance for emotion processing is not modality specific, but extends across facial, lexical, and prosodic channels, and is supported by converging evidence across a broad range of research paradigms, including clinical, imaging, and behavioral investigations. Numerous clinical studies assessing patients with unilateral brain damage have found that right hemisphere damage is more likely to cause emotion-processing deficits than left hemisphere damage. The emotion production problems experienced by patients with right hemisphere damage encompass the full spectrum of emotional conveyance, from facial expressions of emotion to the ability to interpret prosody in other people’s speech (see Borod, 1993, for review). For example, Lai and Reilly (2015) found that following right hemisphere perinatal stroke children produced significantly fewer facial expressions of emotion, and half as much affective content in their speech, than children who had had a left hemisphere perinatal stroke or typically developing children. Similar findings have been previously reported for adults following right hemisphere stroke (Blonder et al., 1993; Borod et al., 1988a,b), illustrating that the right hemisphere’s dominant contribution to emotion production is evident throughout the course of human development.

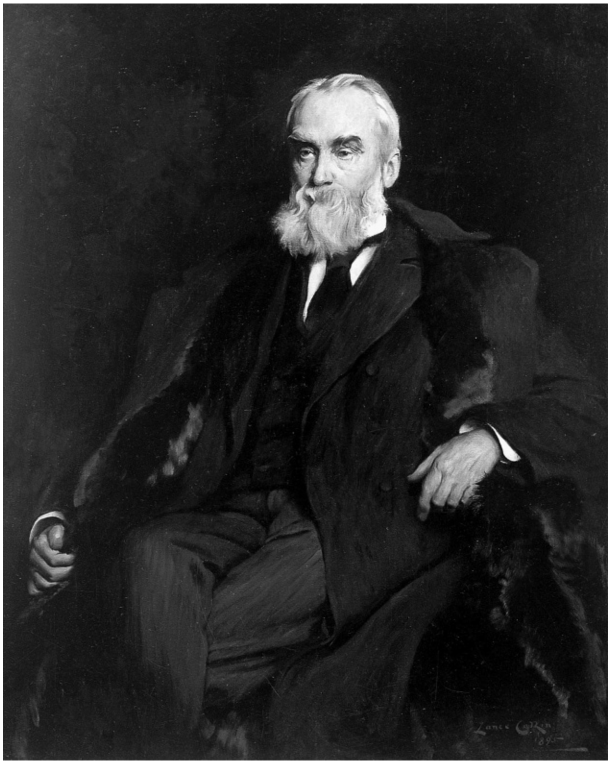

FIG. 1

John Hughlings-Jackson (1834–1911).

Photogravure after Lance Calkin (1859–1936). Public domain.

In addition to adversely affecting emotion production, right hemisphere damage also compromises emotion perception, prompting difficulties recognizing the facial expression of emotion (e.g., Abbott et al., 2014; Harciarek et al., 2006), understanding emotional words (e.g., Borod et al., 1998), and interpreting emotional prosody (e.g., Tucker et al., 1977). Indeed, Dara et al. (2014) have recently demonstrated that deficits in understanding emotional prosody better predict right hemisphere dysfunction than unilateral neglect. Unilateral neglect is a common neurological disorder resulting from right hemisphere damage in which patients neglect the left-hand side of space, resulting in a lack of awareness of, and attention to, stimuli falling in their left visual field (Ocklenburg and Güntürkün, 2017). Given that unilateral neglect is widely considered to be the cardinal cognitive characteristic of right hemisphere damage (Dara et al., 2014), the fact that deficits in understanding prosody are even more intimately associated with right hemisphere damage underscores the dominant role of the right hemisphere in emotion perception.

Consistently, imaging research demonstrates that emotion processing produces greater activity in the right than left hemisphere. Regardless of whether participants are making judgments about emotion communicated via facial expressions (Gorno-Tempini et al., 2001), pictures (Lane et al., 1999), or prosody (Wildgruber et al., 2005), functional imaging shows that emotion-related processing prompts more right than left hemisphere activation. Behavioral investigations offer further support. For example, when emotional faces are presented in the left visual field (projecting to the right hemisphere), participants respond faster and more accurately than when identical stimuli are presented in the right visual field (projecting to the left hemisphere; Ley and Bryden, 1979). Similarly, emotional films are rated as more unpleasant or horrific when presented in the viewer's left, than right, visual field as they immediately project to the emotion-dominant right hemisphere (Dimond et al., 1976). Though there is typically a right visual field (left hemisphere) advantage for visual word recognition, consistent with the left hemisphere's superiority for language processing, right hemisphere (left visual field) performance is enhanced for words that convey emotional content (e.g., KISS, AGONY) in comparison with neutral words (e.g., ITEM, AMOUNT; Nagae and Moscovitch, 2002). Thus the right hemisphere's dominance for emotion appears to offset the left hemisphere's dominance for language, resulting in no difference in lexical decision accuracy between emotional words presented in the left and right visual fields (projecting to the right and left hemispheres, respectively; Nagae and Moscovitch, 2002).

The right hemisphere's advantage for emotion processing is similarly evident for auditory stimuli. For example, Godfrey and Grimshaw (2016) showed that the typical right ear (left hemisphere) advantage for speech stimuli in dichotic listening tasks is attenuated when the words are spoken with emotional prosodic cues (e.g., happiness, sadness, fear). Such findings demonstrate that the right hemisphere's ability to process speech is enhanced by the inclusion of emotional content. In a similar vein, when emotional prosodic cues are absent, but the words used have emotional (e.g., LOVING) rather than neutral meanings (e.g., COMBINE), Sim and Martinez (2005) demonstrated that participants have a stronger memory for emotional words presented in their left ear (projecting predominantly to the right hemisphere) than in their right ear (projecting predominantly to the left hemisphere). The fact that right hemisphere performance is enhanced when the stimuli contain emotion content—whether prosodic or semantic—appears completely consistent with right hemisphere dominance for emotion processing.

Overall, evidence from a wide variety of clinical, imaging, and behavioral research paradigms indicates that the right hemisphere plays the dominant role in human emotion processing. However, it should be noted that the right hemisphere hypothesis for emotion lateralization is not the sole contender; a number of alternate theories have been put forward. These include the valence hypothesis, which proposes that the right hemisphere controls negative emotions, whereas the left hemisphere controls positive emotions (see Demaree et al., 2005), and the approach-withdrawal model (also known as the BAS BIS [behavioral approach system/behavioral inhibition system] model), in which the left hemisphere is argued to control approach-related behaviors that drive the organism toward positive stimuli, and the right hemisphere controlled avoidance-related behaviors that deter the organism away from negative stimuli (see Rutherford and Lindell, 2011). Ocklenburg and Güntürkün (2017) provide a comprehensive review of the different models of emotional lateralization. However, though the precise nature of the lateral division of emotion control remains contentious (e.g., Demaree et al., 2005; Ocklenburg and Güntürkün, 2017; Rutherford and Lindell, 2011), there is overwhelming evidence, indicating that the right hemisphere plays a greater role in emotion processing than the left hemisphere (Lindell, 2013a; Mandal and Ambady, 2004), in keeping with Hughlings-Jackson's (1874/1915) early observation.

2 HEMIFACIAL ASYMMETRIES IN EMOTIONAL EXPRESSIVITY

Darwin (1872) (Fig. 2) was famously the first to formally report that the two sides of the face express emotion differently. His treatise entitled "The Expression of the Emotions in Man and Animals" set out to document the biological underpinnings

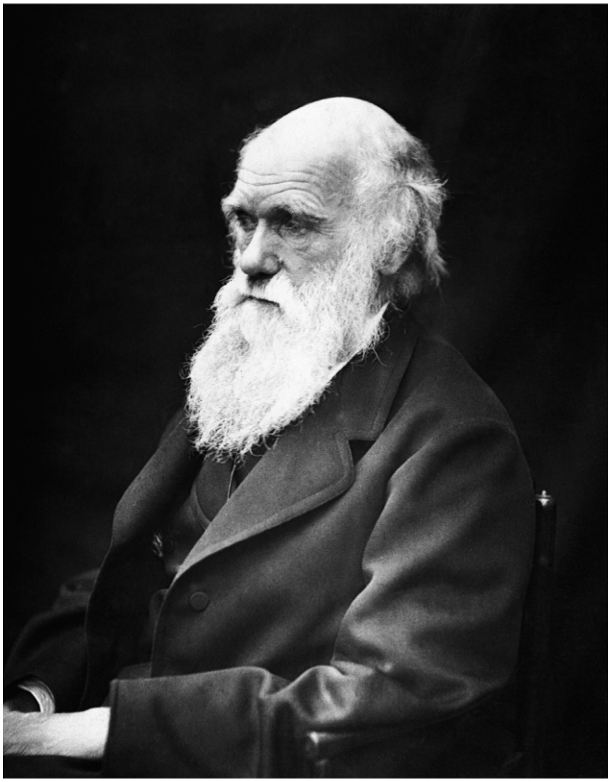

FIG. 2

Charles Darwin (1809–1882). Public domain.

of emotional expressions, including vocal, bodily (e.g., erection of dermal appendages including hair and feathers when experiencing anger and terror), and facial expressions. In keeping with his evolutionary theory (On the Origin of Species had been published 13 years earlier in 1859), Darwin keenly drew attention to parallels in the expressions of humans and other animals, for he believed that human expressions shared much with those of other animals. For example, Darwin noted that the facial actions involved in the human sneer are the same as those of a snarling dog. Darwin's view ran contrary to prevailing thought at the time, with eminent facial anatomist Sir Charles Bell instead arguing that God designed humans with a unique pattern of facial musculature necessary to express uniquely human emotions (Matsumoto and Ekman, 2008).

In addition, Darwin's (1872) thorough descriptions of the facial muscles involved in human expressions ranging from sulkiness to devotion carefully detailed cross-cultural similarities in the expressions of both children and adults. These cross-cultural observations were made by Darwin's numerous correspondents who confirmed that the expressions he personally observed in the United Kingdom were also exhibited by residents of other countries and people of other races (e.g., Darwin's correspondents confirmed that just as in England, excessive laughter prompts tears in "hindoos… Chinese… Malays… aborigines of Australia … (and tribes in) Southern Africa" [Darwin, 1872, p. 209]).

Critically for our purposes, Darwin (1872) reported that the expression of sneering defiance was asymmetric, involving the uncovering of the "canine tooth on one side of the face alone" (p. 250). Nine of Darwin's international correspondents, in regions ranging from Australia to China to North America, confirmed that although the expression is rare, it is reliably asymmetric. Of course evidence of asymmetries in facial expressivity was available well before Darwin observed the phenomenon. However, it had not previously been explicitly noted (indeed, Darwin himself refers to an engraving in Parsons, 1746 that clearly illustrates an asymmetric expression of sneering defiance). Darwin goes on to observe that the asymmetry in facial expressivity is not restricted to sneering defiance: "… some persons smile more on one side of their face than on the other" (p. 251). However, he admitted to being at a loss to explain why such expressions should be so commonly confined to one side. Hughlings-Jackson's (1874/1915) proposal that, akin to language, emotion was also lateralized, offers a likely explanation for Darwin's observation of asymmetric human facial expressivity.

The muscles of the face are predominantly innervated by the seventh cranial nerve: the facial nerve (Korb and Sander, 2009). Whereas the upper face is under bilateral cortical control (Matsumoto and Lee, 1993), the lower two-thirds of the face is contralaterally innervated (Patten, 1996; Rinn, 1984). Consequently, from the lower eyelid downward, the left side of the face is controlled by the right hemisphere, and the right side of the face is controlled by the left hemisphere (see Fig. 3). Because of the right hemisphere's emotional dominance, the contralateral innervation of the lower face results in greater expressivity, and thus more intense emotional expressions, on the left than right hemiface. Therefore, whether we are grinning or grimacing, we tend to express stronger emotion on the left side of the face (Borod et al., 1983; Lindell, 2013a).

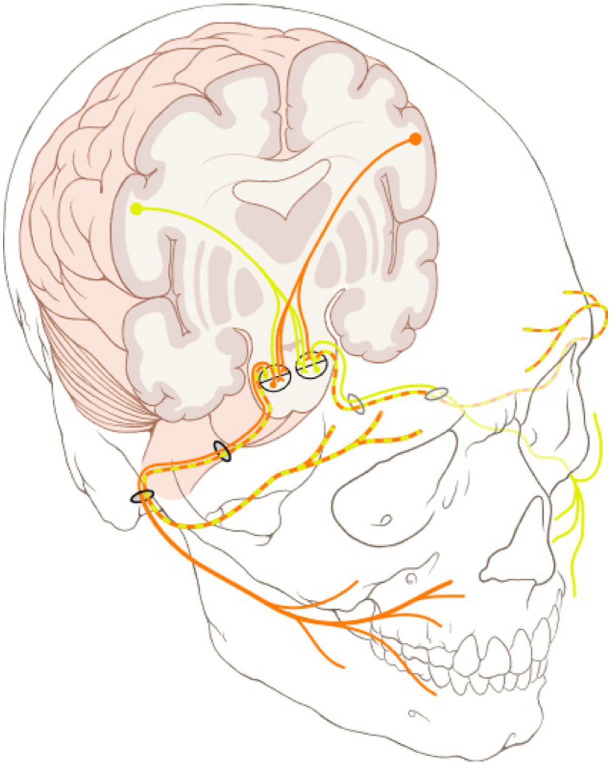

FIG. 3

Cortical projections of cranial nerve VII: the facial nerve. Note that the *upper face* is bilaterally innervated, whereas the *lower face* is innervated contralaterally: the right hemisphere controls the left hemiface, and the left hemisphere controls the right hemiface.

Image courtesy of Patrick J. Lynch, medical illustrator. Creative Commons Attribution 2.5 License 2006.

Research confirms that the muscles of the left side of the face move more than those on the right when we express emotion. The difference in movement can be measured using facial electromyography (EMG) to record facial muscle activity. This objective technique provides instantaneous measurement of the electrical potentials generated by muscular activity and has sufficient precision to permit the detection of muscle movements that are too small to be overtly visible (Dimberg, 1990). For example, Dimberg and Petterson (2000) used EMG to measure activity of the *zygomaticus major* and *corrugator supercilii* muscle, while participants viewed images of happy and angry faces. These muscles were selected for investigation because the *zygomaticus major* muscles draw the corners of the mouth up and back when we smile, and the *corrugator supercilii* muscles draw the eyebrows downward and inward, creating vertical wrinkles, as the forehead is furrowed into a frown (Achaibou et al., 2007; Dimberg, 1990). As expected, viewing happy faces caused greater zygomatic EMG activity while looking at angry faces prompted stronger corrugator EMG activity. Crucially, there was greater EMG activity recorded from the left than right side of the face, irrespective of the valance of the emotion. As Dimberg and Petterson (2000) suggest, these findings support the notion that the right hemisphere is predominantly involved in the control of spontaneous emotional reactions, and hence produces greater movement of the contralaterally innervated left, compared with the right, side of the face.

Wylie and Goodale (1988) consistently found that the left side of the mouth moves more than the right when we smile spontaneously. They applied white makeup to the facial area surrounding participants' lips and then outlined the lips using black eyeliner. Participants' mouth movements were videorecorded as they smiled spontaneously (cleverly prompted when an experimenter made a comment about the participant's rather unusual appearance!), or posed a smile (verbally cued by asking participants to show the expression they would make when "Somebody has given you a nice birthday gift"). Computer analysis of the video recordings revealed that the left side of participants' mouths moved more than the right for the spontaneous, but not the posed, smiles. Like Wylie and Goodale (1988), Dopson et al. (1984) reported a stronger left cheek bias for spontaneous than posed (i.e., nonnaturally occurring) smiles. Because spontaneous expressions of emotion are, by definition, more genuine than posed expressions, these findings converge in supporting right hemisphere dominance for emotion control. However even for posed expressions, the left side of the face has been found to move more than the right across a range of both positive (happiness, pleasant surprise, sexual arousal) and negative (fear, anger, confusion, disgust, sadness) emotions (e.g., Borod et al., 1988a). Indeed, Borod et al. (1983) found that the magnitude of the left hemiface bias for emotional expressivity is not influenced by whether the expression was posed or spontaneous (see Borod et al., 1983, and Borod et al., 1997, for reviews of the posed vs spontaneous expression literature).

In one of the most precise analyses of facial expression reported to date, Nicholls et al. (2004) used a 3D physiognomic range finder to analyze hemifacial movement asymmetries across the entire face. This technique is ideally suited because it provides replicable, objective, and precise measurements of hemifacial movements (Strőmland et al., 1998). Nicholls et al. (2004) asked participants to pose under three conditions, producing the most intense expressions of happiness and sadness they could, as well as posing a "neutral" expression. Analysis of the 3D digital images confirmed that regardless of emotional valence, the left side of the face moved more than the right side of the face during the expression of emotion. Such findings appear consistent with the findings of meta-analyses: both Borod's (1993) and Skinner and Mullen's (1991) meta-analyses ($N=14$ and $N=47$ studies, respectively) confirm that the left hemiface produces more intense emotion expressions than the right hemiface. Borod et al. (1997) offer further confirmatory evidence. Their review of 49 facial asymmetry experiments similarly concluded that the left hemiface had greater involvement in facial expressions of emotion than the right. Borod et al.'s (1998) subsequent analysis of the 49 experiments identified by Borod et al. (1997) indicated that the magnitude of the left cheek bias for emotional expressivity was influenced by study methodology. The left cheek bias is clear in studies that have used trained judges or recording of muscle movements, but less apparent in investigations that have relied on self-report measures. Overall, these findings converge to confirm greater expressivity of the left hemiface. Such hemifacial differences are not exclusive to humans but are evident across primate species (Lindell, 2013b), indicating homology in the expression of facial emotions between humans and other animals, consistent with Darwin's (1872) evolutionary argument.

Holowka and Petitto's (2002) findings suggest that the left cheek's greater expressivity is already evident prior to age one. They videotaped 5- to 12-month-old babies at the point at which the infants started syllabic babbling. On achieving this developmental milestone, the babies were videorecorded and their oral movements were coded according to whether they were babbles, nonbabble vocalizations, or smiles. Images 50 ms after the onset of mouth opening were extracted, and two independent judges scored each image, indicating whether there was greater opening on the left, right, or both sides of the baby's mouth. Results confirmed that where the right side of babies' mouths opened more for babbles (confirming that babbling is fundamentally linguistic, given that the right side of the mouth is controlled by the language dominant left hemisphere), babies' smiles were instead left sided. These findings show that as early as 5 months, infants exhibit a left hemiface bias in emotional expressivity, consistent with the adult literature, implying that right hemisphere emotion dominance is already established in early infancy.

Nagy's (2012) findings, however, are not consistent, indicating that left hemiface dominance for facial expressions does not emerge until adulthood. She gathered photos of infants (0–5 months; 6–12 months) and children (3–8 years) from the American Baby Beauty Contest website, and photos of adults from her colleagues' professional and family collections. Left–left and right–right chimeras were created from the original images; 90 judges rated the strength of each chimera's smile using a 5-point Likert scale. Results revealed no hemiface bias for any of the infant or child groups. However, for adults, left–left chimeras showed stronger smiles than right–right chimeras. Although Nagy's (2012) findings for infants are not consistent with Holowka and Petitto's (2002) results, the fact that Nagy (2012) used smiling photographs submitted for a Baby Beauty Contest (i.e., posed images), whereas Holowka and Petitto (2002) used still images from videos of spontaneous smiling expressions, may help account for the differences in results. Given that previous adult research indicates that the left hemiface bias is stronger for spontaneous than posed expressions (Dopson et al., 1984; Wylie and Goodale, 1988), one would anticipate a stronger left cheek bias for experiments that investigate infants' spontaneous expressions (e.g., Holowka and Petitto, 2002) than those that focus on infants' posed expressions (e.g., Nagy, 2012). Further research is needed to determine whether the left hemiface bias reported by Holowka and Petitto (2002) for infants as young as 5 months might be evident in even younger babies.

The difference between posed and spontaneous facial expressions may also help account for the findings of perhaps the first study to explicitly examine hemifacial differences in expressivity. Lynn and Lynn (1938) asked three judges to observe the involuntary (i.e., posed) smiling expression of 429 participants (age range 4–80 years; 60% of the sample aged 6–15 years) and determine whether the expression was a "definite right" (i.e., more expression on the right side), "definite left" (i.e., more expression on the left side), or "even" (i.e., balanced: no clear-cut asymmetry). Complete agreement from all three judges was found for only 229 participants (57.5% of cases), with the majority of disagreements involving the perception that the expression was symmetrical rather than asymmetrical (155 participants; 38%), highlighting a limitation of this subjective methodology. Of the 229 participants for whom there was unanimous agreement, 105 were judged to have a definite right or left asymmetry, with 47.5% right and 52.5% left. Thus though there was a slight left cheek bias for expressivity, the magnitude was very small. Had Lynn and Lynn (1938) examined spontaneous, rather than posed, facial expressions, perhaps a stronger left cheek bias would have emerged (e.g., Wylie and Goodale, 1988).

Research confirms that, in addition to being more expressive, the left side of the face starts moving earlier than the right side when we produce spontaneous facial expressions. Using high-speed videography to record participants making facial expressions (smile, surprise, frown), Ross and Pulusu (2013) found that spontaneous facial expressions commence 20 ms earlier on the left than right side of the face. Carr et al. (2014) subsequently demonstrated that participants are faster and more accurate in detecting expressions that onset in the left hemiface, implying that our perception of facial expressions is sensitive to hemifacial differences in the onset of the expression. It is important to note that the earlier left hemiface expression onset is exclusive to spontaneous facial expressions; for posed expressions the right hemiface starts moving first (by approximately 10 ms; Ross and Pulusu, 2013). This suggests that temporal differences in the onset of emotional expressions in the two sides of the face may be used as a clue to distinguish genuine (i.e., spontaneous) from fake (i.e., posed) facial expressions. Carr et al. (2014) confirmed this prediction using avatar faces: participants perceive expressions that start earlier on the left side of the face as more spontaneous than identical expressions that start earlier on the right side of the face. Such findings confirm that, although we may not be consciously aware of it, hemifacial asymmetries in the timing of expression onset offer subtle cues that index the veracity of an expresser's emotional expression.

Viewers' perceptions are influenced by the greater anatomic expressivity of the left side of the face, as demonstrated in Sackeim et al.'s (1978) seminal work. They created chimeric faces composed of mirrored left cheeks (left–left composites) and mirrored right cheeks (right–right composites) of models expressing each of the six basic emotions as well as a neutral condition. Participants were presented with trios of stimuli (left–left composite, right–right composite; normal face) and rated the intensity of the emotional expressions using a seven-point scale. Consistent with right hemisphere lateralization of emotion, left–left composites were rated as expressing emotion more intensely than right-side composites. Subsequent chimeric face investigations by the same group (e.g., Indersmitten and Gur, 2003; Sackeim and Gur, 1978) and independent research groups (e.g., Asthana and Mandal, 1998; Moreno et al., 1990; Okubo et al., 2013) have similarly found that left–left chimeras are judged to express emotion more intensely than right–right chimeras, in keeping with right hemisphere emotion lateralization.

The mirroring of models' left or right hemifaces in chimeric face investigations (e.g., Sackeim et al., 1978) creates artificial stimuli in which differences in the emotional expressivity of each side of the face are magnified via reflection. Importantly, investigations using more natural stimuli, such as 3/4 view portrait photographs, confirm that perception of the left cheek's greater expressivity is not limited to the chimeric face paradigm. Nicholls et al. (2002a) presented participants with portrait photographs of models adopting a pleasant neutral expression and posing facing 15 degree to the left (right cheek pose), 15 degree to the right (left cheek pose), or straight-ahead (full face pose). Participants were asked to imagine the person in each photo and rate how emotionally expressive they were using four six-point Likert-scale items from Kring et al.'s (1994) Emotional Expressivity Scale (EES). Results confirmed that models shown in left cheek poses were rated as significantly more emotionally expressive than identical models shown in right cheek poses. Critically, this effect remained even when the images had been mirror-reversed, making a true left cheek pose look like a right cheek pose and vice versa. The fact that models adopting left cheek poses appear more emotionally expressive even when the images have been digitally reversed confirms that perceived differences in the expressivity of the two sides of the human face stem from the greater anatomic expressivity of the left cheek, rather than an aesthetic or perceptual bias.

Further investigation has confirmed that models posing for portraits using a left cheek pose appear happier, even when the images have been digitally reversed. Harris and Lindell (2011) presented participants with pairs of left and right cheek portrait images of the same models and asked participants to make forced choice decisions indicating which image in each pair appeared happier. Unbeknownst to participants, half the image pairs had been digitally reversed. Confirming the left cheek's greater anatomic expressivity, left cheek poses were selected as looking happier, even when the images had been digitally manipulated. Furthermore, after presenting the same type of forced-choice task to children aged 3–7 years, Lindell et al. (2017) recently found that the left cheek bias for happiness perception is already established in 3-year olds. Such findings demonstrate that the greater physiognomic expressivity of adults' left hemifaces can be distinguished by children as young as three.

Importantly, the left cheek bias for emotional expression is not unique to humans: nonhuman primates also display greater emotion on the left side of their faces (see Lindell, 2013b, for review). Evidence indicates more intense left- than right hemiface expressions across many nonhuman primate species, including rhesus macaques (Hauser, 1993), baboons (Wallez and Vauclair, 2011), and chimpanzees (Fernández-Carriba et al., 2002a,b). As cortical control of the lower face is contralateral in nonhuman primates (Morecraft et al., 2001), just as it is in humans (Patten, 1996), greater expressivity in the left hemiface of rhesus macaques, baboons, and chimpanzees is entirely consistent with right hemisphere dominance for emotion control in nonhuman primates. Such findings are important for they confirm organizational continuity in the neural substrates supporting emotion processing across primate species. The fact that the expressional asymmetry is evident in Old World monkey species (e.g., baboons, macaques) suggests that the right hemisphere's dominance for emotion processing must have emerged early in primate evolution and was then conserved across phylogeny (Old World monkeys, apes, and humans are thought to have had a shared ancestor 30–40 million years ago; Stewart and Disotell, 1998). Whether the left cheek bias is similarly evident in more phylogenetically distant nonhuman primates (e.g., prosimians like lemurs and lorises) remains an important but as yet unanswered question, offering an opportunity to shed light on the degree to which expressional asymmetries have developed over the course of primate evolution (see Lindell, 2013b).

Overall, data from a variety of paradigms, including both objective measures (e.g., Dimberg and Petterson, 2000; Nicholls et al., 2004) and subjective ratings (e.g., Nicholls et al., 2002a,b; Sackeim et al., 1978), converge to confirm that the left side of the face expresses emotion more intensely than the right in both human and nonhuman primates. Given the contralateral innervation of the lower two-thirds of the face, such findings support the right hemisphere hypothesis: the left side of the face expresses stronger emotion because it is controlled by the emotion-dominant right hemisphere. Because the left side of the face is anatomically more expressive and starts moving earlier than the right when we spontaneously express emotion, these findings appear entirely compatible with Wolff's (1933, 1943) early suggestion that the left side of the face reveals our true, spontaneous, unconscious self; the right side of the face instead appears more controlled and socially appropriate.

3 HUMANS ARE INTUITIVELY AWARE OF THE LEFT CHEEK'S GREATER EXPRESSIVITY

In day-to-day life few people appear consciously aware of differences in the emotional expressivity of the two sides of their face. Indeed, when people learn about this research, they typically express profound surprise! However, an intriguing group of studies suggests that humans possess an intuitive awareness that the left side of the face expresses emotion more strongly, and this intuitive understanding influences a broad range of human behaviors, from how we pose for portraits (see Lindell, 2011, for review), to how we cradle infants (Vauclair and Donnot, 2005). For example, Nicholls et al. (2002b) asked participants to rate their own levels of emotional expressivity using the Kring et al. (1994) EES, and then pose for a photograph "as themselves." Results revealed that people who posed showing their left cheek had significantly higher EES scores than those who posed showing their right cheek, indicating that those who are more emotionally open are more inclined to offer their more emotionally expressive cheek in a portrait. Harris and Lindell (2011) have subsequently demonstrated that these findings are not restricted to emotional expressivity considered broadly, but extend to the communication of specific emotions, such as happiness. They found that when asked to pose for a portrait photo expressing as much happiness as possible, people were more likely to offer their left than right cheek, again suggesting an innate understanding that the left cheek expresses emotion more intensely than the right.

Nicholls et al. (1999) offer further evidence indicating an intuitive awareness of the left cheek's greater emotional expressivity. They asked participants to pose for a photograph in one of the two conditions: half of the participants were asked to imagine that they were traveling overseas for a year and wanted to leave their family with a portrait that shows how much they love them (emotive family condition), while the other half were instructed to imagine that they were a scientist who had just been accepted into the Royal Society and they wanted to pose for a portrait that shows that they are intelligent but not smug or arrogant, and so should avoid depicting emotion (impassive scientist condition). Nicholls et al.'s findings showed that participants aiming to express emotion in the emotive family condition were more likely to offer their left cheek, whereas those participants seeking to conceal emotion in the impassive scientist condition were more inclined to present their right cheek. Given that people aiming to express emotion (Nicholls et al., 1999) and those who are naturally more emotionally expressive (Nicholls et al., 2002b) are both more likely to offer the left cheek when posing for a portrait, it seems that we are intuitively aware that the left cheek expresses stronger emotion than the right.

Assessment of eye movements as people make emotional expressivity judgments offers further evidence supporting an innate understanding that the left cheek expresses emotion more intensely. Thomas et al. (2014) presented participants with faces displaying minimal happiness and sadness (chosen to reflect the less extreme facial expressions humans typically encounter in everyday life). In Experiment 1, participants were asked to rate how emotionally expressive the models were using three items from Kring et al.'s (1994) EES, while in Experiment 2, participants made explicit judgments about the valence of the emotion expressed (e.g., rating "how happy (sad) he or she believes they are"). Eye movements were recorded while participants inspected the stimuli. Across both experiments participants made significantly more fixations on the left than right hemiface. As half of the stimuli had been mirror-reversed, this does not reflect a perceptual bias favoring faces appearing in the left visual field. Instead, Thomas et al.'s (2014) findings indicate that viewers intuitively focus more on the more expressive left hemiface—whether or not it is presented on the left or right side of the stimulus image—when making expressivity judgments, consistent with a right hemisphere advantage for emotion processing.

The bias to preferentially attend to the left hemiface appears to be evident early in life. For example, when Mather et al. (2015) presented a 33-month-old infant with familiar faces that were smiling, frowning, or crying, the child exhibited far greater attention, as indexed by the number of fixations, to the left than right side of the familiar faces. This case study implies that the left hemiface preference noted by Thomas et al. (2014) arises early in life, with other studies showing that this left side preference is present in infants as young as 4 months old. Guo et al. (2009) found that 6-month olds already show a left visual field preference when viewing faces, whether human, nonhuman primate (Rhesus monkey), or other mammal (dog; see also Wheeler, 2010). Similarly, Liu et al. (2011) reported that 4- to 9-month olds already show a trend ($P=0.054$) toward a left-side preference in eye gaze patterns. This intuitive bias to focus more on the left hemiface is likely to facilitate efficient decoding of facial expressions which would benefit social interactions, given the importance of decoding and responding appropriately to emotional expressions in day-to-day interactions (Dimberg, 1990).

The left cheek's greater expressivity may also help explain why humans are more likely to cradle infants on the left (Salk, 1960; Vauclair and Donnot, 2005). This preference is evident in research adopting a variety of experimental methodologies, including picking up either a doll or a live infant and cradling it (Manning and Chamberlain, 1991), and simply imagining cradling an infant (Harris et al., 2001). Post hoc examination of photographs of infants being cradled (Harris and Fitzgerald, 1985) similarly confirms that mothers, in particular, are more likely to cradle an infant to the left. And humans are not alone: research indicates that a diverse range of both marine and other terrestrial mammals, including walrus, reindeer, whales, and kangaroos (Karenina et al., 2017), also exhibit a leftward bias when interacting with their infants. The fact that this preference is also evident in great apes (Manning and Chamberlain, 1991) offers evidence of evolutionary continuity in the leftward cradling bias.

Accounts based on sex and handedness fail to adequately explain the left-sided cradling preference in humans (Todd and Banjeree, 2016; Vauclair and Donnot, 2005). However, Manning and Chamberlain's (1991) emotion lateralization argument appears to hold promise. When an infant is cradled to the left maternal/paternal monitoring is enhanced as facial and emotional information from the infant projects predominantly to the mother/father's right hemisphere, which is dominant for face processing (e.g., Weibert and Andrews, 2015), as well as emotion processing (e.g., Mandal and Ambady, 2004). In addition, infant monitoring of the parent's emotional state is optimized because the child is exposed to the more expressive left side of the parent's face. Thus as a consequence of right hemisphere emotion lateralization, leftward cradling facilitates social/emotional communication between parent and infant, enhancing bonding. The fact that the leftward cradling bias is absent, or even reversed to a rightward bias, in people with known emotion-processing deficits and atypical patterns of hemispheric lateralization (e.g., people with autism spectrum disorders, Pileggi et al., 2013; people with depression, Weatherill et al., 2004) is completely compatible with an emotion lateralization account of the leftward cradling bias. Overall, research in humans confirms that we are more likely to cradle an infant to the left than to the right.

In sum, the evidence indicates that human behavior is sensitive to differences in the expressivity of the two sides of the face, despite a lack of conscious awareness of this phenomenon of expressional asymmetry. People who are naturally more emotionally expressive are more inclined pose for photos with their left cheek forward (Nicholls et al., 2002a,b). Similarly, when asked to pose explicitly expressing as much emotion as possible, people are more likely to offer their left cheek (Harris and Lindell, 2011; Nicholls et al., 1999). Not surprisingly then, eye movement recordings confirm that both infants (Mather et al., 2015) and adults (Thomas et al., 2014) intuitively spend more time looking at the more expressive left hemiface, with the adult left cradling bias affording infants an optimal view of the more expressive side of the parent's face (e.g., Vauclair and Donnot, 2005).

4 SUMMARY AND CONCLUSIONS

We all know that our facial expressions convey emotion (e.g., a grin when we receive great news; a grimace when the verdict is grim). What few know consciously, however, is that these facial expressions are not symmetrical. Humans display stronger emotion on the left side of the face, with this expressional asymmetry representing an external manifestation of the functional lateralization of the human brain. As the right hemisphere plays the dominant role in emotion control (Lindell, 2013a), and the lower two-thirds of the face is innervated contralaterally (Patten, 1996; Rinn, 1984), the left cheek expresses emotion more intensely. The research reviewed in this chapter provides strong evidence, indicating that when expressing emotion, the muscles of the left hemiface move more (e.g., Dimberg and Petterson, 2000; Nicholls et al., 2004), and earlier (e.g., Ross and Pulusu, 2013), consequently producing more intense emotional expressions than the muscles of the right hemiface. Given that the left cheek is physiognomically more expressive, it is not surprising that viewers perceive the left cheek as showing stronger emotion (e.g., Nicholls et al., 2002a,b; Sackeim et al., 1978) and thereby spend more time looking at the left side of the face (e.g., Thomas et al., 2014) when making emotional judgments.

What is surprising, however, is that our behavior indicates an intuitive understanding that the left cheek is more expressive. When asked to pose for a photo expressing emotion, we are more inclined to offer the left than right cheek (Nicholls et al., 1999). Consistently, people who rate themselves are more emotionally expressive are more likely to pose offering the left cheek (Nicholls et al., 2002a,b). In a similar vein, when cradling an infant, both right- and left-handers (the majority of whom share the same pattern of cerebral lateralization) are more likely to cradle to the left (Vauclair and Donnot, 2005). This intuitive preference enhances parental monitoring of the child (leftward cradling results in facial and emotional information from the infant projecting predominantly to the parent's right hemisphere), while simultaneously optimizing infant monitoring of the parent's emotional state (leftward cradling provides the infant with a clear view of the more expressive side of the parent's face). The evidence reviewed in this chapter thus suggests that we are sensitive to differences in the expressivity of the two sides of the face, despite typically lacking conscious awareness that the left side of our face is more expressive.

The age at which asymmetries in expression are evident in human primates is a prime candidate for further investigation. Results from studies to date are not consistent: whereas Holowka and Petitto's (2002) analysis of videos of infants smiling and babbling indicates that by 5 months of age the left cheek is already more expressive, Nagy's (2012) analysis of chimeric faces generated from Baby Beauty Contest photos indicated that the left cheek expressivity bias does not emerge until adulthood. Given the relative dearth of developmental research assessing the left cheek bias, systematic (and ideally longitudinal) investigation is vital to determine whether the left cheek's greater anatomical expressivity develops and/or changes over the course of development. As the left cheek expressivity bias is present in nonhuman primates, indicating that it has a strongly biological basis that is conserved across phylogeny, one would anticipate that the left cheek bias would be present in infants at, and potentially before, birth. The advent of in utero 3D and 4D ultrasound fetal scanning offers the potential for investigating expressional asymmetries prenatally. This type of research, combined with longitudinal follow-up, would allow determination of the point at which the left cheek's greater anatomic expressivity evinces, and the extent to which it alters in magnitude over the course of development.

While Darwin (1872) first noted that human facial expressions are often one-sided, he was at a loss to explain the phenomenon. The research reviewed in this chapter supports the view that the expressional asymmetries Darwin described are an external manifestation of the right hemisphere's dominant role in emotion processing. The left cheek is predominantly controlled by the right hemisphere, resulting in greater muscular contraction and consequently stronger emotional expressions on the left, than right, side of our faces. Our behavior, from posing for photographs to cradling infants, implies an intuitive understanding of the left cheek's greater expressivity, despite a lack of conscious awareness of this expressional asymmetry. Whether we are born expressing stronger emotion on the left hemiface, and whether this bias increases as we age, remains to be determined.

