

# Scientists shed light on how serotonin works

October 5 2010

---

Scripps Research Institute scientists have shown for the first time that the neurotransmitter serotonin uses a specialized signaling pathway to mediate biological functions that are distinct from the signaling pathways used by hallucinogenic substances. The new findings could have a profound effect on the development of new therapies for a number of disorders, including schizophrenia and depression.

The study was published in the October 6, 2010 issue of the *Journal of Neuroscience*.

[Serotonin](#) has tremendous influence over several brain functions, including the control of perception, cognition, sleep, appetite, pain, and mood and mediates these effects through interactions with receptors located throughout the central and peripheral nervous systems.

"Our study shows that while both serotonin and hallucinogens act at the serotonin 2A receptor, serotonin utilizes a very specific pathway and its actions are independent of those produced by hallucinogens," said Laura Bohn, an associate professor on the Florida campus of The Scripps Research Institute. "Future drug discovery efforts to identify lead compounds for treatment of depression may consider focusing upon those that only engage that pathway. This work may also lend insight into the mechanisms that underlie the hallucinations that occur in schizophrenia."

This may be particularly important, Bohn said, for the treatment of depression because traditional therapies, which focus on elevating

serotonin levels, can sometimes produce serious side effects such as a serotonin syndrome. This syndrome is often accompanied by hallucinations, and is especially serious when antidepressant treatments such as [selective serotonin reuptake inhibitors](#) (SSRIs) are mixed with monoamine oxidase inhibitors (MAOIs).

The scientists' current study supports a long-standing hypothesis that hallucinations may arise from the metabolites formed from elevated serotonin levels. Since there is a difference in the way the two neurotransmitters signal, this may represent a means to preserve the effects of serotonin while preventing the adverse side effects caused by the metabolites.

## **Serotonin Versus Hallucinogens**

The study, coauthored by Cullen Schmid, a graduate student in the lab, showed that serotonin signals through the serotonin 2A receptor by recruiting a regulatory protein called  $\beta$ arrestin2, and that the actions of serotonin at the receptor are far different than those produced by hallucinogenic N-methyltryptamines, a class of naturally occurring substances found in several plants and in minute amounts in the human body and which includes the abused drug, DMT. The study found that the N-methyltryptamines activate the serotonin 2A receptor independently of  $\beta$ arrestin2.

Both serotonin and the N-methyltryptamines produce what is known as a head twitch response in animal models, which indicates that the serotonin 2A receptor has been activated. Any interruption in the exclusive serotonin pathway prevents that behavioral response to serotonin, but has no effect on N-methyltryptamine-induced head twitches, indicating a distinct divergence in the signaling pathways utilized by these two neurotransmitters.

"Despite the fact that they activate the same receptor, serotonin leads to the assembly of a number of proteins associated with the receptor that the metabolites of serotonin do not produce," Bohn said. "But whether the lack of this complex formation is why compounds like DMT lead to hallucinations is not clear."

Bohn continues to investigate these and other questions.

**More information:** "Serotonin, But Not N-Methyltryptamines, Activates the Serotonin 2A Receptor via an Arrestin2/Src/Akt Signaling Complex in Vivo," *Journal of Neuroscience*.

Provided by The Scripps Research Institute

Citation: Scientists shed light on how serotonin works (2010, October 5) retrieved 26 April 2024 from <https://medicalxpress.com/news/2010-10-scientists-serotonin.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--