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Substance use disorders increase the odds of subsequent mood disorders

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ABSTRACT

Background: There is a well-known association between mood disorders and substance use disorders (SUD), but little research has been conducted on SUDs as risk factors for the development of subsequent mood disorders.
Methods: We analyzed data from the National Comorbidity Survey Replication study. Diagnoses were determined using DSM-IV criteria. Odds ratios (aORs) of subsequently developing mood disorders were adjusted for age, sex and race/ethnicity.
Results: Data from 5217 individuals were included (6.6% male; mean age 45.3 years; 72.6% White, 11.2% Black, 12.5% Hispanic and 3.7% other). Subsequent mood disorders developed in 26.4% of individuals with primary adolescent-onset SUD (12–17 years), 21.7% of those with SUD onset at 18–25 years, and 14.0% of those with SUD onset between the ages of 26 and 34 years. The mean lagtime between SUD onset and development of a mood disorder was about 11 years. Controlling for demographic variables, the aORs of developing a mood disorder in these three age groups were 2.44, 3.65, and 3.25. Substance dependence was associated with higher odds of mood disorders than was abuse. Among the specific mood disorders, the increased odds of developing bipolar disorder were particularly high among individuals with drug dependence.
Conclusions: Individuals with adolescent and young adult-onset SUD had increased odds of developing a secondary mood disorder. This indicates that adolescents and young adults with SUD should be closely monitored for both positive and negative mood symptoms. SUD treatment and aftercare offer opportunities for the early identification of secondary mood disorders.
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1. Introduction

Individuals with mood disorders have high rates of substance use disorders (SUD; Conway et al., 2006; Grant et al., 2005) and are over-represented among people with SUD (Conner et al., 2009; Grant et al., 2004; Lai and Huang, 2009). About 30–50% of individuals with bipolar disorder (BPD) have a primary SUD (Fossey et al., 2006; Strakowski and DelBello, 2000; Strakowski et al., 2005; Winokur et al., 1995), and 30–55% of individuals with major depressive disorder (MDD) have a primary alcohol use disorder (AUD) (Boschloo et al., 2012; Falk et al., 2008; Swendsen et al., 1998). Because the dual diagnosis of both SUD and a mood disorder is associated with very high rates of morbidity (Blanco et al., 2012; Dutta et al., 2007; Gao et al., 2008) and mortality (Oquendo et al., 2010; Sublette et al., 2009; Waller et al., 1999), understanding the trajectory of mood disorders among individuals with SUD will help clinicians improve the quality of life among patients with this dual diagnosis.

Primary SUD might be a result of self-medication of prodromal mood disorder symptoms (Strakowski and DelBello, 2000) or may be a causal factor for mood disorders perhaps by triggering an underlying susceptibility (Fergusson et al., 2011; Strakowski and DelBello, 2000; Boschloo et al., 2012). Thus, a better understanding of the connection between primary SUD and the development of subsequent mood disorders may lead to opportunities for the early detection, intervention, and perhaps even prevention, of mood disorders among people with SUD.

Unfortunately, only a few studies have assessed primary SUD as a potential risk factor for the development of a subsequent mood disorder. In longitudinal studies of depression, nonmedical opioid dependence was a predictor of subsequent MDD (adjusted Hazard Ratio = 5.21; Martins et al., 2009); alcohol or illicit drug use in childhood or adolescence predicted MDD in one's late 20s (Brook et al., 2002); AUD in adolescence predicted depression in early adulthood

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(OR = 2.3; Rohde et al., 2001); and binge drinking increased the risk of depressive symptoms five years later by about two-fold (Paljarvi et al., 2009). In studies of BPD, opioid dependence from nonmedical use increased risk of subsequent BPD type I (adjusted Hazard Ratio = 5.0; Martins et al., 2009), and adolescents with SUD were 2.8 times more likely to have BPD than were adolescents without SUD (Wilens et al., 1997).

Although comparisons among studies are hindered by different study populations and outcome variables, the available research suggests that individuals with specific primary SUDs may be at higher risk of developing mood disorders. For instance, the higher risk of mood disorders associated with opioid dependence as compared to binge-drinking or combined SUD suggests that substance dependence may be a greater risk factor for mood disorders than is substance abuse. Consistent with this, 34.0% of individuals with a lifetime diagnosis of drug abuse had a lifetime mood disorder, as compared to 61.7% of individuals with drug dependence in a national survey (Conway et al., 2006). On the other hand, Falk et al. (2008) found that alcohol abuse, but not dependence, was associated with an increased frequency of secondary mood disorders. Further study is needed to elucidate the potential relationship between substance use disorder diagnosis and the development of mood disorders.

