

Brief Report

Methylphenidate Increases Choice of Cigarettes Over Money

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Abstract

Introduction: Stimulants increase cigarette smoking in the naturalistic environment and laboratory. The effects of methylphenidate on a 9-trial, discrete cigarette versus money (\$0.25) choice task were tested to elucidate the mechanisms underlying stimulant-induced increases in smoking.

Methods: Eleven participants who reported smoking 10–20 cigarettes/day completed the study. Four doses of methylphenidate (0, 10, 20, and 40 mg) were administered across 5 experimental sessions, with placebo administered twice. One hour following medication administration and at 30-min intervals thereafter, participants chose between smoking a cigarette and receiving US\$0.25. The primary behavioral outcome measure was number of cigarette choices.

Results: Methylphenidate increased the number of cigarette choices over money. Puffs per session and carbon monoxide levels increased significantly and caloric intake decreased significantly following methylphenidate administration relative to placebo.

Conclusions: The results of this study suggest that methylphenidate increases the relative reinforcing efficacy of cigarette smoking. Stimulant use may thus be an important consideration for individuals attempting to quit smoking.

Introduction

Cigarette smoking is a leading cause of preventable death in the United States (Adhikari, Kahende, Malarcher, Pechacek, & Tong, 2008). Approximately 24% of U.S. residents aged 12 years or older report current cigarette smoking, with certain state prevalence rates exceeding 30% (Substance Abuse and Mental

Health Services Administration [SAMHSA], 2008, 2009). Research examining factors that contribute to cigarette use can inform treatment and intervention efforts to reduce morbidity and mortality associated with cigarette smoking.

One known factor that increases the likelihood of cigarette smoking is the use of stimulant drugs. Nearly 75% of active cocaine users also report cigarette smoking (SAMHSA, 2009). Illicit use of prescription stimulants, particularly by young adults, also increases the likelihood of cigarette smoking (Darredeau, Barrett, Jardin, & Pihl, 2007; McCabe, Knight, Teter, & Wechsler, 2005; Teter, McCabe, Boyd, & Guthrie, 2003; Teter, McCabe, LaGrange, Cranford, & Boyd, 2006). Current nonmedical stimulant use was estimated at 2.1% in one sample of college students, similar to national prevalence rates of cocaine use (McCabe et al., 2005; SAMHSA, 2009). Moreover, students reporting nonmedical stimulant use were nearly three times more likely to report current cigarette smoking than students that did not report nonmedical stimulant use (McCabe et al., 2005).

A number of human laboratory-based experiments have explored the link between stimulant use and cigarette smoking (Cousins, Stamat, & de Wit, 2001; Henningfield & Griffiths, 1981; Rush et al., 2005; Schuster, Lucchesi, & Emley, 1979; Sigmon, Tidey, Badger, & Higgins, 2003; Stoops, Vansickel, Glaser, & Rush, 2008; Tidey, O'Neill, & Higgins, 2000; Vansickel, Stoops, Glaser, & Rush, 2007; Vansickel et al., 2009). The results of several of those studies demonstrate that experimental administration of stimulants like cocaine, D-amphetamine, and methylphenidate markedly increases *ad libitum* cigarette smoking (Cousins et al., 2001; Henningfield & Griffiths, 1981; Rush et al., 2005; Schuster et al., 1979). Stimulants possibly increase smoking due to enhanced levels of synaptic dopamine and synergistic interactions between nicotine and dopamine (Gerasimov et al., 2000; Stoops et al., 2008; Vansickel et al., 2007). This effect may result in stimulants increasing the reinforcing effects of smoking (Sigmon et al., 2003; Tidey et al., 2000).

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Several previous studies in our laboratory have shown that methylphenidate increases *ad libitum* smoking under controlled conditions (Rush et al., 2005; Stoops et al., 2008; Vansickel et al., 2007, 2009). The purpose of the present experiment was to further determine the mechanisms involved in methylphenidate-induced increases in cigarette smoking. To this end, a range of doses of methylphenidate (0, 10, 20, and 40 mg) was administered to adult cigarette smokers who were then allowed to self-administer cigarettes using a nine-trial, discrete cigarette versus money choice procedure. This procedure has been used previously and is sensitive to the reinforcing effects of cigarettes and money (Tidey et al., 2000).

