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A tale of two stimulants: mentholated cigarettes may play a role in cocaine, but not methamphetamine, dependence

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Abstract

Background—Research suggests that mentholated cigarettes may play a role in cocaine dependence. The purpose of the present study was to expand upon the research on mentholated cigarettes and cocaine dependence and to evaluate the role of mentholated cigarettes in methamphetamine dependence.

Methods—Secondary analysis of a multisite, randomized trial evaluating the impact of smoking-cessation treatment in stimulant-dependent outpatients (N=538). Participants' reasons for concurrent use of cigarettes and illicit stimulants were assessed via self-report. Stimulant-abstinence was measured by self-report and urine drug screens. Smoking cessation was assessed via self-report and carbon monoxide levels.

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Contributors

Dr. Winhusen conceptualized the research hypotheses, contributed to the analysis and interpretation of the data, and led the drafting of the manuscript. Mr. Lewis conducted analyses and critically reviewed the manuscript. Dr. Adinoff, Dr. Brigham, Dr. Gardin, Dr. Sonne, Mr. Theobald, and Dr. Ghitza contributed to the interpretation of the findings and critically revised the manuscript for important intellectual content. All authors have approved the final manuscript.

Conflict of Interest

The authors have no potential conflicts of interest to report.

Results—Of the 301 cocaine-dependent participants, 201 (67%) were menthol and 100 (33%) were non-menthol cigarette smokers. Cocaine-dependent participants who smoked menthol, compared to non-menthol, cigarettes were significantly more likely to report that cigarettes prolong their cocaine high ($X^2(1)=16.3$, p<.0001, OR=3.58 [95% CI: 1.88–6.79]) and were less likely to be stimulant abstinent during active treatment (W=3.6, p<0.001, d=.39 [95% CI: 0.16–0.62]), at 3-month follow-up ($X^2(1)=14.4$ p<0.001, OR=.32 [95% CI: 0.17–0.58]), and at 6-month follow-up ($X^2(1)=4.6$, p=0.03, OR=.53 [95% CI: 0.29–0.95]). No parallel differences were found between menthol and non-menthol methamphetamine-dependent smokers. The prevalence of Caucasian menthol smokers was significantly greater in the cocaine-dependent participants (37.2%) than in the methamphetamine-dependent participants (17.61%), ($X^2(1)=14.4$ p<.001, OR=2.77 [95% CI:1.62–4.73]). Smoking cessation was not significantly associated with cigarette type for either cocaine- or methamphetamine-dependent participants.

Conclusions—The present results suggest that mentholated cigarettes play a role in cocaine, but not methamphetamine, dependence.

Keywords

menthol; cigarettes; cocaine dependence; methamphetamine dependence

1. INTRODUCTION

In 2009, the Family Smoking Prevention and Tobacco Control Act granted the Food and Drug Administration (FDA) regulatory power over particular aspects of tobacco products, including flavor additives (Family Smoking Prevention and Tobacco Control Act, 2009). Since that time, the FDA has banned flavored cigarettes, with the exception of mentholated cigarettes, and commissioned an advisory committee to report on the impact that mentholated cigarettes have on public health (Benowitz and Samet, 2011). The report from the advisory committee noted that, while there is not conclusive evidence to suggest that menthol, relative to non-menthol, cigarette smokers have worse disease outcomes, there is evidence that mentholated cigarettes lead to more smoking initiation and greater difficulty with smoking cessation and, thus, public health would benefit from the elimination of mentholated cigarettes (Benowitz and Samet, 2011). However, there has been reluctance to ban menthol cigarettes based on concern that such a ban would lead to a black market for menthol cigarettes (Carter, 2013). Additional data on the potential impact of mentholated cigarettes on public health would be helpful in weighing the potential costs and benefits of banning them.

