When Outgoing and Incoming Signals Meet: New Insights from the Zona Incerta

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In the sense of touch, it is the motion of the sensory receptors themselves that leads to an afferent signal—whether these receptors are in our fingertips sliding along a surface or a rat's whiskers palpating an object. Afferent signals can be correctly interpreted only if the sensory system receives information about the brain's own motor output. In this issue of *Neuron*, Urbain and Deschênes provide new insights into the physiological and anatomical interplay between tactile and motor signals in rats.

Rats and mice generate touch signals by palpating objects through self-controlled whisker motions called "whisks." Such "active sensing" endows the animals with the capacity to rapidly and accurately judge the physical features of objects—their position, size, shape, and texture (Brecht et al., 1997; Krupa et al., 2001; Knutsen et al., 2006; von Heimendahl et al., 2007). But signals traveling from the receptors in the whisker follicle are uninterpretable unless the nervous system can integrate them with knowledge of the sensor motion that generated the tactile signal to begin with (Kleinfeld et al., 2006). Likewise, motor output can be optimized only if updated with sensory signals. The complex interaction between sensory and motor systems is the problem addressed in an article by Urbain and Deschênes (2007) in this issue of *Neuron*.

They focus on a nucleus named the Zona Incerta (ZI). Although ZI catches the eye as a large, horizontally elongated region wedged just below the ventral tier of the thalamus (Jones, 2007), its possible functions have been overlooked; indeed, its very existence is unknown to many neuroscientists. From recent work (reviewed in Urbain and Deschênes, 2007), it is known that ZI forms part of the "paralemniscal" somatosensory pathway, one of the four streams traveling in parallel from periphery to cerebral cortex.

(The other three pathways synapse in various sectors of the ventral posterior medial nucleus of the thalamus [VPM].) In particular, the ventral division of ZI (ZIv) receives vibrissal input from the spinal subdivision of the brainstem trigeminal complex and projects to the medial subdivision of the posterior complex (POm), the thalamic relay of the paralemniscal pathway (Diamond et al., 1992; Yu et al., 2006). In addition to ZIv input, POm receives direct projections from the brainstem trigeminal complex and from the cortex. However, since ZIv cells are GABAergic, their activity *suppresses* sensory responses in POm. This intriguing circuit raises a critical question: under what conditions is ZIv active or inactive, thus inhibiting or releasing (respectively) the flow of signals through POm? The present study shows that in anesthetized rats, electrical microstimulation of primary motor cortex (M1) excites one neuronal population in ZIv through a direct corticofugal pathway. The activated ZIv neurons, through a local GABAergic circuit, suppress the sensory responsiveness of another population of ZIv neurons; this second population projects to POm and, if active, would act to inhibit POm. In other words, the net effect of M1 activity is to *release* POm from the inhibitory influence of ZIv, opening up the flow of whisker signals through POm.

The present work thus shows that ZIv is one of the crucial nodes for the integration and distribution of both sensory and motor information. But what functions are served by ZIv inhibiting the paralemniscal pathway, or releasing it from inhibition? We suggest that it will be fruitful to consider the question on two different timescales.

On a timescale of seconds, the behavior of the animal switches back and forth between two states: one in which the animal is quiet and immobile and does not whisk, and another in which it explores, whisks, and palpates objects. In the quiescent periods, neurons in the lemniscal pathways are unadapted and bursty (Sherman and Guillery, 2002; Castro-Alamancos, 2004)—object contact with the passively resting whisker produces an enormous response in cortex (Hentschke et al., 2006; Crochet and Petersen, 2006). In the active periods, neurons in the lemniscal pathways are adapted and tonic (Sherman and Guillery, 2002; Castro-Alamancos, 2004)—object contact with the protracting whisker produces a linear response in VPM and cortex. This state is believed to be characterized by high capacities for processing information (i.e., for forming object-specific spatial and temporal patterns of activity). The present study predicts that in these epochs, M1 output to ZIv would act to release the paralemniscal system

from ZIv inhibition. Many POm cells carry self-induced whisking signals (Yu et al., 2006), which are under strong somatosensory cortical gating when ZIv is active (Diamond et al., 1992; H. Bokor et al., 2007, Soc. Neurosci., abstract): releasing POm from ZIv inhibition during the active state thus allows a detailed record of whisking to flow freely from sensory receptors to cortex.

What about quiescent periods characterized by low motor output? The lemniscal pathways would operate in the burst mode while POm neurons would be suppressed by ZIv. In this latter state, the lemniscal pathways may act primarily to "alert" the cortex to the presence of an object or a threat. Whisking response in this case will not be generated automatically, due to ZIv inhibition, but will depend on higher-order, probably context-dependent processing.

Understanding ZIv in the behaving animal will also require working out network activity on the timescale of milliseconds. Consider the active whisking periods, when ZIv presumably receives strong inputs from M1. ZIv responses to whisker deflection occur in two phases: a rapid one (up to 10 ms latency), due to direct trigeminal input, and a later prolonged one (10–25 ms latency), due to descending input from somatosensory cortex (Urbain and Deschênes, 2007). So, on each whisker contact, POm potentially receives two successive waves of inhibition from ZIv. Would motor cortex suppression of ZIv release both waves, or act preferentially on one of the two? In short, what sort of signals will pass through POm, and at what latency? These issues are critical to understanding the detailed temporal dynamics of sensory-motor interaction.

Let us step back from the details of spike timing to consider ZIv's possible role in the modulation of whisking. Control theory teaches that multilevel closed loops allow monitoring of overt motor variables by internal reference signals (Powers, 1973). In the control theory framework, motor cortex is situated within a high-level loop and controls whisking via a set of reference signals projected onto lower-order sensory-motor loops. POm's connections suggest that it belongs to an intermediate level—higher than brainstem and collicular loops, but lower than cortical loops. If a POm loop controls a motor variable (e.g., whisking frequency: whisks per second), the most elegant and efficient way for a higher-order station to control whisking frequency would be to modulate a reference signal in the POm loop. For example, if POm is engaged in a negative-feedback control loop, whereby increased whisking frequency causes decreased POm firing rate (which in turn causes decreased whisking frequency), such a loop will stabilize at fixed values of whisking frequency and POm firing rate (e.g., eight whisks per second and X spikes/whisk). For M1 to shift whisking frequency to a higher, stable level, it can simply shift the set-point of the POm loop by adding a fixed number of spikes to POm's output. And here we return to the possible function of ZIv: by controlling the amount of ZIv inhibition on POm, M1 could add or subtract spikes from POm's output and thus shift the whisking frequency upward or downward.

Elucidating the functions of these complex sensory-motor loops will require sampling of neuronal activity from behaving rats across a number of tasks and behavioral states—a tall order! However, the remarkable findings presented by Urbain and Deschênes have uncovered the functional organization of cortical-subthalamic-thalamic circuits and paved the way for testing specific hypotheses in actively whisking and touching rats.

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