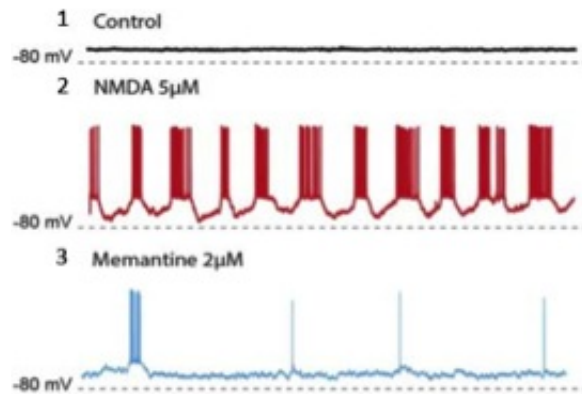


Readying the neural network

November 17 2014, by Poncie Rutsch



Extrasynaptic receptors are essential for producing activity in this striatal neuron. Neurons were recorded from brain tissue slices in three different conditions. In graph 1, the researchers electrically stimulated a neuron without any extrasynaptic response, or in a “down” state. In graph 2, the researchers added the neurotransmitter NMDA. This lifted the membrane potential, and made it possible to provoke many action potentials with electric stimulation. In graph 3, the researchers added memantine and showed that the drug blocks nearly all action potentials by blocking most extrasynaptic activity.

Synapse, the name for the signal-receiving site on a neuron, comes from the Greek word for contact. Neuroscientists used to maintain that neurons form one-to-one relationship to contact one another. Yet more researchers are finding evidence that shows how neurons function as part of a network. An incoming excitation does not always provoke an outgoing signal. Some excitations change the state of the neuron, readying the neuron for the next signals. Okinawa Institute of Science

and Technology Graduate University researchers in Professor Gordon Arbuthnott's Brain Mechanism for Behavior Unit have just completed a study where they found neurons receiving signals in the area just outside of their synapses, and those signals changed the way that the neurons interpreted the next signals.

Led by researchers Marianela Garcia-Munoz and Violeta Lopez-Huerta, the results offer insight on a mechanism reputed for triggering [cell death](#), and the work was published online in *Neuropharmacology* on September 18, 2014.

For years, neuroscientists thought only the synapse could contain [receptors](#), the neurotransmitter catching-mitts on [neurons](#). But when they applied a neurotransmitter called NMDA to the area around the synapse they realized that they could trigger different responses. Any receptor located near, but not on the synapse, became known as an extrasynaptic receptor. However, stimulating extrasynaptic receptors sometimes triggers a molecular pathway that kills the neuron. Yet extrasynaptic receptors puzzled Professor Arbuthnott, who reasoned that it does not make evolutionary sense to have a group of receptors that act only as self-destruct buttons. "Maybe there are things you can do with this path," he said.

Garcia-Munoz and Lopez-Huerta looked for the extrasynaptic receptors' purpose by first targeting slices of brain. The slices they used connected the striatum, part of the brain involved in movement, to the cortex, which they knew signals to the striatum. However, when they tried to provoke the striatum by stimulating the cortex, the [striatal neurons](#) were silent. Next, they added the neurotransmitter NMDA to the brain slice, where NMDA would interact with both synaptic and extrasynaptic receptors. This changed the sensitivity of the neuron by lifting the membrane potential, or the charge of the neuron. The higher the membrane potential, the less additional stimulation a neuron requires to

fire an action potential. With the higher membrane potential in place, the researchers could trigger many [action potentials](#). Finally, Garcia-Munoz and Lopez-Huerta added memantine, an Alzheimer's drug that slows the progression of dementia by blocking extrasynaptic receptors, and thus blocking the pathway that triggers cell death. With the memantine in effect and the extrasynaptic receptors out of commission, the researchers could only trigger a few action potentials using electricity. In this way, the researchers could tell that the extrasynaptic receptors were necessary to lift the membrane potential of the striatal cell, putting it in a more sensitive state.

Next, Garcia-Munoz and Lopez-Huerta used calcium imaging to watch how extrasynaptic receptors changed the neural network. When a neurotransmitter interacts with a receptor, the cell opens gated channels. This allows positively charged [calcium ions](#) to enter through the cell's membrane, lifting the membrane potential. Garcia-Munoz and Lopez-Huerta added a dye to the system so that when calcium ions enter the cell, they interact with the dye, causing that cell to fluoresce. "Because the calcium is a direct measure of the electrical activity, you can see when the neuron is activated," Lopez-Huerta explained. "We can see the activity of hundreds of cells at the same time," she said. "Like fireflies," Garcia-Munoz added. Then, the researchers once again applied memantine to block the extrasynaptic receptors. The neurons fluoresced far less frequently and less synchronously.

Based on these experiments, Garcia-Munoz and Lopez-Huerta concluded that the extrasynaptic receptors were essential for establishing a plateau, a relatively long 200-millisecond lift in the membrane potential. Although plateaus do not cause action potentials, which last closer to one millisecond, the lift in electric charge gives the neuron a kind of leg up. In fact, Arbuthnott says that the plateau appears necessary for signaling. "The cells in the striatum don't fire action potentials unless they're up and in some kind of plateau state," said Arbuthnott. If this is the case for

other parts of the brain, which the group thinks is possible, extrasynaptic receptors are essential for communication brain-wide. As Arbuthnott concluded, "If you need this plateau, you might need these extrasynaptic receptors."

More information: "Extrasynaptic glutamate NMDA receptors: Key players in striatal function." *Neuropharmacology* DOI: [10.1016/j.neuropharm.2014.09.013](https://doi.org/10.1016/j.neuropharm.2014.09.013)

Provided by Okinawa Institute of Science and Technology

Citation: Readyng the neural network (2014, November 17) retrieved 20 March 2024 from <https://medicalxpress.com/news/2014-11-readyng-neural-network.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--