Drug and Alcohol Dependence 134 (2014) 391–395

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Short communication

Achieving smoking abstinence is associated with decreased cocaine use in cocaine-dependent patients receiving smoking-cessation treatment

Theresa M. Winhusen*, Frankie Kropp, Jeff Theobald, Daniel F. Lewis

Addiction Sciences Division, Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine, 3210 Jefferson Avenue, Cincinnati, OH 45220, USA

ARTICLE INFO

Article history:
Received 28 August 2013
Received in revised form
18 September 2013
Accepted 19 September 2013
Available online 27 September 2013

Keywords:
Cocaine
Smoking cessation
Methamphetamine

ABSTRACT

Background: Past research suggests that a significant relationship exists between cigarette smoking and illicit-stimulant abuse. The present study evaluated the association between achieving smoking abstinence in response to smoking-cessation treatment (SCT) and illicit-stimulant abstinence in cocaine- and/or methamphetamine-dependent participants.

Methods: Secondary analysis of a randomized, 10-week trial conducted at 12 substance use disorder (SUD) treatment programs. Two hundred and sixty seven adults, meeting DSM-IV-TR criteria for cocaine and/or methamphetamine-dependence and interested in quitting smoking were randomized to SUD treatment as usual plus SCT consisting of weekly individual smoking cessation counseling, extended-release (XL) bupropion (300 mg/day), nicotine inhaler, and contingency management for smoking abstinence. Illicit-stimulant-abstinence was measured by self-report and urine drug screens. Smoking abstinence was assessed via self-report and carbon monoxide levels.

Results: A significant effect was found for the cocaine-dependent subsample ($N = 147$) in which participants who stopped smoking were abstinent for illicit stimulants an average of 78.2% of the post-smoking-quit weeks (weeks 4–10) relative to 63.6% in participants who continued smoking ($X^2(1) = 8.55$, $p < .01$, $d = 0.36$). No significant effects were found for the sample as a whole ($N = 249$) or for the methamphetamine-dependent subsample ($N = 102$).

Conclusions: The present results suggest that cocaine-dependent patients achieving smoking abstinence in response to SCT might evidence not only improved smoking outcomes but improved cocaine-use outcomes as well. Future research to replicate this finding appears warranted.

1. Introduction

A link between cigarette smoking and cocaine abuse has been established in pre-clinical, human laboratory, and clinical studies. In mice, exposure to nicotine prior to cocaine increases behaviors associated with cocaine and results in synaptic changes in the striatum and amygdala that are not associated with nicotine or cocaine alone (Huang et al., 2013; Levine et al., 2011). Pre-treatment of rhesus monkeys with nicotine prior to cocaine enhances the preference for cocaine (Mello and Newman, 2011) while the combination of nicotine and cocaine results in greater drug administration than either substance alone (Mello et al., 2013; Mello and Newman, 2011). Human laboratory studies have found that cocaine administration increases the rate of cigarette smoking (Nemeth-Coslett et al., 1986; Roll et al., 1997) and that mecamylamine, a nicotine antagonist, reduces cue-induced cocaine craving (Reid et al., 1999) while nicotine increases it (Reid et al., 1998).

Clinically, the rates of cocaine dependence are significantly higher in cocaine users who initiated cocaine after having started smoking compared to both non-smokers and those who initiated cocaine before smoking (Levine et al., 2011). The rate of smoking in cocaine abusers is 75–80% (Budney et al., 1993; Gorelick et al., 1997; Sees and Clark, 1993) and smoking cigarettes is associated with more severe cocaine addiction, 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). In addition, smoking status is a significant predictor of cocaine use (Frosch et al., 2000; Patkar et al., 2003; Roll et al., 1996) and cocaine users who smoke concurrently smoke more cigarettes (Brewer et al., 2013; Roll et al., 1996) and experience greater cravings for both nicotine and cocaine (Brewer et al., 2013).

