Original Investigation

Alcohol and Marijuana Use in the Context of Tobacco Dependence Treatment: Impact on Outcome and Mediation of Effect

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Abstract

Introduction: Alcohol and marijuana are among the most commonly used substances together with tobacco worldwide, but their relationship to smoking cessation is unclear. Although alcohol use decreases the likelihood of abstinence from tobacco, mechanisms of this effect have not been identified. Moreover, a small literature has yielded inconsistent findings regarding the effect of marijuana use on tobacco dependence treatment outcome. The aims of this study were to test increased positive-reinforcement smoking urge as a mediator of the relationship between alcohol and cigarette use and evaluate the impact of marijuana use on abstinence from tobacco.

Methods: Participants were adult cigarette smokers ($N = 739$) from 3 randomized clinical trials of smoking cessation treatment. Alcohol consumption and marijuana use were assessed at pretreatment and postcessation. Biochemically verified, 7-day point prevalence smoking abstinence was determined at Weeks 12, 24, 36, and 52, as were urges to smoke as measured by the Questionnaire of Smoking Urges.

Results: Increased positive-reinforcement urge mediated the effect of postcessation alcohol use on smoking abstinence. Although pretreatment alcohol use was associated with a decreased likelihood of abstinence from tobacco, increased positive-reinforcement urge did not account for this relationship. Marijuana use was not associated with abstinence from tobacco.

Conclusions: Smoking cessation treatments should provide those who drink during a quit attempt techniques designed to mitigate positive-reinforcement urge to smoke. Additional research is needed to determine how pretreatment alcohol consumption exerts its effect on cigarette use. Modifying the use of marijuana might not be critical to the success of tobacco interventions.

Introduction

Along with tobacco, alcohol and marijuana are among the most widely used substances on the planet (e.g., United Nations Office on Drugs and Crime, 2010; World Health Organization, 2011). In addition, those who smoke cigarettes consume alcohol more frequently and heavily and use marijuana at higher rates than those who do not smoke tobacco (Agrawal, Silberg, Lynskey, Maes, & Eaves, 2010; Kahler et al., 2009). These observations have prompted researchers to investigate the effects of alcohol and marijuana use on tobacco smoking cessation (e.g., Auguston et al., 2008; Burns, Mattick, & Wallace, 2008; Dollar, Homish, Kozlowski, & Leonard, 2009; McDermott, Dobson, & Owen, 2009). One purpose of this line of research is to advance existing tobacco treatments by identifying individual characteristics to which such treatments may be tailored.

A number of tobacco use intervention studies have demonstrated that alcohol consumption is associated with a decreased probability of nonsmoking (Hays et al., 1999; Humfleet, Muñoz, Sees, Reus, & Hall, 1999; Hymowitz et al., 1997; Kahler, Spillane, & Metrik, 2010; Leeman et al., 2008; McClure, Wetter, de Moor, Cinciripini, & Gritz, 2002; Murray, Istvan, Voelker, Rigdon, & Wallace, 1995; Sherman, Wang, & Nguyen, 1996; Smith, Kraemer, Miller, DeBusk, & Taylor, 1999). Although these investigations have illuminated the association between alcohol consumption and smoking cessation treatment outcome, none have explored mediators of this relationship. Human laboratory research suggests that consistent with appetitive motivational theories of craving (e.g., Stewart, de Wit, & Eikelboom, 1984), alcohol consumption increases positive-reinforcement smoking urge (i.e., the desire to smoke for positively reinforcing, pleasurable outcomes; Epstein, Sher, Young, & King, 2007; King & Epstein, 2005; McKee, Krishnan-Sarin, Shi, Mase, & O'Malley, 2006; Sayette, Martin, Wertz, Perrott, & Peters, 2005). Thus, alcohol use may interfere with tobacco dependence intervention by intensifying the urge to smoke for

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positive reinforcement. Nevertheless, no prior longitudinal research, intervention or otherwise, has attempted to determine how alcohol use exerts its influence on cigarette smoking cessation. Unearthing such mechanistic processes is critical because it provides explicit information with which to inform the tailoring of existing treatments (see Hendricks, Delucchi, & Hall, 2010; Kazdin, 2007). For example, whereas the finding that alcohol use impedes smoking cessation has informed the guideline that alcohol intake be limited during a quit attempt (Fiore et al., 2008), understanding how it does so would allow for specific intervention in the more likely eventuality that alcohol use persists.

