

Bullying alters brain chemistry, leads to anxiety

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Bullies and the brain. Mice that have been repeatedly bullied by dominant males show an unusual reluctance to approach new, even nonthreatening mice. Above a bullied mouse (right) keeps as much distance as it can from its corralled counterpart.

(PhysOrg.com) -- Being low mouse on the totem pole is tough on murine self-esteem. It turns out it has measurable effects on brain chemistry, too, according to recent experiments at Rockefeller University. Researchers found that mice that were bullied persistently by dominant males grew unusually nervous around new company, and that the change in behavior was accompanied by heightened sensitivity to vasopressin, a hormone involved in a variety of social behaviors. The findings suggest how bullying could contribute to long-term social anxiety at the molecular level.



"We found that chronic social stress affects neuroendocrine systems that are paramount for adaptive mammalian social behaviors such as courtship, pair-bonding and parental behaviors," says Yoav Litvin, M. S. Stoffel Postdoctoral Fellow in Mind, Brain and Behavior. "Changes in components of these systems have been implicated in human disorders, such as social phobias, depression, schizophrenia and autism."

Litvin and colleagues in Donald Pfaff's Laboratory of Neurobiology and Behavior set up a rough-and-tumble school yard scenario in which a young mouse is placed in a cage with a series of larger older <u>mice</u> — a different one in each of 10 days. The mice, being territorial, fight it out in a contest that the new arrival invariably loses. Following the 10-minute battle, the mice were separated in the same cage by a partition that keeps them physically apart but allows them to see, smell and hear one another, a stressful experience for the loser.

Given a day to rest, the test mice are then put in the company of nonthreatening mice of comparable size and age. The biggest change in behavior was that the traumatized mice were more reluctant to socialize with their fellow mice, preferring to keep their distance compared to their unbullied counterparts. The mice that had lost their battles were also more likely to "freeze" in place for longer periods of time and to frequently display "risk assessment" behaviors toward their new cagemates, behaviors that have been shown to be valid indices of fear and anxiety in humans. The researchers also gave a group of mice a drug that blocked vasopressin receptors, which partly curbed some of the anxious behavior in the bullied mice.

The researchers then examined the brains of the mice, particularly sections in the middle of the forebrain known to be associated with emotion and <u>social behavior</u>. They found that mRNA expression for vasopressin receptors — specifically V1bRs — had increased in the bullied mice, making them more sensitive to the hormone, which is



found in high levels in rats with innate high anxiety. In humans, the hormone is associated with aggression, stress and anxiety disorders. The surge of vasopressin receptors was especially notable in the amygdala, Litvin and colleagues reported this month in *Physiology & Behavior*.

How long these effects last remains an open question. Other studies have found, for instance, that chronic stress can impair some cognitive functions in rodents and people, but that their brains can bounce back, given time to recuperate.

Still, many studies in rodents, primates and people have shown that early psychological trauma can have ill effects on health throughout life. Litvin says his study suggests that victims of bullying may have difficulty forming new relationships, and it identifies the possible role for a specific vasopressin receptor.

"The identification of brain neuroendocrine systems that are affected by stress opens the door for possible pharmacological interventions," Litvin says. "Additionally, studies have shown that the formation and maintenance of positive social relationships may heal some of the damage of bullying. These dynamic neuroendocrine systems may be involved."

More information: Physiology & Behavior online: March 11, 2011. Effects of chronic social defeat on behavioral and neural correlates of sociality: Vasopressin, oxytocin and the vasopressinergic V1b receptor by Yoav Litvin, Gen Murakami and Donald W. Pfaff. dx.doi.org/10.1016/j.physbeh.2011.03.007

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