Methods

Participants

Eleven adult smokers (six male and five female) completed this study, which is a sample size to similar to that of other within-subjects repeated measure experiments that detected significant effects of stimulants on smoking (e.g., Rush et al., 2005; Tidey et al., 2000; Vansickel et al., 2007). One additional subject was enrolled into the study but was lost to follow up prior to completing any sessions. Participants ranged in age from 21 to 35 years (mean \pm SD = 24 \pm 5). Participants reported smoking 10–20 cigarettes/day (mean \pm SD = 14 \pm 4) and consuming between 15 and 328 mg caffeine/day (mean \pm SD = 150 \pm 109). Participants had completed 11–18 years of education (mean \pm SD = 14 \pm 43). Other than having to report smoking 10–20 cigarettes/day to meet inclusion criteria, participants had to be in good physical and mental health to enroll in the protocol.

General Procedures

The Institutional Review Board of the University of Kentucky Medical Center approved the conduct of this study. Prior to enrollment, all participants had to provide sober and written informed consent to participate. Sobriety was assessed using a standard field test and breath sample that had to test negative for alcohol (e.g., 0.00% BAC; Alcosensor, Intoximeters, St. Louis, MO). Participants enrolled as outpatients at the Laboratory of Human Behavioral Pharmacology at the University of Kentucky Medical Center Monday through Friday for six sessions (one practice and five experimental).

With the exception of having to choose between cigarettes and money, sessions were conducted using methods similar to those reported previously (Rush et al., 2005; Vansickel et al., 2007). Briefly, participants arrived at the laboratory at approximately 08:00 a.m. Baseline testing and sobriety measures were completed between 08:00 and 09:00 a.m. At this time, a breath sample was assayed for carbon monoxide (CO; piCO Smokerlyzer; Bedfont, Medford, NJ). This sample had to be below 10 ppm for session to continue. Methylphenidate or placebo was administered at 09:00 a.m. Video recording of the session began at 10:00 a.m., when participants made their first choice between a cigarette of their preferred brand, cut to 50% of its tobacco-containing length, and money (US\$0.25). Participants made choices at 30-min intervals for the next 4 hr for a total of nine choices. Sessions were timed to capture the time course of the effects of methylphenidate (i.e., peak and return to baseline; Parasrampur et al., 2007). Participant-rated and cardiovascular measures were recorded at 10:00 a.m., 12:00 p.m., and 02:00 p.m.

At 02:00 p.m., after receiving their final choice, participants were paid and released. Participants earned \$40 per session, which was paid to them at the end of each session along with the amount of money they chose over cigarettes. Participants also earned a \$40 per session completion bonus that was paid to them at the end of the final experimental session.

Outcome Measures

Outcome measures for smoking included number of cigarette choices, number of puffs per session (summed from the puffs per cigarette), and peak CO level recorded from the 1, 3, and 5 (e.g., 10:00 a.m., 12:00 p.m., and 02:00 p.m.) hr postdose physiological measurements. As an additional measure of the effects of methylphenidate on consumptive behavior, caloric intake, and number of items consumed during the 4-hr smoking period were also recorded. The food that was available consisted of a variety of prepackaged items (e.g., frozen meals, crackers and cookies, caffeine-free soda, juices). At enrollment, participants were queried about items they preferred and whether they had any food allergies. The preferred items were available in all sessions individualized for each participant, while items that participants indicated an allergy to were unavailable. Participant-rated drug effect questionnaires included the Adjective Rating Scale (Oliveto et al., 1992), a Drug Effect Questionnaire that consisted of 20 items sensitive to the effects of stimulant drugs, which was developed in our laboratory (Rush, Stoops, Hays, Glaser, & Hays, 2003), and Cigarette and Food Rating Scales (Vansickel et al., 2007). Cardiovascular measures included heart rate and blood pressure.

Medication Administration

The drug conditions were placebo and methylphenidate (10, 20, and 40 mg). These doses were selected based on previous work showing that doses in this range reliably increase *ad libitum* cigarette smoking, function as discriminative stimuli, and produce positive subjective effects (Rush et al., 2005; Stoops, Lile, Glaser, & Rush, 2005; Vansickel et al., 2007). Each active dose of methylphenidate was tested once, while placebo was tested twice. Doses were administered orally in mixed order with the exception that the highest dose of methylphenidate was never administered during the first experimental session for safety reasons. Dose conditions were administered using double-blind conditions.

Data Analysis

Data were analyzed statistically as raw scores for all measures. Effects were considered significant for $p \leq .05$. Planned comparisons were used to compare data from each of the active dose conditions to the average from the placebo conditions. For the Adjective Rating Scale, Drug Effect Questionnaire, and cardiovascular measures, data collected after the first hour were considered uninterpretable because participants determined the amount they smoked (i.e., they smoked varying numbers of cigarettes with different nicotine contents). For this reason, only data from the first hour were used in the analyses for those measures.

