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Alcohol Use History and Panic-Relevant Responding among Adolescents: A Test using a Voluntary Hyperventilation Challenge

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Abstract

Given the onset of alcohol use, neurological sensitivity, and enhanced panic-relevant vulnerability, adolescence is a key period in which to study the documented linkage between alcohol and panic-related problems. The current study was designed to build upon and uniquely extend extant work via (1) utilization of well-established experimental psychopathology techniques, and (2) evaluation of unique associations between alcohol use and panic symptoms after controlling for theoretically-relevant behavioral, environmental, and individual difference variables (i.e., age, gender, negative affectivity, anxiety sensitivity, child and parent tobacco use, and parental panic disorder). Participants were 111 community-recruited adolescents ages 12–17 years ($M = 15.76$ years; $n = 50$ girls). Youth completed a battery of well-established questionnaires and a voluntary hyperventilation challenge, and parents present at the laboratory completed a structured clinical interview. Adolescent alcohol use was categorized as Non-Users, Experimenters, or Users. Panic symptoms were indexed via retrospective self-report and adolescents' response to a biological challenge procedure (i.e., voluntary hyperventilation). After controlling for theoretically-relevant covariates, Users evidenced elevated panic-relevant symptoms and responding compared to Non-Users; Experimenters did not differ from Non-Users. Findings suggest alcohol use history is uniquely associated with panic symptomatology among youth, including "real-time" reactivity elicited by a laboratory challenge. While there is significant work yet to be done, these data advance extant work and lay the groundwork for the types of sophisticated designs that will be needed to answer the most pressing and complex questions regarding the link between alcohol use and panic symptoms among adolescents.

Problematic alcohol use and anxiety psychopathology commonly co-occur (see Blumenthal, Leen-Feldner, Badour, & Babson, 2011; Brady & Lydiard, 1993; Kushner, Sher, & Beitman, 1990; Schuckit & Hesselbrock, 1994; Wilson, 1988 for reviews). One area receiving increasing empirical attention is the relation between alcohol use behaviors and panic-related problems (e.g., panic attacks, panic disorder; Bunaciu et al., 2010; Domalanta, Risser, Roberts, & Risser, 2003; Hayward et al., 1997; Seguí et al., 2001; Zimmerman et al., 2003). Adolescence is a key developmental period in which to study the alcohol-panic linkage for at least three reasons. First, initiation and experimentation with alcohol is common during this phase (Johnston, O'Malley, Bachman, & Schulenberg, 2008; Chen, Yi, & Faden, 2011; Wittchen et al., 2008). For example, recent epidemiological work indicates that over 70% of high school students in the United States have at least experimented with

alcohol, 41.8% report having consumed alcohol in the past 30 days, and 24.2% report heavy consumption (i.e., 5 or more drinks within a couple hours) in the past 30 days [Centers for Disease Control and Prevention (CDC), 2010]. Second, the rapid somatic and neurological development that characterizes the period of adolescence, particularly during puberty, sets the stage for enhanced vulnerability for somatic and neurological damage related to alcohol consumption (Brown et al., 2008; Nixon & McClain, 2010), as well as distinct acute effects when compared to adults (e.g., attenuated motor impairment, enhanced social facilitation, Nixon & McClain, 2010; Windle et al., 2008). Indeed, discrepant neurophysiologic effects (as a function of developmental stage) may lead to increased consumption as well as greater risk for alcohol use (Deas, Riggs, Langenbucher, Goldman, & Brown, 2000) and alcohol-related (including panic-relevant) problems among adolescents (Masten, Faden, Zucker, & Spear, 2010). Finally, the onset of panic-relevant responding (e.g., fearful reactivity to somatic perturbation) and panic-related problems (e.g., recurrent panic attacks) often occur during adolescence (Goodwin & Gotlib, 2004; Reed & Wittchen, 1998; Von Korff, Eaton, & Keyl, 1985). For example, a growing body of work indicates that progression through puberty, which is a “hallmark” of adolescence (Hayward & Sanborn, 2002), predicts enhanced panic-relevant vulnerability (Leen-Feldner, Reardon, & Zvloneksy, 2007) as well as the onset of panic attacks (Hayward et al., 1992). Together, these data highlight adolescence as an important developmental period in which to study the onset and progression of alcohol- and panic-related problems as they occur(cf., as retrospectively reported by adults; Cicchetti & Rogosch, 2002; Masten et al., 2010).

Building on studies conducted with adults (e.g., Falk, Yi, & Hilton, 2008), an emerging body of research (albeit limited and not entirely uniform), including prospective work (Goodwin et al., 2004; Zimmerman et al., 2003), suggests a correlation between alcohol use behaviors and panic-related problems among youth. For instance, qualitative (Gardner & Kutcher, 1993) and quantitative work with incarcerated adolescents (Domalanta, Risser, Roberts, & Risser, 2003) suggests a high rate of co-occurrence between problematic alcohol use and panic attacks among treatment-seeking youth. Conversely, Clark and colleagues’ (1995) study with adolescent inpatients with a current alcohol use disorder found that rates of panic disorder were comparable to those seen in community-based samples. Similarly, after methodologically controlling for age, pubertal status, and ethnicity, Hayward and colleagues (1995) found no relation between a positive history of panic attacks and current alcohol consumption (i.e., at least 2–4 full beverages or “being drunk” over the past 30 days) within a group of 160 young adolescent girls. However, in a subsequent study involving more than 1,000 adolescent girls, Hayward and colleagues (1997) found that participants reporting a history of both cued (i.e., situationally bound) and uncued (i.e., in the absence of identifiable fear-relevant stimuli) panic attacks evidenced a threefold increase in rates of current alcohol consumption as compared to girls who had never had a panic attack (even after controlling for ethnicity).

