Psychiatry and Clinical Neurosciences 2013; **67**: 167–173 doi:10.1111/pcn.12030

Regular Article

Anxiety disorders and drug dependence: Evidence on sequence and specificity among adults

Renee D. Goodwin, PhD, MPH[1,2]* and Dan J. Stein, MD, PhD[3]

[1]*Department of Psychology, Queens College and The Graduate Center, City University of New York (CUNY),* [2]*Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, USA, and* [3]*Department of Psychiatry, University of Cape Town, Cape Town, South Africa*

Aim: The goal of this study was to investigate the relation between specific anxiety disorders and substance dependence, adjusting for potentially confounding demographic factors (e.g. sex) and comorbidity (e.g. alcohol dependence, major depression), among adults in the USA.

Methods: Data were drawn from the National Comorbidity Survey (NCS), a nationally representative population sample of the US adult population aged 15–54. The temporal sequence of onset of anxiety and substance dependence disorders was examined.

Results: Substance dependence temporally precedes several anxiety disorders, particularly panic disorder. Specifically, a history of past substance dependence predicts current panic disorder (odds ratio [OR] = 2.62, 95% confidence interval [CI] = 1.29, 5.32), social phobia (OR = 1.7, 95%CI = 1.12, 2.41), and agoraphobia (OR = 1.78, 95%CI = 1.08, 2.94). Conversely, in more than 50% of substance abuse disorder cases, in nearly 40% of post-traumatic stress disorder (PTSD) cases, and in nearly 30% of generalized anxiety disorder (GAD) cases, the anxiety disorder has first onset. Similarly, a lifetime history of social phobia, PTSD, or GAD significantly predicts lifetime substance dependence (OR = 1.51 for social phobia, 2.06 for PTSD, 1.45 for GAD).

Conclusion: For any particular anxiety disorder, a diagnosis of substance abuse can occur prior to or subsequent to an anxiety disorder. Nevertheless, there is also evidence for the specificity of some associations between anxiety and substance dependence disorders; these are independent of the effects of sex and other comorbid disorders, may be causal in nature, and deserve particular attention in clinical settings. The possibility that within a particular anxiety disorder there are a variety of mechanisms of association with various substances should be addressed in future work.

Key words: anxiety disorders, comorbidity, depression, epidemiology, substance-related disorders.

SUBSTANCE DEPENDENCE IS a tremendous global public health problem.[1–4] Substance dependence (i.e., dependence on illicit drugs) is associated with occupational disability, increased risk of depressive and psychotic disorders, social impairment, incarceration, and physical health problems.[5–7] The causes of drug dependence are not known, though previous data suggest that risk factors may be identifiable relatively early in life, even prior to the initiation of use and abuse.

Previous research has focused on examining the relation between depressive symptoms, antisocial, oppositional, and disruptive behavior disorders, which are thought to precede and predict onset of substance dependence.[8–11] Other factors, such as familial history of mood, alcohol, and drug use disorders, are also thought to contribute to the

*Correspondence: Renee D. Goodwin, PhD, MPH, Department of Epidemiology, Mailman School of Public Health, Columbia University, 722 West 168th St, New York, NY 10032, USA.
Email: rdg66@columbia.edu
Received 8 August 2012; revised 11 January 2013; accepted 15 February 2013.

risk of substance use,[12–15] as do childhood abuse and deviant peer affiliations.[16,17] For instance, longitudinal research has shown that deviant peer affiliations are related to persistence and course of cannabis use across the lifespan.[18] Also, Merikangas (1998) has demonstrated links between familial mood disorders and substance dependence.[19] The determining factors that govern the shift from vulnerability to onset of substance dependence remain unknown and there are recent data suggesting an interaction between genetic and environmental influences in comorbid substance dependence and mood disorders.[20]