Results

Smoking Measures

The intermediate and high dose of methylphenidate increased the number of cigarette choices over money relative to placebo

(absolute t_{10} values > 2.1 , $p \leq .05$; Figure 1). The high dose of methylphenidate increased the number of puffs per session relative to placebo (absolute $t_{10} = 3.0$, $p < .05$; Figure 1), while the low and high dose of methylphenidate increased peak CO (absolute t_{10} values > 2.2 , $p < .05$; Figure 1). The intermediate dose of methylphenidate produced increases in peak CO, but due to higher variability at this dose, the effect did not attain statistical significance.

Food Intake

The intermediate and high dose of methylphenidate decreased caloric intake and number of items consumed relative to placebo (absolute t_{10} values > 2.9 , $p < .05$; see Figure 1 for number of items consumed).

Participant-Rated Drug Effect Questionnaires

No significant differences were observed on any participant-rated drug effect questionnaires, with the exception that the intermediate dose of methylphenidate produced a small increase relative to placebo (i.e., an increase of 0.36 on a 0 to 4 scale) on

participant ratings of Performance Improved on the Drug Effect Questionnaire (absolute t_{10} value = 2.4, $p < .05$; data not shown).

Cardiovascular Measures

No significant differences were observed on heart rate, systolic pressure, or diastolic pressure.

Discussion

The finding that methylphenidate increased a number of smoking-related outcomes in the present experiment is concordant with results of previously published research (Cousins et al., 2001; Henningfield & Griffiths, 1981; Rush et al., 2005; Schuster et al., 1979; Sigmon et al., 2003; Stoops et al., 2008; Tidey et al., 2000; Vansickel et al., 2007, 2009). Importantly, the results of the present experiment indicate that methylphenidate increased choice of cigarettes relative to money, which extends previous findings with D-amphetamine (Sigmon et al., 2003; Tidey et al., 2000). In the more recent study, D-amphetamine increased cigarette-maintained responding on a progressive-ratio schedule in a subset of individuals while not altering responding

