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Three Hundred Million Years of Attentional Selection

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In this issue of *Neuron*, Winkowski and Knudsen reveal striking parallels between the attentional systems of the barn owl and the rhesus macaque. The observation of close similarities between the attentional systems of such distantly related organisms strongly suggest that key computational principles are at work.

The discovery of parallels between the attentional systems of the barn owl and the rhesus macaque is profoundly interesting because amniotes, the common ancestors of macaque and owl, diverged during the Carboniferous period, some 300–360 million years ago. This divergence resulted in two major evolutionary lineages, the Synapsids, which eventually gave rise to mammals, and the Sauropsids, which eventually gave rise to birds. The experiments described in the Winkowski and Knudsen article (Winkowski and Knudsen, 2008 [this issue of *Neuron*]) were inspired, in part, by a series of elegant studies implicating the frontal eye field region (FEF) of the rhesus macaque in the control of spatial attention.

FEF, part of the frontal cortex, plays a key role in the control of eye movements. It forms a retinotopic map of visual space, with electrical stimulation of neurons at a given FEF site eliciting eye movements to a position in visual space known as the movement field (MF) of the stimulation site. Stimulating current can be reduced to a level just below the threshold current required to elicit an eye movement. This causes an improvement in perception at the MF location. The effect of stimulation is similar to what is observed with spatial attention: a reduction in the minimum luminance contrast at which the monkey can accurately discriminate a stimulus appearing at the movement field location (Moore and Fallah, 2001). FEF projects both directly and indirectly to visual cortical areas involved in attentional selection, including visual area V4, an intermediate stage of processing within the ventral stream. Lesions of V4 markedly impair performance on attention-demanding tasks (De Weerd et al., 1996). Neurophysiological studies of V4 have found that when attention is directed to a stimulus within a V4 neuron's receptive field, this modulates the neuron's response so as to enhance processing of the attended stimulus while simultaneously suppressing neuronal responses to task-irrelevant distracters (Reynolds and Chelazzi, 2004). Both of these forms of attentional modulation are observed under low levels of FEF stimulation (Moore and Armstrong, 2003; Armstrong et al., 2006), suggesting that FEF modulates the circuitry within V4 to yield attentional selection.

The present study builds on earlier work from Winkowski and Knudsen that followed a similar logic (Winkowski and Knudsen, 2006). They applied small amounts of electrical current to neurons in the arcopallial gaze fields (AGF), a premotor region in the owl's forebrain that is a possible homolog of mammalian FEF. As with FEF, AGF plays a central role in the control of gaze direction and mediates memory-guided saccades. As with FEF, AGF projects in parallel to the deep layers of the optic tectum (OT, the avian equivalent of the mammalian superior colliculus) as well as to saccade-generating premotor neurons in the brainstem. Consistent with this putative homology, Winkowski and Knudsen found that AGF stimulation increases the responses of downstream sensory neurons located in the deep layers of the OT. On the basis of these experiments, they concluded that owl AGF plays a role in attentional allocation that is similar to the role of FEF in the macaque.

In the present study, they take this parallel a major step forward by quantifying the effects of AGF stimulation while parametrically varying the auditory stimulus used to drive OT neurons. They find that AGF stimulation modulates OT neuronal responses in ways that closely parallel attentional modulation in the macaque and the human (Reynolds et al., 2000; Martinez-Trujillo and Treue, 2002; Li et al., 2008; Ekstrom et al., 2008). The first of these primate studies was motivated by a relatively simple model of the circuitry

that transforms attentional feedback signals into improved visual processing. According to the normalization model of attention, evolution has co-opted the circuits that enable the visual system to automatically adapt its sensitivity to changes in the strength of visual input (Reynolds and Chelazzi, 2004; Reynolds et al., 1999). Feedback from attentional control centers including FEF multiplicatively scales the inputs to a normalization circuit (Heeger, 1992). This normalization circuitry transforms the scaled inputs to give rise to a variety of observed forms of attentional modulation. Under appropriate sensory conditions, the model predicts that these feedback signals will cause an increase in contrast gain, reflected in a leftward shift of the neuron's contrast response function. This prediction has been validated in several experiments, including extracellular recording experiments in areas V4 (Reynolds et al., 2000) and MT (Martinez-Trujillo and Treue, 2002), an fMRI study of attention in humans (Li et al., 2008), and an fMRI study of the effects of FEF stimulation in the macaque (Ekstrom et al., 2008).

Winkowski and Knudsen find that AGF stimulation causes a leftward shift in the auditory equivalent of the contrast response function. They varied the intensity of an auditory stimulus that fell within the receptive field of the OT neuron under study. As is typically the case for visual neurons tested at different levels of luminance contrast, they find that OT neurons exhibit a saturating neuronal response as a function of stimulus intensity. When they applied current to the AGF site corresponding to the location of the auditory stimulus (inside the OT neuron's receptive field), they observed a leftward shift in the response profile. This suggests that similarities between the owl and the macaque attentional systems hold not only at the level of gross anatomy, with the oculomotor systems of both animals providing attentional feedback to sensory systems, but also at the level of the microcircuitry that is modulated by this feedback. OT appears to share key computational properties with the mammalian neocortical circuits that receive attentional feedback from FEF.

