Experience sculpts brain circuitry to build resiliency to stress

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Rats develop 'illusion of control'

It's long been known that experiencing control over a stressor immunizes a rat from developing a depression-like syndrome when it later encounters stressors that it can't control. Now, scientists funded by the National Institute of Mental Health (NIMH), part of the National Institutes of Health (NIH), have unraveled the workings of the brain circuitry that inoculates against such hard knocks - the circuitry of resilience.

Control not only activated the brain's executive hub, the prefrontal cortex, but also altered it so that it later activated even when the stressor was not controllable. This activation turned off mood-regulating cells in the brainstem's alarm center. The immunizing effect was so powerful that even a week later, when confronted with an uncontrollable stressor, the cells behaved as if the stressor was controllable and the rat was protected.

"It's as if the original experience with control leads the animal to later have the illusion of control even when it's absent, thereby producing resilience in the face of challenge," explained NIMH grantee Steven Maier, Ph.D., University of Colorado. "The prefrontal cortex is necessary for processing information about the controllability of stressors as well as applying this information to regulate responses to subsequent stressors."

A report on this first study exploring the neural mechanisms by which an

initial experience with a controllable stressor can block the later behavioral effects of an uncontrollable stressor, by Maier, Jose Amat, Ph.D., and colleagues, appears in the December 20, 2006 issue of the Journal of Neuroscience.

"Lack of control over stressful life experiences has been implicated in mood and anxiety disorders," noted NIMH Director Thomas Insel, M.D. "Understanding how the brain encodes the experience of control to protect against such adverse consequences should help us develop better treatments for these disorders."

Rats exposed to uncontrollable stress develop a syndrome similar to depression (http://www.nimh.nih.gov/health/topics/depression/index.shtml) and post traumatic stress disorder (PTSD) (http://www.nimh.nih.gov/health/topics/post-traumatic-stress-disorder-ptsd/index.shtml) in which they lose the ability to learn how to escape stressors and behave more fearfully.

Maier's research team had last year reported that the prefrontal cortex quelled the brainstem center's alarmist tendencies. The current study sought to pinpoint how and when the cortex influenced the alarm center to produce the stress immunity.

The researchers chemically inactivated the cortex at critical stages of experiencing and reacting to controllable and uncontrollable stress while measuring neurotransmitter activity and gene expression in cells of the alarm center via chemical monitoring and brain mapping techniques. Increased secretion of serotonin (a mood regulating chemical) and gene expression in the alarm center, as well as the depression-like behavioral changes, no longer occurred following an uncontrollable stressor, if a controllable stressor had been experienced as much as a week earlier.

When the prefrontal cortex was experimentally turned off during the controllable stressor, the animal failed to develop such immunity. Similarly, turning the cortex area off prior to the uncontrollable stress also abolished the usually protective effect of a prior controllable stress experience. Thus, the prefrontal cortex was required both at the time of the initial control experience and then later at the time of challenge for protection to occur.

"Perceived control, or coping, can buffer individuals against the negative emotional and physiological impact of stress," said Maier. "Enhancing the cortex's control over brainstem and other stress-responsive structures appears to be critical for preventing and treating mood and anxiety disorders."

Source: NIH/National Institute of Mental Health