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Nicotine increases alcohol self-administration in non-dependent male smokers

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Abstract

Background: Alcohol and tobacco are commonly co-administered, yet little is known about the effects of acute nicotine administration on alcohol consumption in humans. This study sought to determine how nicotine delivered by tobacco smoke influences alcohol intake in humans using a double-blind placebo controlled repeated measures design.
Methods: During two randomized 120 min sessions 15 male occasional smokers smoked four nicotine-containing or four denicotinized cigarettes at 30 min intervals. Throughout the session, subjects could earn units of their preferred alcoholic beverage and glasses of water using a progressive-ratio (PR) task.
Results: Wilcoxon signed-rank tests indicated that nicotine increased alcohol self-administration in a significant proportion of participants ($P \leq 0.03$) without affecting water consumption ($P \geq 0.16$). A two-way ANOVA supported this observation further, and, compared to denicotinized cigarettes, the nicotine-containing cigarettes increased PR breakpoints for alcohol but not water, as reflected by a Cigarette × Beverage interaction ($P \leq 0.055$).
Conclusions: The present data suggest that acute nicotine administration increases alcohol consumption in at least a subset of smokers.

Keywords: Alcohol; Nicotine; Addiction; Self-administration; Polysubstance use; Progressive ratio

1. Introduction

The two most commonly abused substances in the general population, alcohol and nicotine, are frequently co-administered (e.g., Batel et al., 1995). The prevalence of tobacco smoking in alcoholics is thought to be as high as 90%, compared to less than 30% in the general population (e.g., Sobell et al., 1990; Romberger and Grant, 2004). Similarly, smokers are 50% more likely to drink regularly than adult non-smokers (Kozlowski and Ferrence, 1990). Some evidence suggests that these associations reflect an ability of ethanol and nicotine administration to increase motivation to obtain the other substance. In smokers, acute alcohol administration is consistently reported to increase cigarette self-administration (Griffiths et al., 1976; Mello et al., 1980; Keenan et al., 1990). In comparison, the converse association is less well understood. There are several reports that, in rodents, chronic or repeated nicotine administration increases alcohol consumption (Smith et al., 1999; Le et al., 2000, 2003; Clark et al., 2001; Soderpalm et al., 2000), but this effect has not been uniformly replicated, and decreased alcohol self-administration has also been reported (Sharpe and Samson, 2002). Similarly, acute nicotine administration has been reported to increase (Gauvin et al., 1993), decrease (Nadal et al., 1998), and have no effect on alcohol intake (Nadal and Samson, 1999). Such inconsistent findings may be related to differences in doses, administration regimens, or rodent strains (Le, 2002). The contribution of these factors to the co-administration of nicotine and alcohol in humans remains unknown; to our knowledge, the effect of nicotine on alcohol self-administration in humans has yet to be determined. In a previous investigation acute cigarette smoking was found to increase alcohol related responding in male social drinkers (Perkins et al., 2000). However, because this study did not have a placebo smoking

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condition it was not possible to determine the extent to which the findings resulted from a pharmacological effect of nicotine.

In the present study, we sought to determine how nicotine delivered by tobacco smoke influences alcohol administration in humans using a double-blind placebo controlled repeated measures procedure, in which cigarettes made of nicotine-containing or denicotinized tobacco were smoked throughout the course of a drinking session. Since nicotine withdrawal may affect alcohol craving and consumption in dependent smokers (Palfai et al., 2000; see also Cooney et al., 2003; Colby et al., 2004), the present protocol examined non-dependent occasional smokers to avoid this potential confound.

2. Methods

2.1. Participants

Fifteen non-dependent male 'occasional' smokers (80% Caucasian) between the ages of 18 and 30 (mean = 22.3 ± 1.8) were recruited from the community through advertisements placed in local community newspapers and on university websites. All were medically healthy, free from current or previous mental illness including past or present substance use disorders (including nicotine dependence) as determined by a semi-structured clinical interview using DSM-IV criteria (First et al., 1995), and all scored a 0 on the Fagerström test for nicotine dependence (Heatherton et al., 1991). None reported the use of illegal drugs in the 30 days prior to the study, none were daily users of tobacco and none had a history of social, occupational or legal problems involving alcohol as determined by the Michigan Alcoholism Screening test (Pokorny et al., 1972). All had reached the minimum age to legally consume alcohol and tobacco in Quebec Canada and all reported having smoked a minimum of four cigarettes throughout the course of a drinking session on at least one occasion during the preceding year without experiencing any adverse consequences. On average participants reported consuming cigarettes on 2.7 ± 1.6 days and alcohol on 2.3 ± 0.8 days per week. Average daily consumption on days when the substance was used was 5.4 ± 1.6 cigarettes per day and 5.9 ± 2.1 drinks per day. Participants were informed that the study involved smoking two different brands of tobacco but not that one of the sessions used denicotinized cigarettes. Following a description of the study, all participants provided written informed consent. The study was conducted in accordance with the Declaration of Helsinki and was approved by a McGill University Research Ethics Committee.

2.2. Cigarettes

Prior to the study participants were asked to identify the brand(s) of cigarettes that they smoked in order to ensure their unfamiliarity with the specific brands of tobacco used during the testing sessions. Participants were informed that on each test day that they would be required to smoke four cigarettes over a 2-h period and that on each test day that a different brand of tobacco would be used. All cigarettes contained 65 g of tobacco, and were prepared to appear identical. The 'denicotinized' cigarettes were prepared using *Quest 3* tobacco (Vector Tobacco Inc., USA), and provided maximum nicotine yield of 0.05 mg and a tar yield of 10 mg. The 'nicotine' containing cigarettes were prepared using *Player's Light* tobacco (Imperial Tobacco Limited, Montreal Canada) and they provided nicotine and tar yields of 1.2 and 12 mg, respectively. This tobacco was selected for its relatively high nicotine to tar ratio and its relatively similar average tar yields to the denicotinzed tobacco.

2.3. Alcoholic beverages

Prior to the study sessions, each participant identified a preferred alcoholic beverage. The beverage could consist of any 80-proof liquor with a non-alcoholic mixer; the same beverage was to be consumed on both days. Choice of beverage was restricted to 80-proof liquors due to the high variability in the alcohol contents of commercially available brands of beer, wines and coolers. Participants were informed that on each test day they would be required to consume a minimum of one standard drink containing 12 g of 80-proof alcohol (38 ml) and that the maximum dose of alcohol that could be consumed on any day was 72 g or the equivalent of six-full standard drinks.

2.4. Subjective state

Participants were administered visual analogue scales (VAS) at baseline and immediately following the completion of each cigarette on each test day. Items were rated on a ten cm line labelled with the integers 1–10 and anchored with the words "least" and "most". Items included in the VAS were 'high', 'stimulated', 'energetic', 'anxious', 'sedated', 'intoxicated', 'want alcohol', 'like cigarette', 'crave cigarette', and 'crave alcohol'. Similar scales have been widely used to collect information about subjective drug effects in humans (e.g., Fischman and Foltin, 1991) and this method of data collection has been demonstrated to have acceptable psychometric properties (Bond and Lader, 1974).

2.5. Design

The research protocol was comprised of two test sessions. Each was conducted between 12 pm and 4 pm in the afternoon, was a minimum of 3 and a maximum of 14 days apart, was double blind, and was given in counterbalanced randomized order. In one condition subjects were required to smoke four 'nicotine' cigarettes and in the second condition four 'placebo' cigarettes were smoked. In both conditions, cigarettes were smoked at 30 min intervals throughout the