Although promising, the current literature is characterized by a number of important limitations. First, the overall body of work is relatively small, and although research generally suggests a correlation between problematic alcohol use and panic-related problems, findings are mixed. Importantly, within the limitations of the extant literature there also are plausible explanations for documented discrepancies. For example, with few exceptions (e.g., Zimmerman et al., 2003), very little work has examined the specificity of the association between alcohol and panic outcomes and none has considered theoretically-relevant “process variables,” including individual difference factors (e.g., anxiety sensitivity; Taylor, 1999), behavioral variables (e.g., nicotine use; Johnson et al., 2000), or parental factors (e.g., parental panic disorder; Nocon et al. 2008), all of which evidence substantial overlap with indices of panic among adolescents. Inclusion of these variables represents a timely and important extension to extant work seeking to evaluate the *unique* association

between alcohol use and panic-relevant problems among youth. Further, work to date has relied exclusively on adolescent self-report of alcohol use and panic symptomatology (Blumenthal et al., 2011). Ethical constraints preclude alcohol administration to adolescents (cf., Behar et al., 1983), but there is a rich tradition of safe and effective use of biological challenge procedures to elicit physiological arousal and panic-relevant responding among adolescents (e.g., Leen-Feldner, Feldner, Bernstein, McCormick, & Zvolensky, 2005; Rabian, Embry, & MacIntyre, 1999; Unnewehr, Schneider, Margraf, Jenkins, & Florin, 1996). The value of this procedure from a theoretical perspective is that it allows us to model, or create a state analogous to that of panic (Olatunji, Leen-Feldner, Feldner, & Forsyth, 2007). Accordingly, factors related to enhanced fearful responding to such arousal can be directly examined and even subjected to causally-oriented hypothesis testing, thereby informing etiologic models of panic and co-occurring problems, such as alcohol use. Further, without eliciting bodily sensations in “real time” under controlled laboratory conditions, it is difficult to rule out affective and memory biases (Nisbett & Ross, 1980) as alternative explanations for observed relations between alcohol and panic among adolescents. For instance, it may be that youth with a history of alcohol use simply demonstrate a recall bias for bodily-oriented experiences, and not necessarily enhanced fearful reactivity to somatic perturbation. Finally, laboratory-based procedures may tap into factors not captured by standard self-report assessments such as indirect learning experiences, automatic responding, or genetic disposition (Eifert, Forsyth, Zvolensky, & Lejuez, 1999; Unnewehr et al., 1996). Utilization of experimental psychopathology techniques in which panic-relevant responding is elicited in the laboratory (e.g., voluntary hyperventilation; stair-stepping) therefore represents a key next step in this line of work (Zvolensky, Lejuez, Stuart, & Curtin, 2001).

With this backdrop, the current study utilized both self-report as well as a biological challenge procedure (i.e., voluntary hyperventilation; Hornsveld, Garssen, Dop, & Van Spiegel, 1990; Leen-Feldner et al., 2005; Unnewehr et al., 1996) in an effort to better understand panic-relevant symptoms and responding as a function of alcohol use history among adolescents. It was hypothesized that adolescents who reported alcohol use, as compared to non-drinkers, would evidence higher levels of panic symptomatology as indexed via a well-established questionnaire as well as immediately following the voluntary hyperventilation challenge. Moreover, these effects were expected to remain significant even after accounting for the panic-relevant variables of age, gender (Chorpita, Yim, Moffitt, Umemoto, & Francis, 2000; Reed & Wittchen, 1998), negative affectivity (Craske, Poulton, Tsao, & Plotkin, 2001; Hayward, Wilson, Lagle, Killen, & Taylor, 2004), anxiety sensitivity (Leen-Feldner et al., 2005; Schmidt et al., 2010), child tobacco use (Isensee, Wittchen, Stein, Höfler, & Lieb, 2003; Johnson et al., 2000), parental panic disorder (Hayward, Killen, Kraemer, & Taylor, 2000; Hayward et al., 2004; Nocon et al., 2008) and parental tobacco use (Goodwin, Lewinsohn, & Seeley, 2005).

Method

Participants

Participants were 111 adolescents ages 12 to 17 years ($M = 15.76$, $SD = 1.56$; $n = 50$ girls), recruited from the general community, who took part in a larger investigation focused on adolescent emotional vulnerability. Exclusionary criteria, assessed via structured interview, were as follows: (1) respiratory problems (e.g., asthma), (2) heart problems (e.g., hypertension), (3) pregnancy, (4) the inability to provide written informed assent, and (5) lifetime history of panic disorder (e.g., Leen-Feldner et al., 2005; 2007). Participants selected for analysis in the current study ($n = 115$) were those with complete predictor (e.g., alcohol use history) and criterion (e.g., panic symptoms) data; four participants were removed as outliers on an a priori basis (i.e., criterion variable values greater than 2.5

standard deviations above the mean; Osborne & Overbay, 2004; Zimmerman, 1994), resulting in the final sample of 111 youth. It is important to note that participants selected for analysis did not differ significantly from those in the larger study across any of the selected variables (e.g., age, race, anxiety sensitivity, parental panic disorder).