A potential negative impact of mentholated cigarettes that has received minimal attention is their potential role in cocaine dependence. Cocaine dependence represents a significant problem as evidenced by the sheer number of lives affected, its associated medical and legal consequences, and the difficulty finding effective treatments (Winhusen et al., 2007). The scope of the cocaine problem is largely attributed to the advent of crack, an inexpensive, smokable and, thus, particularly addictive form of cocaine, in the mid-1980s. In 2010, over one million people in the United States were abusing or dependent on cocaine (Substance Abuse and Mental Health Services Administration (SAMHSA), 2011). Because psychosocial interventions are associated with high relapse rates, an impressive amount of resources have been devoted to finding pharmacological treatments that could be used in conjunction with psychosocial treatments; yet there still is no widely used, safe and effective treatment for cocaine dependence (Kuehn, 2009). A link between cigarette smoking and cocaine abuse has been established in both clinical and laboratory studies. The rate of smoking in cocaine abusers is 75–80% (Budney et al., 1993; Sees and Clark, 1993; Gorelick et al., 1997) and smoking cigarettes is associated with more severe cocaine dependence,

including more frequent cocaine use, a greater likelihood of injecting or smoking cocaine, and more severe employment and legal difficulties (Budney et al., 1993; Roll et al., 1997). Human laboratory studies have found that cocaine administration increases the rate of cigarette smoking (Nemeth-Coslett et al., 1986; Roll et al., 1996), and that mecamylamine, a nicotine antagonist, reduces cue-induced cocaine craving (Reid et al., 1999) while nicotine increases it (Reid et al., 1998).

Menthol has been shown to enhance transdermal and transbuccal absorption of other drugs (Ahijevycht and Garrett, 2004). It has been posited that, when inhaled, menthol may increase the permeability of drugs in the lungs as well, thereby increasing the pulmonary absorption of constituents found in smoke (Ahijevycht and Garrett, 2004; Clark et al., 1996). If used together with other substances of abuse, menthol may enhance the reinforcing effects of other substances by affecting the calcium conductance of cells involved in drug reinforcement (Clark et al., 1996). Research suggests that the association between cigarette and cocaine use may be more pronounced for patients who smoke mentholated cigarettes. Specifically, Sees and Clark interviewed cocaine-dependent patients about their cigarette and cocaine use to better understand why these behaviors co-occur at such high rates (1993). In the course of these interviews, participants noted that mentholated cigarettes prolong the cocaine high, allow them to smoke crack for longer periods due to the cooling effects of menthol, and even produce feelings similar to the effects of cocaine in the absence of cocaine use (Sees and Clark, 1993). Consistent with this report, a small study by Wiseman and McMillan found that cocaine-dependent participants preferring mentholated cigarettes cited the ability of menthol to make the cocaine high last longer and as a substitute for cocaine among the reasons for their preference (1998). Wiseman and McMillan (1998) hypothesized that irritants in menthol cigarettes may increase lung permeability increasing exposure to smoked cocaine. If menthol increases the subjective effects of cocaine then one might expect greater dependence severity, as indicated by more difficulty abstaining from cocaine, in cocaine-dependent patients using menthol, relative to non-menthol, cigarettes.

A recent multi-site trial conducted by the National Institute on Drug Abuse (NIDA) National Drug Abuse Treatment Clinical Trials Network (CTN) evaluated the impact of concurrent substance use disorder (SUD) and nicotine dependence treatment for cocaine and/or methamphetamine-dependent patients who were also nicotine dependent. The present study utilized this dataset to explore the potential role of mentholated cigarettes in cocaine dependence. Specific aims included evaluating participants' reasons for using cocaine and cigarettes together, the relative level of cocaine dependence severity, and success in achieving smoking cessation, all as a function of cigarette type (i.e., menthol vs. non-menthol). It was predicted that menthol, relative to non-menthol, cocaine-dependent cigarette smokers would be more likely to report that cigarettes prolong the cocaine high, and would be less likely to be illicit-stimulant abstinent and to achieve smoking cessation. Finally, while smoking rates are estimated to be 87% or higher in methamphetamine abusers (Grant et al., 2008; Weinberger and Sofuoglu, 2009), past research has not evaluated the potential role of mentholated cigarettes in methamphetamine; completing an initial evaluation of a potential relationship was an aim of the present study.

