Published in final edited form as:

Drug Alcohol Depend. 2007 March 16; 87(2-3): 139–145.

Sub-Diagnostic Psychiatric Comorbidity in Alcoholics

George Fein^a, Victoria Di Sclafani^a, Peter Finn^b, and Diane L. Scheiner^a

^a *Neurobehavioral Research, Inc., 201 Tamal Vista Boulevard, Corte Madera, CA 94925-1110, USA*

^b *Department of Psychological and Brain Sciences, Indiana University, 1101 East Tenth Street, Bloomington, IN 47405-7007, USA*

Abstract

Background—Psychiatric comorbidity in alcohol use disorders is clearly established, however most studies ignore data on psychiatric symptom counts that do not meet criteria for a diagnosis. We examined psychiatric symptom counts and psychological measures in the domains of anxiety, mood and externalizing pathology in 48 long-term abstinent alcoholics (LTAA) compared to 48 age/gender comparable light/non-drinking controls (NC).

Methods—Continuous measures of pathology (i.e., symptoms counts and psychological assessments) in each domain were compared between groups for: 1) all study participants, 2) excluding individuals with a lifetime psychiatric diagnosis in the domain, and 3) excluding individuals with a current psychiatric diagnosis in the domain.

Results—Psychiatric symptom counts and psychological pathology were greater in LTAA than NC. The differences between groups on these measures were not reduced by removal of individuals with lifetime or current diagnoses.

Conclusions—The bulk of the difference between LTAA and NC in psychiatric illness was carried by sub-diagnostic psychopathology. In comparison to the limited view provided by using only symptomatology that meets criteria for a diagnosis, the use of continuous measures of psychiatric symptomatology and psychological abnormality yields a much more accurate picture of psychiatric illness co-occurring with alcoholism.

Keywords

Alcoholism; psychiatric comorbidity; long-term abstinence; antisocial personality

1. Introduction

The high prevalence of comorbid psychiatric disorders in substance use disorders (SUDs) has been clearly established (Brady and Sinha, 2005; Grant et al., 2004a; Grant et al., 2004b; Hasin and Grant, 2002; Hirschfield et al., 1990; Kessler et al., 1996). Psychiatric comorbidity is a major issue that needs to be addressed in all studies of SUDs in order to disentangle those phenomena that are consequent to the alcohol or drug abuse/dependence vs. those that are consequent to the comorbid psychiatric disturbance. However, most studies of SUDs, including the very large epidemiological studies (Grant et al., 2004a; Grant et al., 2004b; Kessler et al.,

Address reprint requests and correspondence to: Dr. George Fein, Neurobehavioral Research, Inc. 201 Tamal Vista Boulevard, Corte Madera, CA 94925-1110, Tel: 415.927.7676, Fax: 415.924.2903, Email: george@nbresearch.com

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

1997;Regier et al., 1990) that have a major impact on our understanding of the magnitude of comorbid psychiatric disorders in SUDs, fail to measure psychiatric illness on a continuum. Instead, almost all investigations of psychiatric comorbidity coincident with substance use disorders only measure psychiatric illness that meets diagnostic thresholds. Subthreshold psychiatric disorder data (i.e., symptom counts that are short of the diagnostic threshold) are not presented, and one is left with the strong impression that diagnostic measurements (i.e., threshold measurements) completely address the presence of psychiatric morbidity in SUDs. In truth, relying only on diagnoses results in a great loss of sensitivity, in that only the 'tail' of the distribution of psychiatric comorbidity is examined, leaving the bulk of the data unexplored (Angst et al., 2003;Hankin et al., 2005;Krueger et al., 2005;Markon and Krueger, 2005;Merikangas et al., 1998;Merikangas et al., 2003).

