Medical Xpress

Rewrite the textbooks: Findings challenge conventional wisdom of how neurons operate

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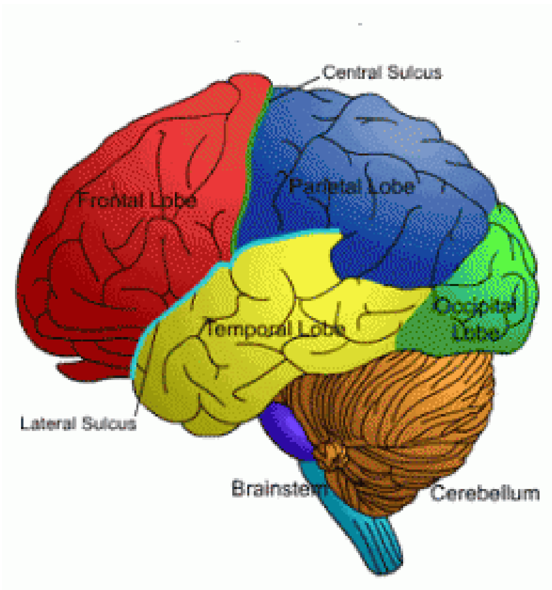

Brain diagram. Credit: dwp.gov.uk

(PhysOrg.com) -- Neurons are complicated, but the basic functional concept is that synapses transmit electrical signals to the dendrites and cell body (input), and axons carry signals away (output). In one of many surprise findings, Northwestern University scientists have discovered that axons can operate in reverse: they can send signals to the cell body, too.

It also turns out axons can talk to each other. Before sending signals in reverse, axons can perform their own neural computations without any involvement from the cell body or dendrites. This is contrary to typical neuronal communication where an axon of one neuron is in contact with another neuron's dendrite or cell body, not its axon. And, unlike the computations performed in dendrites, the computations occurring in axons are thousands of times slower, potentially creating a means for neurons to compute fast things in dendrites and slow things in axons.

A deeper understanding of how a normal neuron works is critical to scientists who study neurological diseases, such as epilepsy, autism, Alzheimer's disease and schizophrenia.

The findings are published in the February issue of the journal Nature Neuroscience.

"We have discovered a number of things fundamental to how neurons work that are contrary to the information you find in neuroscience textbooks," said Nelson Spruston, senior author of the paper and professor of neurobiology and physiology in the Weinberg College of Arts and Sciences. "Signals can travel from the end of the axon toward the cell body, when it typically is the other way around. We were amazed to see this."

He and his colleagues first discovered individual nerve cells can fire off signals even in the absence of electrical stimulations in the cell body or dendrites. It's not always stimulus in, immediate action potential out. (Action potentials are the fundamental electrical signaling elements used by neurons; they are very brief changes in the membrane voltage of the neuron.)

Similar to our working memory when we memorize a telephone number for later use, the nerve cell can store and integrate stimuli over a long period of time, from tens of seconds to minutes. (That's a very long time for neurons.) Then, when the neuron reaches a threshold, it fires off a long series of signals, or action potentials, even in the absence of stimuli. The researchers call this persistent firing, and it all seems to be happening in the axon.

Spruston and his team stimulated a neuron for one to two minutes, providing a stimulus every 10 seconds. The neuron fired during this time but, when the stimulation was stopped, the neuron continued to fire for a minute.

"It's very unusual to think that a neuron could fire continually without stimuli," Spruston said. "This is something new -- that a neuron can integrate information over a long time period, longer than the typical operational speed of neurons, which is milliseconds to a second."

This unique neuronal function might be relevant to normal process, such as memory, but it also could be relevant to disease. The persistent firing of these inhibitory neurons might counteract hyperactive states in the brain, such as preventing the runaway excitation that happens during epileptic seizures.

Spruston credits the discovery of the persistent firing in normal individual neurons to the astute observation of Mark Sheffield, a graduate student in his lab. Sheffield is first author of the paper.

The researchers think that others have seen this persistent firing behavior in neurons but dismissed it as something wrong with the signal recording. When Sheffield saw the firing in the neurons he was studying, he waited until it stopped. Then he stimulated the neuron over a period of time, stopped the stimulation and then watched as the neuron fired later.

"This cellular memory is a novelty," Spruston said. "The neuron is responding to the history of what happened to it in the minute or so before."

Spruston and Sheffield found that the cellular memory is stored in the axon and the action potential is generated farther down the axon than they would have expected. Instead of being near the cell body it occurs toward the end of the axon.

Their studies of individual neurons (from the hippocampus and neocortex of mice) led to experiments with multiple neurons, which resulted in perhaps the biggest surprise of all. The researchers found that one axon can talk to another. They stimulated one neuron, and detected the persistent firing in the other unstimulated neuron. No dendrites or cell bodies were involved in this communication.

"The axons are talking to each other, but it's a complete mystery as to how it works," Spruston said. "The next big question is: how widespread is this behavior? Is this an oddity or does in happen in lots of neurons? We don't think it's rare, so it's important for us to understand under what conditions it occurs and how this happens."

More information: The title of the paper is "Slow Integration Leads to Persistent Action Potential Firing in Distal Axons of Coupled Interneurons." www.nature.com/neuro/journal/v … n2/full/nn.2728.html

Provided by Northwestern University