Relatively few studies, on the other hand, have examined the effect of marijuana use on smoking cessation. Whereas longitudinal community studies suggest that marijuana use is associated with a reduced likelihood of abstinence from tobacco (Abrantes et al., 2009; Burns et al., 2008; Ford, Vu, & Anthony, 2002; McDermott et al., 2009; Richter, Ahluwalia, Mosier, Nazir, & Ahluwalia, 2002), the four studies reported to date that have examined the relationship between marijuana and tobacco use among those receiving tobacco dependence interventions (Gourlay, Forbes, Marriner, Pethica, & McNeil, 1994; Humfleet et al., 1999; Metrik, Spillane, Leventhal, & Kahler, 2011; Stapleton, Keaney, & Sutherland, 2009) present an unclear picture. Indeed, whereas Gourlay et al. (1994) demonstrated that any pretreatment use of marijuana decreased the odds of cessation, Humfleet et al. (1999) found no relationship between the presence of marijuana use at either pretreatment or postcessation and tobacco abstinence, and Metrik et al. (2011) found no differences among pretreatment patterns of marijuana use on tobacco outcomes. Furthermore, while Stapleton et al. (2009) found that any use of illicit substances at pretreatment reduced the likelihood of abstinence from tobacco, the quit rate among marijuana-only users (40%) was greater than the quit rate among users of other illicit substances (11%), though less than the quit rate among nondrug users (55%). Thus, it is not known whether tobacco dependence interventions should account for comorbid marijuana use (e.g., recommend that marijuana use be reduced).

The current research had two specific objectives: (a) to examine urge to smoke for positive reinforcement as a mediator of the relationship between alcohol use and smoking cessation intervention outcome and (b) to evaluate the influence of marijuana use on tobacco use treatment success. We hypothesized a mediational pathway wherein alcohol intake would increase positive-reinforcement urge to smoke, which in turn would decrease the likelihood of abstinence from tobacco. Given conflicting findings on the association between marijuana use and tobacco cessation, we offered no specific hypothesis regarding this relationship.

Methods

This study used participants from three randomized clinical trials of smoking cessation treatment. These investigations employed parallel assessment procedures, and the rates of alcohol and marijuana use were equivalent among trials and treatment conditions within each trial. Though target populations and interventions differed across the three studies, data were

combined to maximize statistical power and the generalizability of findings. More detailed descriptions of the methods of these three trials have been reported elsewhere (Hall, Humfleet, Reus, Muñoz, & Cullen, 2004; Hall et al., 2002; Humfleet, Hall, Sees, Muñoz, & Reus, 2002). We briefly describe the methods here.

Participants

As summarized in a previous publication by our research group (Lawhon, Humfleet, Hall, Muñoz, & Reus, 2009), participants ($N = 739$) were recruited by advertising, public service announcements, and flyers. Studies 1 ($N = 219$; Hall et al., 2002) and 2 ($N = 160$; Hall et al., 2004) required that participants smoke at least 10 cigarettes/day, and Study 3 ($N = 360$; Humfleet et al., 2002) required that participants smoke at least 15 cigarettes/day and report either smoking within 30 min of waking or smoking when so ill that one remains in bed for most of the day. Each study required participants to be at least 18 years of age. Exclusion criteria across the three studies included the use of antidepressant medication, presence of conditions that contraindicated use of pharmacotherapy, or presence of conditions that might interfere with compliance or greatly complicate treatment.

Procedures

Individuals who met the screening criteria during a telephone interview were invited to an orientation meeting, where informed consent was obtained from those choosing to participate. Participants then completed a pretreatment assessment that included a brief medical exam, clinical interview, and measures of demographic and smoking-related variables. Following pretreatment assessment, participants were stratified and randomly assigned to one of the several treatment conditions involving pharmacological and/or psychosocial intervention for tobacco dependence.

Study 1 examined psychological intervention and antidepressant therapy using a two (medical management vs. psychological intervention) by three (bupropion vs. nortriptyline vs. placebo) design. Study 2 investigated the effects of extended treatment using a two (nortriptyline vs. placebo) by two (brief vs. extended treatment) design. All participants in Study 2 were provided with 8 weeks of transdermal patch nicotine replacement therapy and five group counseling sessions. Study 3 examined the effects of extended treatment using a two (clinical management vs. clinical management plus psychosocial support) by two (brief vs. extended treatment) plus one (extended simulated over-the-counter treatment) design. All participants in Study 3 were provided with 12 weeks of nicotine gum therapy; those in extended conditions were provided with nicotine gum therapy as needed for up to one year. As the three studies were conducted prior to the recommendation that counseling be provided for nonnicotinic drugs (Fiore et al., 2008), the interventions did not address alcohol or marijuana use in any systematic fashion.