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CHAPTER

Split-brain patients: Visual biases for faces

10

Giulia Prete[1], **Luca Tommasi**
Department of Psychological, Health and Territorial Sciences, 'G. d'Annunzio'
University of Chieti and Pescara, Chieti, Italy
[1]Corresponding author: +39-871-3554209; Fax: +39-871-35542163,
e-mail address: giulia.prete@unich.it

Abstract

Split-brain patients constitute a small subpopulation of epileptic patients who have received the surgical resection of the callosal fibers in an attempt to reduce the spread of epileptic foci between the cerebral hemispheres. The study of callosotomy patients allowed neuropsychologists to investigate the effects of the hemispheric disconnection, shedding more light on the perceptual and cognitive abilities of each hemisphere in isolation. This view that callosotomy completely isolates the hemispheres has now been revised, in favor of the idea of a dynamic functional reorganization of the two sides of the brain; however, the evidence collected from split-brain patients is still a milestone in the neurosciences. The right-hemispheric superiority found in the healthy population concerning face perception has been further supported with split-brains, and it has been shown that the right disconnected hemisphere appears superior to the left hemisphere in recognizing and processing faces with similar characteristics as the observers' (e.g., gender, identity, etc.). Even more controversial is the field of hemispheric asymmetries for processing facial emotion, some evidence suggesting a right-hemispheric superiority for all emotions, some others showing a complementary hemispheric asymmetry depending on the positive or negative emotional valence. Although the practice of callosotomy is mostly abandoned today in favor of pharmacological alternatives, further studies on the remaining split-brain patients could help advance our understanding of hemispheric specialization for social stimuli.

Keywords

Split-brain patients, Face perception, Hemispheric asymmetry, Social cognition, Visual processing

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1 SPLIT-BRAIN PATIENTS

The expression "split-brain patient" typically refers to individuals suffering from epilepsy, who underwent the surgical resection of the *corpus callosum* (CC), in an attempt to reduce the spread of epileptic *foci* between the cerebral hemispheres (Zaidel and Iacoboni, 2003). This invasive treatment has been mostly abandoned today (Prete and Tommasi, 2017), due to the introduction of pharmacological therapies that are more efficient than those available some decades ago. Nevertheless, it is still used in the most drug-resistant forms of epilepsy (Englot et al., 2017). The surgery has been shown to effectively reduce the spread of epileptic activity between the hemispheres and improve the quality of life of patients (Unterberger et al., 2016).

The CC is the largest bundle of white matter connecting the left and right hemispheres, and it is composed of different functional portions (Fabri and Polonara, 2013). As shown in Fig. 1, the most posterior portions of the CC are the *splenium* and the *isthmus*, and they connect occipital, parietal, and temporal areas across the two hemispheres. Frontal and temporal cortices are connected via the *trunk*, whereas prefrontal areas are connected through the *genu* and the *rostrum* (Fabri and Polonara, 2013). The surgical section of the CC can either be complete (complete callosotomy), or it can involve only one or more specific portions of the fiber bundle (partial callosotomy). In some cases, additional interhemispheric commissures (i.e., anterior, hippocampal, posterior, and collicular commissures) are sectioned (commissurotomy; e.g., Uddin, 2011).

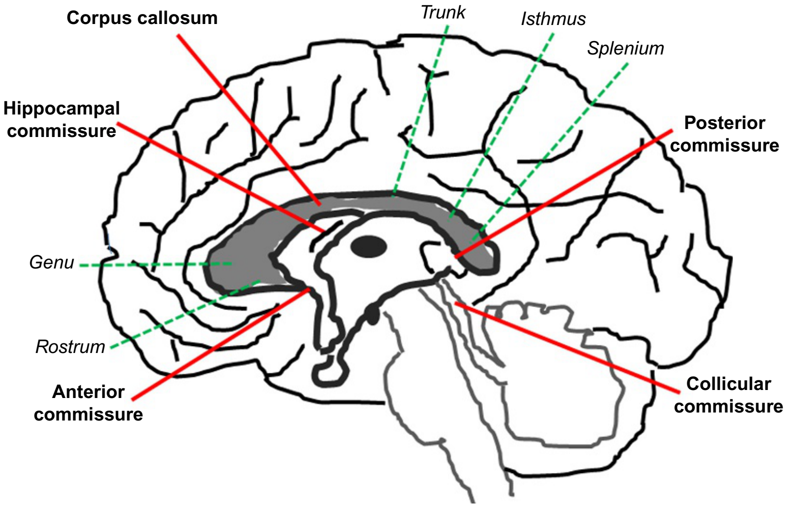

FIG. 1

Schematic representation of the interhemispheric commissures (the corpus callosum is represented in *gray*; portions of the corpus callosum are labeled in *italics*).

The absence of callosal fibers can also result from a congenital condition, and in this case it is defined as *callosal agenesis* (e.g., D'Antonio et al., 2016). Even if callosal agenesis was previously considered to be "asymptomatic" (thanks to an interhemispheric reorganization due to cerebral plasticity), it has been found that patients with callosal agenesis show a syndrome similar to that of split-brain patients, both in the perceptual and in the motor domains (Lassonde et al., 1995).

In the 1940s, Akelaitis described the positive clinical outcome of the first surgical resections of the CC carried out on epileptic patients by van Wagenen (Akelaitis, 1941a,b; Akelaitis et al., 1942; Mathews et al., 2008). Akelaitis (1941a,b) and Akelaitis et al. (1942) described the medical improvement in seizure control after complete or partial callosotomy: according to these pioneering observations, the intervention did not affect the patient's perceptual (Akelaitis, 1941a) and motor abilities (Akelaitis et al., 1942), nor their psychiatric condition (Akelaitis, 1941b). Possibly the first paper describing the cognitive outcome of an epileptic patient who underwent the surgical resection of the CC was that published about two decades later, in 1962, by Gazzaniga, Bogen, and Sperry (previous cases were described for instance by Sperry in 1961, but no cognitive effects had been noticed). The authors confirmed that the surgical intervention improved the clinical condition of the patients, by decreasing the frequency of seizures, but they presented the so-called classical disconnection syndrome (see Section 2).

Conducting research with split-brain patients constitutes a milestone for the neurosciences, but it is a hard and provides limited opportunities, due to the patients' difficulties in maintaining a high level of attention, the effect of patient medications, and often an unfamiliarity with the use of computers used for presenting experimental paradigms (see Corballis and Häberling, 2017). Nevertheless, the research carried out with split-brain patients over the last decades has continued to help clarify hemispheric competences in disparate domains, such as language (Bogen, 1997; Levy, 1983), music perception (Prete et al., 2015c), spatial abilities (Corballis et al., 2010; Hausmann et al., 2003; Prete et al., 2017a, 2018b), memory (Zaidel, 1995), attention (Berlucchi et al., 1997; Luck et al., 1994; Ptito et al., 2009), and moral reasoning (Miller et al., 2010), among others.

Because the CC is the main connection between the left and right hemispheres, the first observations of split-brain patients were centered on the evaluation of the specific skills of each hemisphere, based on the idea that the functional separation was so sharp and strong to give rise to two "minds" or two "consciousnesses": LeDoux et al. (1977) described the case of a split-brain patient who showed preserved linguistic skills in both of his disconnected hemispheres, so that the authors concluded that "*human conscious processes can be doubled by cerebral commissurotomy*" (LeDoux et al., 1977, p. 420). When detailing the clinical case, the authors reported that "On a day that this boy's left and right hemispheres equally valued himself, his friends, and other matters, he was calm, tractable, and appealing. On a day when testing indicated that the right and left sides disagreed on these evaluations, the boy became difficult to manage behaviorally. It is as if each mental system could read the emotional differences harbored by the other. When they were discordant, a feeling of anxiety, which appeared to be read out by hyperactivity and general aggression, was engendered. This clear example of surgically produced psychological dynamism, seen for the first time in P. S., raises the question whether such processes are active in the normal brain, where different mental systems, using different neural codes, coexist within and between the cerebral hemispheres" (LeDoux et al., 1977, p. 420).

The idea of a split consciousness was also proposed by Dimond (1978) who pointed out that the *splenium* was the site in which a general consciousness circuit takes place. In the same vein, Zaidel and Iacoboni (2003) wrote "*Soon after surgery there are episodes of intermanual conflict, in which the hands act at cross-purposes. Patients sometimes complain that their left hand behaves in a 'foreign' or 'alien' manner, and they routinely express surprise at apparently purposeful left-hand actions (autocriticism)*" (p. 320). The issue of one integrated vs two separated conscious entities in the human brain remained a central core to the neurosciences, so much so that after 40 years of research, the "unity of consciousness" is still one of the most debated issues in the split-brain literature (e.g., Bayne, 2008; Colvin et al., 2017; Volz and Gazzaniga, 2017).

Over time the idea of callosal fibers as mere connection between two independent hemispheres has been replaced by the softer interpretation of two cooperating halves of the brain that continue to interact even in the absence of callosal connections, thanks to subcortical bilateral projections (e.g., Funnell et al., 2000). Similarly, also the idea of a "dominant" hemisphere has been replaced with that of a possible superiority of one hemisphere over the other, but with the possibility that the processing of information can occur in each half of the (disconnected) brain (see Corballis and Häberling, 2017). Support for this view can be found in some studies with split-brain patients. For instance, split-brain patients were able to make perceptual judgments, such as matching of nonsense shapes, across the vertical meridian (Zaidel, 1995), showing that unilateral information can reach the contralateral hemisphere in the absence of callosal fibers, even if spatial information is more efficiently processed by the right hemisphere (Funnell et al., 1999). In summary, the findings highlighted by testing split-brain patients add important evidence about the role of interhemispheric connections, as well as about the specific competences of the two halves of the brain and the mechanisms involved in neuroplasticity.

1.1 THE CALLOSAL DISCONNECTION SYNDROME

The so-called callosal disconnection syndrome manifests itself in a combination of several impairments, mainly concerning bimanual coordination (Berlucchi, 2012), spatial attention, and language impairment of the nonlinguistic hemisphere (e.g., Lausberg et al., 1999). The central core of this syndrome is rooted in the associationist theory proposed by Wernicke (1874), and then revised by Geschwind (1965a,b), according to which all cognitive functions emerge from white matter connections with different cerebral areas. In this view, cognitive, behavioral, and psychological dysfunctions occur as the result of white matter lesions. In this frame, the expression "disconnection syndromes" is used to define all of the disorders due to an acquired lesion involving neuronal projections, which leads to specific high-level disorders, including language disability (aphasia), motor disorder (apraxia), sensory processing deficit (agnosia), reading disorder (alexia), and so on (Catani and ffytche, 2005). When referring to split-brain patients, the "callosal syndrome" is mainly defined as the linguistic inability of the right hemisphere, which is evident in higher order deficits in the left hemispace, such as the inability in reading, moving, and recognizing objects in the left hemispace (Zaidel, 1983).

In the past, the classic view posited that callosal fibers simply allow the exchange of information between the two hemispheres: "*a copy of the visual world as seen in one hemisphere is sent over to the other*" through the callosum (Gazzaniga, 1967, p. 29). Similarly, Geschwind and Kaplan (1962) asserted that the callosal disconnection syndrome was the exact result of the interrupted exchange of information between the two sides of the brain. However, besides being the largest group of fibers connecting the two halves of the brain, the CC also plays a role in functional asymmetries. Only recently it has been found that the CC is not solely constituted of white matter, but it contains active cells: a series of functional magnetic resonance imaging (fMRI) studies highlighted functional activation in different portions of the CC depending on the nature of stimuli presented (Fabri et al., 2014; Gawryluk et al., 2009). It is now considered that symptoms following callosal disconnection are attributable to the loss of a distributed balance mediated by the callosal fibers together with the other cortical and subcortical commissures. The notion of an equilibrating role of the callosum was initially put forward by Kinsbourne (2003), based on evidence that callosal fibers are both excitatory and inhibitory and that some excitatory fibers activate inhibitory interneurons. On these grounds, the callosal disconnection syndrome could be seen as the result of a lack of response of the "uninformed" hemisphere, assuming that information reaches it anyway by means of subcortical pathways. With regard to the subcortical interhemispheric connections, Doty (1989) previously proposed that the serotonergic raphe system in the pons and the mesencephalon could be responsible for bilateral subcortical activation.

The prevalent interpretation nowadays is that callosal connections are mainly involved in interhemispheric communication, but they also have a functional role and they are crucial in determining cerebral functional asymmetries. For instance, Barnett and Corballis (2005) found that the right-to-left information transfer time was faster than the opposite route (left-to-right), and they attributed this finding to the faster axonal speed arising in the right rather than in the left hemisphere, due to the greater number of fast-conducting, myelinated fibers in the right hemisphere. This idea had been previously proposed by Marzi et al. (1991, 1997) who argued that callosal projecting neurons are more numerous in the right hemisphere than in the left hemisphere. Based on this observation, the authors also proposed an explanation for a number of impairments following right-hemispheric damage that were possibly attributable to the callosal projections, as the deficit in attention to and awareness of the left visual field (LVF), namely, spatial hemineglect

(Berlucchi and Vallar, 2018), and the inability to consciously perceive stimuli presented in the LVF when they are presented together with stimuli in the right visual field (RVF), namely, visual extinction (Chen and Spence, 2017). According to the hypothesis proposed by Marzi et al. (1997), a right-lateralized brain injury should cause a greater loss of callosal fibers, resulting in a stronger impairment of interhemispheric transmission. Thus, the information reaching the left hemisphere can project to the right, but the information reaching the right hemisphere cannot be projected to the left: the result is the extinction (or neglect) of the stimuli presented in the LVF (Heilman et al., 1987). The model explained the case of right-damaged patients who did not show extinction as rare cases due to the preserved callosal projections despite the right hemisphere lesion.

The view of axonal fibers involved in functional asymmetries and lateralized attentional deficits (e.g., spatial hemineglect, extinction) has been widely referenced in a number of studies and neuropsychological models (Corbetta and Shulman, 2011; De Schotten et al., 2005; He et al., 2007; Gaffan and Hornak, 1997). Furthermore, Corballis et al. (2005) described a case of alternating hemineglect present in a split-brain patient with a complete callosal resection, further supporting the role of the callosal projections in attentional processes: the patient showed slower reaction times for stimuli flashed in the LVF, but he did not show attentional bias when stimulus location was defined by continuous markers presented in both visual fields.

It should be noted that when we refer to complex perceptual stimuli, the disconnection syndrome could be weakly evident, unless it is studied with specific methodologies. In the visual domain, for instance, the most exploited paradigm is that of the divided visual field presentation (Bourne, 2006). In this paradigm, a visual stimulus is presented in the left or in the RVF, for a duration shorter than that needed to make a saccadic movement (about 150ms, computer-based, tachistoscopic presentation), and the observer is required to gaze ahead centrally, without moving their gaze directly to the location of the stimulus. When the stimulus is presented in a lateralized fashion, it is projected to the nasal portion of the retina, which is directly connected with the contralateral hemisphere (e.g., left eye/right hemisphere). This procedure allows researchers to be confident that a stimulus is directly processed by one hemisphere.

The computer-based presentation of lateralized stimuli has been widely exploited to investigate hemispheric skills in healthy observers. The performance of split-brain patients in this type of tasks gives researchers a unique opportunity to evaluate the ability of each hemisphere "in isolation." Brown et al. (1999) recorded event-related potentials (ERPs) during a matching task in which letters and dots were presented unilaterally and bilaterally, in a group of six patients with either complete or partial (posterior) agenesis, in a commissurotomy patient, and in healthy controls. The authors found that none of the patients presented the early visual ERP components (P1/N1) related to visual perception without high-level cognitive processing, in the hemisphere ipsilateral to the stimulus presentation, showing that posterior callosal projections are necessary for an interhemispheric exchange of visual information. Interestingly, they also found that the commissurotomy patient was not capable at correctly comparing bilaterally presented letters, but that the patients with callosal agenesis—with an intact anterior commissure—carried out the task successfully, indicating that the anterior projections are sufficient to allow for a bilateral visual matching.

To conclude, the “callosal syndrome” is mainly evident in higher order deficits occurring in the left hemispace (Zaidel, 1983). The classical view of the CC as a mere connection between the two hemispheres (Seymour et al., 1994) is now out of date, in favor of an integrative view of interhemispheric communications taking place by both white matter connections and bilateral subcortical projections. Anatomical and functional studies on the interhemispheric commissures allowed neuroscientists to define the specific functional role of each portion of the CC (Fabri et al., 2014; Gawryluk et al., 2009), and the evidence collected with patients with different degrees of callosal resection further confirmed these findings (e.g., Fabri and Polonara, 2013).

2 HUMAN FACES AS SPECIAL STIMULI

Humans are able to recognize identity, gender, age, and a number of different characteristics from the face of conspecifics, and this ability seems to be innate, being also present in newborns (e.g., Johnson et al., 1991). It has been consistently shown that face processing mainly takes place in the right hemisphere (e.g., Bruce et al., 1981; Gross et al., 1972; McCarthy et al., 1997; Prete et al., 2015e; Rizzolatti et al., 1971; Yovel, 2015), and that a right temporal region, the fusiform gyrus, is specifically devoted to facial analysis, so much so that this area has been defined “fusiform face area” (FFA; Kanwisher and Yovel, 2006; Kanwisher et al., 1997). These findings are further supported by the evidence that a unilateral right-hemispheric lesion can cause the inability at recognize faces (prosopagnosia), whereas a unilateral, left-hemispheric lesion does not alter face recognition (e.g., Barton et al., 2002), even if some evidence suggest that prosopagnosia is more severe with bilateral than unilateral lesions (Barton, 2008).

The right-hemispheric superiority in face processing has been supported by behavioral, electrophysiological, and neuroimaging studies examining healthy participants. Starting from the behavioral findings, a right-hemispheric superiority has been shown in the processing of facial stimuli by means of the divided visual field paradigm (e.g., Bourne and Hole, 2006; Verosky and Turk-Browne, 2012). For instance, in a face identity recognition task, it has been shown that when a sample and a target face were serially presented in different orientations (e.g., sample upright and target upside down) and decomposed (e.g., different portions of the images presented detached from each other), the right hemisphere is more efficient than the left hemisphere in identity recognition, with a better performance for target stimuli presented in the left than in the RVF (Prete et al., 2015e). Moreover, electroencephalographic studies corroborate this evidence, showing enhanced and faster ERP components in the right than in the left hemisphere during face perception (e.g., Prete et al., 2015a; Yovel, 2016). Also, brain stimulation techniques provide further evidence of this asymmetry (Jonas et al., 2015; Parvizi et al., 2012; Rangarajan et al., 2014) and fMRI definitively supports the strong right-hemispheric involvement in face analysis (e.g., Dricot et al., 2008; O'Neil et al., 2014). This hemispheric asymmetry has been explained with reference to the right-hemispheric superiority for global vs local analysis of faces (Karim and Kojima, 2010), for configural vs analytic processing of faces (Chance, 2014), and for low vs high spatial frequency detection of faces (Faubert et al., 2017; Keenan et al., 1989), among others.

Despite the amount of evidence in support of the right-hemispheric superiority in face processing, interhemispheric cooperation in face analysis has been revealed in different studies. For instance, Davies-Thompson and Andrews (2012) presented a sample of 72 right-handed participants with the images of faces, bodies, inanimate objects, places, and scrambled images, during fMRI acquisition. The results suggest the involvement of a face-processing network, including FFA and occipital face area (OFA), as well as different temporal sites, inferior frontal cortex, and subcortical structures such as amygdala and superior colliculus. The authors found that facial processing increased the functional connectivity among these areas, mainly in the right hemisphere—particularly between FFA and OFA. Importantly, they also reported that the covariation in activity between corresponding areas in the two hemispheres (e.g., left and right FFA) was stronger than the intrahemispheric connectivity among different facial processing areas (e.g., right FFA and right OFA). This result supports the hypothesis that, in addition to the right-hemispheric superiority for facial stimuli, interhemispheric connections are involved in face processing. In line with this evidence, Geiger et al. (2016) found a strong interhemispheric connectivity between the left and right fusiform gyrus during memory consolidation of facial images. Finally, in a divided visual field paradigm during fMRI carried out with 20 right-handed and 20 left-handed participants, Frässle et al. (2016) found a stronger left-hemispheric FFA involvement during face processing in left handers compared to right handers, whereas no difference between the two groups was found for objects and scrambled images. The authors concluded that handedness preference affects cerebral asymmetries for faces.

To conclude, the right-hemispheric superiority in face processing is widely accepted: it has been shown by means of behavioral paradigms (Bourne and Hole, 2006; Prete et al., 2015e; Verosky and Turk-Browne, 2012), neurological patients (Barton et al., 2002), electrophysiological findings (Prete et al., 2015a; Yovel, 2016), brain stimulation methods (Jonas et al., 2015; Parvizi et al., 2012; Rangarajan et al., 2014), and neuroimaging techniques (Dricot et al., 2008; O'Neil et al., 2014). Despite this unquestioned cerebral asymmetry, the interhemispheric connections have been proven to have a crucial role in facial processing (Davies-Thompson and Andrews, 2012; Geiger et al., 2016).

2.1 HEMISPHERIC ASYMMETRY FOR FACES IN THE DISCONNECTED BRAIN

The performance of callosotomized patients could shed more light on the issue of hemispheric asymmetry for face perception and on the possible hemispheric imbalance for the different features constituting the complexity of facial stimuli.

For instance, patients with callosal agenesis showed no difficulties in a facial gender discrimination task, but they revealed poor performance with respect to a control group in facial emotion coding, which seems to be related to a different pattern of gaze pointing involving the lowest part of the facial stimuli rather than the eye region (Bridgman et al., 2014). The authors suggested that this peculiarity in facial scanning could be the reason why acallosal patients often show a deficit in social interactions and in particular in facial emotion detection, attributable to the reduced interhemispheric connectivity. Also in callosotomy patients the gender recognition of facial stimuli has been tested (Prete et al., 2016), but the results are controversial. In a divided visual field paradigm with a male split-brain patient (DDC), the accuracy of gender categorization resulted at chance level when stimuli were presented tachistoscopically in the RVF and thus directly projected to the left hemisphere. Nevertheless, when facial stimuli were presented in the LVF, the patient carried out the task successfully, but only when stimuli were male faces (Prete et al., 2016). Thus the study revealed a right-hemispheric lateralization of the Own-Gender Bias; the preference in recognizing persons belonging to the same gender as the observer's (e.g., Wright and Sladden, 2003). The bias, often found in favor of the right hemisphere for those stimuli having the same characteristics as the observers', has been explained by making reference to the right-hemispheric involvement in self-recognition (Keenan et al., 2005). In fact, the substrates of self-representation and self-consciousness are lateralized to the right hemisphere, mainly involving temporal and prefrontal areas (e.g., Devue and Brédart, 2011; Feinberg and Keenan, 2005; Keenan et al., 2005).

However, the same gender categorization task as the one carried out by patient DDC was also administered to a control group of healthy female and male participants did not reveal the same asymmetry as DDC (Prete et al., 2016). Healthy participants showed a right-hemispheric superiority for female face, and a left-hemispheric superiority for male face categorization, independently of the gender of participants (see also Parente and Tommasi, 2008; Prete et al., 2017b). This crossed bias in healthy participants has been attributed to an innate right-hemispheric superiority in the processing of female faces (Parente and Tommasi, 2008; Prete et al., 2017b). This asymmetry would be due to the fact that newborns are mainly cradled on the left side of the maternal body, so that the "social" right hemisphere of both newborn and mother is more directly connected, favoring an optimal social interaction between cradler and newborn. The specular left-hemispheric superiority for male faces has been attributed to a complementary cerebral specialization (the leftward cradling bias being present only in females; Todd and Banerjee, 2016). A different result was found by Luo et al. (2011) who tested a male patient with a lesion involving the splenium and the left medial occipitotemporal region. When the patient was presented with chimeric faces constituted by a female hemiface juxtaposed to a male hemiface to form one face, he reported not to see the chimeras and based his gender categorization on the left hemiface, showing a right-hemispheric superiority in this task. It has to be noted that the combination of the left-hemispheric lesion and the partial callosal resection does not allow for a clear-cut conclusion about the patient's performance in gender discrimination.

A different divided visual field paradigm was used by Mason and Macrae (2004) during a gender categorization task and an identity recognition task, carried out by both the male split-brain patient JW and a control group. In two different blocks, participants had to respond whether two faces presented together either in the left or in the RVF were of the same gender (gender categorization) or the same person (identity categorization). Results showed no asymmetry during the gender categorization task, neither in the patient nor in the control group, but a right-hemispheric superiority was found for identity matching. A similar right-hemispheric superiority for facial identity recognition was also described in a seminal study involving four split-brain patients described by Levy et al. (1972).

A possible explanation of the different results found in gender recognition paradigms could be the specific task required. On one hand, the task carried out by DDC (Prete et al., 2016), revealing the right-hemispheric lateralization for the Own-Gender Bias, was a pure categorization task (response: female/male). On the other hand, the task carried out by JW (Mason and Macrae, 2004), revealing no asymmetries, was a gender matching task in which a direct comparison between two stimuli was required (response: same/different). Moreover, JW was also tested by Turk et al. (2002) in a divided visual field paradigm in which morphed faces, created by mixing the photograph of the patient and that of a familiar person, were presented in one visual field at time. The authors found a right-hemispheric superiority in the recognition of familiar faces, but a left-hemispheric superiority in self-face recognition, even if both disconnected hemispheres carried out the identity task with an accuracy higher than chance (response: yes/no, for both blocks of trials in which JW was required to respond whether the stimulus was either the familiar face, or it depicted his own face). The authors attributed this left-hemispheric bias to a “self-memory system,” i.e., a distributed network responsible for the autobiographical knowledge and the idea of self (Turk et al., 2002). On the other hand, some months later the opposite pattern was described by Keenan et al. (2003), who presented morphed faces centrally and required the left-handed male patient ML to use the left or the right hand to respond whether the stimulus contained his own face or a familiar person’s face. They found that the patient reported seeing his own face more frequently when the left hand was used, showing a right-hemispheric superiority in self-face processing, in accordance with previous galvanic recordings described by Preilowski (1977). They also found a better performance in classifying familiar persons’ faces with the right hand (left hemisphere). Finally, the female patient NG was tested by Uddin et al. (2005) in a divided visual field paradigm in which stimuli were facial morphs, mixing the patient’s own face and an unknown face, or mixing a familiar female face and an unknown female face. Results showed that both hemispheres were capable of self-recognition, but that only the right hemisphere could also successfully recognize the familiar face. All these findings seem to suggest that individual differences, together with the specific experimental manipulations used, lead to different patterns of hemispheric asymmetries.

To summarize, it is still uncertain whether the recognition of familiar faces in general, or that of self-face in particular, is clearly lateralized to one hemisphere.

One possibility is that the left- and right-hemispheric superiorities found from time to time could be specifically attributed to the task required. In general, we can conclude that the majority of studies have revealed a superiority of the right hemisphere in the processing of faces, mainly for those faces having the same characteristics as the observer's, e.g., own-gender (Luo et al., 2011; Prete et al., 2016), own-face (Keenan et al., 2003; Preilowski, 1977), and a right-hemispheric superiority has also been consistently found for facial identity (Levy et al., 1972; Mason and Macrae, 2004) and familiarity (Turk et al., 2002; Uddin et al., 2005).

2.2 EMOTIONS AS VIEWED BY A DISCONNECTED BRAIN

A crucial piece of information conveyed by a face is the emotional state of that person. Emotional expressions are automatically detected (e.g., Stefanics et al., 2012), and this ability allows us to understand the mood of other person and to adequately respond in terms of both behavioral reactions and physiological adjustments (e.g., Jessen et al., 2016). Emotional coding has been widely studied by psychologists, neuroscientists, and clinicians, due to its central role in our daily interactions. A debated point in this frame is concerning hemispheric asymmetries for emotional processing. Two main theories are alternatively supported by research (for a meta-analysis see Fusar-Poli et al., 2009): on one hand, according to the valence hypothesis (VH), a left-hemispheric/right-hemispheric superiority exists for positive and negative valence emotions, respectively (Baijal and Srinivasan, 2011; Davidson et al., 1987); on the other hand, according to the right hemisphere hypothesis (RHH), positive and negative emotional processing both take place in the right hemisphere (Gainotti, 1972, 2012; Levy et al., 1983; Lindell, 2013).

In a divided visual field task (Stone et al., 1996) each of the disconnected hemispheres of the split-brain patient JW was better than chance at matching facial expressions with emotional words. However, in accordance with the RHH, only the right hemisphere appeared to be able at matching two facial expressions, suggesting a right-hemispheric superiority for emotion processing. Nevertheless, other evidence support the validity of both the VH and the RHH (Prete et al., 2014b): it was suggested that the number of emotional stimuli which have to be processed at once could be the main variable influencing hemispheric asymmetries for emotional stimuli. In this view, when just one emotional face is presented, a right-hemispheric superiority appears (in accordance with Stone et al., 1996); when the load increases—due to the presentation of two emotional stimuli—each hemisphere shows its specialization for positive or negative emotions. Support for this speculation can be found in a task carried out by both a patient with an anterior callosal resection saving the splenium (AP) and a patient with a complete callosal resection (DDV; Prete et al., 2014b). Both patients and a control group of healthy participants were asked to rate the emotional content of chimeric faces constituted by a combinations of happy, sad, and neutral hemifaces, and auditory stimuli constituted by a syllable with happy or sad emotional valence presented in one ear and white noise simultaneously presented in the other ear. AP's responses were driven by the stimulus directly projected to the right hemisphere during unimodal presentation (left hemiface and syllable presented in the left ear), but his performance supported the VH during audiovisual presentations (chimeric faces and dichotic stimuli presented simultaneously). However, DDV's judgments were based on the emotional expression of the right hemiface in all conditions. This pattern of results supports the need of an intact splenium in order to maintain the hemispheric imbalance for positive and negative emotions found in healthy participants.

2.3 SUBLIMINAL EMOTIONS AND THE DISCONNECTED BRAIN

Besides the evidence of hemispheric asymmetries for consciously perceived emotional stimuli, different studies also revealed a subcortical asymmetry concerning subliminal emotions: as reviewed by Johnson (2005), a number of neuroimaging, electrophysiological, and neuropsychological studies suggest the existence of a subcortical route specifically involved in a fast and subliminal analysis of facial features. This subcortical route primary includes the amygdala and is responsible for emotional encoding, based on the analysis of low spatial frequencies (LSF). The output of this route would be then conveyed to cortical areas, which are mainly responsible for the processing of the high spatial frequencies (HSF); it also modulates the cortical activity in a bottom-up pathway. A dissociation in hemispheric lateralization for subliminal and supraliminal emotion processing was revealed by Làdavas et al. (1993), in a split-brain patient. The authors exploited a divided visual field paradigm in order to investigate the possible lateralization for emotional (disgusting and sex-related) and neutral stimuli presented below the conscious perceptual threshold (20 ms) and above the conscious perception threshold (150 ms). For both subliminal and supraliminal conditions the heart rate (HR) raised when emotional contents were presented, with respect to neutral stimuli. Moreover, when the stimuli were consciously perceived by the patient, both behavioral responses and HR did not differ across LVF and RVF presentations. However, when the stimuli were presented below the consciousness threshold, the HR was increased when emotional stimuli were presented in the LVF (right hemisphere) but not in the RVF (left hemisphere). The authors concluded that the right hemisphere is dominantly involved in the physiological modulation due to emotional detection, even in the absence of conscious perception of the stimulus.

The involvement of the subcortical route in LSF emotional detection has also been found in a study with emotional "hybrid faces" (Laeng et al., 2010). These stimuli are created by superimposing the photograph of an emotional face filtered at LSF to the photograph of the same person with a neutral pose filtered at HSF. Emotional hybrid faces have been then exploited in a number of paradigms involving both healthy participants and split-brain patients, in order to investigate the relationship between emotional detection, spatial frequencies, and hemispheric asymmetries. The emotional expressions mostly used have been happiness and anger, namely, those receiving the highest and lowest friendliness evaluation in the original study by Laeng et al. (2010), meaning that their LSF emotional content was correctly decoded by observers. In a divided visual field paradigm, hybrid happy, hybrid angry, and neutral faces were presented to healthy participants in a divided visual field paradigm (Prete et al., 2014a). The results showed that the hidden LSF content also modulates the friendliness judgments when presented lateralized. Importantly, stimuli were evaluated as less friendly when they were presented in the LVF than in the RVF, supporting the VH (the left/right hemisphere were more prone to express positive/negative judgments, respectively). In a following study, a different divided visual field paradigm was used: pairs of hybrid or unfiltered angry, happy, and neutral faces were shown in a bilateral presentation task. Two facial stimuli were simultaneously presented, one in each visual field, and a friendliness evaluation task was carried out by healthy participants, the complete split-brain patient DDC, and AP (with the anterior callosal resection; Prete et al., 2015b). The results revealed that when stimuli were hybrid faces, the friendliness judgments were influenced more by the emotional expressions presented in the LVF, supporting a stronger involvement of the right hemisphere in the detection of all subliminal emotions (as suggested by the RHH). This pattern of results was also revealed with unfiltered stimuli both in healthy participants and in AP, whereas the evaluation by the split-brain patient DDC was mainly based on the emotional expression shown in the RVF. The interpretation was that the processing of implicit emotions, contingent upon the LSF analysis of the stimuli, does not require the integrity of callosal fibers and involves the subcortical route lateralized in the right hemisphere. In a further study the patient AP and a control group were presented with hybrid faces during a unilateral presentation paradigm at three different tachistoscopic presentation times (28, 75, 128 ms), and during a bilateral presentation paradigm obtaining by means of chimeric hybrid faces (Prete et al., 2015d). Consistent with previous results, findings showed the unilateral presentation led to a right-hemispheric superiority for all emotions (i.e., RHH), whereas the bilateral presentation revealed a right-hemispheric superiority for negative emotions and a left-hemispheric superiority for positive emotions (i.e., VH). This pattern of results can be considered as a further support for the hypothesis that hemispheric asymmetries for emotions are contingent upon the number of emotional stimuli presented at once: with just one emotional stimulus, the RHH is confirmed, when two different emotional stimuli are presented together, the results support the VH.

Finally, ERPs recorded during the central presentation of hybrid stimuli in healthy participants showed a persistent enhancement of the emotional components P1 and P2 in the right hemisphere for both positive and negative emotions (Prete et al., 2015a), a pattern further supported also by using unfiltered emotional faces (Prete et al., 2018a).

We can conclude that both healthy participants' and split-brain patients' performances reveal different patterns of hemispheric asymmetries depending on the specific paradigm used. When one emotional face is presented, the superiority of the right hemisphere in emotion detection appears, supporting the RHH (Prete et al., 2014a). However, when the cognitive load becomes heavier due to the presentation of different emotional stimuli, the left and the right hemispheres appear to be specialized in positive and negative emotion detection, respectively, supporting the VH (Prete et al., 2015d). This conclusion is true when posterior callosal connections, namely, the *splenium*, are intact and it allows for a sensory information exchange between the two hemispheres (Prete et al., 2015b).

3 CONCLUSIONS

Evidence collected with split-brain patients provide us with a better understanding of the cerebral correlates of cognitive processes. The "split-brain literature" has been a very important resource for shedding more light on hemispheric asymmetries in the most disparate domains of perception and cognition. The growing introduction of pharmacological treatments for epilepsy has resulted in a reduction in the exploitation of invasive surgical resections of the callosal projections, even if callosotomy is still performed in the most drug-resistant forms of epilepsy (Englot et al., 2017; Prete and Tommasi, 2017). The view according to which each disconnected hemisphere reflects—in an amplified fashion—the functioning of that hemisphere in the intact brain is now less supported than in the past decades (Corballis and Häberling, 2017). The overall clinical condition of split-brain patients best explains some extreme evidence of asymmetry due, for instance, to the cerebral plasticity and to the effect of patient medications (e.g., Corballis and Häberling, 2017). Evidence collected in split-brains precipitated Roger Sperry's 1981 Nobel Prize in Physiology or Medicine for the discoveries on the functional specialization of the cerebral hemispheres and constitute a milestone for the neurosciences. With regard to facial processing, split-brain patients' results have revealed a right-hemispheric superiority for the processing of facial features, primarily when they are shared between the observed face and the observer (e.g., own-race bias), as well as a right-hemispheric superiority in emotional detection. The scarce group of split-brain patients still available to be tested today could provide an invaluable contribution to the unresolved issues concerning facial processing and hemispheric asymmetries.

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SECTION

3

Methodological considerations

CHAPTER

Manual laterality and cognition through evolution: An archeological perspective

11

Natalie T. Uomini[*,1,2], **Lana Ruck**[†,‡,1,2]

*Department of Linguistic and Cultural Evolution, Max Planck Institute for the Science of Human History, Jena, Germany
†Cognitive Science Program, Indiana University, Bloomington, IN, United States
‡Department of Anthropology, Indiana University, Bloomington, IN, United States
[1]Corresponding authors: Tel.: +49-177-393-0323 (N.T.U.); +1-812-606-4962 (L.R.),
e-mail address: traduck@gmail.com; lruck@iu.edu

Abstract

To understand the evolution of lateralized motor biases and cognitive functions, we rely on archeological methods to give us a window onto the past. Currently, the overwhelming majority of prehistoric data on asymmetry and laterality concern only the hominin lineage, spanning the time period from the presumed evolutionary split with the other great apes around 6–8 million years ago until the present day. We present an overview of these data from paleontology and archeology. Lateralized motor biases and anatomical asymmetries are evident throughout prehistory, showing increases in the predominance of right-handedness over time. Laterality was a key feature of the motor-cognitive development of extinct human ancestors. However, further research in living humans is needed to resolve the extent of colateralization of functions in the human brain, so we urge caution when inferring functional cognitive laterality from behavioral markers of handedness.

Keywords

Archeology, Fossils, Handedness, Hominins, Human evolution, Laterality, Lithics, Stone tools, Paleoanthropology, Paleoneurology

1 INTRODUCTION

Through the ages, laterality has been considered a hallmark of humanity. From the predominance of right-handers in human societies to the functional specialization of the hemispheres in human brains, our salient laterality has captured the attention

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[2] Both authors contributed equally.

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of scholars worldwide. Although lateralized cognition and motor behaviors are widespread in the animal kingdom—as discussed in the other chapters in this volume—and lateralities are also ubiquitous in plants, molecules, and galaxies (McManus, 2004; Myrgorodska et al., 2017; Rosenberg et al., 2008; Shamir, 2012), it is clear that our species has a unique system of distributing behavior and cognition across the midline, with its unusual species-level preponderance of extreme side biases and lateralized functions.

