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Specificity of Social Anxiety Disorder as a Risk Factor for Alcohol and Cannabis Dependence

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Abstract

Social anxiety disorder (SAD) is highly comorbid with alcohol use disorders (AUDs) and cannabis dependence. However, the temporal sequencing of these disorders has not been extensively studied to determine whether SAD serves as a specific risk factor for problematic substance use. The present study examined these relationships after controlling for theoretically-relevant variables (e.g., gender, other Axis I pathology) in a longitudinal cohort over approximately 14 years. The sample was drawn from participants in the Oregon Adolescent Depression Project. After excluding those with substance use disorders at baseline, SAD at study entry was associated with 6.5 greater odds of cannabis dependence (but not abuse) and 4.5 greater odds of alcohol dependence (but not abuse) at follow-up after controlling for relevant variables (e.g., gender, depression, conduct disorder). The relationship between SAD and alcohol and cannabis dependence remained even after controlling for other anxiety disorders. Other anxiety disorders and mood disorders were not associated with subsequent cannabis or alcohol use disorder after controlling for relevant variables. Among the internalizing disorders, SAD appears to serve as a unique risk factor for the subsequent onset of cannabis and alcohol dependence.

Keywords

Alcohol; Marijuana; Cannabis; Social Phobia; Social Anxiety; Substance Use

I. Introduction

Social anxiety disorder (SAD) is frequently comorbid with both alcohol abuse and dependence (Davidson et al., 1993; Grant et al., 2005; Kessler et al., 1997) as well as cannabis dependence (Agosti et al., 2002; Lynskey et al., 2002). For instance, 48% of individuals with a lifetime diagnosis of SAD also meet criteria for a lifetime diagnosis of an AUD (Grant et al., 2005). The 12-month prevalence of AUDs among individuals with SAD is 13.1% (Grant et al., 2005) compared to only 8.5% among the general population (Grant et al., 2004). Similarly, findings from the National Comorbidity Study (NCS) indicate that there is a 4.2% lifetime prevalence rate for cannabis dependence in the general population, whereas among individuals with SAD, the prevalence rate of cannabis dependence is elevated to 29.0% (Agosti et al.,

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2002). Yet, little is known about the specificity or temporal sequencing of the relationships between SAD and these substance use disorders. Elucidation of these relationships could have important implications for the prevention and treatment of these conditions among socially anxious individuals (Heimberg & Becker, 2002).

The high rates of comorbidity between SAD and AUD and cannabis dependence are cause for concern because misuse of alcohol or cannabis tends to compound the already significant problems of patients with SAD. For example, SAD patients with AUD report more severe impairment than patients with SAD without AUD (Schneier et al., 1989) and alcoholics with SAD demonstrate more severe symptoms of alcohol dependence and display more depressive symptomatology than alcoholics without SAD (Thomas et al., 1999b). Cannabis dependence among individuals with SAD is problematic because smoking cannabis has a larger effect on respiratory function than smoking tobacco (Bloom et al., 1987; Sherrill et al., 1991), including cellular changes that may serve as a risk factor for cancer (Fligiel et al., 1997; Sarafian et al., 1999). Long-term cannabis use is associated with legal problems and increased alcohol and tobacco use (Patton et al., 2002; Reilly et al., 1998) and driving under the influence of cannabis leads to increased automobile crash risk (Ramaekers et al., 2004).

Among the anxiety disorders, SAD appears to show a particularly problematic risk profile for comorbid AUD and CUD. For example, SAD is associated with higher rates of AUD relative to most other anxiety disorders (Kessler et al., 1997). SAD is also correlated with cannabis dependence at rates more than twice that of any other anxiety disorder (Agosti et al., 2002). On the matter of sequencing, evaluation of typical age of onset of SAD and AUD suggests that SAD serves as a risk factor for subsequent AUD (Kessler et al., 1997; Randall et al., 2001a; Randall et al., 2001b; Schneier et al., 1989). Additionally, in a 13-year longitudinal investigation (Crum & Pratt, 2001), individuals with subclinical symptoms of SAD showed a greater risk for AUD relative to individuals without subclinical SAD symptomatology. Unexpectedly, individuals diagnosed with SAD using DSM-III standards did not show an increased risk of subsequent AUD, but changes in diagnostic criteria for SAD from DSM-III to DSM-IV-TR complicate interpretation of these findings in relation to contemporary diagnostic definitions. In particular, DSM-III criteria included avoidance as a necessary symptom for social phobia and avoidance is no longer a necessary criterion for SAD. This change is not trivial because it may very well be those individuals with SAD who do *not* avoid social situations who are most vulnerable to problematic alcohol use, especially if they use alcohol in social situations in an attempt to attenuate anxiety reactions. Similarly, among German adolescents, SAD is associated with subsequent regular and hazardous alcohol use but not DSM-IV alcohol abuse or dependence at 4-year follow-up (Zimmermann et al., 2003). That study, however, did not follow participants very far into the typical period of onset of alcohol dependence, thereby limiting its interpretability. Although there are no known longitudinal investigations of the relationship between SAD and cannabis abuse and/or dependence, given that marijuana users report they use to marijuana to cope with stress and anxiety (Hathaway, 2003; Ogborne et al., 2000), it follows that a similar temporal relationship would occur between SAD and cannabis dependence.

