

# Psychiatric medication effects on brain structure

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It is increasingly recognized that chronic psychotropic drug treatment may lead to structural remodeling of the brain. Indeed, clinical studies in humans present an intriguing picture: antipsychotics, used for the treatment of schizophrenia and psychosis, may contribute to cortical gray matter loss in patients, whereas lithium, used for the treatment of bipolar disorder and mania, may preserve gray matter in patients.

However, the clinical significance of these structural changes is not yet clear. There are many challenges in executing longitudinal, controlled, and randomized studies to evaluate this issue in humans, particularly because there are also many confounding factors, including illness severity, illness duration, and other medications, when studying patients.

It is therefore critical to develop animal models to inform the clinical research. To accomplish this, a group of researchers at King's College London, led by Dr. Shitij Kapur, developed a rat model using clinically relevant [drug exposure](#) and matched clinical dosing in combination with longitudinal [magnetic resonance imaging](#). They administered either lithium or haloperidol (a common antipsychotic) to rats in doses equivalent to those received by humans. The rats received this treatment daily for eight weeks, equivalent to 5 human years, and underwent brain scans both before and after treatment.

Dr. Kapur explained their findings, "Using this approach, we observed that chronic treatment with haloperidol leads to decreases in cortical gray matter, whilst lithium induced an increase, effects that were

reversible after drug withdrawal." [Gray matter](#) was decreased by 6% after haloperidol treatment, but increased by 3% after [lithium treatment](#).

"These important observations clarify conflicting findings from clinical trials by removing many of the confounding effects," commented Dr. John Krystal, Editor of [Biological Psychiatry](#). "Whether these changes in [brain structure](#) underlie the benefits or side effects of these medications remain to be seen. However, they point to brain effects of established medications that are not well understood, but which may hold clues to new treatment approaches."

"Whilst these intriguing findings are consistent with available clinical data, it should be noted these studies were done in normal rats, which do not capture the innate pathology of either schizophrenia or bipolar disorder," Kapur added. "Moreover, because the mechanism(s) of these drug effects remain unknown, further studies are required, and one should be cautious in drawing clinical inferences. Nevertheless, our study demonstrates a new and powerful model system for further investigation of the effects of psychotropic drug treatment on brain morphology."

**More information:** The article is "Contrasting Effects of Haloperidol and Lithium on Rodent Brain Structure: A Magnetic Resonance Imaging Study with Postmortem Confirmation" by Anthony C. Vernon, Sridhar Natesan, William R. Crum, Jonathan D. Cooper, Michel Mado, Steven C.R. Williams, and Shitij Kapur ([doi: 10.1016/j.biopsych.2011.12.004](https://doi.org/10.1016/j.biopsych.2011.12.004)). The article appears in *Biological Psychiatry*, Volume 71, Issue 10 (May 15, 2012)

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