



Anxiety disorders moderate the association between externalizing problems and substance use disorders: Data from the National Comorbidity Survey-Revised

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ABSTRACT

Anxiety disorders and externalizing problems are both associated with substance use disorders. However, the nature of this relationship remains unclear. To examine whether presence of an anxiety disorder changes the association between externalizing problems (conduct disorder, oppositional defiant disorder, and attention deficit hyperactivity disorder) and substance use disorders, we analyzed data from the National Comorbidity Survey-Replication, which is based on a nationally representative sample of 9282 English-speaking adults. Presence of externalizing problems was associated with an increased odds for alcohol abuse (OR: 6.7, CI: 5.6–8.1), alcohol dependence (OR: 7.6, CI: 5.9–9.6), substance abuse (OR: 9.9, CI: 8.1–12.2), and substance dependence (OR: 13.1, CI: 9.6–17.8). Similarly, anxiety disorders were associated with increased odds for substance use disorders. The highest association was found between post-traumatic stress disorder and substance use disorder (OR: 9.2, CI: 5.4–15.5). Individuals who met diagnostic criteria for an anxiety disorder and externalizing problems showed consistently and significantly lower odds for substance use problems than subjects with externalizing problems without a comorbid anxiety disorder. The results suggest that presence of any anxiety disorder reduces the association between externalizing problems and substance use disorders, possibly because the fear of bodily symptoms prevents individuals with externalizing problems from engaging in drug-seeking behaviors.

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Anxiety disorders and substance use disorders are common (Kessler et al., 2004; Kessler, Berglund, Demler, Jin, & Walters, 2005; Kessler, Demler, Frank, et al., 2005) and frequently comorbid conditions (Burns & Teesson, 2002; Grant et al., 2004; Himle & Hill, 1991; Kessler et al., 1997; Kushner, Abrams, & Borchardt, 2000; Saunders & Schuckit, 2006; Schuckit, 2006; Wittchen, Perkonig, & Reed, 1996). For example, it has been shown that substance use problems are common conditions among individuals with high social anxiety (Crum & Pratt, 2001; Morris, Stewart, & Ham, 2005), traumatized people (Hien, Cohen, & Campbell, 2005; Jacobson, Southwick, & Kosten, 2001), and individuals with frequent panic attacks (Katerndahl & Realini, 1999; Zvolensky, Feldner, Leenfeldner, & McLeish, 2005). Some investigators have suggested that substance use disorders directly induce anxiety and other mental

disorders (Wittchen et al., 1996), while others conversely propose that anxiety disorders may lead to substance dependence through a process of self-medication in an attempt to avoid uncomfortable symptoms of an anxiety disorder (Kushner et al., 2000). Others have proposed that a high familial aggregation amongst substance use disorders and anxiety is attributed to a common diathesis, in which a shared vulnerability factor simultaneously explains mutual variation in both substance use disorder and anxiety (Bizzarri et al., 2007; Kendler, Davis, & Kessler, 1997; Kendler et al., 1995).

Other common comorbid conditions of substance use disorders include externalizing problems, such as conduct disorder (CD), oppositional defiant disorder (ODD), and attention deficit hyperactivity disorder (ADHD) (Krueger, Markon, Patrick, & Iacono, 2005; Merikangas et al., 1998; O'Brien & Frick, 1996; Pliszka, 1989). For example, Krueger and colleagues (Krueger et al., 2005) reported data from a large twin sample that are consistent with the notion of a single underlying spectrum of externalizing syndromes, comprised of adult sensation-seeking behaviors, antisocial personality disorder, conduct disorder, alcohol and substance dependence of illicit drugs.

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In sum, there is evidence for a strong association between externalizing problems and substance use disorders on the one hand, and anxiety disorders and substance use disorders on the other hand. In the case of anxiety disorders, some theorists have proposed that substance use problems are the result of attempts to avoid certain anxiety-related sensations. In contrast, in the case of externalizing problems, it has been proposed that substance use problems are the result of general sensation-seeking behaviors. Alternative theories state that associations between these conditions are not functionally linked but rather the result of common vulnerability factors. Despite the high association between substance use and anxiety disorders on the one hand and externalizing problems on the other hand, no study has yet examined the relationship between substance use, anxiety disorders, and externalizing problems.

