

PERSPECTIVE

Pathway-Specific Activation in Sensorimotor Cortical Networks: Perspective on “Projection-Specific Activity of Layer 2/3 Neurons Imaged in Mouse Primary Somatosensory Barrel Cortex During a Whisker Detection Task”

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Animals learn to use diverse sensory signals to meet their needs, such as to obtain food and water. Such abilities have been embedded in the nervous system through millions of years of evolution, resulting in neural networks that associate sensory signals with reward (eg, food and water) and convert the signals into appropriate actions. An active area of research involves recordings and manipulations of neural activity to identify mammalian brain regions critical for this process during trained perceptual tasks.¹⁻⁴ These studies have found a sequential activation of relevant cortical regions and delineated their causal roles in specific task epochs, revealing an overall flow of information from sensory to motor cortex. However, the extensive reciprocal and neuronal subtype-specific connections among cortical regions^{5,6} raise the question of the degree to which recurrent interactions⁷ and the task-dependent recruitment of specific subnetworks⁸ are critical for even simple sensorimotor transformations. To dissect out the precise neural circuits that mediate a sensorimotor transformation, it is critical to monitor specific processing streams within cortex. In this issue, Vavladeli et al.⁹ contribute to this important direction of research by combining pathway-specific labeling techniques and cellular-resolution imaging of populations of cortical neurons. Their results uncover projection-dependent patterns of activity among neurons in primary somatosensory cortex during sensory detection.

Vavladeli et al.⁹ focused on two main corticocortical streams in the mouse whisker system. They used different colors of retrograde dyes to label neurons that send signals from the primary whisker somatosensory cortex (wS1) to the secondary whisker somatosensory (wS2), and neighboring neurons that send signals from wS1 to the primary whisker motor cortex (wM1) (Figure 1A). They enriched a simple whisker detection task by adding auditory stimuli to provide a second rewarded sensory modality. In this new task, mice were trained to lick a water spout if one of their whiskers was deflected or if they heard a brief tone (Figure 1A). Once the mice learned the task, the authors simultaneously measured wS2-projecting (S2p) and wM1-projecting (M1p) populations of single neurons in wS1 using two-photon calcium imaging. This approach offered key advantages compared to the authors' previous whole-cell recordings from these sets of neurons.¹⁰ It allowed the authors to directly compare the two sets under exactly the same conditions: same mouse, same trials. Moreover, it allowed them to probe not only the activity of single neurons, but also to examine correlations in activity among populations of single neurons.

Vavladeli et al.⁹ first asked whether wS1 neurons showed heterogeneous activity based on their projection patterns. They found that S2p neurons showed larger peak responses compared to M1p neurons when the mice licked following whisker

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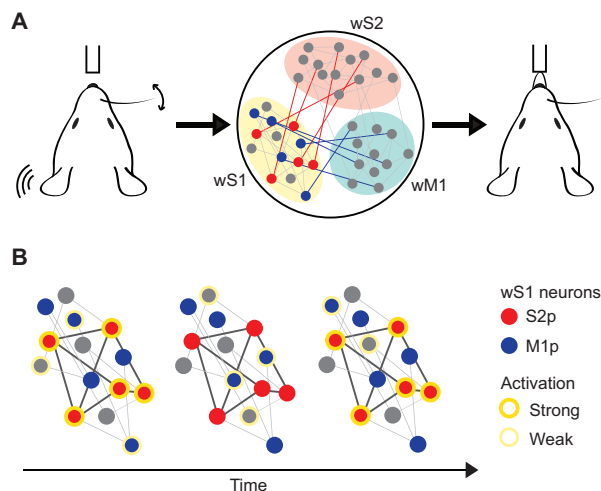


Figure 1. Sensory-Evoked Responses of wS1 Are Projection-Dependent During Touch Perception. (A) Schematic of a distributed corticocortical network highlighting wS2 (S2p, red) and wM1 (M1p, blue) projection neurons in the mouse wS1 during the whisker and auditory detection task. (B) Schematic of projection-dependent activity of wS1 neurons across time. S2p neurons showed larger and more correlated sensory-evoked activity compared to M1p neurons.

deflection, which is consistent with their prior work.¹⁰ The authors then asked whether the activity of S2p neurons was also stronger even in other conditions, where the auditory cue was delivered and/or mice failed to respond. In general, wS1 neurons projecting to wS2 had larger calcium signals compared to the nearby wS1 neurons projecting to wM1 (Figure 1B).

To explore the relationships between neural activity, stimuli, and behavior within each projection group, Vavladeli et al.⁹ selected various combinations of sensory inputs and motor outputs for comparison. The authors first examined the neural correlates of touch-evoked behavioral responses. They compared the whisker trials where the mice licked following the stimulation (hit) and the whisker trials where they failed to do so (miss). Both S2p and M1p neurons had stronger activity in whisker hit trials than in whisker miss trials across different time windows. To understand whether the activity in wS1 depended on the sensory modality of the stimulus, the authors compared whisker and auditory hit trials. In S2p and M1p neurons, whisker hit trials showed larger calcium signals compared to auditory hit trials in the early epoch. In addition to sensory-triggered licking (hit) trials, the authors further investigated spontaneous licking (false alarm) trials where the mice licked the water spout even though there was no sensory stimulation. Under these conditions, S2p neurons showed enhanced responses before lick onsets compared to M1p neurons. Overall, the activity of S2p and M1p neurons built up more when touch stimuli were delivered and when the mice decided to lick. Importantly, S2p neurons showed larger enhancements in comparison to M1p neurons.

Vavladeli et al.'s⁹ data showed clear differential responses of S2p and M1p neurons during an auditory and whisker detection task, despite these neurons being spatially intermingled within cortex. To what extent do S2p and M1p populations form distinct functional subnetworks within wS1? To gain insight into the dynamic interactions occurring within and between the S2p

and M1p populations, the authors examined correlations in spontaneous activity. They found that the S2p–S2p network showed stronger correlations compared to S2p–M1p and M1p–M1p networks (Figure 1B). This result suggests that S2p and M1p neurons may indeed form separate subnetworks and highlights the important future direction of investigating their synaptic properties.

Taken together, the results of Vavladeli et al.⁹ provide further support for the hypothesis that a sensory processing stream from the primary somatosensory cortex to the secondary somatosensory cortex plays a critical role in touch perception. Delineating this functional pathway provides a crucial stepping stone to map the detailed neural circuits underlying a sensorimotor transformation and provides a foundation to study learning, attention, and decision-making. It will be of great interest in future studies to determine how information flows between secondary somatosensory cortex and the motor cortex, the extent to which learning occurs in a pathway-dependent manner,¹⁰ and how attention and context change information flow within these circuits.⁸

Conflicts of interest statement

None declared.

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