

SSRIs may pack more punch at the cellular level than believed

August 16 2010

A new discovery about selective serotonin reuptake inhibitors (SSRIs) suggests that these drugs, which are used to treat mental health disorders like depression and anxiety, have multiple effects on our cells. In a research report published in the August 2010 issue of *GENETICS*, researchers used yeast cells to identify secondary drug targets or pathways affected by SSRIs. Such secondary pathways could help explain why different people taking the same drug may experience different effects, and could also lead to new types of drugs altogether.

"We hope that our study begins to illuminate the full breadth of pharmacological effects of antidepressants on cellular physiology starting with the simple unicellular eukaryote, budding yeast," said Ethan O. Perlstein, Ph.D, a researcher involved in the work from the Lewis-Sigler Institute for Integrative Genomics at Princeton University in New Jersey. "Furthermore, our work validates the notion that simple model organisms may be useful for the study of complex human disease."

Knowing that a high concentration of sertraline (Zoloft®) is toxic to [yeast cells](#), scientists applied a lethal dose to millions of these cells and fished out a few cells that became resistant to the drug. Researchers then identified the underlying mutations in those cells and applied genetic, biochemical, and electron microscopic imaging techniques to characterize the molecular basis of resistance. Their results suggest that SSRIs may actually affect more than one process in a cell, including non-protein targets such as phospholipid membranes. Additionally, the study's results demonstrate that sertraline targets intracellular membranes

and modulate pathways involved in vesicle trafficking that are present in both yeast and human [cells](#). Vesicle trafficking plays an important role in how neural synapses develop and function. More work is necessary, however, to determine the exact clinical relevance of this secondary [drug target](#).

"There's no question that SSRIs help thousands of people with mental health problems," said Mark Johnston, Editor-in-Chief of the journal *GENETICS*, "but as this research shows, there is still some mystery about how they help us. This study a key first-step toward giving us a comprehensive answer to how SSRI's work, and it may open doors to entirely new therapies."

More information: www.genetics.org

Provided by Genetics Society of America

Citation: SSRIs may pack more punch at the cellular level than believed (2010, August 16)
retrieved 19 April 2024 from
<https://medicalxpress.com/news/2010-08-ssris-cellular-believed.html>

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