

Adolescent but not adult hamsters are more aggressive on low dose of fluoxetine

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New research offers tantalizing clues as to why some teenagers taking common anti-depressants may become more aggressive or kill themselves. The research is published in the October *Behavioral Neuroscience*, which is published by the American Psychological Association (APA).

Neuroscientists at the University of Texas at Austin found that juvenile hamsters given low doses of fluoxetine hydrochloride, which is sold in the United States as Prozac, became more aggressive on low doses of the drug. Juveniles given high doses became somewhat less aggressive, but not as much as adult hamsters, who calmed down on both high and low doses.

Doctoral student and lead author Kereshmeh Taravosh-Lahn, BA, says the findings confirm that juvenile and adult brains are different. Thus, she says, "It is unwise to expect a drug to work the same in juveniles as in adults."

Fluoxetine, a selective serotonin reuptake inhibitor (SSRI), is the only medication approved to treat depression in children and adolescents. However, it has carried an FDA "black box" warning since Fall 2004 due to findings of increased risk of suicidal thoughts and behaviors in some children and adolescents on the drugs. Fluoxetine affects the regulation of serotonin, a naturally occurring neurotransmitter thought to be involved in depression, by keeping it available longer in the brain's synapses. It is known to inhibit aggression in adult hamsters. Hamsters

are often used as an animal model for studying the neural basis of social behavior, given how the rodents' youthful play fighting develops in clearly understood stages into adult aggression.

In the study, researchers injected each of the experimental hamsters with high or low doses of fluoxetine. Two hours later, they put a smaller, younger same-sex hamster into the experimental hamster's home cage for 10 minutes, creating a threatening situation to which male hamsters usually respond with aggression. The neuroscientists videotaped the encounters to document behaviors such as attacks, pins, contact time, contact bouts and target of attack.

The adult hamsters treated with either dose of fluoxetine became generally more peaceful, attacking less often and for shorter times. However, the juveniles responded differently, both to high and low doses. The low doses actually resulted in significantly longer, more frequent and intense attacks, whereas the high dose only partly inhibited aggression. Neither set of juveniles responded as well as adults; one set (low dose) actually did worse.

Thus, although fluoxetine consistently calmed the adults in a potentially threatening situation, it differentially affected the juveniles. The effects of fluoxetine on aggressive responses appear to be specific to both age and dose.

The authors say their data add to growing evidence that during puberty, the brain is still maturing and, says Taravosh-Lahn, "could possibly react to drugs given to adults in different and potentially negative ways. We need to understand how these drugs will affect the developing nervous system before giving them to children."

The neuroscientists explain that because adolescents may have lower levels of serotonin than adults, there may not be enough of it in their

systems for the SSRI to work effectively. In addition, the researchers are investigating whether changing ratios of different subtypes of serotonin receptors – some of which inhibit and some of which enhance aggression -- are implicated in the findings of higher aggression on low doses.

Source: American Psychological Association

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