Scientists monitor conversation between sensory perception and behavior in mouse brain

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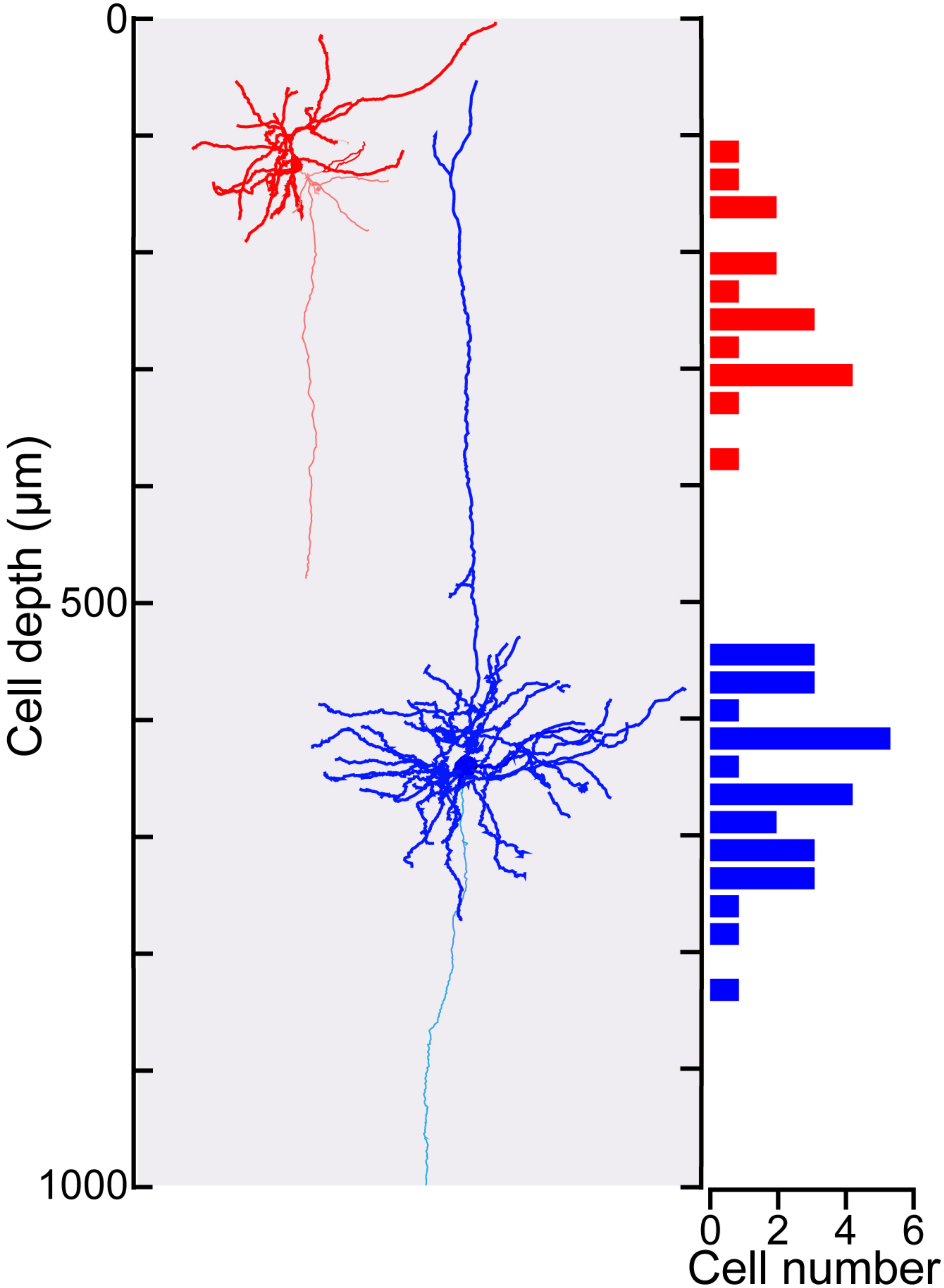

Reconstructions of neurons from layers L2/3 (red) and L5 (blue) of the primary sensory cortex of mice show their structure and relative positions in the brain tissue. The red and blue bars on the right show the depths of individual cells that were measured in each layer. Credit: Wen-Jie Zhao/MDC.

