

Tobacco chippers show robust increases in smoking urge after alcohol consumption

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Abstract

Objective and rationale: Heavy social drinkers often engage in occasional cigarette smoking, especially in the context of consuming large quantities of alcohol. The current study assessed alcohol's effects on smoking urge as a function of alcohol dose and time course in tobacco chippers with heavy social drinking patterns.

Method: The study assessed 39 chippers who underwent three separate evening sessions. Each subject received a placebo (1% volume alcohol as a taste mask), a low alcohol dose (two to three drinks equivalent), and a high alcohol dose (four to five drinks equivalent) in random order. No smoking was permitted during the sessions and the participants were abstinent from smoking for at least 3 h before arrival. Throughout the session, cigarette craving was assessed by the Brief Questionnaire of Smoking Urges and alcohol response was assessed by the Biphasic Alcohol Effects Scale (BAES).

Results: The results showed that alcohol significantly increased cigarette craving in a dose-dependent manner ($p < 0.001$). At the high alcohol dose, craving was heightened during the rising portion of the blood alcohol curve (BAC). There was a strong relationship between BAC and craving for positive reinforcement and this relationship was partially mediated by BAES stimulation, but not sedation.

Conclusions: The findings show that alcohol directly increases smoking urge in chipper smokers. Tobacco chippers may crave cigarettes more during heavier than during lighter drinking bouts, and this effect appears to be driven by heightened stimulation levels rather than as a means to offset alcohol's sedative effects.

Keywords Smoking · Cigarette craving · Brief questionnaire of smoking urges · Alcohol · Tobacco chipper · Light smoker · Stimulation

Introduction

Several studies have established a strong positive association between cigarette smoking and alcohol use. Reports have cited that almost 90% of smokers drink alcohol on a regular basis compared to 60% of non-smokers (Kozlowski and Ferrance 1990), and alcoholism is about ten times more likely to occur among smokers than in non-smokers (DiFranza and Guerrero 1990). Concurrent alcohol and tobacco use contributes to more than half a million deaths each year and is the leading cause of preventable disease and excessive health care costs (Hurt et al. 1996). Despite widespread theories for the direct and indirect causes underlying the covariance between alcohol and cigarette smoking, there is limited direct evidence regarding alcohol's effects on smoking urges. The goal of the current preclinical study was to investigate dose and temporal effects of alcohol on subsequent cigarette smoking urges in regular users of both substances.

In human laboratory studies, alcohol, compared to placebo, acutely increases cigarette smoking in both alcohol-dependent (Griffiths et al. 1976; Henningfield et al. 1983) and non-alcohol-dependent participants (Mitchell

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et al. 1995), as well as in methadone-maintenance patients (Mintz et al. 1985). In terms of time course, alcohol increases cigarette smoking (Mitchell et al. 1995) and smoking urge (King and Epstein 2005) during the interval consistent with the ascending limb of the blood alcohol curve (BAC). Furthermore, studies employing smoking cues (i.e., exposure to a lit cigarette) after alcohol consumption have shown that alcohol increases a participant's ratings of urge to smoke after a moderate to high dose of alcohol (Burton and Tiffany 1997; Sayette et al. 2005), although only one of these studies (Sayette et al. 2005) found that alcohol further augmented craving after the in vivo cigarette cue compared to the neutral cue. A few studies have examined the effects of alcohol on cigarette craving in the absence of acute smoking (Glautier et al. 1996; Mintz et al. 1985) or presentation of in vivo cigarette cues (Burton and Tiffany 1997; Sayette et al. 2005), both of which are likely to confound subsequent craving. As the ascending part of the blood alcohol curve is generally associated with alcohol-induced positive stimulating effects, and the descending part of the curve has been related to feelings of sedation (Martin et al. 1993), understanding smoking urge during both limbs of the blood alcohol curve may help explicate the positive or negative reinforcing properties that promote continued co-abuse.