First, it is important to understand the place of humans in the evolutionary tree of biological life, since *Homo sapiens* evolved in continuity with the ancestral species preceding us. Humans are just one species of great ape, in the primate order, belonging to the class of mammals. Our unique evolutionary lineage extends about 6–13 million years back in time (the exact dates are uncertain), starting from the moment when we shared a common ancestor with other living apes, the chimpanzees (*Pan troglodytes*), and bonobos (*Pan paniscus*), who themselves only diverged into separate species 1.6 million years ago (mya). In the last 7 million years of our evolution, dozens of different hominin species appeared and disappeared, many of them living alongside one another (as do bonobos and chimpanzees today). Ultimately, only *H. sapiens* remained into the present day (albeit with a significant proportion of DNA from Neanderthals, Sankararaman et al., 2014). It is still unclear why only our species survived; current theories propose that the success of *H. sapiens* was due to one or more evolutionary adaptations for sociality, tool-use, cumulative culture, language, increased brain size, or intelligence (McBrearty and Brooks, 2000; Uomini, 2008b). Lateralization might also have contributed to our species' evolution, as for example a stable individual hand preference over time facilitates learning difficult bimanual skills (Todor and Doane, 1977), and having a functionally lateralized brain is suggested to improve the ability to perform tasks that involve both hemispheres (Rogers et al., 2004). Thus, knowing the conditions surrounding the evolution of lateralization helps us to better understand why lateralization exists today.

There has now been over 150 years of scientific research on hemispheric specialization and lateralized functions in living humans, with three major domains being hand preferences, language, and visuospatial skills and attention. Owing to its long history, this research includes assessments of behavioral asymmetries, as well as work on anatomical and functional brain asymmetries; it also includes large-scale studies of laterality-related genes and comparative research on nonhuman species. In other words, the literature on laterality is incredibly vast (see Rogers and Vallortigara, 2017; Seghier, 2016). In the next section, we review some key findings from comparative research and provide a broad overview of the evolutionary perspectives which underlie contemporary laterality research today.

1.1 LATERALITY IN THE ANIMAL KINGDOM

The evidence for lateralized cognition, motor biases, and anatomical asymmetries in nonhuman animals suggests that laterality at the level of the individual is actually quite conserved across animal taxa, with various forms of individual asymmetry across the midline being present in a range of species widely separated by evolution to varying degrees. Thus, while laterality itself is not unique to humans, comparative work shows that *H. sapiens* has a much more extreme degree of functional specialization than other species, even when compared to our closest living relatives among the apes (reviewed in Rogers, 2014; Rogers and Vallortigara, 2017), as we discuss later. Owing to various practical limitations—such as a general inability to conduct task-based functional neuroimaging on nonhumans, the contentious nature of work on nonhuman communicative (or linguistic) capabilities, ethical considerations for animal and human research, etc.—much of the work on hemispheric specialization and laterality in other species comes from behavioral data and, when possible, anatomical comparisons between well-established homologous brain areas.

Driven by the early discovery of a relationship between manual motor skill and other lateralized behaviors in humans (Corballis, 2003, 2009), quite a bit of comparative work relates directly to understanding the basis and the evolutionary context of human *hand preferences*. Although some of this work seek to understand hand preferences in themselves, a majority of research publications situate hand preference *as a proxy* for the other lateralities (Bishop, 2013; Rogers and Vallortigara, 2017). The idea of hand preference as a proxy was certainly based on earlier research, but the spread of this idea throughout the literature was likely facilitated due to a relative ease of studying hand preference (a behavioral trait) compared to the complications of studying functional specialization and hemispheric asymmetries directly.

In the specific case of motor biases in lateralized hand use, which, as discussed earlier, have been more thoroughly investigated than other forms of lateralization, humans are at one end of a continuum on which individual-level and species-level hand preferences can be quantified (Forrester et al., 2013). Nonhuman apes—which also execute complex manipulations with their hands and fingers—commonly have individual hand preferences, just as humans do (although some authors hypothesize that hand preferences in primates can be task specific, as for example in western lowland gorillas (*Gorilla gorilla gorilla*) hand actions are more likely to be right-handed if the target is inanimate, compared to animate targets, Forrester et al., 2011). Hand preferences can also be rather consistent within an individual (i.e., some authors argue that individual apes can be right- or left-handed, in much the same way as us, Hopkins, 2004, 2006; Hopkins et al., 2004, 2011). However, unlike humans, the other apes do not have a species-level bias toward *one* hand preference configuration—that is, handedness (Cashmore et al., 2008; McGrew and Marchant, 1997; Uomini, 2009c).

In other words, all human groups (populations) have a statistically significant majority of right-handers, with proportions across various types of human societies ranging from 77.4% to 96.6% right-handers (Faurie et al., 2016; Faurie and Raymond, 2005), and there are no human groups with a majority of left-handers. On the contrary, nonhuman great ape hand preferences are more evenly distributed to the left or right, in adults, such that various groups have a majority of left-handers, a majority of right-handers, or equal numbers of right-, left-, and ambilateral-handers

(Meguerditchian et al., 2015); for instance, the highest proportion of right-handers in a chimpanzee group does not exceed 70% (Neufuss et al., 2017). The comparative data are on adult hand preferences because in humans, children's hand preferences do not stabilize until age 10 (Michel et al., 2013), but we currently lack thorough comparative research on nonhuman primate hand preferences from similar developmental perspectives. Beyond the primates, group-level limb preferences are found in 61 species of vertebrates—mammals, birds, amphibians, reptiles, and fishes (Ströckens et al., 2013). Some other nonprimate species among the whales and dolphins also show behavioral side biases to 90% at the population level (Karenina et al., 2017; MacNeilage, 2014; Rogers, 2009), which indicates that species-level motor biases can evolve independently in species for different reasons (Rogers, 2014; Rogers et al., 2013).

Some authors have also favored hand preference as a proxy for other forms of lateralization due to the well-known overlaps between bilateral anatomical brain areas subserving manual motor functions to those subserving more complex cognitive functions. In living humans, hand preference and other lateralized functions, such as language and visuospatial attention, share anatomical similarities ranging from white-matter pathways (Bernal et al., 2015; Biswal et al., 1995; Figley et al., 2017; Tzourio-Mazoyer, 2016) to cortical area overlaps (Gotts et al., 2013; Guadalupe et al., 2014; Jung-Beeman, 2005; Marzoli et al., 2014; Mayka et al., 2006; Salmelin and Kujala, 2006). Thus, efforts have also been made to explore additional evidence for the evolutionary roots of human lateralization, specifically to assess and compare brain asymmetries between humans and great apes. Although sample sizes are currently smaller than the behavioral work on manual motor biases, as with the hand preference work in apes, some crucial areas—including primary visual and motor cortices, and even language areas like the planum temporale and frontal operculum—show anatomical asymmetries in apes. These asymmetries are often in the same direction as humans, but to a lesser extent both in absolute size disparities and in the number of individuals presenting such asymmetries (Balzeau et al., 2012a; Gomez-Robles et al., 2013; Holloway et al., 2003; Hopkins and Nir, 2010; Sherwood et al., 2003).

Coupled with the broader comparative work, these studies provide evidence that human asymmetries are elaborations of preexisting biases in related taxa, although confirmations of behavioral or anatomical asymmetries do not directly implicate functional similarities (on this, see Striedter, 2002). In summary, laterality itself is not rare in the animal kingdom, but humans' lateralities have evolved to an extreme form which is unique within our primate lineage in both direction and degree. The comparative approaches are certainly of value in understanding the evolutionary context of lateralization, but because we still lack a general consensus on the relationship between hand preferences, anatomical asymmetries, and functional lateralization, we argue that it is hard to characterize when or how *H. sapiens* shifted away from ancestral patterns of laterality, without learning heavily on implied proxies or speculative logic. Despite these limitations, there is broad evidence that the strong right-handed bias, which occurs at the species-level today in humans, has emerged during our evolution, in the course of the last 7 million years. To understand why right-hand predominance evolved in our lineage, the timing of its emergence can give us clues as to the evolutionary conditions surrounding it. It is our view that this information can also provide some insight into the evolution of other human lateralities.

1.2 EVOLUTION OF LATERALITY AND COGNITION

To track the evolution of lateralized motor biases and cognitive functions, we rely on archeological methods to give us a window into the past. Other sources of data, such as genetics, cannot at present resolve the timing of their evolution. The complex genetic underpinnings of human laterality are still being explored (Brandler et al., 2013; Crow, 2002; Faurie and Raymond, 2013; Francks, 2015; Kavaklioglu et al., 2016; Laval et al., 1998; Loffing and Hagemann, 2012; McManus et al., 2013; Paracchini, 2011; Van Agtmael et al., 2001; Versace and Vallortigara, 2015). Recent works have largely refuted isomorphic polygenic theories, which posited that the genes controlling hand preferences would be identical to those controlling other lateralities (McManus, 1985, 1999; McManus and Bryden, 1991), in favor of a “partial pleiotropy” view, which acknowledges that there is *some* overlap between the genes which affect the development of hemispheric asymmetries in the brain and those contributing to hand preference, but it is likely that there are also genes which affect each system independently (Ocklenburg et al., 2014, p. 195). New genetic evidence from large-population studies finds hand preferences are weakly associated with some pathologies like schizophrenia and dyslexia (Brandler and Paracchini, 2014; Francks et al., 2002, 2003, 2007; Giouzeli et al., 2004; Ocklenburg et al., 2014; Priddle and Crow, 2013; Scerri et al., 2011). In our view, these associations are potential indicators that past evolutionary pressures affected specific cognitive skills with tradeoffs, for example that selection for brain laterality created a higher risk of schizophrenia (Crow, 1998). There is a growing literature on the role of the environment with regard to the development of laterality as well, with recent estimates of the heritability of hand preferences as low as 25%, and much higher contributions coming from external factors (Bishop, 2013; Brandler and Paracchini, 2014; Paracchini and Scerri, 2017; Somers et al., 2015). As the results of these large-scale studies show, there has been a general shift from simple models of laterality—whereby the functional specialization of brain and behavior is seen as largely controlled by simple mechanisms—to more complex perspectives.

Inferences of cognitive function in prehistoric species, paleocognition, relies on anatomical evidence of fossil brains to reconstruct the behaviors of past species. To the best of our knowledge, there is currently only one published study of paleocognition in a nonhominin species. Gaetano et al. (2017) used brain shape measurements from endocasts (fossil brain cases) to infer that extinct maniraptors (a common ancestor of birds and nonbird dinosaurs) could have been cognitively equivalent to modern cormorants. Paleocognitive research on hominins is gaining momentum, especially thanks to the advent of paleoneurology (the study of past brain anatomy from fossil endocasts, Bruner, 2014; Holloway, 2014), which has expanded our ability to reconstruct the neuroanatomy of extinct hominins. Paleoneurology and paleocognition have not yet been applied to animal taxa other than maniraptors and hominins. The main challenges in this research arise from preservation, as many fossil cranial bones are fragmentary, distorted, or the surfaces are too worn to reliably identify features. Linking the data with lateralization and cognition is another challenge, as the features that can be measured are limited to those which are large enough to leave imprints on the endocast, such as overall brain size, arteries, vessels, nerves, sinuses, suture closure, sulci, and gyri of the cortex, and the cerebellum (Bruner, 2017; Falk, 2014b). Inferences about cognition thus necessarily occur at the coarse level, drawing on neuroscience data for these features. Laterality, in particular, is relatively easy to identify in complete and partial fossil skulls, based on asymmetries in size and shape between areas on the two halves of the brain, or between the two hemispheres globally (Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015). Below we discuss in more detail the fossil endocast data presented in Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015. Just as fossil endocasts can give us an insight to brain asymmetries and cognitive lateralities, so do fossil bones provide information about bodily asymmetries and behavioral lateralities.

1.3 VARIETY OF LATERALITIES

Currently, the overwhelming majority of prehistoric data on cognition or laterality concern only the hominin lineage, spanning the time period from the presumed evolutionary split with the other great apes around 6–10 mya until the present day. Below we present an overview of these data from paleontology and archeology.

In this chapter, we focus on behavioral lateralities and related anatomical asymmetries in hominins (i.e., humans, our ancestors, and related extinct human-like species such as Neanderthals, *Homo erectus*, Australopithecines, etc.). As highlighted earlier, reliable preservation is a primary factor which determines the sources of data archeologists can consult in tracking the evolution of laterality in the human lineage (Ruck et al., 2015), and in others. Here we review the major threads researchers have followed in order to assess individual and population-level asymmetries through time. Diverse methods have been used on a wide array of paleoarcheological data, and each provides evidence on the context and evolution of lateralization in our species and our ancestors. Direct evidence of behavioral laterality at one moment in time is found in the artifacts made by people using a right-handed or left-handed manual configuration. Anatomical asymmetries found in the skeleton, due to stronger muscle activity of one arm during the lifetime, provide evidence of more consistently lateralized behavior. Asymmetric neuroanatomy in the brain also indicates directional asymmetries, and these are presumably linked with lateralized *behaviors*, although we do not wish to impose a unidirectional or causal relationship between the two.

These directional asymmetries are canalized genetically and/or developmentally (Fagard, 2013), indicating that hominins experienced selective pressures for the resulting lateralized behaviors during their evolution.

To some degree, cognitive laterality (i.e., functional hemispheric specialization) and manual laterality (i.e., hand preference) should also be treated separately. Although previous work suggested that hand preference was linked directly to brain asymmetries in many other domains, this idea has become more and more contentious over time, and it is heavily debated today (Badzakova-Trajkov et al., 2016; Zago et al., 2016). The central component of contemporary debate revolves around a concept which we term colaterality: namely, that the functional lateralization of one modality—such as language or visuospatial skills—is related in some way to the functional lateralization of another—such as hand preference (Cai et al., 2013; Willems et al., 2014). It is important to note that colaterality does not imply causality, nor does it require that colateralized tasks must be located in different hemispheres; for example, right-handedness and language are both largely subserved by the left hemisphere in living humans, but left-hemisphere dominance for language may also be complementary to right-hemisphere dominance for visuospatial skills (see discussion later; Flöel et al., 2005; Oltedal and Hugdahl, 2017; Zago et al., 2016), with each being a form of colaterality. Thus, the concept simply posits that asymmetry for each of these traits is likely not independent of asymmetry for the others. Although colaterality was widely accepted before researchers had the means to rigorously test it, in recent years a fair amount of research has argued against colaterality. These studies show that language, visuospatial skills, and manual motor behavior are all, indeed, lateralized, but mounting evidence suggests that the three lateralize independently of each other, and thus that no one behavior can be used to infer the laterality of another, as we discuss later.

2 EVOLUTION OF LATERALITY: THE DATA

We now turn to the prehistoric evidence for lateralities. Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015 presents the most comprehensive dataset published to date, compiled from numerous sources. We describe the different categories of data available—artifacts, fossilized skeletal materials, fossilized cut-marked teeth, and fossilized brain cases (endocasts). We then discuss the overall patterns in hominin evolution revealed by the data, which show that brain asymmetry and right-handedness increased over time, although data from earlier hominins are too sparse to make any firm conclusions yet. We then briefly describe a few interesting examples that illustrate the significance of laterality in prehistory.

In Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015, we present data for hominin lateralities obtained from the bodies of evidence which we believe are the most reliable, according to critical assessments by ourselves and others (detailed in Cashmore et al., 2008; Faurie et al., 2016; Gowlett and Uomini, 2014; Jöris and Uomini, in press; Ruck, 2014a, b; Ruck et al., 2015; Ruck and Uomini, in press; Steele and Uomini, 2005, 2009; Uomini, 2001, 2008a, b, 2009a, b, c, 2011, 2014; Uomini and Ruck, in press; see Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015 for specifics on the data and their respective references).

The evidence for behavioral and anatomical hemispheric lateralities consists of:

1. the hand preferences determined—using various methods—from stone tool manufacture and use;
2. the proportions of right- and left-hand prints and stencils found on rocks and cave walls;
3. the right or left diagonal striations on fossil teeth;
4. the measured asymmetries in fossil skeletons, specifically in the arms; and
5. the measured asymmetries in endocasts, which are the imprints left by the brain inside fossilized skulls.

Several methods have been devised and tested experimentally for determining hand preferences from individual stone tools (lithics) or individual flakes, which are the small pieces struck off during stone tool-making. These include reconstructions of the grips used while holding a tool for cutting actions, spatial configuration of the scatter of stone flake waste left behind after making the tool (also called knapping) that shows the seated position of the knapper (stone tool maker), traces of use on stone tools showing directional movement by one hand, asymmetric tool shapes caused by use and resharpening by one hand, microscopic features on stone flakes that indicate striking direction of the fracture while knapping (Bargalló and Mosquera, 2014; Dominguez-Ballesteros and Arrizabalaga, 2015), and diagonal marks on bone pieces that were used to resharpen stone tools using one hand configuration (Semenov, 1964). Stone tools and knapping remnants number millions or even billions around the world, and span nearly all of hominin prehistory, which make them the most accessible evidence to investigate hand preferences and handedness. The real challenge is to develop methods that work reliably for the great diversity of tool types in the archeological record, as each new method needs experimental validation before it can be applied to archeological tools. In Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015, we include methods which have been successfully applied to the archeological record, which result in conferred hand preference data and reveal that a few conspicuous left-handers existed among the majority of right-handers for much of human evolution.

Thousands of hand prints and hand stencils made by prehistoric people survive today on cave walls and rock shelters. Our ability to recognize individual cave painters (as opposed to one individual leaving behind many prints) is only just beginning (Nelson et al., 2017), so we currently assess proportions of right- and left-hand stencils to infer a right-handed majority, consistent with the fact that modern-day right-handers tend to press their *left* hand against the wall to make stencils (Faurie and Raymond, 2004). Hand prints are made by pressing a hand—already covered in liquid pigment—onto the rock surface, but they are relatively rare. Hand stencils are by far more frequent; they are made by the more involved method of placing the hand palm-down onto the rock surface and dabbing or spraying liquid pigment around it, leaving a "negative hand" behind. Dabbing can be done with animal fur or soft leather, and spraying can be done directly from the mouth, or blowing through an arrangement of two tubes in a container of liquid pigment (Uomini, 2009a). The data cover numerous single sites and multisite surveys, showing a universal pattern of high proportions of left-hand stencils, consistent with a right-handed majority among the prehistoric artists (Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015 and references therein).

Some fossil teeth show characteristic diagonal striations that were caused by cultural practices for using the teeth as a "third hand," such as processing leather, plants, or meat (Bruner and Lozano, 2014; Lozano et al., 2008; Uomini, 2008a, 2011). The only documented ethnographic parallels to such behaviors are found in the practice of eating meat by gripping strips of meat in the front teeth and slicing off bite-sized pieces with a knife—or in the case of hominins, a sharp stone flake (examples from around the world are detailed in Uomini, 2008a, 2011). Although nobody has yet studied the teeth of living humans who practice this meat-cutting activity in order to verify the correlation of hand preference to dental striation direction, experiments with simulated Neanderthal teeth confirmed that right-handed and left-handed meat cutting with stone leaves distinct diagonal marks, whose angles and features can be measured under microscopes (Bermúdez de Castro et al., 1988). All available data from hominins, collected in Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015, show that right-handedness comprises the majority of the surveyed individuals, but that some hominins have clear left-handed marks, or a combination of right- and left-oriented striations suggestive of mixed-handedness.

Directional asymmetries in arm bones—in contrast to fluctuating asymmetry, which is caused by developmental stress—relate to regular, unequal biomechanical loading of the muscles in both arms during use. As exemplary cases, athletes who play asymmetric sports like tennis or baseball commonly have a stronger dominant arm and a lesser range of motion in the joints of the nondominant limb (Ellenbecker, 2016; Hagemann et al., 2016), and these differences manifest themselves in the size and robusticity of their arm bones. Directional asymmetry of this form is generally detectable in individuals beyond athletes as well, and the data gathered in Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015 show that hominins generally had strong side biases, showing they habitually performed strenuous asymmetrical activities during their hunter–gatherer daily lives (Shaw and Stock, 2013). Although the lack of clearly paired long bones limits sample sizes for this method, the current data suggest that right-handers were more frequent, but also that some left-handers did exist.

Brain asymmetries occur in several areas and can be assessed with several different measurement methods. Some of these anatomical asymmetries are shared with other apes, but are the most extreme in modern humans relative to other apes, which again shows that the evolution of our species is characteristic of our biological, cultural, environmental, and/or epigenetic heritage, while at the same time highlighting features particular to hominins (Balzeau et al., 2012a; Bruner, 2017; Falk, 2014a, b). Relevant to paleoanthropology are the brain asymmetries, which (1) can be seen in the skull and (2) are related to hand preferences. These asymmetries can be reliably measured in fossil endocasts (Fournier et al., 2011). We focus here on the well-known frontal–occipital petalias, although parietal and temporal petalias are also documented and merit more attention in future research (Kitchell, 2015). Petalias are defined as the protrusion of one hemisphere relative to the other, such as forward (in the frontal lobe) or backward (in the occipital lobe), as related to greater size, greater surface area, or brain torque (Balzeau et al., 2012b). Hand preference is probably correlated with petalia asymmetries. While several studies showed that statistically, right-handed individuals are more likely to have right-frontal and/or left-occipital (RF+LO) petalias and left-handers are more likely to have the opposite petalias (LF+RO) or to have a brain tending toward symmetry (Balzeau et al., 2012a; Galaburda et al., 1978; Kertesz et al., 1990; Kitchell and Schoenemann, 2014; LeMay, 1977; Ruck and Schoenemann, 2018), some other studies failed to find a correlation (Good et al., 2001; Herve et al., 2006). However, it is clear that the RF+LO petalia pattern is unique to humans (Balzeau et al., 2012a; Li et al., 2018; Zollikofer and Ponce de León, 2013); thus the interesting question here is when it emerged in the hominin lineage. Although different measurement methods have been used by researchers, Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015 shows that in most cases, the endocast classifications from different studies are in agreement. We indicate the few instances when different researchers have found conflicting results. The data show that the right-handed petalial pattern (RF+LO) was common among hominins, but that all of the other possible petalia combinations also occurred.

2.1 INTEGRATING MULTIPLE LINES OF EVIDENCE

In Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015, we combine the data from these four categories of evidence, so we can see how they correlate in individuals with more than one type of data. In fact, there are 18 individual hominins with two categories of evidence for hand preference or other forms of laterality. Although these cases would ideally be used to corroborate multiple methods (insofar as multiple assessments of laterality in living individuals, from experimental or comparative work, should result in nonconflicting classifications), the current data are not auspicious. Unfortunately, the data from the two early hominins (OH 16 and OH 7, both from around 1.7 mya) did not yield clearly lateralized results. Out of the eight pre-Neanderthal and *Homo heidelbergensis* specimens (all dated between 200 and 500 kya), three show conflicting results, suggesting potential mixed-handers. Among the eight Neanderthals (dated between 40 and 122 kya), all show data consistent with right-handedness except the adult male Spy 1, who has a left-occipital petalia consistent with right-handedness, but symmetrical arm bones, suggesting he was possibly mixed-handed. No fossils have all four categories of evidence documented, but one individual has three. The adult

Neanderthal of unknown sex, La Quina H5, has two teeth with diagonal right-handed striations and a stronger right arm, although the arm asymmetry might be pathological, and it has a slight left-occipital petalia suggestive of left-handedness, being noted as either symmetrical or slightly rightward by different researchers. Thus, the humeri and endocast data are uncertain and potentially not-right-handed, while the teeth indicate a right-handed use; this individual we have marked as tentatively mixed-handed. As discussed earlier, fossil endocrania are rarely perfectly preserved, but it is possible to reliably measure petalias in many incomplete skulls; in Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015, we include specimens for which there are attributed endocast petalias.

We would like to point out some notable left-handers in our dataset. In prehistoric humans, many left-handed individuals showed a clear left-hand preference already as children. Thus, individual hand preferences were established by adolescence in hominins (Jöris and Uomini, in press), much as they are in living humans today. The data in Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015 show that, for example, two Neanderthal individuals at Krapina who died at age 10 and 15 years old were left-handed, and the left-handed Vergisson 4 Neanderthal was 7–9 years old when it died. The pre-Neanderthal female Atapuerca Sima de los Huesos X died at 15–17 years old and was possibly mixed-handed, as she had tooth striations in all orientations. Finally, the Indonesian *H. erectus* individual Sambungmacan 3, who was not quite adult at death, had left-frontal and right-occipital brain petalias, suggesting it was left-handed. Were left-handers more frequent among the individuals who died younger? Many of the fossils showing left-handedness or mixed-handedness were of unknown age at death. For instance, two *H. erectus* individuals from Zhoukoudian had left-frontal and right-occipital brain petalias. We note the adult male Shanidar 1, who died at 40–50 years old with severe trauma and disease on his skeleton; he most likely was obliged to use his left hand long enough to cause right-arm atrophy and a stronger left humerus. The adult female Liang Bua LB1 was about 30 years old at death and shows pronounced left-frontal and right-occipital brain petalias, making her possibly also left-handed. Still, the fossil record is full of right-handed children who also died young, such as at Atapuerca Sima de los Huesos, El Sidrón, and Krapina. Thus, hominins generally lived dangerous lives, and the present data (Table S1 in the online version at https://doi.org/10.1016/bs.pbr.2018.06.015 and references therein) cannot tell us whether being left-handed might have contributed to their young mortality.

3 COLATERALITY: IS HANDEDNESS A VALUABLE PROXY?

As the data presented earlier make clear, behavioral and anatomical laterality were key features of motor-cognitive development in extinct human ancestors. However, further research in living humans is still needed: the extent of colateralization of functions in the human brain is still unresolved, so we must advise caution when inferring functional cognitive laterality from behavioral markers of hand preference.

Although much is now known about hemispheric specialization for language, hand preference, and visuospatial skills, there is still very little consensus on whether, or how, functional laterality in one modality may interact with asymmetries for other tasks in living humans—and even less in other species (for a review, see Badzakova-Trajkov et al., 2016). We now turn to this topic, as we believe it is a major issue for future works toward understanding the evolution of such lateralities. We present an overview of both sides of the colaterality debate, beginning with a description of the original large-sample studies, which urged caution with regard to colaterality. We then present studies on both visuospatial skills and language laterality, which *are* compatible with the concept of colaterality, considering open questions and future directions with regard to this debate.

3.1 LARGE-SAMPLE STUDIES ON HEMISPHERIC LATERALIZATION AND HAND PREFERENCE

It has long been known that a stark majority of right-handers—about 95%—show left-hemisphere dominance for language processing in the brain; from the initial scientific inquiries on aphasia and apraxia, to split-brain studies in the late 1900s, to newer lines of enquiry enabled by the explosion of technology and neuroimaging methods, many researchers supported the use of hand preference as a proxy for other lateralities, most notably language (Broca, 2011a [1861], 2011b [1865]; Gazzaniga, 2000, 2005; Geschwind and Galaburda, 1987; Springer and Deutsch, 1985, 1998). However, early probes of hemispheric dominance for language in left-handers (using various brain imaging techniques like the Wada test, positron-emission tomography (PET) scans, functional transcranial Doppler sonography (fTCD) measures, functional magnetic resonance imaging (fMRI), and most recently, functional near-infrared spectroscopy (fNIRS)) showed that many left-handers—between 70% and 85%—were *also* left-lateralized for language, as opposed to being right-hemisphere dominant (Flöel et al., 2005; Knecht et al., 2000; Paquette et al., 2015; Tzourio et al., 1998; Tzourio-Mazoyer and Courtin, 2013). As this finding was a direct challenge to the expected relationship between hand preference and language dominance, subsequent studies sought to identify and characterize left-handers with typical language dominance in contrast to left-handers with atypical language dominance.

Knecht et al. (2000) made an early large-sample study using fTCD on the cued word generation task in 326 participants, who were classed into six hand preference categories and familial sinistrality scores. They found a linear relationship between left-handedness and atypical, or right-hemisphere, language dominance, as well as an effect of familial sinistrality. Only 4% of right-handers showed atypical language dominance, with 15% of mixed-handers showing atypical dominance, and 23% of left-handers showing right-hemisphere dominance for language. The authors conclude that: “degree of handedness is linearly and highly significantly related to the side of language dominance… [but that the complexity of their results suggest that] handedness and language dominance are each determined by multiple factors, some of which have a role in both phenomena” (Knecht et al., 2000, p. 2517).

As McManus et al. (2013) point out, inherited hand preferences involve at least 40 genetic loci; thus it is most likely that the other lateralities also involve similarly complex genetics.

Similar subsequent approaches highlight a few major advances in the study of colateralization, including a shift toward treating hand preference as a categorical, rather than binary variable, and the rise of "degree vs direction" discussions in the literature; assessing effects of familial sinistrality (presence of left-handers in the nuclear family); and including study samples enriched in left-handers in general (Willems et al., 2014). This body of work confirmed that the *degree* of left-handedness characterized language lateralization better than binary classifications; and also that familial sinistrality played a small, but often significant role in explaining rightward shifts of hemispheric specialization for language (in both right-handers and left-handers). Despite these advances, an isomorphic relationship between hand preference and language laterality was still lacking, as additional investigations showed little-to-no improvements from using *degrees* of laterality, as opposed to binary classes.

In the past 5 years, several large-sample analyses of hemispheric specialization and colaterality have been published, many coming from the Brain Imaging of Lateralization by the Groupe d'Imagerie Neurofonctionnelle (henceforth BIL&GIN) database of brain and behavioral laterality, containing a battery of tests on over 450 participants enriched in left-handers ($n = 199$ using self-reports; see Mazoyer et al., 2016). In addition to self-reporting hand preference and familial sinistrality, participants completed the Edinburgh Handedness Inventory (henceforth the EHI, Oldfield, 1971), and a behavioral measure of hand preference by finger tapping (FT) (Mazoyer et al., 2016). We will review these works in some detail below, but it is important to note that hand preference classifications for subjects in these large-scale studies comes from a single, survey-based metric for assessing hand preference. As we will argue below, the claim for *independence* between hand preference and language laterality is underpinned almost entirely by publications with this methodological limitation.

Zago et al. (2016) used the BIL&GIN database to explicitly probe the relationship between laterality for visuospatial cognition with that of language processing. This paper includes a good review of the competing hypotheses regarding colaterality:

H1. The relationship between language laterality and visuospatial laterality is *causal*—i.e., the hemispheric specialization in one modality forces the other task to occupy the other hemisphere (essentially a "crowding" hypothesis; see Bryden et al., 1993; Flöel et al., 2005).

H2. These systems are independent—i.e., the typical left-language/right-visual lateralization pattern is common by chance. On this view, all of the other possible combinations of language/visuospatial hemispheric specializations exist (both in left hemisphere; both in right hemisphere; and right language/left-visual), but in smaller proportions, for an unknown reason (see Flöel et al., 2005).

Zago et al. (2016) showed that the *degree* of rightward lateralization for a visual task corresponded to performance on the line bisection task, with right- and left-handers both showing the well-known “pseudoneglect effect” (i.e., left-biased failures), and persons who were more-lateralized performed better overall. However, the degree of laterality in one domain was correlated to the degree of laterality in the other *only* in strong left-handers. In other words, as visual processing shifted more to the right, language processing shifted more to the left, but only for participants with EHI scores below −55. Thus, we argue that these data support our proposal that different hand preference groups (left-handers and right-handers, or weak- and strong-handers) may simply have different systems governing colaterality.

Somers et al. (2015) conducted a cued word generation fTCD study on 310 participants (166 left-handers) divided into five hand preference groups—strong right-handers, right-handers, mixed-handers, left-handers, and strong left-handers—based on EHI scores. Although their data support the idea that nondirectional *variability* in hemispheric specialization for language increases as left-handedness does, they did not find a mirror relationship with regard to direction. We contend that their results raise the possibility of multiple systems (i.e., modeling one system for left-handers and another for right-handers). Following this general schematic, others have argued similar thoughts against the handedness-as-a-proxy concept (Allendorfer et al., 2016; Corballis and Häberling, 2017; Häberling et al., 2016).

Arguing in support of the causal model for hemispheric colaterality, Badzakova-Trajkov et al. (2010) conducted an fMRI study on 155 participants enriched in both left-handers ($n=48$) and monozygotic twin pairs ($n=94$). Using covert word generation, a line bisection task, and a task involving recognizing repeated face stimuli, the team sought to assess colaterality, in much the same manner as the BIL&GIN studies. As with the early studies, despite the use of a relatively balanced sample, overall leftward asymmetry was found for the language task, with overall rightward asymmetry for both the landmark and the faces tasks (i.e., left-handers did not show mirrored patterns of functional laterality). In terms of degrees of laterality, language lateralization was higher in right-handers, with a significant effect of gender (males more lateralized; no effect for twins). For the faces task, right-handers were also more lateralized, but no significant differences were found in lateralization between hand preference groups for the landmark task. In a subsequent paper (Badzakova-Trajkov et al., 2016), the team reviews genetic, developmental, and neuroimaging studies on human lateralization and, in reversal of their earlier (2010) views, they largely favor the statistical independence hypothesis (that laterality in one domain is independent of laterality in another). Perhaps based on their earlier findings, however, they at least acknowledge that the true scenario is likely a mix of both causal and statistical factors; on this they state: “…causality [indicated by language and visuospatial tasks co-lateralizing to opposite hemispheres] is most likely in individuals lacking the innate disposition to asymmetry… paradoxically, then, causality may be restricted precisely to those lacking innate predispositions” (Badzakova-Trajkov et al., 2016, p. 391). This view is compatible with our suggestion that multiple systems could be governing colaterality, although teasing these systems apart would be difficult, if not impossible, using the approaches outlined earlier. We think the "different systems" concept should be the target of future investigations.

To the best of our knowledge, only a few studies have been conducted directly comparing survey-based hand preference classifications with actual performance measures of hand preference (Brown et al., 2004, 2006; Bryden et al., 2011; Corey et al., 2001; Gonzalez et al., 2007). In contrast to these previous approaches, Gonzalez and Goodale (2009) assessed correspondence between the EHI and hand-performance using more naturalistic tasks—a puzzle task and LEGO-building—in 20 subjects. They filmed subjects' hand movements and created laterality indices (LIs) for how often subjects used each hand, and compared these data to EHI scores. They showed high correspondence between the LEGO and puzzle tasks for all subjects, but these data did *not* match well with the EHI scores, especially for left-handers. Although all 10 left-handers in the sample were classed as strongly left-handed by the EHI, at least half of them used their right hand more frequently than their left in the behavioral task (Gonzalez et al., 2007, p. 277). In a later study probing language laterality with a dichotic listening task, the authors assessed correlations between the EHI scores, grip strength (GS), FT, and the LEGO task in 36 subjects (Gonzalez and Goodale, 2009). They found that the LEGO task measures were the only ones significantly correlated with the dichotic listening task. Although there was significant correspondence between the EHI, GS scores, and FT scores, these measures did not correlate with language laterality. The authors suggest that, in their sample, "there is something about visuomotor control and handedness that does not map onto other measures of laterality in motor control" such as the EHI and more common behavioral tasks (Gonzalez and Goodale, 2009, p. 3187). These studies provide initial evidence that left-handers are not left-handed in the way that right-handers are right-handed in their manual motor behaviors. An important distinction follows from this fact, in that perhaps we should not expect left-handers to be lateralized in their hemispheric activation patterns in the way that right-handers are, and thus, that task-based laterality systems for right-handers and left-handers may need to be considered more thoroughly.

The concept of colaterality is a basic hypothesis that the lateralization of one modality has an effect on the lateralization of another. However, many published studies suffer from various methodological flaws, with the most salient being the use of the EHI as a sole hand preference metric, but they also fail to allow for different forms of colaterality to exist in left-handers and right-handers (i.e., they do not acknowledge that left-handers, and even mixed-handers, should not be modeled as atypical right-handers, but instead should be assessed in their own right). As for *how* or *why* different hand preference groups would have different systems governing language (and visuospatial laterality), there are many possible explanations already present in the evolutionary anthropology and paleoarcheology literature (we will briefly speculate on this in our conclusions). Next we discuss very recent works on hand preference modulation of visual perception, and then briefly relate this to potential applications for studying language.

3.2 CONTEXTUALIZING COLATERALITY: ADDITIONAL EVIDENCE

Marzoli et al. (2014) argued that perception–action studies on the relationship between leftward visual biases and right-hand preferences are largely unacknowledged in the laterality literature, and thus, that there are many opportunities for future collaborative studies. These authors note that the early onset of left-biased visual attention to faces and bodies—of which there is much solid evidence (Nagel et al., 2013), and which may stem from both genetic and environmental factors (Cochet, 2016)—may be related to right-hand predominance in human populations. Important here is that preferential attention to the left visual field in dyadic social interactions equates to biased attention to the actions of the right hand (Verfaellie and Heilman, 1990), which could then lead to social modulation of one's *own* manual motor biases toward the right hand (although modeling causality in such a system would be quite fruitless, particularly in archeological contexts as described earlier, as it is much more likely for the two to be interacting dynamically and continuously). In general, the perception–action literature suggests that early visual perception biases can potentially modulate and enable the development of action asymmetries toward the right hand later in life, although this link needs to be confirmed with longitudinal developmental studies (Buckingham and Carey, 2015), and that hand preference plays a key role in modulating visual attention. Several researchers have found that hand location directly impacts spatial attention and reasoning, and vice versa, such that visual attention biases might determine our patterns of space use for grasping. Generally, there is a complex and reinforcing behavioral relationship between the two behaviors (Abrams and Weidler, 2014; Adam et al., 2012; Cai et al., 2013; Colman et al., 2017; Craddock and Lawson, 2009; de Bruin et al., 2014; Gingras and Braun, 2017; Lawson et al., 2016; Reed et al., 2006, 2010; Stone and Gonzalez, 2014; Thomas, 2015; Uomini and Lawson, 2017). The concept is nicely summed up by the following statement: "the origin of the rightward hemispheric dominance for spatial attention may have a manipulospatial origin, neither perceptual nor motor *per se*, but rather reflecting a mechanism by which a spatial context is mapped onto the perceptual and motor activities, including the exploration of the spatial environment with eyes and hands" (Petit et al., 2015, p. 1151).