A smaller body of research also suggests that there is a connection between methamphetamine use and cigarette smoking. In

* Corresponding author. Tel.: +1 513 487 7802/513 310 0442; fax: +1 513 487 7819.
E-mail addresses: winhust@ucmail.uc.edu, winhusen@carc.uc.edu (T.M. Winhusen).

0376-8716/$ – see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.drugalcdep.2013.09.019

rats, co-administration of nicotine and methamphetamine results in expression of different genes in the brain than those expressed when either drug is administered alone (Saint-Preux et al., 2013). It has been suggested that nicotine and methamphetamine may substitute for each other, to some extent (Gatch et al., 2008; Hiranita et al., 2006). In nicotine-naïve rats, nicotine priming alone reinstates methamphetamine-seeking, though to a lesser degree than methamphetamine-priming and cue-induction (Hiranita et al., 2006). In contrast, Neugebauer and colleagues (2010) found that nicotine priming reinstated methamphetamine-seeking only in rats that had been previously treated with nicotine rather than saline. In humans, a laboratory study found that *d*-amphetamine dose-dependently increases cigarette smoking (Tidey et al., 2000). A secondary analysis of a clinical trial of bupropion for methamphetamine dependence revealed a positive association between number of cigarettes smoked and methamphetamine use, but only in the placebo group (Brensilver et al., 2013). The high prevalence of smoking in methamphetamine abusers, estimated to be over 87% (Grant et al., 2007; Weinberger and Sofuoglu, 2009), also suggests a link between cigarette smoking and methamphetamine use.

Given the link between illicit stimulant use and cigarette smoking, we have hypothesized that better illicit stimulant-use outcomes would be obtained for stimulant-dependent patients who achieved smoking cessation abstinence in response to smoking-cessation treatment (Winhusen et al., 2012a). The data to test this hypothesis came from a recent multi-site trial conducted by the National Institute on Drug Abuse (NIDA) National Drug Abuse Treatment Clinical Trials Network (CTN) which 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 primary analyses from the trial revealed that there were no significant treatment effects on stimulant-use outcomes (Winhusen et al., 2013). The present analyses evaluated the association between achieving smoking abstinence and illicit-stimulant abstinence in the post-smoking-quit phase of the study for participants randomized to the smoking-cessation condition. Because there are important differences between cocaine and methamphetamine (Newton et al., 2005; Winhusen et al., 2013a,b), we evaluated the association for the entire sample as well as separately for the cocaine-dependent and methamphetamine-dependent participants.

2. Methods

2.1. Study design

Details of the trial are provided elsewhere (Winhusen et al., 2012a). Briefly, the study was a 10-week, intent-to-treat, 2-group randomized controlled trial with follow-up visits at 3 and 6 months post-smoking quit date conducted at 12 SUD outpatient treatment programs. Treatment programs which did not provide smoking-cessation treatment were eligible to participate. Eligible participants were randomized to treatment as usual (TAU) or TAU with smoking-cessation treatment (TAU + SCT). During the 10-week treatment phase, participants were scheduled to attend two research visits per week for efficacy and safety assessments. There were single follow-up visits at 3-months and 6-months post-quit date. Participants randomized to the TAU + SCT arm participated in the SUD treatment as typically provided by the study site and also received SCT consisting of extended-release (XL) bupropion 300 mg/day, nicotine inhaler, individual 10 min smoking-cessation counseling weekly for 10 weeks, and prize-based contingency management for smoking abstinence (Carbon Monoxide (CO) <4 ppm) during the post-quit phase.

2.2. Participants

Recruitment was primarily from clinic patients entering substance use disorder (SUD) treatment at a participating site. Eligible participants were adults enrolled in outpatient SUD treatment, and interested in quitting smoking. The main inclusion criteria were: meeting DSM-IV-TR criteria for cocaine- and/or methamphetamine-dependence, smoking at least 7 cigarettes daily and a CO level ≥8 ppm, and being in good physical health as determined by medical history, vital signs, and electrocardiogram. The decision to require 7 CPD was based on a prior trial completed

Table 1
Participant demographic and baseline characteristics as a function of dependence diagnosis and smoking-cessation abstinence.

