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Differences Between Daily Smokers, Chippers, and Nonsmokers With Co-occurring Anxiety and Alcohol-Use Disorders

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Abstract

Tobacco use is disproportionately represented among both alcohol-use disorders (AUDs) and anxiety disorders (ANX) compared to the general population (Kalman et al., 2005). Despite this common overlap, little is known about how smokers with co-occurring AUD-ANX differ from their nonsmoking counterparts. Seventy-two patients participated in a larger clinical trial evaluating the efficacy of venlafaxine and cognitive-behavioral therapy for AUD-ANX. Differences between daily smokers ($n = 23$), chippers ($n = 12$) and nonsmokers ($n = 37$) with AUD-ANX were examined with respect to intensity and frequency of alcohol use, anxiety symptoms, depressed mood, and stress. Point prevalence of current daily smoking was 31.9%, which is considerably lower than traditionally reported in AUD studies. Consistent with predictions, daily smokers reported higher levels of alcohol dependence, average drinks per drinking occasion, and peak blood concentration levels in a day than nonsmokers during the 90 days prior to assessment. Chippers were nonsignificantly different from either smokers or nonsmokers. Smokers and nonsmokers did not differ with respect to percent heavy drinking days or emotional symptoms.

Keywords

tobacco; smoking; alcohol; anxiety disorders

1. Introduction

Compared to the general population, tobacco use is disproportionately represented among both alcohol-use disorders (AUDs) and anxiety disorders (ANX; Kalman et al., 2005; Morissette et al., 2007). Among those with AUDs, estimates of tobacco use are as high as 71–97% (Monti, Rohsenow, Colby & Abrams, 1995). Individuals with AUDs smoke more cigarettes than those

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without AUDs (Marks et al., 1997) and are at increased risk for becoming tobacco dependent (Kozlowski & Ferrence, 1990). Current smokers also have more severe alcohol dependence (Daepfen et al., 2000).

With respect to the anxiety disorders, smokers with anxiety disorders have more severe emotional symptoms than nonsmokers (McCabe et al., 2004; Morissette, Brown, Kamholz & Gulliver, 2006; Zvolensky, Schmidt & McCreary, 2003). Specifically, among patients *without* co-occurring AUDs or substance disorders, Morissette et al. (2006) found that smokers with anxiety disorders had greater levels of anxiety sensitivity, anxiety symptoms, agoraphobic avoidance, depressed mood, negative affect, stress, and life interference compared to nonsmokers. However, effect sizes were small and significant effects were primarily related to panic disorder (PD).

Correspondingly, elevated rates of AUDs have been found among those with anxiety disorders (Otto, Pollack, Sachs, O'Neil & Rosenbaum, 1992; Thyer et al., 1986). Rates of AUDs are as high as 29–37% among the anxiety disorders (Petrakis, Gerardo, Gonzalez, Rosenheck, & Krystal, 2002) with the greatest likelihood of having an AUD found among those with PD and generalized anxiety disorder (GAD; Grant et al. 2004). Generally, patients with co-occurring anxiety disorders and AUDs describe worse anxiety (Chambless et al., 1987). The presence of anxiety and depressive disorders is associated with moderate increases in symptoms of alcohol abuse or dependence, particularly among those with PD; conversely, AUDs have little influence on phobic disorder symptoms (Swendsen et al., 1998). Although alcohol can provide short-term relief of anxiety symptoms, the long-term repercussions may ultimately lead to greater severity of anxiety and problem drinking (Brady, Tolliver & Verduin, 2007; Kushner, Sher & Beitman, 1990).

Collectively, these data suggest that tobacco use, alcohol use and anxiety disorders are overlapping and potentially interwoven disorders. Understanding the relative contribution of tobacco use to the expression of alcohol and anxiety symptoms has both theoretical and clinical relevance. Specifically, conditioning theory maintains that this diagnostic trifecta has the potential for cross-conditioning of drug- or anxiety-related cues that may in turn trigger further drug use, anxiety symptoms, or both, with context-specific retrieval of learning and behavior (Bouton, 1994).