Assessment of Participant Characteristics

An extensive range of participant characteristics were assessed at pretreatment and included but were not limited to gender; age; ethnoracial status; cigarettes smoked per day; years smoked

cigarettes; tobacco dependence, measured by the Fagerström Test for Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerström, 1991); urge to smoke, measured by the Questionnaire of Smoking Urges (QSU; Tiffany & Drobes, 1991); and average frequency of illicit substance (cocaine, stimulant, opiate, barbiturate, and hallucinogen) use, assessed with a 5-point scale (1 = *never*, 2 = *monthly or less*, 3 = *two to four times per month*, 4 = *two to three times per week*, 5 = *four or more times per week*).

Assessment of Alcohol and Marijuana Use

The Timeline Followback Interview method (Sobell & Sobell, 1995) was used to assess alcohol and marijuana use at pretreatment and at the first postcessation assessment, which occurred at Week 7 for Studies 1 and 2 and Week 8 for Study 3. Participants reported the number of standard alcoholic beverages they consumed during each day and the specific days they used marijuana in the prior 7 days. This time period was selected as it matched the time period of the outcome variable. Assessment of alcohol and marijuana use in the previous 7 days represents a sampling approach; alcohol and marijuana use during this time were believed to be representative of drinking and marijuana use patterns across the study period (see Del Boca & Darkes, 2003). Alcohol and marijuana use were assessed at both pretreatment and postcessation to account for any potential changes in drinking or marijuana use as a result of abstinence from tobacco and to allow for comparison with previous studies with similar alcohol and marijuana use assessment schedules.

Alcohol use was indexed as the number of alcoholic beverages consumed in the past 7 days. We considered also indexing alcohol use according to National Institute on Alcohol Abuse and Alcoholism (1995) guidelines and number of binge-drinking days in the past 7 days. However, drinks consumed in the past 7 days was strongly associated with these alternative indices of alcohol intake (correlation coefficients ranged from .66 to .88), suggesting redundancy, and its variance was larger than these alternative indices, suggesting that it had greater power to detect significant relationships. Marijuana use behavior was indexed as number of days of marijuana use in the past 7 days. We considered any versus no use of marijuana during the previous 7 days as an alternative index of marijuana use. However, mirroring our findings concerning alternative indices of alcohol use, number of days of marijuana use was strongly correlated with any versus no use of marijuana in the previous 7 days (correlation coefficients = .94 and .95), and its variance was larger.

Outcome Variable

Seven-day point prevalence smoking abstinence was assessed in each of the three studies at Weeks 12, 24, 36, and 52. Smoking abstinence was indicated by self-report ("no smoking, not even a puff") and verified in all studies by breath carbon monoxide levels of less than 10 ppm. In Studies 1 and 2, smoking abstinence also was verified by urinary cotinine levels of 60 ng/ml or less. All participants were contacted for each assessment whether they continued in treatment or not and missing participants were coded as missing.

Mediator Variables

The QSU was administered at pretreatment and Weeks 12, 24, 36, and 52 to assess participants' urge to smoke cigarettes. As

with the assessment of alcohol and marijuana use, the assessment of urge to smoke represents a sampling approach; urge to smoke during these times was believed to be representative of larger smoking urge patterns. The QSU consists of two factor-derived subscales: positive-reinforcement urge (QSU-POS) and negative-reinforcement urge (QSU-NEG). QSU-POS and QSU-NEG scores were evaluated in tests of mediation.

Analytic Approach

To identify potential confounding factors in analyses involving alcohol and marijuana use, the relationships of alcohol and marijuana use indices to participant characteristics were examined with *t* tests, analyses of variance, chi-square analyses, and correlation analyses. To confirm prior research indicating that alcohol use decreases the likelihood of nonsmoking, the effects of alcohol use on 7-day point prevalence smoking abstinence at Weeks 12, 24, 36, and 52 was explored with models using generalized estimating equations (GEEs) to account for the dependence of repeated measures (Liang & Zeger, 1986). Two separate GEE models were used to investigate the relationships of pretreatment alcohol use and postcessation alcohol use to tobacco abstinence. These analyses were conducted with the inclusion of the respective covariates of each of the two indices of alcohol use. Although neither study number nor treatment condition were related to alcohol use, study number and treatment condition were included as covariates in all GEE models to control for any unforeseen confounding effects of these variables.

