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Effects of contingent and noncontingent nicotine on lever pressing for liquids and consumption in water-deprived rats

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ABSTRACT

Nicotine has been proposed to be a primary reinforcer and a reinforcement enhancer. To date, no studies have examined whether nicotine enhances consummatory behaviors or only operant responding (appetitive behaviors). Experiments were designed to test whether contingent and noncontingent nicotine enhance lever pressing for and consumption of fluids in water-deprived rats. Animals were water-deprived throughout all experiments. They were trained to press two levers under a variable interval (VI-20, 1–35 s). Their lever pressing and water consumption were measured after noncontingent subcutaneous (s.c.) injection of nicotine (1 mg/kg), and in 3 choice conditions (water and quinine solution (18 μg/ml); water and nicotine (32 μg/ml) solution; quinine (18 μg/ml) and nicotine (32 μg/ml) solutions) where nicotine was thus delivered contingently upon lever pressing. The effects of nicotine (1 mg/kg; s.c.) on the consumption of water in a time-limited free access (1 h) paradigm were assessed. Nicotine significantly increased lever pressing and the number of earned reinforcements on both levers in the two choice conditions and when administered s.c. compared to all groups that did not receive nicotine. However, under no condition did animals consume more fluids than baseline. Under the time-limited free access condition nicotine reduced water consumption. Although our findings do not support a reinforcing effect for nicotine, they are consistent with the incentive-amplification hypothesis. Its relevance for human smoking is yet unclear.

1. Introduction

It is widely believed that nicotine is a powerful primary reinforcer, and that these primary reinforcing properties are responsible for the persistence of tobacco smoking in humans (U.S. Department of Health and Human Services, 2010). This view has been supported by numerous self-administration studies (Corrigall and Coen, 1989; Donny et al., 1998). In recent years, however, nicotine self-administration appears to be less robust than previously reported, leading several researchers to conclude that nicotine is a weak primary reinforcer (e.g., Sorge et al., 2009).

In the same vein, recent studies have confirmed that visual stimuli paired with nicotine administration, traditionally conceptualized as "cue lights," are in fact more reinforcing than nicotine in this paradigm (Donny et al., 2003). Nicotine appears to have a "synergetic" effect when combined with the VS, such that responding for the VS increases dramatically when animals receive nicotine. Critically, nicotine produces similar increases in lever pressing for the VS when administered non-contingently in yoked animals (e.g. Caggiula et al., 2002; Donny et al., 2003) or injected by the investigator (Palmatier et al., 2007) as it does when administered contingent upon lever presses.

These recent developments led Caggiula et al. (2002) and Donny et al. (2003) to formulate a new hypothesis to explain how non-contingent nicotine increases responding for the VS in this paradigm. The "reinforcement enhancement" hypothesis postulates that nicotine enhances the reinforcing valence of other (non-pharmacological) reinforcers (for review, see Caggiula et al., 2009). According to the reinforcement enhancement hypothesis, nicotine perpetuates smoking by enhancing the reinforcing value of various reinforcements in the smoker's environment, including those involved in the smoking experience itself, such as the flavor and other sensory aspects of cigarette smoking.

As Donny et al. (2011) note, the reinforcement enhancement hypothesis does not specify, and findings to date do not clarify, the processes that might underlie the effects of nicotine on reinforced behavior. A critical relevant distinction, proposed already in the 1950 s, is between appetitive behaviors and consummatory ones. Several studies have suggested that the reinforcement enhancement effects of

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Table 1
Order of the experiments following the establishment of the initial baseline under VI-20 schedule of reinforcement. Abbreviations: Nicotine (Nic), Quinine (Qui), Free Access (FA). The number of sessions appears in parentheses.

	Time →								
Group A	Challenge1 (2)	Nic-Qui choice (10)	Challenge2 (2)	Qui-Water choice (6)	Nic-Water choice (6)	Baseline (6)	FA (5)		
Group B	Challenge1 (2)	Qui-Water choice (10)	Challenge2 (2)	Nic-Water choice (6)	Nic-Qui choice (6)	Baseline (6)	FA (5)		

quinpirole (a dopamine D_2 receptor agonist) pertain to operant responding, rather than consummatory behaviors. For example, Amato et al. (2006) reported that rats that were repeatedly administered with quinpirole progressively took less water from a free-access bottle and increased the rate of pressing on a water-associated lever. Moreover, even when the rats were given the choice between free access to highly palatable saccharine solutions and access to operant responding for tap water, quinpirole shifted the animals towards the operant responding.

To date, no studies have examined whether nicotine enhances consummatory behaviors or only operant responding for non-pharmacological reinforcers, as seems to be the case for other stimulants (the only findings of nicotine increasing consumption of other reinforcers were shown in relation to ethanol; e.g. Potthoff et al., 1983; Blomqvist et al., 1996; Lê et al. 2010; Bito-Onon et al., 2011). The present study aimed to examine the effects of nicotine on water-reinforced lever pressing in relation to the operant responding vs. consummatory distinction.

2. Materials and methods

2.1. Subjects

Twenty male Long-Evans rats weighing about 250 g (Charles River, St. Constant, QC) were housed in individual cages. Rats were maintained in an animal care facility on a 12 h reverse light-dark cycle (lights off at 9:30 a.m.). The rats were maintained on 22 h water deprivation, with *ad libitum* access to quinine-tainted water (18 μg/ml) in their home cages for 1 h/day, available 2 h after the daily self-administration session. All rats were treated in accordance with the guidelines of the Canadian Council on Animal Care and approval for all the experimental procedures was granted by the Concordia University Animal Research Ethics Committee.

2.2. Apparatus

Experiments were conducted in 5 identical operant conditioning chambers (Coulbourn Instruments, Allentown, PA, USA; 29.0 cm×29.0 cm×25.5 cm), placed in individual sound-attenuation cubicles. On each of the 2 sidewalls of each box there was a retractable lever (Coulbourn Instruments) located 9 cm above the grid floor, and a liquid receptacle able to contain 0.3 ml of liquid located about 5 cm above the floor. Responses on a lever resulted in a 6 s activation of an infusion pump (Coulbourn Instruments; 3.3 RPM) equipped with a 20 ml syringe that was connected to the liquid receptacle on same wall as the lever and delivered a 0.2 ml infusion of tap water or a nicotine or quinine solution. A cue-light located above the lever was turned on for the duration of the infusion.

2.3. Drugs and solutions

Quinine and nicotine were procured from Sigma, Canada. The dose of nicotine (32 μg/ml) was chosen since according to the dose-response curve established by Glick et al. (1996), this dose produced the highest rate of lever pressing. In a series of preliminary investigations (not reported here) we determined that 18 μg/ml quinine in the drinking water was mildly more aversive than the nicotine solution as indicated by a two-bottle preference tests in a different group of 20 rats. For subcutaneous (s.c.) administration of nicotine we choose the highest dose used by Dwoskin et al. (1999) in their open field study (1 mg/kg). The dose of s.c. quinine (0.54 mg/kg) reflected the nicotine/quinine ratio in the self-administration phase. Quinine was used for control injections in order to keep conditions as similar as possible to the choice phases (see below), during which the rats consumed the quinine solution, in order to enable statistical comparisons. Doses are expressed as the weight of the salt.