The limited literature in this area makes it difficult to draw firm conclusions regarding the risk for alcohol and cannabis use disorders among those with SAD. Importantly, it is unknown whether the development of AUD or CUD is unique to SAD versus other forms of anxiety. The question of specificity is critical because SAD is highly comorbid with other anxiety disorders (Davidson et al., 1993; Merikangas & Angst, 1995) and other anxiety conditions are associated with increased rates of AUD (Kushner et al., 1990) and cannabis dependence (Zvolensky et al., 2006). When all anxiety disorder diagnoses were combined, anxiety disorders preceded AUD in the Oregon Adolescent Project (Rohde et al., 1996). However this study did not investigate the temporal relations among specific anxiety disorders. The few studies that

have examined specific anxiety conditions and their temporal associations with AUD and CUD suggest that other anxiety disorders were more likely to be sequelae of alcohol and cannabis use, whereas SAD may serve as a risk factor for subsequent AUD and CUD. For instance, among individuals with co-occurring panic and AUD, panic onset tends to follow AUD (Kushner et al., 1990). Age of onset of panic is also later than that of CUD among individuals with both conditions (Zvolensky et al., 2006). Similarly, age of onset of substance use disorder is earlier than that of generalized anxiety disorder (GAD) among individuals with both disorders (Kessler et al., 2002).

It is also unclear whether SAD and/or other anxiety conditions demonstrate specific relationships to AUD or cannabis dependence after accounting for other types of psychopathology related to these substance use disorders. Considering that SAD is highly comorbid with mood disorders (Stein & Kean, 2000) and that depression is related to both alcohol and cannabis use problems (Buckner et al., in press), often preceding the onset of alcohol use (King et al., 2004) and cannabis use (Paton et al., 1977), it may be that the high rates of alcohol and cannabis dependence among individuals with SAD are due to co-occurring mood pathology. Likewise, externalizing disorders, particularly conduct disorder, are highly comorbid with anxiety disorders (Russo & Beidel, 1994; Zoccolillo, 1992) and predict later AUDs and CUDs (Myers et al., 1995), so they must be controlled in analyses of connections between anxiety and substance use disorders. And, of course, alcohol and cannabis use are themselves highly comorbid (Agosti et al., 2002), making it is necessary to examine the effects of one substance after controlling for effects of the other.

Further, the majority of studies in this area tend to combine alcohol abuse and alcohol dependence diagnoses (Crum & Pratt, 2001; Schneier et al., 1989), making it difficult to demarcate whether individuals with SAD are at increased risk for alcohol abuse, dependence or both. This distinction is important because alcohol dependence is a more debilitating disorder (American Psychiatric Association, 1980) and it appears that individuals with SAD are particularly vulnerable to this more severe condition. For example, epidemiological studies using DSM-IV criteria suggest SAD is more likely to be associated with increased risk of alcohol dependence than alcohol abuse (Grant et al., 2005; Kessler et al., 1997). Further, among individuals seeking treatment for alcohol-related problems, 23% to 39% meet diagnostic criteria for SAD (Kushner et al., 1990; Schneier et al., 1989; Smail et al., 1984; Thomas et al., 1999a). Individuals with higher levels of alcohol-related problems also experience significantly higher levels of social anxiety (Buckner et al., 2006c; Lewis & O'Neill, 2000). In regards to cannabis, greater SAD symptoms are associated with greater number of CUD symptoms (Buckner et al., 2006a; Buckner et al., 2006b) and the NCS data indicate that SAD is associated with increased rates of cannabis dependence but not abuse (Agosti et al., 2002).

Given the ambiguities described above, the present investigation contributes to the elucidation of the relations of anxiety disorders with AUDs and CUDs in several ways. First, the comorbidity of specific anxiety disorders and AUDs and CUDs was evaluated. Second, longitudinal analyses examined whether particular anxiety disorders serve as risk factors for subsequent AUDs or CUDs. Third, relevant variables (e.g., depression, conduct disorder) served as covariates to ensure that observed effects were not better accounted for by these conditions. Fourth, the relationships between SAD and specific AUDs and CUDs were examined after also controlling for other anxiety disorders to ensure observed relationships were not due to comorbidity of anxiety pathology. Last, analyses clarified whether observed relations applied to substance abuse, dependence, or both. Given the data suggesting that SAD is particularly associated with alcohol and cannabis dependence, we hypothesized that, after controlling for theoretically relevant variables, SAD would be significantly associated with alcohol and cannabis dependence, but not abuse. Additionally, given other theoretical and empirical work suggesting that other anxiety disorders appear to be a sequelae of substance

use (Kessler et al., 2002; Zvolensky et al., 2006), it was hypothesized that SAD, but not other anxiety disorders, would be associated with the onset of subsequent alcohol and cannabis dependence, thereby demonstrating explanatory specificity.

