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Visual Cortex: The Eccentric Area Prostriata in the Human Brain

Marco Tamietto[1,2,3] and David A. Leopold[4]
[1]Department of Clinical and Medical Psychology and CoRPS - Center of Research on Psychology in Somatic diseases - Tilburg University, Tilburg, The Netherlands
[2]Department of Psychology, University of Torino, Italy
[3]Department of Experimental Psychology, University of Oxford, Oxford OX1 3UD, UK
[4]Section on Cognitive Neurophysiology and Imaging, National Institute of Mental Health, 49 Convent Drive, Bethesda, MD 20892, USA; Neurophysiology Imaging Facility, National Institute of Mental Health, National Institute of Neurological Disorders and Stroke, National Eye Institute, Bethesda, MD 20892, USA
Correspondence: marco.tamietto@unito.it (M.T.), leopoldd@mail.nih.gov (D.A.L.)
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Human area Prostriata is a small, unstudied portion of the visual brain set deep in the calcarine sulcus, next to V1. A recent neuroimaging study in humans indicates that this area is specialized to respond to rapidly moving stimuli in the far periphery, consistent with single-unit responses in other mammals.

Neuroscientists studying the primate brain have spent a disproportionate effort to understand the functional organization of the primary visual cortex, also termed striate cortex or V1, which serves as the bottleneck for virtually all visual information passing into the cerebral cortex. As early as the 1960s, it was recognized that the primate V1 shares a long border with another large visual area, V2, which is present in all placental mammals. The other mammalian area bordering V1, however, has almost completely escaped notice of the vision neuroscience community and is familiar primarily to comparative anatomists. This area, known as prostriata, is diminutive in monkeys and humans, and lurks in the deep recesses of the calcarine sulcus.

The discoverer of prostriata, the German anatomist Friedrich Sanides [1], applied the Latin prefix 'pro' based on the area's primitive limbic cytoarchitecture [2], which suggested it to be an evolutionary precursor of the visual cortex. In monkeys, only approximately 10% of the V1 border lies adjacent to prostriata, whereas in non-primate mammals this fraction is thought to be much higher [3] (Figure 1A). In contrast to adjacent V1, prostriata lacks a clear six-layered structure, has a thinner layer 4, a thicker layer 2, and is lightly myelinated. Anatomically, it is located anteriorly to V1, serving as a bridge to the adjacent retrosplenial and parahippocampal cortices [4] (Figure 1B).

There is a reasonable expectation based on evolutionary conservation that this basic layout should be similar in the human brain. Nonetheless, the small size and relative anonymity of this area has left it untouched by human neuroscientists peering inside the brain with tools such as functional magnetic resonance imaging (fMRI). A new study by Mikellidou *et al.* [5] in *Current Biology* is thus bound to garner a lot of attention by providing the first functional description of area prostriata in the human brain. The authors used a novel method to carry out fMRI mapping of responses to stimuli presented over an unusually wide range of positions, including the far periphery of the visual field. Consistent with single-unit responses in nonhuman primates [6,7], they demonstrated that human prostriata has a map of the opposite visual field that is distinct from that of V1. Responses were strongest for stimuli that moved very fast over large receptive fields at visual eccentricities exceeding 60°, essentially out of the corner of the subjects' eye, suggesting that this area is important for monitoring the fringes of vision. Unlike other visual cortical areas, there was no particular emphasis on central vision, where attention and object recognition reside, as they found a similar proportion of voxels dedicated to the center and the periphery of the visual field (Figure 1C).

Mikellidou *et al.* [5] reached these conclusions using an analysis method called population receptive fields, which treats fMRI signals in a manner analogous to neural spiking responses in electrophysiology experiments [8]. This approach provides a fruitful basis for multimodal integration that can be used to compare the functional characteristics of visual neurons observed previously in the anesthetized marmoset monkeys [6,7]. In both species, the prostriata response properties suggest rapid and coarse analysis of fast moving and unexpected stimuli in the far periphery of the visual field. These physiological characteristics imply a key role of prostriata in initiating visual orienting and implementing postural responses to avoid collision, which is broadly consistent with its known pattern of output projections to structures such as the auditory cortex and cingulate motor areas.

