**Sharpened under Pressure**  
Short stressful events may improve memory

**Chronic stress** can adversely affect physical and mental health and have a detrimental effect on learning and emotion. Acute stress, however, may enhance learning and memory.

In a study published in the August 18, 2009, issue of the *Proceedings of the National Academy of Sciences* UB scientists have shown that acute stress can produce a beneficial effect on learning and memory through the effect of the stress hormone corticosterone (cortisol in humans) on the brain's prefrontal cortex, a key region that controls learning and emotion.

Working with an animal model, they specifically demonstrated that acute stress increases transmission of the neurotransmitter glutamate and improves working memory, the process by which information is coded into memory, actively maintained and subsequently retrieved for guiding behavior.

"Stress hormones have both protective and damaging effects on the body," says Zhen Yan, PhD, professor of physiology and biophysics at UB and senior author on the study. "This paper and others we have in the pipeline explain why we need stress to perform better, but don't want to be stressed out."

Eunice Y. Yuen, PhD, UB research assistant professor of physiology and biophysics, is the first author on the study. To test the effect of acute stress on working memory, Yan, Yuen and colleagues trained rats in a maze until they could complete it correctly 60–70 percent of the time. When the rodents reached this level of accuracy for two consecutive days, half were put through a 20-minute forced swim, which served as acute stress, and then were put through the maze again.

Results showed that the stressed rats made significantly fewer mistakes as they went through the maze both four hours after the stressful experience and one day post-stress, compared to the non-stressed rats.

To determine if the corticosterone-induced neuropathway was responsible for the improved memory, as they proposed, researchers injected one group of rats before the stressful forced-swim with a medicinal compound that blocks the pathway and injected another group with saline. Results showed that the saline group, in which the corticosterone neuropathway was not blocked, performed better in the maze than the blocked group.

The researchers also determined that the stressful experience did not increase depression or anxiety-related behavior in the animals.

"It is known that stress has both positive and negative actions in the brain, but the underlying mechanism is elusive," says Yan. "Several key brain regions involved in cognition and emotions, including the prefrontal cortex, have been identified as the primary target of corticosteroid [cortisol in humans], the major stress hormone."

"Our current study identifies a novel mechanism that underlies the impact of acute stress on working memory, a cognitive process depending on glutamate receptor-mediated excitatory signals in prefrontal cortex circuits."

The investigators have expanded this research in several directions. In two other papers that will be published soon, they have identified the key signaling molecules that link acute stress to the enhancement of glutamate receptors and working memory.

"In addition," notes Yan, "we have discovered that chronic stress suppresses the transmission of glutamate in the prefrontal cortex of male rodents, which is opposite to the facilitating effect of acute stress, and that estrogen receptors in female rodents make them more resilient to chronic stress than male rats."

"All these studies should bring new insights into the complex actions of stress in different circumstances that may be applicable to humans in the future," she notes.

Wenhua Liu, PhD, research scientist, and Jain Peng, PhD, associate professor, both in the UB Department of Physiology and Biophysics, are coauthors on the study, as is Ilia N. Karatsoreos, PhD, and Bruce S. McEwen, PhD, from the Rockefeller University.

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