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The influence of smoking cigarettes on the high and desire for cocaine among active cocaine users

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ABSTRACT

The primary aim was to evaluate whether nicotine use alters the high or desire for cocaine among active cocaine users who concurrently smoke cigarettes. Participants answered the Fagerstrom Test for Nicotine Dependence (FTND), Nicotine-Stimulant Interaction Questionnaire (NSIQ), and Multiple Drug Use Questionnaire (MDUQ). These questionnaires employ subject recall of participants' drug use habits. The participants that smoked (N = 163/188) were primarily African American males who were 45.0 ± 0.5 (mean ± S.E.M.) years of age, and used cocaine for 17.9 ± 0.6 years and 19.8 ± 0.6 days out of the last 30. These individuals smoked 14.0 ± 0.8 cigarettes/day (CPD), scored 4.6 ± 0.2 (on a scale of 0–10) on the FTND, and smoked cigarettes for 23.5 ± 0.7 years. Two questions from the MDUQ, which evaluates the interaction between cocaine and nicotine, (−5: reduces effect, 0: no change, +5: increases effect) included "Does nicotine affect the high that you experience from cocaine?" and "Does nicotine affect your desire for cocaine?", and the scores were 1.3 ± 0.2 and 0.8 ± 0.2, respectively. The NSIQ also evaluated interactive effects of nicotine and cocaine, on a scale of 0 to 100 (0: not at all, 100: most ever). Smokers responded most strongly that using cocaine increased both the urge to smoke and cigarette craving. Additional analyses were performed by separating participants into HighCPD vs. LowCPD groups via median split. The HighCPD group smoked 22.7 ± 1.1 CPD while the LowCPD group smoked 6.4 ± 0.3 CPD [$F(1,161) = 228.4$, $p < 0.0001$], and the HighCPD group had a mean FTND score twice that of the LowCPD group. Significant differences emerged between the two groups on multiple items of the NSIQ, but not the MDUQ. The subjective ratings of high and desire for cocaine, and several subjective effects produced by cocaine, were modestly altered by cigarette smoking. Taken together, these data suggest that cigarette smoking may augment the craving and high produced by cocaine.

1. Introduction

It is well documented that abusers of illicit drugs such as cocaine often use other drugs simultaneously, including alcohol, marijuana, and specific to this report, nicotine (Higgins et al., 1991; Burling and Ziff, 1988; Burling et al., 1991; Miller et al., 1989). In 2011, over 56 million Americans over the age of 12 smoked cigarettes, while 1.4 million Americans over 12 used cocaine (Substance Abuse and Mental Health Services Administration, 2011). Individuals who use cocaine are also more likely to smoke cigarettes than people who do not use drugs (Henningfield et al., 1990). In particular, cocaine users are roughly three to four times more likely than their non-drug-abusing counterparts to smoke cigarettes (Budney et al., 1993; Gorelick et al., 1997; Patkar et al., 2002; Kalman et al., 2005; Weinberger and Sofuoglu, 2009). In addition, several researchers have observed that stimulant use can also lead to increased consumption of nicotine/cigarettes (Roll et al., 1997; Sigmon et al., 2003; Wooters et al., 2008).

Several researchers have also investigated the ability of nicotine to substitute for cocaine (and vice versa) using animal models of drug discrimination, but with varying results. In two studies with monkeys, nicotine failed to fully substitute for cocaine. In the first, injections of nicotine (0.125–16 mg/kg, intramuscular) produced inconsistent responding for cocaine (0.25 mg/kg, i.v.) in Rhesus monkeys; at the highest dose of nicotine, one monkey responded on the cocaine-appropriate lever in more than 90% of responses, while at this dose, the other monkey only responded on the cocaine-appropriate lever in 40% of responses (de la Garza and Johanson, 1983). In contrast, a later study reported that cocaine (0.01–1 mg/kg, i.v.) had no effect on responding for nicotine (0.1 mg/kg, i.v.) in squirrel monkeys (Takada et al., 1988). In a newer report, more complex results were observed. Nicotine (0.032–0.56 mg/kg, i.v.) mostly failed to substitute for cocaine (0.4 mg/kg, i.m.), but nicotine pretreatment (0.32 mg/kg, i.m.) increased cocaine discrimination in 2 out of 3 monkeys (Mello and Newman, 2011). In another report (Gould et al., 2011), nicotine only partially substituted for cocaine (0.01–0.3 mg/kg, i.v.). The mutual