Collectively, these findings [5] draw attention to the importance of the visual periphery in guiding natural behavior. Our understanding of vision is dominated by experiments in which isolated stimuli have been presented on relatively small screens, under the implicit assumption that the same principles and structures also govern perception in the periphery. Much is known about the brain's analysis of visual details, perception of objects, and parafoveal direction of attention, and it is clear from the allocation of the cortex that primate visual cognition places particular emphasis on central vision. But area prostriata is an example of a brain area devoted to monitoring eccentric vision, outside the focus of attention. This can be particularly important when faced with sudden changes in environmental conditions, as in the case of looming stimuli, and is pivotal to self-motion stabilization, head and body orientation

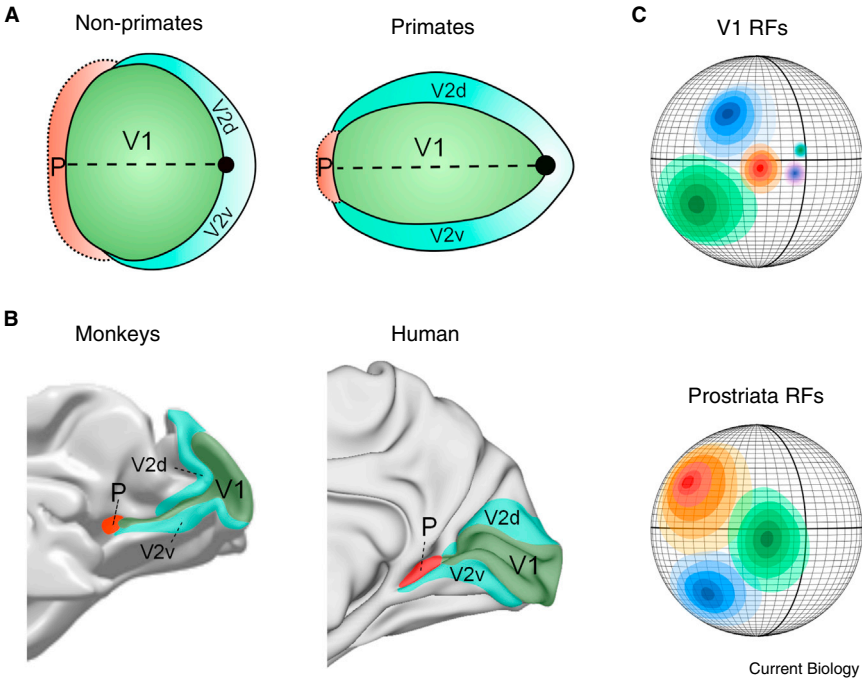

Figure 1. Area prostriata in the monkey and human brain.
(A) Topographical relationships of V1, V2 and prostriata (P) in non-primate and primate brain displaying the comparative reduction of prostriata in primates. (Adapted from [3].) (B) Location of V1, V2 and prostriata in the monkey (macaque) and human brain. (C) Examples of receptive field (RF) sizes of typical neurons in V1 and prostriata. RF sizes increase with eccentricity in V1, whereas they remain relatively constant and comparatively large in prostriata.

[6]. In keeping with this notion, the study by Mikellidou *et al.* [5] provides the first example of functional preference for very fast motion in any human visual area. The physiological, connectional and anatomical properties of prostriata together suggest an anatomical network for the analysis of motion in the far periphery that is largely segregated from that in well-studied cortical areas primarily devoted to central vision.

Clinical studies provide another source of information about the properties of human prostriata. Focal brain lesions in this region of the brain can lead to the 'half-moon syndrome' [9], referring to the loss of vision in the far periphery contralateral to the damage, or delayed attentional habituation to contralateral stimuli [10]. Importantly, the observed deficits are not purely visual, but rather encroach on affective behaviors, which is typically associated with limbic functions. For example, sensitivity to peripheral stimuli related to dysfunctions of prostriata and surrounding areas appear to contribute to panic disorders and agoraphobia [11]. By contrast, selective damage to V1 produces an entirely different syndrome that has virtually no effect on limbic functions [12]. Specifically, V1-damaged patients are clinically blind in the field opposite the lesion, but exhibit no change in their affective state. They are sometimes able to retain non-conscious visual functions, a condition known as 'blindsight' [13,14]. In such patients [15], and in monkeys with comparable lesions [16], looming stimuli typically elicit normal appropriate defensive reactions [17]. These observations may provide clues about the origin of the prostriata visual input, which has never been clear. The preserved response to peripheral moving stimuli after damage to V1 argues against V1 as the primary input source to prostriata. One possibility is that of a parallel and independent input from subcortical areas, such as the pulvinar or more anterior nuclei of the thalamus that receive projections directly from the retina as well as through the superior colliculus [18].