The research on praxis and visuospatial asymmetries inherently adopts an affordance-based view of perception–action, and as we have argued elsewhere, embodiment is the only view of cognition which is compatible with evolutionary theory (Ruck, 2014a, b), and so many of the aspects of the perceptuo-motor research can be easily incorporated into evolutionary discourse. The main concept underpinning the colaterality hypothesis is that the areal and asymmetrical similarities for different modalities—despite being complex and difficult to characterize—are likely not independent of each other, because hand preference, visuospatial skills, and language all interact "online" in the real world every day. In order to tie this finding back to hand preference, and to provide further support for seriously considering multiple systems of colateralization, we close with an fMRI study on functional asymmetry. Gotts et al. (2013) used a short resting-state fMRI paradigm to probe intrinsic levels of intra- and interhemispheric connectivity for the right and left brain hemispheres in 62 right-handed participants. They have several ideas which we adopt here in our own conclusion, although their timescale is more developmental, whereas ours considers evolutionary perspectives. Their conclusions are:

1. The left hemisphere shows greater preference for within-hemisphere interactions; this is likely a consequence of white-matter asymmetries present before birth, as measured near birth (Perani et al., 2011), but it is also undoubtedly related to strong right-handed bias and language functions.
2. The right hemisphere, in contrast, has interactions that are strongly bilateral; this both stems from, and underpins, the bilateral nature of visual perception, and the lack of mirror asymmetry between language and visuospatial networks.
3. The findings of improved cognitive performance in more lateralized participants are consistent with the computational efficiency model for hemispheric specialization.
4. In spite of high individual variability in patterns of connectivity, caused both by developmental considerations and plasticity, an overall pattern of lateralization for cognitive tasks can be found in salient task-positive networks, even using resting state data; this has implications for future comparative work.

4 DISCUSSION

Following each of these points, we will conclude by outlining a basic hypothesis for the evolution of human-specific laterality biases, and set a framework for future works which might help further elucidate colaterality. Based on all that we have discussed in this chapter, we hypothesize a model for the evolution of uniquely human lateral biases:

1. Hemispheric specialization has deep roots in vertebrate taxa, and based on existing primate research, it is plausible that early hominin ancestors inherited systems of preexisting lateral biases for vision, praxis, and communication; these systems became elaborated over time in the hominin lineage.
2. Hemispheric specializations have multifactored genetic underpinnings, but downstream effects of developmental biases and epigenetics may have even stronger effects than genetic factors in driving *directional biases*, and multiple systems may be operating in left- and right-handers today (Schmitz et al., 2017; Vallortigara and Rogers, 2005).
3. One especially critical factor in driving the *typical* directional shifts may be the increasing complexity of manual motor actions, including visually guided bimanual coordinative ones, such as tool-use and tool-making, in hominins (as proposed by Bradshaw and Nettleton, 1982; Uomini, 2009b, c; Tabiowo and Forrester, 2013). On this:

   - **a.** It seems that preexisting visual biases, underpinned by differential hemispheric integration/segregation systems, would have more easily enabled right-hand precision and left-hand support roles, at least on an individual level.
   - **b.** These individual hand preferences (which were, again, being increasingly driven to the right, simply via interactions between preexisting asymmetries and higher task complexity) *then* coupled with increased reliance on social learning in hominins (Högberg et al., 2015; Morgan et al., 2015; Uomini and Lawson, 2017), which (via developmental routes) drove populations' hand preferences even more rightward.
   - **c.** Once a right-handed majority was established, a frequency-dependent selection of the left-handed minority was reinforced and maintained by selective advantages linked to close combat and/or interactive contests (Faurie and Raymond, 2005, 2013; Loffing and Hagemann, 2012), which we can speculate occurred as hominin groups encountered each other in competitive territorial situations.

4. As brain size increased, these once-modest patterns of asymmetry grew exponentially in their complexity (as there is a nonlinear relationship between brain size increases and anatomical–functional changes in the brain, Herculano-Houzel, 2009).

Of course, each of these steps would not have proceeded linearly, but instead in a much more nuanced way, feeding backward and forward in a dynamic fashion. As this is just a speculative sketch, many relevant factors are missing in the earlier outline; most notably is the absence of an explanation for atypical laterality patterns, which is not isomorphic with, but is no doubt related to, the persistence of left-handers. However, until more comprehensive work is conducted to pin down the forms and nature of colaterality, our proposed outline remains an open possibility.

In conclusion, multiple incredibly rich lines of evidence suggest that hand preference, visuospatial skills, and language should be related to each other, but there are more open questions than answers. Much more pragmatic work needs to be conducted on even the most fundamental aspects of colaterality, including a more careful consideration of experimental methods. On this, we recommend to focus on a few easy targets. First is to further probe the efficacy of the EHI in characterizing actual manual behaviors, including communicative gestures, developmental trajectories for the formation of hand biases (see Fagard, 2013), and to continue testing right- and left-handers. Second is to cleverly use the data from current large-sample studies—which unfortunately have the EHI (and other simple hand preference metrics) as their only hand preference measures—because even with their hand preference measure potentially confounded by the EHI, they *can* provide higher frequencies of atypically lateralized persons for language and visuospatial skills, as well as cognitive performance data, and other measures. Additional data from studies like Cai et al. (2013), Pool et al. (2014), and Gotts et al. (2013) can be mined to further probe the disparities regarding colaterality without needing to collect new data. Finally, dependent on replication results for the aforementioned studies—and, of course, continued discoveries from comparative, genetic, and developmental research—we can add hand preferences back into the picture, using more rich, dynamic, and naturalistic tasks, should it seem necessary down the line to do so. As Rogers (2014, p. 566) noted: "it is timely for a more integrated approach to the study of lateralization"; we think these are the best steps forward towards this goal.

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Cognitive archeology, body cognition, and hand–tool interaction

12

Emiliano Bruner[*,1], **Annapaola Fedato**[*], **María Silva-Gago**[*],
Rodrigo Alonso-Alcalde[†], **Marcos Terradillos-Bernal**[‡],
María Ángeles Fernández-Durantes[§], **Elena Martín-Guerra**[§]
[*]*Centro Nacional de Investigación sobre la Evolución Humana, Burgos, Spain*
[†]*Museo de la Evolución Humana, Burgos, Spain*
[‡]*Universidad Internacional Isabel I de Castilla, Burgos, Spain*
[§]*Sociograph Marketing Science Consulting, Valladolid, Spain*
[1]*Corresponding author: Tel.: +34-947-040-800; Fax: +34-947-040-810,*
e-mail address: emiliano.bruner@cenieh.es

Abstract

Body cognition and lateralization can be investigated in fossils by integrating anatomical and functional aspects. Paleoneurology cannot provide strong evidence in this sense, because hemispheric asymmetries are shared in all extinct human species, and motor cortical areas are difficult to delineate in endocranial casts. However, paleoneurological analyses also suggest that modern humans and Neanderthals underwent an expansion of parietal regions crucial for visuospatial integration and eye–hand–tool management. Because of our technological specialization, haptic cognition can be particularly targeted by evolutionary processes. Hand–tool relationships can be investigated through physical and physiological correlates. In terms of metrics, size is the main factor of hand morphological variation among adult humans, followed by the ratio between thumb length and palmar size. In modern humans, emotional changes during hand–tool contact can be measured by electrodermal activity. During tool manipulation, electrodermal response, which is a physiological correlate of emotional engagement, shows differences between males and females, and it is different for distinct Paleolithic technologies. Emotional engagement, hand management, and haptic cognition are part of a specialized prosthetic technological capacity of modern humans and can provide indirect evidence of cognitive discontinuities in the archeological record.

Keywords

Endocranial asymmetry, Paleoneurology, Parietal cortex, Visuospatial integration, Hand morphology, Haptic cognition, Electrodermal activity

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1 PALEONEUROLOGY AND ENDOCRANIAL ASYMMETRIES

Brain and behavioral asymmetries are hallmarks of our species and, accordingly, they have received considerable attention in cognitive science. There have been plenty of reviews investigating this topic in living humans, nonhuman primates, and even fossil human species (e.g., Cashmore et al., 2008; Lozano et al., 2017; Uomini, 2009). Of course, behavioral asymmetries are thought to be a consequence of brain asymmetries, and this is why this issue is of interest in evolutionary neuroscience, particularly when dealing with language (Rilling, 2013, 2014). Taking into consideration that fossils provide the only direct anatomical evidence of species evolution, paleoneurologists have always been interested in hemispheric asymmetries (e.g., Balzeau et al., 2012; Holloway, 1980, 1981). In paleoneurology, brain morphology is inferred by the anatomy of the endocranial cavity, which supplies information on brain size, brain proportions, some sulcal patterns, vascular traits, and cerebral spatial relationships (Bruner, 2017; Holloway et al., 2004). In terms of gross morphology, in modern humans, the frontal cortex is larger on the right side, while the occipital cortex is larger on the left side (Li et al., 2018). Such a pattern generates a "torque" of the brain axis, which is generally called right-frontal left-occipital petalia. This same pattern can also be found in apes, although it is less frequent and less pronounced (Holloway and De La Costelareymondie, 1982). However, brain size is much larger in humans, and there are no extant primates with an intermediate brain volume. Therefore, at present we cannot exclude that the torque and asymmetry displayed by our brain is a scaled version of the same pattern expressed, to a lesser extent, by other primates (Gómez-Robles et al., 2013; Kyriacou and Bruner, 2011). Extinct human species apparently show our same asymmetry pattern (Balzeau et al., 2012), and hence paleoneurology cannot provide any clear information on this topic, at least when investigating evolutionary changes within the human lineage.

Apart from this general background, there are several problems that hamper a reliable approach on hemispheric asymmetries when dealing with fossils. First, asymmetric cortical traits can present large individual (intraspecific) variation and subtle evolutionary (interspecific) differences. Therefore, among the species of the genus *Homo*, any possible mean difference in endocranial asymmetry is easily obscured by the large individual variability. Accordingly, gross volumetric asymmetries could only be investigated through very large samples, in order to guarantee proper statistical power. Of course, this limitation is hardly constrained to paleoanthropology. A second limit concerns the biological meaning of these morphological traits. We estimate asymmetries through volumetric figures and sulcal schemes, but to date the relationships between these macroscopic features and functional or histological factors are scarcely known. Furthermore, for many aspects, we still ignore the degree and patterns of cortical variability in our own species. Any inference on extinct taxa will be seriously affected by such a vast lack of information. A third limit regards the functional matrix associated with the brain and skull growth and development. Brain and braincase are reciprocally integrated in terms of ontogeny and phylogeny, through complex functional and structural relationships between soft and hard tissues (Bruner, 2015; Moss and Young, 1960). Such integration is generally local and driven by physical and spatial interaction between anatomical elements. A complex system of pressures and tensions is generated during morphogenesis, and the final phenotypic and evolutionary output is a balanced result between distinct anatomical influences. Apart from the histological components behind volumetric asymmetries, we currently ignore their general biomechanical and morphogenetic background. In fact, differences in the general volume of two counterlateral regions can be due to a difference in the brain growth force, or to a difference in cranial resistance. Paradoxically, the increase in the surface of a specific lobe can result from a major pressure exerted by its counterlateral hemisphere. Often the falx cerebri, which separates the two hemispheres and attaches the brain to the vault, displays a curved trajectory, evidencing a spatial conflict between the two sides. This differential distribution of the brain mass can also influence sulcal patterns and their degree of expression (Tallinen et al., 2016; Toro, 2012). For example, the frontal and parietal volumes are often larger on the right side, while their gyri (forming the Broca's and Wernicke's area) are most clearly shaped on the left side (see Holloway et al., 2004). Any inference on gross brain asymmetries will be partial and incomplete (and possibly biased) with no information regarding the processes behind this biomechanical redistribution of cortical tissues.

This situation is even more complicated if we deal strictly with the motor cortex. Sulcal morphology and cortical regions in paleoneurology are generally identified by localizing possible traces of the folding elements (bosses and grooves) and by positioning different elements so as to constrain the position of the others (Bruner, 2018a). At present, no reliable methods have been proposed to identify the boundaries of the sensory-motor cortex in fossils. Central, postcentral, and precentral sulci can be tentatively identified on endocranial casts, but the uncertainty is noticeable, and differences among distinct human species were probably subtle, if any. In contrast, there is paleoneurological evidence suggesting specific and localized differences for areas of the posterior parietal cortex involved in the cognitive integration of the body elements, crucial for visuospatial associative functions (Bruner, 2018b).

2 PARIETAL LOBES AND VISUOSPATIAL EVOLUTION

Modern humans have long been said to have "rounded heads" when compared with extinct human species. It turns out that such globularity of the braincase is mainly due to the size and curvature of the parietal bones (Bruner et al., 2004, 2011a). Although the correspondence between brain and cranial elements is not firm and constant, expanded parietal bones in our species are apparently due to an actual expansion of the parietal lobes, probably of their dorsal regions (Bruner, 2010;

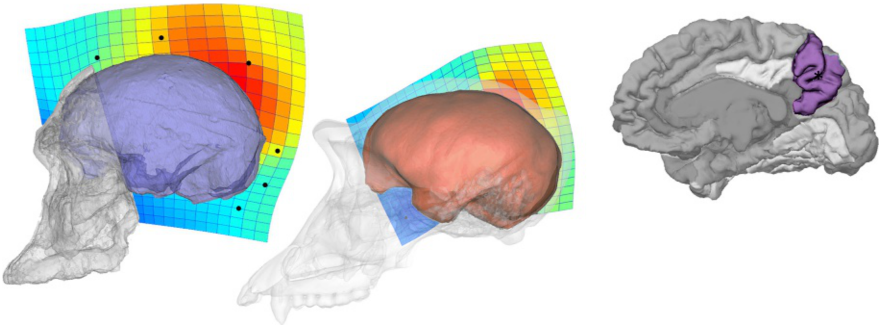

FIG. 1

Compared with extinct hominids (on the *left*, a digital reconstruction of skull and endocast of an *Australopithecus*), modern humans display larger and bulging parietal bones and lobes. Compared with chimpanzees (*middle*), we have a larger parietal cortex because of a larger precuneus (*right*). The same area is also extremely variable among adult individuals.

Bruner et al., 2003, 2018a). Also Neanderthals display wider superior parietal lobules when compared with more archaic hominids, but only modern humans show a general enlargement of the whole dorsal cortex, with an increase in the longitudinal extension of the upper parietal areas (Fig. 1). In this region, morphogenesis is rather linear, with the bone shaped by cortical pressure (Moss and Young, 1960). Therefore, an association between bone and lobe form and size is to be expected. In terms of spatial correspondence, the sagittal region involved in these changes roughly matches the precuneus and the superior parietal lobule, and the lateral region matches the position of the intraparietal sulcus (Pereira-Pedro and Bruner, 2016). The intraparietal sulcus is more complex (and possibly even expanded externally) in humans than in other primates, and it is particularly involved in eye–hand integration, handedness, and tool manipulation (Grefkes and Fink, 2005; Martin et al., 2011; Stout et al., 2015; Tunik et al., 2007; Verhagen et al., 2012). It is hence not by chance that the endocranial surface corresponding to this region underwent a visible enlargement in the two human species (*Homo sapiens* and *Homo neanderthalensis*) that have evolved complex tools and technology. Precuneus is involved in body–vision integration, egocentric spatial coordinates, visual imaging and simulation, and memory retrieval (Cavanna and Trimble, 2006; Freton et al., 2014; Margulies et al., 2009; Zhang and Li, 2012). All these functions are central also for visual representations and imagination, and for integration between physical, chronological, and social spaces (Hills et al., 2015; Land, 2014; Maister et al., 2015; Peer et al., 2015). It is therefore interesting that this cortical element could have undergone a marked expansion in the only species (*H. sapiens*) associated with a remarkable visual and symbolic culture, and with a unique social and technological development. The precuneus is extremely variable among adult humans (Bruner et al., 2014, 2015) and much larger in humans than in chimpanzees (Bruner et al., 2017). Because of its role in visual imaging and simulation, the phylogenetic differences, and spatial correspondence, a specialization of its morphology and role in modern humans is likely (Bruner, 2018b). Interestingly, early modern humans (about 150–300,000 years ago) apparently did not display such morphological changes in the parietal region, suggesting that the origin of modern humans did not match the origin of a modern brain form (Bruner and Pearson, 2013). It is likely that parietal morphology underwent a following and gradual change in later *H. sapiens*, achieving a modern appearance 50–100,000 years ago, roughly at the same time we can find a relevant visual culture in the archeological record (Bruner et al., 2018a; Neubauer et al., 2018).

Parietal cortex is largely involved in body perception and representation (Daprati et al., 2010), namely, processes that intimately combine the sense of the body with self-awareness and action (Borghi and Cimatti, 2010; Gallese and Sinigaglia, 2010). These cognitive mechanisms bridge body perception (an admixture of egocentric, exteroceptive, and interoceptive feedbacks) with psychological and emotional responses (Longo et al., 2010). Accordingly, we can broadly define *body cognition* as those cognitive processes that rely and depend upon the experience, sensing, feedback, and recognition of the own body. Body cognition and visual imaging are essential for a technological species like *H. sapiens*, taking into account that they are crucially involved in tool making, hand–tool management, and symbolic communication. Most of the functions involved in body–environment management are generally labeled as *visuospatial integration* and deal with the capacity of coordinating a *personal space* (the body) with a *peripersonal space* (external reachable elements close to the body) within an *extrapersonal space* (the surrounding environment, out of the body range) (Cléry et al., 2015; Farnè et al., 2005; Maravita and Iriki, 2004; Maravita et al., 2003). Tools are a particular case of environmental elements and can modify the perception of the body and of the peripersonal space through alteration of the visuotactile perception (Brozzoli et al., 2010; Macaluso and Maravita, 2010). In fact, distinct cortical areas and neural networks of the frontoparietal system are involved in processing objects depending upon their distance from the egocentric references of the body (hand, arm, head), with mechanisms that undergo both dynamic and plastic changes after tool use (Cléry et al., 2015).

Body cognition may also have a direct relevance on language. Language and dexterity have long been supposed to be evolutionarily related, sharing functions and cortical resources (Binkofski and Buccino, 2004). Additionally, functional evidence also suggests that motor simulation is associated and integrated with speech comprehension (Buccino et al., 2005; Jirak et al., 2010; Marino et al., 2012). Language and handedness can be hence associated in terms of neural mechanisms and lateralization, but also in terms of body experience.

Such a perceptual system bridging body and cognition is extremely stimulating for current cognitive sciences and can be tentatively investigated in an evolutionary context, within the perspective of the field called *cognitive archeology*.

3 HAPTIC COGNITION AND COGNITIVE EXTENSION

Recent theories in cognitive science suggest that “mind” might not be a *product* of the brain, but instead a *process* generated by the interaction between brain, body, and environment (Malafouris, 2010, 2013). These hypotheses are generally named “extended cognition” and are aimed at evaluating if and to what extent the body and the environment are integrated and necessary parts of our cognitive mechanisms. Our culture is not simply *tool-assisted*, but is actually *tool-dependent* (Plummer, 2004). Like a spiderweb, it should be intended as an essential part of the organism’s cognitive system in both functional and evolutionary terms, even though it is external to the body. For humans, environment also means culture, and in particular material culture, namely, technology. If such a “prosthetic capacity” (Overmann, 2015) has a major role in human evolution, then visuospatial functions may be central to its proper development (Bruner and Iriki, 2016).

Visuospatial integration can be partially tested in extinct human groups by integrating information from their anatomy, archeology, ecology, and social organization (Bruner et al., 2016, 2018b). Of course, there are many difficulties when analyzing behavior and cognition in extinct species, but nonetheless we can collect multiple and independent evidence in order to support or reject a specific hypothesis. Visuospatial integration in Neanderthals is an interesting case study and example. They had similar brain size and ecological niche than modern humans, but apparently distinct behaviors. In fact, as far as we know, Neanderthals did not display modern parietal bulging, they heavily relied on their mouth to handle tools, they did not apparently have any projectile technology or a noticeable visual culture, and they had smaller social groups and smaller territories (Bruner and Lozano, 2014, 2015). All these independent sources of information converge in supporting a lack of visuospatial specialization, at least to a degree comparable with our species. Namely, we can hypothesize that those extinct humans lacked our visuospatial specialization (including aspects of body cognition and body–tool integration), and all the evidence we have on Neanderthals (brain anatomy, archeology, ecology, skeletal morphology, etc.) is not able to reject this possibility, so making the hypothesis more probable.

During the interaction between hand and tool, the body undergoes a structural adjustment to include the information of the tool in the physical management (dynamic touch; Turvey and Carello, 2011), and the tool can be represented as an actual body element in the body schemes of the brain (Iriki and Taoka, 2012; Maravita and Iriki, 2004). The functional unit is hence the hybrid body–tool system, which has new emerging properties, new qualities, and capacities that are generated thanks to the combination of the two elements. Hand–tool integration is therefore directly intermingled with cognitive extension (Iriki, 2006), in which some cognitive functions are exported and delegated to extraneural elements. Apparently, motor behavior and sensorial experience, despite generally associated with distinct cortical territories, are strongly integrated at both neural and behavioral levels

(Ackerley and Kavounoudias, 2015; Tunik et al., 2007). Because of the importance of tool making and tool use in our species, grasping patterns and hand morphology are a major topic in evolutionary anthropology (Marzke, 1997; Marzke and Marzke, 2000; Susman, 1998). These same topics also represent a fruitful research area in ergonomics, orthopedics, robotics, and cognitive science (Feix et al., 2016; Landsmeer, 1962; Napier, 1956; Serino and Haggard, 2010), as well as in experimental archeology (Key and Dunmore, 2015; Marzke et al., 2015; Rolian et al., 2011). It is therefore mandatory, when dealing with cognitive archeology and visuospatial capacity, to investigate the behavioral basis of hand–tool interaction. In Section 4, we present two complementary aspects that can provide quantitative approaches to the study of the hand–tool system: hand morphometrics and electrodermal activity.

4 TOUCHING STONES: HANDS AND EMOTION

4.1 HAND MORPHOLOGY

Hand anatomy has undergone several changes during human evolution (Kivell, 2015; Tocheri et al., 2008), and hand morphological changes are supposed to be directly involved in tool management (Rolian et al., 2011; Williams et al., 2012). Human hand morphology might have evolved from ape-like proportions with longer digits adapted for suspensory behavior and brachiation, or else be based on a primitive and generalized short-fingered primate scheme (Almécija et al., 2015). In this latter case, the human hand retains the primitive nonspecialized features (short fingers and manual dexterity), observed in many quadrupedal monkeys like baboons or macaques, while apes underwent finger elongation because of a suspensory adaptation. The hand fossil record associated with early and archaic humans is scant (see Bruner et al., 2016). However, despite their similar brain size, modern humans and Neanderthals apparently displayed different hand proportions since the evolution of their respective early forms (Niewoehner, 2001). Therefore, it turns out that we modern humans have a distinct morphology of the parietal regions associated with visuospatial integration (the paleoneurological evidence), distinct body and hand proportions (the skeletal evidence), and a distinct cultural capacity (the archeological evidence). Although these evolutionary changes are still not completely clear, they should be considered as associated with our special technological niche.

Of course, before we can design research for and interpret research from fossils, we should investigate general patterns and variations in our own species. In Fig. 2 eight basic hand diameters in a sample of adult modern humans (46 normal right-handed adults; 22 females, 24 males) were analyzed through principal component analysis based on a correlation matrix, showing that the first vector of variation (explaining 75% of differences) is basically associated with an increase in all the diameters. Namely, the main factor channeling hand morphological variability is general hand size, and it is not associated with specific hand proportions. This size component strongly separates males and females (Mann–Whitney $P < 0.001$). In this

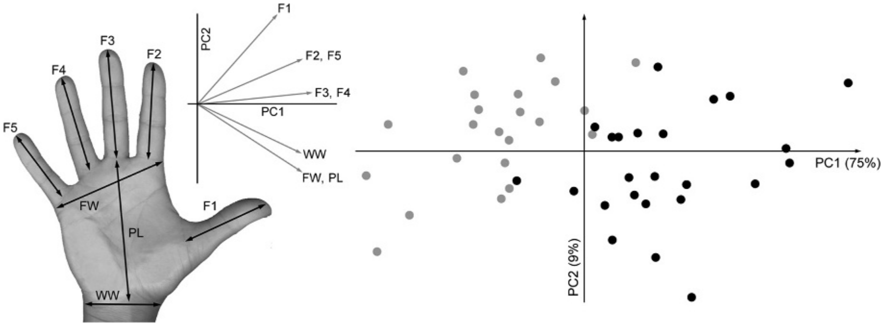

FIG. 2

Principal component analysis computed on eight hand diameters (*F1–F5*: finger 1–5 length; *FW*: fingers width; *PL*: palmar length; *WW*: wrist width). PC1 is associated with size, i.e., increase of all the variables. This vector explains 75% of the variance and separated females (*gray dots*) from males (*black dots*). The second component is associated with longer fingers (mostly the thumb) and smaller palm.

case, the following components are not statistically significant, although the second component is above the Jolliffe cutoff value (a threshold commonly used to evaluate stability of these multivariate vectors) and explains 9% of the variance. It is associated with an increase in finger length (particularly the thumb) and decrease in palmar size. In this case, values are slightly larger, on average, in females ($P=0.02$). A discriminant function using the same hand variables is able to classify sex in 96% of the individuals, and it is correlated to both PC1 ($R=-0.89$) and PC2 ($R=0.37$). This means that 75% of the hand variation is due to size, and 79% of the sex variation is due to size, too. Interestingly, PC2 is moderately correlated to age ($R=-0.45$; $P=0.002$), and aging is therefore associated with relatively shorter fingers and wider palms. In this example, sexes have slightly different ages (males 46 ± 10 years; females 40 ± 11 years; $P=0.04$), and analysis of covariance suggests that PC2 sex differences are no more significant when corrected for age ($P=0.14$).

This simple exploratory survey suggests that morphometric differences between male and female hands concern only size, being larger in males. It also means that hand variation, in terms of general patterns, is not channeled according to some specific finger proportion. The only widely discussed sexual difference in finger length is the ratio between the second and fourth finger (2D:4D), which is larger in females because of a shorter proximal and middle phalanx of the fourth finger, a morphogenetic effect that might be due to early (prenatal) hormonal effects (Zheng and Cohn, 2011). As far as we know, it remains to be evaluated how much these factors are also related to hand size, and the extent of such male–female differences. In our sample, although males have a slightly lower mean value for this ratio, the difference between sexes is not significant ($P=0.21$).

In sum, size is the most common factor involved in our adult hand variability, including sexual differences. Accordingly, hand size should be regarded as a key issue in hand–tool interactions. Hand size is known to influence biomechanical grasping mechanisms, but also sensory features. Smaller hands (more frequent in women) have thinner skin and higher concentration of receptors, and both factors increase tactile sensitivity (Peters et al., 2009). Of course, although size is apparently the principal factor of hand group variation, individual aspects other than size can promote or demote grasping capacity or sensory responses. In this example, the second component deals with the ratio between palm dimension and the length of the fingers, mostly of the thumb, a pattern that accounts for almost 10% of the variance and apparently changing with age. In this case this component does not reach a statistical significance but, if confirmed, such an inverse relationship between palmar size and thumb length could represent a second integrated pattern of hand variation. This can be relevant when considering the role of the thumb in tool use, especially during the transition from Oldowan to Acheulean (Rolian et al., 2011; Williams et al., 2012—see later). The rest of the variation (including specific finger proportions) is probably due to idiosyncratic characters, based on individual features that should be evaluated independently.

4.2 ELECTRODERMAL ACTIVITY

A crucial issue in cognitive archeology concerns whether or not interactions with tools influence brain functions. Obviously, specific tool uses are associated with specific cortical activation, as evidenced though experiments in neuroarcheology (Stout and Chaminade, 2007). Brain imaging largely relies on hemodynamic responses, metabolic processes, expensive technical resources, and complex experimental paradigms. Costs and logistics apart, these methods may involve operational difficulties, mostly when dealing with the observation of complex behaviors in real time (Hecht and Stout, 2015). Additional methodologies come from psychometrics that can be useful to test correlation between cognitive performance and anatomical characters (Bruner et al., 2011b, 2015).

Some generalized cognitive aspects can be also investigated with simpler approaches, like devices for the detection of Electrodermal Activity (EDA; Critchley, 2002; Vecchiato et al., 2014). Electrodermal response is typically quantified in terms of skin conductance levels, mainly in the hands and feet (De Houwer and Hermans, 2010). These systems are based on electric impedance (reduction of electrical resistance and increase in conductance) and are designed to capture and measure emotional reactions in individuals or groups. Following empirical evidence, sensors are employed to detect skin electric signals associated with emotional changes (Boucsein, 2012; Martin and Venables, 1966). *Electrodermal level* (EDL) measures the tonic activity of the skin and is associated with basal level of activation, and its value is interpreted as proportional to attention, namely, the predisposition to receive, analyze, and react to, new incoming information. *Electrodermal response* (EDR) deals with a psychophysiological reaction due to fast conductivity changes and is interpreted as a generalized emotional reaction. These methods were originally applied at the beginning of the past century in psychological

FIG. 3

The three stone tools used in this survey: a chopper (*left*), a handaxe (*middle*), and a scraper (*right*).

experiments regarding arousal and emotion (Boucsein, 1992; Kreibig, 2010; Stemmler, 2002). Since then, their use has increased, applying EDA quantification methodologies in legal contexts, and they are currently employed in neuromarketing, to investigate customer reactions to given commercial strategies and choices (Ariely and Berns, 2010; Boucsein, 2012; Lee et al., 2007; Morin, 2011). These kinds of physiological recordings have been employed often in cosmetics, to test the emotional reaction to haptic (Boucsein et al., 1999) as well as visual and olfactory (Eisfeld et al., 2005) stimulation.

In cognitive archeology, these methods can be used to evaluate different behavioral and emotional responses during interaction with Paleolithic tools, under the null hypothesis of no differences in electrodermal activity between individuals or groups during tool manipulation, or between different tool typologies. We recorded the EDR in the same sample used to analyze hand morphology (see earlier), while handling three representative stone tools belonging to different lithic typology (Fig. 3). The chopper is a classic Oldowan element, associated with the earliest human technology with a robust archeological record, largely used between 1.5 and 2.5 million years ago. It is but a flaked core with a cutting edge, probably handled with a force grip and used to beat and crash, taking advantage of the weight of the stone tool. The toolmaker was historically thought to be *Homo habilis*, although at present this species is not commonly recognized as a real evolutionary unit, probably representing a "basket taxon" in which we have grouped fossils from distinct (and largely undetermined) species. The handaxe is the typical Acheulean element, a technology that was dominant between 1.5 and 0.5 million years ago. The core is refined through a long

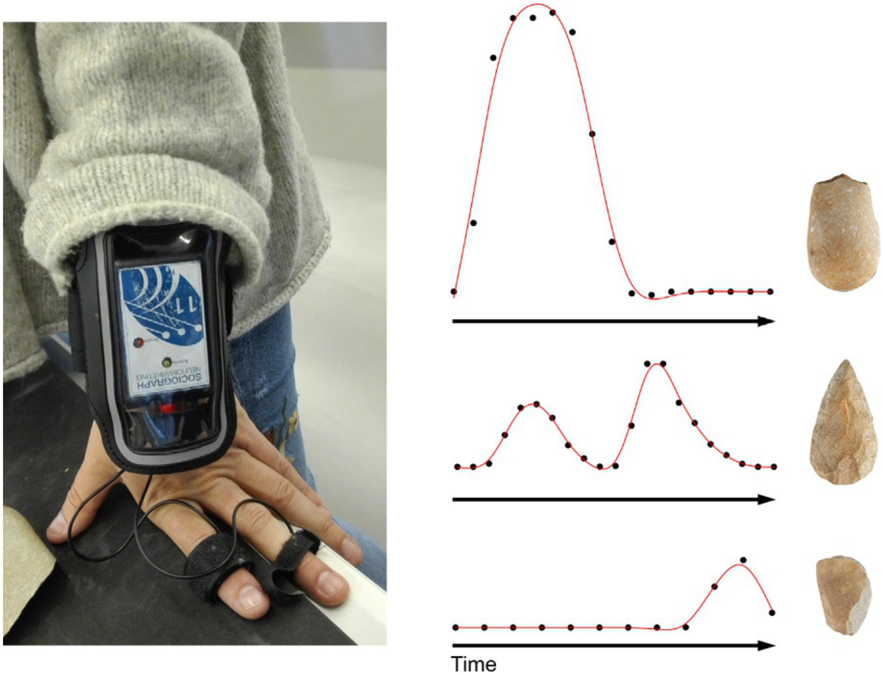

FIG. 4

Electrodermal activity was detected and recorded with a portable remote device wrapped around the forearm (*left*). Electrodermal response (EDR) for each individual was recorded during the handling of the three tools. The same individual (*right*) can show different patterns of emotional engagement for the three tools. Trials were randomized and preceded by a familiarization procedure with a set of lithic tools.

portion of the outline, and the tool is generally elongated, roughly symmetrical, and probably employed in multiple tasks. Handaxes are generally flatter than choppers and can be handled from the base but also grasping the lateral edge. They are generally associated with *H. ergaster*, *Homo erectus* and *Homo heidelbergensis*. The scraper is a much smaller tool also used by *H. heidelbergensis* but typical of large-brained hominids like Neanderthals or early modern humans, and frequently used between 500 and 50 thousand years ago.

We used a remote device that is wrapped on the forearm and senses the bioelectrical responses through electrical resistance at the second and third finger (Sociograph Technology; Martínez Herrador and Garrido Martín, 2003), measuring electrodermal parameters on the left hand, while the participant manipulates the tool with the right hand (Fig. 4). Participants were asked to manipulate the tool until a stable sensation and a comfortable position are reached. We recorded the electrodermal values through the whole trial, from the beginning of the manipulation to the achievement of a stable position. We have therefore quantified the variations in

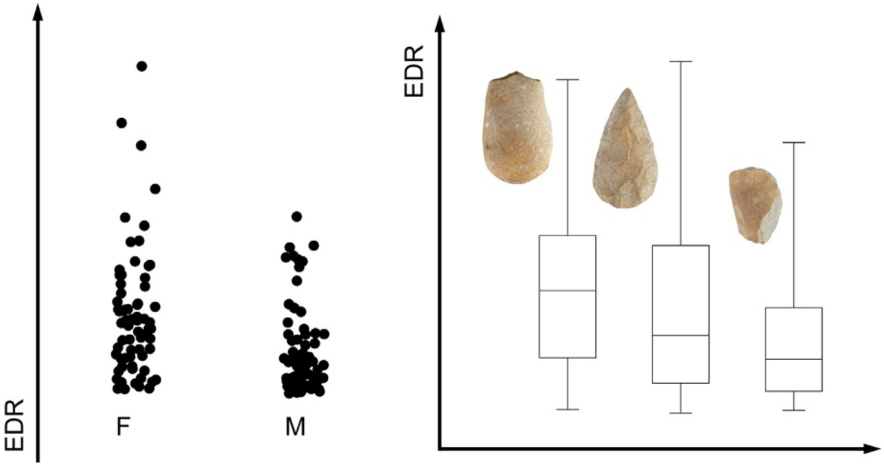

FIG. 5

Mean EDR for males and females (F, M; jitterplot) and for the three tools (nonparametric boxplots) computed from all the sessions.

emotional responses during the haptic experience, according to the hand–tool interaction. Visual inputs play a crucial role in object affordance, grasping mechanisms, and spatial perception (Lacey et al., 2014), although there are distinct and independent neural pathways involved (Goodale et al., 1994). Accordingly, individuals were blindfolded so as to limit the interaction between hand and tool to the haptic experience. Signals were captured with a frequency of 32 recordings per second. For this demonstration survey, we reduced the data to one recording per second after arithmetic mean, and only the mean values for each trial (a single session of one person with one object) were used to compute comparisons.

Fig. 5 shows the distribution of EDR values in males and females, and the differences for the three tools. Females display a stronger emotional involvement when handling the tools ($P < 0.0001$), with a higher average and larger variation. Also the EDR values for the three tools are distinct ($P = 0.005$), particularly because of the difference between chopper and scraper ($P = 0.001$). The handaxe shows an intermediate value, but differences do not reach significance with either the chopper ($P = 0.12$) or with the scraper ($P = 0.10$). According to these results, emotional engagement is lower for the scraper and larger for the chopper, with the handaxe in an intermediate position.

This exploratory survey is aimed at showing how electrodermal activity can be applied in an archeological context. It suggests that even a simple contact can exert an emotional alteration when handling an object, and that this emotional change can be different in distinct lithic tools. This approach can be employed to test responses to different tools or even to different behaviors associated with Paleolithic ecological, economical, or social aspects. Dealing with visuospatial integration, it can be employed to evaluate the response during physical contact or during specific visuospatial tasks (e.g., throwing).

5 PERSPECTIVES IN HAPTIC COGNITION AND COGNITIVE ARCHEOLOGY

Primates “think” with their hands more than any other mammals, by exploring and interacting with the surrounding elements largely through their specialized eyes and hands, imagining and simulating hand-centered actions, and planning according to their body perceptions and body-based expectations (Ackerley and Kavounoudias, 2015; Byrge et al., 2014; Haggard, 2005; Tunik et al., 2007). This specialization is the result of an integrated functional package made of body and brain elements. Humans are particularly specialized in this sense, and it is no coincidence that we display complex cortical areas dedicated to eye–hand and body–environment coordination (Goldring and Krubitzer, 2017). In humans, the intraparietal sulcus is particularly complex, probably because of a specialization in hand–tool interaction (Choi et al., 2006; Grefkes and Fink, 2005; Kastner et al., 2017; Zlatkina and Petrides, 2014). Also the precuneus is larger, and it is a central node for visual imaging, body cognition, and self-consciousness based on body-centered egocentric imagination and memory (Bruner et al., 2017; Cavanna and Trimble, 2006; Freton et al., 2014; Margulies et al., 2009; Zhang and Li, 2012). The body, and particularly the eye–hand ports, is therefore an active interface between brain and environment, and in humans especially between brain and technology. Perception and action are, in fact, intimately associated (Ackerley and Kavounoudias, 2015), and the same cortical regions dedicated to body integration are also involved in attentional, intentional, and executive management (Andersen and Buneo, 2002; Andersen et al., 1997; Bisley and Goldberg, 2003; Freedman and Assad, 2006; Rushworth et al., 2001; Tunik et al., 2007). Technology itself is a crucial part of this cognitive system, although we still do not know to what extent and with what specific roles (Iriki and Taoka, 2012; Malafouris, 2010). In the last 2 million years, humans have evolved a culture that is dependent on technology, and accordingly we have evolved a cognitive system that is dependent on technology too. The “prosthetic capacity” itself can be an evolutionary characteristic, and a behavioral ability targeted by natural selection.