Another important issue is that prior preclinical research on alcohol–smoking associations has primarily focused on habitual or nicotine-dependent smokers. In terms of assessing alcohol-induced smoking urge, regular heavy smokers may present with high baseline craving levels and/or nicotine withdrawal symptoms, which may confound the precise measurement of smoking urge in the laboratory. Our group recently examined a heterogeneous group of light and moderate smokers (King and Epstein 2005) and the results showed that, compared to placebo, alcohol produced dose-dependent increases in smoking urge. The small sample size ($n=16$) unfortunately precluded subgroup analyses in terms of potential differential sensitivity based on smoking patterns. As tobacco chippers have shown more variability in smoking topography than the dependent smokers (Brauer et al. 1996) and studies examining tobacco chippers have differed in terms of levels of smoking background [averaging from 8.3 cigarettes per week (Davies et al. 2000) to 30.1 cigarettes per week (Shiffman 1989)], it is unclear if there may be diverse subgroups within non-dependent, light smokers. Tobacco chippers are a subgroup of interest as alcohol is the most common environmental cue for smoking among this group (Shiffman et al. 1994). Furthermore, tobacco chippers are unique in that they have been hypothesized to have features that protect them from becoming nicotine dependent (Shiffman 1989).

The current study examined smoking urge in tobacco chippers who were also regular heavy social drinkers before and after consumption of a placebo and a low and high dose of alcohol. The primary goal was to examine if alcohol would produce dose-dependent effects on smoking urge in tobacco chippers and if these effects would be more pronounced during the rising vs declining limb of the BAC. The secondary goal was to compare lighter chippers vs heavier chippers on sensitivity to alcohol-induced smoking urges. The final goal was to examine the association of smoking urge to alcohol-related factors. It was hypothesized that positive-like subjective alcohol effects would mediate the relationship between BAC and smoking urge whereas sedation would be unrelated to BAC and smoking urge.

Materials and methods

Participants

Study candidates were recruited through flyers, advertisements in local Chicago newspapers, web sites, and by word-of-mouth referrals. First-line screening of interested candidates over the telephone employed basic study inclusion criteria: age between 21–35 years, body mass index between 19–30, general good health, no major current medical or psychiatric conditions, and the candidate must have met study inclusion qualifications for alcohol and smoking patterns. This study was part of a larger ongoing investigation, the Chicago Social Drinking Project (CSDP), which examines alcohol response (subjective, performance, and physiological) in social drinkers. Data for this study were extracted from a subset of the heavy drinker group in the CSDP who were also current smokers. Heavy drinking criteria in the larger study included reported consumption of 10–45 alcohol drinks per week, with regular weekly binge episodes (i.e., five or more drinks/occasion; four for females) one to four times per week, to be consistent with prior studies on heavy social drinking (King and Byars 2004; King and Epstein 2005; King et al. 2002). For inclusion in the present study sample, the participants must also have reported smoking one to five cigarettes in 2–7 days per week for at least 1 year. These smoking criteria were expanded from previous studies of tobacco chippers (smoking one to five cigarettes at least 4 days per week; Brauer et al. 1996; Shiffman 1989; Shiffman et al. 1990, 1992, 1994, 1995) to include smokers who smoked two or more days per week (Presson et al. 2002; Sayette et al. 2001). As smoking patterns vary considerably in heavy

social drinkers, the participants were still eligible if they reported smoking up to 15 cigarettes on heavier drinking days but also regularly smoked five or fewer cigarettes on non-alcohol drinking days. Those persons who met the basic criteria were subsequently invited for an in-lab screening session, where they provided photo identification to verify age requirements.

During the in-lab screening, all candidates underwent a physical examination by the resident physician, a pregnancy test (females only), a urine toxicology test, a blood test to examine blood chemistry and liver functioning, and a diagnostic interview. They also completed several psychosocial and health history questionnaires. The questionnaires included the Beck Depression Inventory (Beck et al. 1961), State-Trait Anxiety Inventory (Spielberger et al. 1970), Fagerström Test of Nicotine Dependence (Heatherton et al. 1991), and the Short Michigan Alcoholism Screening Test (Selzer et al. 1975). The diagnostic interview included the screening portion of the Structured Diagnostic Interview for the DSM IV (SCID; First et al. 1995) as well as specific modules for mood and substance use disorders. Using standard cutoff thresholds for the questionnaires, as well as the diagnostic interview and medical examination, the participants were excluded if they were taking any psychotropic medications, had any major medical or psychiatric conditions, including past or current alcohol or substance dependence (history of alcohol abuse permitted), or a positive urine toxicology screening (except for marijuana). Persons with alcohol and nicotine dependence were excluded to avoid potential complications of alcohol and nicotine withdrawal during the sessions. Females were excluded if they were pregnant (assessed at screening and before each session), breastfeeding, or did not show evidence of adequate birth control.