2. METHODS

2.1 Study Design

Details of the clinical trial are provided elsewhere (Winhusen et al., 2012a; Winhusen et al., in press). Briefly, the study was a 10-week, two-group, randomized trial to evaluate the impact of providing smoking cessation treatment (SCT) with SUD treatment as usual (TAU), compared to TAU alone, in smokers who are in outpatient treatment for cocaine or methamphetamine dependence. Eligible participants were randomized to TAU or TAU

+SCT in a 1:1 ratio. Follow-up visits were completed at 3 and 6 months following study day 20, which was the target smoking-quit date for the TAU+SCT participants. The trial was completed at 12 SUD outpatient treatment programs that did not provide smoking-cessation treatment as part of their standard treatment. During the 10-week treatment phase, participants were scheduled to attend two research visits per week for efficacy and safety assessments. Participants randomized to TAU participated in treatment as typically provided by the study site, which consisted of at least one non-nicotine SUD treatment session per week during the 10-week treatment phase.

Participants randomized to the TAU+SCT arm received TAU and SCT consisting of extended-release (XL) bupropion 300 mg/day, nicotine inhaler, individual 10 minute smoking-cessation counseling weekly for 10 weeks, and prize-based contingency management for smoking abstinence (Carbon Monoxide (CO)< 4ppm) during the post-quit phase. The CO cut-off of < 4 ppm was based on research findings that the use of 2–3 ppm produces the most accurate identification of smoking abstinence whereas 8–10 ppm, which has been traditionally used to verify abstinence, may occasionally result in smokers falsely being classified as abstinent (Javors et al., 2005; Cropsey et al., 2006).

2.2 Participants

The main inclusion criteria were: being at least 18 years old, meeting DSM-IV-TR criteria for cocaine- and/or methamphetamine-dependence, smoking at least 7 cigarettes daily and a CO level ≥ 8 ppm, being enrolled in outpatient SUD treatment, interested in quitting smoking, and being in good physical health as determined by medical history, vital signs, and electrocardiogram. Exclusion criteria included a medical or psychiatric condition potentially making study participation unsafe, current treatment for nicotine dependence; for women, pregnancy, breastfeeding, or unwillingness to use adequate birth control.

The present study sought to replicate and expand upon prior reports of a connection between menthol cigarette and cocaine use while doing an initial evaluation of a potential relationship between menthol cigarettes and methamphetamine use. Thus the participants included in the present analyses met criteria for either cocaine-dependence (n=301) or methamphetamine-dependence (n=209) while the participants meeting criteria for both cocaine and methamphetamine-dependence (n=27) were excluded.

2.3 Measures

Participants were coded as menthol or non-menthol cigarette smokers based on the Smoking History Survey, which is a modified version of the Mayo Nicotine Dependence Center Patient Questionnaire, administered by a research assistant at baseline. Reasons for using cigarettes with cocaine/methamphetamine were assessed via a self-report questionnaire created for the trial in which participants selected all of their reasons for using the substances together. The choices included: "Cigarette smoking helps the high from crack/cocaine or methamphetamine to last longer," "cigarette smoking is just a habit – no particular reason for using cigarettes with crack/cocaine or methamphetamine, " " cigarette smoking helps to feel more relaxed/calm, " "smoking cigarettes slows down crack/cocaine/methamphetamine use so that the crack/cocaine/methamphetamine lasts longer, " "everyone else is smoking cigarettes and I want to be social, " and "specify other. " Only 21 participants (3.9% of the sample) used the "specify other" option with the most common response (provided by 6 participants) being that the use of cocaine/methamphetamine increases craving for cigarettes. The pre-specified choices were the measures of interest.

Abstinence from cocaine/methamphetamine was defined by stimulant-negative urine drug screens (UDS) and self-report of no stimulant use at each research visit. A rapid UDS

system that screened for drugs of abuse including cocaine, methamphetamine, amphetamine, opioids, benzodiazepines, and marijuana was used to analyze the urine samples (Branan Medical Corporation). To avoid falsification, urine samples were collected using temperature monitoring and the validity of urine samples was checked with the use of a commercially available adulterant test. Self-report of substance use was assessed using the Timeline Follow-back (TLFB) method (Sobell and Sobell, 1992; Fals-Stewart et al., 2000), which is widely employed and well-validated. Achievement of smoking cessation was defined as achieving smoking-point prevalence abstinence (PPA) during the final treatment week (week 10). PPA is a standard measure and is defined as self-report of not smoking in the previous seven days, confirmed by a CO level <8 ppm (Hurt et al., 2003). In accordance with National Institutes of Health policy, participants self-reported their race and ethnicity; reporting was based on the race/ethnicity classifications used in the 2000 United States Census.