Corresponding with the local community (southern Midwest United States; U.S. Bureau of the Census, 2010) the ethnic (Hispanic/Latino; not Hispanic/Latino) and racial composition of the sample was as follows: 17.4% Hispanic/Latino, 80.2% Caucasian, 11.7% African American, 2.7% Native American, 0.9% Asian, and 4.5% “other” or did not respond. A median family income of \$35,000 ($M = \$50,587.10$, $SD = \$46,853.24$) was reported by parents who accompanied participants to the laboratory (73.2% biological mothers). Parental education was as follows: 15.4% did not complete high school, 26.1% received a high school diploma or equivalent degree, 26.1% completed some college, 14.4% held Associate’s or Bachelor’s degrees, 7.2% reported some graduate or professional schooling, and 10.8% completed graduate or professional school. Approximately 63% of parents reported being married or living with someone, 22.5% were divorced, 10.8% separated, 2.7% never married, and 0.9% widowed.

Measures

Alcohol Use History—History of alcohol use was assessed via the well-established Adolescent Alcohol and Drug Involvement Scale (AADIS; Moberg, 2003; Moberg & Hahn, 1991). This face-valid measure asks participants to select a single response that best reflects how often they drink alcohol on a scale of 0 (*never used*) to 7 (*several times a day*). In an effort to capture distinct stages of alcohol use in a non-clinical sample, responses were trichotomized such that participants selecting “0” (*never used*) were categorized as Non-Users, those selecting “1” (*tried but quit*) were categorized as Experimenters, and those selecting a “2” or higher (e.g., 2 = *several times a year*; 3 = *several times a month*) were categorized as Users. Please see Table 1 for sample characteristics as a function of alcohol use history. Finally, for descriptive purposes three items drawn from the widely-used Youth Risk Behavior Survey (CDC, 2006) also are included in Table 1. Specifically, participants responded to the following questions: (1) How old were you when you first had an alcoholic drink (years)?, (2) During the past month (30 days) on how many days did you have at least one drink of alcohol?, and (3) During the past month (30 days) on how many days did you have 5 or more alcoholic drinks in a row, that is, within a couple of hours?

Panic Symptoms—The Revised Child Anxiety and Depression Scale-Panic subscale (RCADS-P; Chorpita et al., 2000) was used to index symptoms of panic. Designed to reflect the dimensions of several DSM-IV defined anxiety and depressive disorders among youth, the nine-item panic subscale asks participants to rate the frequency with which they experience panic-type sensations (e.g., “My heart starts to beat too quickly for no reason”) on a four-point Likert-type scale (0 = *never* to 3 = *always*). Responses are then summed providing a total subscale score. This measure evidences good reliability and validity (Chorpita et al., 2000; Chorpita, Moffitt, & Gray, 2005). For example, an initial alpha coefficient of .85 was reported for the panic subscale by Chorpita and colleagues (Chorpita et al., 2000; $\alpha = .78$ in the current sample), as well as good one week test-retest reliability ($\alpha = .76$). Standardized *T* scores (i.e., for grade and gender; Chorpita et al., 2000) are included for descriptive purposes; however, raw score totals were utilized in all analyses such that comparable analyses could be conducted across criterion variables (i.e., adjusting for age and gender).

Laboratory Challenge—Hyperventilation was selected as the challenge procedure because it can reliably produce bodily arousal, its parametric properties are well studied

(Hornsveld et al., 1990; Hornsveld, Garssen, & van Spiegel, 1995), and it has been safely employed with children and adolescents (Hawks, Blumenthal, Feldner, Leen-Feldner, & Jones, 2011; Leen-Feldner et al., 2005; Leen-Feldner et al., 2007; Unnewehr et al., 1996). The challenge involved a three-minute voluntary hyperventilation during which participants were asked to breathe at a rate of 30 respiratory cycles per minute. Importantly, this rate has been shown to produce an increase in plasma epinephrine, lactate levels, and blood pH, and a decrease in $p\text{CO}_2$ (Fried & Grimaldi, 1993; Hornsveld et al., 1995). Audio-taped instructions were used to standardize procedures and ensure consistency of breathing rates across participants throughout the challenge. These instructions are thoroughly described elsewhere (Leen-Feldner et al., 2006). Immediately after completing the challenge, the Acute Panic Inventory was administered.

Panic Symptoms Following the Challenge—The Acute Panic Inventory (API; Dillon, Gorman, Liebowitz, Fyer, & Klein, 1987) was used to index panic-relevant responding elicited by the hyperventilation challenge. On a four-point scale (0 = *not at all* to 3 = *a lot*) participants rate the degree to which they are currently experiencing 23 items reflecting DSM-IV defined panic attack symptoms (e.g., “Do you feel your heart beating fast?” and “Are you afraid of going crazy?”). Responses are then summed, providing a total symptom level score immediately post-challenge. Importantly, the API has been employed in prior biological challenge work with children and adolescents (Hawks et al., 2011; Pine et al., 2000), and evidences sound psychometric properties (e.g., $\alpha = .85$ in the current sample).