The in-person screening also included interviews to assess for alcohol and smoking patterns using the Quantity–Frequency Index Interview (QFI; Cahalan et al. 1969), the nicotine dependence module of the SCID (First et al. 1995), and the Timeline Follow-Back (TLFB; Sobel and Sobel 1995; Sobel et al. 1979). The TLFB assessed the participants' recollection of daily drinking and smoking behavior over the previous 28-day period. Based on data from the larger Chicago Social Drinking Project study, out of the 112 individuals who were rejected during the in-person screening (i.e., before enrollment), 33.9% ($N=38$) of individuals were excluded based on their drinking patterns, 22.3% ($N=25$) were excluded for having a positive urine toxicology or meeting criteria for alcohol and/or drug dependence, 22.3% ($N=25$) were excluded for meeting criteria for a psychiatric condition, 10.7% ($N=12$) were excluded because they were not interested in participating in the study, and 10.7% ($N=12$) were excluded for medical reasons or high body mass index.

Procedure

During the screening session, the participants signed informed consent, which was approved by the University of Chicago Institutional Review Board (IRB). To control for alcohol expectancies acting as a cue for smoking urge, the participants were informed that they might receive a stimulant, sedative, alcohol, or placebo (Martin and Sayette 1993). All participants actually underwent a placebo session (1% volume of ethanol as a taste mask), a low-alcohol-dose session (0.4 g/kg; 8% volume alcohol), and a high-alcohol-dose session (0.8 g/kg; 16% volume alcohol) in random order. The drinks were prepared with Kool-Aid, water, Nutrasweet, and the appropriate dose of 190-proof ethanol based on body weight. Adjustments were made for women to receive an approximate 90% dose of that for men due to differences in total body water affecting blood alcohol concentrations (Frezza et al. 1990; Sutker et al. 1983). A separate coder prepared the beverages so that the research assistant was kept blind to the beverage content.

The participants completed three early evening 4- to 5-h laboratory sessions, which were conducted in a room with a sofa and chairs to resemble a living room environment. Sessions were separated by at least 48 h. The participants were asked to abstain from alcohol and recreational drugs 48 h before each session, as well as caffeine, food, and cigarettes 3 h before each session. The participants were interviewed upon study arrival to assess their compliance with the alcohol, drug, caffeine, food, and smoking abstinence requirements, along with objective carbon monoxide (CO) verification (Smokerlyzer, Bedfont Scientific, Medford, NJ, USA). The 3-h time interval of smoking abstinence was chosen to maintain a minimal level of smoking deprivation for all participants.

Each participant arrived at the laboratory between 15:00 and 17:00 hours and underwent a urine toxicology screen, pregnancy test (if female), and breathalyzer test. The participants were excluded if their baseline blood alcohol levels were greater than 0.003 ($N=0$) or if pregnancy or urine toxicology tests (except for marijuana) were positive ($N=0$ positive pregnancy, $N=1$ positive urine toxicology). After the participant completed pre-session measures, s/he consumed a low-fat snack (20% daily calories) to avoid hunger effects on mood state and to help reduce the potential for alcohol-induced nausea. At 30 min post-arrival, the participant completed baseline questionnaires and objective measures (CO tests).

At approximately 45 min post-arrival, the participant consumed the allocated beverage through a straw in an opaque cup to help conceal the scent and identification of the alcohol content. The participant drank the beverage over a 15-min interval in the presence of the research assistant and then completed the subjective measures and breathaly-

zer readings at 15 and 45 min (rising limb) and at 105 and 165 min (declining limb) after completion of the beverages. Similar beverage administration procedures have been used in the past and have shown reliable rising and declining blood alcohol curves across participants (King and Byars 2004; King and Epstein 2005; King et al. 2002). After completing the subjective scales, the participant engaged in various performance and objective tests as part of the larger study. The second and third sessions were identical to the first session with the exception of beverage alcohol content. The participant was allowed to read or watch selected videos during the times when study measures were not being obtained. At the end of each session, the participant was transported home by a delivery service to ensure his/her safety. The participant was debriefed at the end of the study and received a check for US\$200 (\$50 per session plus a \$50 bonus) within 2 weeks after study completion.

