Experiment reveals how cells that process sound respond to complex stimuli

June 25 2015, by Charlotte Hsu

Credit: Human Brain Project

If you stimulate an auditory nerve cell over and over in a uniform pattern in the lab, it quickly runs out of the chemicals that it uses to send messages from the ear to the brain.

The cell, in effect, loses its ability to process and transmit information about new sounds.

But does this type of chemical depletion happen in real life, where cells are subject to constant sound stimulation and also fire spontaneously on their own?

This question has been a topic of debate among scientists for years, and a new University at Buffalo study is helping to provide an answer.

Matthew Xu-Friedman, PhD, an associate professor in the UB Department of Biological Sciences, and Hua Yang, a research assistant professor in the same department, have published a new paper in the *Journal of Neuroscience* showing that the strength of an auditory nerve cell's response to sound does change in nonrandom ways in response to complex, ongoing activity. Some level of chemical depletion does occur in these situations, Xu-Friedman says.

The research, published May 27, was funded by the National Institutes of Health and National Science Foundation.

Using a trick

To draw their conclusions, the researchers used a clever experiment: They did their study in the lab, but mimicked real-world conditions by exposing auditory nerve cells to a string of stimuli occurring at irregular intervals.

Then, they ran the same test again on the same cells, but skipped a single beat, removing one of the stimuli toward the end of the chain.

This small change had a significant effect: When the beat was missed, the cells' response to subsequent stimuli—those at the end of the string—was stronger than when no beats were missed, with the cells releasing more of the neurotransmitter chemicals used to signal the brain. The effect lasted for about 60 milliseconds after the skipped stimulus.

The more active response is likely due, in part, to the cells having a larger supply of neurotransmitter on hand.

"There have been past studies saying that these kinds of short-term changes only happen in vitro, in the artificial environment of the lab where the cells are separated from the ear and are unnaturally silent," Xu-Friedman said. "But what we saw in our study is that even in a situation where you have irregular, ongoing activity, we do see these types of changes."

Difference from past research

Previous experiments by other researchers addressed the same topic by studying auditory nerve cells' activity within animals.

"They looked at spontaneous nerve activity, and measured the resulting synaptic currents—an indicator of the strength of the cells' response," Xu-Friedman explained. "These researchers expected to see depression, so when two synaptic responses were close together, the second should be small, and when the two were well spaced, the second should be large. Instead, they got nothing predictable, and concluded there was no depression."

Xu-Friedman said new ways of looking at the responses were needed to draw a conclusion about a system that is very complex. Like the previous researchers, his team looked at synaptic currents, which indicate how much neurotransmitter is released.

But by measuring cells' response to an entire chain of irregular stimuli with just a single stimulus removed, and not just two events, the UB team was able to capture changes that previous studies might have missed, he said.

Though he and Yang did not see any cells go "silent" and run out of neurotransmitter completely, their results suggest that neurotransmitter supplies can shrink in response to random, ongoing activity, depressing the strength of the cells' response, Xu-Friedman said. That's why cells' overall response to stimuli were weaker when no beats were missed, he said.

"If this kind of short-term plasticity didn't exist, you would expect to see no change in activity if you took one stimulus out," Xu-Friedman said. "But in fact, we see a significant change."

More information: "Skipped-Stimulus Approach Reveals That Short-Term Plasticity Dominates Synaptic Strength during Ongoing Activity." *Journal of Neuroscience*, 27 May 2015, 35(21): 8297-8307; DOI: 10.1523/JNEUROSCI.4299-14.2015

Provided by University at Buffalo