

## Authors and Disclosures

### Journalist

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## From Medscape Medical News > Psychiatry Juvenile Abuse Induces Sex-Specific Behavior in Animal Model



Caroline Helwick

June 24, 2011 — New animal research shows repeated abuse can induce behaviors in a sex-specific manner that resemble mood disorders in humans.

Specifically, young, abused, female animals showed numerous signs of greater susceptibility to the abuse than their male counterparts and female controls, Bradley M. Cooke, PhD, reported at the 16th Annual International 'Stress and Behavior' Neuroscience and Biopsychiatry Conference.

"Rates of depression and anxiety are approximately 2 times higher in women than in men, and this sex difference emerges during puberty. The origin of this sex difference in mood disorders is unknown, although it has been suggested that it may be due to an increased susceptibility of females to stress," he said.

Dr. Cooke noted that early adverse experience is a major risk factor for anxiety and depression, and it encompasses a broad range of experiences, including physical and sexual abuse and bullying.

He and his colleagues developed an animal model of child abuse in which juvenile rats were subjected to repeated attacks from aggressive adult male rats. Several weeks after the abuse ended, the animals were evaluated for behaviors that mimicked depression and anxiety in humans.

Beginning at day 28 of life, juvenile rats were placed into cages with aggressive male rats (rats selected for their aggressive behavior out of a larger population). Each rat experienced one 10-minute abuse episode with a different aggressive resident each day for a total of 10 episodes during 12 days.

Males and females received equal numbers of kicks, dominance postures, and pins. Controls were treated identically, except that they were housed in clean empty cages without exposure to the aggressors.

As adults, the rats were observed in a variety of stressful test situations, including the open field test (which evaluated for exploratory behavior), the forced swim test (learned helplessness), the elevated-plus maze (fearfulness), and a social interaction test (sociability and fearfulness).

In addition, blood was sampled for stress-evoked corticosterone levels after the first forced swim and on day 87 for baseline corticosterone (at the circadian nadir).

### Females More Reactive

The male and female juveniles received nearly identical levels of abuse, with a total of 173 episodes observed in the males and 187 in the females; however, the males and females had different reactions to the abuse.

"Juvenile abuse induced behaviors that resembled mood disorders in a sex-specific manner," Dr. Cooke reported.

Abused females were more prone to learned helplessness in the forced swim test compared with their controls and the males. Male rats exhibited the same immobility latency as controls, but latency was significantly shorter for female rats vs controls. Reduced latency to stop swimming indicates a tendency toward helplessness and despair, he noted.

"The females were more prone to learned helplessness, whereas there was no effect of the abuse experience on the male in this test."

Juvenile abuse increased anxiety levels in the elevated-plus maze in both sexes, but the effect was greater in females. Abused females also made fewer investigatory approaches during the social interaction test, whereas there was no effect on males, he reported.

Juvenile abuse also sensitized the hypothalamic-pituitary-adrenal (HPA) axis in a sex-specific manner, judging by adrenal weight (corrected by body weight). The females had significantly higher stress-evoked corticosterone levels than their controls, whereas males showed no difference. In contrast, baseline levels of corticosterone were unaffected by juvenile abuse in both males and females.

"We found that in females, juvenile abuse increased learned helplessness, fearfulness, antisocial behavior, and HPA activity," Dr. Cooke reported.

Because the level of juvenile abuse was equivalent across the sexes, these results indicate that female rats are more susceptible to juvenile abuse than males, a pattern that resembles clinical findings in humans, he suggested.

### **Novel Model of Abuse**

"Juvenile abuse may therefore potentially be used as a model of sex differences in the susceptibility to mood disorders," he added. "We are now investigating the neurobiological mechanisms that underlie the sex-specific processing of abuse stimuli."

Additional laboratory experiments point to the amygdala as the substrate with which males and females process the experience of abuse differently.

"The posterodorsal subnucleus of the medial amygdala is the most likely location in the amygdala because we have discovered this area is sexually dimorphic in many ways," he said. "If you think of the medial amygdala as the filter of experiences, then this filter seems to be different for males and females. We want to know whether the neuroanatomical sex differences in this area are responsible for the functional outcomes we observed."

Conference organizer Allen V. Kalueff, PhD, of Tulane University School of Medicine, New Orleans, Louisiana, called the rat model of juvenile abuse "a very novel model and very promising."

He added the model has a strong neurobiological basis and that it produces clinical features that closely resemble human abuse-related behaviors. "That's what makes this story very convincing," he said.

*Dr. Cooke and Dr. Kalueff have disclosed no relevant financial relationships.*

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