2. Method

2.1. Participants and Procedures

The sample was drawn from the Oregon Adolescent Depression Project (Goodwin et al., 2005; Goodwin et al., 2004; Lewinsohn et al., 1993). Participants were randomly selected from nine senior high schools representative of urban and rural districts in western Oregon. A total of 1,709 adolescents completed the initial (T1) assessments between 1987 and 1989, with an overall participation rate of 61%. Approximately one half of the T1 sample was female (53.7%), with a mean age of 16.6 years (*SD* = 1.2). As participants reached their 24th birthday, a third wave of questionnaire and diagnostic interview assessments (T3) was conducted with a selected subset of time 2 (T2) participants. On the basis of T1-T2 diagnostic information, three groups were selected for the T3 diagnostic interview: (a) 360 participants with a T2 lifetime history of major depressive disorder, (b) 284 participants with a T2 lifetime history of nonaffective Axis I disorder, and (c) 457 participants with no history of mental disorder at T2. The no-disorder comparison group was representative of the entire group of participants with no mental disorder at T2 (*n* = 863) in terms of age and gender within age; all participants with non-white ethnicity were invited to participate in the T3 assessment. This sampling strategy was intentional due to the expense of running this longitudinal investigation.

At age 30 (*M* = 30.6 years, *SD* = 0.6), the participants who completed the T3 interview were invited to participate in a fourth wave (T4) of data collection. Of the 941 eligible participants, 816 (86.7%) completed the T4 diagnostic interview. The T4 participants (59% women) were primarily Caucasian (59%) and married (53%). Forty-one percent had a bachelor's degree or higher. For the T4 assessment, the retention rates for the three groups selected for the T3 interview were as follows: 86.5% for individuals in the major depressive disorder group, 82.5% for individuals in the nonaffective Axis I disorder group, and 89.5% for individuals in the no mental disorder group. Significantly higher attrition rates were noted for men than women (16% vs. 11%), as well as for participants with a lifetime history of alcohol use disorders (17% vs. 12% for those with no lifetime alcohol use disorder), and cannabis use disorders (18% vs. 12% for those with no lifetime history of cannabis use disorder).

Given that the age of onset for alcohol abuse and dependence peaks by the early 30s, (American Psychiatric Association, 2000; Grant et al., 2004) this report concerns data collected concerning lifetime diagnostic histories at T1 and T4. By age 30, the adults had been assessed on four occasions. Written informed consent was obtained from participants (and guardians, if applicable) to conduct all assessments.

2.2. Materials

Participants were interviewed at T1 with a version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) that combined features of the epidemiologic version (Orvaschel et al., 1982) and the present episode version (K-SADS-P) and included additional items to derive DSM-III-R diagnoses (American Psychiatric Association, 1980). Both versions of the K-SADS have been found to demonstrate adequate psychometric properties (Ambrosini, 2000). In the present report, lifetime histories of the following disorders at T1 were examined: SAD, PD (with and without agoraphobia), GAD, obsessive compulsive disorder (OCD), specific phobia (SP), overanxious disorder (OD), and separation anxiety disorder. Given that diagnoses at the T1 assessment periods were derived using DSM-III-R criteria, in cases where DSM-III and DSM-IV criteria differed, additional

data were used to ascertain DSM-IV criteria for the diagnoses of interest (American Psychiatric Association, 2000). Lifetime history of adult T4 diagnoses were derived from a joint administration of the Longitudinal Interval Follow-up Evaluation (LIFE; Keller et al., 1987) and the Structured Clinical Interview for DSM-IV, non-patient version (SCID-I/NP; First et al., 1994) to probe for new or continuing psychiatric episodes.

Diagnostic interviewers were carefully selected, trained, and supervised. Interviewers had advanced degrees in a mental health discipline and completed a 70-hour course in diagnostic interviewing. Interrater reliability was evaluated by the kappa statistic (Cohen, 1960). Kappas for the T1 anxiety disorders have been reported elsewhere (Lewinsohn et al., 1997) and were acceptable. Prior to conducting interviews, all interviewers were required to demonstrate a minimum kappa of .80 across all symptoms for at least two consecutive training interviews and on one videotaped interview of a participant with evidence of psychopathology. T4 interviews were audiotaped and 15% ($n = 124$) were randomly selected for reliability purposes. Interrater reliability, as evaluated by the kappa statistic, was moderate to excellent for AUD ($\kappa = .79$) and CUD ($\kappa = .90$).