To further explore the relationship between the development of mood disorders among individuals with primary SUD, we analyzed data from the population-based National Comorbidity Survey Replication (NCS-R) study. The purpose of our analysis was to estimate risk of secondary mood disorders among adolescents and young adults with SUD, including the relationships between specific types of primary SUDs and specific types of secondary mood disorders. We also assessed the frequency of alcohol and specific drug use prior to the onset of mood disorder in this population. Given the association between SUD and mood disorders, we hypothesized that (a) adolescents and young adults with SUD have a higher risk of subsequent mood disorders than do those without SUD, and (b) the risk of mood disorders associated with primary substance dependence is greater than risk associated with substance abuse.

2. Methods

2.1. Data source/participants

The National Comorbidity Survey Replication (NCS-R) study was a cross-sectional study that collected data on symptoms of mental disorders of 9282 individuals age 18 years and older from a nationally-representative population in the continental United States (US) in 2001 through 2003. Part I of the interview was conducted on all participants and included a core diagnostic assessment. A second part asked about additional disorders and was administered to 5692 individuals who met the lifetime criteria for a core disorder in Part I, as well as a probability subsample of other respondents. Additional details of the study procedures have been published elsewhere (Kessler and Ustun, 2004). After excluding individuals with SUDs secondary to mood disorders and individuals who developed SUDs after the age of 34 years, the final sample size for our analysis was 5217.

2.2. Procedures

The NCS-R DSM-IV diagnoses and ages of onset were based on self-report of symptoms using Version 3.0 of the World Health Organization's (WHO) Composite International Diagnostic Interview (CIDI), a fully-structured lay-administered interview (Kessler and Ustun, 2004). A mood disorder diagnosis was defined as a lifetime diagnosis of MDD, dysthymia or BPD. With regard to BPD, we included type I, type II and subthreshold. We included subthreshold in the bipolar category, because it more closely resembles bipolar disorder than MDD in outcome (Nusslock and Frank, 2011), and that other research has found that the risk of lifetime (Merikangas et al., 2007) and secondary (Kenneson et al., 2013) SUD is also increased among subthreshold bipolar disorder in addition to type I and type II. Subthreshold bipolar disorder was defined as (a) recurrent subthreshold hypomania and intercurrent MDE, or (b) recurrent hypomania without recurrent MDE, or (c) recurrent subthreshold hypomania without intercurrent MDE. Subthreshold hypomania was defined as meeting two or more criterion B symptoms and all other criteria for hypomania. Cases with plausible organic causes were excluded. Additional details regarding the categorization of bipolar disorder in the NCS-R study have been previously published (Merikangas et al., 2007).

SUD was defined as lifetime alcohol abuse or dependence, or drug (cocaine, cannabis, prescription, or other) abuse or dependence. The "other" category included sedatives, tranquilizers, stimulants, analgesics, inhalants, hallucinogens, and heroin. Among individuals with more than one of the above four lifetime SUD diagnoses, the one that occurred first was used to determine the individual's age of SUD onset. Primary SUD was defined as SUD onset occurring at an earlier age than mood disorder onset. Within the NCS-R dataset, age at onset is reported in years; therefore, we excluded individuals who had the same age of onset for both conditions ($n = 64$), because it was impossible to determine sequence of onset of the two conditions. We categorized individuals by age at SUD onset as adolescents (age 12–17 years), emerging adults (18–24 years) and young adults (25–34 years). We have chosen these age categories because SUDs among children are uncommon, and because as the age of SUD onset increases the percent of people with mood disorders that develop after, compared to before, the onset of SUD decreases. As a consequence, the sample sizes are small for people with childhood ($n = 23$) or older adult onset ($n = 76$) primary SUD and a subsequent mood disorder in this study population.

2.3. Analysis

All statistical analyses were conducted using Statistical Analysis Software (SAS) version 9.2. To account for the complex design structure and weighting of NCS-R, we used the survey applications, which utilize the Taylor series linearization method (An, 2002). Chi-square analysis was used to compare the frequency of mood disorders between groups with different ages of SUD onset, with p-values of less than 0.0083 considered to be statistically significant (based on the Bonferroni method of correction for multiple comparisons). Logistic regression, controlling for current age, race/ethnicity (White, Black, Hispanic or Other) and sex, was used to determine adjusted odds ratios (aORs) of developing a subsequent mood disorder. The comparison group for each analysis was comprised of individuals who did not have lifetime SUD or mood disorder at the age in question. Thus, each comparison group included individuals who did not have a lifetime SUD at the time of the survey, as well as those that developed an SUD after the upper limit of the age group in that analysis (e.g., when analyzing the 12–17 year age group, the comparison group included individuals who develop an SUD at the age of 18 or later). Reported p-values are not corrected for multiple comparisons. We calculated 16 aORs per age group; therefore, aORs with p-values < 0.0015 were considered to be significant in this study.

2.4. Approvals

The study procedures were approved by the institiutional review board of the Syracuse Veterans Affairs Medical Center.

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