The objective of the present study was to examine the relationship between these three different diagnostic groups (externalizing problems, anxiety disorders, and substance use disorders). More specifically, our goal was to examine whether the co-occurrence of an anxiety disorder and an externalizing problem heighten or lower the likelihood for a comorbid substance disorder (i.e., alcohol use and illicit substance use disorders). If anxiety disorders and externalizing problems are independently associated with substance use problems, one would predict that individuals with comorbid anxiety and externalizing problems are more likely to meet criteria for a substance use disorder than individuals with either disorder alone. In order to answer this question, we analyzed data from the National Comorbidity Survey-Replication (NCS-R; Kessler & Merikangas, 2004), a large, nationally representative survey of mental disorders among English-speaking residents of the continental United States 18 years and older.

1. Methods

Data were drawn from the public release of the National Comorbidity Survey-Replication. Diagnoses were derived from the World Mental Health Survey Initiative Version of the World Health Organization Composite International Interview (WMH-CIDI), which is a fully structured lay-administered diagnostic interview that generates DSM-IV diagnoses. Interviews were conducted in person with 9282 respondents (47.4 male), with the mean age of respondent equaling 44.73 (S.D. = 17.5). Verbal informed consent was obtained before data collection (Kessler & Merikangas, 2004). The NCS-R was carried out by the professional field staff of the Survey Research Center at the Institute for Social Research, University of Michigan, between February 2001 and April 2003. Sampling was based on a multi-stage clustered area probability design. The response rate was 70.9%. Respondents received \$50 for participation. The human subjects committees of Harvard Medical School and the University of Michigan, Ann Arbor, approved these recruitment and consent procedures.

The NCS-R interview was administered in two parts. Part I included a core diagnostic assessment of all respondents ($N = 9282$). A probability sub-sample of 5692 respondents was also administered a Part II interview that assessed disorders of secondary interest plus a wide range of correlates. A variety of weighting options are available in the NCS-R, depending on the research question at-hand. We opted to use the consolidated weight for Part I, which corresponded to the diagnostic variables of interest. The consolidated weight was compiled primarily on the basis of a non-response adjustment approach, which awarded a greater weight to individuals unlikely to be sampled by the NCS-R. This was determined by computing the joint product of the following five sub-weights: (1) a locked building sub-sampling

weight, (2) a within-household probability of selection weight, (3) an unadjusted non-response weight (4) a post stratification selection weight, and (5) a Part II selection weight. Therefore, cases drawn from an underrepresented group (as determined by the sub-weights) were awarded a greater “influence” vis a vis the consolidated weight, to compensate for the fact that fewer cases in the sample (versus the population) were available. A more detailed discussion of NCS-R sampling and weighting is provided elsewhere (Kessler & Merikangas, 2004). Sample weights were incorporated into the current analyses using SPSS Complex Samples module in order to obtain more precise parameter estimates corresponding to individual case weights.

We compared the lifetime odds ratios (OR) for substance use disorders (alcohol abuse/dependence, substance abuse/dependence) among: (1) individuals with an anxiety disorder (agoraphobia without panic disorder, panic attacks, panic disorder, generalized anxiety disorder [GAD], post-traumatic stress disorder [PTSD], specific phobia and social anxiety disorder) but with no externalizing problems; (2) individuals with externalizing problems (i.e., conduct disorder, oppositional defiant disorder, and attention deficit hyperactivity disorder) but no anxiety disorder; and (3) individuals with externalizing problems and an anxiety disorder using adjusted odds ratios based on adjustments provided by relative weights in the NCS-R. It should be noted, that although antisocial personality disorder can be considered part of the externalizing spectrum disorders, this syndrome was not included amongst NCS-R diagnoses and therefore could not be incorporated into the current study.