2.3. Statistical Procedures

First, odds ratios and confidence intervals were computed to examine the relationships between T1 predictor variables and T4 criterion variables (alcohol abuse, alcohol dependence, cannabis abuse, cannabis dependence). Next, hierarchical logistic regression analyses were performed with each of the T4 criterion variables. T1 anxiety and mood disorders found to be associated with T4 criterion variables served as predictor variables. For each model, a dichotomous variable was created representing the absence (“0”) or presence (“1”) of the covariate Axis I disorders of interest. Given that gender is associated with anxiety disorders (Lewinsohn et al., 1998) and with substance use (Siqueira et al., 2001), gender was also included as a covariate in level 1 of all regression models. For the cannabis models, participants with a T1 lifetime history of CUD were excluded from the analyses. Both cannabis models were divided into three levels. At level 1, gender was entered and at level 2, T1 “other Axis I disorder” variable was entered. At level 3, the anxiety condition of interest was entered. For the alcohol models, participants with a T1 lifetime history of AUD were excluded from the analyses and T1 lifetime history of CUD was entered at level 2 (rather than T1 AUD). These models ensured that observed effects for T1 anxiety disorder at level 3 cannot be attributed to shared variance with the variable at levels 1 (Cohen & Cohen, 1983).

Third, hierarchical logistic regression analyses were performed to examine whether the relationship between SAD and T4 criterion variables occurred above and beyond the association among SAD and other anxiety disorders. For the cannabis models, participants with a T1 lifetime history of CUD were excluded from the analyses. Gender was entered at level 1 in the model and “other Axis I disorder” was entered at level 2. This procedure ensured any observed effects were not due to these variables. For the alcohol models, participants with T1 lifetime history of AUD were excluded from the analyses. At level 2, T1 lifetime history of CUD was entered. At level 3 in the model, SAD was entered. These models ensured that observed effects for T1 SAD at level 3 cannot be attributed to shared variance with the variable at levels 1 and 2 (Cohen & Cohen, 1983).

Univariate and multivariate survival analysis methods developed to deal with censored time-to -event data were used to test time to onset of alcohol dependence and cannabis dependence. Univariate Kaplan-Meier models were used to estimate onset rates and generate survival curves for participants with and without a lifetime history of SAD at T1. Cox proportional hazards models were specified for multivariate analysis of time to onset. Survival analysis is a powerful and informative method for identifying clinically important effects that may be obscured by analytic techniques that examine the proportion of individuals who develop a disorder at a

single point in time. In contrast to end-point analytic techniques that restrict the sample to individuals with known event occurrences, computation of the hazard function in time-to-event analyses includes censored participants who are lost to follow-up or who do not experience the target event during the data collection period and thereby maximizes statistical power (Willett & Singer, 1993).

The Kaplan-Meier method estimates risk of onset at a particular moment as the ratio of the number who onset at that time to the number of individuals currently at risk of onset. The Cox proportional hazard model, a regression-based method for time-to -event analysis, is a technique that allows for the simultaneous estimation of hazard ratios for multiple explanatory variables (Bull & Spiegelhalter, 1997). The hazard ratio with 95% confidence interval can be used as a measure of effect size with a positive ratio of 1.44, 2.48, and 4.28 representing small, medium, and large effects, respectively (Lipsey & Wilson, 2001). Proportional hazard models assume that the log-hazard profiles represented by all possible values of the predictors share a common shape and are mutually parallel (Singer & Willett, 1991). The proportional hazards assumption was tested by including a time x predictor interaction term in the Cox model. As recommended (Willett & Singer, 1993), if the time x predictor interaction term was significant, the term was retained in the model to ensure appropriate estimation of the effects of interest. If the proportional hazards assumption was not violated, the interaction term was removed from the model.

In accordance with the logistic regression models described above, participants with a lifetime history of alcohol dependence or cannabis dependence were excluded from each respective model. T1 anxiety, conduct, and mood disorders as well as gender were included in the Cox models as covariates.

3. Results

3.1. Descriptive Information

Table 1 summarizes demographic characteristics of the sample. Diagnostic frequencies, odds ratios, and confidence intervals were computed to examine the relations between T1 predictor variables and T4 criterion variables (alcohol abuse, alcohol dependence, cannabis abuse, cannabis dependence) (Table 2). Additionally, 84 (4.9%) reported a T1 lifetime history of AUD and 92 (5.4%) participants reported a T1 lifetime history of CUD.

