Head-mounted microscope captures brain activity in freely behaving mice

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Researchers have developed a head-mounted miniature microscope that can be used to image activity from the entire outer part of the brain, or cortex, in freely behaving mice. When combined with implantable see-through skulls, the new microscope can capture the brain activity of mice for more than 300 days.

Mice are often used to study the brain because they have many of the same brain structures and connectivity as humans. The new microscope, known as the mini-mScope, offers an important new tool for studying how neural activity from multiple regions of the cortex contribute to behavior, cognition and perception.

Mathew L. Rynes from the University of Minnesota, Twin Cities, USA will present the research at the all-virtual 2021 OSA Biophotonics Congress: Optics in the Life Sciences to be held 12-16 April. Daniel Surinach co-led the study. The presentation is scheduled for Thursday, 15 April at 10:00 PDT (UTC-07:00).

Although scientists have made much progress in understanding how neural activity in specific regions of the brain's cortex contribute to behavior, it has been difficult to study activity from multiple cortical regions at once. For mice, even the simple task of moving a single whisker in response to a stimulus involves processing information in several cortical areas.

"The mini-mScope enables most of the dorsal cortex to be imaged during free and unrestrained behaviors," said Rynes. "This could allow neuroscientists to investigate the brain during complex behaviors holistically, or to understand how cortical regions interact during behaviors. This opens up research into understanding how connectivity changes in diseased states, traumatic brain injury or addiction."

The new mini-mScope is a fluorescence microscope that can be used for calcium imaging, a technique commonly used to monitor the electrical activity of the brain. The head-mounted device captures images at near cellular level, making it possible to study connections between regions across the cortex.

The researchers created the miniaturized microscope using LEDs for illumination, miniature lenses for focusing and an sCMOS camera for capturing images. It includes interlocking magnets that let it be easily affixed to morphologically realistic, 3-D-printed transparent polymer skulls known as See-Shells that the researchers developed previously. When implanted into mice, the See-Shells create a window through which long-term microscopy can be performed. In previous experiments, mice have lived with implanted See-Shells for up to a year.

They demonstrated the mini-mScope by using it to image mouse brain activity in response to a visual stimulus to the right eye, a vibrational stimulus to the right hindlimb and a somatosensory stimulus presented to the right whisker. They also created functional connectivity maps of the brain as a mouse wearing the head-mounted microscope interacted with another mouse. They saw that intracortical connectivity increased when the mouse engaged in social behaviors.

"Our team is creating a suite of tools that will enable us to access and interface with large parts of the cortex at high spatial and temporal resolution," said Rynes. "This study shows that the mini-mScope can be used to study functional connectivity in freely behaving mice, making it an important contribution to this toolkit."

The researchers are now using the mini-mScope to investigate how cortical connectivity changes in a variety of behavioral paradigms, such as exploring a novel space. They are also working with collaborators to use the mini-mScope to study how cortical activity is altered when mice learn difficult motor tasks.

Provided by The Optical Society

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