Physiological Arousal—To evaluate psychophysiological arousal elicited by the challenge, a J&J Engineering I-330-C2 system was used to digitally record skin conductance levels (SCL) and respiration rate (breaths-per-minute) throughout the procedure. Data were collected at a rate of 1024 samples per second across all channels using J&J Engineering PhysiLab Software. Converted to microsiemens (μS), SCL was monitored via SE-35 electrodes placed on the middle segment of the index finger and connected to an RV-5 skin resistance lead. Breaths-per-minute (BPM) were assessed via a Pnemograph sensor cable with two elastic PS-2 sensors filled with conductive fluid: stretching across the sensors causes a voltage change, thus providing a gross measure of chest exertion during respiration. Average values for SCL and BPM were computed for the baseline and challenge periods.

Covariates—Chronological age, gender (Chorpita et al., 2000; Reed & Wittchen, 1998), negative affectivity (Craske et al., 2001; Hayward et al., 2004), anxiety sensitivity (Leen-Feldner et al., 2005; Schmidt et al., 2010), child tobacco use (Isensee et al., 2003; Johnson et al., 2000), parental history of panic disorder (Hayward et al., 2000, 2004; Nocon et al., 2008) and recent parental tobacco use (Goodwin et al., 2005) were selected as covariates. General proclivity toward negative affect was measured via the negative affect scale of the *Positive and Negative Affect Schedule for Children* (PANAS-C; Joiner, Catanzaro, & Laurent, 1996); a measure that evidences good internal consistency (e.g., $\alpha = .89$ in the present sample) and validity (Joiner et al., 1996). The negative affect scale of the PANAS-C asks participants to use a five-point Likert-type scale (1 = *very slightly* to 5 = *extremely*) to rate how they have been feeling during the past few weeks in terms of 15 descriptors (e.g., upset, nervous, sad). Anxiety sensitivity was indexed using the well-established *Child Anxiety Sensitivity Index* (CASI; Silverman, Fleisig, Rabian, & Peterson, 1991). On the 18-item CASI participants rate perceptions of the aversive nature of anxiety symptoms (e.g., “It scares me when I have trouble getting my breath”) using a three-point scale (1 = *none*, 2 = *some*, 3 = *a lot*); this measure has consistently demonstrated good reliability and validity (e.g., Silverman et al., 1991; $\alpha = .78$ in the current sample). Tobacco use was evaluated using the National Cancer Institute’s *Smoking History Questionnaire* (SHQ). Specifically,

both parents and adolescents (separately) were asked about the number of cigarettes smoked over the past 30 days. Importantly, this widely-used measure has been successfully employed in research with both adults and adolescents (e.g., Dino et al., 2001; Horn et al., 1999). Finally, lifetime history of parental panic disorder was assessed using the *Structured Clinical Interview for DSM-IV* (SCID-I; First, Spitzer, Gibbon, & Williams, 2002). Trained interviewers administered the panic subscale of this instrument to parents who accompanied participants to the laboratory; this instrument has demonstrated adequate psychometric properties (Kranzler, Kadden, Babor, & Tennen, 1996; Zanarini et al., 2000).

General Procedure

All study procedures were approved by the University Institutional Review Board prior to participant contact. Interested participants and parents responding to community advertisements (e.g., flyers; radio) were fully informed about the study and adolescents were screened for the exclusionary criteria noted above. Eligible youth were scheduled for a laboratory visit, at which time written informed assent and parental consent (for self and child participation) were obtained. Written consent procedures were followed by verbal review and confirmation that participants understood each element of informed consent/assent, including confidentiality (e.g., from one-another), limits to confidentiality (i.e., mandated reporting), and the voluntary nature of participation. The panic subscale of the SCID, SHQ, and a small questionnaire battery, including demographics, were then administered privately to parents, after which parents were thanked, debriefed, and compensated \$5 for their time. Adolescent participants completed a battery of randomly ordered questionnaires, including demographics, the PANAS-C, CASI, SHQ, and RCADS, followed by a series of laboratory-based activities including the hyperventilation challenge. After completion of the laboratory procedures adolescent participants were thanked, debriefed, and compensated \$45 for their time.

Analytic Approach

A paired-samples *t*-test was used to examine physiological reactivity to the biological challenge, and hierarchical regression analyses were utilized to assess API scores as a function of physiological arousal (i.e., manipulation check). Chi-square analyses, independent samples *t*-tests, and one-way analyses of variance were used to examine zero-order relations among predictor and criterion variables. All follow-up analyses were Bonferroni corrected for interpretation (i.e., $p < .017$). Analyses of covariance were conducted to examine the primary hypotheses. Specifically, RCADS-P and API scores were entered as dependent variables. Across both analyses, alcohol use history (0 = *Non-Users*; 1 = *Experimenters*; 2 = *Users*) was entered as a fixed factor, and gender (0 = *male*; 1 = *female*), chronological age, parental history of panic disorder (0 = *negative*; 1 = *positive*), average number of cigarettes smoked per day by child and parent (separately), PANAS-C, and CASI scores were entered as covariates. Effect size was indexed via eta squared (η^2). Follow-up analyses (i.e., pairwise) were conducted to examine group differences in RCADS-P and API scores among Non-Users, Experimenters, and Users.