2.4 Data Analysis

All analyses were completed on the intent-to-treat (ITT) sample using SAS, Version 9.1.3 (SAS Institute, Inc.). Statistical tests were conducted at a 5% Type I error rate (two-sided) for all measures. It has been recommended that effect sizes be provided rather than using the Bonferroni procedure to adjust for multiple-comparisons (Nakagawa, 2004) thus effect sizes (i.e., Cohen's d (Cohen, 1988) or odds ratio) were calculated for each statistically significant effect.

Analyses were completed separately for the cocaine-dependent (n=301) and methamphetamine-dependent (n=209) participants. Initially, the significance of cigarette type (i.e., menthol vs. non-menthol) was tested using a simple between-group comparison consisting of either a Pearson Chi Square or Fisher's exact for each binary measure, and either a Wilcoxon Rank Sum or a Student’s t for each numeric variable. To ensure that any observed effect was not due to significant baseline differences between menthol and non-menthol smokers (see Table 1), these baseline differences were included in regression analyses of outcome variables.

Regressions with binary response variables used either logistic models or logistic mixed models, and the remaining regressions used either ordinary least squares or ordinary mixed models. For all regressions, treatment effects (e.g., TAU vs. TAU+SCT) could be selected for inclusion in the model by corrected Akaike Information Criteria (AICC). Whenever the results of these analyses suggested a significant effect, the regression results were used in place of the simple comparison.

3. RESULTS

3.1 Participants

Demographic and baseline characteristics are provided in Table 1. Of the 301 cocaine-dependent participants, 201 (67%) were menthol and 100 (33%) were non-menthol cigarette smokers. Of the 209 methamphetamine-dependent participants only 33 (16%) were menthol cigarette smokers. The cocaine-dependent menthol and non-menthol cigarette smokers differed significantly on race and ethnicity, which is consistent with the greater prevalence of menthol smokers in African Americans (Giovino et al., 2004; Allen and Unger, 2007). As noted in section “2.4 Data Analysis,” analyses controlled for the effect of race and ethnicity in cases in which they were related to the outcome of interest. The methamphetamine-dependent menthol and non-menthol cigarette smokers differed significantly on age and number of smoking years, which are significantly correlated. As noted in section “2.4 Data

Analysis," analyses controlled for the effect of smoking years/age and ethnicity in cases in which they were related to the outcome of interest.

3.2 Reasons for concurrent use of cigarettes and cocaine/methamphetamine as a function of cigarette type

Analyses of the cocaine-dependent participants revealed two significant differences between menthol and non-menthol cigarette smokers on reasons for using cigarettes with cocaine. As can be seen in Table 2, menthol, relative to non-menthol, smokers were significantly more likely to report that cigarettes help their cocaine high to last longer ($X^2(1)=16.3$, $p<.0001$, OR=3.58 [95% CI: 1.88–6.79]) while non-menthol smokers were more likely to report that their use of cigarettes with cocaine was just a habit ($X^2(1)=5.1$, p=.025, OR=0.56 [95% CI: 0.34–0.93])). To evaluate whether the ability of menthol cigarettes to prolong the cocaine high is dependent on cocaine being smoked, the analyses were repeated with participants using cocaine via the smoked route (n=192) and those using cocaine through either the nasal or IV route (n=102). As can be seen in Table 2, menthol, relative to non-menthol, smokers were significantly more likely to report that cigarettes helped their cocaine high to last longer regardless of cocaine administration route and, thus, the potential impact of mentholated cigarettes is not entirely dependent on cocaine being smoked. Analyses of the methamphetamine-dependent participants revealed no significant differences between menthol and non-menthol cigarette smokers for reasons for using cigarettes with methamphetamine (Table 2).