Measures

The main dependent measure was the ten-item Brief Questionnaire of Smoking Urges (BQSU; Cox et al. 2001). Each statement is scored on a Likert scale from 1 (strongly disagree) to 7 (strongly agree), where higher scores indicate stronger smoking urges. In addition to a total score, the BQSU has two factor-derived subscales: factor 1 reflects desire to smoke for reward, and factor 2 reflects urge to smoke to relieve negative affect or nicotine withdrawal. The BQSU has established reliability within controlled laboratory settings and has been shown to have the advantage of capturing multidimensional features of craving compared to a single-item craving rating (Cox et al. 2001). However, as some research designs may preclude the use of multiple-item scales (i.e., imaging studies), the single item within the BQSU (item 1: “I have a desire for a cigarette right now.”) was examined separately in an exploratory analysis to determine its sensitivity to alcohol-induced cigarette craving.

The secondary measure was the Biphasic Alcohol Effects Scale (Martin et al. 1993), a 14-item adjective rating scale that consists of Stimulation and Sedation subscales. Each adjective item is scored on an 11-point scale from 0 (not at all) to 10 (extremely), where higher scores indicate greater levels of stimulation and sedation. The Stimulation scale includes the sum of: elated, energized, excited, stimulated, talkative, up, and vigorous. The Sedation scale is comprised of: down, heavy head, difficulty concentrating, inactive, sedated, slow thoughts, and sluggish. The BAES has been validated to yield higher stimulation scores during ascending BACs and higher sedation scores during descending BACs (Martin et al. 1993). The participants were also asked a beverage discrimination question, (“Do you think you received a

sedative, stimulant, alcohol, or placebo?”) at 15 min (rising limb) and 165 min (declining limb) after drink consumption. Finally, BAC readings at baseline were measured by the Alco-Sensor III (Intoximeter, St. Louis, MO, USA), and during the session by the Alco-Sensor IV breathalyzer. The Alco-Sensor IV displays readings of 0.000 regardless of alcohol content, with the true values stored and later downloaded to a computer.

Statistical analyses for primary measures

BQSU and BAC measures were analyzed using repeated-measures analyses of variance (ANOVA), with dose (placebo, low dose, and high dose) and time (baseline, and 15, 45, 105, and 165 min after drink consumption) as within-subject factors. Consistent with a priori hypotheses, simple effects tests were performed to examine differences across dose and limb for each significant interaction. As BAES scores were not the main dependent measures in this study, the results from this measure are only described in the context of mediating-variables analyses.

Results

Participant characteristics

The final sample consisted of 39 participants (22 men, 17 women). The details on participant demographics are displayed in Table 1.

Main outcome measures

As expected, alcohol increased BAC levels in a dose-dependent manner [dose \times time; $F(10, 340)=312.88$, $p<0.001$]. Figure 1 depicts the breathalyzer readings and shows that, particularly for the high dose, BACs peaked rapidly by 45 min after alcohol consumption and slowly declined during the descending limb.

As seen in Fig. 2, alcohol increased smoking urge (BQSU total scores) in a dose-dependent manner [dose \times time; $F(8, 304)=12.76$, $p<0.001$]. Comparisons of smoking urge across doses showed that the high alcohol dose produced the greatest urges, the low dose produced intermediate urges, and placebo beverage produced no changes in smoking urges (high $>$ low $>$ placebo, simple effects; $p<0.005$; T15–T105). Both the high and low alcohol dose increased initial smoking urge at 15 min ($p<0.001$, T0–T15), whereas the placebo beverage did not affect smoking urge over time. While the high dose produced sharp increases in smoking urge that declined steadily after the rising limb ($p<0.005$), the low dose

Table 1 Participant characteristics (*n*=39)

General	
Age (years)	25.0 (3.3)
Sex (male)	22 (56.4%)
Race (Caucasian)	32 (82.1%)
Education (years)	15.8 (1.4)
BMI (kg/m ²)	25.1 (3.2)
Smoking behavior	
FTND	0.4 (0.9)
Smoking days/week	3.5 (1.9)
Cigarettes/smoking day	4.9 (2.6)
Total cigarettes/week	21.1 (17.4)
Smoking duration (years)	6.3 (3.5)
Daily smokers	7 (17.9%)
Drinking behavior	
Drinking days/week	3.3 (1.0)
Alcohol drinks/drinking day	6.6 (5.0)
Total drinks/week	20.7 (11.1)
Binges ^a per month	9.7 (4.4)
Lifetime alcohol abuse	17 (43.6%)
Smoking/drinking co-use ^b	
Cigarettes on a non-drinking day	1.3 (2.1)
Cigarettes on a light drinking day	2.7 (2.9)
Cigarettes on a binge drinking day	5.8 (3.9)

Data presented are Mean (SD) or N (%), where indicated
BMI Body mass index, *FTND* Fagerström Test for Nicotine Dependence

^a Binge—five or more drinks per drinking occasion, four for females (obtained from QFI)

^b Drinking and smoking combination based on a 28-day TLFB assessment; light drinking day—one to four drinks per occasion for men, one to three drinks per occasion for women; binge drinking day—five or more drinks per occasion for men; four or more drinks per occasion for women

initially increased urge ratings and these remained at a consistent intermediate level throughout the BAC.