Figure 1a and b illustrate the hypothesized mediational pathways of alcohol use on smoking abstinence. To infer a causal

Figure 1 a. Hypothesized mediational pathway of pretreatment alcohol use on smoking abstinence through positive-reinforcement urge to smoke. Pretreatment alcohol use, derived from the Timeline Followback Interview administered at baseline and measuring alcoholic beverages consumed in the past 7 days, is connected to 7-day point prevalence smoking abstinence at Week 52 through direct (*c'*) and indirect (*a* and *b*) paths. b. Hypothesized mediational pathway of postcessation alcohol use on smoking abstinence through positive-reinforcement urge to smoke. Postcessation alcohol use, derived from the Timeline Followback Interview administered at the first postcessation assessment and measuring alcoholic beverages consumed in the past 7 days, is connected to 7-day point prevalence smoking abstinence at Week 52 through direct (*c'*) and indirect (*a* and *b*) paths.

pathway in mediation models, the independent variable (i.e., alcohol use) must temporally precede the mediator (i.e., change in positive-reinforcement smoking urge), which must temporally precede the outcome (i.e., smoking abstinence; Kazdin, 2007). To establish such a timeline, mediation analyses (MacKinnon, Lockwood, Brown, Wang, & Hoffman, 2007; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002) assessed the effect of alcohol intake on abstinence at Week 52. To explore the degree to which change in positive-reinforcement urge mediated the effect of pretreatment drinking quantity, change was computed by subtracting QSU-POS scores at baseline from QSU-POS scores at Week 36. To determine the degree to which change in positive-reinforcement urge mediated the effect of postcessation drinking quantity, change was computed by subtracting QSU-POS scores at Week 12 from QSU-POS scores at Week 36. Tests of the mediated effect were conducted via a bootstrap approach with all paths adjusted for the influence of the two alcohol use indices' respective covariates as well as study number and treatment condition (Preacher & Hayes, 2008). The proportion of mediated effect was estimated by methods based on the product of regression coefficients (see MacKinnon et al., 2007).

To test the discriminant validity of the mediational role of positive-reinforcement urge to smoke, negative-reinforcement urge to smoke was evaluated as a mediator of the relationship between alcohol intake and abstinence at Week 52. As with positive-reinforcement urge to smoke, change was computed by subtracting QSU-NEG scores at baseline from QSU-NEG scores at Week 36 to investigate the effect of pretreatment drinking quantity and by subtracting QSU-NEG scores at Week 12 from QSU-NEG scores at Week 36 to test the effect of postcessation drinking quantity.

Two separate GEE models were used to investigate the relationships of pretreatment marijuana use and postcessation marijuana use to smoking abstinence at Weeks 12, 24, 36, and 52. These analyses were conducted with the inclusion of the respective covariates of each of the two measures of marijuana use. As with alcohol analyses, though neither study number nor treatment condition were related to marijuana use, these variables were included as covariates in all GEE models to control for any unanticipated confounding.

Results

Participant Characteristics

Participant characteristics are displayed in Table 1. Negative binomial regression analyses indicated that whereas the decrease in alcohol use from pretreatment to postcessation was statistically significant ($B = -.23, p = .01$), the decline in marijuana use during this time period was not ($B = -.17, p = .25$).

Attrition

Attrition rates were low through Week 52 (Week 52 attrition rate = 18.8%). Pretreatment ($B = -.04, p = .009$) and postcessation ($B = -.08, p = .0003$) drinking quantity were both associated with a lower likelihood of missing outcome data across assessment periods. However, for both of these variables, missing participants were no more likely to be smoking than non-missing participants. Marijuana use was unrelated to attrition.

Table 1. Participant Characteristics

Male (%)	60.8
White, non-Hispanic/Latino (%)	75.0
Mean number of cigarettes smoked per day (<i>SD</i>)	21.64 (8.22)
Mean years smoked cigarettes (<i>SD</i>)	22.37 (10.87)
Mean score at baseline (<i>SD</i>)	
FTND total score	5.16 (2.15)
QSU positive-reinforcement urge	4.57 (1.18)
QSU negative-reinforcement urge	2.86 (1.24)
Cocaine use at baseline (%)	
Never	78.7
Monthly or less	21.3
Stimulant use at baseline (%)	
Never	96.8
Monthly or less	3.2
Opiate use at baseline (%)	
Never	97.0
Monthly or less	3.0
Barbiturate use at baseline (%)	
Never	98.6
Monthly or less	1.4
Hallucinogen use at baseline (%)	
Never	97.6
Monthly or less	2.4
Mean drinks consumed in the past 7 days (<i>SD</i>)	
Pretreatment	4.92 (6.66)
Postcessation	3.90 (6.65)
Mean days used marijuana in the past 7 days (<i>SD</i>)	
Pretreatment	0.74 (1.74)
Postcessation	0.62 (1.61)

Note. FTND = Fagerström Test for Nicotine Dependence;
QSU = Questionnaire of Smoking Urges.