Individual substances included in the illicit substance abuse/dependence included marijuana, cocaine, psychoactive medications, hallucinogens, heroin and an “other” category, which included a more comprehensive list in a written prompt, including drugs from other categories such as barbituates, sedatives, etc. Nicotine dependence was not subsumed under the substance-related disorders in the current study.

Odds ratios were computed for each cross categorization of interest (i.e., substance abuse with or without externalizing problems), and focused on lifetime prevalence of relevant disorders. The odds ratio is a measure of the effect size defined as the ratio of the odds of an event (presence of substance use disorder) occurring in one group (individuals with an anxiety disorder) to the ratio of the event in another group (individuals without an anxiety disorder). An odds ratio of 1 indicates that the event is equally likely in both groups. If the odds ratio of 1 is outside the 95% confidence interval, the odds ratio is significant at the $p < 0.05$ level. Furthermore, two odds ratio are significant at $p < 0.05$ if the confidence intervals are non-overlapping. All analyses were conducted utilizing the entire NCS-R dataset ($N = 9282$).

2. Results

Tables 1 and 2 present the odds ratios and the 95% confidence intervals for a diagnosis of alcohol abuse, alcohol dependence, illicit substance abuse, and illicit substance dependence among (1) individuals with an anxiety disorder but without externalizing problems, (2) individuals with externalizing problems without an anxiety disorder, and (3) individuals with comorbid anxiety disorders and externalizing problems.

2.1. Association between anxiety disorders, externalizing problems, and alcohol use disorders

Results in Table 1 showed that externalizing problems (without a comorbid anxiety disorder) were associated with increased odds

Table 1

Odds ratios for the lifetime diagnoses of alcohol use disorders among DSM-IV anxiety disorders without externalizing problems, anxiety disorders with externalizing problems, and externalizing problems without anxiety disorders.

	Alcohol dependence			Alcohol abuse		
	OR (95% CI)	N	p	OR (95% CI)	N	p
Agoraphobia w/o panic	2.4 (1.4–4.2)	20	<0.01	3.0 (1.4–6.3)	11	<0.01
Agoraphobia w/o panic + externalizing	1.3 (0.6–2.8)	17	ns	1.4 (0.6–3.3)	9	ns
Panic attacks	2.7 (2.2–3.1)	322	<0.001	2.9 (2.1–3.8)	134	<0.001
Panic attacks + externalizing	1.2 (0.9–1.7)	181	ns	1.7 (1.1–2.4)	110	<0.01
Panic disorder	2.7 (2.2–3.1)	72	<0.001	3.4 (2.3–5.1)	37	<0.001
Panic disorder + externalizing	1.2 (0.9–1.7)	55	ns	1.9 (1.2–3.1)	35	<0.01
GAD	2.4 (1.9–3.1)	101	<0.001	2.2 (1.5–3.3)	41	<0.001
GAD + externalizing	1.2 (0.8–1.8)	68	ns	2.2 (1.4–3.4)	51	<0.001
PTSD	3.8 (2.8–5.0)	96	<0.001	4.6 (3.1–6.9)	50	<0.001
PTSD + externalizing	1.1 (0.7–1.6)	69	ns	1.7 (1.1–2.5)	47	<0.05
Specific phobia	2.8 (2.2–3.4)	164	<0.001	3.2 (2.2–4.5)	71	<0.001
Specific phobia + externalizing	1.1 (0.8–1.5)	95	ns	1.5 (1.0–2.3)	65	<0.05
SAD	2.8 (2.2–3.4)	163	<0.001	3.5 (2.5–4.8)	76	<0.001
SAD + externalizing	1.5 (1.1–2.1)	119	<0.05	1.8 (1.2–2.7)	73	<0.01
Externalizing	6.7 (5.6–8.1)	320	<0.001	7.6 (5.9–9.6)	268	<0.001

Note: OR, odds ratios; GAD, generalized anxiety disorder; PTSD, post-traumatic stress disorder; SAD, social anxiety disorder. N reflects non-overlapping cases with a given disorder (anxiety or anxiety plus externalizing) and alcohol use disorder.

for comorbid alcohol abuse (OR: 6.7, CI: 5.6–8.1) and alcohol dependence (OR: 7.6, CI: 5.9–9.6). Furthermore, all anxiety disorders (without a comorbid externalizing disorder) were associated with increased odds of a comorbid alcohol use disorder (range of ORs: 2.2–4.6).