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substitution of nicotine and cocaine has also been investigated in Sprague–Dawley rats. In one study, nicotine (0.03–0.56 mg/kg) fully substituted for cocaine, yet cocaine (1–17 mg/kg) failed to fully substitute for nicotine (Desai et al., 1999). In addition, the authors had previously reported, under otherwise identical experimental conditions, that nicotine (0.03–0.56 mg/kg) fully substituted for cocaine, yet cocaine (1–17 mg/kg) failed to fully substitute for nicotine, a phenomenon dubbed "asymmetrical substitution" by the author (Desai et al., 1999).

Studies involving self-administration paradigms have also been conducted in non-human primates and rodents. First, a 9-day regimen of nicotine exposure (0.6 mg/kg, s.c.) facilitated the acquisition of cocaine self-administration (0.25 mg/kg, i.v.) in Sprague–Dawley rats (Horger et al., 1992). Additional data have been reported in Rhesus monkeys. In one study, (Gould et al., 2011) nicotine (0.01–0.1 mg/kg) was not self-administered in monkeys previously trained on cocaine (0.017–0.1 mg/kg/injection). In the other study (Mello and Newman, 2011), nicotine (0.001, 0.0032, and 0.01 mg/kg, i.v.) increased self-administration of the combination of cocaine and nicotine at low doses of cocaine.

Clinical data on the effects of nicotine on cocaine use have also provided inconsistent results. In one of the first studies on this topic, cocaine-dependent smokers self-reported using more cocaine in the past 30 days and more days per week, using more grams per week, and spending more money on cocaine on a weekly basis than cocaine-dependent non-smokers (Roll et al., 1996). More recent reports have investigated the subjective and/or reinforcing effects of nicotine and cocaine. In one report, acute exposure to transdermal nicotine patches (22 mg) enhanced cue-induced craving for cocaine without affecting physiological measures such as skin temperature and conductance (Reid et al., 1998). A subsequent report investigated the subjective and physiological responses of both nicotine (0.75, 1.5, and 3.0 mg/70 kg, i.v.) and cocaine (10, 20, and 40 mg/70 kg, i.v.) in cocaine-dependent cigarette smokers (Jones et al., 1999). Nicotine and cocaine produced similar subjective responses (e.g. "good effects", "like drug", "high", etc.) although the magnitude of these responses tended to be greater for nicotine than cocaine. Physiological measures such as heart rate, diastolic and systolic blood pressure, and skin temperature were similar for both nicotine and cocaine as well. In another report, transdermal nicotine (14 mg) attenuated subjective responses to cocaine (0.9 mg/kg, intranasal), including "stimulated" and "high" without altering heart rate, skin temperature, or blood pressure (Kouri et al., 2001). On the contrary, chronic nicotine maintenance (21 mg/day for 14–25 days, transdermal) did not alter subjective responses to cocaine (15 and 30 mg/70 kg, i.v.), including "good effects", "like drug", and "high" (Sobel et al., 2004). Last, a report investigated the hypothesis that nicotine substitutes for cocaine in cocaine-dependent participants, and that upon successful treatment for cocaine dependence, increases in aspects of smoking would be observed (Patkar et al., 2006). The study revealed no differences in cigarettes smoked per day or FTND scores.