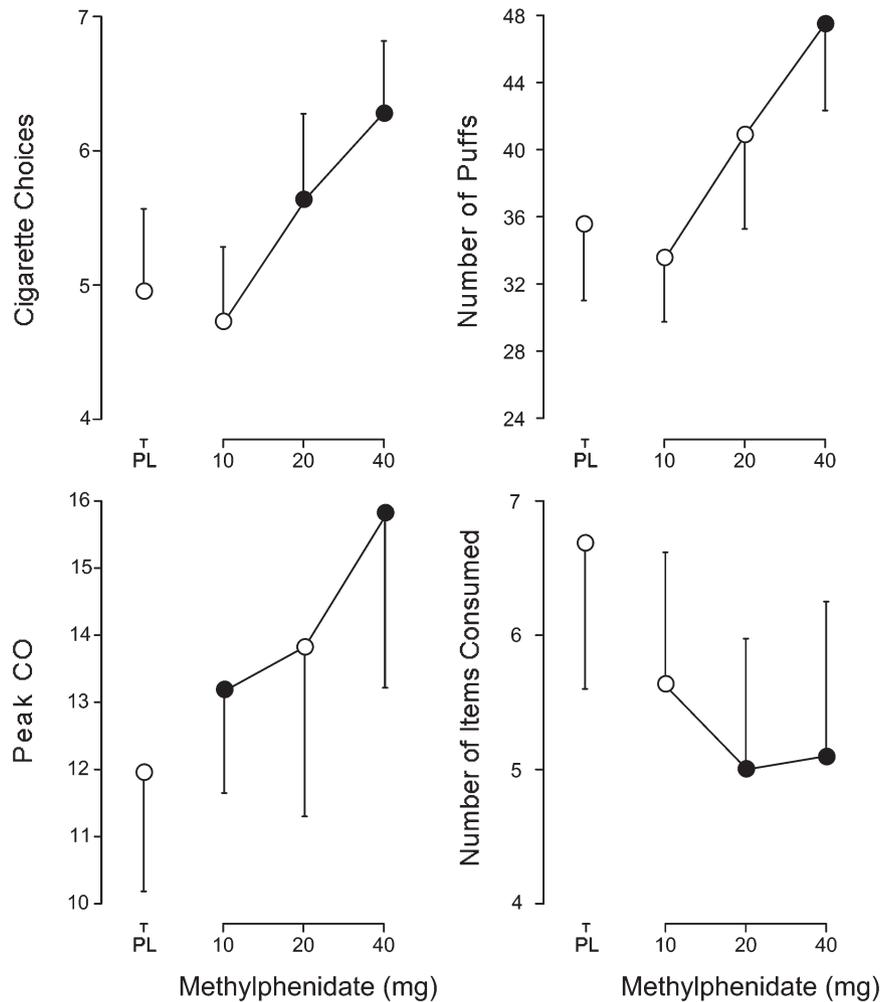


Figure 1. Dose effects of methylphenidate for number of cigarettes chosen (top left panel), number of puffs per session (top right panel), peak CO (bottom left panel), and number of food items consumed (bottom right panel). x-Axis: dose in milligrams. Data points above PL designate averaged values from the placebo sessions. Unidirectional brackets indicate 1 SEM. Filled symbols indicate values that are significantly different from placebo.

for money, also available on a progressive-ratio schedule albeit during separate sessions (Sigmon et al., 2003). In the earlier study, d-amphetamine increased choices for cigarettes in a cigarette versus money choice task very similar to the one described here (Tidey et al., 2000). Taken together, these data suggest that stimulant-induced increases in cigarette smoking are likely due to stimulants enhancing the reinforcing efficacy of cigarettes over money. This effect is probably mediated by the increase in synaptic dopamine levels produced by stimulant drugs, given that non dopaminergic drugs do not increase smoking (Stoops et al., 2008; Vansickel et al., 2007). Overall, increased smoking following stimulant administration is most likely driven by interactions of behavioral and pharmacological factors (i.e., smokers engage in increased drug-taking behavior due to increased synaptic dopamine levels following stimulant administration).

The results also indicate that methylphenidate decreased caloric intake during sessions, which is concordant with previous findings from our laboratory (Rush et al., 2005; Stoops et al., 2008; Vansickel et al., 2007, 2009). While subjects were not required to choose between food and money (i.e., the reinforcing effects of food were not being tested), these results further support the notion that methylphenidate-induced increases in intake appear specific to cigarette smoking and are not due to an increase in overall behavior or activity.

Several limitations to the present experiment should be acknowledged. First, we generally did not observe any significant effects of methylphenidate on participant-rated or physiological measures, which is discordant with the results of a number of previous studies (Rush et al., 2005; Stoops et al., 2005; Vansickel et al., 2007). This discrepancy is likely due to the limited data analysis possible based on the study design (i.e., only data gathered 1 hr after dosing were analyzed). Second, we only examined cigarette versus money choice using a single monetary value, US\$0.25, a value selected because it does not suppress cigarette choice behavior (Tidey et al., 2000). Perhaps different money values would have changed cigarette choice behavior (i.e., lower values resulting in increased cigarette choice and higher values resulting in decreased cigarette choice). Even though only a single money value was tested, the results of this study have implications for cigarette tax policy. That is, in the present study, half of a cigarette cost US\$0.25, making a full pack price US\$10.00. Subjects chose to smoke even though the pack price was substantially higher than what has been reported in the literature (e.g., Hyland, Higbee, Bauer, Giovino, & Cummings, 2004). It is likely that much higher money values would be needed to suppress cigarette choice experimentally and that higher cigarette taxes would also be needed to eliminate cigarette smoking. Third, we employed a discrete cigarette versus money choice procedure, without requiring an operant response to earn a choice. Requiring an operant response, either on a fixed- or progressive-ratio schedule, could have altered the reinforcing effects of cigarettes versus money. Fourth, although the increase in the number of cigarette choices was statistically significant, the absolute number was approximately 1.3 choices or 0.65 cigarettes, higher on average relative to placebo. While this increase may appear small in magnitude, given that some studies have demonstrated a dose-response relationship between cigarettes smoked per day and risk for serious disease, any increase in smoking could be clinically significant (e.g., Law, Morris, Watt, & Wald, 1997; Pope et al., 2009).

The results of the present experiment suggest that stimulants increase cigarette smoking through an increase in the reinforcing efficacy of cigarettes relative to money. By revealing the factors that contribute to smoking, like stimulant-induced increases in cigarette use, smoking intervention and prevention efforts can be improved. For example, a body of literature now exists which suggests that stimulant users are more likely to smoke. This link is probably driven by complex behavioral pharmacological interactions. Considering stimulant use when delivering smoking cessation treatment may be important, particularly to young adults who are likely to use these drugs.

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Declaration of Interests

None declared.

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