Public Abstract

First Name: Kelli
Middle Name: Renee
Last Name: Rodvelt
Degree: M. A.
Department: Psychological Sciences
Advisor's First Name: Dennis
Advisor's Last Name: Miller
Co-advisor's First Name:
Co-advisor's Last Name:
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Schizophrenia is a severe neuropsychiatric disorder that affects cognition and behavior, however, scientists do not fully understand the underlying mechanisms of the disorder. Scientists have developed preclinical methods to study behavioral and neurochemical changes underlying schizophrenia. Pharmacological animal models of schizophrenia, in which neurotransmitters are manipulated by drugs, were developed to investigate positive and negative symptoms and cognitive dysfunction associated with schizophrenia.

Acute and subchronic ionotropic glutamate receptor blockade, by ketamine, induces changes in central dopamine and glutamate circuits, which models positive and negative symptoms and cognitive dysfunction associated with schizophrenia in animals. Nicotine evokes dopamine release through activation of nicotinic acetylcholine receptors and temporarily improves negative symptoms and cognitive dysfunction associated with schizophrenia in animals. Taken together, this suggests a common underlying neurobiology between schizophrenia and nicotine addiction.

The purpose of these experiments was to investigate the role of nicotine in schizophrenia. In the present study, ketamine did not alter dopamine release in rat brain. In an acute model of schizophrenia, ketamine increased nicotine-evoked dopamine release in rat brain. In a subchronic model of schizophrenia, ketamine lowered the concentration of nicotine to evoke dopamine release in rat brain. Taken together, ketamine altered rat brain neurocircuitry which increased the sensitivity to nicotine. Overall, these data support a role for nicotinic receptors in schizophrenia treatment.

Beyond schizophrenia, our findings suggest that the integration of multiple neurotransmitter systems could contribute to underlying pathophysiology of disorders and investigating neurotransmitter systems comprehensively could be valuable for treatment research.