Modelling Nicotine Self-Administration Using Drinking-in-the-Dark

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Although cigarette smoking is a widely recognized problem in the United States, few animal models of nicotine self-administration exist. One aim of this study was to develop a new model of nicotine self-administration in animals. The Drinking in Dark (DID) model, in which ethanol access is given for two hours, three hours into the dark cycle, can be easily altered to investigate nicotine intake and withdrawal. We found that animals will readily consume around 6 mg/kg of nicotine per day, which is equivalent to smoking approximately 3-4 cigarettes. A second aim of the study was to test pharmacological manipulations in the model. Two areas of focus for pharmaceutical manipulations involve GABA and acetylcholine. On the fifth day of nicotine DID we administered baclofen, a $GABA_B$ receptor agonist, or mecamylamine, a nicotinic acetylcholine receptor (nAChR) antagonist, immediately prior to nicotine consumption. We found that baclofen, but not mecamylamine, reduced nicotine intake ($p < .05$). The final aim of the study will be to test for face validity of the model. A separate group of mice will be given access to nicotine or saccharin for 5 or 10 days using DID procedures. Face validity of the model will be tested using the elevated plus maze and by observing locomotor activity during spontaneous withdrawal, approximately 55 hours following the last DID presentation. Taken together, these studies suggest that nicotine DID is a valid model of voluntary nicotine intake that can be tested for smoking treatments, as well as the neurobiological underpinnings of repeated nicotine use.

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