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SCHIZOPHRENIA Factsheet

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What are glutamatergic modulators?

Antipsychotic medications predominantly target the dopamine neurotransmitter system, with some efficacy for alleviating the positive symptoms of schizophrenia. However, the persistence of negative and cognitive symptoms suggests that other mechanisms are also likely to be involved. The glutamate hypothesis of schizophrenia proposes that reduction of glutamatergic N-methyl-D-aspartate (NMDA) receptor function represents a primary neuropathology in schizophrenia. Therefore, glutamate receptor modulators have been suggested as an adjunctive therapy to standard antipsychotic treatments, when individuals have sub-optimal responses to treatment. The glutamate receptor modulators that have been trialed in schizophrenia are predominantly amino acids, and act on several different aspects of the glutamatergic neurotransmission system. Agents include glycine, D-serine, D-cycloserine, D-alanine, CX516, sarcosine, N-acetyl cysteine, and memantine. These agents have been studied for efficacy in improving symptom severity and cognitive function.

What is the evidence for adjunctive glutamatergic modulators?

Moderate to high quality evidence shows small improvements in negative, positive, and total symptoms with adjunctive N-methyl-d-aspartate modulators. For negative symptoms, D-serine, N-acetyl-cysteine, and D-alanine were most effective. For positive symptoms, NMDA receptor modulators with non-clozapine adjuncts were most effective. For total symptoms, D-serine, glycine, N-acetyl-cysteine, sarcosine, and D-alanine were most effective.

For memantine, moderate to high quality evidence finds medium-sized improvements in total and negative symptoms, with no significant effects on positive symptoms or general psychopathology. Lower quality evidence suggests there may also be some improvement in cognitive symptoms with adjunctive memantine.

For minocycline, moderate to low quality evidence suggests a small benefit for overall and negative symptoms, with no benefit for positive or depressive symptoms.

Moderate to high quality evidence suggests no overall benefit of adjunctive N-methyl-d-aspartate receptor-enhancing agents for cognition, although it may be beneficial in people aged between 30 and 39 years, and when taking N-acetyl cysteine for working memory.

For more information see the technical table

NeuRA
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NeuRA (Neuroscience Research Australia) is one of the largest independent medical and clinical research institutes in Australia and an international leader in neurological research.

Diseases of the brain and nervous system pose the greatest health, economic and social burden of any disease group because they are chronic, debilitating and have no known cures.

Medical research is the cornerstone of efforts to advance the health and wellbeing of families and the community. Our dedicated scientists are focussed on transforming their research into significant and practical benefits for all patients.

While we hope you find this information useful, it is always important to discuss any questions about schizophrenia or its treatment with your doctor or other health care provider.

HOW YOUR SUPPORT HELPS

We are able to make significant advances due to the generosity of countless people. Your donation allows us to continue to work towards transforming lives. For information on how you can support our research, phone **1300 888 019** or make a secure donation at **neura.edu.au/donate/schizophrenia**.

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