

# An Animal Model for Schizophrenia Identifies a Novel Approach for Treating Cognitive Impairments

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Researchers have been seeking a safe and effective way to treat cognitive impairments associated with schizophrenia by enhancing N-methyl-D-aspartate (NMDA) glutamate receptors. Functional deficits in NMDA receptors may contribute to the underlying neurobiology of this disorder. The first generation of studies trying to stimulate NMDA receptors administered large amounts of substances, like glycine or D-serine, which indirectly enhance NMDA receptor function. While there were some positive reports of efficacy, findings across studies were more inconsistent than was hoped.

New approaches following this line of research are just beginning to be tested in patients. For example, several pharmaceutical companies are studying drugs that block the glycine transporter (GlyT1) and thereby raise synaptic glycine levels. A new study in *Biological Psychiatry*, published by Elsevier, by Dr. Kenji Hashimoto and colleagues may represent a “next step,” which is to prevent the inactivation of D-serine by the enzyme D-amino acid oxidase (DAAO). The authors found that this approach enhances the efficacy of D-serine in an [animal model](#) for deficits in NMDA glutamate receptor function.

To put it more simply, although D-serine is used as a treatment for schizophrenia, it is metabolized by DAAO, reducing its availability in the brain. So, using an animal model of schizophrenia, these scientists co-administered D-serine and a compound that blocks the effects of

DAAO. This increased the levels of D-serine in the mice and therefore its effectiveness in treating the abnormal behaviors in this animal model that may be relevant to schizophrenia.

“We still do not have effective treatments that specifically target the cognitive and functional impairments associated with schizophrenia. These findings are very interesting because there is a continued sense that we have not yet captured the therapeutic promise associated with the glycine site of the NMDA receptor. GlyT1 blockers and DAAO inhibitors may be important new clinical research tools,” comments John Krystal, M.D., Editor of Biological Psychiatry.

Further research is still needed to see whether these findings can be extended to humans, but it is hoped that this combination therapy proves to be a novel and effective treatment of [schizophrenia](#).

Source: Elsevier

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