3.3 Cocaine/methamphetamine abstinence as a function of cigarette type

Figure 1 displays cocaine/methamphetamine abstinence as a function of cigarette type and stimulant-dependence diagnosis. Results of analyses comparing cocaine-dependent menthol and non-menthol cigarette smokers revealed that menthol smokers were significantly less likely to be abstinent for illicit stimulants during active treatment (W=3.6, p<0.001, d=.39 [95% CI: 0.16–0.62]), at 3-month follow-up ($X^2(1)=14.4$ p<0.001, OR=.32 [95% CI: 0.17–0.58]), and at 6-month follow-up ($X^2(1)=4.6$, p=0.03, OR=.53 [95% CI: 0.29–0.95]). In contrast, illicit-stimulant abstinent rates for methamphetamine-dependent patients did not differ significantly between menthol and non-menthol smokers during active treatment (W=0.6, p=.54, d=.01 [95% CI: −0.26–0.28]), 3-month follow-up (F=0.17, p=0.59, OR=.76 [95% CI: 0.28–2.05]), and 6-month follow ($X^2(1)=0.4$, p=0.53, OR=.73[95% CI: 0.28–1.91]).

3.4 Success in achieving smoking-cessation as a function of cigarette type

Logistic regressions were used to evaluate the association between cigarette type (menthol vs. non-menthol) and smoking cessation in the 147 cocaine-dependent and 102 methamphetamine-dependent participants assigned to the smoking-cessation (i.e., TAU +SCT) arm as measured by week 10 PPA. These analyses revealed no significant effect for cigarette type in either the cocaine-dependent ($X^2(1)= 0.06$, p=0.81) or methamphetamine-dependent ($X^2(1)= 0.01$, p=0.9) participants.

3.5 Prevalence of Caucasian menthol smokers as a function of stimulant-dependence diagnosis

As noted above, the prevalence of menthol smokers is lower in Caucasians relative to African Americans; it is estimated that only 22% of Caucasians are menthol smokers. The number of menthol methamphetamine-dependent smokers in the present study was limited, which may reflect the relatively few African Americans in the methamphetamine-dependent group (Table 1). Still, substance abusers tend to look for ways to improve their highs and, thus, one might expect to find an increased prevalence of menthol cigarette smokers in a

given substance-abusing population should menthol have beneficial effects on the high generated by the substance. To test this possibility we compared the prevalence of Caucasian menthol cigarette smokers in the cocaine-dependent, relative to methamphetamine-dependent, participants. In the present sample, 37.2% of cocaine-dependent Caucasian patients smoked menthol cigarettes relative to 17.61% of methamphetamine-dependent Caucasians ($X^2(1)=14.4$ $p<.001$, OR=2.77 [95% CI: 1.62–4.73]).

4. DISCUSSION

The present study sought to replicate and expand upon prior reports of a connection between menthol cigarette and cocaine use while completing an initial evaluation of the relationship between menthol cigarettes and methamphetamine use. While cocaine and methamphetamine are both stimulants, the present results suggest that mentholated cigarettes may play a role in cocaine dependence but not in methamphetamine dependence. Specifically, the present results revealed that cocaine-dependent participants who smoked menthol, compared to non-menthol, cigarettes were significantly more likely to report that cigarettes prolong the cocaine high and were significantly less likely to be cocaine abstinent. These differences were not found between menthol and non-menthol methamphetamine-dependent smokers. The present results also revealed a greater prevalence of Caucasian menthol smokers in the cocaine-dependent, relative to the methamphetamine-dependent, participants, suggesting that the increased incidence of mentholated cigarette use in the cocaine-dependent population was not due to group differences in race. Finally, the results revealed that menthol and non-menthol cigarette smokers did not differ in achieving smoking-cessation abstinence for either cocaine-dependent or methamphetamine-dependent participants.

The finding that cocaine-dependent participants who smoked menthol, compared to nonmenthol, cigarettes were significantly more likely to report that cigarettes prolong their cocaine high is consistent with past research findings (Sees and Clark, 1993; Wiseman and McMillan, 1998). It has been suggested that the potential of mentholated cigarettes to prolong the cocaine high is based on the ability of menthol cigarettes to increase lung permeability, serving to increase exposure to smoked cocaine (Wiseman and McMillan, 1998). However, the reported prolongation of cocaine high following either the smoked or nasal/IV route does not support this hypothesis. Alternatively, menthol may inhibit the metabolism of nicotine (Benowitz et al., 2004) and thereby heighten the interaction between nicotine and cocaine. Anecdotal reports suggest that mentholated compounds are also being added to cocaine to increase its potency and duration of action (e.g., Mint Cocaine, Menthol Cocaine; Internet forum posting, 2009). Whether or not menthol does so, the expectation could impact the cocaine-dependent patient’s experience. Further investigation into mechanisms underlying the potential relationship between mentholated cigarettes and cocaine use is warranted.

