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NONCOMPETITIVE NMDA RECEPTOR ANTAGONISTS INHIBIT APOMORPHINE-INDUCED CLIMBING BEHAVIOR IN RESERPINE-TREATED MICE

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Previous work in our laboratory has shown that noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonists, MK-801, ketamine, dextrorphan and dextromethorphan cause a pronounced inhibition of apomorphine-induced cage climbing behavior in intact mice, suggesting the involvement of NMDA receptors in the glutamatergic modulation of dopaminergic function at the postsynaptic dopamine (DA) receptors. Therefore, in order to definitively establish the involvement of NMDA receptor in the apomorphine-induced dopaminergic response at the postsynaptic DA receptor, it is necessary to investigate whether or not the noncompetitive NMDA receptor antagonists would inhibit these phenomena not only in intact mice but also in the mice that are devoid of any involvement of indirect dopaminergic function. To minimize the risk of any indirect involvement of NMDA antagonists with DA neurons, vesicular DA stores were first depleted with reserpine.

Apomorphine-induced stereotyped cage-climbing behavior is an accepted test for studying postsynaptic DA activity. Climbing behavior was measured using the 3-point rating scale of Protais et al in mice.

The present study showed that noncompetitive NMDA receptor antagonists, MK-801, ketamine, dextrorphan and dextromethorphan attenuated the apomorphine-induced climbing behavior in reserpine-treated mice. Thus, the present results support our previous conclusion that the NMDA receptors play important roles in the glutamatergic modulation of dopaminergic function at the postsynaptic DA receptors.