Winkowski and Knudsen also examined other indices of AGF modulation, including the effect of AGF stimulation on the reliability of the neuronal response, the shape of the neuronal tuning curve, and the capacity of the OT neuron to convey information about the stimulus. All of these observations were in keeping with what would be expected from the AGF-induced modulation of firing rate. In a key comparison condition, they also examined the effect of stimulating an AGF site that fell well *outside* the OT receptive field. In contrast to what they observed with AGF stimulation inside the receptive field, this induced a reduction in the firing rate of the neuronal response across all sound levels—a divisive scaling of the auditory response. This leads them to the interesting conclusion that spatial attention in the owl engages two distinct mechanisms: one that increases contrast gain at the attended location and a second that divisively reduces the firing rates of neurons at unattended locations. The authors speculate that this second form of response modulation may account for the findings of a recent study of visual attention in macaque area V4 that found qualified support for multiplicative scaling of firing rate across the entire contrast response function (Williford and Maunsell, 2006). They suggest that those attention effects may reflect the withdrawal of attention from a location outside the receptive field, which would release the neuron from the divisive effect they observed in the OT. This is an intriguing proposal, though it is unclear why this mechanism would have been activated in some studies and not others.

This second mechanism may instead turn out to reflect a difference between mammalian and avian attentional systems. FEF stimulation studies in the macaque have found no evidence for a reduction in response gain upon stimulation of an FEF site whose MF falls outside the V4 RF, when only a single stimulus appears in the visual field. FEF stimulation outside the receptive field can reduce responses but, in keeping with the predictions of the normalization model of attention (Reynolds and Chelazzi, 2004), this has only been observed when a visual stimulus is present at the MF location outside the V4 neuron's RF. When no stimulus appeared at that location, as in the present study, there was no measurable suppression of the V4 visual response (Moore and Armstrong, 2003). The differences in attentional modulation that have been observed across studies of attention in the macaque may instead reflect differences in task demands or sensory conditions across studies.

A key goal for future research will be to gain a deeper understanding of the circuitry that mediates attentional selection. It is possible, to some extent, to probe this circuitry in the macaque. For example, Mitchell et al. have provided evidence that attention differentially modulates the responses of pyramidal neurons and fast spiking interneurons (Mitchell et al., 2007). However, Winkowski and Knudsen's work suggests that the commonalities between attentional mechanisms in owl and monkey represent a sort of canonical selection mechanism that can be explored in both species. They are therefore poised to link the more detailed circuit insights they will be able to achieve in the owl to related observations in the monkey, potentially yielding key new insights into human attentional mechanisms.

Perhaps the most important consequences of this study are its implications for the evolutionary significance of attentional selection. Winkowski and Knudsen have shown remarkable parallels between attentional selection in owl and macaque. It is tempting to speculate that the owl OT and the mammalian neocortex may have undergone a process of convergent evolution. The microcircuitry that evolved in each structure to allow it to automatically adjust sensitivity upon changes in input strength may have been exploited in both mammals and birds to allow the brain to endogenously control sensory processing to meet moment-to-moment information-processing demands. This correspondence may instead reflect a set of neural mechanisms present in early amniotes, which conferred an evolutionary advantage so great that it has been preserved over the intervening 300 million years. In either case, the present study underscores the essential importance of attentional mechanisms and points to a set of canonical computations that are observed in very distant members of the animal kingdom.

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Toward an Anatomy of Disappointment: Reward-Related Signals from the Globus Pallidus

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The globus pallidus (internal segment, GPi) is traditionally regarded as part of the motor system. In this issue of *Neuron*, Hong and Hikosaka report on a little known projection from the monkey GPi to the lateral habenula that is modulated by reward. This adds an important branch to the brain's reward circuitry.

Disappointment is a not an unfamiliar experience for most of us. A negative outcome may be signaled by an empty hand or more abstractly by a letter starting with a fateful sentence regretting a lack of funds for research. In response to a signal predicting such a negative outcome, an essential part of adaptive behavior is to conserve effort and not expend resources in fruitless pursuits. The brain's reward system, important for guiding reward-seeking behavior and reinforcing successful actions, also responds to signals that predict no reward. In this issue of *Neuron*, Hong and Hikosaka (2008) report on neurons that respond positively to predictors of nonreward.

While the dopaminergic neurons of the midbrain have become widely regarded as a central part of the brain's reward system, particularly in computational models of reinforcement learning (Dayan and Balleine, 2002), relatively little is known about the neural circuitry that controls dopaminergic neuronal activity in the real brain, particularly in relation to signaled nonreward (Hikosaka et al., 2008). The lateral habenula (LHb) has recently emerged as an important component of the control circuitry providing a key source of input to dopaminergic neurons (Ji and Shepard, 2007).

In this issue, Hong and Hikosaka add another limb to this circuitry by an elegant electrophysiological demonstration of reward-related modulation of neurons in the monkey globus pallidus (internal segment, GPi) that project to the LHb. They measured the firing activity of both GPi and LHb neurons during a one-direction reward task. In this task, a visual target is presented randomly on the left or right, and the monkey has to make a saccade to the target. One direction is rewarded, while the other is unrewarded. Two types of responses were observed: some neurons showed an increase in response to the target indicating the absence of upcoming reward and a decrease in response to the target indicating the presence of upcoming reward (reward-negative type). The others showed the opposite, increasing in response to the reward-predicting target and decreasing in response to the no-reward-predicting target (reward-positive type). Reward-negative responses had been described in the LHb, and now for the first time they are reported in the GPi.

The GPi neurons in the current study are a minority group of neurons identified by their antidromic responses to electrical stimulation in the LHb. The GPi to LHb projection is not so well-known, but has been studied in several species, including monkey (Parent et al., 2001). The stimulation in the present study identified a distinct subset of antidromically activated GPi neurons located near the border of the globus pallidus. Their firing pattern differed from the movement-related activity typical of GPi neurons that project to the motor part of the thalamus, and their location was consistent with the anatomical studies of LHb-projecting neurons (Parent et al., 2001).

Could these GPi cells be driving the reward-negative responses of the LHb neurons? That these responses occurred in identified LHb-projection neurons might