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Juvenile golden hamsters engaged in play-fighting (Image: Yvon Delville, University of Texas)

Prozac can make “adolescent” hamsters more aggressive towards their cage-mates, despite the antidepressant drug producing the opposite effect in adult hamsters, making them calmer.

The new findings may help explain why certain antidepressants appear to cause irritability and other abnormal behaviours in teenagers.

Kereshmeh Taravosh-Lahn at the University of Texas at Austin, US, and colleagues gave injections of the drug fluoxetine (sold in pill form as Prozac) to pubescent and mature hamsters. They injected either a low dose (10 milligrams per kilo of body weight) or a high dose (20 milligrams per kilo body weight), while other hamsters received a placebo.

The researchers then introduced a smaller, same-sex hamster into the cage of each experimental hamster and filmed all the fights between the two rodents that were initiated by the subject animals. None of the fights resulted in the skin-breaks or injury to the animals, the researchers stress.

As expected, the pubescent hamsters on a higher dose of drug appeared calmer, initiating about 65% fewer attacks than those on placebo. But surprisingly, those on the lower dose of antidepressant became more aggressive, initiating 40% more fights than those on placebo. [Watch a short movie of the aggression in action.](#)

Adult hamsters on either dose of the drug initiated fewer fights than those on placebo.

Binding on

Taravosh-Lahn speculates that different receptors in the brain may be activated by the different dosages in the younger animals. Fluoxetine, like all selective serotonin reuptake inhibitors (SSRIs), works by increasing the amounts of a mood-altering brain chemical called serotonin.

At low doses, serotonin might bind more readily to serotonin-3 receptors, which promote aggression in the hamsters, she says. But at higher doses of antidepressant, the extra serotonin could bind to serotonin-1a receptors, which inhibit aggressive behaviour, she says.

Mature hamsters may have a fewer serotonin-3 receptors in their brains than “adolescent” hamsters, Taravosh-Lahn suggests.

Some young people with depression receive lower doses of antidepressant drugs because of their relatively small weight and size. But Taravosh-Lahn says the findings of the hamster study should prompt a closer look at the effects of this practice.

“We underestimate the differences between the juvenile brain and the adult brain,” says Taravosh-Lahn. “It seems there needs to be more research on the effects of antidepressants on kids.”

Suicidal thoughts

Previous studies have also indicated a link between SSRIs and violent behaviour. Aggression was the most common reason children discontinued taking the drug Zoloft in two clinical trials conducted by pharmaceutical giant Pfizer (*PLoS Medicine*, DOI: 10.1371/journal.pmed.0030372), for example.

One high-profile case is that of Christopher Pittman, who in 2001 at the age of 12 shot and killed his grandparents before setting their house on fire. Lawyers defending the boy argued the murders were influenced by the antidepressant Zoloft, but a jury disagreed and sentenced him to 30 years in prison in February 2005.

Following a decision by the US Food and Drug Administration in late 2004, all antidepressants in the US now carry strong “black box” warnings, which state that the drugs may cause abnormal behaviours or suicidal thoughts in teenagers.

However, experts stress that antidepressants can dramatically improve the lives of some children. “By in large, children do not become aggressive on Prozac,” says child psychiatrist Stuart Goldman, at the Harvard Medical School in Boston, US.

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