Developing Problem: Why Depression Looks Different In a Kid's Brain; New Studies May Help Explain Links Between Suicide And Antidepressant Use; The Role of Impulse Control

Begley, Sharon . Wall Street Journal , Eastern edition; New York, N.Y. [New York, N.Y]15 Oct 2004: A.1.

ABSTRACT (ABSTRACT)

The brain's prefrontal cortex is the last region to mature. It isn't fully functional until the late teens or early 20s. This region is responsible for controlling impulses and inhibiting dangerous thoughts, including self-destructive ones. "It acts to inhibit intrusive and impulsive thoughts," says Yale neuroscientist George Alexander. "Because their frontal cortex is still developing, kids have less to bring to bear on regulating impulsive acts."

Scientists' growing recognition that the frontal brain lobes don't reach full maturity until at least the late teens has spurred much of the opposition to the execution of juvenile offenders. On Wednesday, the U.S. Supreme Court heard arguments in a case in which Missouri's highest court declared juvenile executions unconstitutional. Several Nobel laureates, as well as scientific and medical groups, filed briefs in the case. They argued that neurobiological evidence shows teens' still-developing brains leave them less able than adults to understand the consequences of actions, to think ahead, or control impulses.

The FDA panel that voted for a "black box" warning heard testimony from families whose children had committed suicide after taking SSRIs for conditions other than depression -- including migraines, nail biting, anxiety and insomnia. The children hadn't shown suicidal tendencies before taking the drug, the families said. That suggests SSRIs may induce "agitation or mood changes" even when there is no underlying depression, says Yale's Dr. King.

FULL TEXT

After more than a year of debate, the link between antidepressant use and a higher risk of suicidal tendencies in some children is persuasive, government regulators say. That has scientists probing an urgent new question: Why kids and not adults?

A growing number of discoveries suggest that depression in young people isn't simply a scaled-down version of depression in adults. The symptoms and the responses to antidepressants are different, indicating different biological activity. Teen brains, scientists are finding, are very different than adult brains.

Instead of feeling deeply and chronically unhappy, teens diagnosed with depression feel bored, moody and irritable. "It isn't the consistently down, sad, depressed feeling that adults have," says Carol Glod of McLean Hospital in Belmont, Mass., who is leading brain- imaging studies of depression in young people.

Adults with depression typically have severe sleep disturbances, including frequent awakening, abnormal brain waves, and a dream-state sleep that comes later in the sleep cycle. Depressed children under 12, however, rarely have these symptoms. "The symptom profile is strikingly different," says psychiatrist Harold Koplewicz of New

York University Medical Center.

These symptomatic differences, experts say, must reflect differences in the underlying biochemistry of the disease in adults and children. One indication is that an older class of antidepressants, called tricyclics, are no more effective than a placebo in young people, but are fairly effective in adults. Even the class of antidepressants at the heart of the current controversy -- called SSRIs, for Selective Serotonin Reuptake Inhibitors -- seem somewhat less effective in young patients.

When it comes to the biological underpinnings of depression in young people and adults, "the differences far outnumber the similarities," says Robert A. King of the Yale University Child Study Center. "We don't even know if depression that begins in childhood is the same disease as adult-onset depression."

Concern that antidepressants may raise the risk of suicidal thoughts and behavior in young people suffering from depression has been growing for more than a year.

After analyses of both published and unpublished studies in which children and adolescents took SSRIs for depression, the Food and Drug Administration concluded that 3.8% of the young people taking one of the drugs became suicidal. Of those on a placebo, 2.1% became suicidal. That represents an increase in risk of 80%.

None of the young patients in the trials committed suicide. Nevertheless, "it seems likely that the effect is real," psychiatrist David Brent of the University of Pittsburgh Medical Center writes in the current issue of the New England Journal of Medicine.

Dr. Brent serves on the FDA advisory panel that voted 15-8 last month to recommend a prominent "black box" warning on SSRIs indicating the drugs increase the risk of suicidal thinking and behavior in a small number of young people. Dr. Brent was among those who voted against requiring it, because he says it could scare doctors and parents away from drugs that have helped many young patients suffering from depression.

The FDA has yet to decide on whether to adopt the panel's black-box recommendation. Psychiatrists who treat depressed children and adolescents warn against a baby-with-the-bathwater reaction. Antidepressants have successfully treated thousands of young people suffering from this disease, they say. Since the introduction of SSRIs, adolescent suicides have been falling, to about eight per 100,000 per year.

No one has a definitive answer about why adolescent depression is different. But researchers are focusing on a handful of possibilities involving the brain's chemistry and structure.

A growing number of studies suggest that the antidepressants called SSRIs stimulate the birth of new neurons in the brain. Boosting this "neurogenesis" might have different effects on a developing brain than a mature one.

Adult brains, according to decades of neuroscience wisdom, weren't supposed to be able to make new neurons. But in a 2003 paper, molecular psychiatrist Ronald Duman of Yale and his colleagues showed that, in lab animals, antidepressants boost neurogenesis in parts of the brain.

The birth of new neurons takes time. Newborn neurons take weeks to travel to their target. Scientists now believe that this explains why SSRIs take weeks to affect depression.