Results

Manipulation Check

Compared to the baseline resting period, significant increases in bodily arousal were evidenced during the hyperventilation challenge (SCL: $M = 10.95$ versus $M = 14.65$, $t(97) = 13.13$, $p < .001$; BPM: $M = 17.16$ versus $M = 24.02$, $t(101) = 15.67$, $p < .001$). Further, API scores did not differ as a function of SCL (standardized $\beta = .11$, $t = 1.12$, $p = .26$) or BPM (standardized $\beta = .06$, $t = 0.67$, $p = .50$). Together these data suggest that participants

followed instructions, the challenge effectively elicited somatic perturbation, and increased challenge response was not a function of elevated physiological arousal alone.

Preliminary Analyses

Consistent with large scale, epidemiological surveys (e.g., CDC, 2010), 23.5% of participants were categorized as Non-Users, 31.5% as Experimenters, and 45% as Users. Further, the percentage of youth meeting criteria for clinically significant impairment on the RCADS-P (i.e., T scores ≥ 65 ; all Experimenters and Users) was comparable to that reported in other unselected, community based samples (approximately 6%; Austin & Chorpita, 2004). Please see Table 1 for data pertaining to predictor and criterion variables as a function of alcohol use history, and Table 2 for zero-order correlations among continuous predictor and criterion variables across the entire sample.

Independent-samples t -tests indicated that girls evidenced significantly higher RCADS-P scores ($M = 4.22$, $SD = 3.24$) than boys [$M = 2.04$, $SD = 2.43$; $t(109) = 4.02$, $p < .001$], although API scores did not differ as a function of gender [$M = 13.20$, $SD = 8.01$ versus $M = 11.63$, $SD = 8.57$, respectively; $t(109) = 0.98$, $p = .32$]. Further, youth with a parent presenting with a lifetime history of panic disorder evidenced significantly higher RCADS-P scores ($M = 6.75$, $SD = 2.62$) than those with a negative history [$M = 2.88$, $SD = 2.95$; $t(109) = 2.57$, $p = .01$], although API scores did not differ as a function of parental panic disorder history [$M = 17.75$, $SD = 6.18$ versus $M = 12.14$, $SD = 8.35$, respectively; $t(109) = 1.32$, $p = .18$].

Primary Analyses

Panic symptoms—Prior to entering covariates, alcohol use history predicted panic symptoms, $F(2, 108) = 4.90$, $p = .009$. Specifically, Users reported significantly higher RCADS-P scores ($M = 3.82$, $SD = 3.19$) as compared to Non-Users ($M = 1.61$, $SD = 1.55$; $p = .002$); Experimenters ($M = 2.94$, $SD = 3.24$) did not differ significantly from either group. In the final model, a significant amount of variance in RCADS-P scores was accounted for by gender [$F(1, 101) = 5.43$, $p = .02$, $\eta^2 = .05$], parental panic disorder [$F(1, 101) = 7.86$, $p = .006$, $\eta^2 = .07$], negative affectivity [$F(1, 101) = 4.16$, $p = .04$, $\eta^2 = .04$], and anxiety sensitivity [$F(1, 103) = 30.35$, $p < .001$, $\eta^2 = .23$]; chronological age, child, and parent smoking history were not significant predictors in the final model [$F(1, 101) = 1.92$, $p = .16$, $\eta^2 = .01$, $F(1, 101) = 1.31$, $p = .25$, $\eta^2 = .01$, and $F(1, 101) = 0.74$, $p = .39$, $\eta^2 = .00$, respectively]. After variance accounted for by covariates (i.e., 41%), alcohol use history predicted RCADS-P scores [$F(2, 101) = 3.27$, $p = .04$, $\eta^2 = .06$]. Follow-up analyses indicated that Users reported significantly higher RCADS-P scores ($M = 3.60$, $SE = .34$) as compared to Non-Users ($M = 1.98$, $SE = .49$; $p = .012$); Experimenters ($M = 2.98$, $SE = .40$) did not differ significantly from either group.

Panic Symptoms Following the Challenge—Prior to entering covariates, alcohol use history predicted post-challenge panic symptoms, $F(2, 108) = 9.10$, $p < .001$. Specifically, Users reported significantly higher API scores ($M = 15.76$, $SD = 8.48$) as compared to Non-Users ($M = 10.46$, $SD = 8.27$; $p = .006$) and Experimenters ($M = 8.85$, $SD = 6.15$; $p < .001$); Non-Users and Experimenters did not differ significantly from one-another. In the final model, a significant amount of variance in post-challenge API scores was accounted for by parental panic disorder [$F(1, 101) = 5.02$, $p = .02$, $\eta^2 = .04$] and negative affectivity [$F(1, 101) = 7.43$, $p = .008$, $\eta^2 = .06$]; conversely, gender [$F(1, 101) = 0.94$, $p = .33$, $\eta^2 = .00$], chronological age [$F(1, 101) = 3.03$, $p = .08$, $\eta^2 = .02$], anxiety sensitivity [$F(1, 101) = 2.51$, $p = .11$, $\eta^2 = .02$], child [$F(1, 101) = 0.99$, $p = .32$, $\eta^2 = .01$] and parental smoking history [$F(1, 101) = 1.80$, $p = .18$, $\eta^2 = .01$] were not significant predictors in the final model. Alcohol use history significantly predicted post-challenge API scores after accounting for all