Cross-sectional studies of adults show strong links between anxiety disorders and substance use disorders.[21,22] Longitudinal studies have also shown associations between anxiety disorders early in life and the subsequent onset of substance use, such as cigarette smoking.[23,24] While results of previous studies consistently show links between anxiety disorders and substance dependence, several questions about the association between anxiety disorders and the onset of substance dependence remain. First, it is not clear whether the association between anxiety disorders and substance dependence applies to any anxiety disorder, or whether it is specific only to some anxiety disorders. Second, it is not known whether the relation between anxiety disorders and substance dependence persists independent of the effects of comorbid depression and alcohol use disorders. Third, it has not been investigated whether the onset of anxiety disorders tends to precede the onset of substance dependence, whether substance dependence occurs prior to the onset of anxiety disorders in the general population.

Against this background, the goal of the current investigation is to examine the relation between anxiety disorders and substance dependence among adults in the community. First, the study will determine the cross-sectional association between anxiety disorders and substance dependence (current and lifetime) among adults in the community. Second, the study will examine the relation between specific anxiety disorders and the odds of substance dependence, adjusting for the effects of depression and alcohol dependence. Third, the study will examine the relation between a history of anxiety disorders (which are not current) and the odds of current substance dependence in order to identify patterns of the temporal sequence of onset of anxiety disorders and substance dependence. We hypothesized that anxiety disorders would be associated with increased likelihood of substance dependence, independent of the effects of depression and alcohol use dependence. In addition, we anticipated that the onset of anxiety disorders would precede the onset of substance dependence in the majority of cases.

METHODS

Sample

The National Comorbidity Survey is based on a national probability sample ($n = 5, 788$) of individuals aged 15–54 in the non-institutionalized US population.[25] Fieldwork was carried out between September 1990 and February 1992. There was an 82.4% response rate. The data were weighted for differential probabilities of selection and non-response. A weight was also used to adjust the sample to approximate the cross-classification of the population distribution on a range of sociodemographic characteristics. Weighting and a full description of study methodology are described in detail elsewhere.[25,26]

Diagnostic assessment

Psychiatric diagnoses were generated from a modified version of the World Health Organization (WHO) Composite International Diagnostic Interview,[27] a structured interview designed for use by trained interviewers who are not clinicians. WHO field trials (WHO 1990) and National Comorbidity Survey clinical reappraisal studies[28–30] documented acceptable reliability and validity of all the diagnoses. Psychiatric disorders included in the current investigation were DSM-III-R major depression, generalized anxiety disorder (GAD), simple phobia, social phobia, panic attacks, panic disorder, post-traumatic stress disorder (PTSD), alcohol dependence, and substance (illicit drug) dependence. Written informed consent was obtained from each participant after the survey had been fully explained.

Analytic strategy

Logistic regression analyses were used to investigate the association between anxiety disorders and substance dependence (past 12-month and lifetime). First, analyses were adjusted for differences in sociodemographic characteristics (age, sex, race, marital status, income, education). Next, sociodemographic characteristics and comorbid alcohol dependence

Table 1. Association between lifetime anxiety disorders and drug dependence among adults in the community

Lifetime	No drug dependence (7469) % (*n*)	Lifetime drug dependence (629) % (*n*)	Model 1† AOR (95%CI)	Model 2‡ AOR (95%CI)	Model 3§ AOR (95%CI)
Mood and anxiety disorders					
Panic attacks	6.52% (493)	19.61% (116)	3.86 (2.7, 5.5)*	2.73 (1.83, 4.08)*	2.21 (1.48, 3.31)*
Agoraphobia	6.81% (403)	16.71% (84)	2.8 (2.1, 3.8)*	2.35 (1.68, 3.28)*	1.98 (1.35, 2.91)*
Panic disorder	6.97% (221)	21.25% (53)	4.1 (2.6, 6.4)*	3.24 (1.94, 5.42)*	2.53 (1.54, 4.17)*
Post-traumatic stress disorder	6.40% (469)	20.90% (122)	4.2 (3.2, 5.7)*	2.84 (1.9, 4.23)*	2.36 (1.52, 3.66)*
Specific phobia	6.59% (751)	14.38% (125)	2.6 (2.08, 4.32)*	1.81 (1.2, 2.1)*	1.49 (.51, 1.73)*
Social phobia	6.20% (886)	15.52% (173)	2.7 (2.13, 3.5)*	2.06 (1.56, 2.72)*	1.8 (1.33, 2.45)*
Generalized anxiety disorder	6.78% (336)	20.36% (79)	3.8 (2.8, 5.2)*	2.53 (1.83, 3.49)*	1.95 (1.4, 2.7)*