Patient characteristics, such as anxiety sensitivity (AS), may also contribute to differential responses to anxiety and drug cues. AS refers to the belief that anxiety-related symptoms have inherent negative somatic, mental, or social consequences (Reiss, 1991) and is often elevated within the anxiety disorders (Taylor, Koch, & McNally, 1992). AS mediates the relationship between some anxiety disorders (i.e., PTSD) and heavy drinking (Stewart, Conrod, Samoluk, Pihl, & Dongier, 2000). Novak and colleagues (2003) further demonstrated that although AS did not directly affect alcohol and tobacco consumption, it had a direct influence on coping-related drinking and moderated the relationship between smoking level and mood-related motives to smoke. Pathways have also been proposed to explain the relationship between AS and the development of panic disorder and smoking, and suggest that sensitivity to fear arousal-based bodily sensations may increase risk for panic disorder and heighten motivation to escape distressing sensations and negative affect through smoking (Zvolensky et al., 2003b). Taken together, these data highlight the importance of understanding patient characteristics, such as AS, which may affect interactions among these diagnostic conditions.

Despite the overlap among these conditions, little is known about the contribution of tobacco use to the co-occurrence of AUDs and anxiety disorders (AUD-ANX). The purpose of the current study was to expand findings by Morissette et al. (2006) to evaluate differences between smokers and nonsmokers with co-occurring AUD-ANX. Differences between daily smokers,

chippers (i.e. nondaily tobacco users) and nonsmokers with AUD-ANX were examined with respect to alcohol-use behavior, alcohol dependence, AS, anxiety symptoms, depressed mood and stress. These variables were selected to evaluate whether smokers and nonsmokers differed with respect to key variables that could theoretically affect outcomes (e.g., worse alcohol or anxiety symptoms). It was hypothesized that, compared to nonsmokers and chippers, daily smokers would be more dependent on alcohol, and exhibit a greater percentage of heavy drinking days, higher blood alcohol concentration during drinking days (measuring peak intoxication), and a lower percentage of days abstinent. Daily smokers were also hypothesized to have higher AS, anxiety symptoms, depressed mood and stress, but effect sizes were expected to be small.

2. Methods

2.1. Participants and Procedures

The sample included 80 outpatients who participated in a larger placebo-controlled clinical trial designed to evaluate the efficacy of venlafaxine, combined with cognitive-behavioral therapy (CBT), for co-occurring AUD-ANX. Participants were recruited using a variety of media strategies, including radio, web and newspaper. Individuals who expressed interest were provided with information about the nature of the study over the telephone and underwent a short screening to determine initial eligibility. Eligible individuals then completed an extensive assessment of alcohol and emotional symptoms followed by two to four sessions of motivation enhancement therapy (MET; Miller et al., 1994) for the treatment of AUD. A second baseline assessment was conducted subsequent to MET and after achievement of at least four days of alcohol abstinence. During this assessment participants completed additional self-report measures, and a clinical interview verified that the anxiety disorder was not alcohol-induced.

Participants who met final eligibility criteria were randomized to one of four treatment conditions: individualized state-of-the-art CBT targeting the primary anxiety disorder plus venlafaxine; CBT plus placebo; relaxation control plus venlafaxine; or relaxation control plus placebo. The focus of this report is on the two baseline assessments, which captured information on tobacco use, DSM-IV (American Psychological Association, 1994) diagnoses of AUDs and anxiety disorders, and associated features via self-report measures.

2.1.1. Inclusion/Exclusion Criteria—Male and female participants, age 18–65, who had co-occurring AUD-ANX were included. Participants were required to meet DSM-IV criteria for alcohol abuse or dependence and DSM-IV criteria for PD with or without agoraphobia, GAD, or social anxiety disorder (SAD). These anxiety disorders were selected based on a review of the literature regarding the hypothesized efficacy of CBT and venlafaxine to be tested as part of the clinical trial. Participants needed to express a desire to completely stop drinking alcohol or reduce alcohol consumption with the possible long-term goal of abstinence.

Participants were excluded if they had DSM-IV diagnoses of bipolar disorder, schizophrenia, bulimia/anorexia, dementia, or a history of psychotic symptoms, severe depression, or suicidal behaviors within the past 30 days. Participants with current or recent (past 30 days) DSM-IV diagnoses of other substance-dependence disorders (with the exception of nicotine, marijuana, and caffeine dependence) were excluded. Aside from these exceptions, other co-occurring diagnoses were allowed.

