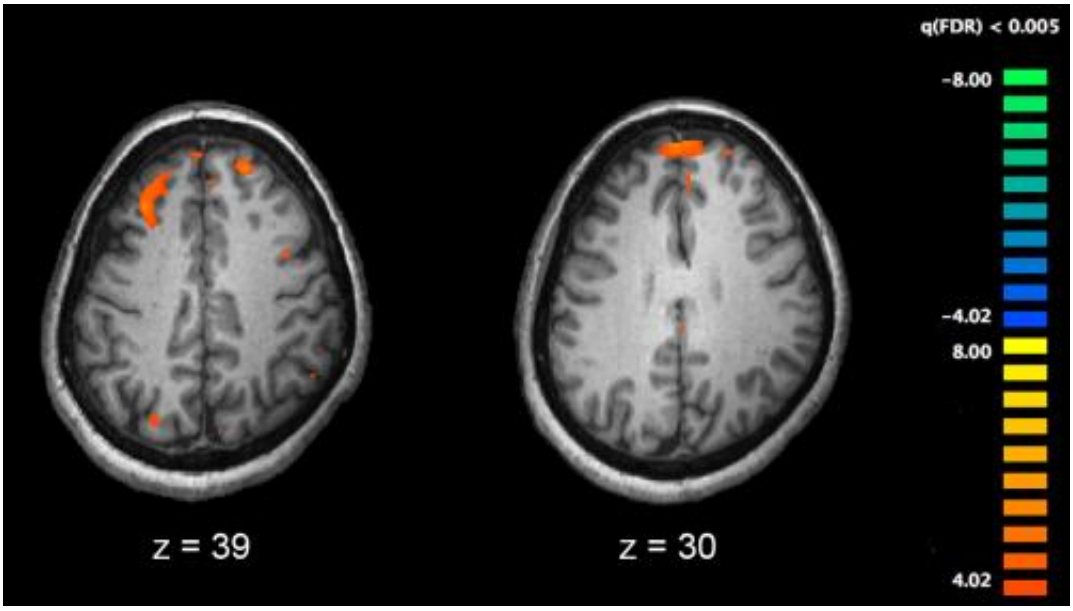
Shining lasers on mouse brains sheds light on cells central to Alzheimer's, schizophrenia

April 9 2019



Functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The image shows two levels of the brain, with areas that were more active in healthy controls than in schizophrenia patients shown in orange, during an fMRI study of working memory. Credit: Kim J, Matthews NL, Park S./PLoS One.

Alzheimer's disease and schizophrenia are some of the most common brain disorders and have been associated with problems in cells that contain a type of protein, called parvalbumin. These parvalbumin-containing cells account for almost one-tenth of the cells in your brain,

however, relatively little is known about what parvalbumin cells do. By stimulating mouse brains with lasers, researchers have started to make surprising findings about how they work.

Researchers in the lab of Dr. Adam Q. Bauer, at Washington University in St. Louis, have found surprising changes in blood volume and flow when parvalbumin-containing cells are stimulated. The technique they used relies on specially bred mice whose brains can be stimulated with laser pulses. They will present their findings at the OSA Biophotonics Congress: Optics in the Life Sciences meeting in Tucson, Ariz., 14-17 April 2019.

One of the main types of the brain's inhibitory cells, parvalbumin-expressing cells have been found to be responsible for keeping the endless signals of the brain in sync. Since proper nervous system development relies on nerves repeatedly firing in concert with one another over time, conducting this neural symphony has been found to be an important part of regulating the connections between brain cells that allow them to develop normally.

The technique of stimulating the brain with light signals, called optogenetics, has produced great leaps in our understanding of how the brain works, including how our brains process fear and our sense of smell, or what causes us to become addicted to drugs.

"Optogenetics is convenient, less invasive and repeatable," Joonhyuk Lee, one of the Bauer group researchers said. "And it's more straightforward. You don't have to stick any probes into mouse brains or anything."

First, the researchers bred mice that expressed a special, light-sensitive protein called channelrhodopsin throughout the brain. Channelrhodopsin was originally found in algae, but scientists can use it to pick which parts

of a mouse brain to turn on. Hit that area of the mouse brain with the right colored laser and you can activate a desired neural circuit.

The team bred mice that had channelrhodopsin stuck to parvalbumin-expressing neurons and mice with channelrhodopsin on excitatory Thy1-expressing cells, for comparison. With each group, they were able to stimulate the mouse brains with lasers and compare the results.

When most neurons are stimulated, Lee said, the brain provides them with more blood and oxygen. This occurred with the excitatory Thy 1 cells, but the lab's findings regarding blood flow and volume revealed the opposite response when parvalbumin-expressing cells were stimulated.

"How activity in specific neural populations is coupled to local changes in blood flow is fundamental to understanding how the brain regulates its blood supply," said Lee.

The scientists concluded that parvalbumin-expressing cells have a way of pulling back and fine-tuning the blood supply in areas where they are activated.

Researchers measured the blood and oxygen levels by shining a separate laser system, called laser speckle contrasting imaging, on the brain. When the mice whiskers were touched, Lee and his colleagues first found that parvalbumin cells could scale down nearby available blood and oxygen when excited. The group then measured different areas of the brain and discovered that parvalbumin cells could help relay messages to faraway corners of the brain to change their hemodynamics, or blood flow, as well.

"We really weren't expecting that activation of parvalbumin-expressing neurons would result in a reduction of local blood flow and volume," Lee said. "Even more so, although it could be an indirect cause, the fact that

we saw similar hemodynamic activity in more distant areas of the brain was very surprising."

Eventually, Lee said, he hopes the findings and techniques will help lead to a better understanding of parvalbumin's role in neurovascular coupling and provide another piece of the puzzle on how it influences brain development or formation of neurological disorders.

Provided by Optical Society of America