

Study explains why Alzheimer's drug is both safe and effective

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Alzheimer's disease destroys brain cells and their connections (called synapses), causing memory loss and other cognitive problems that disrupt work, hobbies and daily life. Symptoms can be alleviated, in part, by the drug memantine (marketed in the United States as Namenda), which is currently FDA-approved to treat moderate-to-severe Alzheimer's disease and was, in part, developed by Stuart A. Lipton, M.D., Ph.D., Director of the Del E. Web Center for Neuroscience, Aging and Stem Cell Research at Sanford-Burnham Medical Research Institute (Sanford-Burnham).

Memantine improves symptoms by blocking abnormal activity of glutamate, a chemical that transmits messages between nerve cells. In a study appearing August 18 in The [Journal of Neuroscience](#), a team of investigators at Sanford-Burnham led by Dr. Lipton unravel exactly how memantine helps Alzheimer's patients without causing serious side effects.

"While memantine is partially effective in treating Alzheimer's disease, one of its major advantages is how safe and well-tolerated it is clinically," said Dr. Lipton

In treating any disease, one of the most difficult parts of designing a new drug is finding ways to maximize its beneficial effect while minimizing harmful side effects. Memantine is a particularly safe treatment for Alzheimer's disease because it dampens excessive glutamate signaling that occurs away from synapses without blocking glutamate activity at

the synapses. This is important because interfering with synaptic glutamate signaling would disrupt normal [brain activity](#).

"We showed definitively for the first time that memantine, the drug our group developed for Alzheimer's disease, works in a unique way," Dr. Lipton said. "It inhibits a protein that binds glutamate called the NMDA receptor, but predominantly blocks NMDA receptors that signal molecularly to cause neuronal injury and death. It spares the synaptic receptors that mediate normal communication between [nerve cells](#) in the brain."

This finding helps explain why the drug is so well tolerated by Alzheimer's patients and might provide hints for the development of future therapies targeting the NMDA receptor and similar cellular machinery in other diseases.

As many as 5.3 million Americans are living with Alzheimer's, currently the seventh-leading cause of death in the United States.

Provided by Sanford-Burnham Medical Research Institute

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