*$P < 0.05$.
†Adjusted for demographic differences. ‡Adjusted for demographic differences and comorbid alcohol dependence.
§Adjusted for demographic differences, comorbid alcohol dependence and major depression.
AOR, adjusted odds ratio; CI, confidence interval.

and major depression were included in the model. The same procedure was used to examine the association between history of anxiety disorders (having lifetime anxiety disorders, but not current) and current drug dependence, and between history of drug dependence and current anxiety disorders. Adjusted odds ratios with 95% confidence intervals were computed.

RESULTS

Association between anxiety disorders and substance dependence

Association between lifetime anxiety disorders and lifetime drug dependence

Each anxiety disorder was associated with a significantly increased likelihood of drug dependence, which persisted after adjusting for differences in sociodemographic characteristics, alcohol dependence and major depression (see Table 1).

Sequence of onset of drug dependence and anxiety disorders

Onset of substance dependence occurred sequentially prior to the onset of anxiety disorder in a majority of cases among those with panic attacks, agoraphobia, GAD, and PTSD (see Table 2). Among those with specific phobia and drug dependence, there seemed almost an equal distribution of first onset, and social phobia appeared to have onset prior to drug dependence in the majority of cases. In more than 50% of social phobia cases, in nearly 40% of PTSD cases, and in nearly 30% of GAD cases, the onset of the anxiety disorder was first.

Association between history of anxiety disorders and current drug dependence

History of each anxiety disorder, with the exception of panic disorder, was associated with a significantly

Table 2. Sequence of onset of anxiety disorders and substance dependence among comorbid cases in the community

Anxiety disorder	Substance dependence onset first	Anxiety disorder onset first
Panic attack	61.77%	38.23%
Agoraphobia	67.24%	32.76%
Panic disorder	80.16%	19.84%
Specific phobia	49.24%	50.76%
Social phobia	43.16%	56.84%
Generalized anxiety disorder	71.84%	28.16%
Post-traumatic stress disorder	61.36%	38.64%

Table 3. Association between history of anxiety disorder and current drug dependence

Lifetime (but not current) anxiety disorders	No drug dependence (7469) % (*n*)	Drug dependence (629) % (*n*)	Model 1[†] AOR (95%CI)	Model 2[‡] AOR (95%CI)	Model 3[§] AOR (95%CI)
Panic attacks	2.31% (219)	5.32% (37)	3.4 (1.64, 7.07)*	2.57 (1.1, 5.98)*	2.26 (0.95, 5.36)
Panic disorder	2.60% (90)	4.19% (14)	2.47 (0.85, 7.22)	1.55 (0.46, 5.2)	1.62 (0.48, 5.45)
Agoraphobia	2.59% (182)	8.06% (39)	3.13 (1.50, 6.53)*	2.93 (1.32, 6.54)*	2.66 (1.17, 6.04)*
Specific phobia	2.39% (161)	5.88% (30)	2.53 (1.06, 6.04)*	1.79 (0.66, 4.87)	1.47 (0.52, 4.14)
Social phobia	2.23% (349)	4.47% (61)	2.15 (1.25, 3.69)*	1.61 (0.88, 2.94)	1.33 (0.7, 2.52)

*$P < 0.05$.
[†]Adjusted for demographic differences. [‡]Adjusted for demographic differences and comorbid alcohol dependence.
[§]Adjusted for demographic differences, comorbid alcohol dependence and major depression.
AOR, adjusted odds ratio; CI, confidence interval.

increased likelihood of current drug dependence (see Table 3). After further adjustment for alcohol dependence, only the links with panic attacks and PTSD remained. Although the pattern of results remained the same, with additional adjustment for comorbid major depression, only the link between history of agoraphobia and substance dependence remained statistically significant.

