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Short communication

Activation of the NMDA/glutamate receptor complex antagonizes the NMDA antagonist-induced antidepressant-like effects in the forced swim test

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Abstract:
The antidepressant activity of NMDA receptor antagonists has been demonstrated, and their mechanism of action was based on the assumption of their selectivity for the NMDA receptor only. However, no direct evidence for the NMDA receptor role in this activity was demonstrated.
Now, in order to prove the NMDA pathway of antidepressant-like action of the NMDA antagonists in the mouse forced swim test (FST) we examined if antidepressant activity of NMDA receptor antagonists is mediated by NMDA receptors and whether the activation of different modulatory sites of the NMDA receptor complex influence the action of the antagonists of different sites of NMDA receptor.
In our study, we used two NMDA ligands: competitive NMDA glutamate site antagonist CGP 37849, and glycine$_B$ antagonist L-701,324; both at doses found to be effective in the FST. The antidepressant-like activity of the compounds was abolished by the N-methyl-D-aspartic acid (NMDA) or by D-serine co-treatment. Ligands at the doses active in the FST did not alter locomotor activity.
The present study indicates the major role of the NMDA/glutamate pathway in the antidepressant-like activity of NMDA antagonists in the mouse FST.

Key words:
NMDA receptor, glutamate site, glycine$_B$ site, ligands, forced swim test, mice