In keeping with a clinical trial investigating the utility of venlafaxine, participants who had previously used a therapeutic dose of venlafaxine were ruled out. Current use of anti-craving agents, medications known to reduce alcohol consumption, medications with known abuse potential (e.g., opioid agonist therapy), medications (or herbal supplements) with clinically-significant interactions with venlafaxine, other anti-depressant or anti-anxiety medications

were prohibited. Medical contraindications for the use of venlafaxine included severe renal disease, cirrhosis, uncontrolled blood pressure, recent cardiovascular problems (e.g., heart attack), and seizure disorders, or current use of a monoamine oxidase inhibitor.

Participants were not permitted to participate if they were pregnant, breastfeeding, planning to become pregnant during the study, or not using a medically-acceptable form of birth control. Participants could not have plans to relocate out-of-state within four months of protocol initiation. Participants who were legally mandated to participate in an alcohol treatment program were not eligible.

The final sample included 80 participants, but self-reported smoking status was known for 72. Thus, 72 are reported here. Participants self identified as daily tobacco users ($n = 23$), chippers ($n = 12$) or current nonsmokers ($n = 37$). Sixty-seven were diagnosed with alcohol dependence and 5 with alcohol abuse. Eight (11.1%) participants carried clinical diagnoses of PD, 39 had SAD (54.2%), and 55 (76.4%) had GAD. (Percents do not add up to 100% because of overlap in diagnoses within participants.) By definition all participants carried at least two diagnoses (AUD-ANX), however participants had up to six clinical diagnoses (excluding tobacco dependence, which was not assessed). Specifically, 20.8% had two, 45.8% had three, 26.4% had four, 2.8% had five, and 2.8% had six clinical diagnoses. Nonsmokers, chippers, and daily smokers differed significantly with respect to number of additional diagnoses [$F(2, 68) = 5.9, p < .01$]. Daily smokers ($M = 3.7$) reported significantly more clinical diagnoses on average than nonsmokers ($M = 2.9$; see Table 1). A tendency ($p = .06$) was observed for daily smokers to report more clinical diagnoses than chippers. The most commonly occurring clinical diagnosis was a mood disorder (61.2%).

Measures

Participant diagnoses were assessed by diagnostic interview using the Anxiety Disorders Interview Schedule – IV: Lifetime Version (ADIS-IV-L; DiNardo, Brown, & Barlow, 1994), which has good to excellent diagnostic agreement (Brown, DiNardo, Lehman, & Campbell, 2001). Self-report measures were selected to target core characteristics of AUDs and the anxiety disorders studied (PD, SAD and GAD), as well as general measures of negative affect and stress.

2.2.1. Form 90 AIR—(Project MATCH Research Group, 1996). The Form 90 employs the TimeLine-Follow-Back (TLFB; Sobell and Sobell, 1992) method for gathering a retrospective account of daily drinking in the previous 90 days. From this calendar of daily drinking, percent days abstinent, percent heavy drinking days (4+ drinks/day for women; 5+ drinks/day for men; NIAAA, 2004; Wechsler & Austin, 1998), and peak blood alcohol concentration (BAC) levels per drinking occasion were calculated. The Form 90 also assesses tobacco use, including average cigarettes smoked per day and time in minutes from waking to first cigarette. As this study was primarily a study of AUD-ANX, more detailed information of smoking characteristics was not collected.

2.2.2. Alcohol Dependence Scale—(ADS; Skinner & Allen, 1982). The ADS is a 25-item self-report instrument designed to assess severity of alcohol dependence (e.g., items evaluate withdrawal symptoms, blackouts, etc.). The ADS has good internal consistency ($\alpha = 0.92$; Davidson, 1987) and test-retest reliability. Higher scores indicate more severe alcohol dependence.

2.2.3. Anxiety Sensitivity Index—(ASI; Reiss, Peterson, Gursky, & McNally, 1986). The ASI contains 16 items that measure fear of physical symptoms of anxiety on a scale from 0 (very little) to 4 (very much) (e.g., “It is important for me not to appear nervous”). The ASI has

three subscales, including physical (ASI-PHYS), mental (ASI-MENT), and social (ASI-SOC) concerns (Zinbarg et al., 1997). The ASI has high internal consistency and test-retest reliability (Peterson & Heilbronner, 1987; Reiss et al., 1986). Total scores range from 0 to 64, with higher scores indicating more AS. Subscale scores range from 0 to 32 (ASI-PHYS) and 0 to 16 (ASI-MENT, ASI-SOC).