The human brain is more plastic than a chimpanzee brain, which in turn is more anchored to genetic inheritance (Gómez-Robles et al., 2015). This sensitivity to environmental influences is probably necessary to delegate cognitive functions to extraneural elements, a process based on loops and feedbacks between biology and culture. Such a cognitive shift, extending the body functional interface through technological components, is likely to have occurred with the evolution of the genus *Homo*, and especially with the evolution of our species, *H. sapiens*. These topics should be investigated within a comprehensive framework, including neurobiology, neuropsychiatry, cognitive science, psychology, robotics, and medicine.

In cognitive archeology, we should evaluate what kind of cognitive alterations can be associated with the contact between body and tools. Body experience can represent a crucial part of the cognitive process, mostly when dealing with the interaction between hand and technology. In fossils, brain anatomy and paleoneurology can only provide minor clues on this topic. Endocasts revealed that modern humans—and partially Neanderthals—underwent an expansion of parietal cortical areas which are relevant nodes for visuospatial integration, and also hand morphology displays interesting changes in our species (Bruner et al., 2016; Patiño et al., 2017). In modern human adults, size is apparently the only main factor involved in overall hand variation. The relationship between thumb length and palmar size also may be based on shared patterns of variability. It is likely that, apart from these two factors, the rest of morphological variation is due to individual and independent features, which should be considered separately.

Further inferences can be supported by evidence in ecology and behavior (Bruner et al., 2018b). For example, the development and use of projectile technology can be an interesting proxy to evaluate visuospatial projecting capacity (Williams et al., 2014). In this sense, discontinuity in the archeological and paleontological record can reveal underlying changes in body cognition and visuospatial capacity in different human lineages.

In terms of emotional engagement, electodermal activity suggests that there are differences between males and females, and also differences associated with different stone tool types. Such differences in cognitive engagement can reveal different haptic responses which, ultimately, are supposed to be associated with part of the processes involved in body technological extension (Bonifazi et al., 2007; Iriki and Sakura, 2008; Malafouris, 2013).

Women apparently display a higher and more diverse emotional reaction. Females have, on average, a smaller parietal cortex and less visuospatial capacity than males, although we still ignore whether this is a genetic or cultural effect (Koscik et al., 2009). Visuospatial cognitive differences between males and females can be in fact the result of specific evolutionary adaptations associated with the distinct social roles (Silverman et al., 2007), or else consequences of different behavioral training due to cultural influences (Burke et al., 2012). It should be considered whether or not such stronger emotional responses in females may be associated with those spatial and visual capacities that are influenced by sex. If this is the case, then increased in visuospatial capacity should be associated with decrease of emotional engagement.

Taking into account that hand size is a major factor channeling hand diversity, and that females have smaller hands than males, it should be also considered to what extent size can influence emotional feedback. Tactile receptors and sweat pores are more densely packed in smaller hand, and generally women are able to perceive finer surface details when compared to men (Edelberg, 1971; Morimoto, 1978; Peters et al., 2009). We ignore if this increased tactile sensitivity in females is a real sexual character or in contrast if it is a secondary (allometric) consequence of having smaller hands. Interestingly, the contact with the large and rough tool (the chopper) induces more emotional reaction than the small and fine one (the scraper). It remains to be tested whether this is mainly due to dimension or to other ergonomic factors like shape, weight, roughness, or other specific properties of the object. A study on a larger and more diverse lithic sample, and a statistical analysis of the whole electrodermal patterns, is in preparation.

Besides any future interpretation, the take-home message concerns the fact that there is an emotional response that alters the cognitive state during the handling of a stone tool, and that this response may be different for males and females, and different for different tools. Trends and discontinuities in the emotional response associated with the archeological record may be able to identify trends and discontinuity in the evolution of the human cognition and prosthetic technological capacity, following genetic, epigenetic, or environmental influences.

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CHAPTER

Evolution and development of handedness: An Evo–Devo approach

13

George F. Michel[*,1], **Iryna Babik**[†], **Eliza L. Nelson**[‡], **Julie M. Campbell**[§]
Emily C. Marcinowski[¶]

[*] *Psychology Department, University of North Carolina Greensboro, Greensboro, NC, United States*
[†] *Department of Physical Therapy, University of Delaware, Newark, DE, United States*
[‡] *Psychology Department, Florida International University, Miami, FL, United States*
[§] *Psychology Department, Illinois State University, Normal, IL, United States*
[¶] *Department of Physical Therapy, Virginia Commonwealth University, Richmond, VA, United States*
[1] *Corresponding author: Tel.: 336-256-0021; Fax: 336-334-5066, e-mail address: gfmichel@uncg.edu*

Abstract

Hand preference is a sensorimotor skill whose development both reflects and promotes the development of hemispheric lateralization for manual and cognitive functions. Extensive comparative, crosscultural, and paleoanthropological evidence demonstrates the prevalence of limb lateralized preferences across vertebrate species and the prevalence of right-handedness within hominid evolution. Many reviews of the evolution and development of human handedness have proposed adaptive explanations for its evolution. However, during the last 3 decades a new approach to understanding evolution (the Extended Evolutionary Synthesis—EES) provided a persuasive alternative to the conventional (Neo-Darwinian Synthetic Theory—ST) evolutionary and developmental accounts. EES combines modern evolutionary and developmental research (Evo–Devo) in ways that alter understanding of natural selection, adaptation, and the role of genes in development and evolution. These changes make obsolete all past accounts of the evolution and development of lateralization and handedness because EES/Evo–Devo requires new study designs. The developmental trajectories of any structural or functional trait must be specified so that it may be related to variations in the developmental trajectories of other traits. First, we describe how the EES/Evo–Devo differs from the conventional ST, particularly for understanding of how traits develop. Then, we apply Evo–Devo to the study of handedness development in infancy and its relation to the development of other cognitive functions. Finally, we argue that identifying the development of atypical traits would benefit from knowledge of the range of individual differences in typical developmental trajectories of hand-use preference and their relation to variations in the developmental trajectories of cognitive functions.

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Keywords

Handedness, Evo–Devo, Evolution, Development, Human, Cognition, Lateralization

1 INTRODUCTION

Our intent in this chapter is to place investigations of human handedness development within a modern Extended Evolutionary Synthesis/Evolutionary–Developmental (EES/Evo–Devo) conceptual framework (cf., Hall, 1999, 2012; Maienschein and Laubichler, 2014; Morange, 2011; Müller, 2017). Recent extensive reviews of the research literature examining the evolution and development of handedness (e.g., Cochet, 2016; Cochet and Byrne, 2013; Ocklenburg et al., 2014a, b; Rogers, 2014; Vallortigara et al., 2011) reduce our need to reiterate the empirical literature. However, previous reviews have used the conventional (Neo-Darwinian Synthetic Theory—ST) account of evolution and development. EES/Evo–Devo requires a reconceptualization of evolution and development and the employment of different research designs. To understand the Evo–Devo approach requires that we first describe how the modern EES differs from the prevalent ST notions of evolution but still retains Darwin's conceptual insights.

2 EVOLUTIONARY THEORY: HOW THE EES DIFFERS FROM THE CONVENTIONAL SYNTHETIC THEORY

Darwin's theory (1859/1968) challenged the notion of species as natural types. By eliminating the need for species members to share common morphological features or physiological processes and traits, Darwin resolved the individual variability problem in species taxonomy. There can be extensive variability of traits among species members because they are united only by common ancestry (homology). To account for the similarities and differences among species members, Darwin appealed to developmental processes (cf., Huxley, 1880). Unfortunately, Darwin's notion of species violates our intuitive expectation that members of any category should be united by some essential features (homoplasy). The rise of population genetics in the early 20th century seemed to account for the inheritance of traits and their resemblance across individuals (common genes) while genetic variance seemed to account for individual diversity (Sarkar, 2017). Thus, our intuitive expectation that species share essential features was satisfied by the notion of species-common genes.

About 8 decades ago, the Neo-Darwinian Modern Synthesis or Synthetic Theory (ST) of evolution integrated concepts about evolution from multiple fields of biology by describing speciation as the operation of natural selection on the distribution of genotypes in populations (cf., Huxley et al., 2010). The ST combined Darwinian principles of individual variation, inheritance of traits, differential reproductive success (natural selection) with Mendelian experimental breeding techniques, the notion that genes are independent units, and the mathematics of population genetics. In the ST, trait variation within a population and across species is explained by adaptation to specific fitness landscapes (ecological conditions) and derives from differences in gene (allelic) frequencies "chosen" by natural selection.

ST required (cf., Laland et al., 2000; Walsh, 2015) that:

1. populations contain genetic variation that arises randomly via mutation and recombination among genes and that populations evolve via changes in gene frequency that reflects primarily the effects of natural selection;
2. genes produce phenotypic traits that enable survival and reproductive success;
3. genetic inheritance alone accounts for the intergenerational transmission of those traits that are naturally selected to "fit" the phenotype to the ecological circumstance;
4. new species (with new traits) arise when gene flow is prevented within a population and these reproductively separated populations exist in ecological circumstances sufficiently different to permit the operation of natural selection;
5. the phenotypic differences among broad taxonomic groups (e.g., hominins vs great apes, or Old-World monkeys, or New World monkeys, etc.) result from the gradual accumulation of large amounts of genetic variation; and
6. natural selection is the only factor that can direct evolution; therefore, each species-typical trait must be an adaptation to a specific identifiable ecological circumstance (this is known as the adaptationist program, Gould and Lewontin, 1979).

Thus, ST proposes that the gene, rather than the organism, is the causal unit for the processes of development, inheritance of traits, adaptive change in population traits, and the origin of novel traits during evolution. Random mutation of genes is the ultimate source of evolutionary novelties. ST minimizes developmental explanations of evolutionary novelties by assuming that development is determined by inheritance: organisms develop what they inherit and individually specific developmental events cannot be inherited. In ST, genes are the privileged and primary explanatory units of development—they are a "code," "script," "program," or "blueprint" that specifies a determinate phenotype (within a delimited range of variability, cf., Goldman and Landweber, 2016). In ST, development is just the process of translation of genetic instructions into biological forms that determine functions; an individual organism's genotype determines that individual's morphological and behavioral traits. Therefore, ST implies that it is possible to know the organism's features and behavioral traits just by knowing its DNA sequence (cf., Sarkar, 2006).

Although the expression of genes is known to vary among individuals and during development, ST assumes that this developmental variability of gene expression is also under genetic control (Müller, 2017). ST accepts that many nongenetic factors can distort development, but those nongenetic factors interfere with the development of adapted traits and cannot contribute to evolution by natural selection. Since differences in gene frequencies among and within populations are sufficient to account for evolution, developmental biology contributes to evolution only by: (1) describing how certain genes regulate the expression of other genes and (2) speculating about how these regulatory genes may have been chosen by natural selection.

New methodologies and modern evidence from molecular genomics, developmental biology, epigenetics (how factors other than DNA control protein production and cellular biochemistry), physiological plasticity, systems biology, network analyses, ecology, and the behavioral, cultural, and social sciences have challenged both the conceptual frame of, and predictions from, the ST models (cf., Annila and Baverstock, 2014; Bateson, 2014; Gilbert et al., 2015; Gilbert and Epel, 2015; Jablonka and Lamb, 2005; Latham, 2017; Müller, 2017; Sultan, 2017). An organism's actions such as niche selection, niche construction activities, physiological adjustment to conditions, and mobility to seek other conditions have all played formative roles in evolution (see Bateson, 2015; Lickliter and Harshaw, 2010 for reviews). Therefore, many have called for EES to unite the new properties of evolutionary change with aspects of ST (e.g., Laland et al., 2000; Pigliucci and Muller, 2010), or even to serve as a new theory of evolution (e.g., Müller, 2017). EES changes our understanding of natural selection, adaptation, and the role of genes in development and evolution.

2.1 EVOLUTIONARY THEORY: NATURAL SELECTION

Oddly, the most distinctive weakness of ST is that it misconstrues Darwin's concept of natural selection (Walsh, 2015). ST proposes that natural selection is a causal process responsible for the adaptiveness of traits. That is, natural selection causes changes in gene frequencies (and hence phenotypes) via differential reproduction. Those individuals with genes that produce phenotypes that better "fit" the environment leave more offspring than those with genes that do not. Natural selection (differential reproduction) ensures that structures and functions are adapted to the environmental circumstances.

For Darwin (1859/1968, p. 114), natural selection is not a force or causal process; rather, the cause of biological fitness and diversity derives from each organism's developmental "struggle" to live and reproduce—nothing more is needed to "guide" evolution. Darwin's "natural selection" is an effect on a population of the variety of causes (physiological and ecological) involved in each individual's developmental adjustments to live and reproduce. When individuals vary in their heritable capacity to survive and reproduce, a population will change the characteristics of its lineage. This change means that a population appears to better match the ecological conditions of its existence not because the circumstances selected particular genes but rather because the individual has adjusted (physiologically and developmentally) to its circumstances.

Treating natural selection as an effect rather than a cause, greatly changes notions about the adaptation of traits. Consider two individuals: one may not "fit" some facet of their common ecological circumstance as well as the other. Nevertheless, the first produces more offspring than the second. If the production of more offspring is passed on to the offspring (via many mechanisms other than gene transfer; cf., Jablonka and Lamb, 2005; West-Eberhardt, 2003), the descendants of that first individual eventually will come to predominate in that population. Natural selection did not cause that change in the population; that change is natural selection. To consider the offspring of the first individual more "fit" to the environment than offspring of the second individual is to miss that the second individual's traits "fit" the environment better than the first individual and that difference continues for their descendants.

For a concrete example, consider the blackcap, a European passerine bird (Bearhop et al., 2005). Typically, these birds are seasonal migrants with spring migration affecting the start of breeding. Until 50 years ago, all European blackcaps migrated back and forth together, spending summers in northern Europe and the British Isles and winters in Portugal, Spain, and North Africa before migrating in spring to breed in southern Germany and Austria. However, some blackcaps began wintering in Britain and Ireland because of increased availability of winter provisioning provided by bird feeders and other human activities. Thus, northern-wintering blackcaps are exposed to the photoperiods that contribute to the initiation of migration and the onset of gonadal development 10 days earlier than their southern-wintering species–mates.

Although all blackcaps continue to gather each year at the same mating sites in Germany and Austria, the northern blackcaps arrive earlier, establish territories and mate with other earlier arriving birds. Southern-wintering blackcaps arrive later and mate with each other, serving to reproductively separate northern-wintering birds from the later-arriving southern-wintering population. This shift in migratory patterns results in the northern-wintering pairs producing one more egg per season than the southern-wintering pairs (Bearhop et al., 2005).

Note that both groups appear to be adapted to their ecological circumstances. Only empirical investigation conducted over many generations would determine the relative fitness between these two groups within this species. The northern blackcap gets to the breeding site earlier and has an advance in breeding but must endure the harsh winter. The additional egg may (or may not) compensate for the losses suffered in winter. In contrast, the southern blackcaps must endure a longer migration. Of course, there are many more differences in the circumstances of these two groups that affect their survival and reproductive success. Natural selection is not guiding their evolutionary changes (if any); rather, developmental processes of plasticity and social influence on migratory activities and overwintering are producing differential reproduction that we note as natural selection. If speciation occurs, we would conclude that the two species are adapted to different ecological circumstances but that would conceal the developmental patterns involved in the establishment of the northern and southern groups. This applies equally well to the evolution of human handedness.

2.2 EVOLUTIONARY THEORY: ADAPTATION

It is misleading to assume that the predominance of a trait in a population automatically means that those individuals with the predominant traits are better fit to the environment than those with traits that do not predominate. As Gould and Lewontin (1979) demonstrated decades ago, not all traits affect reproductive success and not all traits have evolutionarily relevant functions. Many traits derive from developmental events and function within development but may have little consequence on reproductive success (Gould and Vrba, 1982). Acceptance of this view of adaptation, forces the undertaking of empirical investigations to determine whether a trait contributes to reproductive success or simply enables an individual to develop reproductive capacity.

Consider again the Blackcap example: The northern and southern groups may function equally as well in their respective responses to winter. Running computational models with cost–benefit analyses will not answer the question of whether the northern-wintering is an adaptation because we do not have the information about all the causes and consequences of the differences in migratory patterns. The northern-wintering may result in an increase in eggs and chicks but overwintering may result also in a greater loss of juvenile or adult birds. Only systematic assessment of the role of northern-wintering in the survival of the birds can shed light on adaptiveness of the trait.

The ST distortion of Darwinian natural selection and adaptation had profound consequences on accounts of the evolution of adaptive traits, including the evolution of lateral asymmetries (cf., Rogers, 2014). Computational modeling (Ghirlanda and Vallortigara, 2004) revealed that a population bias in the domestic chicken's hemispheric asymmetry emerged when lateralized individuals had to interact with one another. However, the model assumed that only lateralization affected the social interaction. Many factors affect social interaction and each is likely to be related to reproductive success because social interaction is necessary for reproduction. The ST notion that each trait should fulfill a specific requirement of some feature of the environment (or it would have been eliminated by natural selection) is not required by EES. Traits only need to not disrupt survival to remain in the repertoire of the species. It is even possible for some traits to reduce reproductive success but enhance survival because of their crucial functions during development. These traits may be part of a developmental "package" that may work well enough for individuals to leave offspring and hence these traits will continue to be present across generations (cf., Oppenheim, 1984). Therefore, engaging in simulations of the adaptiveness of traits using computational models is unlikely to capture the causes of population change. Nor do these models reveal what makes adaptive evolution "adaptive" (Walsh, 2015).

Just as establishment of dorsal/ventral and anterior/posterior asymmetric dimensions are developmental events that do not contribute directly to reproductive success (rather, they ensure that an organism can function in its environment); so, too, lateralized asymmetry (left/right) may simply derive from the three-dimensionality of an animal and need not represent any specific adaptive function (Cartwright et al., 2004). These 3D bodily asymmetric distinctions permit an animal to orient effectively within its environment. Layering additional specific adaptive functions is not necessary, as they could all derive from effective orientation. Currently, it is unknown whether handedness or its variations are adaptive (i.e., contribute to reproductive success) for humans. Handedness may play a role in development of specific abilities (e.g., tool use and manufacture, gestural communication, and spatial comprehension) without affecting reproductive success. Such developmental functions for handedness can contribute to its continued expression in a population without the need to invoke natural selection.

2.3 EVOLUTIONARY THEORY: THE ROLE OF GENES IN EVOLUTION AND DEVELOPMENT

Whereas ST focuses on genetic and adaptive variation in populations when proposing accounts of the evolution of organismic complexity, EES emphasized constructive processes in development, ecological influences (including social and cultural conditions), and system dynamics (Hall, 2012; Laubichler, 2010; Maienschein and Laubichler, 2014; Müller, 2017). EES dispenses with the privileged role of genes in phenotypic development by adopting multilevel, reciprocal, and coaction causation in the development of traits (Annila and Baverstock, 2014). In EES, the pressures of living to reproduce operate on the development of each of the individual's component systems. As Gould (2002) argued, the developmental processes that produce the phenotypic characteristics of an organism may constrain the course of subsequent evolution or they may facilitate a particular form of evolutionary change. Developmental processes, not genetic mutation and natural selection, help guide evolutionary lineage.

Consistent with EES, Jablonka and Lamb (2005) demonstrated that inheritance of both trait resemblance and difference can be achieved without the process of gene transmission. They argued that control over the pattern of inheritance is distributed throughout the organism–environment system. Although transgenerational transfer of DNA plays a role in some aspects of inheritance (particularly in providing an "alphabet" for protein construction), other aspects of inheritance derived from: epigenetic processes (changes in protein production by modifying gene expression via environmental and other influences on cellular processes), behavioral processes (such as developmental plasticity and learning), and niche construction and selection by parents (Gilbert and Epel, 2015). For humans, social processes of enculturation, education, written records, stories, etc., also are involved in inheritance (Latham, 2017; Michel, 2010).

Unlike ST, EES proposes that the activities of genes in a network are neither independent nor additive (Goldman and Landweber, 2016; Sarkar, 2017), and they are context sensitive (Sultan, 2017). Genes become a resource (like an alphabet) rather than a program governing development. Molecular biology has shown that the architecture of genetic regulatory networks during development and function exhibits feedback loops, cyclical causation, and coaction among multiple regulatory pathways (Annila and Baverstock, 2014; Latham, 2017). The activity of a "gene" in such a network is part of the context of its own activity (Goldman and Landweber, 2016); not the expression of a program or code. This means that even the "alphabet," and certainly the way it is used, is plastic in its character. Consequently, inheritance is not "genetic" or "epigenetic," or "environmental," or "cultural"; it is holistic (Walsh, 2015).

2.4 EVOLUTIONARY THEORY: INHERITANCE HOLISM

Inheritance holism implies that every phenotypic trait is a result of the complex, causal coaction among genomes/epigenomes, organisms, and their environments during development (Annila and Baverstock, 2014; Latham, 2017). All organisms are somewhat modular in that they are composed of relatively independent components or subsystems. Consider the mammalian nervous, endocrine, immune, circulatory, digestive system, skeletal–muscle systems. These systems are integrated in a manner that partially couples them to one another (Michel and Moore, 1995). Partial coupling permits the components to operate somewhat independently from the others, which facilitates compensation for perturbations to the component or for disruptions of other components. However, partial coupling also allows the components to contribute to the regulation of the activities of other components in ways that ensure the robust maintenance of the whole organism's general state and its ability to adjust to changing circumstances (Annila and Baverstock, 2014). The regulatory activities of any individual component of an organism ramify throughout the other components and ultimately reverberate back to the originating component. In complex systems, the activities of a component are among the causes of that component's own activities, via direct and indirect "feedback" loops. All component parts are involved and none is causally privileged or primary. Organisms remain stable because the relations among their components permit compensation for changes around them.

The properties of such partially coupled modular architecture operate throughout development and include the components that compose the cellular biology of the zygote, the tissue differentiation and morphogenesis of the embryo, and development throughout the life span to produce reliably a viable individual typical of its kind despite genetic mutations, epigenetic alterations, or environmental perturbations (cf., Annila and Baverstock, 2014; Latham, 2017). Simultaneously, these properties also allow "exploration" of ecologically neutral traits that could permit "rapid" generation of phenotypic novelties in the event of the emergence of new ecological opportunities (Pigliucci, 2010; remember the northern-wintering blackcaps). The processes of development involve not just the establishment and refinement of these component systems but also the architecture of their coupling. Thus, the individual's "adaptive" resources continue to change and emerge during the life span (Bateson, 2014; Michel, 2013, 2018a). Adaptability of organisms, particularly behavioral adaptability, helps buffer them against extinction in changing conditions. Thus, in EES, the conditions of the environment do not simply set problems to which organisms must evolve solutions; rather, the organism is capable of modulating, and/or creating, or even seeking out an environment in which it can live and reproduce (Lewontin, 1982; Lickliter and Harshaw, 2010; Michel, 2010).

Through its capacity to adjust to conditions, an organism's developmental resources are capable of producing novel, stable, and viable forms (e.g., the northern-wintering blackcaps), without the need for genetic changes (Sultan, 2017; West-Eberhardt, 2003). The evolution of complex forms and functions requires the coordination of an organism's partially coupled developmental systems. What was once considered evidence against the possibility of rapid evolutionary change, because of all the adjustments that would be needed by a major change in one trait now can be accommodated by recognizing the partial coupling of components of a system which makes traits mutually dependent. As organisms continue to occupy new ecological niches, this would inevitably lead to the subsequent emergence of more efficient morphological, physiological, and biochemical adjustments to those niches and the likelihood of speciation (e.g., Pfennig et al., 2010; Pfennig and McGee, 2010). Thus, the individual organism plays an important role in the evolution of its descendants through its actions, its control of the environment, and its phenotypic adjustment to its circumstances (Bateson, 2014).

3 Evo–Devo: CONTRASTS BETWEEN ST AND EES IN DEVELOPMENTAL THEORY

The mid-20th century discovery of a biochemical "code" of nucleotides in the DNA molecule that identified the specific amino acids that comprise peptides, polypeptides, and proteins gave credence to the ST notion that genes (the DNA) sequestered information. This information was assumed to have been established by natural selection and represented the instructions for ensuring the organism's adaptation to its environment. Moreover, since much of the DNA has been conserved across broad phyletic groups, DNA appeared to represent the evolutionary history of the necessary biochemical instructions for life and the development of phenotypes. This fit well with ST notions about development being irrelevant to evolution.

However, observations that the same phenotype may be obtained from different combinations of informational sources in the genotype (cf., Alberch, 1991) and different phenotypes may be obtained from the same genotype (cf., Pigliucci, 2010), challenge the notion that genes specify the development of organismal forms. Rather, the genotype is only one of the several factors operating during development that jointly determine the phenotype, with developmental events both being affected by, and in their turn, affecting genetic expression and protein production (Annila and Baverstock, 2014; Goldman and Landweber, 2016; Latham, 2017; Sultan, 2017). Each specific genotype can play a role in the expression of different phenotypes but this relation depends on the environmental context. The variety of these phenotypic differences is unpredictable from knowledge of the genotype.

Although certain base sequences of DNA relate directly to amino acids and these "chained" arrangements of amino acids in mRNA are translated into specific peptide, polypeptide, and protein products, the arrangement of amino acids is controlled by biochemical processes (the epigenome) that permit (or not) parts of DNA to be transcribed into mRNA. Moreover, various DNA parts are combined in unexpected ways before mRNA is created. Since any sequence of DNA could be combined with numerous other sequences for eventual translation into an indefinite number of products (proteins, polypeptides, etc.)—a way of creating "new genes" from "old genes"—research has focused on this regulation of transcription and translation (Sarkar, 2006).

Cells are organized by an intricate and dynamic set of chemical messengers that travel within and between cells to permit the transcription of specific parts of the DNA into mRNA. This layer of biochemical reactions is the epigenome, which affects the pattern and timing of mRNA transcription and translation during developmental transformations as well as the biochemical "signaling" pathways operative at any time in the cell's life. Molecular genetics traces the biochemical networks and signaling pathways that connect the use of various sequences of DNA to the developmental appearance of phenotypic traits. Cellular and nuclear networks and pathways (phenotypes) emerge during development via complex, epigenomically influenced, regulatory processes. These molecular phenotypes, in turn, influence the development of the dynamic traits of physiology and behavior that enable an organism to adjust to and modify its environment.

Epigenomic processes are open to many environmental influences, which can begin before conception during the formation of parental germ cells (eggs and sperm) and continue throughout the life span. Such developmental "plasticity" enables organisms to meet the requirements of their habitat (niche selection) or adjust their habitat to their requirements (niche construction). Such developmental plasticity not only alters "external conditions for the individual… [but also] … for co-occurring plants, animals and microbes in its habitat" (Sultan, 2017, p. 3). Examination of these ecological influences on heredity and individual development became the focus of ecological developmental biology (Eco–Devo, Gilbert and Epel, 2009, 2015).

What appeared from the perspective of heredity across populations as a blueprint-like relation between genes and phenotypic traits became an illusion when an individual's networks of cellular processes were examined. As the concept of heredity expanded to include the epigenetic consequences of environmental events, research revealed that a variety of environmental conditions, inherited from parents, can affect offspring development. These may include: viruses, microbiota (e.g., bacteria, fungi, and various parasites), habitats and shelters, relatives and neighbors, food (prey types and edible vegetation), etc. Incorporation of Evo–Devo and Eco–Devo into the EES is the reason why some have argued that the EES is a distinctly different evolutionary theory from the ST. Evo–Devo and Eco–Devo consider development to be the product of ongoing, bidirectional interactions among DNA, proteins, cells, physiological processes, behavior, and the environment that simultaneously contributes to both the stability and the variability of traits (Gilbert and Epel, 2009; Keller, 2002; Sansom and Brandon, 2007; West-Eberhardt, 2003). Thus, cerebral asymmetries and handedness would be shaped (maintained, transformed, promoted, inhibited, or eliminated) by extensive interactions between the developing individual and diverse environmental influences throughout the life span.

3.1 Evo–Devo: A ST ACCOUNT OF PRIMATE HANDEDNESS

To date, only one theory (the postural origins theory—POT) has been proposed to account for the evolution of primate handedness (MacNeilage, 1987), and this theory illustrates the differences between the ST and the ESS theories. POT includes the ecological context (i.e., where the species lived, what its members ate) to argue that this context shaped a division of labor between the hands. POT proposes that the earliest arboreal primates exhibited left-hand specialization for ballistic smash-and-grab acquisition of insect prey because the right hand was used for postural support that required more feedback control. As later evolving primates shifted to a terrestrial ecology, this ecological change produced a concomitant change in hand use for eating. The feedback mechanisms controlling the right hand became specialized for skilled sensory-controlled hand movements. The presumed shift from the left-hand preference observed in many modern day prosimian species to the right-hand preference seen in great apes, including the right-hand predominance in humans, was considered reconciled by POT.

POT inspired many new studies of primate handedness which provided only mixed support (MacNeilage, 2007; Papademetriou et al., 2005). POT continues to guide investigations, but no studies have been designed to refine the theory or devise an alternative theory. POT accounts for ecology, but in keeping with ST, it invokes a past environment to explain hand-use preferences observed in the present. Little attention has been paid to the function of lateralized hand use within a species' current ecological conditions and life span. Also, by focusing at the population bias level of handedness, there have been few studies of the development of individual handedness or of parsing individual variability into different developmental patterns. Thus, POT does not account for why there is a preference or how it got there.

In EES, parents provide an ecological niche for offspring, which ensures a delimited range of environmental events and potential experiences (West et al., 1988). If organisms, including humans, develop within a niche inherited from parents, then whatever constitutes the environment for an individual cannot be presumed a priori, but must be specified in detail. For example, consider the well-known association of maternal handedness with offspring handedness (Annett, 2002; McKeever, 2000). Parental hand preferences can affect the development of their infant's hand preferences via interactive social factors during dyadic play with objects (Michel, 1992). This is a complicated interaction because whereas right-handed mothers can be strikingly dominant in the use of their right hand during dyadic play, left-handed mothers show only moderate bias toward left-hand use. As a result, infants developing a right-hand preference might have their manual asymmetry strengthened by their strongly right-handed mothers, or only mildly disrupted by their moderately left-handed mothers. In contrast, infants who are developing a left-hand preference could have their manual asymmetry strikingly disrupted by their strongly right-handed mothers, or have a chance to develop their left-hand preference under the influence of a moderately left-handed mother. In the latter case, however, infants' left-hand preference will not be as strong as the preference of infants who are developing a right preference with their right-handed mothers (Michel, 2002). The continuation of such influences beyond the child's first year remains unstudied.

The measurement of any potential environmental influence on development must be defined, in part, by reference to the individual's sensory, biomechanical, and motoric character at that point in development. von Uexküll (1957) labeled this personal quality of environments the Umwelt. The individual engages with its environment via the sensory/perceptual processes and biomechanical/physiological actions possible for that individual at that point in its life span. Both the individual and its Umwelt can change throughout development as a consequence of their continuous coactive engagement. Such change forces developmental investigations to focus on characterizing trajectories in development and the discovery of those factors that maintain consistency in any trajectory, as well as those that foster changes in trajectory vectors. Relations among the developmental trajectories of different phenotypic traits create individual differences, and these trajectories are created by individual–Umwelt coaction (Michel, 2010).

This makes untenable any notion of development as an interaction of two separate/separable influences such as gene–environment, biology–culture, nature–nurture, not because these do not interact, but because they are conceptually and empirically fused in development. Whereas some Umwelt features can be consistent across a wide range of individuals/species (e.g., gravity, atmospheric pressure, oxygen content of the medium, heat from Sun or Earth's core, and social engagement with more developed companions), others are delimited to an ecological niche (e.g., atmospheric pressure in deep seas vs mountain tops, deliberate education of young by more developed companions). The construct of Umwelt ensures that developmental investigations of any human trait must include how human culture can be transduced into epigenomic factors.

3.2 Evo–Devo: THE Evo–Devo APPROACH TO DEVELOPMENT

An Evo–Devo approach to psychological development requires identifying similarities and differences among individuals not according to their expressed traits at any point during development (e.g., handedness or working memory) but rather according to the pattern of their developmental trajectories. Although alterations in trajectories that occur earlier in development have a more noticeable consequence than those that occur later, development continues throughout the life span. Even biological structures, organs, and systems continue their development until death, despite being described as "mature." For psychological traits, describing trajectories requires large sample sizes with carefully defined traits, measured longitudinally more than a few times (Kagan, 2016).

Once trajectory details are the focus of development, Evo–Devo identifies four main developmental processes generating the phenotypic diversity upon which evolution can occur. All four involve changes in a developing trait's relation to other developing traits; hence, trajectory details about trait development are essential for understanding both evolution and development.

1. *Heterochrony* involves changes of the timing or duration of expression of developmental events. It involves two differences in developmental trajectories: (1) the beginning and/or end of one trait's most distinctive trajectory vector relative to those of other traits and (2) the rate (faster or slower) of development of one trait relative to trajectories of other traits. For example, infants who develop a hand preference before their first year exhibit more advanced language and visuospatial skills than those who develop a hand preference in their second year (Michel et al., 2013b).
2. *Heterotopy* involves changes in the organization of developmental traits so that an individual's repertoire exhibits atypical patterns. For example, the newborn's attraction to moderate intensities of stimulation contributes toward establishing familiarity with circumstances, companions, and events. This exposure creates "neural circuits" that permit detection of stimuli that vary from the "familiar" and increases the probability of withdrawal, wariness, or cautious behaviors. We expect that similar early establishment of neural circuits controlling one hand for acquiring objects would increase likelihood that those circuits would be expanded as that hand becomes more employed for tool use and object construction actions (Michel et al., 2013b). Moreover, these circuits may be shared with those involved in developing the understanding of spatial relations among objects.
3. *Heterometry* involves changes in the intensity of expressions of a trait. Thus, individual differences in the strength of handedness would likely have consequences on the development of other differences in sensorimotor, language, and cognitive traits (Michel et al., 2013b).
4. *Heterotypy* involves rearranging a developing trait's relation to other developing traits. For example, the prenatal influence on postnatal postural asymmetry (bias for supine rightward head orientation) combined with the emergence of hominin bipedal locomotion created a right-hand biasing factor in the distribution of human handedness (Michel et al., 2013a) that is not present in most primate species. The prolonged postnatal period of ineffective sensorimotor control in human infants resulted in more frequent supine conditions during early infancy which permitted the rightward bias in head orientation to affect the development of eye hand and proprioceptive arm neural control. This, in turn, led to the distinctive right bias in human handedness.

Incorporating these four developmental processes into the development of hemispheric specialization and handedness alters the interpretation of research designs.

Comparing individual differences in handedness to individual differences in any cognitive, social, or emotional trait (cf., Cochet et al., 2014) or even to differences in neural processes (Joliot et al., 2016) reveals nothing about the developmental relation of that trait/process to handedness. Even our own work on examining the relation of different trajectories in hand preference development during infancy with the language skills of older children only hints at a developmental relation (Michel et al., 2016). We need to adopt new research designs in order to examine the relation of handedness development to the development of any other trait or neural process (Michel, 2018b).

4 RELATIONS OF EES AND Evo–Devo TO HANDEDNESS

Before examining how the modern conceptions of evolutionary and developmental biology affect accounts of the evolution and development of handedness, let us emphasize some important notions:

1. A general overriding notion is that genes are not privileged, nor are they primary explanations of either development or evolution. This has profound consequences on how we approach the study of familial resemblance in handedness and the cross-species comparison of handedness (Michel, 2013). Many genetic models of human handedness postulate a single gene as the responsible agent (e.g., Annett, 2002; McManus, 2002). According to Annett (2002), a biasing (rs+) allele would shift a random distribution of hemispheric specialization toward a left-hemisphere control of language and consequently a shift to a right-handed bias in a continuous distribution of handedness because of the left-hemisphere's control of the right hand. Inheritance of this gene would result in greater resemblance among parents and offspring. Those lacking the left-hemisphere biasing allele are presumed to have their handedness determined by relatively contingent events of culture and development.

   These single gene models are good predictors of handedness distribution in offspring populations given knowledge of handedness in the parental populations. However, no single gene responsible for lateralization has been identified. The evidence is inconsistent even for the notion that several genes are involved in the control of hemispheric specialization (Ocklenburg et al., 2014a, b; Van Agtmael et al., 2002; Warren et al., 2006). Since EES proposes that phenotypes are not controlled by DNA "codes," it should not be surprising that genome-wide association studies fail to provide convincing evidence of a genetic control of handedness or hemispheric specialization of function (cf., McManus et al., 2013). An Evo–Devo approach expands the realm of factors that should be examined when seeking the causes for familial resemblance and individual diversity for handedness to include subtle epigenomic, familial, and sociocultural influences (cf., Ocklenburg et al., 2014a, b; Vuoksimaa et al., 2009).

2. Populations contain much phenotypic variation that arises from developmental processes in coaction with the ecological circumstances of the individual members of the population and those that affected their ancestors. Populations evolve via changes in how well individuals can survive to reproduce. Natural selection is not causing change, it is not a pressure or a guide; it is an effect of individual developmental success in surviving and reproducing. This new notion should alter the way we examine the evolution of handedness in primates and its relation to nonprimate limb asymmetries (cf., Michel, 2013). Although handedness among primates involves the use of the homologous forelimbs, there is no other evidence that handedness is homologous. Nor is there evidence that the different manifestations of handedness throughout development are homologous. Thus, primate handedness may be a developmental phenomenon that enables orientation toward environmental events (e.g., anterior/posterior and dorsal/ventral asymmetries affect orientation) and each manifestation of it during development is not the manifestation of the same underlying characteristic, but rather a cascading concatenation in which later handedness builds on early handedness.
3. Since natural selection is not the cause of changes in lineage traits and characteristics, organisms do not contain bundles of traits, each specifically adapted to particular ecological features. Rather, they develop general "tools" for adjusting to their environments and for adjusting their environments to them so that they can survive to reproduce. This refocuses attention on the functions of a hand preference during the life span and away from trying to identify some important adaptive significance to its occurrence. We must determine empirically how a hand preference contributes to survival and eventual reproduction (however indirectly) during the life span and whether a population bias in handedness affects survival and reproduction. Since natural selection is not a causal agent, we cannot assume that natural selection would have eliminated any polymorphism unless it had important adaptive consequences.
4. Holistic inheritance accounts for the transmission of traits across generations. The individual's developmental processes "carve" the phenotype and the ecological circumstances so that they appear to "fit." The development of handedness must be characterized by trajectory analyses that specify both the factors that maintain a vector as well as those that alter a vector. Then, we can compare handedness trajectories to the developmental trajectories of other traits according to the four developmental processes (heterochrony, heterotopy, heterometry, and heterotypy) that generate both handedness resemblance and diversity in a population. Such comparison with development of gesture, tool use and manufacture, problem-solving abilities, language abilities, and spatial representation should enrich our understanding of both development (and what disrupts typical development) and evolution (and what can lead to novelties for speciation).
5. The phenotypic differences among broad taxonomic groups result from distinct differences in their ecological and developmental histories and not differences in

their genetic information. This new notion should change our investigation of the handedness of other species to determine what ecological niches foster handedness or permit variability in handedness. It should affect also the investigation of those factors that contribute to the appearance of lateralized asymmetries throughout the vertebrate and perhaps invertebrate species. Are there ubiquitous conditions (e.g., the 3D of bodies) shaping such asymmetries of development?