Functional and connectional properties of area prostriata pose challenges to several organization principles commonly applied to the visual system. One such principle concerns the hierarchical progression of visual processing, starting from V1. The projection patterns, response latency, and receptive field characteristics to some extent contradict each other for classifying the hierarchical position of prostriata. For example, short-latency or lack of adaptation and selectivity to motion direction are typical of structures in very early stages of the visual system, whereas large receptive fields are more typical of higher-order areas. Another challenge comes in assigning prostriata to dorsal or ventral visual pathways within the extrastriate cortex, a dichotomy that is itself under renewed scrutiny [19]. While exhibiting short-latency and eccentric responses that bear some similarity to the dorsal 'where' or 'how' cortical pathway, the big receptive field size and efferent connections of prostriata neurons are distinctly different from traditional dorsal stream areas. Might prostriata feed an additional, parallel processing stream with a different function altogether? This is possible, though it is worth noting that the dorsal visual pathway is now conceived as a multiplicity of pathways based on diverse downstream projection targets [20]. One of these subpathways entails a projection to the medial temporal lobe that courses through the posterior cingulate and retrosplenial cortex — in and around prostriata. It is conceivable that this subpathway, whose proposed function is to support multimodal spatial processing and navigation, might contribute to the observed responses and provide a systems-level context for prostriata.

In summary, Mikellidou *et al.* [5] have described for the first time the functional properties of area prostriata in the human brain. This has been possible by introducing several important novelties in the neuroimaging approach to vision: the use of a wide-field projection system able to map the visual periphery, the choice of stimuli moving at varying speeds, and analysis methods that favor comparisons with previous neurophysiological studies in monkeys. The peculiar properties and the paucity of studies on prostriata make a quote from the British novelist Aldous Huxley particularly appropriate to describe its fate in vision neuroscience: "There are things known and there are

things unknown, and in between are the doors of perception''.

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Behavioral Evolution: Can You Dig It?

Michael J. Sheehan*, Caitlin H. Miller, Caleb C. Vogt, and Russell A. Ligon
Department of Neurobiology and Behavior, Cornell University, Ithaca, NY 14853, USA
*Correspondence: msheehan@cornell.edu
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Behaviors are among the most complex phenotypes, making the genetic dissection of behavioral differences extremely challenging. A careful dissection of ontogenetic differences in burrowing behavior between mouse species highlights the importance of integrative approaches to the study of behavioral evolution.

A major goal of researchers studying the evolution of behavior is to link mutations to specific changes in complex behavioral traits [1]. Behavioral evolution may involve changes in sensory systems, in the brain or even anatomical changes in the structures used to carry out a behavior (Figure 1). This complexity often requires significant efforts just to describe behavioral differences between species, let alone to map them genetically. For example, detailed analyses of schooling differences between marine and freshwater sticklebacks revealed multiple distinct behavioral modules that had evolved to reduce schooling in freshwater sticklebacks [2]. Similarly, courtship songs from closely related *Drosophila* species differ in multiple features, controlled by distinct loci [3]. Increasingly, it is clear that careful dissection of the behavioral differences between species is key to linking mutations to changes in specific aspects of behavioral phenotypes. A new study by Hillery Metz, Hopi Hoekstra and colleagues [4] in *Current Biology* details the ontogeny of burrowing in two species of deer mouse and suggests that one locus may influence the motivation to dig burrows. This provides a potential link between the genomic and neuronal architecture of behavioral evolution.

Efforts to uncover the genetic basis of complex behavioral adaptations have been especially fruitful drawing on natural diversity in North American deer mice (*Peromyscus* Spp.). Hopi Hoekstra and colleagues have tackled the genetic differences in burrow architecture [5] between two closely related species of deer mouse, *Peromyscus maniculatus*