2.2.4. Depression Anxiety Stress Scales—(DASS; Lovibond & Lovibond, 1995). The DASS includes 42 items with three empirically-distinct subscales: Depression (DASS-DEP; e.g., “I felt sad and depressed”), Anxiety (DASS-ANX; e.g., “I felt scared without any good reason”) and Stress (DASS-STR; e.g., “I found myself getting upset by quite trivial things”). Good discriminant validity and internal consistency has been established in those with anxiety and mood disorders (Brown et al., 1997). Higher scores indicate greater depression, anxiety and stress (scores on each subscale range from 0 to 42).

2.2.5. Albany Phobia and Panic Questionnaire—(APPQ; Rapee, Craske & Barlow, 1995). The APPQ includes 27 items assessing anxiety focused on activities and situations that trigger panic-related sensations. Situations are rated on a scale from 0 (no fear) to 8 (severe fear). Three subscales are derived: interoceptive sensations (APPQ-I; e.g., “Playing a vigorous sport on a hot day”), agoraphobia (APPQ-A; e.g., “Going through a car wash”), and social anxiety (APPQ-S; e.g., “Talking to people”). Higher scores indicate more symptoms with scores ranging from 0 to 64 for the APPQ-I, 0 to 72 for the APPQ-A, and 0 to 80 for the APPQ-S. High levels of factor determinacy, scale reliability and concurrent validity have been found (Brown, White & Barlow, 2005).

2.2.6. Social Interaction Anxiety Scale—(SIAS; Mattick & Clark, 1998). The SIAS evaluates social interaction anxiety. Items are rated on a 0 (not at all true of me) to 4 (Extremely true of me) scale (e.g., “I am at ease meeting people at parties, etc”). This measure has high internal consistency and test-retest reliability, and good convergent and discriminant validity (Mattick & Clarke, 1998). Higher scores indicate greater social anxiety (total scores range from 0 to 80).

2.2.7. Penn State Worry Questionnaire—(PSWQ; Meyer, Miller, Metzger & Borkovec, 1990). The PSWQ is 16-item trait measure of general life worry (e.g., “Many situations make me worry”). The PSWQ has high internal consistency and good test-retest reliability (Meyer et al., 1990). Higher scores indicating a greater degree of general life worry (total scores range from 16 to 80).

2.3. Data Analytic Plan

Between-groups ANOVAs were conducted to examine differences between daily smokers, chippers and nonsmokers on the primary measures of interest. Tukey’s Honestly Significant Difference (HSD) was employed to control for follow-up comparisons. The small sample sizes precluded conducting analyses by specific anxiety disorder.

3. Results

3.1. Participants

Table 1 summarizes demographical information by smoking status. Between-groups differences were found with respect to age, such that nonsmokers (47.2 years) were significantly older than chippers (36.7 years). Distribution of race also differed across groups, likely due to the small sample size. Smokers and nonsmokers were similar with respect to other demographic characteristics. Consistent with demographics described in the alcohol literature,

but inconsistent with the gender breakdown reported in the anxiety disorders literature, the majority (79.2%; 57/72) of the sample was male.

Daily smokers smoked an average of 12.7 (SD = 6.0) cigarettes per day (cpd) and chippers smoked an average of 3.9 (SD = 3.1) cigarettes per occasion. Among daily smokers, the average time from waking to first cigarette, a predictor of both nicotine dependence and biochemical measures (Heatherton et al., 1989), was 135.6 minutes (SD = 168.2). Thus, the sample generally included light to moderate, non-dependent smokers.

3.2. Smokers Versus Nonsmokers with AUD-ANX on drinking behavior

Overall point prevalence of any current smoking (chippers and daily smokers) was 48.6% (35/72) and of current daily smoking was 31.9% (23/72). Means and standard deviations of alcohol measures by smoking status are presented in Table 2. Self-report data were available for 67 to 72 participants, depending on the variable.

