'Bursting' cells gain the brain's attention for life-or-death decisions

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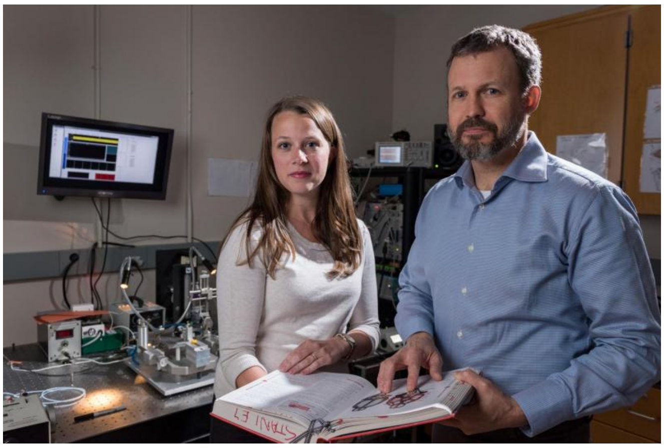

Using optogenetics and other technology, researchers have for the first time precisely manipulated bursting activity of cells in the thalamus, tying it to the sense of touch. Shown are Georgia Tech graduate student Clarissa Whitmire and Georgia Tech professor Garrett Stanley. Credit: Rob Felt, Georgia Tech

As you start across the street, out of the corner of your eye, you spot something moving toward you. Instantly, your brain shifts its focus to assess the potential threat, which you quickly determine to be a slow-moving bicycle - not a car - which will pass behind you as you complete your crossing.

The brain's ability to quickly focus on life-or-death, yes-or-no decisions, then immediately shift to detailed analytical processing, is believed to be the work of the thalamus, a small section of the midbrain through which most sensory inputs from the body flow. When cells in the thalamus detect something that requires urgent attention from the rest of the brain, they begin "bursting" - many cells firing off simultaneous signals to get the attention of the cortex. Once the threat passes, the cells quickly switch back to quieter activity.

Using optogenetics and other technology, researchers have for the first time precisely manipulated this bursting activity of the thalamus, tying it to the sense of touch. The work, done in animal models, will be reported January 14th in the journal *Cell Reports*. The research is supported by the National Institutes of Health's National Institute of Neurological Disorders and Stroke.

"If you clap your hands once, that's loud," explained Garrett Stanley, a professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University. "But if you clap your hands several times in a row, that's louder. And if you and your friends all clap together and at the same time, that's even stronger. That is what these cells do, and the idea is that this mechanism produces bursts synchronized across many cells to send out a very strong signal about a stimulus in the outside world."

Neuroscientists have long believed that such coordinated spikes of activity serve to focus the brain's attention on issues requiring immediate attention. Stanley and graduate student Clarissa Whitmire - working with researchers Cornelius Schwarz and Christian Waiblinger from the University of Tübingen in Germany - used optogenetics techniques to study bursting activity in the thalamus of rats. Their findings could lead to a better understanding of how cells in this walnut-sized portion of the human brain perform a variety of sensory and motor control tasks, switching from one mode to another as needed.

"Clarissa was able to get into the mechanism of synchronized thalamic bursting so we can manipulate it and look at it not only from within individual cells, but also across cells, recording from multiple cells simultaneously," said Stanley, who has been studying the thalamus for more than a decade. "We can now begin to provide a coherent story about how information gets from the outside world to the brain machinery that's in the cortex."

The researchers studied the connection between the rats' whiskers and cells in their thalamus. By stimulating the whiskers in many different ways, they were able to induce signals - including bursting - in the thalamus. The researchers used light-sensitive proteins introduced into the thalamic cells - a technology known as optogenetics - to establish optical control of the bursting activity.

"We were able to turn the bursting mechanism on or off at will," Stanley explained. "This is really the first time we have been able to readily control this, turning the knob in one direction to eliminate the bursting activity and then turning it the other way to make the cells produce these bursts in rapid succession."

The control extended not just to turning the bursting on or off, but also allowed the researchers to create a continuum of cell activity.

"Clarissa could make them act very 'bursty' and very synchronized, or she could turn the knob and move them very smoothly to the opposite end of the spectrum," Stanley said. "There is a range of activity that people had speculated would be there, but nobody had actually done the experiments to show it existed."

The cellular bursting mechanism likely developed very early in mammalian evolution to help creatures survive threats posed by predators. The brain's cortex is always busy with higher-level activity, and the thalamic bursting serves to let it know that critical outside activities need its urgent attention.

Other sensory inputs such as vision can initiate bursting, but Stanley's group chose to study sense of touch in this work. In rats, the whiskers are embedded in follicles that have specialized cells whose function is similar to that of human sensory cells. Thus, these whiskers serve many of the same "touch" functions as human fingers.

"When you reach out with your hand and touch a surface, you are mechanically deforming the skin, stretching the sensors that are in the skin and sending signals to tell the brain about the surface you are touching," Stanley noted. "In the rats, we moved the whiskers, recorded the activity, and identified the presence of a burst."

As a next step, Stanley and his research team plan to connect what they've learned about bursting activity of the thalamus to behavior in an effort to fully confirm the theory. "The next step is to take this to behavior and work with animals that are trained to detect and discriminate between different kinds of inputs," he said.

With the optogenetics and other advanced technology, researchers are beginning to see the big picture of how sensory inputs affect brain activity.

"These thalamic cells are somewhere in between the outside world and the cognitive machinery of the brain, and they have a job that changes rapidly," Stanley said. "In some cases, they are saying 'yes' or 'no' about something in the outside world, and in some cases they are discriminating between the final details of objects in the outside world."

More information: Clarissa Whitmire, Christian Waiblinger, Cornelius Schwarz, Garrett Stanley, "Information Coding Through Adaptive Gating of Synchronized Thalamic Bursting, (*Cell Reports*, 2016).