6. Developmental processes involve coaction of epigenomic/physiological plasticity with ecological (physical, biological, and social) contexts. There is no gene-by-environment interaction for the development of phenotypic traits because the action of DNA cannot be separated from the action of ecological contexts. This notion alters current behavior-genetic approaches that try to partition population variance in handedness characteristics (left-, right-, or ambilateral) into estimates of genetic, environmental, and gene-by-environment influences. These are not substitutes for developmental studies that specify how handedness develops from its precursors, what factors maintain or alter its trajectory throughout the life span, and how its vector relates to the developmental vectors of other traits.

5 AN Evo–Devo APPROACH TO THE STUDY OF HUMAN HANDEDNESS

Both the EES and Evo–Devo approaches require that human handedness be carefully defined and studied longitudinally, so that its developmental trajectory can be compared with the trajectories of other traits, which also must be carefully defined and studied longitudinally. Both also require that comparative studies search for evidence of homology in human handedness. Finding evidence for determining handedness homologies, either phylogenetically across species or even serially within individual development, has been difficult to accomplish (Michel, 2013). Homology requires extensive comparative work on both morphology of structures and the structure–function relation in neural processes underlying handedness across a wide range of species. Finally, identification of homology in handedness requires detailed descriptions of its developmental trajectory, especially in closely related species (Atz, 1970; Michel, 2013). Elsewhere, Michel (2013, 2018b) argued that we lack the type of research that would permit examination of phylogenetic homology for human handedness and the comparison of handedness development with the development of other traits.

Nevertheless, there are two characteristics of the human hand preference that might distinguish it from the forelimb preferences of other vertebrates and even other hominids: (1) the preference is consistent across a variety of manual tasks, even when the "demands" of each task elicit few or no motor skills in common for their execution (McGrath and Kantak, 2016) and (2) the handedness consistency is unevenly distributed in the population toward a distinct right-hand skew. These two characteristics would fit the criterion of special or unusual quality needed for identifying a phylogenetic homology (Michel, 2013). Archeological evidence seems to support the idea that the right bias in human handedness is an evolutionary extension of a right bias in hominin handedness (cf., Uomini, 2009a, b, 2014). Whereas there is some evidence for a right-hand bias in great ape handedness (Hopkins et al., 2011), this bias does not exhibit the same kind of consistency across tasks. Moreover, there are groups of apes with a left-hand bias and some groups for which there is no evidence of a population bias (Uomini, 2009a). By contrast, cross-cultural research does not find any human group with more than 30% left-handers (Raymond and Pontier, 2004).

The Apprenticeship Complexity Theory (Högberg et al., 2015; Uomini, 2009b; Uomini and Lawson, 2017) proposes that as hominins began to manifest complex skills of tool use and manufacture, social learning became important for the transmission of these skills. A group-shared handedness biases would facilitate faster learning of such manual skills through imitation. From an ST perspective, the pressure to quickly and accurately learn tool use and manufacture early in development would likely favor those whose hand preference matched that of their "tutors." Unfortunately, the evidence for the importance of concordance in handedness for the acquisition of manual skills via observation is weak (Michel and Harkins, 1985; Uomini and Lawson, 2017). Moreover, this account provides no explanation for why left-handedness remains in all human groups.

It is unlikely that children are motivated to develop handedness but they do have immediate needs to manually engage with social companions and physical objects. Such interactions have functional demands that require reducing competition between hands in initiating action, reducing the decision time for hand selection for unimanual actions and for distribution of hand actions in complementary bimanual manipulation. These identify a function for handedness, but not for the population-level right bias. The right population bias may be an incidental consequence of a typical developmental "package" and there may be little or no "cost" for left- or ambihandedness. What may be a unique character for humans is how handedness is assembled during development. It is possible that hominins did not "need" to manifest a particular pattern (right handedness) for handedness.

5.1 DEVELOPMENT OF HUMAN HANDEDNESS DURING INFANCY

Early cellular events may have important effects on the development of asymmetries in the embryo. Before the revolution in examining the epigenome, Morgan (1977) argued that the spatial information in the oocyte may affect gene expression that can contribute to subsequent development of structural asymmetries as the asymmetries of the oocyte translate into the morphological asymmetries of the developing organism via differential growth. This could be the early developmental origin of all vertebrate lateral asymmetries of structure and function (Vallortigara et al., 2011). However, despite well-developed theories of oocytic asymmetries, there is no conclusive evidence to support the notion that early neural growth is a necessary condition for establishing the asymmetrical differences in neural processing involved in human hemispheric specialization of function and handedness.

For humans, it is likely that oocytic asymmetries coalesce with other fetal asymmetries and the asymmetrical prenatal environment to create prenatal asymmetries of structural development (Previc, 1991). The asymmetry of the uterus and the specific gravity of the fetus contribute to the fetus' predominant head-down position with the fetus typically facing mother's right side. Mother's bipedal locomotion produces asymmetrical vestibular stimulation of the otolith organs of the fetus to create different patterns of activation in the two hemispheres (Previc, 1991). This asymmetrical development of the otoliths means that unless the head is oriented to the right postnatally, the otoliths will be generating asymmetrical stimulation. Michel and Goodwin (1979) observed that position in utero (the typical "facing mother's right side" vs the much less frequent "facing mother's left side," as estimated during birth) predicted the direction (right and left, respectively) of the neonate's head orientation preference (HOP). The direction of the neonatal HOP predicts the infant's hand preference for acquiring objects up to 18 months of age (Michel and Harkins, 1986). Thus, there may be a prenatal influence on the early organization of postural asymmetries (perhaps, involving spinal lateral asymmetries of development, Ocklenburg et al., 2017) that affect infant hand use.

The differential sensitivity of the left and right otoliths activates the infant's neck muscles producing a neonatal supine HOP during the first 2–3 months of life (Gesell and Ames, 1947; Michel, 2002). This HOP places one hand in the infant's visual field more than the other, and it results in asymmetric activity of the hands and the consequent asymmetric proprioceptive feedback (Michel and Harkins, 1986). It is the hand on the infant's face side during HOP that becomes the preferred hand for initial reaching and object manipulation (Michel, 2002). Indeed, the direction of the infant's HOP was found to be predictive of right- and left-hand preferences at 10 years (Gesell and Ames, 1947). This early HOP induces differences in visual, haptic, and proprioceptive experiences which contribute to differences in the neuromotor control mechanisms, which, in turn, cascade (through continued use of the preferred hand) into distinct differences in neural circuitry between the left and right hemispheres of the brain (Pool et al., 2014; Serrien et al., 2006; Volkmann et al., 1997). As sensorimotor skills get continuously refined by proprioceptive, somatosensory, and other sensory experiences and feedback during early development, the neural control shifts from spinal circuits to brainstem to cortical circuits (Hopkins and Rönnqvist, 1998; Michel et al., 2013a).

The pelvic changes associated with hominin bipedal locomotion and upright posture likely made a shortened gestation period more prevalent. This, in turn, resulted in infants with less developed sensorimotor abilities that required maternal carrying and occasional resting on the ground. This early postural asymmetry, combined with increased time in supine positions as a neonate, may be the unique manner by which human handedness is assembled during development. Other primates do not exhibit such extensive bipedal locomotion during pregnancy, and the newborn is behaviorally much more precocial and is seldom supine. Thus, human-typical prenatal vestibular experience might play a key role in the formation of neonatal postural asymmetries, which are accentuated by the relative behavioral/postural incompetency of the young infant, resulting in more supine experience which, in turn, helps shape hand-use preferences and, perhaps, hemispheric asymmetries for cognitive processing (Michel et al., 2013a). Elevated visual and kinesthetic sensory feedback from the movement of the face–side hand likely establishes sensorimotor circuits in the nervous system that ensures more precise sensory control of face–side hand movements. Such circuits could also serve as the foundation for the development of other sensorimotor neural circuits that would contribute to the embodiment of various cognitive functions (Michel et al., 2016).

The early development of infant hand-use preferences suggests a progressive expansion from an initial preference to a wider range of increasingly complex manual skills (Michel, 2002; Michel et al., 2013b). Handedness for object manipulation is initially observed in a preference for reaching and subsequently for acquiring objects (Michel, 1983). These preferences then concatenate into the preferences for unimanual object manipulation (Campbell et al., 2015; Hinojosa et al., 2003) which, in their turn, influence hand preference for the later-developing role-differentiated bimanual manipulation (RDBM) skill (i.e., the two hands performing different but complementary manipulative movements on one or several objects). RDBM requires sophisticated bimanual coordination and considerable interhemispheric transfer of information (Babik and Michel, 2016a; Michel et al., 1985; Nelson et al., 2013). Eventually, manual preferences for RDBM form the foundation of handedness in artifact construction and tool use skills (Marcinowski et al., 2016; Vauclair, 1984), which involve higher-level cognitive skills such as imitation of complex actions, planning, decision making, and the ability to comprehend the spatial character of objects and situations.

Importantly, hand preference for later-emerging skills might also influence hand use for already established skills. Thus, an apparent decline in the hand-use preference for acquisition observed after 12 months (Ferre et al., 2010) coincides with the development of hand preference for later-developing RDBM skills. Perhaps, as the sensorimotor circuits for acquiring objects become more efficient, they get associated with circuits for RDBM (Michel et al., 1985). Thus, the nonpreferred hand could be employed to obtain the object so that the preferred hand could immediately initiate RDBM without the need to transfer the object between the hands (Michel, 2018b). Such bidirectional developmental transformations in how handedness are assembled during infancy likely produce the occasionally reported variability in longitudinal studies of handedness development.

Oddly (from an Evo–Devo perspective), the developmental trajectory of early handedness for acquiring objects appears to be unrelated to the trajectory for development of early postural control for sitting, crawling, and walking (Babik et al., 2014). Also, the trajectory for the development of general neuromotor control is unrelated to the development of infant hand preference for object acquisition (Campbell et al., 2018). Developmental trajectories of infant hand preferences for acquiring objects, for engaging in unimanual manipulation of objects, and for RDBM seem to relate to one another in a developmental cascade-like pattern (Babik and Michel, 2016a, b, c; Campbell et al., 2015). More research is needed to determine how the developmental trajectories of these different forms of infant hand preferences relate to handedness development and other forms of neuromotor development during childhood.

6 HANDEDNESS AND COGNITION

Hand preferences for manual actions reflect underlying lateralized difference in neural control (Pool et al., 2014), some of which may be shared with manual actions involved in gestural communication, which could link the development of handedness to the development of speech–sound gestures (cf., Arbib, 2006; Greenfield, 2006). Although there is some evidence of an association between handedness for object manipulation and that for gesture (e.g., Cochet, 2016), it is not reliably obtained and may depend on age, research design, and type of skills assessed (e.g., Cochet and Vauclair, 2010; Esseily et al., 2011). Indeed, Ocklenburg et al. (2014a, b) found evidence of some genetic and neural circuit associations between adult handedness and hemispheric lateralization for language, but these associations were weak, at best. Nevertheless, production of manual actions and production of speech both depend upon finely timed and appropriately ordered sequences of acts and the development of each could be facilitated by some shared neural circuits (Abbs and Grecco, 1983; Corballis, 2003).

Embodied cognition theory proposes that symbolic cognitive processes, such as abstract reasoning, concept formation, and language, derive from sensorimotor experiences during infancy that are mediated through alterations in brain structure/functioning (Anderson, 2003; Aziz-Zadeh et al., 2006; Barsalou, 2008; Boulenger et al., 2009). The differential proficiency of their preferred hand means that right- and left-handers receive different sensorimotor experiences, and ought to engage in correspondingly different neurocognitive processing (Michel et al., 2013a). Therefore, the development of handedness and its relation to the development of language and other cognitive abilities should be a good test of embodiment theory.

The early development of hand-use preference is associated with the more effective bimanual control while manipulating objects and the early development of the artifact construction skills (i.e., stacking blocks), both of which reflect and contribute to the development of knowledge of spatial relations (Marcinowski et al., 2016). Hand preference for object acquisition also facilitates the development of object storage skills (Kotwica et al., 2008), an ability considered to reflect the cognitive capabilities of “planning” and early symbolic knowledge (Bruner, 1973). Perhaps, more efficient performance of these manual skills would facilitate the development of higher-level cognitive abilities, such as understanding of spatial and temporal characteristics of objects and situations, comprehending relations between objects, imitation of complex actions, planning, decision making, and language development (Michel et al., 2013a). All these hypotheses need further investigation.

Early development of hand-use preferences seems to predict advances in toddler language skills (Nelson et al., 2014) and consistency of a hand preference across infancy (6–14 months) and toddlerhood (18–24 months) also predicts advances in language skills at the age of 3 years (Nelson et al., 2017). Previous research has shown that preschool design-copying skills are excellent predictors of middle school math, science, and reading achievement test scores (Cameron et al., 2012; Grissmer et al., 2010). Since design-copying skills represent visual-motor manual skills, Michel et al. (2013b) proposed that individuals with early hand-use preferences are likely to excel in copying designs compared to their peers without early hand-use preferences. If early hand-use preference is related to better design-copying skills, then different trajectories of hand-use preferences might represent different trajectories of neurobehavioral development highly relevant for the development of mathematical, scientific, and reading abilities.

Although atypical lateralization is not a sign of pathology, right hemisphere dominance, and more bilateral specialization for fine motor movements and language have been associated with different neurobehavioral dysfunctions (e.g., Illingworth and Bishop, 2009; Ribolsi et al., 2009; Whitehouse and Bishop, 2008). An Evo–Devo approach emphasizes that exploration of the origins of hemispheric specialization of function in human ontogeny is imperative for both understanding typical development and identifying factors that might shift hemispheric specialization and contribute to dysfunctional behavior. Therefore, understanding how handedness is acquired and maintained during the life span can provide insight into why it is often associated with neurobehavioral dysfunctions.

7 CONCLUSIONS

If EES and Evo–Devo are taken seriously when examining studies of handedness, then it is clear that too few studies have been designed to examine the homology of handedness, and the processes of its development or its relation to the developmental trajectories of cognitive functions. The underlying phylogenetic relation among current primates is too small a base upon which to propose notions about the evolution of handedness in primates. It is uncertain whether nonhuman primate handedness is homologous with human handedness (Michel, 2013). Primates homologously share two forelimbs; therefore, any population could show: no population bias, a left bias, or a right bias—there are no other options. Although the limbs are homologous (as demonstrated by careful analysis; see Shubin, 2008), it would be misleading to assume that primate handedness is homologous. It may be that primate handedness is not related by evolution, but rather has been constrained by developmental processes that are common among primates. However, the upright posture of hominims initiated the development of a population-level right-hand bias. Thus, natural selection may play little role in the origin and maintenance of the asymmetry.

Lateral asymmetries seem to be a deep homology throughout animals (vertebrate and invertebrate) that may have something to do with the evolution of multicellular organisms (which created the anterior–posterior and dorsal–ventral asymmetrical organizations; see Cartwright et al., 2004). Although most population biases in the lateral asymmetries of traits might depend in their initial developmental stages on some underlying lateralizing factors that would not address issues about the evolution of human handedness. Too often, it is assumed that the presence of handedness was guided by natural selection (which, according to EES, natural selection does not do) and therefore handedness must be adaptive to a specific environmental circumstance and its development must be genetically controlled. Because of the problems with these assumptions, we tried to set the record straight on what constitutes the study of evolution. We do need to have details about the developmental trajectories for handedness and for other abilities so that we can examine issues of heterochrony, heterotopy, heterometry, and heterotypy. This knowledge would add to our understanding of what is different across primates, mammals, etc., and provide insight into possible evolutionary scenarios. Moreover, understanding of these four issues would provide more insight into how those trait differences, which we identify as atypical, develop. More of this research needs to be done.

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SECTION

4

Cerebral lateralization and behavioral biases as a foundation for higher cognitive function

CHAPTER

A comparative perspective on lateral biases and social behavior

14

Gillian S. Forrester[*,1], **Brenda K. Todd**[†]

[*]*Department of Psychological Sciences, Birkbeck, University of London, London, United Kingdom*
[†]*Psychology Department, City, University of London, London, United Kingdom*
[1]*Corresponding author: Tel.: +44-7814704884, e-mail address: g.forrester@bbk.ac.uk*

Abstract

Cerebral lateralization and associated motor behaviors were historically thought to be characteristics unique to humans. Today, it is clear that these features are present and visible in other animal species. These shared attributes of brain and behavior suggest inheritance from a distant common ancestor. Population-level motor biases are likely to reflect an early evolutionary division of primary survival functions of the brain's left and right hemispheres. In modern humans, these features may provide a foundational platform for the development of higher cognitive functions, inextricably cementing the ties between the evolution and development of cognition. This chapter focuses on the links between a vertebrate-wide right hemisphere dominance for perceiving and producing social signals, left side motor biases (inclusive of visual field preferences), and the evolution and development of cognition in modern humans.

Keywords

Cerebral lateralization, Hand dominance, Social positioning, Social cognition, Left cradling bias, Autism

ABBREVIATIONS

LCB	left cradling bias
SDB	self-directed behaviors

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1 INTRODUCTION

1.1 CEREBRAL LATERALIZATION AND ASSOCIATED MOTOR BIASES

For all animals, motor behaviors are enacted as sequences of action units (Sommerville and Decety, 2006) to achieve biologically adaptive behaviors. In many vertebrates survival behaviors tend to be dominant on one side of the body, resulting from "*cerebral lateralization*" (Rogers and Andrew, 2002; Vallortigara and Rogers, 2005). In essence, cerebral lateralization refers to asymmetric contributions of the left and right hemispheres of the brain for experiencing the world around us. The nerve fibers of the motor cortices project to the opposite side of the body. Therefore, dominant hemisphere processes can manifest as contralateral motor behaviors (Hellige, 1993) and act as informative behavioral markers of brain organization and function (e.g., Toga and Thompson, 2003).

Many species have demonstrated right-biased motor actions for well-learned sequences of motor actions including fish and toads for prey capture (Alonso, 1998), birds for foraging and manipulating food items (Alonso, 1998), and birds (Rutledge and Hunt, 2003), monkeys (Westergaard and Suomi, 1996), and apes (Hopkins et al., 2011) for object manipulation. Additionally, disparate species have demonstrated left-biased eye preferences for predator monitoring and a rightward bias in predator escape behaviors for novel and urgent stimuli including birds (Franklin and Lima, 2001; Koboroff et al., 2008; Rogers, 2000), lizards (in the laboratory: Bonati et al., 2013; and in the wild: Martín et al., 2010), and toads (Lippolis et al., 2002).

These patterns of motor dominances suggest that early in our evolutionary history (e.g., 500 million years ago) the right hemisphere emerged as dominant for responding to novel, and/or threatening situations in the environment (e.g., predators) (e.g., Bonati et al., 2013; Franklin and Lima, 2001; Koboroff et al., 2008; Lippolis et al., 2002; Martín et al., 2010; Rogers, 2000; but see marsupials for evidence of reversed laterality, Giljov et al., 2015). On the other hand, if no urgent response was required, information passed to the left hemisphere, which in turn, emerged dominant for controlling routine and structured motor sequences. Routine motor sequences are found, for example, in the feeding behaviors of animals (e.g., Alonso, 1998; Hopkins et al., 2011; Rutledge and Hunt, 2003; Westergaard and Suomi, 1996).

It is believed that the asymmetric control of different domains was preserved throughout evolution because it has beneficial adaptive outcomes that increase the survival of the individual organism (MacNeilage et al., 2009; Rogers et al., 2013). Specifically, the dissociation of specialized processing of left and right hemispheres may increase neural efficiency by allowing different functions to operate in parallel, decreasing duplication of functioning across hemispheres, and eliminating simultaneous incompatible responses (Rogers, 2002; Vallortigara, 2000). In its simplest form we might think of the two hemispheres as working in tandem to provide an "*eat and not be eaten*" parallel processor.

1.2 CEREBRAL LATERALIZATION AS A FOUNDATION FOR HIGHER COGNITIVE FUNCTION

Placing human cognition within an evolutionary framework is important when considering the emergence of cognitive abilities because our modern sophisticated human abilities will likely be founded upon evolutionarily early vertebrate brain organization and function. Through natural selection, evolutionary innovations build on existing neural architecture. New functional components do not spontaneously emerge. Rather, the existing architecture is extended and/or modified (Finlay, 2007). As a result, sometimes we find that a system that we are using for one cognitive function hardly resembles the foundation components for which it was originally designed (e.g., Finlay, 2007). For example, a left hemisphere dominance for producing routine, goal-oriented sequences of motor actions may have been extended to support the syntactic structure underpinning language function (e.g., Greenfield, 1991). Conversely, a right hemisphere dominance originally designed for avoiding environmental threats may have been extended to support the sophisticated emotion processing present in modern human social cognition (e.g., Forrester et al., in press) (for a review, see Vallortigara et al., 2011).

The presence of lateralized motor function in humans and other animals provides a unique strategy to investigate the evolution and development of cognition within and between species under a common framework of a shared evolutionary history. Although ontogeny (the development of the individual) does not recapitulate phylogeny (the evolution of the species) in the literal sense (Ehrlich et al., 1974), during human development, higher cognitive abilities scaffold, build upon, and bootstrap early perceptual and motor capabilities, which are governed by cerebral lateralization of function (e.g., D'Souza and Karmiloff-Smith, 2011). In humans, we consider primary sensory and motor functions to represent the core building blocks of mental processing (Hommel et al., 2001) (Fig. 1).

This chapter focuses on the evolutionary and developmental links between social motor biases and higher cognitive process in humans and other species (e.g., Bradshaw and Rogers, 1993).

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2 LATERALIZED VISUAL BIASES

2.1 NONHUMAN ANIMALS

The ability to detect novel and/or threatening stimuli in the environment is paramount to the survival of an organism. The approaching and avoiding behaviors of animals with eyes positioned on the sides of their heads are preferentially monitored with the left eye. For example, a left-eye dominance for predator avoidance and species recognition has been reported in fish (De Santi et al., 2001), toads (Robins et al., 1998), lizards (Hews and Worthington, 2001), pigeons (Nagy et al., 2010), chicks (Vallortigara and Andrew, 1991), beluga whales (Karenina et al., 2010), and

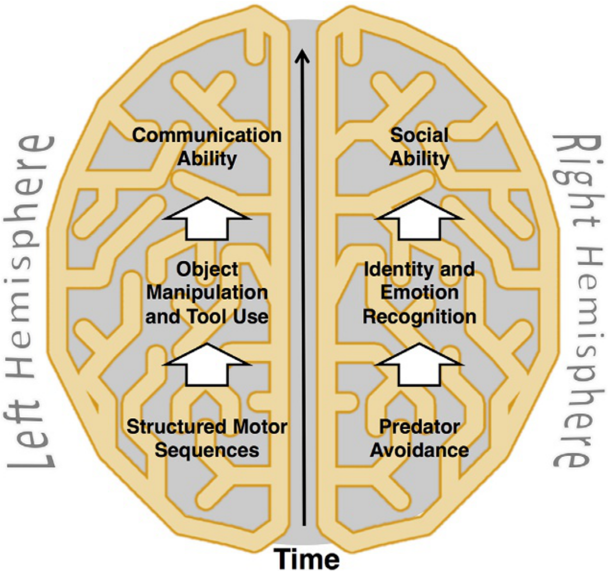

FIG. 1

Illustration of how primitive dominances of the *left* and *right* hemispheres can support the emergence of more abstract and sophisticated cognitive abilities across both evolutionary and developmental time.

Brain image adapted from cover photo.

striped-faced dunnart (Lippolis et al., 2005). These studies suggest a right-hemisphere dominance for perceiving and responding to social stimuli. In animals with forward-facing eyes, a similar pattern is found for the left visual field associated with social behaviors. For example, studies of nonhuman primates that consider spontaneous intraspecies encounters have reported a left visual field preference during aggressive encounters in gelada baboons (Casperd and Dunbar, 1996) and in a zoo-housed group of mangabeys (Baraud et al., 2009) during spontaneous approach behaviors, suggesting a right-hemisphere facilitation for rapid identification of facial expressions and predicting behaviors (Fernández-Carriba et al., 2002). These findings may reflect a common vertebrate characteristic of right-hemisphere dominance for processing social stimuli, for example, reacting to novel and dangerous stimuli in order to facilitate escape behavior and thus increase survival rates (e.g., Rogers et al., 2013; Rosa Salva et al., 2012).

The right-hemisphere bias is not, however, exclusive to novel and threatening social experiences. The requirement to effectively recognize and respond to aggressive facial expressions and postures may have facilitated a social recognition system for identifying conspecifics. Sheep (Peirce et al., 2000), dogs, rhesus monkeys (Guo et al., 2009), and chimpanzees (Morris and Hopkins, 1993) have all been reported to demonstrate a left gaze bias for conspecific face perception (e.g., looking time of centrally presented faces). Additionally, the left side of the face in nonhuman primates has been reported to display emotive expression earlier and more intensely than the right side of the face in chimpanzees (Fernández-Carriba et al., 2002), macaques (Hauser, 1993), marmosets (Hook-Costigan and Rogers, 1998), and baboons (Wallez and Vauclair, 2011).

2.2 HUMANS

Human and nonhuman primates share a common ancestor (Moyà-Solà et al., 1999), and given our understanding of evolutionary progression, we would anticipate a level of continuity in the neural architecture supporting cognitive function. However, despite the presumption that modern human social cognition is likely to have scaffolded upon evolutionarily early right-hemisphere dominance for approach–avoidance behaviors, theories regarding human social behavior have been developed in the isolation of other animals (but see Andrew, 1963; Leopold and Rhodes, 2010) (see also chapter "Sensorimotor lateralization scaffolds cognitive specialization" by Gonzalez et al.).

Human emotion processing is critical to broader social cognition and is considered in light of two primary human unique theories of cerebral lateralization. The right-hemisphere hypothesis (e.g., Borod et al., 1998; Campbell, 1982) proposes that the right hemisphere is solely responsible for the processing of emotion. Alternatively, the valence hypothesis (e.g., Davidson, 1995) purports that both the right and the left hemispheres are involved in affect processing, such that the left hemisphere is dominant for positive affect and the right hemisphere is dominant for negative affect. Although there is debate over which theory more accurately reflects human emotion processing, the right hemisphere and the valence theories share a common theme with evolutionary theories of vertebrate brain function (see Demaree et al., 2005; Harmon-Jones et al., 2010; Rutherford and Lindell, 2011). Specifically, they both support the notion that the right hemisphere is dominant for primary responses to novel and threatening stimuli. Regardless of the differences in the theoretical and methodological approaches to the study of humans compared with other animals, the patterns resulting from studies of human social behavior are relatively consistent with those from nonhuman animal studies. Numerous examples of human right-hemisphere dominance for emotion processing are found in behavioral, neuroimaging, and clinical studies.

Behavioral investigations indicate that humans exhibit a left gaze bias for face perception of other humans (Burt and Perrett, 1997; Kanwisher et al., 1998; for a review, see Demaree et al., 2005). Studies involving chimeric faces demonstrate that humans show a left visual field advantage for detecting emotional expressions (Bourne, 2008; Ley and Bryden, 1979). Moreover, a right-hemisphere advantage was found when participants were presented with identical face stimuli to each visual field. Participants reported a more salient experience when face stimuli were presented to the left visual field compared with the right visual field (Failla et al., 2003).

Functional imaging research also demonstrates right-hemisphere dominance for perceiving face identity and the valence of expression in humans (Gorno-Tempini et al., 2001). Moreover, neuroimaging evidence shows greater activation in the right than left hemisphere when processing the approach of strangers with directed gaze compared to averted gaze (Pelphrey et al., 2004). These findings suggest that not only is the identity and expressive valence of the approaching stranger processed, but also their gaze direction was found to carry information about their intended actions, thus allowing for the viewer to anticipate and respond accordingly.

The vast majority of clinical evidence from brain trauma studies supports a right-hemisphere dominance for human production and perception social stimuli (e.g., face identity and emotive expression). Reports of brain damage indicate that injury to the right, but not the left hemisphere, resulted in a deficit for processing affect (for a review of 23 clinical investigations, see Borod et al., 2002). Additional evidence of a right hemisphere dominance for face and emotion perception comes from split-brain patients (e.g., Benowitz et al., 1983) and patients undergoing intracartoid sodium amytal injections to anesthetize the right hemisphere demonstrate decreased ability to identify emotional expressions (Ahern et al., 1991).

The ability to produce and comprehend social signals is vital to the survival of all animals, including humans. Social signals convey information about the intended nature of future events (Andrew, 1963), allowing the perceiver to make appropriate social responses, whether, for example, to reciprocate a friendly smile or to escape to a safe location. Through the course of human evolution, responses to environmental threats may have laid a foundation for the emergence of negative emotions/affect in humans (Vallortigara et al., 2011) in addition to the more complex social abilities that we have for navigating our complex social environments. Little is known about how a right-hemisphere bias for processing social stimuli influences human behavior in the natural world. There is also a paucity of data relating to how humans operate as social animals outside of the laboratory. The remainder of this chapter focuses on what we do know about human social behavior in the real world, the involvement of the right hemisphere, and continuity with other nonhuman primates. Examples covered include hand dominance for social behavior, social positioning, and infant cradling.

3 LEFT LATERALIZED BIASES IN THE NATURAL WORLD

3.1 SOCIAL HAND DOMINANCE

Most investigations of cerebral lateralization and hand dominance focus on associations between left-hemisphere dominance and right-hand motor actions. Handedness, within the context of object manipulation, is generally established by the time neurotypical children start school (e.g., Gudmundsson, 1993; for a review, see Scharoun and Bryden, 2014) and is typically categorized via self-report as right, left, or mixed. However, more granular measures exist that evaluate the individual or population-level strength of manual dominance along a gradient that ranges from strongly left-handed to strongly right-handed (e.g., Beaton, 2003). To date, few reports focus on hand dominance outside of the context of object manipulation (e.g., tool use).

A significant group-level lateralized preference for left-handed self-scratching and for the fine manipulation of parts of the face was reported in rehabilitated orangutans (Rogers and Kaplan, 1996). While this may not seem particularly interesting in isolation, an increase in left-hand activity has also been reported in great apes for hand reaches to social partners and the self. During the monitoring of naturalistic unimanual hand actions, both gorillas and chimpanzees used the left hand preferentially when engaging in self-directed behaviors (SDBs) or hand actions directed toward social partners compared with hand actions directed toward objects (Forrester et al., 2011, 2012). Additionally, chimpanzees demonstrated a significant group bias for scratching the left side of their bodies, although there was no hand preference for this behavior (Hopkins et al., 2006). Hand dominance, within the context of social interaction or self-directed behaviors, may be under increased control of the right hemisphere in comparison to situations of object manipulation, where hand dominance is known to be preferentially directed by the left hemisphere (e.g., Forrester et al., 2012).

This working theory is supported by studies of typically right-handed humans who, during instances of high social arousal, have demonstrated increased right-hemisphere involvement and left-biased motor actions. For example, in a laboratory setting, right-handed adults responded more quickly to unexpected stimuli with their left hand compared with their right hand (e.g., Fox et al., 2006). Additionally, in a real-world setting, neurotypical children who demonstrated a right-hand bias for tool use also demonstrated a significant left-hand bias for SDBs during situations that involve high emotional arousal (e.g., stress) (Forrester et al., 2014b). In the study, the 4- and 5-year-old children were observed, while they participated in a battery of cognitive tasks. Unimanual hand reaches were evaluated only when both hands were free and the child directed a hand toward an object or the self. While the children displayed a significant right-hand bias for reaching toward objects, they demonstrated a left-hand bias for reaching toward themselves. In this case, SDBs may reflect an increased contribution of the right hemisphere during arousing situations.

Social hand dominance has even been reported in fetuses. Reissland et al. (2014) investigated the association between maternal stress and the fetal choice of hand preference for SDBs. In this study, SDBs were defined as touches to the face or head. They found that maternally reported stress levels were significantly related with fetus SDBs, such that higher reported maternal stress level was positively associated with the proportion of fetal left-handed SDBs.

The findings in this section demonstrate how a right-hemisphere bias for producing emotive behavior can be biased to the left side of the body and act as an indicator of arousal. Conversely, it is possible that in situations of heighted social arousal or raised levels of threat or stress, left-biased motor and visual behavior provide reliable markers of population-level brain organization and function. Nevertheless, it appears that the left manual bias, presumably underpinned by enhanced right hemisphere contributions, is present and visible early in life and impacted by both the prenatal and postnatal environments.

3.2 SOCIAL POSITIONING

The right-hemisphere bias, that appears to provide an advantage for monitoring the threat levels of social stimuli, also seems to be at play when primates navigate their environment. As such, a left visual field preference for detecting and monitoring the threat level of conspecific behavior was arguably co-opted to influence physical positioning during natural social behavior in primates. Although there is a paucity of naturalistic investigations in this area, one study in great apes revealed group-level biases in both gorillas and chimpanzees for keeping conspecifics situated to the left side of the viewer's body (Quaresmini et al., 2014).

Like great apes, physical positioning within a human social group appears to be influenced by cerebral lateralization for the processing of social stimuli. A recent study has provided the first evidence of lateralized social navigation in the natural behaviors of children. Extending upon animal studies of social positioning, the spontaneous navigational routes taken by children around adults, peers, and objects were observed during play (Forrester et al., 2014a). A focal individual was monitored for their directional path (left or right) around a stationary individual when there was equal opportunity to pass on either side. In the control condition, the focal individual was monitored for their directional path around an inanimate object (e.g., a bin) (see Fig. 2). Analyses revealed that children expressed a significant bias for choosing a right vs left navigational path around another human, whereas children expressed no lateral bias for navigating around an object.

A bias to keep conspecifics on the left side provides the navigator with an advantage for viewing the stationary individual within the left visual field. These findings are consistent with studies that have demonstrated a left eye or left visual field preference for monitoring conspecifics in nonprimate animals (e.g., chicks: Vallortigara et al., 2001, fish: Brown et al., 2007). The results are also consistent with investigations of social positioning in chimpanzees and gorillas (Quaresmini et al., 2014) and support the premise that the left visual field would provide the most efficient route to the right hemisphere for processing identity, intention, and angry or fearful facial expressions in order to expedite escape behaviors.

While navigating the social world as an individual, the right hemisphere may provide an advantage for monitoring individual identities and threat levels of conspecifics. However, motor biases that are aligned across a population can also contribute to cooperation between conspecifics (e.g., Ghirlanda et al., 2009). For example, when interacting with offspring, the same social positioning biases that provide an advantage for right-hemisphere processing can facilitate social monitoring based on identity, status, and facial expression (for a review, see Rosa Salva et al., 2012).

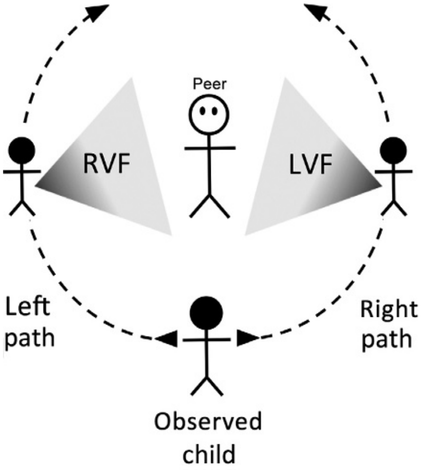

FIG. 2

Illustrations of two possible navigational paths (*left*, *right*) of the observed child around a stationary individual. The path chosen indicates the side of the body that will be presented to the stationary individual. A left navigational path presents the right side of the body and right visual field, while a right navigational path presents the left side of the body and the left visual field.

This figure is reprinted from Forrester, G.S., Crawley, M., Palmer, C., 2014. Social environment elicits lateralized navigational paths in two populations of typically developing children. Brain Cogn. 91, 21–17 with permission from Elsevier.

3.2.1 Comparative social positioning with offspring

At no time would it seem more critical for animals to engage social processes to maximize survival rates than during the rearing of offspring. Recent research has reported that a myriad of animal species possess social positioning biases during mother–infant interactions that favor the right hemisphere and the left eye (or visual field) (Giljov et al., 2018; Karenina et al., 2017). This orientation of social positioning, while nurturing offspring, has also been identified our closest living relatives including chimpanzees (Hopkins et al., 1993; Nishida, 1993), gorillas (Dienske et al., 1995; Manning et al., 1994), and bonobos (Hopkins and De Lathouwers, 2006). The behavior appears to be largely unaffected by setting (e.g., captive or wild rearing) (for a review, see Hopkins, 2004) and suggests that a left side cradling bias was most likely inherited from a common ancestor of great apes and humans (Manning et al., 1994). A left side cradling bias is less evident across New and Old World monkeys (e.g., Regaiolli et al., 2018); however, some studies do not distinguish between comfort holding and nursing, which may impact upon resulting patterns of behavior. It has recently been reported that species as diverse as marine mammals and terrestrial nonprimate mammals adopt mother–baby resting positions with significant population-level side biases. Both walrus and Indian flying fox mother–offspring dyads assume a physical orientation that provides an advantage for the left visual fields for both members of the dyad (Giljov et al., 2018). These examples of population biases across diverse and distant species may represent behaviors akin to human infant cradling and support an evolutionary continuum of right-hemisphere dominance for efficient production and perception of social stimuli that dates back long before a common ancestor of great apes and humans.

