

# ACUTE & SUBCHRONIC NMDA RECEPTOR BLOCKADE ALTERS NICOTINE-EVOKED DOPAMINE RELEASE

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## ABSTRACT

Blockade of ionotropic glutamate receptors can induce changes in central dopamine and glutamate circuits, which model the symptoms of schizophrenia. Nicotine evokes dopamine release through activation of nicotinic acetylcholine receptors, and human research indicates that nicotine improves negative and cognitive symptoms of schizophrenia. The objective was to determine the effect of the glutamate receptor antagonist, ketamine, on the function of nicotinic receptors that mediate dopamine release. Ketamine did not have intrinsic activity to evoke dopamine release from rat striatal or prefrontal cortical slices. Acute NMDA receptor blockade augmented the effect of nicotine to evoke dopamine release. To model progression of schizophrenia, rats received injections of either a high or low dose of ketamine or vehicle for 30 days and then nicotine-evoked dopamine release was measured. Subchronic NMDA receptor blockade altered the effect of nicotine to evoke dopamine release. Overall, these data indicate that nicotinic receptor function is altered in this model of schizophrenia, and support a role for nicotinic receptors in schizophrenia treatment.