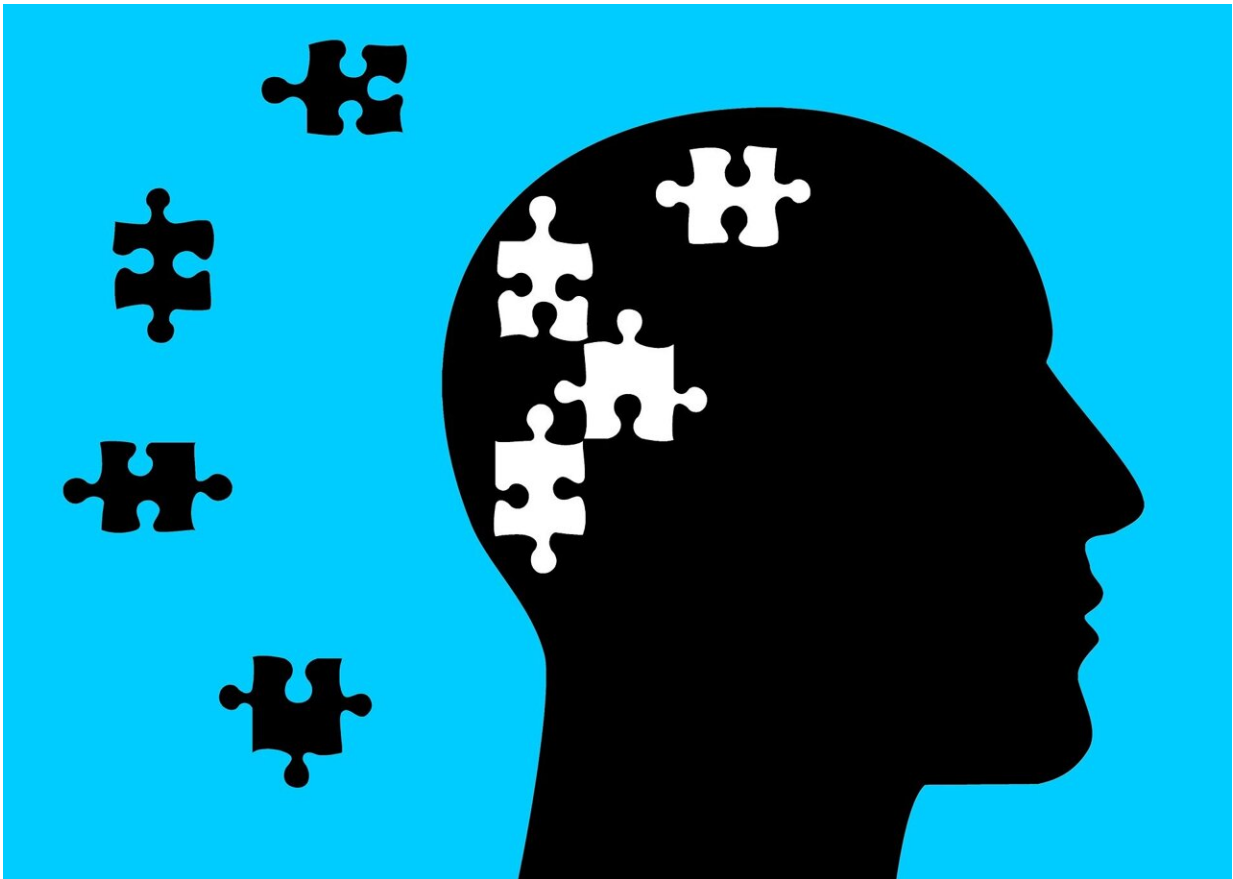


Researchers find two FDA-approved drugs that curb symptoms of Alzheimer's disease

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Two commonly used psychiatric drugs show evidence of improving symptoms of Alzheimer's disease including boosting cognition,

according to a study from researchers at the University of Colorado Anschutz Medical Campus.

"The people who received these drugs developed better cognition and actually improved in their [clinical diagnosis](#)," said the study's senior author Huntington Potter, Ph.D., professor of neurology at the University of Colorado School of Medicine and director of the CU Alzheimer's and Cognition Center. "Compared to those who did not take these drugs, they reverted from Alzheimer's disease to mild cognitive impairment or from [mild cognitive impairment](#) to normal."

The study was published today in the journal *Alzheimer's Research & Therapy*.

The drugs, the antidepressant imipramine and antipsychotic olanzapine, are already approved by the Food and Drug Administration. And since depression and psychosis are common in those with Alzheimer's disease (AD), many patients take other medications for these problems, providing a large control population for the scientists to evaluate the effects.

The CU Anschutz research team, led by Noah Johnson, Ph.D., were looking for drugs that block the effect of the apolipoprotein E4 protein or APOE4, which is encoded by a gene variant that when inherited, confers the strongest risk for developing late-onset Alzheimer's.

"We took a unique approach by targeting APOE4 because the usual [drug](#) targets, amyloid-beta and tau, have not produced a convincingly effective drug for people with AD despite decades of work," said Johnson.

The researchers screened 595 compounds in a drug library from the National Institutes of Health and identified several compounds that

specifically blocked the effect of APOE4 on Alzheimer amyloid formation.

"We then looked into the huge National Alzheimer's Coordinating Center (NACC) database and asked what happened when someone was prescribed these drugs for normal indications but happened to be Alzheimer's patients," Potter said.

That's when they found that [psychiatric patients](#) with AD using imipramine and olanzapine showed significant improvement in AD symptoms.

"The only things these drugs have in common is that they block the catalytic effect of APOE4 on the formation of amyloids in the brain," Potter said, referring to the proteins that form clumps and disrupt cell function in AD.

The results were surprising.

"Our analyses show that, compared to the control populations, subjects taking imipramine or olanzapine had improved cognition and diagnoses, which are direct clinical measures of disease severity," the study said.

"Notably, in our drug screen, we found that imipramine and olanzapine strongly inhibited the apoE4-catalyzed fibrillization of A β ([amyloid beta](#)), whereas none of the other antidepressants or antipsychotics whose use was reported in the NACC database had any such activity and none showed any benefit for AD patients."

Potter cautioned that the study was retrospective, meaning they made the discovery while analyzing data collected for another purpose. The next step, he said, would be to test imipramine, which has fewer side-effects than olanzapine, on a rodent model and if successful conduct a clinical trial.

"The number of human drugs that have shown any benefit to AD patients are maybe one or two or three," Potter said. "So this is a very promising advance."

More information: Noah R. Johnson et al, Imipramine and olanzapine block apoE4-catalyzed polymerization of A β and show evidence of improving Alzheimer's disease cognition, *Alzheimer's Research & Therapy* (2022). [DOI: 10.1186/s13195-022-01020-9](https://doi.org/10.1186/s13195-022-01020-9)

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