First, relations between predictor variables were examined. Consistent with expectation, T1 SAD was significantly correlated with female gender, T1 mood disorder and T1 anxiety disorders, but not T1 conduct disorder. Contrary to expectation, T1 SAD was not associated with any T1 alcohol/cannabis variable. Second, relations among the predictor variables and the T4 alcohol abuse and alcohol dependence dependent variables were examined (Table 2). As predicted, T4 alcohol dependence was significantly associated with T1 SAD, T1 PD, T1 mood disorder, T1 conduct disorder, T1 alcohol abuse, T1 cannabis abuse, T1 cannabis dependence, and male gender. T4 alcohol abuse was not significantly associated with increased odds for T1 SAD and was only significantly associated with male gender and T1 cannabis abuse. Third, patterns of associations among the predictor variables and the T4 cannabis abuse and cannabis dependence dependent variables were examined (Table 2). Consistent with prediction, T4 cannabis dependence was significantly associated with T1 SAD, T1 mood disorder, T1 conduct disorder, T1 alcohol abuse, T1 alcohol dependence, T1 cannabis abuse, and male gender. T4 cannabis abuse was not associated T1 SAD and was only significantly associated T1 alcohol abuse and male gender.

3.2. Prediction of Lifetime History of Cannabis and Alcohol Use Disorders using Anxiety Disorder Diagnoses in Adolescence

Hierarchical logistic regression analyses were performed with each criterion variable, controlling for theoretically relevant variables. Only those T1 affective disorders found to be associated with T4 criterion variables (i.e., SAD, PD, mood disorders) served as predictor variables. Consistent with expectation, T1 SAD was the only anxiety condition to significantly predict T4 AUD or CUD after controlling for theoretically relevant variables. Specifically, T1 SAD was associated with increased odds of T4 alcohol dependence (OR = 4.47, 95% CI= 1.48-13.45, $p < .01$) but not T4 alcohol abuse (OR = 0.39, 95% CI= .05-3.07, $p > .05$). Further, T1 SAD was associated with increased odds of T4 cannabis dependence (OR = 6.58, 95% CI= 1.94-22.34, $p < .01$) but not T4 cannabis abuse (OR = 0.99, 95% CI= .13-7.79, $p > .05$).

Given that T1 PD was associated with significantly increased odds of T4 alcohol dependence, hierarchical logistic regression analyses were performed to determine whether T1 PD was significantly associated with increased odds alcohol dependence above and beyond the covariates. After controlling for T1 AUD, T1 mood disorder, T1 conduct disorder, and gender, T1 PD was not significantly associated with T4 alcohol dependence (OR = 2.36, 95% CI= .25-21.96, $p > .05$).

Similarly, because T1 mood disorder was also associated with significantly increased odds of T4 alcohol and cannabis dependence, hierarchical logistic regression analyses were performed with each relevant criterion variable for T1 mood disorder. After controlling for T1 AUD, T1 conduct disorder, and gender, T1 mood disorder was not significantly associated with T4 alcohol dependence (OR = 1.49, 95% CI= 1.0-2.28, $p > .05$) or T4 cannabis dependence (OR = .86, 95% CI= .45-1.64, $p > .05$).

3.3. Evaluation of the Unique Contribution of Social Anxiety Disorder Relative to Other Axis I Anxiety Disorders in Predicting the Development of Alcohol and Cannabis Use Disorders

Hierarchical logistic regression analyses were performed to examine whether the relation between T1 SAD and T4 criterion variables occurred above and beyond the associations between SAD and other anxiety disorders. After controlling for all theoretically relevant variables (including other anxiety disorder diagnoses and relevant T1 SUDs), T1 lifetime history of SAD continued to be significantly related to T4 lifetime history of alcohol dependence (OR = 3.72, 95% CI= 1.23-11.29, $p < .05$) but not T4 alcohol abuse (OR = 0.36, 95% CI= .05-2.78, $p > .05$). Similarly, T1 lifetime history of SAD continued to be significantly related to T4 lifetime history of cannabis dependence (OR = 4.88, 95% CI= 1.43-16.64, $p < .05$) but not T4 cannabis abuse (OR = 1.07, 95% CI= .14-8.56, $p > .05$).

3.4. Survival Curve Analyses of Social Anxiety Disorder in Predicting the Development of Alcohol Dependence

Based on cumulative sample survival probabilities from the Kaplan-Meier models, 26% of T1 participants *with* a SAD diagnosis developed alcohol dependence by age 24 with the steepest onset slope occurring between 18 to 19 years old. In comparison, only 8.5% of T1 participants *without* a SAD diagnosis developed alcohol dependence by age 24 with total cumulative onset through the T4 assessment of only 11% (see Figure 1). After covarying out the effects of participant sex and T1 anxiety, conduct, and mood disorders, T1 SAD significantly predicted time to onset of alcohol dependence in the Cox proportional hazard model (*hazard ratio* = 1.56; 95% CI = 1.06 - 2.31; $p = .02$) indicating that participants with a T1 SAD diagnosis were 1.56 times more likely to develop an alcohol dependence diagnosis over the period of observation than those without a T1 SAD diagnosis.

