



# Anxiety disorders and substance use disorders: Different associations by anxiety disorder

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## ABSTRACT

Anxiety disorders (ADs) and substance use disorders (SUDs) often occur together, but the strength of this association and their apparent order of onset differ across studies. The goals of this study were to examine: (1) which ADs were associated with which SUDs, and (2) among people who experienced both an AD and a SUD, which disorder had an earlier onset. Lifetime diagnoses from the National Comorbidity Survey-Replication ( $n = 9282$ ) were used. Social phobia, generalized anxiety disorder, panic disorder, and agoraphobia were positively associated with all SUDs. Among people with both an AD and a SUD, the order of onset differed by anxiety type: social phobia nearly always had an onset prior to any SUD; panic disorder and agoraphobia tended to occur prior to some SUDs; and generalized anxiety disorder tended to occur after the onset of at least one SUD. Therefore, all ADs are positively associated with SUDs, but ADs differ in the timing of their onset relative to comorbid SUDs.

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## 1. Introduction

Anxiety disorders (ADs) and substance use disorders (SUDs) often occur together (e.g., Conway, Compton, Stinson, & Grant, 2006; Goodwin, Fergusson, & Horwood, 2004; Kessler et al., 1996; Sareen, McWilliams, Cox, & Stein, 2004), but evidence is mixed regarding the strength of this association and the order of onset (i.e., among individuals with both disorders, it is unclear which disorder tends to have an earlier onset). The purpose of this study was to examine (1) overall associations between ADs and SUDs and (2) the order of onset among people with both types of disorders, with a focus on potential differences by type of AD.

In community-based samples, there is evidence for both ADs increasing risk for SUDs (e.g., Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Kessler et al., 1996; Kushner, Sher, & Erickson, 1999; Merikangas et al., 1998; Swendsen et al., 1998; Woodward & Fergusson, 2001) and SUDs increasing risk for ADs (e.g., also see reviews by Kushner, Abrams, & Borchardt, 2000; Kushner et al., 1999; Morris, Stewart, & Ham, 2005; Schuckit & Hesselbrock, 1994; Swendsen et al., 1998). Part of the increased risk for later SUDs among people with ADs, as well as for the development of social phobia among people with earlier SUDs, may be attributable to using substances for self-medication of anxiety symptoms (Robinson, Sareen, Cox, & Bolton, 2011). Overall, ADs appear to occur earlier (e.g., Costello et al., 2003; Kessler et al., 1996;

Merikangas et al., 1998; Schuckit & Hesselbrock, 1994), though this order of onset might differ for different types of ADs (e.g., Falk, Yi, & Hilton, 2008; see below for a discussion of this possibility).

Although most research on associations between ADs and SUDs indicates that they are positively related, some contradictory evidence exists. In some cases, this may be due to the age of the sample. For example, one study found that ADs were unrelated to risk for SUDs occurring up to mid-adolescence (Costello, Erkanli, Federman, & Angold, 1999). Adding to the possibility that ADs may be protective for some people or situations, a recent study reported that among people with externalizing disorders, the presence of an AD is associated with reduced risk for SUDs (Hofmann, Richey, Kashdan, & McKnight, 2009).

Associations between ADs and SUDs may also differ depending on the type of anxiety. For example, some people with social phobia may be so withdrawn that access to substances is reduced; that is, if people with social phobia are not spending time with substance-using peer groups in adolescence and early adulthood, they may escape peer influences that reinforce substance use. Conversely, panic disorder may increase the desire for self-medication with depressant substances due to the extremely uncomfortable nature of panic attacks. Unfortunately, research directly examining the relationship between different types of ADs and SUDs has been inconsistent and limited by the fact that many studies examine combined AD diagnoses and not each individual diagnosis separately. However, one study of adults reported stronger associations with SUDs for phobias than for panic disorder (Swendsen et al., 1998). In contrast, a study of adolescents and young adults found strong associations for panic disorder and significant, though

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weaker, associations for phobias and no significant association for generalized anxiety disorder (Zimmerman et al., 2003). Although research supports a positive association between social anxiety disorder and alcohol dependence among adults (Buckner, Zvolensky, Sachs-Ericsson, & Schmidt, 2008), among young people social anxiety may be protective: one study found that anxiety/withdrawal (a dimensional scale defined as behaviors associated with an anxious and fearful interpersonal style) in early adolescence was protective against the development of alcohol dependence in early adulthood (Pardini, White, & Stouthamer-Loeber, 2007).

Type of anxiety may also influence the order of onset of ADs and SUDs. In descriptive analyses, Glantz et al. (2009) reported that most cases of social phobia began before alcohol or drug dependence, whereas approximately half of the cases of generalized anxiety disorder, panic disorder, and agoraphobia occurred prior to the onset of substance dependence. Consistent with this, Swendsen et al. (1998) reported that phobias tended to occur prior to SUDs. Falk et al. (2008) reported that alcohol abuse and dependence tended to occur prior to generalized anxiety disorder and panic disorder (but not social phobia). Consistent with this finding, Swendsen et al. (1998) found that panic disorder tended to occur after the onset of SUDs, and Kushner et al. (1999) found that ADs were predicted by SUDs in a sample in which generalized anxiety disorder was the most common AD. Thus, although the literature to date is sparse, it seems likely that social phobia tends to have an onset prior to SUDs, while generalized anxiety disorder and panic disorder may occur after the onset of SUDs.