Significant differences were observed on alcohol dependence, average drinks per drinking occasion, percent days abstinent, and highest and second-highest BAC in a day. Effect sizes were small to moderate (Table 2). Follow-up tests revealed that, with the exception of percent days abstinent, nonsmokers reported lower alcohol symptoms than daily smokers, with chippers being nonsignificantly different from either nonsmokers or daily smokers. In the case of percent days abstinent, although the overall ANOVA was significant ($p = .035$), follow-up tests revealed only a tendency for nonsmokers (19%) to have *fewer* percent days abstinent from alcohol than chippers (37%; $p = .06$), but not daily smokers (31%; $p = .14$). Contrary to hypotheses, smokers and nonsmokers did not differ with respect to percent heavy drinking days (adjusted for gender).

3.3. Smokers Versus Nonsmokers with AUD-ANX on Emotional Characteristics

Between-groups t-tests yielded no significant differences when daily smokers, chippers, and nonsmokers were compared regarding emotional characteristics.

4. Discussion

Overall, just under half (48.6%) of this sample of individuals with co-occurring AUD-ANX reported being smokers, with 31.9% being daily smokers. This prevalence was substantially greater than prior prevalence estimates of smoking among those with anxiety disorders without co-occurring AUDs (14.8%, Baker-Morissette et al., 2004), but lower than traditionally seen among those with AUDs (Monti et al., 1995). Also surprising, using rate of daily smoking (mean = 12.7 cpd) and duration of time to first cigarette (mean = 135.6 minutes) as a proxy for tobacco dependence, smokers with co-occurring AUD-ANX exhibited low levels of tobacco dependence. The reasons for the lower prevalence and tobacco dependence levels are unclear, particularly in light of evidence that elevated levels of anxiety sensitivity commonly found among the anxiety disorders, particularly panic disorder, may increase risk for smoking (Zvolensky et al., 2003a). However, GAD was the modal anxiety disorder diagnosis, and correspondingly, AS levels (mean = 27.7; SD = 10.9) were consistent with scores typically observed for those with GAD versus panic disorder [mean 28.6 (SD = 20.6) and 32.1 (SD = 11.3) for GAD and PDA, respectively; Rapee et al., 1992]. These lower levels of AS, coupled increased levels of health-related worries found among GAD patients, could account for lower tobacco prevalence and dependence levels, and warrants further investigation particularly in light of the dearth of studies published on smoking and GAD.

With respect to alcohol variables, nonsmokers reported lower alcohol dependence, average drinks per occasion, and BACs than daily smokers, with chippers being nonsignificantly

different from either nonsmokers or daily smokers. Notably, daily smokers (0.31%) reported significantly higher peak intoxication levels in a day than nonsmokers (0.19%), which is clinically meaningful with regard to the behavioral impairment associated with each level of intoxication. Significant differences were also observed with respect to percent days abstinent. The overall ANOVA was significant, although follow-up tests revealed only a tendency for nonsmokers (19%) to have fewer percent days abstinent than chippers (37%), who had the highest percent days abstinent. Daily smokers (31%) were intermediate, but not meaningfully different from either chippers or nonsmokers. This could reflect chippers' reliance on alternative substances (i.e. tobacco) in selective ways to refrain from drinking. Overall, these findings suggest that daily smokers and nonsmokers with AUD-ANX differ in terms of their overall level of alcohol dependence and patterns of drinking.

Based on the separate tobacco and alcohol literatures, we expected that patients who use multiple substances (i.e., both alcohol and tobacco) would report worse emotional symptoms than nonsmokers with AUDs by virtue of their being potentially more addicted (Kandel, Huang & Davies, 2001). Contrary to predictions, daily smokers, chippers, and nonsmokers with AUD-ANX did not differ across measures of emotional characteristics. Although the reasons are unclear, this may be due to the relatively small number of patients with panic disorder (who were primarily responsible for emotional differences found between smokers and nonsmokers by Morissette et al., 2006). Unfortunately, the overall sample size was relatively small and precluded evaluation of findings based on anxiety diagnosis. Future studies with larger sample sizes are clearly needed to explore differences by specific anxiety disorder.

Several interpretive caveats warrant discussion. First, participants included in this study were willing to volunteer for a fairly intensive clinical trial, and because of the medication being investigated, needed to meet considerable inclusion and exclusion criteria. Although recruitment efforts were as broad possible, this affects the generalizability and nature of the sample, and could account for the low tobacco prevalence and rates found. Second, the sample size was small, which could have resulted in a lack of significance with respect to emotional measures. That differences between daily smokers and nonsmoker on alcohol symptoms were still found with mostly moderate effect sizes, suggests that alcohol findings were relatively robust. Third, only self-reported tobacco use was assessed and no biochemical validation of smoking status was conducted. Thus, it is possible that under-reporting could have occurred, resulting in the lower prevalence and rate of smoking observed.

