Medical Xpress

Neuroscientists isolate molecular 'when' and 'where' of memory formation

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Neuroscientists from New York University and the University of California, Irvine have isolated the "when" and "where" of molecular activity that occurs in the formation of short-, intermediate-, and long-term memories. Their findings, which appear in the journal the *Proceedings of the National Academy of Sciences*, offer new insights into the molecular architecture of memory formation and, with it, a better roadmap for developing therapeutic interventions for related afflictions.

"Our findings provide a deeper understanding of how memories are created," explained the research team leader Thomas Carew, a professor in NYU's Center for Neural Science and dean of NYU's Faculty of Arts and Science. "Memory formation is not simply a matter of turning molecules on and off; rather, it results from a complex temporal and spatial relationship of molecular interaction and movement."

Neuroscientists have previously uncovered different aspects of molecular signaling relevant to the formation of memories. But less understood is the spatial relationship between molecules and when they are active during this process.

To address this question, the researchers studied the neurons in Aplysia californica, the California sea slug. Aplysia is a model organism that is quite powerful for this type of research because its neurons are 10 to 50 times larger than those of higher organisms, such as vertebrates, and it possesses a relatively small network of neurons—characteristics that readily allow for the examination of molecular signaling during memory formation. Moreover, its coding mechanism for memories is highly conserved in evolution, and thus is similar to that of mammals, making it an appropriate model for understanding how this process works in humans.

The scientists focused their study on two molecules, MAPK and PKA, which earlier research has shown to be involved in many forms of memory and synaptic plasticity—that is, changes in the brain that occur after neuronal interaction. But less understood was how and where these molecules interacted.

To explore this, the researchers subjected the sea slugs to sensitization training, which induces increased behavioral reflex responsiveness following mild tail shock, or in this study, mild activation of the nerve form the tail. They then examined the subsequent molecular activity of both MAPK and PKA. Both molecules have been shown to be involved in the formation of memory for sensitization, but the nature of their interaction is less clear.

What they found was MAPK and PKA coordinate their activity both spatially and temporally in the formation of memories. Specifically, in the formation of intermediate-term (i.e., hours) and long-term (i.e., days) memories, both MAPK and PKA activity occur, with MAPK spurring PKA action. By contrast, for short-term memories (i.e., less than 30 minutes), only PKA is active, with no involvement of MAPK.

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