Association between history of drug dependence and current anxiety disorders

History of drug dependence was associated with a significantly increased likelihood of current panic attacks, agoraphobia, panic disorder, and social phobia (see Table 4). These associations persisted after adjusting for demographic characteristics, alcohol dependence and major depression. The association was strongest for panic disorder. History of drug dependence did not appear to be associated with increased likelihood of specific phobia or GAD.

DISCUSSION

The community data here confirm clinical impressions and previous findings that the relationship between anxiety disorders and substance dependence are complex. These results suggest that for any particular anxiety disorder, comorbid substance use disorders may have an earlier onset and possibly contribute to the pathogenesis of anxiety symptoms, or comorbid substance dependence can have a later onset perhaps reflecting the outcome of behaviors associated with an attempt to self-medicate anxiety symptoms. The data here also provide evidence for: (i) strong lifetime associations between specific anxiety disorders and substance dependence among adults in the community; (ii) the possibility that associations between specific disorders are independent of the influence of demographic characteristics and comorbid major depression and alcohol dependence; and (iii) the specificity of associations between particular anxiety disorders and substance dependence.

Table 4. Association between history of drug dependence and risk of current anxiety disorders (past 12 months)

History of drug dependence (not current)	Current anxiety disorder AOR (95%CI)					
	Panic attacks	Agoraphobia	Panic disorder	Specific phobia	Social phobia	GAD
	1.79 (1.05, 3.06)*	1.78 (1.08, 2.94)*	2.62 (1.29, 5.32)*	1.24 (0.82, 1.87)	1.7 (1.12, 2.51)*	1.19 (0.74, 1.9)

*$P < 0.05$.
AOR, adjusted odds ratio (adjusted for differences in demographic characteristics, alcohol dependence and major depression); CI, confidence interval; GAD, generalized anxiety disorder.

By controlling for the effects of sex and comorbid disorders we were able to demonstrate that the association between anxiety and substance dependence is not simply a methodological artifact. While there is growing awareness amongst clinicians of obtaining an alcohol history in all patients with anxiety disorders, and of determining a history of mood and anxiety disorders in all patients with alcohol dependence, there is perhaps less focus on other substances in clinical assessment of patients presenting with anxiety disorders. Substance abuse and dependence are stigmatized conditions, and may be underreported especially upon initial presentation as well as being overshadowed by more clinically obvious comorbid mood symptoms. As such, this may contribute to the relative underdiagnosis and undertreatment of anxiety disorders among persons with comorbid substance dependence, despite its prevalence. In fact, reviewing literature on treatment of patients with comorbid anxiety and substance use disorders shows that there is relatively little evidence of specific treatments for both disorders.

The strongest association between past substance dependence and current anxiety disorder was observed in panic disorder. This finding is consistent with the frequent observation that panic disorder can be precipitated or exacerbated by substance use or withdrawal.[31–33] It is also consistent with current understandings of the neurobiology of panic attacks. This theory suggests that panic attacks are underpinned by a distributed neurocircuitry involving the amygdala that may be sensitized or activated by a range of different stressors, including changes in either the external or internal milieu.[34,35] While data here cannot be used as evidence to confirm this pathway, these results may be useful in pointing to patterns of specificity that may be fruitfully investigated in future, more detailed, studies.