These findings are consistent with the assumption that outcome data were missing completely at random (see Schneider, Hedeker, Bailey, Cook, & Spring, 2010).

Relationships of Alcohol Use to Participant Characteristics

Pretreatment drinking quantity was positively associated with cocaine use ($r = .15, p = .001$) and negatively associated with tobacco dependence ($r = -.09, p = .01$). Thus, cocaine use and tobacco dependence were added as covariates in the model predicting smoking abstinence from pretreatment drinking quantity, and the mediational paths of pretreatment drinking quantity on smoking abstinence through smoking urge were adjusted for the influence of these variables.

Postcessation drinking quantity was greater among men than women (mean difference = 1.30, $p = .01$), positively associated with cocaine use ($r = .20, p < .001$), and negatively associated with age ($r = -.12, p = .001$), years smoked tobacco ($r = -.11, p = .002$), and tobacco dependence ($r = -.10, p = .006$). Gender, cocaine use, age, years smoked tobacco, and tobacco dependence were therefore added as covariates in the model predicting smoking abstinence from postcessation drinking quantity, and the mediational paths of postcessation drinking quantity on smoking abstinence through urge to smoke were adjusted for the effect of these constructs.

Table 2. Results of the GEE Model Predicting Smoking Abstinence From Pretreatment Drinking Quantity, Tobacco Dependence, and Cocaine Use

Variable	χ^2	OR	95% CI	p Value
Time	35.10	.98	.97, .98	<.001
Pretreatment drinking quantity	6.81	.96	.94, .99	.009
Tobacco dependence	4.58	.92	.85, .99	.03
Cocaine use	4.47	.63	.41, .97	.03

Note. Study number and treatment condition were included in the model as covariates. Seven-day point prevalence smoking abstinence was assessed at Weeks 12, 24, 36, and 52. Pretreatment drinking quantity was derived from the Timeline Followback Interview administered at baseline and measuring number of alcoholic beverages consumed in the previous 7 days. Tobacco dependence was assessed at baseline with the Fagerström Test for Nicotine Dependence. Cocaine use was measured at baseline with a self-report questionnaire that assessed average frequency of use. GEE = generalized estimating equation.

Relationship of Alcohol Use to Smoking Abstinence

Results of the GEE model predicting smoking abstinence from pretreatment alcohol use and its covariates are presented in Table 2, and results of the model predicting smoking abstinence from postcessation alcohol use and its covariates are displayed in Table 3. As seen in the tables, pretreatment and postcessation drinking quantity were both independently associated with a decreased likelihood of abstinence.

Mediation Analyses

Pretreatment drinking quantity was not associated with change in urge to smoke for positive reinforcement ($B = .02$, $p = .14$), and thus the test of mediation indicated a nonsignificant effect (95% CI $[-.003, .03]$). However, postcessation drinking quantity was associated with increased positive-reinforcement urge ($B = .04$, $p = .004$). Increased positive-reinforcement urge was, in turn, associated with a decreased likelihood of abstinence while controlling for the effect of postcessation drinking quantity ($B = .67$, $p < .0001$). The test of mediation indicated a significant effect of postcessation drinking quantity (95% CI $[.007, .05]$) on abstinence through increased positive-reinforcement urge. Estimates of the proportion of the mediated effect ranged from .56 to .64.

Although positive-reinforcement urge to smoke was assessed before abstinence at Week 52, those relapsing to cigarette use before Week 52 may have experienced an increase in positive-reinforcement urge to smoke. Thus, the mediation of postcessation alcohol use on smoking abstinence at Week 52 through positive-reinforcement urge to smoke may in fact reflect mediation via previous outcome. To explore for this possibility, abstinence status at Weeks 12, 24, and 36 were added as covariates to the mediation analysis evaluating the effect of postcessation drinking quantity on smoking abstinence at Week 52 through positive-reinforcement urge to smoke. Change in positive-reinforcement urge to smoke remained a significant mediator of the relationship between postcessation drinking

quantity and abstinence at Week 52 while controlling for abstinence at Weeks 12, 24, and 36 (95% CI $[.001, .03]$), suggesting that positive-reinforcement urge to smoke was not simply a consequence of earlier tobacco use.