Research has consistently found that the prevalence of menthol smokers is lower in Caucasians relative to African Americans, with approximately 22% of Caucasian smokers using mentholated cigarettes (Giovino et al., 2004). In the present sample, 37.2% of cocaine-dependent Caucasian patients smoked menthol cigarettes relative to 17.61% of methamphetamine-dependent Caucasians, which suggests that mentholated cigarettes may have beneficial effects for the cocaine high that they do not have for methamphetamine. Although cigarette type was not associated with smoking cessation, this finding is consistent with past research that failed to find a significant relationship between cigarette type and difficulty with quitting smoking (Alexander et al., 2010; Fu et al., 2008; Hyland et al., 2002).

To our knowledge, this is the first study to evaluate the potential role of mentholated cigarettes in methamphetamine dependence. Given that methamphetamine and cocaine are both stimulants, it may seem counterintuitive for cocaine use to have significant associations with mentholated cigarettes and for this relationship not to be observed for methamphetamine use. However, methamphetamine and cocaine have a key difference that could account for the differential relationship, which is the relative length of subjective effects, which is considerably shorter for cocaine than for methamphetamine (Newton et al., 2005). In other words, menthol may noticeably increase the length of a cocaine high which lasts, at most, 30 minutes while not having a noticeable effect on the methamphetamine high, which can last six hours or more.

The present study has several strengths and a few limitations. First, this trial was conducted at 12 sites, which enhances the generalizability of the results, and included a large sample of stimulant-dependent participants. Another study strength is that it was conducted with individuals seeking treatment at SUD treatment programs and, thus, the results are likely generalizable to individuals in treatment for stimulant-dependence disorders (Winhusen et al., 2012b). A limitation of this study was the relatively small sample of methamphetamine-dependent menthol smokers. Also, this study included a treatment-seeking population of outpatients, so the findings may not be generalizable to those individuals not seeking treatment. In addition, the findings are correlational in nature and, thus, cause and effect determinations cannot be made. Finally, the present trial utilized a standard definition of smoking abstinence, which was self-report of not smoking in the previous seven days confirmed by a CO level <8 ppm (Hurt et al., 2003), but there is research to suggest that a CO level of 8–10 ppm may occasionally result in smokers falsely being classified as abstinent (Javors et al., 2005; Cropsey et al., 2006); consequently, the reported smoking abstinence rates for this study may have been artificially inflated.

In conclusion, the present results suggest that mentholated cigarettes might play a role in cocaine dependence but not in methamphetamine dependence. The potential import of the present study is two-fold. First, cocaine clinical trialists should assess whether participants smoke mentholated cigarettes since the present results suggest that this easily-assessed variable is associated with cocaine-use outcomes. Second, the results suggest that the concurrent use of mentholated cigarettes with cocaine is associated with more severe cocaine dependence as measured by significantly lower rates of cocaine abstinence. Cocaine dependence is a significant public health problem (SAMHSA, 2011) and the present results revealed that 67% of the cocaine-dependent participants smoke menthol cigarettes. This potential negative impact on public health should be considered when weighing the potential costs and benefits of banning mentholated cigarettes.