The odds ratio for alcohol abuse among individuals with externalizing problems but without comorbid anxiety disorder was significantly greater than the odds ratios for alcohol abuse among individuals with externalizing problems and comorbid anxiety disorders (range of ORs: 1.1–2.5). Similarly, the odds ratio for comorbid alcohol dependence and externalizing problems but without an anxiety disorder was significantly greater than the odds ratios for alcohol dependence among anxious individuals with comorbid externalizing problems (range of ORs: 1.4–2.2).

The difference in odds ratios between anxious individuals with and without externalizing problems was significant for alcohol abuse in individuals with panic attacks, panic disorder, GAD, PTSD, specific phobia, and social anxiety disorder. In contrast, the difference in odds ratios between anxious individuals with and without externalizing problems was only significant for alcohol dependence in individuals with PTSD.

2.2. Association between anxiety disorders, externalizing problems, and illicit substance use disorders

A similar pattern of results emerged for illicit substance use disorders (Table 2). Externalizing problems (without a comorbid anxiety disorder) were associated with increased odds for

Table 2

Odds ratios for the lifetime diagnoses of substance use disorders among DSM-IV anxiety disorders without externalizing problems, anxiety disorders with externalizing problems, and externalizing problems without anxiety disorders.

	Substance abuse			Substance dependence		
	OR (95% CI)	N	p	OR (95% CI)	N	p
Agoraphobia w/o panic	2.2 (1.0–4.6)	9	<0.05	3.9 (1.4–10.9)	5	<0.001
Agoraphobia w/o panic + externalizing	1.4 (0.7–3.0)	14	ns	1.5 (0.6–3.8)	7	ns
Panic attacks	2.4 (1.7–3.6)	188	<0.001	4.5 (2.9–7.1)	69	<0.001
Panic attacks + externalizing	1.4 (1.0–2.0)	161	<0.05	1.6 (1.0–2.4)	84	<0.05
Panic disorder	3.0 (2.4–3.8)	40	<0.001	3.1 (1.8–5.7)	16	<0.001
Panic disorder + externalizing	1.8 (1.1–2.8)	45	<0.05	1.9 (1.1–3.2)	26	<0.05
GAD	2.3 (1.6–3.2)	56	<0.001	2.3 (1.3–3.9)	19	<0.01
GAD + externalizing	1.4 (0.9–2.2)	59	ns	1.6 (0.9–2.6)	32	ns
PTSD	4.7 (3.3–6.6)	64	<0.001	9.2 (5.4–15.5)	32	<0.001
PTSD + externalizing	1.1 (0.8–1.7)	59	ns	2.1 (1.3–3.3)	41	<0.01
Specific phobia	2.2 (1.7–3.0)	78	<0.001	3.8 (2.3–6.3)	34	<0.001
Specific phobia + externalizing	1.1 (0.8–1.6)	81	ns	1.5 (1.0–2.4)	46	ns
SAD	2.6 (2.0–3.4)	89	<0.001	4.1 (2.7–6.5)	40	<0.001
SAD + externalizing	1.9 (1.4–2.8)	107	<0.05	2.5 (1.6–3.8)	62	<0.001
Externalizing only	9.9 (8.1–12.2)	263	<0.001	13.1 (9.6–17.8)	132	<0.001

Note: OR, odds ratios; GAD, generalized anxiety disorder; PTSD, post-traumatic stress disorder; SAD, social anxiety disorder. N reflects non-overlapping cases with a given disorder (anxiety or anxiety plus externalizing) and substance use disorder.

substance abuse (OR: 9.9, CI: 8.1–12.2), and substance dependence (OR: 13.1, CI: 9.6–17.8). Furthermore, all anxiety disorders (without comorbid externalizing problems) were associated with increased odds of a comorbid substance use disorder (range of ORs: 2.2–9.2).

