

Cognitive Control Signals in Visual Cortex: Flashes Meet Spotlights

At the intersection of two intensely belabored fields, primary visual cortex (V1) function and neural mechanisms of cognitive control, Jack et al. (in this issue of *Neuron*) report a neural signal that is neither related to stimulus representation nor spatial attention. Instead, this endogenous signal correlates with task structure and raises new questions.

Across several species, primary visual cortex (V1) is arguably the most heavily studied and best understood brain area. The investigation of its functional response properties was heralded by the seminal work of Hubel and Wiesel who were first in eliciting reliable and selective responses of single neurons to sensory stimuli. These stimulus-related response properties included retinotopic receptive fields and orientation selectivity and have appeared in every neuroscience textbook. Along these lines, V1 is still often thought of as a camera-like device that provides a somewhat distorted and fractured but fairly veridical representation of the retinal image. Yet its neurons seem to be involved in functions going beyond mere image representation.

This insight comes as no surprise if one considers the anatomical connectivity of V1 and realizes that retinogeniculo-cortical afferents provide only a fraction of its input (Casagrande and Kaas, 1994). Despite these anatomical clues, it has proven more difficult to evoke V1 responses by mechanisms other than sensory stimulation, as for instance by visual imagery or spatial attention, cognitive processes that are associated with strong activity changes elsewhere in the brain. Following initial sparse electrophysiological reports of attentional V1 activity modulation, significant progress came from functional magnetic resonance imaging (fMRI) studies that mapped activations during covert spatial attention to corresponding retinotopic representations of the attended visual field locations (reviewed in Posner and Gilbert, 1999).

Given the number and quality of studies at the crossroads of V1 function and spatial attention, one would have believed this gold mine to be fully exploited, but the study by Jack et al. (2006) in this issue of *Neuron* comes up with a novel neuroscience nugget: they report transient V1 activations that are neither associated with stimulus processing nor with spatial attention. Separation in time (between stimulus presentation and behavioral reporting) and space (within retinotopic cortical maps) allow them not only to reproduce previous findings on spatial attention but also to distinguish from these signals a novel endogenously generated V1 response.

Spatial attention (orienting) induces signal increases that are maximal at the time of stimulus presentation and at the cortical representation of stimulus location. Across retinotopic areas, these signals grow in size

and/or strength the higher one moves into the cortical visual hierarchy. Conversely, the novel V1 signal reported by Jack et al. (2006) occurs at task on- and offset, manifests throughout V1 with a preference for the peripheral visual field representation, and is less pronounced in higher retinotopic visual areas. In the initial experiment, the task-related signal also correlates with auditory signals cuing stimulus appearance and response timing, but it persists in experiments where responses are self-initiated as well as in no-go trials. These control experiments rule out direct confounds from auditory stimulation and response cuing as well as from actual execution of a motor response. Even more interestingly, yet another experiment with alternating visual and auditory targets establishes that this novel type of V1 response is even observed in trials with auditory targets and no visual stimuli.

It is remarkable that despite previous intensive research on V1 function and neural mechanisms of spatial attention, such a relatively strong signal modulation as described by Jack et al. (2006) should have passed unnoticed or uncommented upon in previous studies using similar paradigms. Visual cortex responses to afferent signals of nonsensory origin have traditionally received less attention than sensory responses. Within this comparably small literature, most reports deal with the effects of ascending neuromodulatory systems, eye movements and attention to space, features, or objects. There are only anecdotal reports on task-related responses (e.g., Watanabe and Iwai, 1996), and their spatiotemporal properties, neural origins, and functional significance have never been thoroughly elucidated. One reason why such signals have been largely neglected previously may be that their adequate characterization falls into the gap between the spatial sampling characteristics of traditional single-cell recordings in laboratory animals and mainstream neuroimaging studies in humans. However, approaches based on detailed cortical mapping in single human subjects as used here by Jack et al. (2006) and by others before seem capable of partially bridging this gap.

The observations reported in the study by Jack et al. are sound and solid, and they considerably advance our phenomenological understanding of an interesting component of V1 activity. Yet the functional, let alone behavioral, significance of this signal remains puzzling. What good could this signal do any particular perceptual or behavioral process? The same features that permit us to distinguish this signal from that related to spatial attention also raise doubt as to whether it is useful in perceptual processing. Jack et al. (2006) propose a functional interpretation in the context of marking task boundaries. One could think of this as a transient reset mode, a tenable and tempting hypothesis that nonetheless awaits further, more conclusive confirmation in dedicated experiments.

In their experiments, Jack et al. (2006) also replicate activity modulations related to spatial attention, and these latter signals can more obviously endorse perceptual processing. Overall, several studies have shown

that the cortical “spotlight” of spatial attention reflects a sophisticated and versatile neural mechanism. In accord with behavioral effects, the V1 correlates of the attentional spotlight display a Mexican hat configuration with a contrast-enhancing antagonistic surround (Müller and Kleinschmidt, 2004), and they can flexibly adapt to incorporate object shape-related processing, even in lower-tier visual areas (Müller and Kleinschmidt, 2003). By contrast, the V1 activity modulation reported by Jack et al. appears primitive from a functional perspective, and by analogy this signal could hence be called a cortical “flash.”

