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# Memory molecule, deja vu

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A second high-profile paper in as many months has found an important role in learning and memory for calpain, a molecule whose academic fortunes have ebbed and flowed for 25 years.

USC's Michel Baudry (then at the University of California, Irvine) and Gary Lynch (UC Irvine) first pointed to calpain as the key to memory in a seminal 1984 paper in Science on the biochemistry of memory.

In a paper published Jan. 20 in the *Journal of Neuroscience,* Baudry and graduate student Sohila Zadran report that calpain mediates the effects of brain-derived neurotrophic factor (BDNF).

BDNF is a modulator that some neuroscientists consider a potential "fountain of youth" for its effect on synapses, the chemical junctions that neurons use to communicate.

"Calpain is a key element in synaptic remodeling that underlies learning and memory," Baudry said. "Our findings also suggest that learning and memory is an emerging property of cell movement."

"All these great things that we're seeing about BDNF indeed involve calpain," Zadran said.

Last month, in a paper published in the Proceedings of the National Academy of Sciences, Baudry and Zadran showed that estrogen's beneficial effects on learning and memory seem to occur through calpain.

The findings matter for anyone who seeks to understand the biochemical machinery that leads to memory formation. They also are likely to guide the development of drugs for memory and learning enhancement.

In her experiments, lead author Zadran used a biochemical probe to measure calpain activation in cultured neurons. She found that BDNF added to the cultures caused the activation of calpain, and she discovered how BDNF was doing it in the dendritic spines, the mushroom-like structures where communication between neurons takes place.

When calpain was activated through BDNF, the spine structure changed in ways similar to those that occur during learning.

But when activation was blocked with calpain inhibitors, the addition of BDNF had no effect - implying that this modulator, which is essential for learning and memory, requires calpain to act.

For Zadran and Baudry, the experiments represent vindication for calpain, which has gone in and out of favor.

"Calpain's back. Calpain is there, it's activated, it's involved in all of these things," Zadran said.

If Zadran has indeed settled the 25-year debate over calpain's relevance, she has done it in the blink of an eye. She is expected to complete her Ph.D. at USC in two years. This summer, she will head across town to the California Institute of Technology for postdoctoral work.

Provided by University of Southern California