

Prozac during adolescence protects against despair in adulthood, study finds

January 20 2014, by Melissa Healy

Adolescents treated with the antidepressant fluoxetine - better known by its commercial name, Prozac - appear to undergo changes in brain signaling that result in changed behavior well into adulthood, says a new study.

Adult mice and rats who were administered Prozac for a stretch of mid-adolescence responded to daunting social and physical challenges with less despair than animals who passed their teen years unmedicated, a team of researchers found. But, even as adults long separated from their antidepressant days, the Prozac veterans reacted to [stressful situations](#) with greater anxiety than did the adult Prozac virgins.

The latest research, published this week in the *Journal of Neuroscience*, offers evidence that treatment with a selective serotonin reuptake inhibitor - an SSRI antidepressant - has long-lived effects on the developing brain. It also zeroes in on how and where fluoxetine effects those lasting changes: by modifying the cascade of chemical signals issued by the brain's ventral tegmentum - a region active in mood regulation - in stressful situations.

Yet, the new research raises more questions than it answers, since the changes in adults who were treated with Prozac as adolescents seem contradictory. Sensitivity to stress appears to predispose one to developing depression. So how does a medication that treats depression in children and teens - and that continues to protect them from depression as adults - also heighten their sensitivity to stress?

"These findings underscore the complexity of drug and intracellular manipulations in the immature brain," the authors write. Perhaps, [anxiety and depression](#) - often treated as if they were indistinguishable - have a far more complicated relationship to one another than has been appreciated. Perhaps, they suggest, the chemical signaling changes brought about by Prozac treatment have surprising and contradictory effects somewhere else in the brain. Or perhaps the adolescent brain and the adult brain respond differently to stress, so that a Prozac effect unseen in adolescence will become evident in adulthood.

Answering such questions should be urgent, given that an estimated 5 percent of U.S. children are expected to experience a bout of major depression - and that, at last count (in 2002), some 3.9 percent of American adolescents were prescribed an antidepressant.

Wednesday's study was conducted by a team of researchers from California State University, San Bernardino; Florida State University; Mount Sinai School of Medicine; University of Maryland and the Massachusetts Institute of Technology. Starting 35 days after the animals' birth - the equivalent of mid-adolescence for such rats and mice - the researchers put large groups of undepressed animals first through a 15-day regimen either of daily Prozac or a placebo, and then returned them to live peacefully in their cages until they were adults - about 70 days old.

The researchers then put the mice and rats through a gantlet of psychological tests that reliably reveal the presence or absence of depression and anxiety in the animals. In one that tests the animal's response to "social defeat," a mouse or rat is housed in sight of, and briefly exposed to, a highly aggressive peer every day for 10 days, then afforded the opportunity to socialize with a new, more peaceable peer. The resilient will gladly socialize; the socially beaten will withdraw to a corner. In another, mice or rats are dropped into a bowl of water from

which they can't escape. The resilient keep swimming, persistent in their efforts to escape. The depressed quickly give up, exerting only enough effort to keep their nose above water to breathe.

In both of those tests, mice and rats treated with Prozac as adolescents proved significantly more resilient than those who got a placebo.

But in the elevated-plus maze, which tests anxiety behavior, rats and mice who had been treated with Prozac as adolescents showed themselves more sensitive to stress. Dropped in a maze under low-light conditions, timid, stressed animals tend to stay in enclosed areas where they feel more protected, while bolder creatures strike out for the maze's open spaces. In the current experiments, Prozac-treated animals showed greater anxiety and retreated to the maze's covered parts more than did those who had gotten placebo in their youth.

The researchers found that among mice and rats who exhibited more resilient behaviors, and those treated with Prozac, there was more evidence that a protein called brain-derived neurotrophic factor was actively at work in the ventral tegmentum. The work may help shed light on biomarkers that could predict an adolescent's propensity toward depression, and his likely response to antidepressant treatment. And it certainly underscores that medicating [depression](#) in adolescence has long-term effects that can change an adult's behavior in ways that are both positive and slightly worrisome.

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