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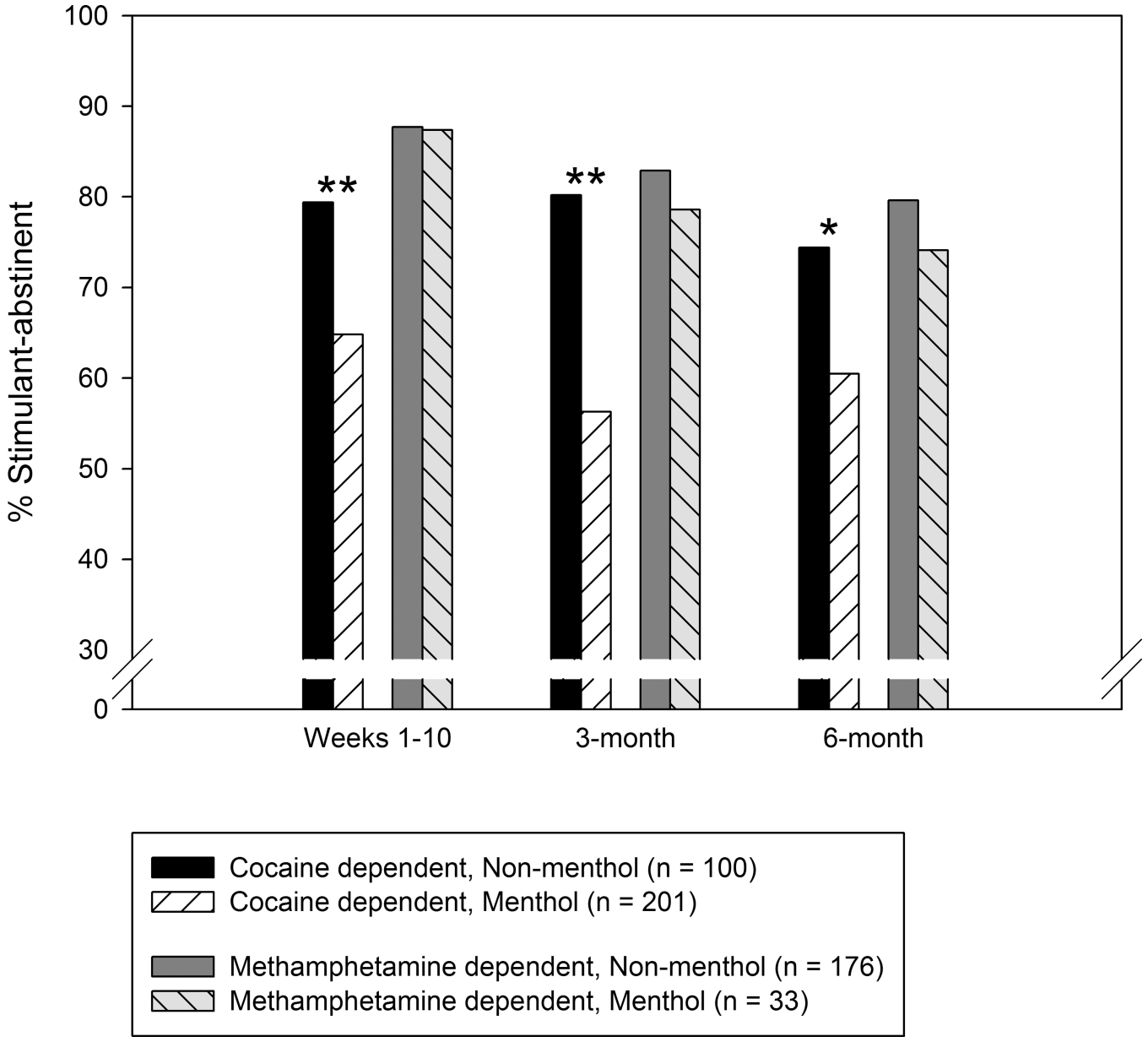

Figure 1.
Stimulant abstinence as a function of stimulant-dependent diagnosis and cigarette type. * p < .05; ** p <.001.

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Table 1

Participant demographic and baseline characteristics as a function of stimulant diagnosis and cigarette type

	Cocaine-Dependent			Methamphetamine-Dependent		
	Non-Menthol N=100	**Menthol N=201**	**Cigarette Analysis[a]**	**Non-Menthol N=176**	**Menthol N=33**	**Cigarette Analysis[a]**
Age (Years)	39.5 (10.1)	39.7 (9.8)	W=−0.3	33.1 (8.9)	29.3 (6.5)	t (57.0)=2.8**
Sex (% Male)	58.0%	56.2%	$X^2(1)=0.1$	48.3%	30.3%	$X^2(1)=3.6$
Race (%)			F=0.0***			F=0.0143
African-American	15.2%	74.6%		2.3%	3.0%	
Caucasian	76.8%	22.4%		82.4%	93.9%	
Other/mixed	8.1%	3.0%		15.3%	3.0%	
Ethnicity (% Hispanic)	18.0%	4.0%	$X^2(1)=16.3$***	18.2%	12.1%	$X^2(1)=0.7$
Stimulant-positive UDS[b]	20.0%	38.3%	$X^2(1)=10.2$**	12.5%	12.1%	F=0.2260
Stimulant-use route (%)			F=0.002			F=0.0005
Smoked	59.0%	66.2%		60.8%	57.6%	
Nasal	31.0%	27.4%		10.2%	6.1%	
IV	7.0%	4.0%		27.3%	24.2%	
Other/no answer	3.0%	2.5%		1.7%	12.1%	
Fagerström score	5.6 (2.4)	5.7 (2.2)	W=−0.2	5.6 (2.2)	5.3 (2.2)	W=−0.5
No. of Smoking years	21.0 (9.6)	22.8 (10.5)	W=−1.4	17.2 (8.7)	12.3 (6.1)	t (58.9)=3.9**
No. of cigarettes/day	17.5 (7.1)	16.4 (7.9)	W=1.6	15.0 (7.3)	16.5 (8.6)	W=1.1