	Pooled sample TAU + SCT (*N* = 249)			Cocaine-dependent TAU + SCT (*N* = 147)			Methamphetamine-dependent TAU + SCT (N = 102)		
	Continued smoking *N* = 174	Smoking abstinent *N* = 75	Smoking analysis[a]	Continued smoking *N* = 107	Smoking abstinent *N* = 40	Smoking analysis[a]	Continued smoking *N* = 67	Smoking abstinent *N* = 35	Smoking analysis[a]
Age, mean (SD), y	37.7 (9.9)	36.2 (10.1)	$W = 1.1$	41.4 (9.1)	40.4 (9.9)	$W = 0.3$	31.8 (8.0)	31.5 (8.2)	$W = 0.4$
Sex, male, *n* (%)	89 (51.1)	47 (62.7)	$X^2(1) = 2.8$	57 (53.3)	29 (72.5)	$X^2(1) = 4.4^*$	32 (47.8)	18 (51.4)	$X^2(1) = 0.1$
Race, *n* (%)			$X^2(2) = 0.9$			$F = 0.017$			$X^2(1) = 0.1$
African-American	56 (32.4)	27 (36.0)		56 (52.8)	27 (67.5)		0 (0)	0 (0)	
Caucasian	105 (60.7)	41 (54.7)		48 (45.3)	12 (30.0)		57 (85.1)	29 (82.9)	
Other/mixed	12 (6.9)	7 (9.3)		2 (1.9)	1 (2.5)		10 (14.9)	6 (17.1)	
Ethnicity, Hispanic, *n* (%)	20 (11.6)	11 (14.7)	$X^2(1) = 0.5$	10 (9.4)	1 (2.5)	$F = 0.117$	10 (14.9)	10 (28.6)	$X^2(1) = 2.7$
Baseline use (prior 28 days)									
Days/stimulant use	2.3 (5.2)	1.3 (4.1)	$T(174.0) = 1.5$	2.7 (5.7)	2.2 (5.5)	$W = 1.4$	1.5 (4.1)	0.3 (0.9)	$T(76.6) = 2.3^*$
Stimulant-free, *n* (%)	118 (67.8)	61 (81.3)	$X^2(1) = 4.7^*$	68 (63.6)	31 (77.5)	$X^2(1) = 2.6$	50 (74.6)	30 (85.7)	$X^2(1) = 1.7$
Days/drug use	5.1 (8.7)	2.1 (5.4)	$T(218.4) = 3.3^{**}$	5.7 (9.3)	3.5 (6.9)	$T(93.1) = 1.6$	4.1 (7.8)	0.5 (1.6)	$T(76.3) = 3.6^{***}$
Drug-free, *n* (%)	90 (51.7)	55 (73.3)	$X^2(1) = 10.1^{**}$	51 (47.7)	26 (65.0)	$X^2(1) = 3.5$	39 (58.2)	29 (82.9)	$X^2(1) = 6.3^*$
Smoking history									
No. of Smoking years	21.1 (9.5)	19.4 (9.7)	$W = 1.4$	24.2 (9.0)	22.4 (9.8)	$W = 1.0$	16.1 (8.1)	16.0 (8.4)	$W = 0.2$
No. of cigarettes/day	17.1 (8.6)	14.8 (7.6)	$W = 2.1^*$	18.1 (8.9)	16.1 (7.5)	$W = 1.4$	15.5 (7.7)	13.3 (7.5)	$W = 1.3$

$^*p < .05$, $^{**}p < .01$, $^{***}p < .001$. Where not specifically indicated, numbers represent means (standard deviations).
[a] W = Wilcoxon rank-sum test; $X^2(df)$ = Pearson chi-square test; $T(df)$ = Student's *t*-test; F = Fisher's exact test.