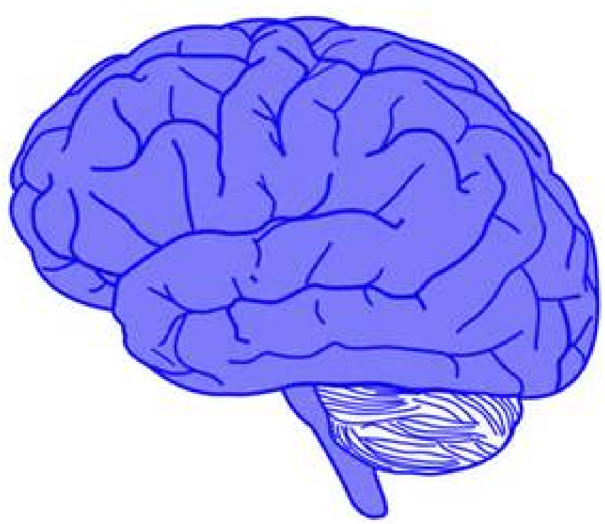
Neuroscientists call for more comprehensive view of how brain forms memories

July 5 2017



Credit: public domain

Neuroscientists from the University of Chicago argue that research on how memories form in the brain should consider activity of groups of brain cells working together, not just the connections between them.

Memories are stored as "engrams," or enduring physical or chemical changes to populations of neurons that are triggered by new information and experiences. Traditional thinking about how these engrams form centers on the ability of connections between neurons to strengthen or weaken over time based on what information they receive, or what's known as "synaptic plasticity." The new proposal, published this week in the journal *Neuron*, argues that while synaptic plasticity establishes the map of connectivity between individual neurons in an engram, it is not enough to account for all aspects of learning. A second process called "intrinsic plasticity," or changes in the intensity of activity of neurons within an engram, plays an important role as well.

"Synaptic plasticity does not fully account for the complexity of learning mechanisms that we are aware of right now," said Christian Hansel, PhD, professor of neurobiology and senior author of the new paper. "There were elements missing, and with the introduction of intrinsic plasticity, all of a sudden you see a system that is more dynamic than we thought."

In recent studies using optogenetic tools, which enable scientists to control the activity of neurons with light, researchers have been able to monitor memory storage and retrieval from brain cells. Optogenetic tools give scientists a window to the activity of the brain as a whole, even in living animals. These new studies show how both individual neurons and groups, or ensembles, of neurons work together while memory and learning processes take place—often without requiring any changes to the connections between synapses.

For instance, synaptic plasticity relies on repeated conditioning to develop stronger connections between cells, meaning that an animal has to experience something several times to learn and form a memory. But, of course, we also learn from single, brief experiences that don't necessarily trigger changes in the synapses, meaning that another, faster learning process takes place.

The authors point to several studies showing that intrinsic plasticity is a nearly instantaneous mechanism that likely has a lower threshold, or takes fewer experiences, to initiate. Thus, it might be more appropriate for fast learning resulting from single experiences, instead of the slow, adaptive process involved with synaptic plasticity.

Theories about memory formation also don't account for the relative strength of activity in neurons once connections between them have been established, the authors write. If you think of how memories are stored as working like the lights in a room, synaptic connections are the electrical wiring that determine how the lights are connected and what input (electricity) they receive. Changing how the lights are wired (i.e. the synaptic plasticity) obviously affects how they function, but so do the switches and light bulbs. Intrinsic plasticity is the ability to manipulate the intensity of the light without changing the wiring, like using dimmer switches or three-way bulbs. Both kinds of changes have an effect independently, but they work together to light the room.

"They are two ideas that are very important to learning and memory and we bring them together in this paper," said postdoctoral scholar Heather Titley, PhD, first author of the paper. "They're not mutually exclusive."

The authors emphasize that this new line of thinking is just a starting point. More experiments should be designed, for instance, to tease out the relative effects of synaptic versus intrinsic plasticity on learning and memory. But given the evidence produced by new technology, they argue that it's time to expand our thinking about how memories form.

"People might argue whether this intrinsic plasticity is really something that plays a major role or not," said Nicolas Brunel, professor of neurobiology and statistics, and another author of the paper. "But I don't think people can argue that it doesn't play any role, because there is an increasing amount of evidence that it does."

More information: *Neuron* (2017). DOI:

10.1016/j.neuron.2017.05.021

Provided by University of Chicago Medical Center