With respect to testing the discriminant validity of the mediational role of positive-reinforcement urge to smoke, pretreatment drinking quantity was not related to change in urge to smoke for negative reinforcement ($B = .01$, $p = .24$), and therefore the test of mediation indicated a nonsignificant effect (95% CI $[-.004, .01]$). Similarly, postcessation drinking quantity was not associated with change in urge to smoke for negative reinforcement ($B = .02$, $p = .07$), and the test of mediation failed to yield significant results (95% CI $[-.0002, .02]$).

Relationships of Marijuana Use to Participant Characteristics

Pretreatment marijuana use frequency was negatively associated with age ($r = -.13$, $p < .001$) and years smoked tobacco ($r = -.13$, $p < .001$) and positively associated with cocaine ($r = .43$, $p < .001$), stimulant ($r = .10$, $p = .02$), opiate ($r = .09$, $p = .04$), and hallucinogen ($r = .21$, $p < .001$) use. Consequently, age, years smoked tobacco, cocaine use, stimulant use, opiate use, and hallucinogen use were added as covariates in the model predicting smoking abstinence from pretreatment marijuana use frequency.

Postcessation marijuana use frequency was negatively associated with age ($r = -.12$, $p = .002$) and years smoked tobacco ($r = -.11$, $p = .005$) and positively associated with cocaine ($r = .29$, $p < .001$), stimulant ($r = .10$, $p = .02$), opiate ($r = .10$, $p = .02$), and hallucinogen ($r = .14$, $p = .001$) use. Age, years smoked tobacco, cocaine use, stimulant use, opiate use, and hallucinogen use were thus added as covariates in the model predicting smoking abstinence from postcessation marijuana use frequency.

Table 3. Results of the GEE Model Predicting Smoking Abstinence From Postcessation Drinking Quantity, Gender, Age, Years Smoked Tobacco, Tobacco Dependence, and Cocaine Use

Variable	χ^2	OR	95% CI	p Value
Time	29.94	0.98	0.97, 0.98	<.001
Postcessation drinking quantity	6.07	0.97	0.95, 0.99	.01
Gender	0.70	0.86	0.61, 1.21	.40
Age	0.11	0.99	0.95, 1.03	.73
Years smoked tobacco	0.04	0.99	0.95, 1.03	.84
Tobacco dependence	2.81	0.93	0.86, 1.01	.09
Cocaine use	4.35	0.62	0.40, 0.97	.03

Note. Study number and treatment condition were included in the model as covariates. Seven-day point prevalence smoking abstinence was assessed at Weeks 12, 24, 36, and 52. Postcessation drinking quantity was derived from the Timeline Followback Interview administered at the first postcessation assessment and measuring number of alcoholic beverages consumed in the previous 7 days. Gender was dummy coded as 0 = male and 1 = female. Tobacco dependence was assessed at baseline with the Fagerström Test for Nicotine Dependence. Cocaine use was measured at baseline with a self-report questionnaire that assessed average frequency of use. GEE = generalized estimating equation.

Table 4. Results of the GEE Model Predicting Smoking Abstinence From Pretreatment Marijuana Use Frequency, Age, Years Smoked Tobacco, and Cocaine, Stimulant, Opiate, and Hallucinogen Use

Variable	χ^2	OR	95% CI	p Value
Time	33.10	.98	.97, .98	<.001
Pretreatment marijuana use frequency	0.20	.97	.87, 1.08	.65
Age	0.07	.99	.95, 1.03	.78
Years smoked tobacco	0.19	.99	.95, 1.02	.66
Cocaine use	4.36	.58	.34, .97	.03
Stimulant use	0.04	.92	.43, 1.94	.83
Opiate use	0.20	1.14	.63, 2.06	.65
Hallucinogen use	0.60	1.51	.51, 4.51	.43

Note. Study number and treatment condition were included in the model as covariates. Seven-day point prevalence smoking abstinence was assessed at Weeks 12, 24, 36, and 52. Pretreatment marijuana use frequency was derived from the Timeline Followback Interview administered at baseline and measuring number of days used marijuana in the previous 7 days. Cocaine, stimulant, opiate, and hallucinogen use were measured at baseline with a self-report questionnaire that assessed average frequency of use. GEE = generalized estimating equation.