Results also showed associations between past substance dependence and other current anxiety disorders, such as social phobia. Withdrawal from regular social activities is commonly seen among individuals who spend significant amounts of their time and effort on drug seeking and drug taking. There may also be more direct relations between substance abuse and social anxiety; for example, withdrawal of a range of substances leads to decreased levels of striatal D2 receptors, a finding that is also seen in social anxiety disorder patients.[36,37] Speculatively, there may be overlaps between the neurobiological sequelae of substance use or withdrawal, and the neural substrate of social anxiety. In addition, it is conceivable that use of substances may begin as an attempt to self-medicate feelings of isolation and distress related to lack of social relationships associated with social anxiety.[38,39] While only a minority of instances of substance use lead to the development of dependence, it has been shown that social phobia is associated with increased risk of development of substance dependence, once substance use is initiated. For instance, one study[40] showed very high rates of nicotine dependence among those with social phobia who initiated nicotine use (31.5%), compared with rates of nicotine dependence among those without social phobia (15.4%). As such, it may be that exposure to some substances and learning (through exposure) of the anxiety-relieving effects may lead to the onset of substance use among those with social phobia.

Our findings also indicate that anxiety disorders may contribute to the onset of substance dependence. While the cross-sectional nature of these data and lack of more detailed information on factors influencing onset do not permit conclusions based on these data alone, the persistence of these associations after adjusting for differences in comorbid depression and alcohol use disorders suggest that the link is not purely attributable to comorbidity. This is consistent with growing evidence emphasizing the relatively early onset of anxiety disorders and associated vulnerability to later comorbid disorders. In more than 50% of social phobia cases, in nearly 40% of PTSD cases, and in nearly 30% of GAD cases, anxiety disorders had first onset. Similarly, a lifetime history of social phobia, PTSD, or GAD significantly predicted lifetime substance dependence, an association that was strongest for PTSD. Furthermore, the greater the number of lifetime anxiety disorders, the higher the risk for past and for current substance dependence.

Several limitations of this study should be emphasized. First, as noted above, the cross-sectional nature of the dataset does not allow inferences about the causality or mechanisms of these observed associations. Second, participants were aged 15–54 only, therefore these results are not generalizable to other age groups. Third, we were unable to analyze the data according to specific type of substance with confidence (mainly due to small cell size; e.g. benzodiazepines); future work needs to explore also the specific relations between specific substance use disorders and the range of anxiety disorders. Replication in a

larger national dataset, such as the National Epidemiologic Study on Alcohol and Related Conditions (NESARC), may be informative. Fourth, while these results are generalizable to the USA, they may not be relevant to other countries.

Nevertheless, these data provide preliminary evidence on the potential significance in emphasizing specific associations between particular anxiety disorders and substance dependence. These findings have clear clinical implications, including the need to maintain a reasonable level of suspicion for anxiety disorders in patients with substance use disorders, and the need for early detection and robust intervention for anxiety disorders in order to help prevent subsequent morbidity. Further research is needed to investigate the precise mechanisms, which account for the temporal relations apparent in this dataset, and to extend the work to include the range of specific substance use disorders.

ACKNOWLEDGMENTS

This study was supported by grants MH64736 and DA20892 from NIH. The authors have no conflicts of interest.