As in the case of alcohol use disorder, the odds ratio for comorbid substance abuse and externalizing problems (without anxiety disorders) was significantly greater than the odds ratios for comorbid substance abuse and externalizing problems among individuals with comorbid anxiety disorders (range of ORs: 1.1–1.9). Similarly, the odds ratio for comorbid substance dependence and externalizing problems (but without an anxiety disorder) was significantly greater than the odds ratios for substance dependence among individuals with an anxiety disorder and comorbid externalizing problems (range of ORs: 1.5–2.5).

Consistent with results observed among alcohol use disorders, comorbid externalizing problems generally lowered the odds for substance use disorders among individuals with some anxiety disorders. This difference was significant in individuals with PTSD and specific phobias for substance use disorder, and in individuals with panic attacks and PTSD for substance dependence.

2.3. Post-traumatic stress disorder

PTSD (without externalizing problems) was the anxiety disorder most consistently associated with the highest odds of alcohol use disorder (OR: 3.8, CI: 2.8–5.0), alcohol dependence (OR: 4.6, CI: 3.1–6.9), substance use disorder (OR: 4.7, CI: 3.3–6.6) and substance dependence (OR: 9.2, CI: 5.4–15.5). When externalizing problems were comorbid, the odds ratios decreased significantly (range of ORs: 1.1–1.7; see Tables 1 and 2).

2.4. Differentiation between externalizing problems

In order to determine whether certain individual externalizing diagnoses were differentially associated with particular anxiety disorders, additional analyses were conducted in a logistic regression framework, computing odds ratios between each anxiety diagnosis and CD, ODD and ADHD. Specifically, we computed odds ratios for each externalizing disorder relative to each alcohol and substance use disorder in cases with and without an anxiety disorder (i.e., all anxiety diagnoses were collapsed into a single dummy variable coded true or false, and analyses were conducted in parallel for each group). For all subanalyses, cases endorsing both oppositional defiant disorder and conduct disorder were collapsed into the conduct disorder category due to the DSM-IV hierarchy rule.

For the nonanxious group, alcohol abuse was significantly related to ODD (OR: 3.2, 95% CI: 1.5–6.7), CD (OR: 5.3, 95% CI: 2.6–10.8) and ADHD (OR: 3.2, 95% CI: 1.4–7.8), although no one predictor emerged as superior as evidenced by overlapping confidence intervals. For the anxious group, however, all externalizing disorders significantly predicted alcohol abuse, although ADHD (OR: 1.4, 95% CI: 1.1–2.0) was outperformed by CD (OR: 3.5, 95% CI: 2.5–4.9) but not ODD (OR: 2.3, 95% CI: 1.6–3.1). Similar comparisons were made for alcohol dependence, wherein non-anxious cases were significantly more likely to endorse dependence in the presence of comorbid CD (OR: 8.0, 95% CI: 3.3–19.4) or ADHD (OR: 3.3, 95% CI: 1.1–10.2) but not ODD (OR: 0.8, 95% CI: 0.2–2.7). In anxious cases alcohol was related to CD (OR: 3.1, 95% CI: 2.1–4.7) and ODD (OR: 2.8, 95% CI: 1.9–4.1) but not ADHD (OR: 1.5, 95% CI: 1.0–2.2).

In the case of substance use disorders, similar analyses were performed. All predictors were comparable in terms of predicting substance abuse in nonanxious cases as well as anxious cases (for

the sake of space we omitted these analyses). However, only conduct disorder was related to substance dependence in nonanxious cases (OR: 5.7, 95% CI: 1.6–20.8). For anxious cases, all predictors were significantly related to substance dependence however we also omitted these results for space considerations.

Overall, no single consistent pattern of results emerged across the externalizing disorders as they related to the substance use disorders in anxious versus nonanxious cases, and in many cases predictors were statistically equivalent. This suggests that the meaning of “externalizing” is not consistently different for anxious versus nonanxious cases.