Existing evidence from human studies comes mainly from cradling behaviors of parents of newborn infants and young children. Cradling bias is typically measured by considering the ventral position of the infant with a focus on the position of the infant's head in relation to the midline of the mother's chest. When the infant's head is orientated to the left of the mother's midline (regardless of the torso and limbs), the bout is recorded as left-sided (e.g., Manning and Chamberlain, 1990). Like great apes, human mothers and fathers prefer to position their offspring on the left side of their bodies (Scola, 2009; Scola and Vauclair, 2010a,b). Naturalistic field observations of infant holding are comparatively rare for humans and generally relate to infant transport rather than cradling. Nevertheless, Saling and Cooke (1984) found a significant left-side bias during infant transport when midline holds (both ventral and dorsal) were excluded. The same was true when Sri Lankan women were observed carrying young children in a variety of contexts and locations (Bruser, 1981). Moreover, the positioning is not always the decision of the mother. Even when carried in back packs, young infants in Dakar showed a left, rather than right, head placement when aged under, but not over, 1 year (Lockard et al., 1979), suggesting that social positions are biased to favor the right hemisphere for both individual and dyadic benefit.

3.2.2 The human left cradling bias

At the population level, approximately 70% of human mothers prefer to cradle their infants on the left side of their own bodies. The left cradling bias (LCB) appears robust across baby positioning (e.g., lateral, upright) (e.g., Bourne and Todd, 2004; Donnot, 2007; Hopkins, 2004; Matheson and Turnbull, 1998; Reissland, 2000; Reissland et al., 2009; Salk, 1973; Sieratzki and Woll, 2002, 2004; Todd and Banerjee, 2016; Turnbull and Bryson, 2001; Turnbull et al., 2001; Vauclair and Donnot, 2005), mother's handedness (Previc, 1991; Sieratzki and Woll, 1996, 2002; Vauclair and Donnot, 2005; but see Van der Meer and Husby, 2006), and mother's culture (Richards and Finger, 1975).

The causal nature of the LCB is debated via a variety of theoretical propositions. Explanations of the left-holding bias include (1) facilitating infant access to the soothing sound of the holder's heartbeat (Salk, 1960), (2) responding to the infant's own bias to position the head on the right (Bundy, 1979; Ginsburg et al., 1979), and (3) freeing the holder's dominant hand to perform other tasks (Van der Meer and Husby, 2006). The first two of these theories have been challenged by findings that the left-side preference remains when the infant is held away from the torso and by a lack of correlation between holding side and immediate infant head position (Scola and Vauclair, 2010b; Todd and Banerjee, 2016). There is evidence that infants are held in the contralateral arm when the dominant hand is in use (Van der Meer and Husby, 2006) yet the preference remains in situations where this demand does not apply (Todd and Banerjee, 2016) and a left holding bias has been found in some groups of left-handed individuals (e.g., Bogren, 1984; Donnot, 2007; Salk, 1960) but not others (Donnot, 2007; Scola and Vauclair, 2010b). The most promising theory to date relies on cerebral lateralization of function. The physical positioning is thought to facilitate the processing of social–emotional stimuli (e.g., gaze, facial expression) by establishing a direct route to the right hemisphere (for a review, see Scola and Vauclair, 2010b). This theory is further supported by a study investigating lateral biases in adult embracing, where women demonstrated a leftward preference for embracing a social partner that was unrelated to handedness (Turnbull et al., 1995). Moreover, recent investigations into kissing (Karim et al., 2017) and embracing (Packheiser et al., 2018) behaviors also demonstrated a bias to engage with the left side of the face or body that was unrelated to handedness.

The LCB facilitates a mutual (mother–baby) right-hemisphere advantage for producing and perceiving social signals across modalities, including visual, auditory, and tactile social stimuli (Scola and Vauclair, 2010b; Sieratzki and Woll, 2002). As the mother holds to the left, the infant is provided with the more expressive side of the mother's face (Vauclair and Donnot, 2005), which may serve to promote bonding and social development (Huggenberger et al., 2009). However, a recent longitudinal investigation found a left-side bias for infant cradling may be time sensitive. Todd and Banerjee (2016) reported that a LCB decreased below significance by 12 weeks of age. A similar left-side bias was reported in rhesus monkeys, where infants demonstrated a preference for the mother's left nipple; as in humans, the bias was only significant during the first 3 weeks of life and decreased in subsequent weeks (Tomaszycki et al., 1998). It is possible that in both human and nonhuman primates, a left-side positioning of the infant against the mother's body facilitates maternal monitoring of the infant state, while the infant is most vulnerable (for a review, see Todd and Banerjee, 2016).

Evidence of an LCB in men has been inconsistent (Harris et al., 2006; Manning, 1991; Turnbull and Lucas, 1991). Some investigations used a doll as stimulus (Bundy, 1979) or asked participants to imagine feeding a baby in the absence of any stimulus (Harris et al., 2000; Nakamichi and Takeda, 1995), making it difficult to draw any robust conclusions. Some studies have reported that in men, the LCB is isolated to fathers (Bogren, 1984; Dagenbach et al., 1988; Scola and Vauclair, 2010b) and men with experience of infant care (De Château, 1983). These findings suggest that sex differences may be underpinned by developmental and/or experiential component(s) to the LCB. To date, it is unclear if the LCB population strength differences found in men and women are mediated by experience or innate predisposition, nor do we understand what specific characteristics of a stimulus elicit the LCB to emerge in both men and women. Nevertheless, evolutionary explanations of LCB would support its appearance early in ontogeny among both males and females without prior experience of holding infants (e.g., see Todd and Banerjee, 2016).

Further research of the LCB has been conducted with child participants, using dolls as social stimuli. For example, evidence from cradling studies of girls and boys showed that a propensity to cradle left is present and visible prior to parenthood. Girls and boys (aged 2–16 years) demonstrated an LCB using a doll (Pileggi et al., 2015; Souza-Godeli, 1996). However, no lateral preferences in doll holding were found among girls (aged 2–5 years) (De Château and Andersson, 1976; Manning and Chamberlain, 1991) or in boys younger than 16 years of age (De Château and Andersson, 1976). Disparity in the rates of left holding in child and youth studies may be explained by variation in stimuli size and procedures. Additionally some younger participants were reported to have had difficulty in following task instructions (De Château and Andersson, 1976; Souza-Godeli, 1996).

Across cultures, gender-specific socialization and family experience might impact the presence of the LCB in young male and female children. In Western countries, girls are preferentially socialized to interact with dolls from a young age (Todd et al., 2018) and may gain formative experience through these interactions. Additionally, experience of observing the care of a younger sibling (as measured by birth order) may provide important experiences triggering or influencing the strength or propensity for a cradling bias in children. These factors and how they might contribute to a population-level LCB have yet to be addressed in a systematic fashion.

4 LATERAL BIASES AND COGNITION

While we are not suggesting a direct correlation between phylogeny and ontogeny (e.g., Gould, 1977), intact motor capabilities are considered to be a key precursor to typical cognition across both evolutionary and developmental trajectories. For example, while evolutionary psychology provides evidence for a common cognitive system underpinning goal-oriented object manipulation and language (e.g., Higuchi et al., 2009), developmental psychology suggests that structured motor actions that underlie object manipulation and gesture set the stage for the acquisition of symbolic systems required for typical language acquisition (Iverson, 2010). Thus, for example, typical language development requires the mastering of fine motor coordination prior to language production. Any anomalies present in early motor processes, due to genetic or experiential factors, will cascade to influence emerging higher cognitive functions (e.g., Karmiloff-Smith, 2009; see Section 5). As such, there is an inextricable link between motor action and cognitive outcomes.

4.1 LATERAL BIASES IN EARLY SOCIAL DEVELOPMENT

One might predict that newborns would not benefit from early exposure to social stimuli received through cradling positions in the first days and weeks of life, due to their underdeveloped sensory and motor systems. However, brain-imaging studies suggest that neonates possess face-sensitive subcortical neural regions (Umiltà et al., 1996), associated with an evolutionarily early predisposition to respond to stimuli that are comprised of the most basic face components representing the eyes, nose, and head boundary (Johnson et al., 2015). Early social development research also suggests that even though neonates have underdeveloped sensory processing channels (Simion et al., 2001), faces are still salient stimuli from birth (e.g., Farroni et al., 2005) and newborns preferentially attend to patterns that contain the basic configuration of high-contrast areas of a face (e.g., Johnson, 2007). Moreover, infants tested at birth demonstrate a preference for faces above other types of stimuli (Bower, 2001; Cassia et al., 2008; Goren et al., 1975; Leppanen et al., 2007; Simion et al., 2001; Umiltà et al., 1996; Valenza et al., 2006). In fact, babies might already be sensitive to face stimuli before birth. New evidence suggests that basic visual face-orienting abilities are in place prenatally as early as 30 weeks' gestation (Reid et al., 2017). Using 4D ultrasound technology to evaluate fetal head turns, Reid and colleagues projected face-like stimuli through the mother's uterine wall. They found that like newborn infants, neonates were more likely to engage with upright face-like stimuli compared with the same inverted stimuli, suggesting that a social-orienting mechanism sensitive to face-like stimuli precedes birth (Reid et al., 2017). These early behavioral and neural attributes coupled with a reflexive rightward head-turning bias (in the final weeks of gestation through the first 6 months after birth, Güntürkün, 2003) and a mother's inclination to exhibit an LCB create ideal conditions for both the infant's survival and development of a social brain.

4.2 MOTOR BIASES AS A MARKER OF COGNITIVE ABILITY

Associations are regularly drawn between right-handedness and the cognitive domain of language, dominant within the left hemisphere (Hervé et al., 2006). In this example, hand dominance is thought to reflect the strength of left cerebral lateralization for the structured motor sequencing that underpins language processing (e.g., Toga and Thompson, 2003), whereby early and strong handedness is associated with early and typical language development (e.g., Leask and Crow, 2001; Nelson et al., 2013, 2017). Specifically, the development of hand dominance in children has been linked with the successful hemispheric specialization for language. Thus, by proxy, the manual motor bias serves as a marker of brain organization and also as a marker of cognitive ability (see chapter "Evolution and development of handedness: An evo–devo approach" by Michel et al.).

The association between right-hemisphere dominance for social–emotional processing and left motor biases has yet to be explored within the scope of social cognitive ability. Understanding the links between motor biases, brain organization, and cognitive ability has the capability to yield significant advances in the areas of developmental psychology and clinical aspects of diagnosis and therapeutic interventions. There is a paucity of data linking cradling side with cognitive outcomes. Here we discuss the findings of the two studies that address this area in part.

Vervloed et al. (2011) revealed differences in the social perceptual abilities of adults who (as babies) were held with a left arm vs a right arm preference. Based on family photos, this retrospective investigation found that adults who had been held with an LCB developed a left visual field (right hemisphere) bias for faces on chimeric face tests. This is the expected bias for the majority of the typically developed population. In turn, this exposes the most expressive side of the mother's face to the infant. Adults who had been reared with a right arm cradling bias, however, did not develop any visual field bias for faces. One consideration relevant to these findings is that faces of right cradlers were less visible from the "infant viewpoint" compared to those of left cradlers (Hendriks et al., 2011). What is more interesting is that not only did the right-side cradlers not demonstrate the expected left visual field/right-hemisphere bias for chimeric faces, social cognitive abilities differed between the two groups. Although all participants could effectively identify the identity and emotional expression of face stimuli, those who had been cradled on the left were significantly faster at doing so.

These findings suggest that there is significant variation in the social ability levels of the typically developed population and that adults who as babies were cradled on the left may develop enhanced right hemisphere bias for processing social emotional stimuli, compared with their right-cradled counterparts. However, at this time it is impossible to reconcile whether right-cradled babies were predisposed to decreased cerebral lateralization through heritability (for a genetic account of cradling, see Manning and Denman, 1994) or if the cradling side influenced development. While bearing in mind the findings discussed earlier, there is currently no evidence suggesting an association between the side of the mother's body on which babies were cradled during the early weeks of infancy and the level of subsequent cognitive development. Moreover, population patterns do not necessarily translate to the individual; one cannot be certain of an individual's brain organization based on motor biases. Nevertheless, the findings suggest that experiential factors have the capacity to influence the development of cerebral lateralization of social cognitive function.

A more recent investigation considered the relationship between cradling side biases, hand dominance, and sociocommunicative abilities in young children (Forrester et al., in press). This research attempted to address some gaps in the literature regarding motor biases, their relationship with cognition (e.g., Lindell and Hudry, 2013), and the factors required to elicit the LCB. Findings from the study, conducted on a relatively large population of 4- and 5-year old neurotypical children ($N = 98$), showed a population-level LCB for holding an infant human doll that was not influenced by hand dominance, sex, age, or experience of having a younger sibling. Moreover, a proto-face pillow's schematic face symbol was sufficient to elicit a population-level LCB, whereas the no-face pillow elicited no cradling side bias (see Fig. 3A), suggesting that an LCB requires minimal triggering. However, an infant primate doll elicited a population-level right-side cradling bias, which may have been induced by stress due to the novelty of the stimulus (see Fig. 3).

Previous studies have noted that mothers who held their babies on the right side of their bodies reported higher stress levels than those who held their babies with an LCB (Reissland et al., 2009; Vauclair and Scola, 2009), which may be the result of an "inaction–withdrawal" response (Davidson et al., 1990; Harris, 2010). This response may be analogous to the threat avoidance behavior, known to favor the left eye or left visual field (in animals with forward facing eyes) and the right hemisphere

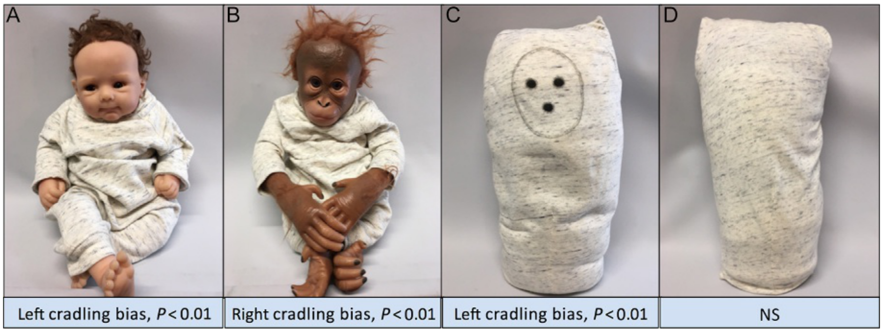

FIG. 3

Illustrations of the cradling stimuli used by Forrester et al. (in press) (A) infant human doll held with a significant left cradling bias, (B) infant primate doll held with a significant right cradling bias, (C) proto-face pillow held with a significant left cradling bias, and (D) no-face pillow held with no side bias. The proto-face pillow was created based on schematic face stimuli (Johnson et al., 2015).

This figure is reprinted from Forrester, G.S., Davis, R., Mareschal, D., Malatesta, G., Todd, B.K., in press. The left cradling bias: an evolutionary facilitator of social cognition? Cortex, https://doi.org/10.1016/j.cortex.2018.05.011 with permission from Elsevier.

across a disparate range of vertebrate species during heightened arousal associated with negative affect (e.g., MacNeilage et al., 2009). The findings suggest that the LCB is present and visible early in development and is likely to represent evolutionarily old domain-specific brain organization and function.

Most recently, Forrester et al. (in press) found a significant relationship between cradling side and social ability. Compared with children who exhibited a right cradling bias, children with an LCB scored significantly higher on a social ability survey (completed by their teacher). The findings suggest that individuals with a predisposition to use the LVF to process social stimuli may benefit from enhanced social abilities compared to their right cradling counterparts. In this study, children who cradled on the left or the right were all from a neurotypical population. As such, there are likely to be multiple and varied social developmental trajectories associated with typical cognitive development. The implementation of longitudinal investigations to map the development of motor profiles and their association with cognitive abilities may offer a valuable method for predicting neurotypicality and identifying children at risk for nonneurotypicality.

5 DISRUPTED MOTOR BIASES AND SOCIAL COGNITION

The behavioral biases discussed within this chapter have thus far focused on population-level patterns in healthy populations. Although it is clear that a small but significant minority (e.g., 10%) of the healthy population demonstrate reversed behavioral biases (e.g., left-handedness) (e.g., Knecht et al., 2000), in other cases, a decrease in behavioral biases has been associated with decreased cognitive performance and neurodevelopmental conditions. Here we present the available data of visual and motor biases associated with social stimuli from cases of: deprivation, maternal stress, and/or depression and autism.

5.1 DEPRIVATION

Nonhuman primates and other mammals suffer from care deprivation and adverse events experienced early in life, which results in enhanced stress responsiveness, susceptibility to psychopathology and difficulty in relating to conspecifics (Cirulli et al., 2009). However, such studies generally refer to absence of maternal care or peer-rearing rather than variations in the quality of maternal care.

In humans, the experience of maltreatment in infancy and childhood has been associated with difficulties in the expression, recognition, understanding, and communication of emotion (Curtis and Cicchetti, 2007). Moreover, early trauma, including neglect, emotional abuse, and physical abuse, can affect the development of the right hemisphere (Schore, 2003). Such developmental insult can result in long-term consequences including reduced right hemisphere volume and critical deficits in reception and expression of facial expressions, communication of emotional states, exhibiting empathy and self-reflection, and regulating affective states (Schore, 2003).

5.2 STRESS AND DEPRESSION

Social development of an infant relies on dynamic dyadic coordinated interactions. Maternal depression may affect emotional development; for example, 3- to 6-month-old infants of depressed mothers were less likely to look at the facial expressions of their mothers or a stranger during peek-a-boo games. Additionally, they exhibited less positive, more negative emotions, greater relative right frontal EEG asymmetry, and elevated cortisol levels compared with infants of nondepressed mothers (Field, 2007).

In studies of cradling behavior, mothers who held their infants on the right side reported higher stress levels than those holding on the left (Reissland et al., 2009; Vauclair and Scola, 2009). The immediate and temporary circumstantial effect of stress is also associated with a reversal of the LCB. For example, women who participated a bilateral cold pressor task, which significantly increased their blood pressure and heart rate, were more likely to hold a baby doll on the right than control participants (Suter et al., 2007). A decline in, or reversal of, the typical LCB is evidenced in adults undergoing temporary or prolonged stress and may reflect an “inaction–withdrawal” response rather than approach and engagement (e.g., Harris, 2010). Holding on the right side during episodes of high arousal may alleviate over-stimulation of the dominant social processing areas of the holder’s right hemisphere.

In our own study of motor biases and social behavior in young children we introduced an infant primate doll (orangutan) in an attempt to decrease gendered social biases young boys and girls for engaging with test stimuli (Forrester et al., in press). However, in direct contrast to our prediction (that children would hold the primate doll with a left-side bias), children held the primate doll significantly more often in a right vs left cradling position. Cradling the unfamiliar primate doll might have aroused mild anxiety in our young participants. Indeed, some boys and girls indicated that they had found the primate doll "scary." Several children were reluctant or even refused to pick it up, a response not found in the "baby doll" or "pillow" conditions. While we did not envisage that the commercially available primate doll would appear novel or threatening, it was perhaps unexpected in the experimental situation and therefore increased arousal levels in these children. Consequently, stress may have been responsible for the reversal of the LCB in this condition (Forrester et al., in press).

5.3 AUTISM

Individuals diagnosed with autistic spectrum disorders (ASDs) offer a unique opportunity to investigate the associations between motor biases and cognitive ability. Individuals with autism exhibit a decrease in functional brain lateralization and associated contralateral motor biases compared with the neurotypical population. For example, neuroimaging research demonstrates that individuals with autism show face-processing deficits associated with decreased activation of the right fusiform gyrus (for a review, see Curby et al., 2009) and the absence of a left visual field bias for face faces in infants (Dundas et al., 2012). The condition of ASD has been classed as one of atypical connectivity (Gershwind and Levvitt, 2007; for a review of different theories involving disrupted cerebral lateralization see chapter "Atypical structural and functional motor networks in autism" by Floris and Howells).

Additional evidence of anomalous cerebral lateralization comes from an investigation of social hand dominance from children with and without autism (Forrester et al., 2014b). In this behavioral study, SDBs were monitored as children participated in a battery of cognitive tests used to diagnose autism (Autism Diagnostic Observation Scales: Lord et al., 2000). An SDB was classified as any manual action where the child directed their hand to touch or manipulate their own body, face, hair, or clothes. Children who were categorized as "right-handed" by their parents and teachers for tool use activities were all significantly left-handed for SDBs while children diagnosed with autism (also categorized as right-handed by parents and teachers) presented no hand preference for either context. The findings suggest that children with autism have less distinct cerebral lateralization compared with neurotypical children manifesting as a decrease in motor biases, including those within a social context (e.g., Forrester et al., 2014b).

Several recent studies of cradling have also reported a decrease, absence, or reversal of the LCB in individuals with autism. For example, Fleva and Khan (2015) looked the cradling behaviors of typically developed adults who scored high on autistic traits and found that these individuals demonstrated reduced tendency to cradle on the left compared to participants who scored within the normal range on autistic traits. Additionally, Pileggi et al. (2013) investigated cradling behaviors in children with autism. They found that unlike neurotypical children who demonstrated an LCB, children with autism exhibited no preference for cradling side. A follow-up study evaluated the impact of intelligence and executive function measures on cradling bias (Pileggi et al., 2015). Ninety-three children aged 5–15 years where identified as: neurotypical, intellectually disabled, or autistic. While both intellectually disabled and neurotypical children exhibited an LCB, no such preference was found in the ASD group. The results suggest that disrupted cerebral lateralization is present and visible early in development, manifesting as weakened or absent motor biases. As such, motor behavior acts as a useful behavioral marker of cognitive development.

We have yet to fully understand the relationship between behavioral biases and cognitive ability. Going forward, we need to consider the developmental trajectory of these characteristics to gain a better perspective on what longitudinal profiles result in typical and atypical cognitive outcomes. Of course there are some limitations to this approach. The investigations highlighted within this chapter indicate that lateralized motor actions reveal valuable information about brain organization and function. However, these findings should be treated with some caution, as cerebral lateralization of function is never solely processed by one hemisphere. For instance, studies of social perception in monkeys (e.g., Pinsk et al., 2005), dogs (Guo et al., 2009), and sheep (Peirce et al., 2000) also indicate small contributions from the left hemisphere. Indeed, in humans, cerebral lateralization refers only to dominances and not absolute domain-specific processing in one hemisphere. Thus, there are limitations to the extent to which we can attribute a single function to a single hemisphere. Nevertheless, motor biases tend to be robust across disparate methodologies, further investigations of the patterns inherent in these context-specific behavioral biases (e.g., social interaction, object manipulation) and their associations with cognitive ability may be key to a better understanding how cognitive abilities emerge and contribute to cognitive ability different populations.

6 CONCLUSIONS

The early delineation of hemisphere dominances in our vertebrate ancestors may have served to carry out adaptive survival strategies in parallel. Good delineation of function across the hemispheres associated with efficient neural organization is resulted in effective behavioral responses and better survival rates of the individual (e.g., fitness) (Vallortigara and Rogers, 2005). Motor dominance serves as a valuable and informative behavioral marker of brain organization (e.g., MacNeilage et al., 2009) and affords insight into how primary motor systems may have evolved in our ancestor and how they still develop in modern human infants to support higher cognitive function.

Although traditionally, motor and sensory behavior was investigated in isolation of higher cognitive functions (e.g., social and communication abilities), we now understand that these behaviors critically underpin the development of all higher cognitive functions, and therefore should be treated as one component of a "dynamic systems framework" (Whyatt and Craig, 2012). In this chapter, we touch only on tip of the proverbial iceberg relating to possible links between motor biases, brain organization, and cognitive function. These associations are not likely to be isolated to visual fields and manual dominances, but are also present and detectable across modalities as suggested, for example, in studies of tactile interaction (e.g., embracing: Packheiser et al., 2018) and audition (e.g., prosody: Reissland, 2000).

Placing human behavior within an evolutionary framework provides a window not only to view modern cognitive abilities within the landscape of an evolutionary continuum but also to contemplate the developmental associations between behavior, cognition, neuropathology, and prognosis. Via this approach we may reveal fresh avenues for exploring alternative and complementary diagnostic and intervention practices.

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FURTHER READING

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CHAPTER

15

Sensorimotor lateralization scaffolds cognitive specialization

Claudia L.R. Gonzalez[*,†,1], **Nicole A. van Rootselaar**[*,†], **Robbin L. Gibb**[†]

*The Brain in Action Laboratory, Department of Kinesiology, University of Lethbridge,
Lethbridge, AB, Canada

†Department of Neuroscience, Canadian Centre for Behavioral Neuroscience,
University of Lethbridge, Lethbridge, AB, Canada

[1]Corresponding author: Tel.: +1-403-329-2147; Fax: +1-403-380-1839,
e-mail address: claudia.gonzalez@uleth.ca

Abstract

In this chapter, we review hemispheric differences for sensorimotor function and cognitive abilities. Specifically, we examine the left-hemisphere specialization for visuomotor control and its interplay with language, executive function, and musical training. Similarly, we discuss right-hemisphere lateralization for haptic processing and its relationship to spatial and numerical processing. We propose that cerebral lateralization for sensorimotor functions served as a foundation for the development of higher cognitive abilities and their hemispheric functional specialization. We further suggest that sensorimotor and cognitive functions are inextricably linked. Based on the studies discussed in this chapter our view is that sensorimotor control serves as a loom upon which the fibers of language, executive function, spatial, and numerical processing are woven together to create the fabric of cognition.

Keywords

Left hemisphere, Right hemisphere, Haptics, Visuomotor, Grasping, Speech, Executive function, Spatial abilities, Musical training, Numerical processing

1 INTRODUCTION

One of the oldest and most intriguing questions in behavioral neuroscience relates to the nature of localization of function, with the extreme case being the hemispheric lateralization. In 2018, we know that the neural processes underlying motor control, language, haptic processing, and spatial abilities are lateralized either to the left or right hemisphere, but how and why these functions are lateralized remains a matter of scientific inquiry. Indeed, we still do not know exactly *what* is lateralized, nor how lateralized functions relate more generally to sensory inputs (e.g., visual vs haptic) or cognition.

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Because brain lateralization is conserved across the animal kingdom, the left/right differences must provide an important advantage for the individual. A prevailing thought is that lateralization makes efficient use of brain tissue and allows for increased neural capacity while avoiding unnecessary duplication (Gunturkun and Ocklenburg, 2017; Vallortigara and Rogers, 2005). Given its ubiquity, functional lateralization has been extensively studied as distinct elements of behavior. Two unequivocal examples are the specialization of the left hemisphere for language and the right hemisphere for spatial processing. As we write this chapter, we resonate with the proposal put forward by Koziol et al. (2012) that studying brain and behavior in a compartmentalized fashion detracts from the fact that the brain works as an "integrated whole." We will come back to this idea at the end of the chapter, but in the following sections we draw parallels between sensorimotor and cognitive abilities as discrete functions localized to specific regions of the brain.

Because sensorimotor functions are lateralized, our proposal is that this lateralization served as a platform for the later development of cognitive specializations. It has been argued that every psychological construct (e.g., language, executive function, etc.) derives from sensorimotor experiences (Pezzulo, 2011). This is the basis of the embodied cognition theory, which proposes a relationship between sensorimotor, cognitive, and affective neurological processes (Shapiro, 2007). This theory—despite its criticisms (e.g., Goldinger et al., 2016)—has brought the sensorimotor system back to "front and center" in the field of human cognition.

In this chapter, we highlight the lateralization of the sensorimotor system and its interplay with language, executive function, music, spatial, and numerical processing. None of these sections is intended to be an exhaustive review of the literature, but rather provides the reader with a taste of the many studies that have examined these relationships.

2 CEREBRAL LATERALIZATION FOR VISUOMOTOR CONTROL (LEFT HEMISPHERE)

2.1 DEFINING "HANDEDNESS"

One of the most salient correlates of cerebral asymmetry is the expression of population-level right-handedness. Ninety percent of the human population self-identify as right-handed, preferring to use this hand for numerous activities such as grasping, writing, and using tools. It is important to acknowledge that handedness is a reliable predictor or hemispheric lateralization of function in right-handed individuals. Right-hand preference for manual actions develops early. Fetuses prefer their right hand for thumb-sucking as early as 15 weeks gestation (Hepper et al., 1998), and this preference is strongly correlated with right-handedness in adolescence (Hepper et al., 2005). Right-hand preference in infants is also well documented (Nelson et al., 2013; Sacrey et al., 2013), although some studies have shown that this preference is not consistent until 4 years of age (Schneiberg et al., 2002).

We have argued that the nature of the task should be considered when measuring hand use in children (Sacrey et al., 2013). We showed that 3-year-old children display a robust right-hand preference when picking up small food items to bring to the mouth, but no hand preference when picking up similar sized and colored objects for construction (i.e., building blocks; Sacrey et al., 2013). We expanded on this finding by conducting a comprehensive examination of hand preference for grasp-to-eat and grasp-to-construct in participants who ranged from 2 to 90 years of age. The results showed a right-hand preference for both actions, but this preference was greater for the grasp-to-eat action across all ages (Gonzalez et al., 2015). This finding suggests two things; first, that there is a left-hemisphere specialization for the visual control of reach-to-grasp actions, and second, that similar actions (reach-to-grasp) with unique end goals (eat vs construct) make use of distinct networks with different degrees of lateralization. This is important because checklists (e.g., handedness questionnaires) on the basis of which handedness is usually determined do not consider the end goal of the movement, but only the hand preference for different tasks.

On this note, we have recently conducted a study designed to investigate the usefulness of handedness questionnaires (Flindall and Gonzalez, in press). We were particularly interested to know if self-reported handedness correlates with actual hand preference for manual action (grasping). The main finding was that reported handedness was not useful in predicting actual hand preference for grasping. In fact, we found that hand preference in the self-reported inventory showed limited test–retest reliability across a short (2-week) interval. Clearly, the common understanding of what handedness is deserves focused rethinking (see chapter "A review of performance asymmetries in hand skill in nonhuman primates with a special emphasis on chimpanzees" by Hopkins for a discussion of this issue in nonhuman primates).

2.2 BEHAVIORAL DISTINCTIONS ACCORDING TO TASK AND ACTOR INTENT

Returning to functional specialization for visuomotor control, in his doctoral thesis Woodworth (1899) noted an advantage of faster movement times and greater precision of the right hand during pointing movements, even among left-handers. This observation led him to propose that the right hand was guided by "a superior neural motor center." More recently, numerous studies examining the kinematics of left- and right-handed pointing have supported this early observation of a right-hand advantage for this type of movement. Pointing is executed in less time, with higher peak velocities, and with greater end point accuracy (Barthélémy and Boulinguez, 2002; Carnahan, 1998).

Manual asymmetries for grasping movements have been more difficult to demonstrate which has led some researchers to speculate that the differences are minimal (Flindall et al., 2014; Grosskopf and Kuhtz-Buschbeck, 2006; Tretriluxana et al., 2008). This is a difficult finding to reconcile with the previously mentioned kinematic advantage for right-handed reaching movements (which is an intrinsic component of grasping behavior) and with the overwhelming evidence that humans prefer to use their right hand for grasping and manipulating objects (Bryden and Roy, 2006; Stone and Gonzalez, 2015).

Several studies from our lab have demonstrated right-hand advantage during ecologically valid tasks: grasp-to-drink and grasp-to-eat actions. We have argued that it is in these real, everyday life scenarios that manual actions should be studied. Consistent with the reach-to-point literature, in the grasp-to-drink task (Flindall et al., 2014) we found faster movement times and more accurate grasps when executed with the right hand. In the grasp-to-eat study (Flindall and Gonzalez, 2013) participants were required to reach for and grasp a food item to either bring it to the mouth for consumption or bring it to a receptacle near the mouth, to place. The results showed that grip apertures were produced with a smaller margin of error when bringing the item to the mouth for eating, but *only* during right-handed grasps; grip apertures in the left hand were similar between the two actions (i.e., eating or placing; Flindall and Gonzalez, 2013). This finding is independent of handedness (Flindall and Gonzalez, 2015), providing convincing evidence of a left-lateralized network for the grasp-to-eat action.

Intriguingly, we have found that such right-hand differentiation between the two slightly different food-grasping actions is present regardless of whether the food item is eaten (Flindall and Gonzalez, 2017). Based on this last finding we have revised our initial theory of a left-hemisphere specialization for grasp-to-eat actions to that of a left-hemisphere specialization for *hand-to-mouth* grasping actions (Flindall and Gonzalez, 2017). Of note, the two tasks in which hand differences were observed required a grasp coupled with a hand-to-mouth movement to bring the glass of water or the food item to the mouth for consumption. These findings suggest a unique left-lateralized motor plan for bringing a to-be-grasped object to the mouth. We have argued that the lateralization for the hand-to-mouth action may predate the development of specialized circuits for praxis (gestures and tool use) and language, an idea, which we return to expand upon later in the chapter.

2.3 NEUROIMAGING PERSPECTIVES

Research using neuroimaging techniques has also shown the major role that the left hemisphere plays in visuomotor processing and control. In one EEG study, researchers investigated if hemispheric asymmetries associated with object manipulability depended on the hand used. They had previously observed that the presentation of graspable objects led to larger EEG responses in the left vs the right hemisphere (Proverbio et al., 2011). Subsequently, they wondered if this enhanced activation might be linked to right-hand use or more generally to hemispheric specialization. They presented participants with pictures of objects that afforded one- or two-hand manipulation (spoon vs a pair of drumsticks) while measuring EEG activity. The results showed greater left premotor cortex activation regardless of object nature suggesting a left-hemisphere asymmetry for the neural representation of grasping actions (Proverbio et al., 2013).

In a different EEG study, researchers looked at a more basic manual action, key-presses. Right- and left-handed participants used their right, left, or both hands to tap buttons in a sequence. What the study showed is that regardless of handedness or hand used, there was increased functional activity of the left hemisphere (Serrien and Sovijärvi-Spapé, 2015). Although more fMRI research is needed to uncover the specific contributions of the left hemisphere to visuomotor control, one study has suggested that the left hemisphere is particularly important in the timing of movements under visual control (Floegel and Kell, 2017).

Lastly, a study investigating brain–behavior relationships of the motor system revealed a correlation between anatomical connectivity and motor skill (Barber et al., 2012). The authors recruited typically developing right-handed children and assessed them on a battery of gross and fine motor skill. The children also underwent functional connectivity MRI scans. The results showed compelling evidence for the central role that the left hemisphere plays in motor control. Greater left-lateralized connectivity in motor areas predicted better motor skill. The authors suggest that "the consistency of the findings across motor measures support the observation [hypothesis] that left lateralized motor connectivity is associated with superior motor performance in children" (Barber et al., 2012, p. 55).

3 CEREBRAL LATERALIZATION FOR VISUOMOTOR CONTROL AND ITS RELATIONSHIP TO LANGUAGE

3.1 MOTOR OUTCOMES OF LANGUAGE AND MANUAL INTERACTIONS

There is a strong historical link between motor control and language. Over 100 years ago, Liepmann (1908) suggested that the left-hemisphere specialization for language evolved from an earlier specialization of this hemisphere for the control of skilled movements of the hands and limbs. Behavioral studies have provided support for the close link between language and manual skill. In an early study Klatzky et al. (1989), participants were presented with a word on a screen, and based on the instruction they were required to execute a manual action or a vocal response. The results showed that manual responses were faster than vocal responses. This study demonstrates that the motor system plays an important role in the processing of verbal cues and action. In a later study, Gentilucci and Gangitano (1998) asked participants to pick up different sized rods with the words "long" or "short" printed on them. They found that the kinematics of the reach were affected by the printed words even though word reading was not required for the task. Similarly, Glover et al. (2004) asked participants to pronounce different noun-words while reaching and picking up two different-sized blocks. What they found was that the grip aperture (the distance between thumb and index finger) was influenced by the words the participant produced. When they said a noun signifying a relatively larger item (i.e., apple), grip aperture was larger than when they pronounced a word that signified a smaller object (i.e., grape) even though both objects were the same size. In these previous examples, words influenced (interfered) with the execution of manual actions suggesting shared neural substrates for mouth and hand articulation. Corballis et al. (2012) proposed that lateralized hand use during praxis or tool use is closely linked to neural lateralization of language. Neural areas (mainly around the left frontoparietal network) are activated not only during execution of communicative action but also during execution of nonsymbolic praxis/grasping tasks (Frey, 2008). Taking into account that predominant speech areas (i.e., Broca's, and the arcuate fasciculus (AF); a white matter tract connecting Broca's and Wernicke's areas) are also located in the frontoparietal network, the observed interference between language processing/pronunciation and movement of the hand may be due to interaction in processing two motor acts through similar neural structures.

Although less studied, the converse has also been found where manual action influences speech. A common method has been the investigation of speech changes due to manual action by looking at formants; variations in resonance of the vocal tract during vowel production (Clark et al., 2007; Delattre, 1951; Hardcastle et al., 2009). These transformed frequencies of speech can be compared to other pronunciations to infer changes in mouth shape and tongue position during vowel production. Similar to kinematics, changes in acoustic characteristics (formants) driven by manual actions are noted across studies, regardless of age of the speaker. For example, 11- to 13-month-old babies were given objects of different sizes (small or big) and the authors noted significant changes in their vocalizations (babbling and words) depending on object size (Bernardis et al., 2008). Similarly, adults show a larger mouth aperture, which results in altered phoneme pronunciation during execution of power grasps compared to precision grasps, despite pronouncing the same syllable (Gentilucci, 2003; Gentilucci et al., 2004). An important consideration is that these studies all used nonsense syllables as opposed to meaningful words.

A recent study completed in our lab examined changes in voice spectra of verb/noun homophones—words that sound the same but have different meaning; fall (as in the act of falling) and fall (as in the season)—during a grasping task. Results showed that vowel pronunciation in verbs differed significantly from nouns during a reach-to-grasp action (van Rootselaar et al., in preparation-a,b). Specifically, the height and frontness of the tongue in the mouth during vowel pronunciation changed significantly when pronouncing the identical word as a verb compared to a noun (fall vs fall). This finding suggests that during manual action, speech is differentially affected depending on the classification of a word (i.e., verbs or nouns); manual actions appear to have a greater impact on verb than on noun pronunciation. Because manual actions affect speech, it is possible that pronouncing a verb alters hand movements differently than do nouns (for other instances of this, please see Boulenger et al., 2006; Nazir et al., 2008; Silva et al., 2018). This distinction in limb kinematics in turn changes speech, ultimately suggesting a bidirectional interaction between these motor skills.