3.5. Survival Curve Analyses of Social Anxiety Disorder in Predicting the Development of Cannabis Dependence

Of the participants with a T1 SAD diagnosis, 13% developed cannabis dependence by age 24 compared to only 4% of T1 participants without a SAD diagnosis. Total cumulative onset through the T4 assessment (roughly age 30) was 22% for T1 SAD participants and 5% for those without T1 SAD (see Figure 2). Findings for the Cox proportional hazard model predicting onset of cannabis dependence were similar to those predicting onset of alcohol dependence. Again, participants with a T1 SAD diagnosis were significantly more likely to develop a cannabis dependence disorder over the observation period (*hazard ratio* = 1.94; 95% CI = 1.21-3.13; $p = .01$) than those without a T1 SAD diagnosis, after controlling for relevant T1 covariates.

3.6. Evaluation of the Specificity of Social Anxiety Symptoms in Predicting the Development of Alcohol and Cannabis Dependence relative to Other Axis I Anxiety Disorders

To determine whether SAD uniquely predicts alcohol and cannabis dependence (but not other Axis I conditions), hierarchical logistic regression analyses were performed with each criterion variable (with gender serving as level 1 covariate). For each regression, participants with a T1 lifetime history of the T4 criterion variable were excluded from the analyses. T1 lifetime history of SAD only demonstrated significantly increased odds of T4 lifetime history of separation disorder (OR = 3.96, 95% CI= 1.06-14.79, $p < .05$) but not mood disorder (OR = 7.36, 95% CI= .85-63.58, $p > .05$), CD (OR = .00, $p > .05$), PD (OR = 1.70, 95% CI= .37-7.86, $p > .05$), OCD (OR = .00, $p > .05$), GAD (OR = 3.17, 95% CI= .39-25.93, $p > .05$), or SP (OR = 4.94, 95% CI= 1.03-23.76, $p = .05$).

4. Discussion

The present study serves as the first known prospective investigation of the temporal relationship between current definitions of SAD and specific alcohol use and cannabis use disorders after controlling for baseline AUDs and CUDs, as well as other relevant variables. Results indicated that SAD may serve as a unique and significant risk factor for subsequent alcohol and cannabis dependence, but not abuse. These effects were above and beyond the variance accounted for by a variety of theoretically-relevant covariates, including prior CUD and AUD, mood disorders, conduct disorder, gender, and other anxiety disorders. The identification of SAD as a specific risk factor for the development of these SUDs is not trivial, as it may be that treatment of adolescent SAD could reduce the incidence of adult SUD (Kendall & Kessler, 2002).

Consistent with one of our key hypotheses, the current findings indicate that among the anxiety disorders, SAD appears to be unique in its role as a risk factor for subsequent cannabis and alcohol dependence. This finding is consistent with previous research suggesting that problematic substance use typically precedes the development of other anxiety conditions (Kessler et al., 2002; Zvolensky et al., 2006). Given the specific nature of the various anxiety disorders, it is not surprising that individuals with other anxiety disorders are less likely than individuals with SAD to use substances to self-medicate anxiety reactions. For example, patients with PD are characterized by intense fears of physiological arousal sensations, which can be brought on by illicit substances. Consequently, some patients with PD have been found to avoid cannabis, particularly when the use of cannabis has led to increased anxiety (Szuster et al., 1988). In fact, current models of the panic-cannabis nexus posit that cannabis dependence serves as a risk factor for the development of panic (Zvolensky et al., 2006). Individuals with GAD possess exaggerated worries that often focus on issues such as health and illness (Craske et al., 1989; Wells & Carter, 1999). These worries could readily focus on the consequences of substance dependence (e.g., health, legal, social stigma). Thus, fear of physiological arousal

as well as heightened worry may serve as protective factors, decreasing the risk for subsequent alcohol and cannabis dependence.

The question arises as to why SAD is associated with dependence specifically. Patients with SAD use substances with anxiolytic properties such as alcohol and cannabis to cope with social anxiety reactions (Schneier et al., 1989; Smail et al., 1984). As a result, these individuals may come to believe that they need these substances to cope with negative affective states related to social anxiety. Consequently, they become less likely to engage in adaptive coping strategies as they are ever more reliant on substances to regulate affective states. Reliance on alcohol or cannabis to cope with social anxiety increases the likelihood that these individuals will be vulnerable to substance-related problems, thereby increasing their risk for substance dependence. The use of substances to regulate emotions appears to be particularly related to *dependence*. For example, using alcohol to regulate emotions is associated with the dependence symptoms of withdrawal and tolerance (Cooper, 1994; Cooper et al., 1992) and the use of alcohol and cannabis to cope with negative emotions is associated with increased risk for the development of substance-related problems regardless of quantity/frequency of alcohol use (Cooper et al., 1995).

