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EDITORIAL

Understanding structure–function relationships in the mammalian visual system: part two

Hiromasa Takemura[1,2,3] **· Marcello G. P. Rosa**[4,5,6]

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Over the last several decades, the mammalian visual system has been arguably the most widely studied subject in systems neuroscience. Research on the mammalian visual system has provided important insights for our understanding of the brain in general, artificial neural networks (Yamins et al. 2014), and intervention strategies for visual disorders (Beauchamp et al. 2020). Despite these extraordinary advances, some aspects of the neurobiology of vision remain mysterious.

In December 2018, we discussed with the late Founding Editor Karl Zilles the idea of organizing a *Brain Structure and Function* special issue dedicated to the structure and function of the visual system. At the level of retinal circuitry, it is evident that there is a strong relationship between structure and function. For example, anatomical knowledge such as the spatial distribution of photoreceptors and the synaptic connections between different cell types both provide fundamental constraints to current models of how we see. However, there is less clarity about how the anatomy of subsequent visual processing structures, including subdivisions of the visual thalamus and cortex, influences function. This limits the biological plausibility of computational models on visual processing, as well as the precision of interventions aimed at alleviating visual disturbances related to the central nervous system. After Karl's departure, the project of a special issue on the structure and function of the visual system persisted and became reality through the collaborative efforts of the present co-editors (H.T. and M.G.P.R.), as well as tireless support from the editorial team.

The response from the scientific community exceeded our expectations: one volume of the journal would not be enough. Accordingly, we published 22 papers in part one of the "Structure and Function of the Visual System" special issue last year (Takemura and Rosa 2021). We present here the second half of the papers. Papers were assigned to the first and second parts based on the order of acceptance; together, these two volumes represent an integrated collection of current research on the structure–function relationships in the mammalian visual system.

Part two starts with an attempt to understand the logic of the differentiation of visual structures during early development, and the formation of their retinal connections. Puelles (2022) provides a comprehensive review of the "prosomeric model" as it applies to the mammalian visual system, with focus on its explanatory merits relative to the earlier "columnar model". The author highlights how the prosomeric model helps the formulation of new hypotheses that explain the organization and evolution of subcortical visual centers.

Understanding similarities and differences of the anatomical and physiological organization of the brain across species can be a powerful paradigm illuminating structure–function relationships, and the following three papers in this issue adopt this approach. Graïc et al. (2022) investigate the primary visual cortex (V1) of Cetartiodactyls that live on land, in the sea, or in an amphibious environment.

✉ Hiromasa Takemura
htakemur@nips.ac.jp

Marcello G. P. Rosa
marcello.rosa@monash.edu

1 Division of Sensory and Cognitive Brain Mapping, Department of System Neuroscience, National Institute for Physiological Sciences, Okazaki, Japan

2 Department of Physiological Sciences, School of Life Science, SOKENDAI (The Graduate University for Advanced Studies), Hayama, Japan

3 Center for Information and Neural Networks (CiNet), Advanced ICT Research Institute, National Institute of Information and Communications Technology, Suita, Japan

4 Biomedicine Discovery Institute, Neuroscience Program, Monash University, Clayton, VIC 3800, Australia

5 Department of Physiology, Monash University, Clayton, VIC 3800, Australia

6 Australian Research Council, Centre of Excellence for Integrative Brain Function, Monash University Node, Melbourne, VIC 3800, Australia

The authors not only described several unexpected features, in comparison with more intensively studied mammals, but also uncover systematic differences between aquatic and land-dwelling animals. Arcaro et al. (2022) explore the relationship between the sulcal anatomy of the occipital lobe and the retinotopic representation of V1 in human and macaque brains. They demonstrate that the relationship between sulci and retinotopy is highly consistent across individuals, but variable across species. This result has implications for models that attempt to explain the formation of retinotopic maps on the basis of constraints related to the biomechanics of the developing cortex (e.g. Schira et al. 2012). Another take-home message is that extrapolations between species of primates need careful consideration of anatomical differences, a topic that is also prominent in the paper by Rapan et al. (2022). Here, the authors used receptor autoradiography to compare multiple visual areas in both macaque and human brains. The paper demonstrates that the hierarchical flow of visual information follows similar organizational principles in human and macaque, even though the receptor architectures of putative homologous areas are not exactly equal in the two species.

A key aspect of the function of V1 are the computations performed by local circuits, through intrinsic connections. Two papers in this volume take on the challenge of understanding how this local anatomy informs models of visual processing. Using the tree shrew (*Tupaia belangeri*) as an animal model, Mohan et al. (2022) examine neuronal response properties in V1 to evaluate the relationship between structure (laminar location) and function (feature selectivity). The results support a model whereby the sharp feature selectivity found in supragranular layers can be established by weakly biased inputs from layer 4. Based on similarities and differences from previous reports in cats and primates, the authors suggest a fundamental computation. In another paper, Chavane et al. (2022) challenge the notion that intrinsic connections in V1 are always biased towards linking neurons with similar orientation selectivity. By reviewing the anatomical and physiological evidence, and linking this to computational models and theory, the authors conclude that the functions of V1 are subserved by a distance-dependent connectivity rule, which incorporates a like-to-like connectivity bias at short horizontal distances, and long-distance like-to-all connectivity. The authors speculate that this anatomical structure enables this area to perform its functions in a manner that enables a more flexible, context-dependent performance.

