Impulsive Behavior is Influenced by Interactions Between Cholinergic and Dopaminergic Neurotransmitter Systems

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INTRODUCTION

Our lab is interested in examining relationships between different neurotransmitters in influencing behavior. Two important neurotransmitters are acetylcholine (ACh), which has a role in optimal attentional performance, and dopamine, which is involved in impulsive behavior.

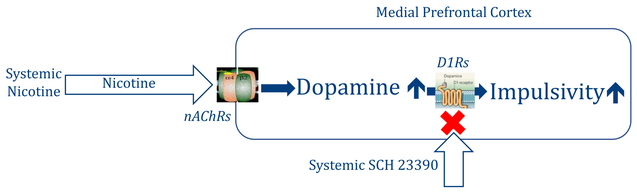
As an initial part of a project in our lab, we wanted to examine the previously reported relationship between ACh and dopamine in impulsive behavior. Dopamine neurons in the prefrontal cortex, which is an important brain region for both attention and impulsive behavior, have nicotinic subtypes of ACh receptors (nAChRs) on the presynaptic terminals. Release of ACh in the prefrontal cortex results in stimulation of dopamine neurons to release dopamine via binding of nAChRs by ACh. Dopamine then mediates impulsive behavior via binding of dopamine-1 receptors (D1Rs).

Adult Long-Evans rats of both sexes were trained to peak performance on the 5-Choice Serial Reaction Time Task (5-CSRTT), which assesses both attention and impulsive behavior. We then tested the effect of nicotine, a nAChR agonist, and SCH 23390, D1R antagonist, alone and together to better examine the relationship between ACh and dopamine on impulsive behavior, as well as attention.

PROJECT HYPOTHESES

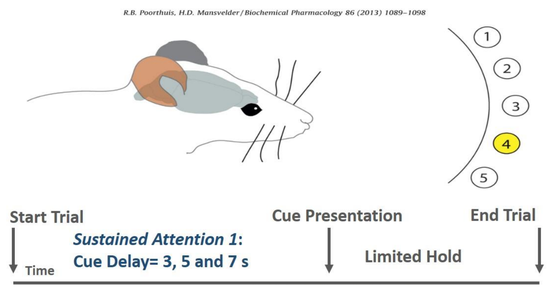
Examining the Effects of Cholinergic and Dopaminergic Neurotransmitter Systems on Impulsive Behavior

Nicotine will increase both attention and impulsive behavior in the 5-CSRTT.
SCH 23390 will decrease impulsive behavior but not affect attention.
Nicotine and SCH 23390 Combined will normalize the effect of both drugs on impulsive behavior.



EXPERIMENTAL DESIGN

5-Choice Serial Reaction Time Task (5-CSRTT) Rats were trained over 21 days (7 blocks of 3 days each) to monitor holes for a cue light and then to poke their nose in the hole where the cue light illuminated. The delay until the light illuminated (intertrial interval or ITI) varied within each testing session by 3, 5, or 7s.



Dependent measures:
% Accuracy (measures attention)
% Premature (measures impulsivity)
Changes in % accuracy and % premature over the initial 21 days of testing are shown in Figures 1 and 2, and as a result of drug testing in Figures 3 and 4.

Drug Trials Rats were given drug injections of nicotine, SCH 23390, or both I.P. after a baseline level of 5-CSRTT performance was attained. Nicotine was given 30 min and SCH 23390 20 min prior to testing based on the pharmacokinetics of the drugs. Saline vehicle (control) injections were given 20 min prior.

Drug	Dose (mg/kg)
Nicotine	0.5
SCH 23390	0.01
	0.02
Combination	
Nicotine + SCH 23390	0.5 + 0.01
	0.5 + 0.02

Drug Schedule:
Monday: No drug – testing only.
Tuesday: Drug
Wednesday: No drug – testing only.
Thursday: Vehicle
Friday: Drug

RESULTS

Percent accuracy prior to drug trials

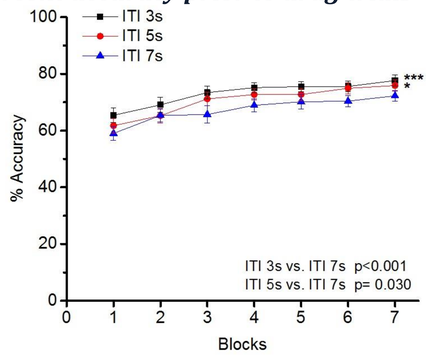


Figure 1. Percent accuracy was significantly higher at ITIs 3s and 5s compared to ITI 7s. This shows that it is harder to pay attention as the cue delay increases. Rats also improved their ability to pay attention as they learned the task.

Percent premature prior to drug trials

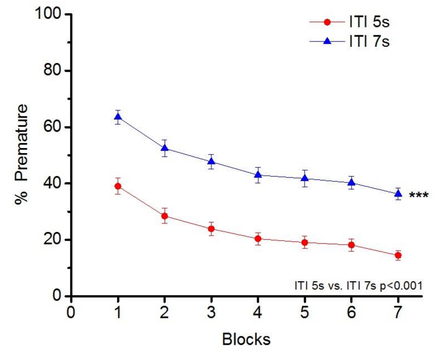


Figure 2. Percent premature responding was greater at ITI 7s than ITI 5s. This aligns with literature where the animals show greater impulsive behavior with increases in cue delay. Impulsivity decreased as rats learned the task.

Effect of drugs on percent accuracy

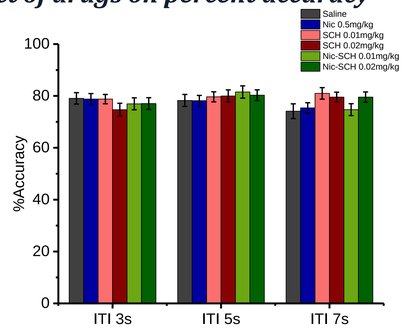


Figure 3. Nicotine and SCH 23390, alone and in combination, did not affect attention.

Effect of drugs on percent premature

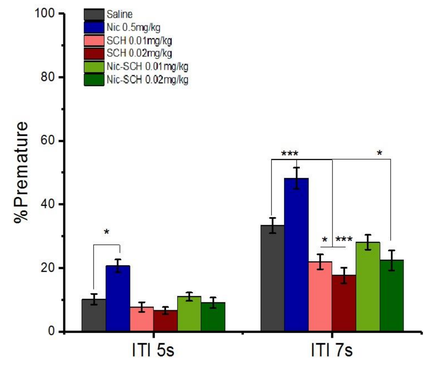


Figure 4. Premature responding increased at both ITIs when the rats received 0.5mg/kg of nicotine. Both doses of SCH 23390 decreased impulsive behavior at ITI 7s. Combinations of nicotine and SCH 23390 reduced premature responding caused by nicotine, but not to the level of premature responding seen from SCH 23390 alone.

DISCUSSION

We found that at baseline performance the ability to pay attention decreased and impulsive behavior increased as the delay until the cue (ITI) became longer, which inherently makes sense.

Nicotine increased impulsive behavior while SCH 23390 reduced impulsive behavior, which matched our hypotheses. Neither drug, at the doses given, affected attention. We predicted that nicotine would affect attention. One possibility is that the nicotine dose was too low to see an effect on attention.

When nicotine and SCH 23390 were combined, the effect of nicotine on impulsive behavior was reduced. This confirms that there is a relationship between ACh and dopamine in their effects on impulsive behavior. We will use these findings in future studies in which we examine the effects of environmental factors, such as changes in daily circadian rhythms, which are mediated by the cholinergic system, on impulsive behavior.

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