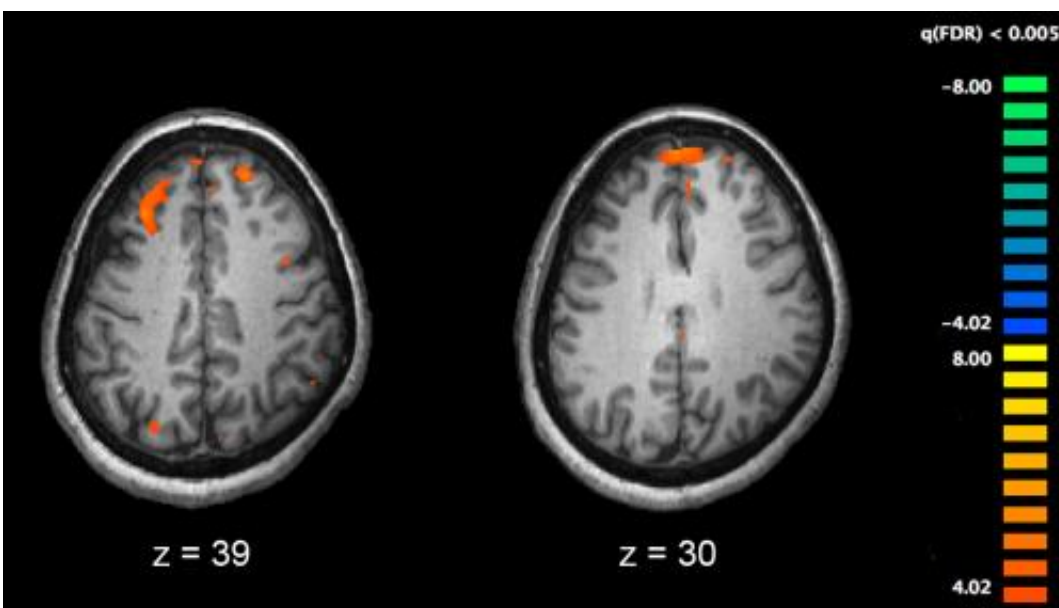


Commonly used anticholinergic drugs for schizophrenia linked to greater cognitive impairment

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Functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The image shows two levels of the brain, with areas that were more active in healthy controls than in schizophrenia patients shown in orange, during an fMRI study of working memory. Credit: Kim J, Matthews NL, Park S./PLoS One.

Writing in the May 14, 2021 issue of *The American Journal of Psychiatry*, a multi-institution team of scientists led by researchers at

University of California San Diego School of Medicine report that medications commonly prescribed to reduce the severity of physical and mental health symptoms associated with schizophrenia may have a cumulative effect of worsening cognitive function in patients.

Psychotropic medications are often necessary and beneficial, but they possess other secondary properties that are not directly related to reducing symptoms, including [anticholinergic](#) properties. That is, apart from their actual intended effects, they also inhibit acetylcholine, a neurotransmitter that is important in brain signaling and in a number of other body functions. Apart from schizophrenia, which is estimated to affect roughly 1.5 million Americans, drugs with anticholinergic properties are used to treat a wide variety of conditions, including urinary incontinence, chronic obstructive pulmonary disorder and some muscle disorders.

"Many medications have anticholinergic effects, and we are becoming increasingly aware about their potential long-term risks," said lead study author Yash Joshi, MD, assistant professor in the Department of Psychiatry at UC San Diego School of Medicine.

In fact, anticholinergic drugs have been linked to [cognitive impairment](#) and increased dementia risk in healthy adults. For example, a 2020 study by UC San Diego School of Medicine researchers found an association between anticholinergic medications and increased risk of Alzheimer's disease. Another study cited by authors reported that taking just one strong anticholinergic medication for three years was associated with a 50 percent increase in the odds of developing dementia over the 11-year study period.

Persons living with schizophrenia commonly experience significant difficulties with attention, learning, memory, executive function (such as reasoning and planning) and social cognition. Since these [mental](#)

[processes](#) are critical for many [daily activities](#), cognitive impairment in schizophrenia can lead to significant disability.

In the latest study, Joshi and colleagues sought to comprehensively characterize how the cumulative anticholinergic burden from different classes of medications impact cognition in patients with schizophrenia.

"We wanted to better understand how anticholinergic medication burden impacted cognitive functioning in individuals who may have already some cognitive difficulties due to schizophrenia," he said.

Researchers assessed medical records, including prescribed medications, of 1,120 study participants with schizophrenia. They found that 63 percent of participants had an anticholinergic cognitive burden (ACB) score of at least 3.

"This is striking because previous studies have shown that an ACB score of 3 in a healthy, older adult is associated with cognitive dysfunction and a 50 percent increased risk for developing dementia," said Joshi.

Notably, roughly one-quarter of the schizophrenia patients in the study had ACB scores of 6 or more.

The authors wrote that while such numbers may be high for persons living without any psychiatric illness, they are not difficult to achieve in patients receiving routine psychiatric care, which often includes medications with anticholinergic properties. For example, a patient prescribed daily olanzapine for symptoms of psychosis already starts with an ACB score of 3; add hydroxyzine for anxiety and insomnia in the same patient and their ACB score doubles. Many patients with schizophrenia are treated with multiple psychotropic drugs—other medications for other health conditions could increase this burden further.

"It is easy even for well-meaning clinicians to inadvertently contribute to anticholinergic medication burden through routine and appropriate care," said Gregory Light, Ph.D., professor of psychiatry and senior author. "The unique finding here is that this burden comes from medications we don't usually think of as typical anticholinergic agents."

The authors said ACB should be considered when physicians prescribe medications for patients with schizophrenia, noting that emerging data suggests reducing anticholinergic burden is associated not only with cognitive benefit, but an improved quality of life.

"Brain health in schizophrenia is a game of inches, and even small negative effects on cognitive functioning through [anticholinergic medication](#) burden may have large impacts on patients' lives," said Joshi.

"Everyone caring for those living with [schizophrenia](#)—mental health providers, primary care providers, specialists, and loved ones—should be vigilant in trying to reduce anticholinergic burden in a holistic way so that we can be good stewards of our patients' long-term cognitive health. If clinically feasible and safe, this could include reducing the number of [psychotropic medications](#), changing some psychotropic medications to others with lower anticholinergic properties, or using complementary approaches to enhance [cognitive functioning](#)."

More information: Yash B. Joshi et al. Anticholinergic Medication Burden—Associated Cognitive Impairment in Schizophrenia, *American Journal of Psychiatry* (2021). [DOI: 10.1176/appi.ajp.2020.20081212](https://doi.org/10.1176/appi.ajp.2020.20081212)

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