As highlighted in the special issue of *Brain Structure and Function* dedicated to structural connectivity (Takemura and Thiebaut de Schotten 2020), anatomical connections between brain areas deeply influence their functions. Five papers published in this special issue report or review findings on structural connectivity in the visual system. Gămănuţ and Shimaoka (2022) review our current understanding of hierarchical processing in the mouse visual system, based on both anatomical connections and physiological measurements. They propose that the hierarchical organization is relatively shallow compared to that observed in primates, again reinforcing the message that one needs to understand species differences to interpret functional results. The following paper addresses the issue of parallel processing: by combining retrograde tracer injection and intrinsic signal optical imaging, Fang et al. (2022) demonstrate that anatomical connections between macaque areas V2 and V4 are specific with respect to stimulus selectivity. These findings indicate that information about color and form remain separate in ventral mid-level visual processing, further highlighting the exquisite specificity of the structure–function relationship in the primate brain.

Understanding the specificity of visual connections in the human brain is challenging, given the impossibility of applying the high-resolution cellular tracing methods that have contributed so much to our knowledge of the nervous system in other mammals. An additional challenge is understanding functional specificity in the white matter, which is a highly important topic (for example, for interpreting the consequences of stroke), but has been relatively less studied. This requires new methodological approaches, such as the ones highlighted in the next four papers in this volume. Caspers et al. (2022) used polarized light imaging (Axer et al. 2011) to obtain high-resolution views of the sagittal stratum, a prominent compartment of the primate occipital white matter. The study demonstrates that this stratum sagitale has a more complex organization than previously realized, beyond the fact that it contains the optic radiations. In the following paper, Grotheer et al. (2022) review recent neuroimaging approaches combining functional MRI (fMRI) and diffusion MRI (dMRI) to identify subcomponents of white matter tracts terminating near specific functional regions in individual humans. In addition, Rizzi et al. (2022) combine anatomical dissection studies with dMRI and stereoelectroencephalographic experiments to obtain a more precise view of the dorsal loop of the human optic radiation, a topic of significant interest for neurological practice. Finally, still on the topic of developing and understanding methods applicable to the human brain, Fracasso et al. (2022) compare negative blood oxygen level-dependent (BOLD) responses and intracranial electrophysiological measurements acquired from the same human subjects, thus demonstrating that negative BOLD responses are associated with an absence or decrease of electrophysiological activity.

Four papers are related to categorical processing, which has often been discussed in relation to ventral visual stream of extrastriate areas (Ungerleider and Mishkin 1982; Goodale and Milner 1992). Hatanaka et al. (2022) used two-photon microscopy to compare the physiological activity of neurons in macaque V1 and V4 during viewing of naturalistic videos. Using a sophisticated statistical modeling technique, they demonstrate not only significant differences between these areas, but also a clustering of neurons in V4 according to the optimal type of stimulus. Using fMRI, Silson et al. (2022) evaluate the relationship between a measure of retinotopic representation (bias towards the contralateral hemifield) and category selectivity in human lateral–occipital and ventral–temporal cortex. This analysis revealed that visual areas on the lateral surface of the brain show a stronger contralateral than face or scene bias, while those on the ventral surface regions show the opposite pattern of selectivity. Taubert et al. (2022) review the current evidence on whether or not the cortical networks of areas selective for face and body information are separable, including a discussion of four competing hypotheses. This systematic analysis helps highlight the fact that significant complexity lies behind the apparently simple nature of this question, which demands new experimental and analytical approaches. In addition, Stenger et al. (2022) address the issue of structure–function relationship by reporting probability maps of several cytoarchitectonic areas in the human caudal parahippocampal cortex, and evaluating their likely functions by comparisons with previous fMRI studies on place selectivity, visuo-spatial processing, and memory processing.

While the overall distinction between the dorsal and ventral streams of extrastriate areas (and their respective associations with spatial categorical processing tasks) has been widely accepted, significant evidence supports their anatomical integration (Rosa et al. 2009). In particular, recent work has highlighted the significance of white matter tracts connecting these streams, such as the Vertical Occipital Fasciculus (VOF) (Yeatman et al. 2014; Takemura et al. 2016). Two papers in this special issue focus on this topic. Vinci-Booher et al. (2022) investigate the development of a group of human white matter tracts within and between dorsal and ventral streams by comparing dMRI datasets acquired from adults and children. The study concludes that the tissue properties of white matter tracts connecting the parietal and inferotemporal cortex are more adult-like compared with those forming the dorsal stream and less adult-like compared with those forming the ventral stream. Based on this finding, the authors suggest that tracts connecting dorsal and ventral stream areas may play a role in developing the dorsal stream. Further, Abdolalizadeh et al. (2022) report on how the VOF is affected in multiple sclerosis patients, demonstrating significant associations between its tissue properties and visual symptoms.

Two additional papers published in this special issue involve novel data acquisition and analysis methods, which will likely push forward future understanding of structure–function relationships in the visual system. Ip and Bridge (2022) review recent advances in magnetic resonance spectroscopy (MRS), a technique which enables non-invasive measurements on biologically relevant chemicals, including neurotransmitters, and recent studies using this approach to investigate human visual function. In addition, Tu et al. (2022) propose a novel analysis method applicable to fMRI-based retinotopic mapping. This method enables diffeomorphic registration of multiple visual areas, and improves the accuracy of the group analysis of fMRI datasets on the human visual system.

Lastly, Meikle and Wong (2022) address one of the most obvious ways in which knowledge about the structure and function of the visual system can have direct impact on human societies, by reviewing how understanding the anatomical and physiological properties of different visual areas can help in the design of prostheses designed to restore vision to the blind.

We believe that two special issue volumes (Part 1 and Part 2) demonstrate the significant progress of visual neuroscience in a manner that reflects the diversity of approaches that characterizes this field. At the same time, they also highlight the need to integrate knowledge obtained by different methods (at different spatial scales) and species. We hope that this special issue can prompt many future collaborative efforts that will help address the existing knowledge gaps.

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