

Why Antidepressants May Worsen Symptoms Before Kicking In

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Emerging research helps explain the delayed, even paradoxical effect of certain antidepressants.

Clinicians have known that some medications may actually worsen symptoms before helping patients feel better.

The new findings, publishing online in the journal *Trends in Cognitive Sciences*, may eventually help investigators fix the problem as well as create new classes of drugs to treat depression.

Selective serotonin reuptake inhibitors (SSRIs) are the most widely prescribed class of antidepressant drugs, and they work by increasing levels of the neurotransmitter serotonin.

While this boost in serotonin occurs within minutes to hours after an SSRI is taken, patients usually have to take the medication for about two weeks before experiencing any relief of symptoms. During this delay, the drug may actually aggravate depression, in some cases even increasing the risk for suicide.

Adrian Fischer of Otto-von-Guericke University in Germany and his colleagues said new research shows that serotonin neurons transmit a dual signal that consists of the release of serotonin as well as glutamate, another brain chemical. The investigators say that SSRIs may affect these two components of the dual signal in different ways.

<http://psychcentral.com/news/2014/12/18/why-antidepressants-may-worsen-symptoms-before-kicking-in/78794.html>

"While the serotonergic component is immediately amplified following SSRI administration, the glutamate component is acutely suppressed and is only normalized after several days of drug treatment," said Fischer.

He notes that the serotonin component of the dual signal has been linked to motivation, while the glutamate component has been linked to pleasure and learning.

"These differential time courses may help to explain the paradox of acute versus chronic SSRI effects," he said.

Experts believe a better understanding of serotonin neurons' dual signal and its varied response to acute and chronic drug treatment may help resolve some of the paradoxes observed with SSRIs.

Researchers believe delineating the contributing factors of each aspect of the dual signal may point to new drug targets. Also, improved knowledge about the signal will aid the development of new drugs that reduce the time of onset.

Investigators believe the discovery of the dual signal helps explain why the delayed onset of clinical efficacy seen with SSRIs is not evident with other antidepressant drugs that instead target glutamate receptors.

Source: Cell Press/EurekAlert

Abstract of the neurotransmitter serotonin in the brain photo by shutterstock.

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