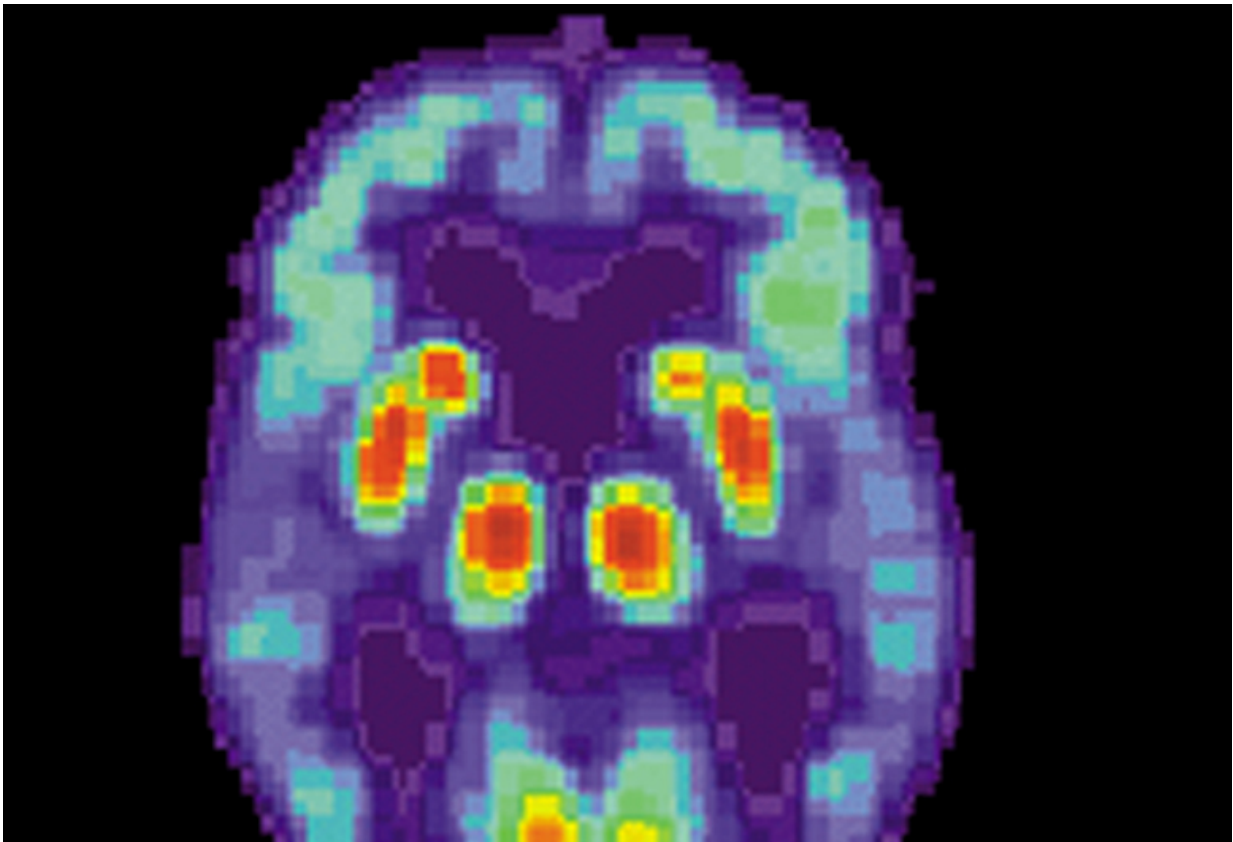


# Anti-seizure medication improves cognitive function in some Alzheimer's patients

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PET scan of a human brain with Alzheimer's disease. Credit: public domain

An inexpensive anti-seizure medication markedly improves learning and memory and other cognitive functions in Alzheimer's patients who have epileptic activity in their brains, according to a study published in the

Sept. 27th issue of *JAMA Neurology*.

