## Accepted Manuscript

Accepted Date:

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PII: DOI: Reference:	S0306-4522(17)30935-1 https://doi.org/10.1016/j.neuroscience.2017.12.045 NSC 18215
To appear in:	Neuroscience
Received Date:	22 August 2017

26 December 2017

Please cite this article as: W-j. Zhang, H-h. Wang, Y-d. Lv, C-c. Liu, W-y. Sun, L-



Please cite this article as: W-j. Zhang, H-h. Wang, Y-d. Lv, C-c. Liu, W-y. Sun, L-j. Tian, Downregulation of Egr-1 expression level via GluN2B underlies the antidepressant effects of ketamine in a chronic unpredictable stress animal model of depression, *Neuroscience* (2017), doi: https://doi.org/10.1016/j.neuroscience.2017.12.045

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## ACCEPTED MANUSCRIPT

Downregulation of Egr-1 expression level via GluN2B underlies the antidepressant effects of ketamine in a chronic unpredictable stress animal model of depression

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## Abstract

Ketamine is a non-competitive antagonist of N-methyl-D-aspartate receptors (NMDARs). Growing evidence suggests that a single dose of ketamine produces a series of rapid and remarkable antidepressant properties. However, the mechanisms remain unclear. In our study, the antidepressant properties of a single dose of ketamine (10 mg/kg, i.p.) in mice exposed to chronic unpredictable stress (CUS) was assessed using the open field test (OFT) and the forced swimming test (FST). Early growth response 1 (Egr-1) and postsynaptic density protein 95 (PSD-95) mRNA and protein expression levels were examined using qRT-PCR and western blot, respectively. Dendritic spine density in the CA1 region of the hippocampus was detected by Golgi staining. AMPAR currents in hippocampal slices were measured by electrophysiology. Our study showed that CUS induced a significant depression-like behavior accompanied by an upregulation of Egr-1 and downregulations of PSD-95, spine density, and AMPAR currents in the

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