Three additional findings are particularly noteworthy. First, the relationship between SAD and cannabis dependence emerged after controlling for the effects of AUD and the relationship between SAD and alcohol dependence remained after controlling for CUD. These data indicate that observed relationships cannot simply be accounted for by the co-occurrence of SAD and AUD (Kessler et al., 1997) or the co-occurrence of AUD and CUD (Patton et al., 2002; Reilly et al., 1998). Second, the association between SAD and alcohol/cannabis dependence emerged even after controlling for CD. Given that CD was an especially strong predictor of subsequent AUD and CUD, the current findings suggest the relationship between SAD and these substance use disorders is not better accounted for by the relationship between CD and anxiety disorders (Russo & Beidel, 1994; Zoccolillo, 1992). Third, mood disorders were not found to predict subsequent AUD or CUD after controlling for theoretically relevant variables, suggesting that SAD may not only serve as a unique risk factor for alcohol and cannabis dependence among anxiety disorders, but among internalizing disorders generally.

The present findings should be considered in light of several limitations that point to interesting areas for further work. First, there were very few subjects in some diagnostic categories, resulting in odds ratios with large confidence intervals. Although, these prevalence rates are consistent with those found in other studies of adolescent populations (McGee et al., 1990), replication with larger samples of anxiety disorders is needed. Second, although a psychometrically sound interview was employed to identify psychopathology, future work could benefit from the use of multiple measures to address the limitations inherent in the assessment of adolescent psychopathology (Loney & Lima, 2003). Third, baseline assessments were conducted using DSM-III criteria. Although sufficient information was obtained to derive DSM-IV diagnoses, future research is necessary to ascertain whether the present findings would replicate on data collected specifically using DSM-IV criteria. Fourth, given that not all students participated T1 assessments, generalizability to those students who refused to participate is limited. Fifth, attrition over the course of 14 years was high, particularly among those with substance use disorders. Although our data suggest that SAD is correlated with alcohol and cannabis dependence despite the increased attrition rates among this group, we cannot rule out the possibility that attrition may have obscured certain effects.

Despite these limitations, the findings of the present investigation suggest that individuals with SAD are at an increased risk for a lifetime history of alcohol and cannabis dependence above and beyond a rich array of relevant factors. Moreover, the relationship between SAD and alcohol and cannabis dependence appears relatively specific, as no such effect was evident for

other anxiety or mood disorders. Further elucidation of the mechanisms underlying why SAD serves as a risk factor for subsequent cannabis and alcohol dependence could have important implications for the development of prevention and treatment programs for at-risk individuals.

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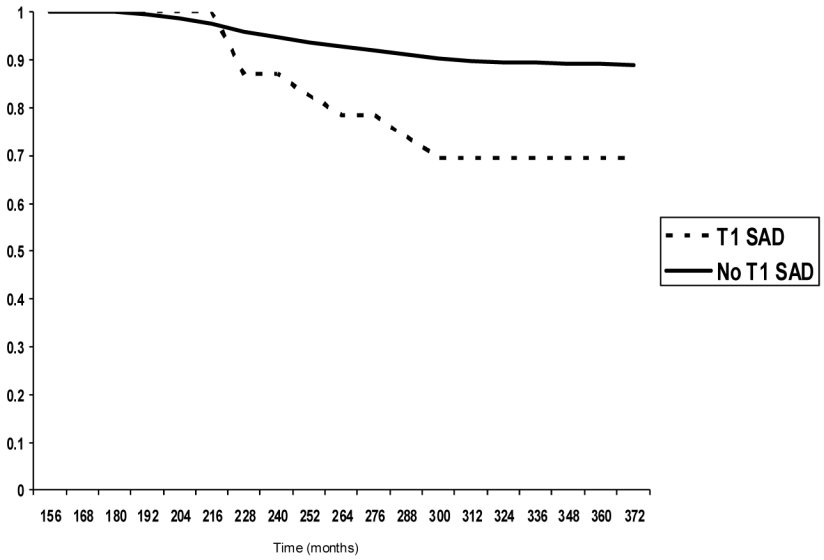

Figure 1.
Cumulative survival curve for alcohol dependence onset, excluding participants with T1 AUD.