"This is a drug that's used for epilepsy," says Keith Vossel, MD, MSc, director of the Mary S. Easton Center for Alzheimer's Disease Research at UCLA, and the principal investigator on the clinical trial. "We used it in this study for Alzheimer's [patients](#) who had evidence of silent [epileptic activity](#), which is seizure-like brain activity without the associated physical convulsions."

Alzheimer's [disease](#) (AD) is the leading cause of dementia worldwide. Early symptoms include short-term memory loss, decline in problem solving, word-finding difficulties, and trouble with spatial navigation. Among Alzheimer's patients, an estimated 10-22% develop seizures, while an additional 22-54% exhibit silent epileptic activity.

Dr. Vossel showed in earlier studies that patients who experience silent epileptic activity in their brains have a more rapid decline in cognitive function. The researchers chose to test the anti-seizure medication levetiracetam, which was approved by the FDA in 1999 and had also performed well in animal models of Alzheimer's disease. Now available as a generic, levetiracetam costs around \$70 per year. The dose tested in the trial was 125 mg twice a day, far less than a typical dose used for epilepsy.

In the study, 54 patients with mild Alzheimer's symptoms were screened for silent epileptic activity using an electroencephalogram (EEG) to monitor them overnight, as well as an hour-long magnetoencephalogram (MEG) to record magnetic waves generated from electrical activity.

"MEG can pick up epileptic activity that EEGs miss because it's looking at a different population of brain cells," Dr. Vossel explained.

Among the patients screened for the study, 34 patients were eligible to

participate, with nearly 40% having epileptic activity, and the remainder having no epileptic activity (patients on anti-seizure medications due to preexisting seizure disorders were excluded prior to screening).

These patients were then divided into two groups with one group receiving placebo for four weeks, followed by a 4-week period of receiving no drug and then a 125 mg dose of levetiracetam twice a day for four weeks. The second group received these same treatments in reverse order. This crossover design allowed the intervention to be tested on all participants with neither the patients nor the researchers knowing whether the patient was taking the actual drug on any given week.

During the study period, the researchers tested skills like the patients' abilities to problem solve, reason, remember words and how well they could navigate. For example, using a driving simulator on a computer monitor, they had participants learn to navigate a street route through a virtual city.

The researchers found that the patients treated with levetiracetam showed trends toward improvement in cognitive function, but when the patients were separated into those with silent epileptic activity and those without, the patients with silent epileptic activity showed clear benefit from being on the drug.

"There were very clear differences between the groups," Dr. Vossel says. "There's a subtype of Alzheimer's disease, consider it an epileptic variant, that's quite common, occurring in approximately 60% of patients. Patients with this form of Alzheimer's disease show symptomatic improvement with levetiracetam."

When doctors diagnose Alzheimer's disease, they do not typically test for silent seizures, so findings from the study may prompt them to consider whether a patient is potentially experiencing epileptic activity.

"There are some clinical features that indicate Alzheimer's patients are more likely to be having silent epileptic activity," he says. "The main one is being under the age of 65 when symptoms begin." In fact, he says, the drug also appeared to benefit younger patients even if they didn't have detectable epileptic activity.

Patients in the study were already taking currently approved medications for Alzheimer's, and this study demonstrates that levetiracetam improves cognitive function better than current treatments alone. Future studies will be needed to find out whether taking the drug long-term can slow disease progression.

"This study was intended to look for cognitive improvement during a short course of treatment," Dr. Vossel says. "There are other studies that are ongoing to see if the drug can help slow the disease course over longer periods," adding that future studies at UCLA will focus on recruiting a more diverse study population and testing other anti-seizure medications.

Dr. Vossel began the study in 2014, while he was at the University of California, San Francisco and enrolled patients at UCSF and the University of Minnesota. The research was supported by grants from the Alzheimer's Association, the National Institutes of Health, and other private gift funds.

**More information:** Keith Vossel et al, Effect of Levetiracetam on Cognition in Patients With Alzheimer Disease With and Without Epileptiform Activity, *JAMA Neurology* (2021). [DOI: 10.1001/jamaneurol.2021.3310](https://doi.org/10.1001/jamaneurol.2021.3310)

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