REFERENCES

1. de Graaf R, Bijl RV, Spijker J, Beekman AT, Vollebergh WA. Temporal sequencing of lifetime mood disorders in relation to comorbid anxiety and substance use disorders: findings from the Netherlands Mental Health Survey and Incidence Study. *Soc. Psychiatry Psychiatr. Epidemiol.* 2003; **38**: 1–11.
2. Stinson FS, Grant BF, Dawson DA, Ruan WJ, Huang B, Saha T. Comorbidity between DSM-IV alcohol and specific drug use disorders in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Drug Alcohol Depend.* 2005; **80**: 105–116.
3. Degenhardt L, Bucello C, Calabria B *et al*. What data are available on the extent of illicit drug use and dependence globally? Results of four systematic reviews. *Drug Alcohol Depend.* 2011; **117**: 85–101.
4. Degenhardt L, Hall W. Extent of illicit drug use and dependence, and their contribution to the global burden of disease. *Lancet* 2012; **379**: 55–70.
5. Dawson DA, Grant BF, Stinson FS, Chou PS. Psychopathology associated with drinking and alcohol use disorders in the college and general adult populations. *Drug Alcohol Depend.* 2005; **77**: 139–150.
6. Grant BF, Stinson FS, Dawson DA, Chou SP, Ruan WJ. Co-occurrence of DSM-IV personality disorders in the United States: Results from the national epidemiologic survey on alcohol and related conditions. *Compr. Psychiatry* 2005; **46**: 1–5.
7. Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC. Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the national comorbidity survey. *Arch. Gen. Psychiatry* 1997; **54**: 313–321.
8. Compton WM, Conway KP, Stinson FS, Colliver JD, Grant BF. Prevalence, correlates, and comorbidity of DSM-IV antisocial personality syndromes and alcohol and specific drug use disorders in the United States: Results from the national epidemiologic survey on alcohol and related conditions. *J. Clin. Psychiatry* 2005; **66**: 677–685.
9. Kessler RC, Adler LA, Barkley R *et al*. Patterns and predictors of attention-deficit/hyperactivity disorder persistence into adulthood: Results from the national comorbidity survey replication. *Biol. Psychiatry* 2005; **57**: 1442–1451.
10. Strakowski SM, DelBello MP, Fleck DE *et al*. Effects of co-occurring alcohol abuse on the course of bipolar disorder following a first hospitalization for mania. *Arch. Gen. Psychiatry* 2005; **62**: 851–858.
11. Wiesner M, Kim HK, Capaldi DM. Developmental trajectories of offending: Validation and prediction to young adult alcohol use, drug use, and depressive symptoms. *Dev. Psychopathol.* 2005; **17**: 251–270.
12. Fu Q, Heath AC, Bucholz KK *et al*. Shared genetic risk of major depression, alcohol dependence, and marijuana dependence: Contribution of antisocial personality disorder in men. *Arch. Gen. Psychiatry* 2002; **59**: 1125–1132.
13. Houston RJ, Bauer LO, Hesselbrock VM. Depression and familial risk for substance dependence: A P300 study of young women. *Psychiatry Res.* 2003; **124**: 49–62.
14. Lieb R, Merikangas KR, Hofler M, Pfister H, Isensee B, Wittchen HU. Parental alcohol use disorders and alcohol use and disorders in offspring: A community study. *Psychol. Med.* 2002; **32**: 63–78.
15. Nurnberger JI, Jr, Wiegand R, Bucholz K *et al*. A family study of alcohol dependence: Coaggregation of multiple disorders in relatives of alcohol-dependent probands. *Arch. Gen. Psychiatry* 2004; **61**: 1246–1256.
16. Bailey JA, McCloskey LA. Pathways to adolescent substance use among sexually abused girls. *J. Abnorm. Child Psychol.* 2005; **33**: 39–53.
17. DuBois DL, Silverthorn N. Do deviant peer associations mediate the contributions of self-esteem to problem behavior during early adolescence? A 2-year longitudinal study. *J. Clin. Child Adolesc. Psychol.* 2004; **33**: 382–388.
18. Li F, Barrera M, Jr, Hops H, Fisher KJ. The longitudinal influence of peers on the development of alcohol use in late adolescence: A growth mixture analysis. *J. Behav. Med.* 2002; **25**: 293–315.
19. Merikangas KR, Stolar M, Stevens DE *et al*. Familial transmission of substance use disorders. *Arch. Gen. Psychiatry* 1998; **55**: 973–979.