The creation of new neurons in the brain had been assumed to be beneficial. In depressed adults, the

hippocampus -- the part of the brain responsible for learning, memory and emotion -- is typically shrunken. By restoring it to full size, and presumably, full health, depression might be lifted.

But in young people with depression, the hippocampus isn't shrunken. It may be that the influx of new neurons is somehow detrimental to adolescents. Some scientists wonder whether the new neurons could destabilize fragile brain circuits in kids suffering from mental illness.

In another key difference, young patients with depression usually don't show elevated levels of the stress hormone called cortisol. In adults, in contrast, scientists are discovering more and more evidence that depression is caused by abnormally high levels of cortisol flooding the brain.

Cortisol shrinks the hippocampus, the brain's center of learning and memory. But scientists don't yet understand why depressed adults have higher levels of cortisol than depressed teens do.

The human brain isn't fully mature for two decades. The way it matures suggests reasons why young people might be vulnerable to the worst side effects of SSRIs.

Using a new imaging technology called proton magnetic resonance spectroscopy, David Rosenberg and colleagues at Wayne State University School of Medicine in Detroit have been peering into the brains of children and adolescents suffering from major depression.

From the grey smudges on the scans, they discovered that in the brains of many of 9-to-17-year-old patients, the left side of the prefrontal cortex -- the seat of higher thought, analysis and planning -- is clearly larger than the right side. In adults with depression, in contrast, the left prefrontal cortex is often shrunk. While the significance of the difference isn't clear, it adds to the evidence that depression leaves different marks on young brains and adult ones.

Other scans, of young people suffering their first bout of major depression, found the part of the brain that is the seat of fear and anxiety is much larger than the part that is the center of learning and memory. That difference is much less extreme in adults with depression.

The brain's prefrontal cortex is the last region to mature. It isn't fully functional until the late teens or early 20s. This region is responsible for controlling impulses and inhibiting dangerous thoughts, including self-destructive ones. "It acts to inhibit intrusive and impulsive thoughts," says Yale neuroscientist George Alexander. "Because their frontal cortex is still developing, kids have less to bring to bear on regulating impulsive acts."

As a result, young people are more prone to act on their impulses, including self-destructive ones, than adults are, scientists say. Antidepressants have what scientists call a "disinhibiting effect," and that may loosen the already-loose impulse control that characterizes even healthy adolescent brains. "If you're stressed and irritable, your chances of being sensible and making the right decisions plummet," says NYU's Dr. Koplewicz.

Scientists' growing recognition that the frontal brain lobes don't reach full maturity until at least the late teens has spurred much of the opposition to the execution of juvenile offenders. On Wednesday, the U.S. Supreme Court heard arguments in a case in which Missouri's highest court declared juvenile executions unconstitutional. Several Nobel laureates, as well as scientific and medical groups, filed briefs in the case. They argued that neurobiological evidence shows teens' still-developing brains leave them less able than adults to understand the consequences of actions, to think ahead, or control impulses.

One difference receiving increased attention is that young people diagnosed with depression are more likely to develop bipolar disorder than adults are. Patients with bipolar disorder suffer from alternating episodes of depression and mania, which is marked by euphoric bursts of energy. As many as 20% to 40% of depressed children and adolescents experience a manic episode within five years of their first episode of major depression, Yale's Dr. King and colleagues reported in a 2001 review paper.

"In young people with underlying bipolar disorder, antidepressants can flip them into a mixed state of mania and depression," says Pittsburgh's Dr. Brent, making them agitated enough to contemplate ending their troubles once and for all.

But an interaction between SSRIs and depression isn't the whole story. These drugs are also given to young patients with other mental illnesses, and the adverse side effects have included suicidal thoughts and behavior, according to testimony before the FDA panel.

The FDA panel that voted for a "black box" warning heard testimony from families whose children had committed suicide after taking SSRIs for conditions other than depression -- including migraines, nail biting, anxiety and insomnia. The children hadn't shown suicidal tendencies before taking the drug, the families said. That suggests SSRIs may induce "agitation or mood changes" even when there is no underlying depression, says Yale's Dr. King.

DETAILS

Subject:	Mental depression; Suicides &suicide attempts; Teenagers; Antidepressants
Classification:	9190: United States; 8641: Pharmaceuticals industry; 8320: Health care industry; 1220: Social trends &culture
Publication title:	Wall Street Journal, Eastern edition; New York, N.Y.
Pages:	A.1
Publication year:	2004
Publication date:	Oct 15, 2004
Publisher:	Dow Jones &Company Inc
Place of publication:	New York, N.Y.
Country of publication:	United States, New York, N.Y.
Publication subject:	Business And Economics--Banking And Finance
ISSN:	00999660
Source type:	Newspapers

Language of publication:	English
Document type:	News
ProQuest document ID:	398873045
Document URL:	https://proxy.lib.wayne.edu/login?url=https://www.proquest.com/docview/398873045?accountid=14925
Copyright:	Copyright (c) 2004, Dow Jones &Company Inc. Reproduced with permission of copyright owner. Further reproduction or distribution is prohibited without permission.
Last updated:	2017-11-02
Database:	ProQuest Central

LINKS

Check for full text via 360 Link, Check for full text via 360 Link