covariates, $F(2, 101) = 9.18, p < .001, \eta^2 = .15$. Follow-up analyses indicated that Users reported significantly higher API scores ($M = 15.86, SE = 1.10$) as compared to Non-Users ($M = 10.84, SE = 1.57; p = .015$) and Experimenters ($M = 8.42, SE = 1.29; p < .001$); Non-Users and Experimenters did not differ significantly from one-another.

Discussion

Adolescence is a key developmental period in which to study the linkage between alcohol and panic-related problems (Hayward et al., 1997; Masten et al., 2010; Windle et al., 2008; Zimmerman et al., 2003); however, the existing body of work is limited both in terms of size and methodological approach (Blumenthal et al., 2011). The current study was designed to build upon and uniquely extend extant work. Specifically, this investigation evaluated panic-relevant symptoms and responding to somatic perturbation as a function of alcohol use history among adolescents. Findings indicated that users, as compared to those who have abstained or have tried but quit, evidence elevated panic symptoms as indexed via retrospective self-report as well as in response to a voluntary hyperventilation challenge. These data are consistent with prior work suggesting a link between alcohol use and panic-related problems (e.g., Falk et al., 2008; Hayward et al., 1997; Zimmerman et al., 2003), and make a novel contribution to the literature on alcohol use and psychopathology in at least two important ways.

First, the current study is the first to employ well-established experimental psychopathology techniques in an attempt to better assess the relation between alcohol use and panic-relevant responding among adolescents. This methodological approach addresses a key criticism of existing work as it reduces concerns related to affective or memory biases inherent in more naturalistic designs (Kleinknecht, 2002; Nisbett & Ross, 1980; Zvolensky et al., 2001). Indeed, extant work relying solely on retrospective accounts of behavior and experience are consistent with the hypothesized linkage; however, in the absence of more methodologically rigorous demonstrations, conclusions remain tentative (Askew & Field, 2008; Kleinknecht, 2002). The current study included examination of panic symptoms in response to a controlled, laboratory-based induction of bodily arousal, and thus is the first to provide evidence for the linkage between adolescent alcohol use history and panic-relevant responding utilizing a “real-time” assessment. An important next step in this line of work will be to incorporate biological challenge procedures into longitudinal studies seeking to address etiologic, maintenance, and treatment characteristics of the alcohol-panic association among youth. Such endeavors will be key to better understanding the nature and progression of co-occurring alcohol use and panic-related problems as they unfold over time.

Second, alcohol use history was uniquely predictive of panic symptomatology after accounting for several theoretically-relevant behavioral, environmental, and individual difference variables not previously addressed in the empirical literature (i.e., child tobacco use, anxiety sensitivity, negative affectivity, parental history of panic disorder and tobacco use). Effect sizes were small to moderate (i.e., 6–15%; Cohen, 1992), but they are notable given the large amount of variance attributable to theoretically-relevant covariates (i.e., 16–41%; Abelson, 1985). The current statistical approach to culling out the unique effects of alcohol use history was an important starting place given the under-developed state of the literature, and findings underscore specificity in the alcohol-panic linkage, thus setting the stage for more refined tests of this association. Indeed, methodological controls (e.g., matching) and studies designed and powered to test more sophisticated, multivariate models of the alcohol-panic association will be critical for addressing questions related to mechanisms and processes that underlie this linkage (e.g., risk accumulation in terms of both additive and sequential effects; Dodge et al., 2009; Miller & Chapman, 2001).

While the current methodological and statistical approach represents an important advance in this domain of research, the cross-sectional design of this investigation precludes conclusions regarding temporal patterning. Importantly, theory and evidence provide support for “both directions,” and a critical next step will be to evaluate the alcohol-panic association over time with an eye on better understanding the nature and progression of co-occurrence (e.g. Masten, Faden, Zucker, & Spear, 2010; Yamaguchi & Kandel, 1984a; 1984b). Specifically, elevated consumption may precipitate or exacerbate panic symptomatology (e.g., Falk et al., 2008), but panic-related problems also may increase risk for problematic alcohol consumption (e.g., Zimmerman et al., 2003). In regard to the former, and akin to the substantial body of work examining the role of smoking in the development of panic-related problems (Breslau & Klein, 1999; Johnson et al., 2000; West & Hajek, 1997; Zvolensky, Schmidt, & Stewart, 2003), theorists propose a “kindling” process, such that repeated exposure to somatic perturbation following periods of heavy/repeated alcohol consumption and/or disruptions to neurological functioning (e.g., neurotransmitter activity) as a function of excessive consumption may increase risk for panic-related problems (Allan, 1995; Brady & Lydiard, 1993; Kushner et al., 1990; Stewart & Conrod, 2008). Consistent with this perspective, Falk and colleagues (2008) examined retrospective age of onset data collected in the National Epidemiological Survey on Alcohol and Related Conditions and found that among individuals presenting with co-occurring panic disorder and alcohol use disorders (AUDs), AUD onset occurred primary to panic disorder in a significant proportion of cases (i.e., 73% alcohol abuse; 67.7% alcohol dependence). Importantly, order of onset is a necessary, but insufficient criterion for determining causality (e.g., Chilcoat & Breslau, 1998), and no work to date provides a direct test of this model. Future laboratory-based work in this area could include anxious responding to physiological arousal following priming techniques designed to elicit alcohol-relevant cognitions and neurobiological compensatory activity (e.g., via linguistic or pictorial cues Lowman, Hunt, Litten, & Drummond, 2000; Tapert et al., 2003).

