Making waves in the brain: Researchers use lasers to induce gamma brain waves in mice

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Scientists have studied high-frequency brain waves, known as gamma oscillations, for more than 50 years, believing them crucial to consciousness, attention, learning and memory. Now, for the first time, MIT researchers and colleagues have found a way to induce these waves by shining laser light directly onto the brains of mice.

The work takes advantage of a newly developed technology known as optogenetics, which combines genetic engineering with light to manipulate the activity of individual nerve cells. The research helps explain how the brain produces gamma waves and provides new evidence of the role they play in regulating brain functions — insights that could someday lead to new treatments for a range of brain-related disorders.

"Gamma waves are known to be [disrupted] in people with schizophrenia and other psychiatric and neurological diseases," says Li-Huei Tsai, Picower Professor of Neuroscience and a Howard Hughes Medical Institute investigator. "This new tool will give us a great chance to probe the function of these circuits."

Tsai co-authored a paper about the work that appears in the April 26 online issue of *Nature*.

Gamma oscillations reflect the synchronous activity of large interconnected networks of neurons, firing together at frequencies ranging from 20 to 80 cycles per second. "These oscillations are thought to be controlled by a specific class of inhibitory cells known as fast-spiking interneurons," says Jessica Cardin, co-lead author on the study and a postdoctoral fellow at MIT's McGovern Institute for Brain Research. "But until now, a direct test of this idea was not possible."

To determine which neurons are responsible for driving the oscillations, the researchers used a protein called channelrhodopsin-2 (ChR2), which can sensitize neurons to light. "By combining several genetic tricks, we were able to express ChR2 in different classes of neurons, allowing us to manipulate their activity with precise timing via a laser and an optical fiber over the brain," explains co-lead author Marie Carlén, a postdoctoral fellow at the Picower Institute.

The trick for inducing gamma waves was the selective activation of the "fast-spiking" interneurons, named for their characteristic pattern of electrical activity. When these cells were driven with high frequency laser pulses, the illuminated region of cortex started to produce gamma oscillations. "We've shown for the first time that it is possible to induce a specific brain state by activating a specific cell type" says co-author Christopher Moore, associate professor of neuroscience and an investigator in the McGovern Institute. In contrast, no gamma oscillations were induced when the fast-spiking interneurons were activated at low frequencies, or when a different class of neurons was activated.

The authors further showed that these brain rhythms regulate the processing of sensory signals. They found that the brain's response to a tactile stimulus was greater or smaller depending on exactly where the stimulus occurred within the oscillation cycle. "It supports the idea that these synchronous oscillations are important for controlling how we perceive stimuli," says Moore. "Gamma rhythms might serve to make a sound louder, or a visual input brighter, all based on how these patterns regulate brain circuits."

Because this new approach required a merger of expertise from neuroscience and molecular genetics, three different laboratories contributed to its completion. In addition to Tsai, Moore and Carlén of MIT, co-authors include Jessica Cardin, research affiliate at the McGovern Institute and the University of Pennsylvania, and Karl Deisseroth and Feng Zhang at Stanford University. Other co-authors were Konstantinos Meletis, a postdoctoral fellow at the Picower Institute, and Ulf Knoblich, a graduate student in MIT's Department of Brain and Cognitive Sciences.

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