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NMDA Receptor Antagonists Enhance 5-HT Receptormediated Behavior, Head-Twitch Response, in Mice

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The purpose of this study was to determine the behavioral interaction between glutamatergic and serotonergic receptors. In the present study, both the competitive (AP-5 and D-CPP) and the noncompetitive (MK-801, ketamine, dextrorphan and dextromethorphan) N-methyl-D-aspartate (NMDA) receptor antagonists markedly enhanced 5-HT(5-hydroxytryptamine)-induced selective serotonergic behavior, head-twitch response (HTR), in mice. These results suggest that the glutamatergic neurotransmission may modulate serotonergic function at the 5-HT receptor. The precise relationship between glutamatergic and serotonergic system is as yet undefined. However, these are the first data available regarding glutamatergic modulation of serotonergic function at the 5-HT receptor in intact mice, and the present results support the notion that the NMDA receptors may play important roles in the glutamatergic modulation of serotonergic function at the 5-HT receptor.