Secondary analyses of the factors that comprise the BQSU total showed that alcohol increased smoking urges for both positive reinforcement [factor 1 dose × time, $F(8, 304)=11.23, p<0.001$] and negative reinforcement [factor 2

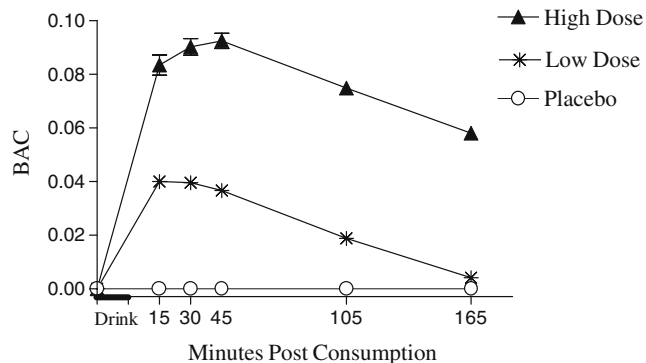


Fig. 1 Blood alcohol curve. The results show the BAC at the pre-drink baseline and at 15, 30, 45, 105, and 165 min after drink consumption

dose × time, $F(8, 304)=9.18, p<0.001$]. Although overall smoking urges were of a greater magnitude for factor 1 than for factor 2, for both factors alcohol increased smoking urge in a linear dose-dependent manner (high > low > placebo). Additional exploratory analyses revealed that alcohol dose-dependently increased ratings for the single item within the BQSU (item 1: “I have a desire for a cigarette right now”) [dose × time, $F(8, 304)=7.21, p<0.001$]. Alcohol increased the BQSU total score by 75% (baseline 18.7 to peak 32.7) compared to the single item which increased by 67% (baseline 2.4 to peak 4.0)]. The remaining analyses focus on BQSU Total scores as this was the primary outcome measure.

As the sample was comprised of a heterogeneous group of tobacco chippers, a median split was conducted to dichotomize heavier tobacco chippers (individuals who smoke at least 20 cigarettes per week, $N=19$) and lighter chippers (individuals who smoke 2–19 cigarettes per week, $N=20$) on smoking urge (BQSU total). As seen in Fig. 3, a repeated-measures ANOVA with smoking group as a between-subjects factor showed that the high alcohol dose increased smoking urge for both groups, whereas the low dose only increased smoking urge in the light chippers [group × dose × time, $F(8, 296)=2.38, p<0.05$]. As expected, overall smoking urge was greater for the heavy chippers compared to the light chippers [$F(1, 37)=12.92, p<0.001$].

Beverage identification ratings during the rising and declining BAC limbs were largely similar for any given dose (average 35 and 36% incorrect beverage guessing, respectively). For ease of presentation and to be consistent with prior studies assessing alcohol identification, further analyses were conducted using only the latter interval. The results showed that, in the placebo session, 36% ($N=14$ of 39) of participants were incorrect in their beverage identification (i.e., guessing that they received something