Sensory information enters the brain at the primary sensory cortex, where they are processed by different layers of cells in ways that ultimately influence an animal's perception and behavioral response. Scientists have now watched the flow of information between the different layers of the cortex for the first time in awake, active mice. Their work provides new insights into links between sensory stimuli and behavior.

Many types of sensory information enter the brain at a structure called the primary sensory cortex, where they are processed by different layers of cells in ways that ultimately influence an animal's perception and behavioral response. James Poulet's group at the Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC) has now watched the flow of information between the different layers of the cortex for the first time in awake, active mice. Their work, which is published in the June 2 edition of *Cell Reports*, provides new insights into links between sensory stimuli and behavior.

An ultimate goal of neurobiological research is to understand how a brain integrates a constant flow of various types of stimuli, makes sense of it, and helps coordinate an appropriate behavioral response. When many types of sensory information arrive simultaneously, they need to be prioritized, integrated, and passed along to the parts of the brain that are needed to deal with it. The new study from James Poulet's lab helps to elucidate these fundamental and yet unsolved issues.

Understanding the most basic principles of this system will require careful studies of regions of animal brains that are simple enough to keep track of nerve impulses as they enter, and yet complex enough to follow different types of signals as they exit along different routes.

Wen-Jie Zhao and Jens Kremkow in James' lab focused on the primary sensory cortex, a region in the parietal lobe of the brain. It consists of a six-layered stack composed of neurons and functions a bit like an editing booth in a television newsroom. Scientists knew that the region is the collection point for "feeds" from nerves involved in several perceptual systems around the mouse body. They also knew it is required for the perception of stimuli that a mouse experiences in activities such as touching a food pellet. It also helps coordinate some fast movements in reaction to sensory stimulation.

The structure of the tissue suggested that individual layers might handle impulses in different ways while remaining coordinated with each other to provide the right output. Finding out required stimulating the cortex in precise ways and monitoring how specific nerves within the layers responded. The easiest way to achieve this was to through the front paw, whose nerves transmit touch information into the cortex. Then the scientists could observe movements of the paw to study reflexive and voluntary movements. The latter would only happen if the animals were awake.

This required inserting probes into an upper and lower layer of the cortex to monitor incoming nerve impulses and the types of signals they generated. This is the first study to take measurements from multiple layers at the same time. The scientists stimulated nerves in the paw by placing it on a metal platform and tapping on one of its digits with a small metal arm. This stimulated nerves in different layers of the sensory cortex. The scientists monitored the firing of dozens of individual nerves in each layer to which probes had been attached, measuring the strength and timing of the impulses they generated.

Interestingly, they discovered, the firing of nerves in the deeper layer didn't have much effect on their neighbors in the same layer. Previous studies had shown that when mice are resting, nerves in the cortex fire spontaneously and generate slow impulses that have a large amplitude. The movement of these signals leads to a synchronization of some of the layers. These waves of activity disappear in animals that are active and moving, and as a result the layers become desynchronized. Researchers believe that these differences reflect a physiological signature of distinct mental states related to arousal and sensory perception. Here the results showed that a single stimulation had different effects on the behavior of neurons in each layer because even when the overall state of the brain changed, layers had distinctive characteristics.

One interesting outcome of the study was to show that an animal's movement triggers more firing among nerves in the deeper layers than in those nearer the surface of the brain. While all layers experienced new impulses that could be traced back to sensations, their nerves began firing at slightly different times. This might influence the way animals perceive the strength of a particular stimulus, or the way they store a memory of it, or other aspects of its processing.

The study, James says, represents a first step toward an understanding of more general issues. "Deepening our understanding of the connection between brain structure and function will require watching how the properties and activity of single nerves and tissues change under several behavioral conditions," he says. "By precisely controlling the stimulation of the paw, we could take measurements of different layers of the same tissue during the processing of a stimulus and during phases when the mouse was moving or at rest."

One message from the study is that brain functions depend not only a matter of the arrangement of nerves, or overall physical structure - which remain the same under many different conditions. Differences in brain tissues create specialized environments for nerves that alter the meaning of the impulses they generate. Now that scientists can listen in on these conversations between cells, they will need many more controlled, simultaneous measurements to understand what is being said.

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