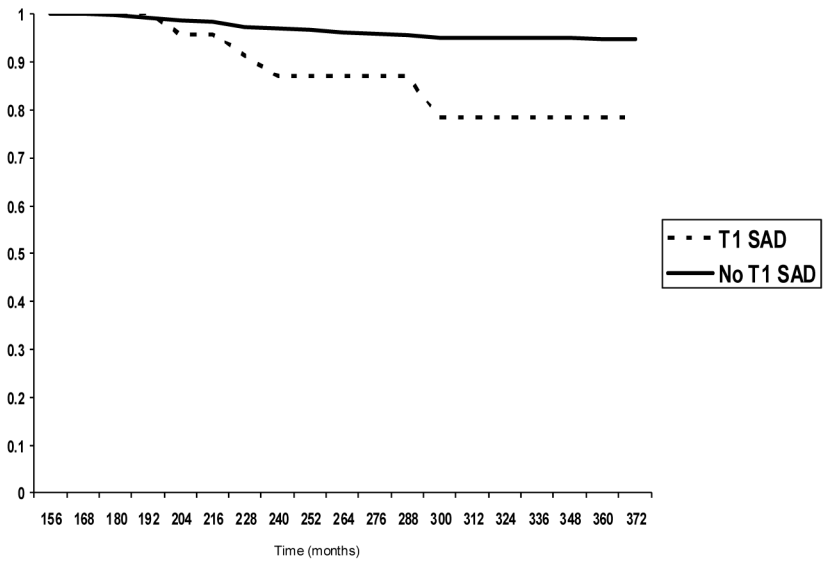

Figure 2.
Cumulative survival curve for cannabis dependence onset, excluding participants with T1 CUD.

Table 1

Demographic Information for Entire Sample and by Social Anxiety Diagnosis

	Entire Sample				No Social Anxiety Diagnosis				Social Anxiety Diagnosis			
Variable	***n***	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***
Age (years)			16.56	1.19			16.56	1.19			28.76	10.91
Gender (female)	891	52.1			870	51.7			21	84.0		
Race/ethnicity (Caucasian)	1557	91.1			1535	91.2			22	88.0		
Annual income												
$0-14,999	373	21.9			365	21.6			8	32.0		
$15,000-29,999	312	18.3			305	18.1			7	28.0		
$30,000+	248	14.5			246	14.6			2	8		

Table 2

Associations between T1 Anxiety Disorders and T4 Criterion Variables

Predictor Variable	T4 alcohol abuse	T4 alcohol dependence	T4 cannabis abuse	T4 cannabis dependence	Frequency (% total sample)
T1 SAD	.48 (.11-2.11)	3.98 (1.51-10.47)**	1.01 (.23-4.50)	4.89 (1.82-13.15)**	25 (1.5%)
T1 PD	.52 (.06-4.23)	5.82 (1.38-24.57)*	1.09 (.13-8.92)	4.06 (.96-17.25)	12 (0.7%)
T1 OCD	2.44 (.41-14.72)	5.18 (.86-31.26)	1.91 (.21-17.24)	4.48 (.74-27.14)	8 (0.5%)
T1 OD	.28 (.04-2.12)	1.37 (.43-4.43)	.58 (.08-4.48)	.51 (.07-3.90)	22 (1.3%)
T1 SP	.78 (.22-2.73)	1.89 (.69-5.18)	1.65 (.46-5.84)	.41 (.05-3.11)	34 (2.0%)
T1 separation anxiety disorder	.56 (.23-1.35)	.87 (.41-1.85)	.35 (.08-1.46)	1.51 (.68-3.34)	72 (4.2%)
Frequency (% total sample)	176 (10.3%)	185 (10.8%)	95 (5.6%)	107 (6.3%)	

Note. Values are expressed as odds ratios (95% confidence interval). T1 and T4 diagnoses reflect lifetime history. Abbreviations: social anxiety disorder (SAD), panic disorder (PD), obsessive compulsive disorder (OCD), overanxious disorder (OD), specific phobia (SP).

* $p < .05$.

** $p < .01$.

Table 3

Associations between T1 Covariates and T4 Criterion Variables

Predictor Variable	T4 alcohol abuse	T4 alcohol dependence	T4 cannabis abuse	T4 cannabis dependence	Frequency (% total sample)
Gender	1.73 (1.23-2.42)**	1.91 (1.38-2.66)**	1.46 (.95-2.25)	1.68 (1.12-2.53)*	52.0% female
T1 mood disorder	.72 (.49-1.06)	1.57 (1.11-2.22)*	1.00 (.63-1.62)	1.78 (1.17-2.71)**	347 (20.3%)
T1 conduct disorder	3.86 (1.81-8.27)**	6.69 (3.03-14.77)**	3.22 (1.38-7.54)**	16.79 (7.37-38.26)**	56 (3.3%)
T1 alcohol abuse	-	7.92 (2.71-23-08)**	18.75 (6.36-55.28)**	12.08 (4.29-33.98)**	32 (1.9%)
T1 alcohol dependence	.91 (.36-2.25)	-	1.55 (.58-4.14)	10.13 (4.75-21.51)**	53 (3.1%)
T1 cannabis abuse	3.40 (1.36-8.49)**	2.55 (1.01-6.43)*	-	5.13 (2.01-13.06)**	31 (1.8%)
T1 cannabis dependence	1.88 (.92-3.84)	7.69 (3.76-15.71)**	1.90 (.81-4.46)	-	61 (3.6%)
Frequency (% total sample)	176 (10.3%)	185 (10.8%)	95 (5.6%)	107 (6.3%)	

Note. Values are expressed as odds ratios (95% confidence interval). T1 and T4 diagnoses reflect lifetime history.

* $p < .05$.

** $p < .01$.