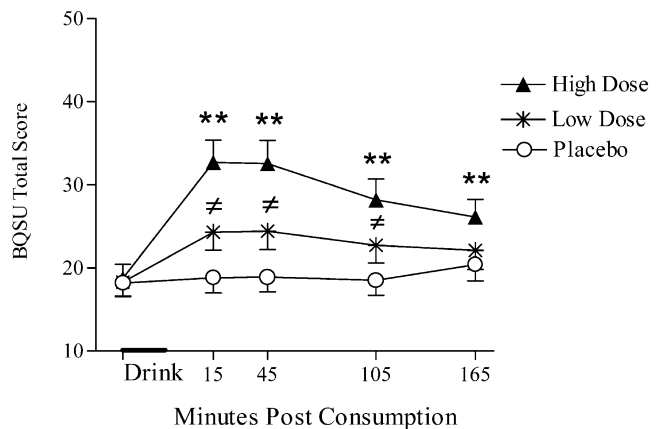
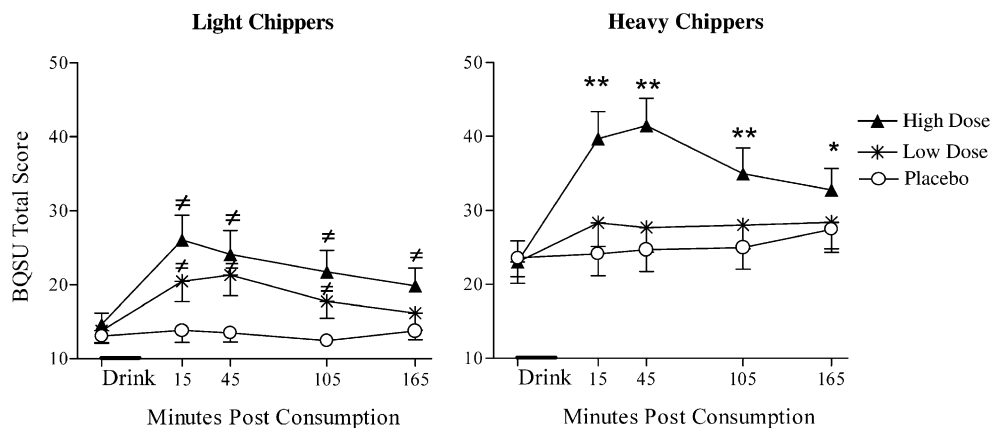


Fig. 2 Brief Questionnaire of Smoking Urges total. High alcohol dose 0.8 g/kg (approximately four to five drinks equivalent) and low dose 0.4 g/kg (approximately two to three drinks equivalent). † $p<0.05$, represents significantly greater than placebo beverage; ** $p<0.01$, represents significantly greater than both low-dose and placebo beverages

Fig. 3 Brief Questionnaire of Smoking Urges total in light vs heavy tobacco chippers. High alcohol dose 0.8 g/kg (approximately four to five drinks equivalent) and low dose 0.4 g/kg (approximately two to three drinks equivalent). $\#p<0.05$, represents significantly greater than both low-dose and placebo beverages; $*p<0.05$, $**p<0.01$, represents significantly greater than placebo beverage



other than placebo), compared to 51 and 21% who were incorrect in identifying the low- and high-dose sessions, (i.e., guessing that they received a placebo, sedative, or stimulant), respectively. Exploratory analyses of beverage content identification as a between-subjects factor revealed no differences between these groups in their degree of alcohol-induced smoking urge [$F(4, 148) < 2.32, p = ns$].

Mediating variables

Following the model of Baron and Kenny (1986), analyses examined whether alcohol subjective stimulation and/or sedation mediated the relationship between BAC and craving (BQSU total). This was done by testing the indirect (mediated) effect using the Sobel (1988) procedure, as reviewed in MacKinnon et al. (2002). As craving was most heightened during the high alcohol dose, the relationships among variables were examined only during the high-dose session. There were 4 out of the 39 participants who were excluded because they failed to report any desire to smoke throughout the sessions and therefore would have negatively skewed the distribution of craving scores. Similar exclusion procedures have been used in other pharmacology study analyses with non-responders (e.g., Kouri et al. 2004). Craving values were transformed to change scores from baseline so that the alcohol's effects on craving could be isolated. To examine how these variables are related as they change over time within each participant, the data were analyzed using hierarchical linear modeling (HLM; Bryk and Raudenbush 1992). BAC, stimulation, and sedation were evaluated as random variables so that there was essentially a separate regression for each person. The "average" regression coefficients and standard errors across all participants are the fixed effects in the HLM model and were used in the mediation analyses.

BAES stimulation and sedation were examined as potential mediators in the relationship between BAC and smoking urge. First, BAC significantly predicted craving

($B=158.0, SE=44.2, p<0.001$). Second, BAC significantly predicted stimulation ($B=257.5, SE=66.3, p<0.005$) but not sedation ($B=44.4, SE=61.2, p=0.47$). Because the predictor BAC was not related to the potential mediator sedation, the subsequent analyses consider only stimulation as a potential mediator (Fig. 4). Finally, when stimulation and BAC were included in the regression, the direct effect of BAC on craving decreased but was still significant (from $B=158.0$ to $B=120.4, SE=41.3, p<0.01$), and the indirect effect of BAC through stimulation to craving was also significant ($B=41.0, SE=20.4, p<0.05$). Stimulation accounted for 26.0% (41.0 of 158.0) of the total relationship between BAC and craving.