In summary, data from the current study suggest that daily smokers with AUD-ANX demonstrated worse alcohol, but not anxiety symptoms, than their nonsmoking counterparts. Consistent with the alcohol literature (Daepfen et al., 2000), compared to nonsmokers with AUD-ANX, daily smokers reported worse alcohol dependence, greater drinks per drinking occasion, and higher peak blood alcohol concentrations. Clinicians may need to take tobacco use into account when treating patients with co-occurring AUD-ANX. Nonsignificant findings with respect to emotional symptoms are generally inconsistent with data from studies investigating tobacco and anxiety. Specifically, in the absence of AUDs, smokers have been shown to have worse emotional symptoms than nonsmokers (e.g., Morissette et al., 2006), and irrespective of tobacco use, those with AUDs report worse anxiety (e.g., Chambless et al., 1987). Future research with larger and more diverse samples is needed to better understand characteristics of patients with these highly co-occurring disorders so that appropriate interventions to address their unique needs can be developed. The health consequences of tobacco use, AUDs and anxiety disorders are notable, and the potential synergistic effects of these disorders are of significant public health concern.

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Table 1

Sample Characteristics.

Measure	Smoker (n =23)	Chipper (n = 12)	Nonsmoker (n = 37)
Age**	41.6 (10.5)	36.7 (8.9)	47.2 (9.5)
Education	14.4 (2.5)	14.6 (3.3)	15.8 (3.2)
# clinical psychiatric diagnoses *	3.7 (1.1)	3.0 (0.6)	2.9 (0.7)
Gender			
Male	27.8%	11%	40.3%
Female	4.2%	5.6%	11.1%
Race *			
Caucasian	23.6%	12.5%	48.5%
African American	4.2%	1.4%	1.4%
Asian	0%	1.4%	0%
More than one race	0%	1.4%	1.4%
Other	4.2%	0%	0%
Employment			
Employed full-time	18.1%	12.5%	31.9%
Employed part-time	4.2%	1.4%	9.7%
Unemployed	8.3%	2.8%	6.9%
Retired	1.4%	0%	2.8%
Income			
\$0–14,999	7.1%	0%	5.7%
\$15,000–29,999	4.3%	7.1%	4.3%
\$30,000–44,999	8.6%	2.9%	10.0%
\$45,000–59,999	1.4%	1.4%	4.3%
\$60,000–74,999	4.3%	1.4%	2.9%
\$75,000–89,999	4.3%	0%	5.7%
\$90,000 or higher	2.9%	4.3%	17.1%
Marital Status			
Never married	15.3%	11.1%	9.7%
Married	8.3%	4.2%	29.2%
Separated/divorced	6.9%	1.4%	11.1%
Widowed	1.4%	0%	1.4%

* p < .05

** p < .01

Table 2
Means (Standard Deviations) for, and Differences Between, Daily Smokers, Chippers and Nonsmokers with Co-Occurring Alcohol and Anxiety Disorders on Self-Reported Alcohol Symptoms.

Measure	Smoker (n = 23)	Chipper (n = 12)	Nonsmoker (n = 37)	F	η^2
<u>Alcohol Characteristics</u>					
Average drinks per drinking occasion	13.8 (6.5)	9.9 (4.5)	9.7 (6.4) *	3.2	0.09
Alcohol Dependence Scale	18.9 (8.3)	14.8 (7.3)	13.3 (5.6) *	4.8	0.12
% Days Abstinent	31% (27%)	37% (27%)	19% (18%) *	3.5	0.10
% Heavy Drinking Days	64% (26%)	54% (31%)	64% (28%)	.65	0.02
Highest BAC (g/dl)	.31 (.15)	.30 (.16)	.19 (.12) **	6.2	0.15
Second Highest BAC (g/dl)	.35 (.20)	.28 (.15)	.18 (.12) **	8.4	0.20

* p < .05

** p < .01

Note: η^2 < 0.10 is considered a small effect size; 0.10 to 0.25 medium; and > 0.25 strong (Jaccard & Becker, 1990).