20. Compton WM, Thomas YF, Conway KP, Colliver JD. Developments in the epidemiology of drug use and drug use disorders. *Am. J. Psychiatry* 2005; **162**: 1494–1502.
21. Henquet C, Murray R, Linszen D, van Os J. The environment and schizophrenia: The role of cannabis use. *Schizophr. Bull.* 2005; **31**: 608–612.
22. Windle M, Wiesner M. Trajectories of marijuana use from adolescence to young adulthood: Predictors and outcomes. *Dev. Psychopathol.* 2004; **16**: 1007–1027.
23. Goodwin RD, Fergusson DM, Horwood LJ. Association between anxiety disorders and substance use disorders among young persons: Results of a 21-year longitudinal study. *J. Psychiatr. Res.* 2004; **38**: 295–304.
24. Johnson JG, Cohen P, Pine DS, Klein DF, Kasen S, Brook JS. Association between cigarette smoking and anxiety disorders during adolescence and early adulthood. *JAMA* 2000; **284**: 2348–2351.
25. Kessler RC, McGonagle KA, Zhao S *et al*. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch. Gen. Psychiatry* 1994; **51**: 8–19.
26. Kessler RC, Little RJ, Groves RM. Advances in strategies for minimizing and adjusting for survey nonresponse. *Epidemiol. Rev.* 1995; **17**: 192–204.
27. Wittchen HU. Reliability and validity studies of the WHO–Composite International Diagnostic Interview (CIDI): A critical review. *J. Psychiatr. Res.* 1994; **28**: 57–84.
28. Blazer DG, Kessler RC, McGonagle KA, Swartz MS. The prevalence and distribution of major depression in a national community sample: The National Comorbidity Survey. *Am. J. Psychiatry* 1994; **151**: 979–986.
29. Wittchen HU, Kessler RC, Zhao S, Abelson J. Reliability and clinical validity of UM-CIDI DSM-III-R generalized anxiety disorder. *J. Psychiatr. Res.* 1995; **29**: 95–110.
30. Wittchen HU, Zhao S, Abelson JM, Abelson JL, Kessler RC. Reliability and procedural validity of UM-CIDI DSM-III-R phobic disorders. *Psychol. Med.* 1996; **26**: 1169–1177.
31. Deacon BJ, Valentiner DP. Substance use and non-clinical panic attacks in a young adult sample. *J. Subst. Abuse* 2000; **11**: 7–15.
32. O'Brien MS, Wu LT, Anthony JC. Cocaine use and the occurrence of panic attacks in the community: A case-crossover approach. *Subst. Use Misuse* 2005; **40**: 285–297.
33. Valentiner DP, Mounts NS, Deacon BJ. Panic attacks, depression and anxiety symptoms, and substance use behaviors during late adolescence. *J. Anxiety Disord.* 2004; **18**: 573–585.
34. Gorman JM, Kent JM, Sullivan GM, Coplan JD. Neuroanatomical hypothesis of panic disorder, revised. *Am. J. Psychiatry* 2000; **157**: 493–505.
35. Stein DJ, Goodman WK, Rauch SL. The cognitive-affective neuroscience of obsessive-compulsive disorder. *Curr. Psychiatry Rep.* 2000; **2**: 341–346.
36. Schneier FR, Liebowitz MR, Abi-Dargham A, Zea-Ponce Y, Lin SH, Laruelle M. Low dopamine D(2) receptor binding potential in social phobia. *Am. J. Psychiatry* 2000; **157**: 457–459.
37. Volkow ND, Fowler JS, Wang GJ, Swanson JM. Dopamine in drug abuse and addiction: Results from imaging studies and treatment implications. *Mol. Psychiatry* 2004; **9**: 557–569.
38. Chartier MJ, Walker JR, Stein MB. Considering comorbidity in social phobia. *Soc. Psychiatry Psychiatr. Epidemiol.* 2003; **38**: 728–734.
39. Zimmermann G, Pin MA, Krenz S *et al*. Prevalence of social phobia in a clinical sample of drug dependent patients. *J. Affect. Disord.* 2004; **83**: 83–87.
40. Sonntag H, Wittchen HU, Hofler M, Kessler RC, Stein MB. Are social fears and DSM-IV social anxiety disorder associated with smoking and nicotine dependence in adolescents and young adults? *Eur. Psychiatry* 2000; **15**: 67–74.