Thus, these findings indicate that the relationship between BAC and craving was partially mediated by stimulation but not by sedation. Furthermore, additional analyses were conducted to examine between-persons differences and showed that high stimulators (based on a median split of BAES stimulation scores) reported significantly higher craving scores than low stimulators during the high-dose session [$group \times time F(4, 148)=4.55, p<0.005$]. Therefore, both within-subject and between-subjects analyses support the strong positive relationship between level of alcohol subjective stimulation during heavy alcohol drinking and corresponding smoking urge.

Discussion

The findings of the present study show that both a relatively low (two to three drinks equivalent) and high (four to five drinks equivalent) amount of alcohol can produce robust increases in urges to smoke in tobacco chippers who are heavy social drinkers. Comparisons across doses showed that the high alcohol dose produced the greatest increases in smoking urge for both positive and negative reinforcement compared to the low dose and placebo beverage. The light tobacco chippers also appear to be more sensitive to lower

doses of alcohol compared to the heavy chippers. These results replicate the main findings of our prior study (King and Epstein 2005) showing dose-dependent effects of alcohol on smoking urge in the absence of in vivo smoking cues, and extend them in several ways. First, assessing craving more frequently throughout the session showed that craving levels, in fact, peaked very early in the drinking episode (i.e., at 15 min). Second, sharp alcohol-induced increases in smoking urges were found in the present study in a well-characterized, diverse group of light smokers. These findings show that alcohol has profound effects on the desire to smoke in both occasional and more regular non-dependent smokers. Finally, an increased sample size allowed for more specified analyses of mediation results, which indicated that alcohol stimulation, rather than sedation, mediates the relationship between acute alcohol drinking and cigarette craving.

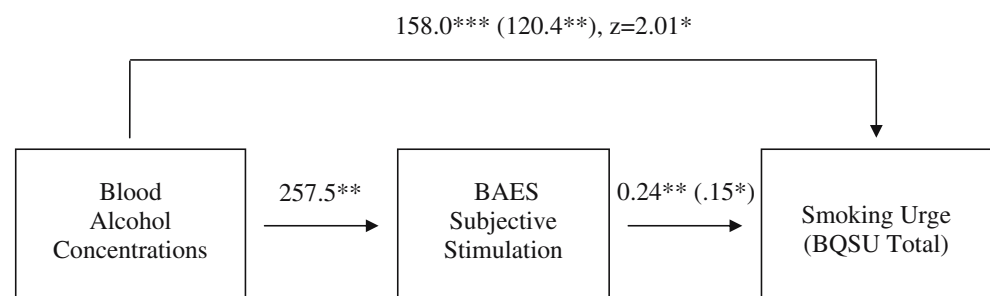
These laboratory findings support the premise that non-dependent smokers who regularly binge drink may be habitually exposing themselves to situations in which they are likely to crave cigarettes and therefore may be at risk for escalation of their smoking behavior. Although these tobacco chippers reported low pre-drink baseline smoking urges (mean=18.7; scale range=10–70), after alcohol consumption their smoking urge scores increased to levels (mean=26.1) comparable to that reported in minimally deprived regular smokers (Epstein et al., 2006, unpublished data). As craving is considered to be one of the hallmarks of addiction and often precedes increases in smoking behaviors and relapse (Killen and Fortmann 1997; Shiffman et al. 1997), it is conceivable that heavy drinkers who show heightened cigarette cravings during their drinking episodes may be at increased risk to show progression of smoking over time and/or potentially develop nicotine dependence. Smoking behavior may also be related to greater risk for continued binge drinking and render such persons at heightened risk for progression to alcohol dependence over time. Light smokers have higher risks of dying from ischemic heart disease (in both sexes) and from lung cancer

(in women) compared to non-smokers (Bjartveit and Tverdaln 2005). Therefore, there is no safe level of cigarette smoking, especially if their concurrent substance use increases over time.