2.5. Sex differences

In order to explore whether the association between externalizing problems and substance use is more strongly related to males than females, we examined sex as a potential moderator. This was accomplished by testing the interaction between the presence of externalizing problems and sex in a stepwise logistic regression framework in accordance with Baron and Kenny (1986), entering sex and externalizing at step one, and the product term at step two. Moderational analyses were conducted for each of the four dependent variables of interest (alcohol abuse, alcohol dependence, illicit substance abuse, and illicit substance dependence). Interestingly, a moderational effect was observed for both alcohol use disorders, but neither substance use disorder. For instance, it was found that in the case of alcohol abuse, exponentiated beta (Exp β ; computationally equivalent to odds ratios) for the interaction was statistically significant (Exp β = 1.5, 95% CI: 1.1–2.1, $p < 0.05$), which was also true for alcohol dependence (Exp β = 1.88, 95% CI: 1.2–2.8, $p < 0.05$), although in both analyses, the interaction term was less robust than each main effect, as evidenced by non-overlapping confidence intervals. Follow-up analyses were conducted in order to probe the nature of the interaction, and it was discovered that a greater proportion of females ($N = 290$) versus males ($N = 238$) without an externalizing disorder endorsed alcohol abuse, although this difference was nonsignificant, $\chi^2(1, N = 528) = 1.99, p > 0.09$. However the reverse was true in cases with an externalizing disorder (i.e., males with externalizing were more likely to endorse alcohol abuse), $\chi^2(1, N = 320) = 3.96, p > 0.05$. A similar pattern was observed in the case of alcohol dependence, wherein females were significantly more likely to endorse alcohol dependence in the absence of externalizing disorders, $\chi^2(1, N = 672) = 8.57, p > 0.01$, and less likely to endorse alcohol dependence in the presence of externalizing disorders, $\chi^2(1, N = 176) = 4.00, p > 0.05$.

In the case of substance abuse (Exp β = 1.4, 95% CI: 0.8–1.7, $p = 0.36$) and substance dependence (Exp β = 1.2, 95% CI: 0.7–2.0, $p = 0.55$) it was found that sex did not moderate the relationship between anxiety and substance use.

3. Discussion

The literature reports a strong association between substance use disorders and various forms of anxiety disorders (e.g., Grant et al., 2004; Merikangas et al., 1998). In addition, there is also a strong relationship between externalizing problems and alcohol and illicit substance use disorders. However, the nature of the association between anxiety disorders and substance use disorders on the one hand and externalizing problems and substance use disorders on the other hand is not well understood. Based on the literature, our central prediction concerned the patterns of association between these conditions. If anxiety disorders and externalizing problems are independently associated with substance use problems, then anxious participants with a comorbid

externalizing problems should have the same or perhaps increased odds for meeting criteria for a substance use disorder than anxious participants without comorbid externalizing problems or individuals with externalizing problems without a comorbid anxiety disorder. In order to examine this issue, we analyzed the NCS-R data in terms of adjusted (weighted) odds ratios, which ultimately provided a standardized means of comparing various morbidities in isolation and in concert.

Results consistently supported the notion that although anxiety disorders and externalizing problems were each uniquely associated with increased odds for substance use disorders, the comorbid state *reduced* these odds. A particularly dramatic difference was observed between externalizing problems with and without comorbid anxiety disorder. More specifically, among individuals with externalizing features, every anxiety disorder significantly *decreased* the odds for all substance use disorders. Similarly, participants with certain anxiety disorders, in particular GAD and PTSD, were less likely to meet criteria for substance use problems when they also met criteria for an externalizing problem than participants without externalizing problems.

These results suggest that externalizing problems and anxiety disorders may be associated with substance use disorders for different reasons. Individuals with an anxiety disorder might be more likely to use substances to avoid anxiety-related sensations than other individuals. In contrast, participants with externalizing problems might use and abuse psychoactive substances because of their heightened sensation-seeking tendencies. When these disorders co-occur, the functional relationship between these conditions may change. For example, the sensation-seeking tendency of a person with externalizing problems may be inhibited because of the discomfort associated with certain sensations that are common in many anxiety disorders.