Neurochemically, both nicotine and cocaine alter dopaminergic activity in brain, which may account for their common subjective and physiological effects (Koe, 1976; Ritz et al., 1987; Bergman et al., 1989; Imperato et al., 1986; Mereu et al., 1987; Corrigall, 1991). Specifically, preclinical work in rodents and nonhuman primates has shown that both nicotine and cocaine increase dopaminergic activity in the brain (Bergman et al., 1989; Di Chiara and Imperato, 1988) and increase the release of dopamine in the nucleus accumbens (Zernig et al., 1997). It has been suggested that when present simultaneously, there may be an additive dopaminergic effect (Budney et al., 1993). If true, then it is logical that nicotine may augment subjective responses to cocaine.

The purpose of this study was to further investigate the link between concurrent nicotine and cocaine use by attempting to determine whether cigarette smoking influences the subjective response to cocaine in non-treatment seeking volunteers.

2. Experimental methods

2.1. Participants

The current study includes data obtained between February 2010 and May 2011 as part of the "Stimulant Addiction Research Program" at the Baylor College of Medicine (BCM) and Michael E. DeBakey VA Medical Center (MEDVAMC). Participants were recruited from the Houston metropolitan area through newspaper and radio advertisements. All participants completed an initial telephone screen in order to assess basic eligibility. Candidates were then invited to complete an in-person assessment at the Research Commons of the MEDVAMC. During the in-person interview, candidates received an explanation of the study purpose and requirements and were allowed to review, inquire about, and sign the informed consent form. At the time of the assessment, all individuals were participating in a preliminary screening interview for possible enrollment into one of several inpatient, non-treatment seeking phase I clinical trial studies. These studies were sponsored by the National Institute on Drug Abuse, and approved by the Institutional Review Board of BCM and the Research and Development Committee of the MEDVAMC. All volunteers provided consent after being fully informed about potential risks of study participation. The participants were compensated with a $40 gift card for completing the in-person screen.

For the current report, participants met the following inclusion/exclusion criteria: (a) met DSM-IV criteria for cocaine dependence, (b) were 18–65 years of age, and (c) were not seeking treatment for cocaine use. Participants were excluded if they met any of the following exclusion criteria: (a) were dependent on any drugs other than cocaine or nicotine or (b) met DSM-IV criteria for any neuropsychiatric disorder other than major depressive disorder, mania, or PTSD.

2.2. Drug use

Drug use was assessed with a 14-item, self-report questionnaire with frequency assessed in terms of date of last use, days used in the past 30, years of use, and route of administration. In addition to cocaine, substance use frequency was also assessed for alcohol, methamphetamine, opiates, marijuana, and nicotine. Recent illicit drug use was assessed via qualitative urine toxicology (testing for cocaine metabolites, amphetamine, methamphetamine, marijuana, and opiates). Also, recent nicotine use was confirmed via measurement of breath carbon monoxide and recent alcohol use was assessed via breathalyzer.

2.3. Multiple Drug Use Questionnaire (MDUQ)

The MDUQ (see Table 2) is an internally created questionnaire developed to assess the interaction between nicotine and cocaine among individuals who simultaneously use both. When completing the questionnaires, individuals were advised to recall and estimate their subjective experiences to both nicotine and cocaine. The first section investigates the quantity of nicotine used and if and when nicotine is used concurrently with cocaine. The second section assesses how much nicotine affects the high and desire for cocaine that individuals experience while smoking cigarettes ($N = 161–163$ for these questions). Responses may vary on the first section, but the second section uses a scale of -5 (reduces effect) to 0 (no change) to $+5$ (increases effect) for both questions. A score of -5 indicates the maximum negative effect, whereas a score of $+5$ indicates the maximum positive effect.

2.4. Nicotine-Stimulant Interaction Questionnaire (NSIQ)

The NSIQ (Table 2) is an internally created 11-item questionnaire that assesses the subjective responses to the cocaine use of individuals. When completing the questionnaire, individuals were advised