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Walk This Way

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The neural mechanisms that decide when and where to walk are not well understood. In this issue of *Neuron*, Felsen and Mainen use an olfactory-guided orienting task to show that the superior colliculus is necessary in rodents for the normal execution of spatial locomotor choices.

The superior colliculus (SC), also called the optic tectum in many vertebrate species, plays a central but only partly understood role in sensory-motor processing and decision-making (Wurtz and Albano, 1980). Perhaps the most distinctive feature of the SC is that it holds its sensory and motor signals in the form of neatly organized spatial maps that provide a topographic representation of the world. The maps are often dominated by vision, but they can also represent auditory, somatosensory, vibratory, and even infrared or electrical signals, depending on the sensory capabilities of the animal. In most vertebrates, the SC is the premier brain center for integrating sensory inputs from multiple modalities and for governing how the animal orients and interacts with its environment (Holmes and Spence, 2005). In primates, the SC is best known for its role in the motor control of saccadic eye movements, but recent work shows that the primate SC in fact participates in a broad range of functions, including the control of head movements, smooth pursuit, target selection, and perhaps even spatial attention (Krauzlis et al., 2004). The range of functions touched on by the SC is striking, and it also makes it more difficult to pinpoint the particular neural computations that are accomplished by this structure.

In this issue of *Neuron*, Felsen and Mainen (2008) employ an olfactory discrimination task that they have pioneered over the past several years (Uchida and Mainen, 2003) in a novel attempt to address these issues. In their task, rats first sampled an odor or odors presented at a central port and then moved to an adjacent port on either the left or right side to receive a potential water reward. The job of the rats was to identify which of two odors was presented at the central port and then move to the appropriate reward port. In some sessions, Felsen and Mainen recorded neural activity from the SC of the freely moving rats using tetrodes, and in other sessions they made focal and reversible lesions in order to establish causal relationships between SC activity and choice. Their findings show that the SC plays a surprisingly important role in generating locomotor choices.

A majority of the neurons recorded by Felsen and Mainen (2008) in the deeper layers of the rat SC exhibited directional selectivity during specific phases of the task. Some showed selectivity while the rats were still standing at the central odor port, whereas others showed selectivity as the rats walked to the left or right port to claim their potential reward. Still others retained their directional selectivity even after the movement was completed and the rat lingered at the reward port. Although a few other studies have studied SC activity in freely moving rats (e.g., Pond et al., 1977; Weldon et al., 2007), this is the first time in the rat that SC activity has been studied in a discrimination choice task.

More significantly, the authors also show that reversible inactivation of the SC on one side causes a spatial bias in the choices made during the task. For these experiments, the rats were presented with mixtures of two odors at the central port. Each odor was associated with a reward port, and the rat chose the port corresponding to the odorant with the greater concentration. Task difficulty was modulated by manipulating the relative ratio of the two odors. Just before the behavioral session, the SC on one side was infused with muscimol, which decreases neuronal activity by binding to the inhibitory $GABA_A$ receptor. Consistent with the spatial organization of the SC (e.g., the left SC represents the right side of space), inactivation biased choices away from whichever odor was associated with the inactivated side. Moreover, when rats did choose with the inactivated side, their reaction times for those responses were longer. These results provide strong evidence that SC is necessary for spatial locomotor choices in the rat.

Nevertheless, it remains unknown which aspects of task performance were impaired by lesion of the SC. Successful completion of the task presumably requires a variety of separate processes including perception of the odorants, localizing the odorants in space, evaluating the sensory evidence indicating that one port or the other will be rewarded, selection of the appropriate response, and planning the movement. In considering these many processes, it is common to employ a conceptual dichotomy between the activity associated with perception, or sensory decision-making, and that associated with action, or locomotion.

Do the results of Felsen and Mainen (2008) mean that the rat SC is directly involved in controlling locomotion? Their data are consistent with this possibility, but some alternatives warrant discussion. The motor aspects of the choice task used by Felsen and Mainen are complex, including movements of the eyes, head, pinnae, vibrissae, and trunk, as well as the legs. The SC is well known for its role in orienting movements of the eyes and head but also, for example, plays an important role in the control of whisking movements in the rat (e.g., Hemelt and Keller, 2008). The relatively high number of SC neurons that preferred ipsiversive movements in the locomotor task may be related to SC involvement in the spatial control of one or more of these other motor outputs. Similarly, inactivation may have undercut performance by impairing other components of spatial orienting rather than locomotion itself. On the other hand, there is evidence that SC activity is related to control of the legs and arms (e.g., Werner, 1993; Fitzmaurice et al., 2003), consistent with the idea that the SC plays an important role in the skeletal motor system. Teasing apart these different aspects of motor control is a major challenge, but one that might be more readily addressed with the experimental approach taken by Felsen and Mainen (2008).

Do these results mean that the SC is involved in olfactory decision-making? The SC is clearly one of the few major sites in the brain where information from different senses are merged (Stein and Meredith, 1993), but historically, most causal studies of SC function (e.g., microstimulation, inactivation) have addressed how SC activity biases motor responses rather than how SC activity might also bias sensory processing. For example, the classic Sprague effect dramatically demonstrates how activity in the SC is part of a push-pull network for prioritizing motor responses in space, and that disruption of this activity can cause motor neglect (Sprague and Meikle, 1965; Sprague, 1966); only recently has it been shown that the biasing effect of SC activity may also apply to the sensory detection or discrimination that precedes the motor response (Fitzmaurice et al., 2003). In the current study, SC inactivation clearly biased choice in the task; in contrast, it is unclear that any particular motor function was impaired, nor does it necessarily follow that impairment of any particular motor function would have led to the observed biasing of choice. New variants of this task will be required to determine the extent to which the SC is involved in the formation of sensory judgments versus the control of motor responses.

One of the striking features of the task used by Felsen and Mainen (2008) is that it is relatively natural and unconstrained. Most SC studies use very constrained sensory-motor paradigms and find a fairly limited range of directional preferences and stereotyped timing of neuronal activity. In contrast, Felsen and Mainen report heterogeneous directional preferences and an unexpected diversity in the timing of selective activity, including persistent activity that extends through the reward period. These findings hint at a wealth of possible functional roles for SC neurons far greater than that explicated in previous tasks. In light of the diversity of these responses, it might seem surprising that inactivation of the SC would lead to such a stereotypical and reproducible bias in choice. This suggests that these neurons are components of networks besides those described in the motor control of orienting. For example, some of this activity may be related to projections from the SC to the basal ganglia related to detecting salient events (Comoli et al., 2003), or to ascending projections to thalamic nuclei involved in evaluation of reward (CMPf) and regulation of sensory processing (pulvinar, TRN) (e.g., Minamimoto et al., 2005).

The various layers that make up the SC are party to a wide variety of neural circuits, and it is likely that our understanding of SC function has itself been biased by our choices of experimental tasks and the consequent emphasis on some circuits over others; investigations such as that of Felsen and Mainen (2008) are only the beginnings of a larger endeavor required to understand this diversity in SC function.

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