One other point worthy of mention pertains to the possibility of differential rates of alcohol/substance use disorders in men versus women. More specifically, because externalizing features are highly correlated with both disorders, and because externalizing features are more prevalent in men than women (Moffitt, Caspi, Rutter, & Silva, 2001), one would expect that men would more frequently endorse alcohol and substance use disorders, based partially on the increased expectancy of externalizing disorders in one group versus the other. We explored this issue by testing the interaction between gender and externalizing to predict the four substance disorders, and ultimately found that consistent with existing literature implicating a male-limited subtype of alcohol and substance use disorders (Krueger, Markon, Patrick, Benning, & Kramer, 2007), we found that although females were more likely to endorse alcohol dependence but not abuse in the absence of externalizing features, males were significantly more likely to endorse both in the presence of externalizing disorders.

Although we believe that the current study represents an important step by documenting the association between anxiety disorders, externalizing problems, and substance use disorders in a large nationally representative sample, an important next step will be to identify the neurobiological correlates linking anxiety disorders, substance use disorders, and externalizing disorders. The neural circuits involved in many behavioral problems and emotional problems include the hypothalamic–pituitary–adrenal axis, the locus coeruleus, the amygdala, and the prefrontal cortex (e.g., Vermetten & Bremner, 2002). A critical neurochemical link between substance use disorders, anxiety disorders, and externalizing problems might be the dopaminergic system (e.g., Nutt, 1996). Specifically, neuroadaptive processes associated with chronic drug use on subcortical dopamine can secondarily impair the function of prefronto-striatal loops, resulting in externalizing behaviors (DiChiara & Bassareo, 2007). It has also been shown that

subjects with low central nervous system serotonin functioning show anxiety symptoms, excessive alcohol consumption, and symptoms of externalizing problems (Higley & Linnoila, 1997). Finally, we suggest that future investigators more closely examine ASPD in relation to substance use and anxiety. In the current study, because ASPD is not included as a diagnostic category in the NCS-R, it was not possible to incorporate it into our composite externalizing variable (which included conduct disorder, oppositional defiant disorder and ADHD). This is clearly an important area for future research.

Although the current results contribute to existing knowledge in the area of substance abuse and anxiety, as with any study the findings must be considered in light of study limitations. First and foremost, the data analysis was limited to the NCS-R. Antisocial personality disorder, which can be considered part of the externalizing spectrum disorders, was not included amongst NCS-R diagnoses and, therefore, could not be incorporated into the current study. Instead, the externalizing disorders included in this study were primarily childhood diagnoses (conduct disorder, oppositional defiant disorder, and attention deficit hyperactivity disorder). Therefore, the results cannot be generalized to all externalizing problems, because it remains unknown whether the same relationship exists in individuals with antisocial personality disorder. This question may be answered by analyzing other epidemiological data, such as the National Epidemiological Survey on Alcohol and Related Conditions (NESARC; Grant et al., 2003, 2004). Second, the underlying reason for the comorbidity pattern remains unknown. It is possible that the reason for the lower comorbidity between substance use disorders and externalizing problems in the presence of an anxiety disorder might be related to other causal links that were not assessed in this study. It could further be argued that substance use disorders are a form of externalizing problems that develop at around the same time. The precise nature of the comorbidity pattern would be clarified if the temporal relationship between the onset of the anxiety disorders, externalizing problems, and substance use disorders was known. Unfortunately, retrospective data provide little reliable information to clarify this issue. However, this question is important to address in future studies. Third, the results reported here are post-hoc analyses of an existing data set (the NCS-R) necessarily relying somewhat on retrospective reporting, which can be subject to various interpretive biases. Finally, the data are limited by the assessment procedures of the clinical syndromes because they were based on fully structured diagnostic interviews rather than clinician-administered diagnostic interviews. Despite these weaknesses, these results shed some light on the association between substance use disorders, externalizing problems, and anxiety disorders.

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