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Editorial

Cognitive and Neurophysiological Models of Brain Asymmetry

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Abstract: Asymmetry is an inherent characteristic of brain organization in both humans and other vertebrate species, and is evident at the behavioral, neurophysiological, and structural levels. Brain asymmetry underlies the organization of several cognitive systems, such as emotion, communication, and spatial processing. Despite this ubiquity of asymmetries in the vertebrate brain, we are only beginning to understand the complex neuronal mechanisms underlying the interaction between hemispheric asymmetries and cognitive systems. Unfortunately, despite the vast number of empirical studies on brain asymmetries, theoretical models that aim to provide mechanistic explanations of hemispheric asymmetries are sparse in the field. Therefore, this Special Issue aims to highlight empirically based mechanistic models of brain asymmetry. Overall, six theoretical and four empirical articles were published in the Special Issue, covering a wide range of topics, from human handedness to auditory laterality in bats. Two key challenges for theoretical models of brain asymmetry are the integration of increasingly complex molecular data into testable models, and the creation of theoretical models that are robust and testable across different species.

Keywords: neuroscience; brain; asymmetry; laterality; functional hemispheric asymmetries; structural hemispheric asymmetries; theoretical models

Citation: Ocklenburg, S.; Güntürkün, O. Cognitive and Neurophysiological Models of Brain Asymmetry. *Symmetry* **2022**, *14*, 971. https://doi.org/10.3390/sym14050971

Received: 5 May 2022
Accepted: 6 May 2022
Published: 9 May 2022

1. Introduction

Research on symmetry and asymmetry in the nervous system is a central part of neuroscience [1–4]. Over the last decade, tremendous progress has been made in research on brain asymmetries, due to large-scale consortium or databank studies [5]. For example, large-scale databank studies have investigated the genetics of structural brain asymmetries [6] and handedness [7–10], as well as the influence of early life factors on handedness [11], and the role of epigenetic processes in handedness ontogenesis [12]. Unfortunately, despite the vast number of data-driven studies on brain asymmetries, more recent publications featuring theoretical models that aim to provide mechanistic explanations of hemispheric asymmetries are sparse in the field. This is in line with the larger development in psychology and neuroscience, which has been called the "theory crisis" [13]. Following earlier works [14], Eronen and Bringmann (2021) argue that the theoretical foundations of psychology are shaky, and that, instead of gathering more and more data, the field needs to shift to developing better theories, which, in turn, inform empirical research.

Research on symmetry and asymmetry in the brain has always been a field driven by influential theories. A few examples are the McManus dextral/chance (DC) model of handedness and language dominance [15], the pathological left-handedness model [16], the right-hemisphere and valence model of emotional lateralization [17], and the Geschwind–Galaburda–Behan model [18–20]. However, since approximately the year 2000, the number of new, influential theories about symmetry and asymmetry in the brain has declined considerably. Moreover, many of the older theories were formulated before the widespread use of modern genetic and neuroimaging techniques, and were often not in line with newer empirical findings obtained with such techniques [21]. Unfortunately, not all authors updated their theories to reflect newer empirical findings, leading to a lack of theoretical models that aim to provide mechanistic explanations of hemispheric asymmetries. Therefore, it was the aim of the present Special Issue to highlight empirically based mechanistic models of brain asymmetry. To this end, we invited several experts in the field of hemispheric asymmetries to contribute theoretical or empirical papers on models of brain asymmetries. Both submissions covering research in humans and research in non-human model species were welcome. Overall, ten excellent articles were submitted to the Special Issue, covering a broad range of theoretical models on hemispheric asymmetries in a wide range of species. Six articles were review papers and four presented new empirical research. In the following sections, we will shortly discuss each of these contributions to the Special Issue.

2. Theoretical Articles

As mentioned above, the McManus DC model of handedness and language dominance [15] was one of the most influential models of handedness ontogenesis. In his contribution to the Special Issue, entitled "Cerebral Polymorphisms for Lateralisation: Modelling the Genetic and Phenotypic Architectures of Multiple Functional Modules", McManus presents an update and extension of this model with two central changes [22]. Building upon the 2014 polygenic revision of the DC model [21], McManus presents an extended polygenic DC model informed by recent studies on the genetics of handedness and, in particular, the role of cilia. Moreover, the model is further extended to include cerebral polymorphisms that are based on a multitude of functional modules for different lateralized cognitive systems, such as language, praxis, and visuo-spatial functioning. This idea is in line with recent findings showing that multidimensional phenotypes improve the genetic analysis of laterality traits [23]. It is very encouraging to observe how a leading model in the field is adjusted to fit with recent empirical findings, even decades after it was first published.

Similarly to McManus, Paracchini focusses on human handedness in her contribution, entitled "Recent Advances in Handedness Genetics" [24]. She highlights several recent advances in the understanding of the genetics of handedness, based on databank studies with large sample sizes, but also highlights the importance of phenotyping, i.e., which handedness measure is used in a study.

The contribution by Guy Vingerhoets, Robin Gerrits, and Helena Verhelst, entitled "Atypical Brain Asymmetry in Human Situs Inversus: Gut Feeling or Real Evidence?" [25], is also related to the ontogenesis of handedness and other forms of hemispheric asymmetries in humans. Whether or not individuals with situs inversus also show inverted hemispheric asymmetries has been discussed for decades [26,27]. While the data pattern found in previous studies in humans has been inconclusive, Vingerhoets et al. (2021) suggest a model that assumes that cilia play a critical role in determining whether someone with situs inversus shows reversed hemispheric asymmetries or not. They suggest that greater attention needs to be paid to the subtypes of situs inversus, and that situs inversus with a ciliary etiology is related to reversed hemispheric asymmetries, while situs inversus with a non-ciliary etiology is related to typical hemispheric asymmetries.