It is not clear whether the mean age of onset of ADs or SUDs differs for people with and without comorbid disorder(s) of the other type. Although not directly addressing the issue of causality, if ages of onset do differ that would imply that the processes involved in the development of the disorders differ for people with and without comorbid disorders of the other type. Alternatively, if the ages of onset are similar for those with and without this comorbidity, that would imply that age-of-onset patterns are more related to overall developmental patterns. For example, social phobia tends to start in early adolescence, while SUDs tend to have later onsets, making a social phobia-precedes-SUD pattern likely regardless of whether social phobia affects risk for SUDs. However, if the average age of onset of SUDs is earlier among people who also have social phobia than those without social phobia, that would imply that the presence of social phobia is indicative of risk for early SUDs (perhaps due to the social phobia itself, or perhaps due to another factor that is associated with the presence of social phobia). Thus, this question indirectly addresses the issue of whether these developmental patterns (which disorder tends to occur first) are related simply to differences in the typical ages of onset of disorders or whether one disorder—or something closely associated with it—may increase risk for the other disorder.

In order to comprehensively examine associations between specific ADs and SUDs in a community-based sample, this study examined: (1) lifetime associations between specific ADs and SUDs; (2) the order of onset among people with both types of disorders, with a focus on potential differences by type of AD; and (3) whether the average age of onset of each disorder varied based on the presence or absence of a comorbid disorder of the other type. Using the National Comorbidity Survey-Replication (NCS-R) sample, we examined four different ADs: social phobia, generalized anxiety disorder, panic disorder, and agoraphobia. These ADs were examined in relation to the following types of SUDs: alcohol abuse, alcohol dependence, drug abuse (any illicit drug), drug dependence (any illicit drug), and any SUD (alcohol abuse, alcohol dependence, drug abuse, or drug dependence).

Based on the literature described above, we examined the following hypotheses. We expected all ADs to be significantly

positively associated with all SUDs, though based on previous research we expected the association between social phobia and SUDs to be relatively weaker than those for other ADs. We predicted that social phobia would tend to occur prior to all SUDs. We also expected that agoraphobia would tend to occur prior to SUDs, while generalized anxiety disorder and panic disorder might occur after SUDs, although these hypotheses were considered tentative due to the sparse evidence on these disorders. We did not make specific predictions regarding whether mean ages of onset would differ for those with and without comorbidity due to the exploratory nature of these analyses, though if differences were found we expected them to be in the direction of younger ages of onset among people with comorbidity of the opposite type (due to the likelihood that those with multiple disorders experience more severe pathology than those with a single disorder).

## 2. Methods

### 2.1. Participants

Participants from the National Comorbidity Survey-Replication (NCS-R), a cross-sectional sample of adults in the contiguous United States ( $n = 9282$ ), were used. The sample is representative of English-speaking adult household residents, and the response rate was 70.9%. Informed consent was obtained, and the study was approved by the IRBs of Harvard Medical School and the University of Michigan.

The weighted percentages of participants completing the entire assessment (including part II, which all of these participants did) were: male = 47%, female = 53%; non-Hispanic white = 73%, non-Hispanic black = 12%, Hispanic = 11%, other = 4%; education less than or equal to 12 years = 49%, education at least 13 years = 51%. Detailed information about the study design, sample, and assessment procedures can be found elsewhere (Kessler et al., 2004; Kessler & Ustun, 2004).

### 2.2. Measures

Diagnoses of ADs and SUDs were based on an in-person survey that was administered by trained, supervised interviewers using computer-assisted personal interview (CAPI) methods. The diagnoses were based on a modified version of the Composite International Diagnostic Interview (CIDI; World Health Organization; Kessler et al., 1998). Lifetime diagnoses were used in this study. Specific information about the assessment of each diagnosis is provided below.

#### 2.2.1. ADs

Social phobia, generalized anxiety disorder, panic disorder, and agoraphobia were assessed according to DSM-IV diagnostic criteria. Prevalence rates, as well as the unweighted number of participants with each disorder, are reported in the top row of Table 1. Panic disorder with agoraphobia diagnoses was not included in this study due to low prevalence (1.4%).

#### 2.2.2. SUDs

Alcohol abuse, alcohol dependence, drug abuse, and drug dependence were assessed according to DSM-IV criteria. Prevalence rates, as well as the unweighted number of participants with each disorder, are reported in the leftmost column of Table 1. Hierarchies were not applied; therefore, a participant who met criteria for dependence on a substance was still diagnosed with abuse of that substance if he or she met criteria for it. All illicit drugs were combined into the drug use disorder diagnoses. In addition, a

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