Note:

[a] W=Wilcoxon Rank Sum, t(df)=Student's t, X^2(df)=Chi-square, F=Fisher's Exact;

[b] UDS=Urine drug screen.

* p < .05;

** p < .01;

*** p <.001

Table 2

Summary of reasons for using cigarettes with illicit stimulant as a function of stimulant diagnosis and cigarette type

	Cocaine-Dependent			Methamphetamine-Dependent		
	Non-Menthol	**Menthol**	**Cigarette Analysis**	**Non-Menthol**	**Menthol**	**Cigarette Analysis**
All participants	**N=100**	**N=201**	**Test statistic[a], OR (95% CI)**	**N=176**	**N=33**	**Test statistic[a], OR (95% CI)**
Helps illicit-stimulant high to last longer	15.1%	38.8%	X^2=16.3***, 3.58 (1.88, 6.79)	19.3%	24.2%	X^2=0.4, 1.34 (0.55, 3.25)
Just a habit, no reason for using with illicit stimulant	60.2%	45.9%	X^2=5.1*, 0.56 (0.34, 0.93)	65.7%	57.6%	X^2=0.8, 0.71 (0.33, 1.52)
Helps to feel relaxed/calm	55.9%	58.5%	X^2=0.2, 1.11 (0.67, 1.84)	50.6%	42.4%	X^2=0.7, 0.72 (0.34, 1.53)
Slows use of illicit stimulant	10.8%	16.4%	X^2=1.6, 1.63 (0.76, 3.49)	7.2%	9.1%	F=0.2, 1.28 (0.34, 4.82)
Used to fit in socially	6.5%	7.7%	X^2=0.1, 1.20 (0.45, 3.24)	15.1%	12.1%	F=0.2, 0.78 (0.25, 2.41)
Smoked route	**N=59**	**N=133**	**Test statistic[a], OR (95% CI)**			
Helps illicit-stimulant high to last longer	12.7%	37.8%	X^2=11.3**, 4.17 (1.74, 10.01)	-	-	-
Just a habit, no reason for using with illicit stimulant	61.8%	46.2%	X^2=3.7, 0.53 (0.28, 1.02)	-	-	-
Helps to feel relaxed/calm	63.6%	58.8%	X^2=0.4, 0.82 (0.42, 1.58)	-	-	-
Slows use of illicit stimulant	10.9%	16.0%	X^2=0.8, 1.55 (0.58, 4.13)	-	-	-
Used to fit in socially	3.6%	5.0%	F=0.3, 1.41 (0.28, 7.21)	-	-	-
Non-smoked route	**N=38**	**N=64**	**Test statistic[a], OR (95% CI)**			
Helps illicit-stimulant high to last longer	16.7%	41.7%	X^2=6.4*, 3.57 (1.29, 9.86)	-	-	-
Just a habit, no reason for using with illicit stimulant	58.3%	45.0%	X^2=1.6, 0.58 (0.25, 1.35)	-	-	-
Helps to feel relaxed/calm	44.4%	58.3%	X^2=1.7, 1.75 (0.76, 4.03)	-	-	-
Slows use of illicit stimulant	11.1%	16.7%	X^2=0.6, 1.69 (0.42, 6.84)	-	-	-
Used to fit in socially	8.3%	13.3%	F=0.2, 1.10 (0.15, 8.13)	-	-	-

Note:

[a] X^2=Pearson Chi-square, OR=Odds ratio, F=Fisher's Exact.

* $p < .05$;

** $p < .01$;

*** p <.001