Relationship of Marijuana Use to Smoking Abstinence

Results of the GEE model predicting smoking abstinence from pretreatment marijuana use and its covariates are presented in Table 4, and results of the GEE model predicting smoking abstinence from postcessation marijuana use and its covariates are presented in Table 5. As shown in the tables, marijuana use failed to predict abstinence. However, in both models, cocaine use was associated with a decreased probability of tobacco cessation.

Discussion

Numerous investigations suggest that alcohol use undermines the efficacy of tobacco dependence intervention (e.g., Humfleet et al., 1999; Kahler et al., 2010; Leeman et al., 2008); however, the mechanisms underlying this effect have not been identified. Accordingly, the first objective of the present study was to evaluate a mechanism of alcohol use's action on smoking cessation treatment outcome. Consistent with our hypothesis, positive-reinforcement smoking urge mediated the effect of postcessation alcohol intake on smoking abstinence, accounting for 56%–64% of the effect of postcessation drinking quantity on cigarette use. Specifically, increased postcessation alcohol use occasioned an increase in positive-reinforcement smoking urge, which in turn decreased the likelihood of successful abstinence from tobacco. Alcohol use was unrelated to negative-reinforcement urge to smoke, highlighting the distinct mediational role of positive-reinforcement urge. These findings are consistent with appetitive motivational theories of craving (e.g., Stewart et al.,

1984), corroborate human laboratory investigations indicating that alcohol consumption elicits positive-reinforcement urge to smoke (Epstein et al., 2007; King & Epstein, 2005; McKee et al., 2006; Sayette et al., 2005), and suggest that those who drink after a quit attempt are less likely to achieve abstinence because their urge to smoke for positive reinforcement is amplified. Although greater pretreatment alcohol use was associated with reduced odds of abstinence from tobacco, change in positive-reinforcement urge was not a significant mediator of this relationship.

Considering that a small number of studies have yielded indeterminate results, it is uncertain whether marijuana use impacts the efficacy of tobacco dependence treatment. For this reason, the second objective of the current study was to clarify the relationship between marijuana use and tobacco intervention outcome. We found that neither pretreatment nor postcessation marijuana intake predicted abstinence from tobacco. While these findings conflict with community research (e.g., Abrantes et al., 2009; Ford et al., 2002) and one prior smoking cessation study (Gourlay et al., 1994), they are consistent with two tobacco intervention investigations (Humfleet et al., 1999; Metrik et al., 2011) as well as a study suggesting that the independent effect of marijuana use on tobacco intervention is weak relative to the oft-comorbid use of other illicit substances (Stapleton et al., 2009). Inconsistencies in the literature may be explained by differences between the studies' samples of marijuana users (e.g., regional differences). It is worth noting that the current investigation is the first intervention study to evaluate the relationship between marijuana use and tobacco cessation outcome while controlling for the influence of other substance use. Although marijuana use frequently co-occurs with other drug use (see Agrawal & Lynskey, 2006) and rates of

Table 5. Results of the GEE Model Predicting Smoking Abstinence From Postcessation Marijuana Use Frequency, Age, Years Smoked Tobacco, and Cocaine, Stimulant, Opiate, and Hallucinogen Use

Variable	χ^2	OR	95% CI	p Value
Time	33.06	.98	.97, .98	<.001
Postcessation marijuana use frequency	1.16	.93	.82, 1.06	.28
Age	0.10	.99	.95, 1.03	.75
Years smoked tobacco	0.16	.99	.95, 1.03	.68
Cocaine use	4.62	.59	.37, .96	.03
Stimulant use	0.03	.93	.43, 2.00	.86
Opiate use	0.31	1.17	.64, 2.14	.57
Hallucinogen use	0.65	1.50	.53, 4.18	.42

Note. Study number and treatment condition were included in the model as covariates. Seven-day point prevalence smoking abstinence was assessed at Weeks 12, 24, 36, and 52. Postcessation marijuana use frequency was derived from the Timeline Followback Interview administered at the first postcessation assessment and measuring number of days used marijuana in the previous 7 days. Cocaine, stimulant, opiate, and hallucinogen use were measured at baseline with a self-report questionnaire that assessed average frequency of use. GEE = generalized estimating equation.

comorbid drug use in the present sample appear to be commensurate with other clinical samples (e.g., Metrik et al., 2011), elevated levels of substance use may have obscured the relationship between marijuana and tobacco. It also is possible that use of marijuana greater than was observed in the present research could decrease the likelihood of abstinence from tobacco. However, the rates of marijuana use reported in the current study were either greater than (Gourlay et al., 1994) or equivalent to (Humfleet et al., 1999; Stapleton et al., 2009) those of prior tobacco cessation investigations. Thus, despite suggestions that marijuana use may complicate the tobacco cessation process (e.g., Humfleet & Haas, 2004), evidence that marijuana use as observed among those presenting for tobacco dependence treatment affects the outcome of such treatment is tenuous.