In addition to these theoretical articles that were mainly focused on research in human subjects, three theoretical articles integrated findings from human subjects with comparative research. In her contribution, "It Is Not Just in the Genes", Martina Manns integrates human and animal research, with a focus on birds, to create a new multi-level model for asymmetry formation [28]. The model focuses on the cellular processes that determine hemispheric asymmetries during embryonic patterning, neural differentiation, and refinement of neural circuits.

In their contribution, entitled "Structural Brain Asymmetries for Language: A Comparative Approach across Primates", Yannick Becker and Adrien Meguerditchian also take a strongly comparative look at hemispheric asymmetries, but focus on primates instead of birds [29]. They highlight how in several non-human primate species, human-like structural brain asymmetries can be found in brain areas that are homologous to key language regions in the human brain. This finding proposes a challenge for models of human language lateralization, as it suggests that these structural asymmetries in language areas did not develop for language per se, as they are also present in non-linguistic primates. Becker and Meguerditchian suggest that gestural communication may be a key factor here. Intriguingly, this idea is very much in line with the "from hand to mouth" theory about the origins of language, proposed by Mike Corballis 20 years ago [30]. Mike Corballis also contributed a theoretical paper to this Special Issue [31]. Entitled "Asymmetry research in human subjects and in non-human species—How Asymmetries Evolved: Hearts, Brains, and Molecules", this article gives a cross-species overview of the evolution of asymmetries in the body and brain, and their potential molecular basis.

3. Empirical Articles

In addition to these six theoretical articles, the Special Issue includes four empirical articles. Pamela Villar González and co-workers presented a study on dichotic listening in Silbo Gomero, a form of whistled Spanish, entitled "Lateralization of Auditory Processing of Silbo Gomero" [32]. Whistled languages are highly interesting in the context of theoretical models of language lateralization [33]. While whistled languages typically use the full lexical and syntactic properties of the spoken languages they are derived from, their acoustic properties differ from the acoustic properties of spoken languages. While the left hemisphere typically shows dominance for processing spoken languages, the right hemisphere is dominant for processing spectral cues, pitch, and melodic lines [34], all of which are central for understanding whistled languages. Testing the assumptions of theoretical models of language lateralization using both spoken and whistled stimuli may allow us to better disentangle which lateralized processes are relevant for language.

The contribution by Stuart Washington and co-workers also belongs to the acoustic domain, entitled "Hemispheric and Sex Differences in Mustached Bat Primary Auditory Cortex Revealed by Neural Responses to Slow Frequency Modulations" [35]. This study convincingly shows how unusual model species can yield very informative results in research on hemispheric asymmetries. Washington et al., (2021) investigated hemispheric asymmetries in the primary auditory cortex of mustached bats (*Pteronotus parnellii*). Similarly to humans, these bats show leftward asymmetry for complex social vocalizations. Washington et al., (2021) demonstrated that this asymmetry is driven by spectro-temporal processing differences, which, to some extent, mirrors the findings in humans. This work highlights that using a broader range of model species in laterality research than those typically used (e.g., rats, mice, pigeons, and chickens) could be very beneficial to test laterality models in an evolutionary context.

The contribution by Gisela Kaplan and Lesley J. Rogers, entitled "Brain Size Associated with Foot Preferences in Australian Parrots", shows another important empirical technique to test laterality models in an evolutionary context [36]. In this study, the authors did not analyze data from one species, but assessed foot preferences and brain masses in 25 psittacine species from Australia. Importantly, they found that birds with larger brain masses showed stronger foot preferences. We expect to observe more multi-species studies aimed at testing evolutionary models of laterality in the future. Clearly, a theoretical model is stronger if its predictions hold true across different species.

Finally, the contribution by Hao Cheng and co-workers, entitled "A Simulation on Relation between Power Distribution of Low-Frequency Field Potentials and Conducting Direction of Rhythm Generator Flowing through 3D Asymmetrical Brain Tissue", reported an EEG simulation, taking into account brain asymmetries [37]. Their work may be helpful for testing theoretical models of EEG asymmetries.

4. Conclusions

Taken together, the ten articles included in the present Special Issue, "Cognitive and neurophysiological models of brain asymmetry", give several insights into theoretical models of hemispheric asymmetries in 2022. Clearly, one of the key challenges identified in several articles is integrating the increasingly complex findings of molecular genetic and epigenetic studies in humans and non-human animal species into testable theoretical models. Before the wide availability of molecular research methods, models were typically based on statistical distributions of phenotypes. Molecular research has clearly shown that many of these models were oversimplified, and that the field needs to adjust. Particularly, cilia function needs to be integrated into theoretical models about the ontogenesis of hemispheric asymmetries. In addition, we are convinced that the next decade will observe stronger cross-species integration in theoretical models of hemispheric asymmetries, particularly in the context of evolutionary models. Along with this, more research in non-typical model species, to test specific aspects of theoretical models, will emerge. We hope that the theoretical and empirical articles presented in this Special Issue will lead to empirical studies testing these models in various contexts.

Author Contributions: Conceptualization, S.O. and O.G.; writing—original draft preparation, S.O. and O.G.; writing—review and editing, S.O. and O.G. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

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