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NMDA receptor antagonists for depression: Critical considerations.

Serafini G[1], Gonda X, Rihmer Z, Pompili M, Girardi P, Nasrallah HA, Amore M.

Author information

Abstract

BACKGROUND: Research studies suggest that glutamate dysfunction, in particular N-methyl-D-aspartate receptors (NMDARs) abnormalities, may be involved in the pathophysiology of major neuropsychiatric conditions. Increased glutamatergic excitotoxic activity may be found in some brain circuits of patients with major depression. According to several published reports, NMDAR antagonists may exert antidepressant activity, but the molecular changes associated with abnormal glutamatergic neurotransmission remain unclear.

METHODS: We have critically reviewed the current literature in order to investigate the role of NMDAR antagonists in major depression.

RESULTS: NMDAR antagonists, such as ketamine, may be considered novel and promising pharmacological options for the rapid treatment of treatment-resistant depression patients. This is in contrast to the delayed action of the currently available antidepressant medications. Studies suggest that glutamatergic receptor modulation may enhance neuroplasticity mechanisms and neurogenesis together with the release of some neurotransmitters. Unfortunately, the use of ketamine is currently limited by some transient adverse events, including dissociative symptoms.

CONCLUSIONS: Targeting NMDARs using antagonists represents an important alternative antidepressant option in major depression. However, NMDAR antagonists may exert different actions based on the differential brain location of NMDAR.

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