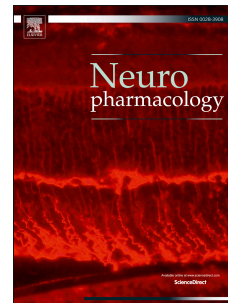


# Accepted Manuscript

Two Cellular Hypotheses Explaining Ketamine's Antidepressant Actions: Direct Inhibition and Disinhibition

Oliver H. Miller, Jacqueline T. Moran, Benjamin J. Hall



PII: S0028-3908(15)30035-6

DOI: [10.1016/j.neuropharm.2015.07.028](https://doi.org/10.1016/j.neuropharm.2015.07.028)

Reference: NP 5935

To appear in: *Neuropharmacology*

Received Date: 26 May 2015

Revised Date: 20 July 2015

Accepted Date: 22 July 2015

Please cite this article as: Miller, O.H., Moran, J.T., Hall, B.J., Two Cellular Hypotheses Explaining Ketamine's Antidepressant Actions: Direct Inhibition and Disinhibition, *Neuropharmacology* (2015), doi: 10.1016/j.neuropharm.2015.07.028.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

A single, low dose of ketamine has antidepressant actions in depressed patients and in patients with treatment-resistant depression (TRD). Unlike classic antidepressants, which regulate monoamine neurotransmitter systems, ketamine is an antagonist of the N-methyl-D-aspartate (NMDA) family of glutamate receptors. The effectiveness of NMDAR antagonists in TRD unveils a new set of targets for therapeutic intervention in major depressive disorder (MDD) and TRD. However, a better understanding of the cellular mechanisms underlying these effects is required for guiding future therapeutic strategies, in order to minimize side effects and prolong duration of efficacy. Here we review the evidence for and against two hypotheses that have been proposed to explain how NMDAR antagonism initiates protein synthesis and increases excitatory synaptic drive in corticolimbic brain regions, either through selective antagonism of inhibitory interneurons via cortical disinhibition, or by direct inhibition of cortical pyramidal neurons.

Download English Version:

<https://daneshyari.com/en/article/5813613>

Download Persian Version:

<https://daneshyari.com/article/5813613>

[Daneshyari.com](https://daneshyari.com)