One important question is whether this flash can be related to attentional functions. Alerting is a more primitive attentional function than spatial orienting. Neuroimaging studies have reported that signal modulations from alerting can be constrained to task-relevant sensory cortex (Thiel et al., 2004). From a functional perspective, alerting could account for some of the response properties observed by Jack et al. A flash could simply boost neural resources available to one or several of the senses prior to the arrival of fine-grained spatial information required for orienting. A flash could prioritize the periphery of the current visual field to facilitate future reorienting away from the current (foveal) focus of attention. And finally, if considered a primitive mechanism, a spatially nonspecific flash mechanism might also show less selectivity and thus be associated with a high number of false alerts. If, for instance, within a given experiment (with low perceptual load) half the trials involve visual and half the trials involve auditory targets, why not send alerting flashes to visual (and presumably auditory) cortex on every trial and thus also on trials where only auditory targets appear? Or why not send alerting signals to visual cortex whenever auditory stimulation cues motor responses, given that half the trials closely associate timing of visual input and motor responses?

These latter considerations point at an important issue that is worth dwelling upon when interpreting cognitive neuroscience studies. Imagine training subjects to say “bah” in response to a red light. You then scan their brains while comparing two conditions. In one, a green cue lights up, instructing them to say “bah” in response to a subsequent red light; in another, a blue cue lights up, instructing them to generate no response to a subsequent red light. Chances are that the trials with blue lights will evoke nearly as much activity in neural circuits preparing articulation as trials with green lights. This is not a shortcoming of the particular study by Jack et al. (2006) but a generic concern across the entire behavioral neurosciences. Artificial dissection of natural and ecologically optimized perception-to-action loops is one problem, for instance when introducing delays that would not occur in real life. Another problem illustrated by the aforementioned thought experiment is that explicit requirements in one experimental condition can spill over into implicit effects in another condition, especially when the two are bound together in a single paradigm. It is hence conceivable that in an ecologically meaningful context, the signal reported by Jack et al. would offer more obvious behavioral benefits than when considered within the framework of the experimental paradigm that was used (and necessary) to detect it.

That even a seemingly tightly tuned area as adult V1 can be sensitive to effects from associative learning, and that this may cast open the door to nonretinal influences, is illustrated by recent work in rat visual cortex (Shuler and Bear, 2006). When rats had learned that flashes to the left or the right eye predicted shorter or longer timing of a subsequent reward, respectively, many of the initially only stimulus-sensitive visual cortical neurons displayed additional activity that was maintained up to or even restricted to the expected time points of reward. Once established, this neural behavior no longer required actual reward to occur but persisted into the posttraining period. As in the case of Jack et al. (2006), Shuler and Bear (2006) can currently only speculate about the putative neural mechanisms that might underpin their discovery of reward expectancy coding in visual cortex activity.

Help to unravel mechanisms may come from pursuing one obvious future question, namely, where in the brain such effects originate. At first glance, this is a suitable question for functional neuroimaging, but in their related whole-brain analyses, Jack et al. found no cortical candidates activating in parallel with the V1 flash. But should we necessarily expect a cortical source of the flash? The study by Jack and colleagues also reminds us to regularly revisit labels used in simple heuristics of cortical function. Spatial attention, for instance, is often considered a “top-down” process that relies on “feedback” connections from higher-order areas, and combined functional neuroimaging and electrophysiological studies have provided evidence in favor of such a view on the spotlight (Martinez et al., 1999). There is abundant evidence of candidate cortico-cortical connections innervating V1, but extrageniculate subcortical modulation should neither be forgotten nor underestimated. In a usual hierarchical view, these projections could readily be classified as bottom-up and feedforward. Of note, sensitivity of conventional functional neuroimaging to subcortical effects may be low not only because of limitations in spatial resolution but also due to high tonic activity in such structures.

Single-cell studies of the thalamic reticular nucleus in monkeys have recently reintroduced subcortical mechanisms into the arena of putative contributors to the attentional spotlight in retinotopic areas as V1. Neurons in this thalamic structure are good candidates. As pulvinar neurons, they code retinotopic information required for spatial orienting, but they could act on geniculocortical transmission instead of projecting to V1 (McAlonan et al., 2006). A well known direct thalamic projection to V1, however, the intralaminar nuclei, does not preserve retinotopy (Perkel et al., 1986) and preferentially innervates the peripheral field representation in V1, as does the claustrum (Minciacchi et al., 1995). Although these latter functional response properties would be compatible with the flash characterized by Jack et al. (2006), this neuroanatomical account remains as speculative as the structural and functional interpretations proposed by the authors. In conclusion, the result of the study by Jack et al. (2006) is clearly not an endpoint but a stimulating and thought-provoking starting point for future research into V1 activity and its modulation by cognition.

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Selected Reading

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