In contrast to kindling models, affect regulation models suggest that problematic alcohol use may result from alcohol consumption aimed at reducing anxious arousal (e.g., self-medication; Carrigan & Randall, 2003; Robinson, Sareen, Cox, & Bolton, 2009; Sayette, 1999). Prospective data from the Munich Early Developmental Stages of Psychopathology study provide support for this model (e.g., Goodwin et al., 2004; Zimmerman et al., 2003). For example, after controlling for several demographic and psychological variables (e.g., age, other anxiety disorders), a positive history of panic attacks at baseline predicted the onset of hazardous drinking [odds ratio (OR): 2.5] and alcohol abuse (OR: 2.7), as well as the persistence of an AUD (OR: 18.7) across a four-year follow-up period (Zimmerman et al., 2003). Importantly, the opposite pattern (e.g., baseline alcohol use predicting panic-related problems) was not empirically evaluated. Experimental psychopathology designs assessing the desire to consume alcohol following a panic-relevant challenge, particularly in conjunction with tension reduction expectancies and/or coping-related motives for use (Christiansen, Smith, Roehling, & Goldman, 1989; Comeau, Stewart, & Loba, 2001; Kuntsche, Knibbe, Gmel, & Engels, 2005; Mulligan & McKay, 2001), would further shed light on the relative role of panic-related symptoms in increasing risk for subsequent alcohol use behaviors. Overall, a convergence of methodological techniques will be required to draw meaningful conclusions about the strength, direction, and larger context in which the alcohol-panic linkage develops (e.g., experimental and prospective designs; multi-informant/-modal assessment; ecological momentary sampling); the current study was designed to extend and address important limitations of the extant body of work, and thus sets the stage for causally-oriented, multivariate hypothesis testing in this domain.

Finally, it is worth noting that alcohol use history broadly (i.e., non-users, experimenters, and users), rather than more clinically-relevant indices (e.g., alcohol abuse; dependence) or

patterns (e.g., frequency of use; quantity consumed per occasion), was selected as the index of alcohol use behavior, and participants were screened for the presence of lifetime panic disorder. While this design affects the generalizability of findings, it also represents a strength of the current study in terms of informing etiologic models of co-occurring alcohol and panic-related problems. In terms of alcohol use, prominent researchers have suggested it is as important to study alcohol use *behavior* as it is to evaluate alcohol use *disorders* among youth (Masten et al., 2010; Windle & Zucker, 2010). Such recommendations are based on empirical evidence suggesting (1) adolescent alcohol use (broadly) is related to increased mortality (e.g., motor vehicle accidents, drowning; Levy, Miller, & Lox, 1999; National Highway Traffic Safety Administration, 2002) and an array of problem behaviors (e.g., risky sexual behavior, delinquency; Hingson & Kenkel, 2004), (2) adolescents progress more rapidly from initial use to symptomatic and diagnostic status as compared to adults (Deas et al., 2000), and (3) the use of alcohol during adolescence is positively correlated with problematic alcohol use in adulthood (Rohde, Lewinsohn, Kahler, Seeley, & Brown, 2001; Wittchen et al., 2008). Nonetheless, extending the current findings to designs that employ more sophisticated assessments of alcohol use (e.g., frequency of binge drinking; parental alcohol use behaviors/AUD) as well as theoretically-relevant neurobiological correlates (e.g., dysregulation of the HPA, Abelson, Khan, Liberzon, & Young, 2007; Anthenelli, 2010) would allow for a richer understanding of the role of elevated (lifetime) exposure to alcohol in enhancing risk for panic-related problems.

Similarly, panic was indexed via overall symptom level rather than history/elicitation of DSM-IV-defined panic attacks in the current study. Importantly, the assessment of prodromal/sub-clinical responding, particularly in the context of an elicitation of bodily arousal, speaks to panic-relevant *vulnerability*, and thus provides a snapshot of adolescent alcohol use behavior in relation to increased risk for panic development (Bouton, Mineka, & Barlow, 2001; Leen-Feldner et al., 2005). However, it is important to note that the current study employed a differential, cross-sectional design and thus cannot speak to the temporal patterning or causal mechanisms that are at the heart of this work; longitudinal designs will be required to address these types of questions. Taken together, the current findings suggest a linkage between alcohol and panic may form in advance of clinically significant impairment in either domain, and thus there is merit in studying non-clinical as well as at-risk samples of youth. Nonetheless, extension of these findings to clinical samples of youth remains a necessary step in forwarding this literature, particularly in terms of better understanding processes related to maintenance and/or exacerbation of existing risk.