Blinding participants to alcohol dose condition was performed in the present study to minimize expectancies about the drug (Kirsch 1997). If smoking urge increases were only apparent in participants who correctly identified alcohol and not in those who could not discriminate alcohol, then this would have supported the notion that alcohol cues or expectancies may be a main factor underlying alcohol-induced smoking urges. However, alcohol increased smoking urges similarly in subjects who were alcohol discriminators and nondiscriminators. Although alcohol placebos have certain limitations (Martin and Sayette 1993) and the current paradigm cannot completely eliminate all alcohol cues inherent in an oral dose (i.e., taste, smell, etc.), the data do support that the pharmacological properties of alcohol in the central nervous system, rather than a paired-associate mechanism, may be playing a key role in alcohol-induced cigarette craving. The data also show that a single item of smoking urge (item 1: “I have a desire for a cigarette right now.”) yielded similar results as the full BQSU scale. Therefore, although a single item measuring cigarette craving would lack the multidimensional nature of craving for positive and negative reinforcement, studies with experimental constraints on time or measurement choice may be able to validly measure alcohol’s effects on cigarette craving using a single item, if necessary.

Although this study was not a treatment trial, there are some potential clinical implications of the data. First, because both low and high doses of alcohol increased smoking urges, persons desiring to quit or reduce smoking may be well advised to refrain from alcohol drinking altogether. As the higher dose produced more profound increases in smoking urge, such individuals could at least reduce harm or relapse potential by alternatively choosing beverages with lower alcohol contents or consuming their

Fig. 4 Model for the association of blood alcohol concentrations and smoking urge, mediated by subjective stimulation. The values outside the parentheses are unstandardized coefficients obtained from the HLM-based mediation model which represent the total effects; the values inside the parentheses are the effects after controlling for the other independent variable in the model. The z value is the test of the indirect effects of BAC on smoking urges through the mediator. *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$



drinks at a slow pace. Second, in the absence of potent cues, alcohol-related smoking urges appear to be transient, so patients could be advised that urge increases will dissipate within the first few hours after drinking, i.e., when their BACs decline. However, the results cannot be extrapolated to extended binge drinking over longer periods or to BACs higher than 0.08–0.09, and it remains to be determined whether or not smoking urge is further increased under such circumstances.

Some limitations should be noted. First, although the findings in the current study showed clear evidence of alcohol dose-dependent increases in smoking urge in tobacco chippers, these findings may not apply to a heavy-smoking and/or nicotine-dependent population who often show high baseline craving levels. While a recent study found that alcohol increased smoking urge in heavy smokers (Sayette et al. 2005), preliminary data by our group in a small sample ($N=7$) of regular smokers (>10 cigarettes per day) show that alcohol does not increase smoking urge beyond that of placebo in a minimally deprived state (Epstein et al. 2006, unpublished data). However, our preliminary data differ from Sayette's in that we required a shorter period of smoking abstinence (3 vs 12 h), used a different measure of smoking urge (BQSU vs a 100-point rating scale), eliminated smoking cues, and examined regular smokers of a lower smoking threshold (>10 cigarettes per day vs ≥ 20 cigarettes per day). Second, as the present study indicated that alcohol subjective stimulation partially mediates the relationship between alcohol and smoking urges, it remains to be determined whether our findings would apply to lighter drinkers who have been shown to have significantly lower levels of alcohol subjective stimulation than heavy drinkers (King et al. 2002). Finally, the current study results may not generalize to "real-world" settings such as smoking bars or restaurants as we eliminated olfactory and visual smoking cues that have been demonstrated to elicit potent cigarette craving (Burton and Tiffany 1997; Sayette et al. 2005). However, the fact that alcohol directly increased smoking urges in an environment without in vivo smoking cues may have particular relevance to the increasing number of "smoke-free" cities, states, and countries that have been gaining momentum in recent years.

In sum, these findings lend support for a direct, alcohol-induced pharmacological mechanism underlying smoking urge after drinking in light, non-dependent smokers. The results also suggest that tobacco chippers may crave cigarettes more during heavier than lighter drinking bouts. Cigarette cravings were partially mediated by heightened subjective stimulation levels but not mediated by alcohol's sedative effects. This finding suggests that individuals may crave cigarettes during heavy drinking episodes to enhance the reinforcing stimulating properties of alcohol, rather than

as a means to offset alcohol's sedative or unpleasant effects. Therefore, individuals who exhibit heightened alcohol stimulation may be at risk for both continued binge drinking (King et al. 2002) as well as robust cigarette cravings, creating a potential reinforcement loop underlying the co-misuse of these substances. Longitudinal studies may provide clues to understanding the role of alcohol's direct effect on smoking urges and behavior and the potential trajectories from non-dependent, occasional use of both substances to addiction propensity.

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