There are several implications of the present research. First, while curtailing alcohol use during a quit attempt should continue to be among the priorities of smoking cessation therapies (Fiore et al., 2008; see Kahler et al., 2008), the current findings indicate for the first time one way how tobacco dependence interventions might aid those who persist in drinking: by providing strategies designed to alleviate positive-reinforcement urge to smoke. Such strategies might include positively reinforcing pleasurable behaviors that replace the use of cigarettes (e.g., the adoption of a new hobby). Second, although greater pretreatment alcohol intake should be recognized as a risk factor for poorer treatment outcome, the mechanisms of this effect remain unknown. Perhaps pretreatment alcohol use was unrelated to change in urge to smoke because pretreatment alcohol use inaccurately approximated drinking behavior across the study period or because the effect of alcohol consumption on smoking urge was muted with concurrent cigarette use. It is possible that pretreatment alcohol intake is related to smoking abstinence because it reflects a generalized risk for substance use conferred by trait vulnerabilities, such as personality characteristics (see Elkins, King, McGue, & Iacono, 2006). Nevertheless, it can only be concluded that more intensive treatment might be warranted among smokers who present with higher levels of alcohol consumption and additional research is needed to determine how these tobacco users might be best assisted. Finally, consistent with the interpretation that most marijuana users do not suffer from its use (Earleywine, 2002), tobacco interventions may not need to concern themselves with this substance, *per se*. However, as the legal status of marijuana changes in conjunction with the stigma surrounding its use, marijuana intake may serve as an easily assessed marker of other behaviors (e.g., cocaine use) known to impact the efficacy of tobacco interventions.

Methodological limitations and other considerations should be weighed when evaluating the current findings. First, source data were collected approximately 10 years ago, challenging the degree to which results can be generalized to the current population of smokers. However, it should be noted that among U.S. adults, the prevalence of cigarette, alcohol, and marijuana use, as well as comorbidity among tobacco and alcohol/drug use, appears to have remained stable over the past 10 years (Guydish et al., 2011; Substance Abuse and Mental Health Services Administration, 2010), and there is no evidence to suggest that the characteristics of treatment-seeking smokers in the United States have changed since the data were collected (e.g., Hughes, 2011). Second, cigarette smokers from the San Francisco Bay

Area, where marijuana drug law enforcement is relatively lenient and lifetime prevalence of marijuana use is 62% (Reinarman, 2009), may not be representative of smokers elsewhere. Third, alcohol and marijuana use in the past 7 days at pretreatment and shortly after cessation may not be representative of larger patterns of use, the number of days in which marijuana was used may be a less than ideal measure of marijuana use behavior (see Temple, Brown, & Hine, 2011), and change in urge between two time points may not be representative of the dynamic pattern of urge over time (see Piper et al., 2011). Real-time techniques may have allowed for a more accurate evaluation of the effects of alcohol and marijuana on tobacco abstinence. Fourth, the distributions of alcohol and marijuana use were skewed, and though categorization of these variables did not meaningfully alter results, the distributions of these variables may have unduly influenced findings. Finally, a number of constructs other than positive-reinforcement urge to smoke were not tested as mediators in the current investigation and may account for the relationship between alcohol intake and abstinence from tobacco (e.g., motivation to quit, abstinence self-efficacy).

Future studies should continue to explore the relationships between alcohol and marijuana use and tobacco cessation treatment outcome across diverse settings and samples of smokers. We advocate that a specific focus be centered on the mechanisms that explain how alcohol and marijuana might affect the process of cessation. In the interim, findings from the current study serve to inform the tailoring of existing tobacco use interventions and in doing so improve their efficacy.

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Declaration of Interests

Dr. Hall has a material grant from Pfizer Pharmaceuticals. Drs. Hendricks, Delucchi, and Humfleet have no competing interests to declare.

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