Additional limitations also must be considered in conclusions drawn from the current study. First, the current investigation included a relatively homogeneous sample (e.g., largely White; single-site recruitment), and was underpowered to address more complex models of the alcohol-panic relation. Relatedly, the present study required repeated analysis of a single sample; independent replication as well as future work designed to examine the specific role of demographic/cultural (e.g., ethnicity, gender), individual difference (e.g., negative affectivity), behavioral (e.g., additional substance use), and environmental (e.g., parental psychopathology and substance use) variables is warranted. For example, research suggests that particular facets of anxiety sensitivity (e.g., physical concerns) have more predictive validity in terms of panic outcomes than others (e.g., social concerns; Carter, Such day, & Gore, 2001; Leen-Feldner et al., 2005). Interestingly, although anxiety sensitivity was significantly correlated with challenge response at a zero-order level, it was not a predictor of challenge response in the final model. Additional research is now needed to examine the nature and direction of the relations among alcohol use, panic-relevant responding, and the global as well as specific facets of anxiety sensitivity (e.g., Mulligan & McKay, 2001; Steward, Peterson, & Pihl, 1995). Finally, the current study included a relatively healthy sample of adolescents (and parents) who chose and were able to participate in a laboratory

study for a monetary award; thus, research employing alternative sampling (e.g., via schools, community programs) and assessment (e.g., via primary care providers, at home) techniques will be required in order to rule out potential sampling biases. Indeed, adolescents and/or parents experiencing significant panic- or alcohol-related problems may not attend a laboratory appointment, perhaps limiting the generalizability of the current findings. For example, in the final models not all selected covariates consistently predicted panic-relevant responding and this may be due, in part, to limited upper-end variability.

In conclusion, findings from the current study of adolescents suggest alcohol use history is uniquely associated with panic symptomatology, including “real-time” panic-relevant reactivity elicited by a voluntary hyperventilation challenge. While there is significant work yet to be done in this important area of research, these data advance extant work and lay the groundwork for the types of sophisticated research designs that will be needed to answer the most pressing and complex questions in this domain.

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Table 1
Demographic and Psychological Characteristics as a Function of Alcohol Use History.

	Non-Users	Experimenters	Users	Group Differences [*]	Total
% Girls	38	40	52	--	45
Age <i>M</i> (<i>SD</i>)	14.46 (1.81)	15.91 (1.23)	16.33 (1.24)	U, E > N	15.76 (1.56)
% Parental panic disorder	0	11.4	0	E > N, U	3.6
# Cigarettes per day (Child) <i>M</i> (<i>SD</i>)	1.35 (5.89)	0.89 (1.92)	5.03 (5.98)	U > N, E	2.86 (5.37)
# Cigarettes per day (Parent) <i>M</i> (<i>SD</i>)	3.38 (6.68)	7.51 (10.65)	6.20 (8.51)	--	5.95 (8.94)
PANAS-C ^a <i>M</i> (<i>SD</i>)	24.19 (10.15)	27.00 (10.40)	28.22 (9.53)	--	26.88 (9.99)
CASI <i>b</i> <i>M</i> (<i>SD</i>)	25.26 (3.72)	26.08 (4.68)	27.22 (5.45)	--	26.40 (4.88)
RCADS-p ^c T score <i>M</i> (Range)	42.34 (36–57)	46.65 (36–69)	48.10 (36–73)	U > N	46.29 (36–73)
Age first drank ^d <i>M</i> (Range)	N/A	13.14 (9–16)	13.20 (8–16)	--	13.17 (8–16)
Days drank in past 30 ^d <i>M</i> (Range)	N/A	0.10 (0–1)	3.49 (0–30)	U > E	2.14 (0–30)
Days drank 5+ drinks in past 30 ^d <i>M</i> (Range)	N/A	0.07 (0–1)	1.64 (0–10)	U > E	1.01 (0–10)

Note. *N* = 111; *n* = 26 Non-Users (N), *n* = 35 Experimenters (E), *n* = 50 Users (U).

^aPositive and Negative Affect Schedule for Children, Negative affect subscale.

^bChild Anxiety Sensitivity Index.

^cRevised Child Anxiety and Depression Scale – Panic subscale.

^dQuestions completed from Youth Risk Behavior Survey (CDC, 2006); *n* = 30 Experimenters, *n* = 47 Users (Non-Users did not complete).

* Group differences significant at the *p* < .05 level, Bonferroni corrected.

Table 2

Zero-order Correlations among Continuous Predictor and Criterion Variables.

	1	2	3	4	5	6
1. Age	--					
2. # Cigarettes/day (Child)	.34**					
3. # Cigarettes/day (Parent)	-.04	.10				
4. PANAS-C ^a	.16	.01	.02			
5. CASI ^b	.08	-.12	.04	.43**		
6. RCADS-P ^c	.10	.04	.04	.44**	.59**	
7. API ^d	.02	.15	.15	.32**	.29**	.39**

Note. *N* = 111^aPositive and Negative Affect Schedule for Children, Negative affect subscale.^bChild Anxiety Sensitivity Index.^cRevised Child Anxiety and Depression Scale – Panic subscale.^dAcute Panic Inventory.***
p < .01.