New protein synthesis not essential to memory formation

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New research from the University of Illinois challenges the premise that the brain must build new proteins in response to an experience for that experience to be recorded in long-term memory.

The findings, published this month in the *Proceedings of the National Academy of Sciences*, could alter basic assumptions about the role of protein synthesis in memory formation.

Brain researchers have long used drugs that enhance or hinder memory formation to gain insight into the mechanisms at play. Early experiments in rats found that protein synthesis inhibitors injected into brain regions involved in memory processing could disrupt long-term memory formation. This led some to hypothesize that new protein synthesis was essential to the creation of long-term memories.

A research team led by neuroscientist Paul E. Gold discovered an alternate explanation for this effect. The researchers observed that the protein synthesis inhibitor anisomycin, which is commonly used in memory studies, causes dramatic changes in brain chemistry – apart from protein synthesis inhibition – that interfere with memory formation. They found that exposing rat brains to anisomycin sets off wild fluctuations in neurotransmitter levels in the brain region targeted in the experiment – the amygdala, one of several brain structures involved in processing memories and emotions. Large fluctuations in neurotransmitter levels in the amygdala are known to interfere with memory formation.

The researchers were surprised by the intensity of the brain's response to anisomycin. Shortly after they injected the drug into the rat amygdala, they saw huge increases – from 1,000 to 17,000 percent – in levels of the neurotransmitters norepinephrine, dopamine and serotonin.

"This is far above anything we've seen physiologically in any experiment," Gold said. "Normally you think of a 200 percent increase as a really solid result and 300 percent as outrageously high. I wouldn't have thought that there was that much (neurotransmitter) to be released."

Shortly after this spike, dopamine and norepinephrine levels plummeted, dropping well below baseline for up to 48 hours after the initial exposure to anisomycin.

As expected, the rats exposed to anisomycin prior to training had impaired long-term recall of the events. To determine whether the inability to form lasting memories was caused by the anisomycin or by changes in neurotransmitter levels, the researchers repeated the experiment, adding drugs designed to counter the fluctuations in neurotransmitter levels. When the neurotransmitter imbalances were neutralized or blunted – even in the presence of anisomycin – memory formation was significantly restored.

"If we block anisomycin's effects on the neurotransmitters, then we block many of its effects on memory," Gold said. "We still have the protein synthesis inhibition, but it no longer causes the (same level of) amnesia."

It is possible that some of the amnesia is due to the cessation of protein synthesis, Gold said. But, he said, the evidence suggests otherwise. "I think the protein synthesis inhibition itself is causing cells to act in unusual ways," he said.

“No one would deny that protein synthesis is needed to maintain normal brain functions, including memory,” Gold said. “But the idea that new protein synthesis is required to make long-lasting memories should be reexamined.”

Source: University of Illinois at Urbana-Champaign