In addition to acoustic evidence, kinematic measures such as vocal reaction time and peak lip velocity or lip aperture inform changes in pronunciation. Gentilucci (2003) found that the size of a grasped block was reflected in changes of maximum lip aperture. Both the internal and the external positioning of the mouth appears to reflect the type of grasp executed simultaneously with speech. Another study, which measured changes in oral kinematics while executing repetitive precision grasps (threading beads) and pronouncing a sentence, found overall decreased variability and displacement in jaw movement (Dromey and Benson, 2003), suggesting that the hand action provided a template for the mouth to follow resulting in consistency of mouth movements during speech. Supporting this speculation, Forrester and Rodriguez (2015) demonstrated that in typically developing children, tongue protrusion was associated with fine motor movement and it was left lateralized for precision grips.

However, not all investigations have found relationships between hand movement and speech. Several studies, despite using similar methods of simple finger movement or even more drastic hand movement such as full precision grasps, showed no reliable change in voice spectra (Tiainen et al., 2016; van Rootselaar, 2017). The fact that not all studies found a relationship between manual action and speech suggests that other factors (e.g., task complexity) are also at play during this interaction.

Precise manual action while producing speech is a normal part of daily life. Another category of actions commonly performed with the hand is writing. Using EEG, researchers found that compared to typing, handwriting produced significantly higher levels of brain activation (van der Meer and Van Der Weel, 2017). This study supports the proposition by Ardila (2018) that the diminished practice of handwriting (replaced by increased keyboard use) in school children may be responsible for some of the language and learning difficulties seen in recent years. Lack of manual action may be at the heart of the issue. These findings highlight the important role the hand plays in both oral and written communication.

3.2 LATERALIZATION MEDIATES DEVELOPMENT

Before children can speak, they rely on gestures for communication. A simple and universal gesture is pointing. In a review, Cochet and Vauclair (2010) noted a host of previous studies which found (1) a right-hand bias for pointing in infants and toddlers, and (2) that right-hand preference related to stronger language skills later in development. For example, in infants, right-hand use for pointing correlated with analytic/receptive aspects of language at 13 months of age (Nelson et al., 2014) and with larger vocabulary at 14 months of age (Esseily et al., 2011). Furthermore, consistent right-hand use at 18–24 months of age correlated with better expressive and receptive language at 3 years of age (Nelson et al., 2017). Research from our lab provides further support for a link between lateralized hand use and vocabulary. Children (3–10 years of age) assessed on the Peabody Picture Vocabulary Test (PPVT-4; Dunn and Dunn, 2007) were significantly more likely to use their right hand (as compared to the left) to select a correct answer (van Rootselaar et al., in preparation-a,b). These examples serve to illustrate the role that lateralized gestural communication plays in the development of verbal communication.

Studies investigating grasping behavior have also noted the association between right-hand use and language skill during development. For example, Nelson et al. (2014) found that infants who consistently showed a right-hand preference for grasping toys from 6 to 14 months of age demonstrated better language performance on the Bayley Scales of infant and toddler development at 24 months. We further investigated if hand preference for grasping would be a predictor of the maturity of the language production system. Studies have shown that the separation of the "s" and "sh" sounds is relatively late to develop (i.e., between 3 and 7 years of age; Sander, 1972) given the high motor demand for articulation (Kent et al., 1992). Examining these sounds, we demonstrated that in 4–5 year olds, the greater the right-hand use for picking up small objects, the greater the differentiation between the production of these two sounds (Gonzalez et al., 2014a,b). Taken together, this evidence strongly links right-hand preference for pointing and grasping with enhanced reception and production of language.

Another research field that has provided compelling evidence of the link between manual action and language is in the study of developmental disorders. There are a host of studies demonstrating additional motor delays among children diagnosed with a language impairment or speech impediment compared to typically developing peers (for a review, see Hill, 2001; Rechetnikov and Maitra, 2009). One investigation found that children with a familial risk of childhood apraxia of speech scored significantly lower on expressive language, speech development, and fine motor skills between the early ages of 9 and 24 months (Highman et al., 2013). Another study demonstrated slower performance of fine motor tasks in children with specific language impairment compared to typically developing children (Zelaznik and Goffman, 2010).

One limitation of these cited examples is that the hand used for these motor tasks is not discussed. Therefore, the link between lateralization of both speech and hand use may initially appear weakened. However, there are other forms of evidence for this relationship, such as the increased rate of speech disorders in children with higher rates of left-hand use (Bishop, 1990, 2002). In addition, children with developmental language disorder show less cortical lateralization for language (Preston et al., 2010). Behavioral studies support this finding, as Helly and Nathanel (2007) found that, in a population of children aged 5–17 years, those with a developmental coordination disorder (DCD) displayed greater instances of left-hand use for writing, throwing a ball, and grasping a spoon, suggesting a less lateralized brain. Another study indicated that, during a reaching task, children with specific language impairments or DCD used both hands together at a higher rate than did control children, who predominately selected their right hand for reaching and grasping (Hill and Bishop, 1998). These studies examining motor or language disability support the idea that motor control and language are connected, as individuals with deficits in one domain (i.e., motor) typically also demonstrate some degree of impairment in the other (i.e., language).

3.3 NEUROIMAGING PERSPECTIVES

Neuroimaging studies have shown that Broca's area in the left hemisphere is involved during both speech production and hand/arm movements (for a review, see Jirak et al., 2010; see also Olivier et al., 2007; Stout and Chaminade, 2012). For example, Higuchi et al. (2009) showed overlapping activation in Broca's area during a language task and during manual action related to tool use (e.g., cutting with scissors, using chopsticks to move beads from one end of a string to another). A more recent study in deaf signers demonstrated activation in Broca's area during sign execution and perception (Okada and Slevc, 2016). Signing or gesturing is not a practice unique to a deaf population. In adults, fMRI studies indicate that when interpreting speech or manual gestures, Broca's area is similarly activated (Willems et al., 2007). Combined, these studies caution the pervasive portrayal of Broca's area as solely dedicated to speech production. While the described literature does not offer conclusive evidence, it does demonstrate activation is present in the area during manual action, suggesting that Broca's area and therefore speech, a "higher" cognitive function, is intricately connected to manual action.

Other imaging studies have demonstrated the opposite phenomenon, activation in motor areas during language processing. For example, a study by Moseley and Pulvermuller (2014) had participants listen to verbs and nouns—including both abstract and concrete (i.e., feel and luck vs walk and cake)—while undergoing fMRI. Differences were found in activation between the abstract and concrete word classes; while abstract words did not activate the motor-related areas, concrete words yielded strong activation of premotor and motor cortex, with nouns activating more anterior sites. These findings suggest that the brain processes words based on our ability to recognize their potential for motor interaction. Similar research (Pulvermüller, 2001; Pulvermüller et al., 2000) has shown activation in sensorimotor areas for action words (e.g., jump), manipulable objects (e.g., scissors), and adjectives that denote dimensions (e.g., small). In fact, it has recently been shown that *even* highly abstract words, such as emotion labels (Moseley et al., 2012) and mental state terms (e.g., logic and thought; Dreyer and Pulvermüller, 2018), could activate sensory and motor regions.

3.4 SUMMARY

In conclusion, the importance of hemispheric lateralization as a mediator of the interaction between motor control and language should be at the forefront of any discussion centering on language and manual action. Several fMRI studies highlight this assertion by demonstrating a relationship between the pattern of lateralization for speech and manual control. Individuals who are strongly left-lateralized for language also demonstrate greater left-hemisphere activation during manual gestures, regardless of the hand used to perform the action (Kroliczak and Frey, 2009). Those with atypical language lateralization (i.e., bilateral or right-hemisphere lateralized) also showed parallel motor activation (i.e., either mixed or right-lateralized; Króliczak et al., 2011). A MRI study revealed how language lateralization relates to the self-reported direction (predominantly right or left) and degree (consistent use or inconsistent use) of handedness (Propper et al., 2010). According to Propper et al. the degree, rather than the direction of the individuals' handedness, predicted the shape of the AF. Individuals who regularly used one hand demonstrated stronger left-hemisphere development of the AF, while those who reported inconsistent hand use did not display hemispheric differences in AF size. The implications of this connectivity study suggest that the processes of language and manual action benefit from their common lateralization.

4 CEREBRAL LATERALIZATION FOR VISUOMOTOR CONTROL AND ITS RELATIONSHIP TO EXECUTIVE FUNCTION (AND MUSICAL TRAINING)

4.1 DEFINING EXECUTIVE FUNCTION

Executive function (EF) refers to a suite of processes that inform and adapts goal-directed behavior. These functions serve the best interests of the individual and ultimately enhance survival. The behaviors that comprise the EF construct are thought to be distinct yet interrelated (Miyake et al., 2000). The frontal cortex, which includes the prefrontal subareas, has been identified as the primary neural domain of EF. Based on the behavioral profiles of EF some have been characterized as "cool" while others are considered "hot" (Perone et al., 2018). Key elements of "cool" or metacognitive EF (cEFs) include working memory (the ability to hold and manipulate information in mind), inhibitory control (the ability to maintain focus on, and pursue a goal in the face of distraction by inhibiting the impulse to follow the distraction), and cognitive flexibility (the ability to engage alternate means of thinking about an experience). The dorsolateral prefrontal cortex (DLPFC) is the neuroanatomical area that has been shown to support the cEF, and its connection with the hippocampus is thought to provide context for decision-making that relies on conscious control (Koziol et al., 2012).

Our traditional view of EF has embraced only cEF, and these skills are those most frequently studied and assessed. Hot EF (hEF) processes emerge in contexts with motivational cues that involve reward assessment and social interactions and judgments. Importantly, hEF processes are guided by emotional valence and provide the visceral element in driving decision-making (Tsermentsali and Poland, 2016). The medial frontal and orbitofrontal (OFC) cortices provide the neural underpinning for hEF through their strong connections with the basal ganglia and limbic areas (Koziol et al., 2012). It has been proposed that the understudied hEF is evolutionarily older but equally important in driving "successful" behavior (Ardila, 2018). EF is typically assessed using either subjective self-report measures (questionnaires, e.g., Behavioral Rating Inventory of Executive Function [BRIEF; Gioia et al., 2000], Amsterdam Executive Function Inventory [Van der Elst et al., 2012]) or objective measures (direct measures like Dimensional Change Card Sort, Stroop, or Tower of Hanoi; Coelho et al., in preparation; Zelazo, 2006).

4.2 LIFELONG COORDINATION OF EF AND MOTOR CONTROL

The developmental trajectory of EF skills is remarkably protracted and coincides with the extended period of maturation that characterizes the frontal lobes. EF skills emerge in the latter half of the first year of life and can continue to be refined well into adulthood. Privileged periods for EF development have been demonstrated by the rapid expansion of EF skills observed in both preschoolers and in adolescents (Perone et al., 2018; Weintraub et al., 2013).

A host of recent studies has established a connection between EF and motor control. It is no coincidence that premotor and primary motor areas are also located in the frontal lobes. Development of motor skills in very young children has been shown to influence later cognitive function. In a study by Piek et al. (2008), gross motor skill development in preschoolers (assessed using the Ages and Stages Questionnaire [Squires and Bricker, 2009]) predicted working memory performance in elementary school. A more recent study by Luz et al. (2015) demonstrated the relationship between motor control and EF (measured by the cognitive assessment system; Naglieri and Das, 1997) in 9–10 year olds. This study revealed that better motor control was linked to superior performance on planning tasks, and Luz and colleagues cite this as evidence that both skills share common neurological territory.

In a study of community-dwelling older adults, Poranen-Clark et al. (2018) assessed EF and participants' mobility through the community: how often they left their homes, how far they traveled, and if they needed assistance to get around. Higher EF scores predicted more expansive life-space mobility; those with higher EF had better lower extremity function and less need for assistance to get around. Another study of older adults compared psychomotor speed and EF in those who had normal cognitive function, mild cognitive impairment (early stage or late stage), and Alzheimer's disease (Kim et al., 2016). Psychomotor speed and EF showed deficits at even the earliest phases of mild cognitive impairment. These studies show that reduced mobility and motor impairments are often associated with cognitive decline in older adults suggesting deterioration of both sensorimotor and cognitive functions; as sensorimotor function wanes, so too does EF.

4.3 LET US TALK ABOUT EF: THE ROLE OF LATERALIZATION IN LANGUAGE AND EF

A clear link between EF and language development has also been well established (Kuhn et al., 2014; Miller and Marcovitch, 2015; Netelenbos et al., 2018; Roello et al., 2015). In one of the largest longitudinal developmental studies ($N = 1117$), Kuhn et al. (2014) recorded the communicative gestures of 15-month-old babies and documented their language and EF at 2, 3, and 4 years of age. They found that early communicative gestures prospectively predicted the child's EF at 4 years of age. They argue that language development "enables a certain type of thought that provides for the emergence of higher order cognitive abilities" and conclude that gestures (preverbal communication) are key in the development of language and EF.

Hemispheric lateralization also seems to play an important role in the development of EF skills. In a 2007 study, Marlow and colleagues assessed EF in children with extreme preterm birth (<25 weeks) but without cerebral palsy, at 6 years of age. They describe impairments of visuospatial and sensorimotor function as well as lagging EF in this group compared to full-term controls. Perhaps most interestingly, the preterm children showed reduced laterality for hand preference; 28% were nondominant for right-hand use compared to 10% of the controls. In addition, the preterm children showed more overflow movements or unintended mirroring when completing the motor tests. Based on this evidence and other studies that have found robust relationships between language and EF (Gioia et al., 2000; Miller and Marcovitch, 2015; Roello et al., 2015), we wondered if a similar laterality could be demonstrated for EF.

To this end we asked parents or caregivers of 5–6 year olds to complete the BRIEF questionnaire. We then asked children to recreate a Lego® model that required pieces of bricks equally distributed on both their right and left (i.e., the same numbers and types of blocks). The children were filmed during the model building and their hand use was assessed. The results showed that the stronger the right-hand preference, the better the child's reported EF (Gonzalez et al., 2014b). We have expanded this finding to include 3–4 year olds and direct measures of EF, including modified versions of the Stroop Test (Animal Stroop, see Fig. 1) and Dimensional Change Card Sort test (DCCS; Zelazo, 2006; Snap, see Fig. 2). Again, the greater the degree of right-hand preference demonstrated by the participant, the better the performance on these EF tests (Coelho et al., in preparation).

A recent study by Gottwald et al. (2016) explored if the planning of motor actions was related to EF in 18-month-old babies, as assessed via tests of simple inhibition and working memory. A reach-to-place task allowed assessment of motor control during reaching, the kinematics of which were recorded allowing the authors to capture peak velocity on the first movement unit. The authors discovered that the studied EFs were positively related to prospective motor control and from these data proposed an embodied view of the development of EF suggesting that an individual's need to control and plan actions begins in infancy and that the development of

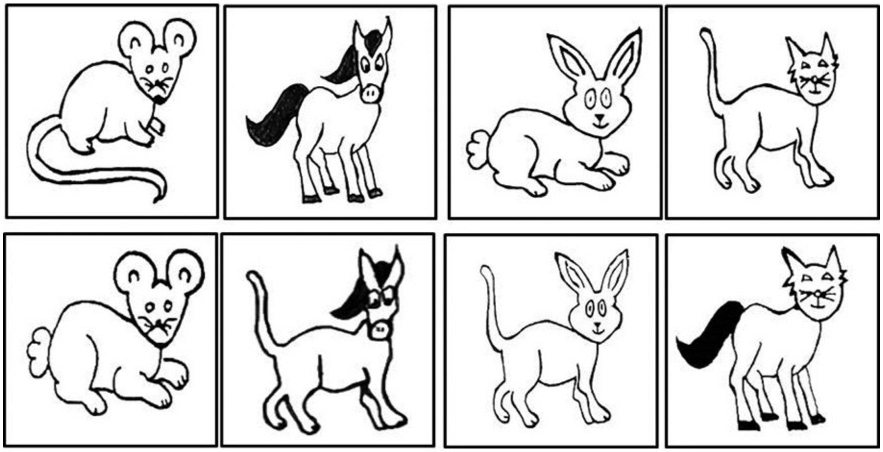

FIG. 1

Animal Stroop. The *top row* features the training images of normal or congruent animals. After naming the animals featured in the *first row*, children are then required to complete the incongruent portion, the *second row*. Here, they name the body of the animal, inhibiting the urge to name the animal according to its face.

FIG. 2

Snap. The game features three different *shapes*, which can be presented in four different *colors*. Participants take turn flipping over the cards. If a scenario occurs as in (A) where the *colors* do not match, the participant would name the shape of the object on the card they just overturned. However, if a scenario occurs as in (B), where the *colors* match, then they are required to switch to different rules, pronouncing the *color* of the shape. If the color of the following card also matches then the participant will resume using the original rule and continues naming the shape.

EF is based on prospective motor control from this early period onward. Perhaps most compelling is their report is that right-hand reaching was most commonly observed—and left hand or bimanual reaches only rarely performed—in this infant participant sample.

4.4 "EXECUTIVE" FUNCTIONAL MAGNETIC IMAGING

Since our first study on hand use and EF (Gonzalez et al., 2014a,b), other studies have documented the anatomical correlates of EF lateralization. In 2017, two studies were published that demonstrated a clear lateralization for EFs. In the first, Ambrosini and Vallesi (2017) used EEG to study the anatomical correlates of Stroop performance. The Stroop test demands an ability to resist interfering, irrelevant information in order to produce an accurate response. The authors looked at resting-state activity in both hemispheres and reported that higher left-hemisphere-lateralized activity was associated with better performance on the Stroop task. Resting-state activity in various prefrontal cortex areas was higher in the left hemisphere in subjects who were more capable of inhibition of irrelevant information. This led to Ambrosini and Vallesi's proposal that there is left-hemispheric specialization for the cognitive control processes that underlie Stroop performance. The second study looked at cEF and hEF in an attempt to determine if these abilities are both functionally and structurally independent. Here, Nejati et al. (2017) tested participants cEF using Go/No-Go (inhibitory control) and Tower of Hanoi (planning and problem solving) tests, and hEF's using temporal discounting (delayed gratification) and balloon analogue risk task tests (see Nejati et al., 2017 for details). Participants were given either anodal (i.e., excitatory), cathodal (i.e., inhibitory), or sham transcranial direct current stimulation for 5 min followed by testing on all four EF tests. An interval of 72 h between each stimulation/EF session ensured no residual effects of previous stimulation parameters. The authors report that inhibitory control, and planning and problem solving (all cEF processes) benefited from anodal stimulation of the left DLPFC and cathodal stimulation of right OFC. Risk-taking behavior and risky decision-making (both hEF processes) also benefited from this stimulation. In addition, these behaviors showed improvement after anodal stimulation of right OFC and cathodal left DLPFC. These results imply that EF processes present on a spectrum rather than as individual constructs, with lateral PFC areas contributing to cEF and medial areas supporting hEF. This chapter also highlights left-hemisphere involvement for the cEF processes and, to some degree, also for the hEF processes.

4.5 FUNCTIONAL MUSIC: THE EFFECT OF MUSICAL TRAINING ON EF AND LANGUAGE

Lastly, we briefly consider musical training as new research indicates that it is a powerful modulator of EF and language. Although melody is processed preferentially by the right hemisphere (Kimura, 1973), musical training has been shown to alter both hemispheres. Recently, musicians have been widely studied in neuroscience as they provide a powerful means to model the effects of experience (musical training) on brain plasticity. Fundamental to musical training is its impact on sensorimotor function and its ability to hone cognitive processing skills including language and EF. In a review of how music modifies the functional and structural organization of the brain, Miendlarzewska and Trost (2014) emphasized the importance of temporal processing and orienting attention in musical training. They also proposed that rhythmic entrainment may support both learning and EFs. They concluded that musical training provides a foundation for developing a host of skills by fostering cognitive development.

Moussard et al. (2016) studied older musicians and nonmusicians using EEG. They gave their participants the Go/No-Go test of behavioral inhibition EF and recorded event-related potentials and discovered that while both groups showed similar competency on the Go trials, the musicians outperformed their age-matched counterparts on the No-Go trials. The musician group showed stronger amplitude of the N2 wave, which was associated with their behavioral accuracy. The authors concluded that life-long musical training was associated with a cognitive advantage for executive control in the older musicians. An fMRI study by Du and Zatorre (2017) examined how musical training changed the ability to identify syllables at varying ratios of signal-to-noise. Their study demonstrated that musicians are superior to nonmusicians on this task, and the enhanced skill in musicians was associated with stronger brain activation in left inferior frontal and right auditory areas.

Developmental studies have also shown the influence of musical training in cognitive function. Habib et al. (2017) recruited 6-year-old children from low socioeconomic backgrounds; some involved in music training, others in sports training, and others in no formal after-school program. The children were given structural MRIs at the outset of the study with no between-group differences observed. After a 2-year interval, the children were given another MRI and those in the musically trained group had higher connectivity via the corpus callosum in superior frontal, sensory, and motor areas as compared to the children in the other two groups. In addition, the group with musical training had a slower rate of cortical thinning (maturation) in the right superior temporal gyrus, compared to the left—an area just outside of the auditory cortex (AC) but associated with the processing of complex sounds including music. The authors suggested that these findings point to musical training as a powerful intervention program that could support brain development in disadvantaged children.

But how does musical training influence cognition? Elmer and Jancke (2018) used both MRI and EEG to gain a better understanding of how musical training mediated improvements in speech processing and word learning. The authors noted that phonetic perception is managed by both left and right AC with the left AC processing fast-changing vocal cues and the right managing vowel processing. They also emphasized that, at rest, gamma oscillations which are thought to track the fine structure of the acoustic signal are stronger in left AC and may arise from stronger local connectivity within the AC. Furthermore, the planum temporale (PT)—which is strongly lateralized to the left hemisphere—is structurally altered by musical training. Elmer and Jancke demonstrated that musicians have increased connectivity between left and right PT and that the stronger activation of left PT in musicians may result from this higher degree of callosal connectivity. In musicians, the PT was more strongly responsive to both spectrotemporal speech cues and spoken sentences.

In a follow-up study (Elmer and Jancke, 2018) they examined functional connectivity by computing neural oscillation alignment and, here, described a left-hemispheric functional asymmetry in the dorsal auditory stream (DAS) for theta oscillations, which are typically detected over long-range neural connections. The DAS supports sound-to-articulation mapping and may contribute to building motors codes for new phonological demands. The authors suggest that musical training strengthens the neural coupling from the AC and inferior parietal lobe to Broca's area (i.e., DAS) via the AF. Finally, the authors propose that advantages enjoyed by musicians for new word learning are thought to arise from the overlap of music and language processing areas, the higher demand of music on these networks than speech, the ability of music to produce strong positive emotion, repetition required by musical activities, and finally the recruitment of attention networks when engaged in musical activities.

Taken together these studies point to widespread behavioral and anatomical changes that are wrought by musical training. Both instrumental and vocal training rely on activation in sensorimotor areas and the subsequent changes in these areas may support the observed superior performance in language and EFs. Importantly, the anatomical changes reported in these studies are highly lateralized and occur on both sides of the brain.

5 CEREBRAL LATERALIZATION FOR HAPTIC CONTROL (RIGHT HEMISPHERE)

5.1 BEHAVIORAL EVIDENCE OF RIGHT-HEMISPHERE HAPTIC ADVANTAGE

In addition to vision, haptics allow us to interact with and manipulate our world. Haptics refers to the sense of touch and proprioception (i.e., body awareness of its location in space), and it is through haptics that we understand object properties, such as surface texture, temperature, weight, size, and shape. Much less is known about lateralization for haptics, but some studies have shown that haptic processing appears to be primarily driven by the right hemisphere. Two early papers by Hermelin and O'connor (1971a,b) investigated hand use during Braille reading in blind participants. They asked if left-hemisphere specialization for language processing (Kimura, 1966) would give Braille readers an advantage when using their right hand. Alternatively, because Braille consists of dots with different spatial arrangements, Hermelin and O'Connor reasoned that the right-hemisphere specialization for spatial function (Kimura, 1966) could provide an advantage to Braille readers when using the left hand. In both studies, participants were faster and made fewer errors when using the left hand. In fact, the authors noted (Hermelin and O'connor, 1971a) that one of the participants was unable to read because he had hurt his "reading hand" which happened to be his left hand.

In another early paper, Milner and Taylor (1972) described the performance of seven patients, with complete transections of the corpus callosum, on a tactile matching-to-sample task. Patients were presented with one of four nonsensical wire figures to manipulate with the right or left hand and, after a short delay, were tasked with finding the previously manipulated figure from the array of four. The main result was that patients performed much better when the objects were manipulated with the left vs the right hand. This result was replicated for common use objects (rubber band, key, quarter, scissors; Milner and Taylor, 1972). Most surprising to the authors was the extent of the deficit that patients demonstrated when using the right-hand commenting, "it seems as though the left hemisphere is unable to obtain enough of a representation of the form palpated to be able to distinguish it from similar ones, even with practice" (Milner and Taylor, 1972, p. 13). But is the left hemisphere unable to process haptic information for object recognition?

Using a competition design, Smith et al. (1977) demonstrated that the left hemisphere can support haptic processing. In their study, participants haptically inspected (with one hand or the other) Braille symbols, listened to music (presented to one ear or the other) or both tasks simultaneously. The most interesting result was that when music was presented in the left ear (i.e., processed by the right hemisphere) performance of the right hand for haptic recognition improved significantly. The authors suggested that the left hemisphere retains the ability to recognize objects haptically but that it is inhibited by the right-hemisphere's superiority for this ability. Subsequent studies have demonstrated the left-hand/right-hemisphere superiority for haptic discrimination (for a review, see Stone and Gonzalez, 2014, 2015).

Developmentally, the left-hand lateralized advantage for haptic processing is evident in early life. Premature infants at 28 weeks already demonstrate haptic ability for recognizing novel shapes placed in their left hand (Marcus et al., 2012). A study of 2-month-old babies (Lhote and Streri, 1998) and another with 4- to 6-month olds (Morange-Majoux, 2011) showed that infants spent more time manipulating objects using their left hand and that retention of haptic information was better when the object was manipulated with this hand. Studies in babies, children, and adults have found that haptic object identification is better and faster with the left hand (Morange-Majoux, 2011; Stone and Gonzalez, 2015). Some early-imaging studies used mah-jongg tiles to investigate hemispheric differences in spatial processing. The tiles are engraved with lines, circles, or Chinese characters, and participants were required to categorize them accordingly using their right or left hands to palpate the engravings. Using positron emission tomography (Yoshii et al., 1989) and transcranial Doppler ultrasonography (Kelley et al., 1993), both of these studies showed contralateral activation during right-hand exploration but bilateral activation during left-hand palpation. More recently, a fMRI study demonstrated only right-hemisphere engagement during haptic exploration of complex objects (Marangon et al., 2016). These findings support the notion of the right-hemisphere superiority for haptic ability but also highlight the importance of this hemisphere during spatial processing.

6 CEREBRAL LATERALIZATION FOR HAPTIC CONTROL AND ITS RELATIONSHIP TO SPATIAL (AND NUMERICAL) ABILITIES

6.1 HOW TO TEST WHAT YOU CANNOT SEE

We have known for decades that right-hemisphere damage leads to a condition called hemispatial neglect; a condition in which a patient is unable to respond, attend, and orient toward stimuli presented (usually) the left side of space, despite retaining intact motor and sensory function (Heilman et al., 2003). Additionally, studies in neurologically intact individuals have demonstrated the key role that the right hemisphere plays in spatial processing (see de Schotten et al., 2011;

Koch et al., 2013 for a review). In one early study (Kimura, 1973), a dot was presented briefly (100 ms) to either the left or right visual field of healthy participants. The dot was placed randomly within a circle, and the participant's task was to identify the location within the circle where the dot had appeared. Participants more accurately indicated the location when the dot was flashed to the left visual field (processed by the right hemisphere). Kimura suggested that the right hemisphere was better equipped to "incorporate components of a system of spatial coordinates that facilitates the location of a point in space" (p. 73). Many tests have been developed to study spatial abilities; most notably the paper-based test of mental rotation described by Shepard and Metzler (1971), which asks participants to determine which two (out of four) perspective drawings of three-dimensional objects match a target. The drawings are in different orientations so a participant must "mentally rotate" them to find those that match the target (see Fig. 3). Using this task, Ditunno and Mann (1990) demonstrated the superiority of the right hemisphere for mental rotation in both healthy participants and patients with brain damage.

To study spatial abilities in the lab, we developed a hands-on task of low- and high-mental rotation demands using Lego bricks (see Fig. 4; deBruin et al., 2016). This hands-on building task has several advantages over the paper-based tests. It requires real-world object manipulation and features a "game" structure. These characteristics make this task more suitable and appealing for young children, seniors, and people with cognitive disabilities. We have validated this hands-on task against the paper-based Shepard and Metzler mental rotation task, showing high correlation between the two experimental methods, particularly with the high-mental rotation demand task (Aguilar et al., in preparation). We are currently investigating the contributions of each hemisphere to the task. Participants are required to build using the left, right, or both hands, and the time to complete the task and the number of errors are recorded. We have also added a condition in which participants identify a target brick from an array of bricks using haptics (i.e., while blindfolded; see Fig. 5). Preliminary data analyses have confirmed a relationship between the tasks: participants who scored better on the mental rotation tests (both hands-on and paper-based) were also more accurate and rapid during the haptic test. Importantly, this association was stronger when participants used their left hand for the haptic task suggesting greater right-hemisphere involvement.

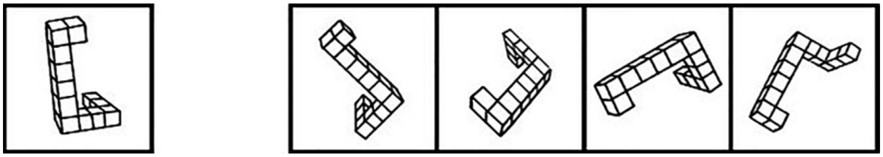

FIG. 3

Paper-based mental rotation task. This is a modified example of the test originally designed by Shepard and Metzler (1971) where participants look at the figure on the *left* (sample) and select the two rotated figures from the *right* that match the sample figure.

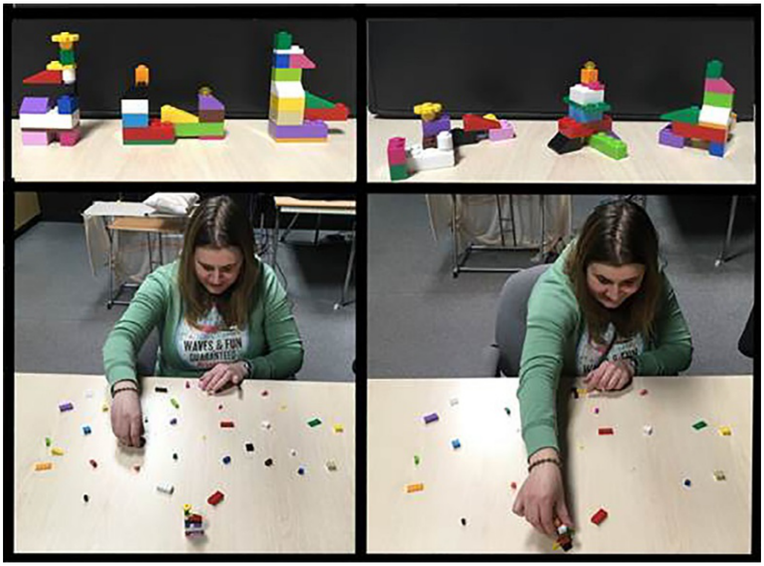

FIG. 4

Hands-on mental rotation task. Pictured above are the low- and high-demand mental rotation models (*left* and *right*, respectively). *Bottom panels* show a participant completing the task. Please note that participants physically (and mentally) rotate the high-demand models in order to accurately replicate them (picture on the *right*).

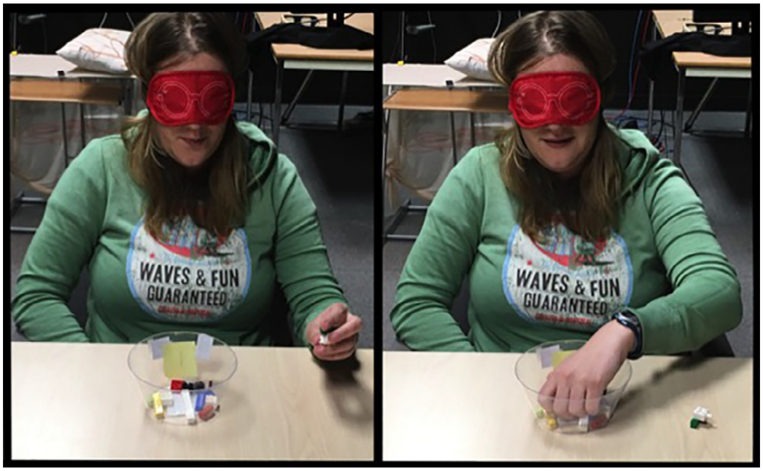

FIG. 5

Haptic task. Participants were blindfolded and required to haptically explore a model constructed from two blocks. After feeling the model for 10 s, participants then tried to find the pieces that composed the model by haptically searching in a bowl with 12 other blocks.

It must be noted that some early studies investigating spatial abilities used tactile/haptic tasks. For example, Witelson (1974, 1976) “used a new behavioral test procedure involving tactual [tactile] perception, which was devised specifically to assess the relative participation of the two hemispheres in spatial processing” (Witelson, 1976, p. 425). The task required participants (6–13 year olds) to use each hand to haptically explore two different meaningless shapes simultaneously. Left-handed trials were more accurate than right-handed trials providing support for the idea that spatial processing occurs preferentially in the right hemisphere. Similarly, those studies previously described investigating hemispheric asymmetries for haptic processing (Hermelin and O’connor, 1971a,b; Milner and Taylor, 1972), emphasized the spatial nature of the tasks although they failed to specifically draw parallels between haptic and spatial processing.

More recently, Lohmann et al. (2017) have explicitly investigated the interaction between tactile and mental rotation, finding mental rotation to be affected by a concurrently perceived tactile rotation. Specifically they found compatibility effects; participants were faster to respond when a tactile rotation cue matched the direction of a mental rotation problem and they were slower when there was a mismatch. It is important to note that the tactile stimulation was always applied to the left hand. Although the authors do not discuss this point, it is tempting to speculate that no compatibility effect would be found if the tactile stimulus was presented to the right hand. From this section (Section 6.1), it is clear that more research is needed to evaluate the interactions between spatial and haptic processing with a focus on hemispheric asymmetries.

6.2 NUMERICAL PROCESSING NOTES

Besides spatial ability, another cognitive function in which the right hemisphere appears to play a special role is numerical processing (see Semenza and Benavides-Varela, 2018 for a discussion on the role of each hemisphere for calculation). Recent imaging studies have provided evidence for this relationship. Edwards et al. (2016), for example, used functional near-infrared spectroscopy to measure brain responses to numerosity changes (e.g., 8 dots followed by 16 dots) in 6-month-old babies, observing distinct activation in the right parietal cortex specific to changes in numerosity. Another imaging study also investigating numerosity found greater activation in the right parietal cortex in 3- to 4-year-old children (Kersey and Cantlon, 2017). Behavioral studies have found links between spatial and numerical processing, particularly early during development. For example, performance on a visuospatial task at 6 and 13 months of age is related to the children’s symbolic math concepts (counting, simple arithmetic problems) at 4 years of age (Lauer and Lourenco, 2016). Another study found that numerical associations are influenced by spatial information as early as 7 months of age (de Hevia et al., 2014). However, the origins of these associations remain unknown.

Given that haptic perception also involves right parietal areas (Hegner et al., 2017; Peltier et al., 2007), we hypothesize common substrates for numerical and spatial functions based on networks supporting haptic processing. There is evidence to substantiate this idea; for example, a recent study showing that tactile information influences performance in a mental rotation task, a key aspect of spatial abilities (Lohmann et al., 2017). Another study has found that listening to numbers affects performance in a haptic bisection task (Cattaneo et al., 2012). Current studies in our lab include measures of numerical processing (numeracy) and measures of spatial numerical associations (i.e., Spatial-Numerical Association of Response Codes [Dehaene et al., 1993] effect). Studies of the SNARC effect have led to the notion that numerical processing is represented as a mental number line in which low numbers are associated with the left side of space and high numbers with the right side of space (Dehaene et al., 1993). Results from our lab (in children, adolescents, and adults) showed that number magnitude influenced the selection of hand and hemispace used for grasping in accordance with the SNARC effect (Mills et al., 2014). In future investigations, we plan to expand on this finding by adapting this task to the haptic domain such that haptic, spatial, and numerical processes can be studied within the same design.

7 CONCLUSION AND FUTURE DIRECTIONS

We began this chapter by acknowledging that the functions discussed in this chapter are deeply imbricated and by studying the "whole brain"—rather than its parts—we will advance the field of cognitive neuroscience. We acknowledge the correlational nature of these studies, which is inherent in cognitive neuroscience. It is important for readers to appreciate that correlation does not imply causation. Cognitive measures, even those that include imaging and neuropsychology, provide insight into brain function, but determining the mechanisms supporting these functions is necessarily left to researchers working with human patients undergoing required neurosurgery. A more holistic approach is bound to reveal the inseparable qualities of sensorimotor and cognitive processes. Further, by understanding how cerebral lateralization shapes brain function we may be able to design strategies to optimize it. At the end of the day, the acid test of the quality of the relationship between sensorimotor and cognitive abilities would be to demonstrate that focused training of sensorimotor abilities, could influence cognitive outcomes, something our lab is currently investigating. We have proposed that a brief, interactive, motor training program (pointing and grasping with the right hand) may provide a means to enhance performance in language, and executive function, in preschool-aged children. Similarly, we are using the hands-on spatial Lego test and haptic discrimination tasks to investigate if we can enhance spatial, and numerical abilities in children. Such intervention studies provide a means to mitigate the limitation in demonstrating causality. The ultimate goal is to foster academic and life success by enhancing sensorimotor abilities to support better cognitive performance.

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238

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Cerebral Lateralization and Cognition: Evolutionary and Developmental Investigations of Behavioral Biases

EDITED BY
Gillian S.Forrester, William D. Hopkins, Kristelle Hudry and Annukka Lindell

In this special volume of Progress in Brain Research we introduce the most up-to-date research examining associations between cerebral lateralization, behavioral biases and cognition. Drawing on evidence from species as disparate as the honeybee, the Indian flying fox and the human, we consider how these linked features manifest through evolution and development. The theories, methodologies and experimental findings presented within this volume reveal the relationships between the functional dominances of the left and right hemispheres and their associated behavioral biases. We also provide convincing evidence that behavioral biases are not distinct from cognition, but rather represent foundational components of a single system that supports cognition.

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