We have recently demonstrated an increased lifetime and current psychiatric comorbidity in long-term abstinent alcoholics (LTAA, abstinent an average of 6.7 years) compared to age and gender comparable normal controls (Di Sclafani, V., Finn, P., and Fein, G., Psychiatric Comorbidity in Long-Term Abstinent Alcoholics, submitted manuscript, June 2006). In that study, we acquired data on symptom counts that go into making the diagnoses of psychiatric disorders and on measures of the psychological abnormalities underlying the psychiatric disturbances. In this manuscript, we revisit the data from that study, examining psychiatric symptom counts and psychological measures both in individuals who did and in individuals who did not meet criteria for comorbid psychiatric disorders. We examine the question of whether there are differences between LTAA and NC in subthreshold psychiatric illness. We then examine the question of whether removing individuals with frank comorbid psychiatric diagnoses (i.e., removing those with supra-threshold symptom counts and keeping only those with subthreshold symptom counts) removes (i.e., controls for) differences in psychiatric morbidity between LTAA and NC.

2. Methods

2.1. Participants

A total of 96 participants were recruited from the community by postings at Alcoholics Anonymous meeting places, and through posters in restaurants, newspaper and Internet advertisements. Two groups were recruited: LTAA (25 men and 23 women), and age and gender matched normal control (NC) light/non-drinkers. LTAA needed to meet the lifetime criteria for alcohol dependence (American Psychiatric Association, 2000), and be abstinent from alcohol for at least 6 months at the time of study entry. NC needed to have a lifetime drinking average of fewer than 30 drinks per month with no periods of more than 60 drinks per month. Exclusion criteria for both groups were: (1) history of, or current, drug abuse or dependence (other than nicotine or caffeine); (2) history of neurological disease; (3) history of head trauma, or cranial surgery; (4) history of diabetes, stroke, or hypertension that required medical intervention; (5) clinical evidence of Wernicke-Korsakoff syndrome, and (6) history of schizophrenia / schizophreniform disorder.

All participants were informed of the study's procedures and aims, and signed a consent form approved by Independent Review Consulting, Inc. (IRC), the IRB that approved the study protocol, before participating. All individuals participated in four testing sessions (clinical, neuropsychological, electrophysiological, and neuroimaging); each session lasted between 1.5 and 3 hours. NC were asked to abstain from drinking alcohol for at least 24 hours before laboratory visits, and a Breathalyzer test (Draeger, Durango, CO) was administered to all participants before each session (all Breathalyzer tests were negative). Individuals who completed a session were paid for their time and travel expenses, and those who completed the entire study were also given a completion bonus.

2.2. Assessment

Medical histories and liver functions were evaluated. Participants were interviewed about their drug and alcohol use using the lifetime drinking history methodology (Skinner and Sheu, 1982; Sobell and Sobell, 1990; Sobell et al., 1988). All individuals were assessed for psychiatric diagnoses and the presence and severity of anxiety, mood, and externalizing disorder symptoms using the computerized Diagnostic Interview Schedule-IV (cDIS) (Robins et al., 1998).

2.2.1. Symptoms counts (SX#)—The number of symptoms of anxiety, mood, and externalizing disorders were quantified as the sum total of the positive responses to all direct symptom questions for each diagnosis screened by the cDIS. Unfortunately, the cDIS does not gather information on whether symptoms are current, unless criteria for a lifetime diagnosis are met. The symptom count for a disorder did not include the positive responses to indirect symptom questions (e.g., for depression: “Was there any time in the last 12 months when you wanted to talk to a doctor or other health professional about feeling sad, depressed, or empty most of the time?”). Affirmative responses to indirect symptom questions are counted by the cDIS as criteria toward a positive diagnosis of a disorder, but in our study were considered secondary consequences of the direct symptoms, and therefore not counted toward a disorder’s symptom count.

2.2.2. Anxiety Disorder Domain Measures—Anxiety was assessed using the Reiss-Epstein Anxiety Sensitivity Index (ASI) (Reiss et al., 1986) and the State and Trait Scales of the State-Trait Anxiety Inventory for Adults (STAI-S and STAI-T) (Spielberger, 1983). Anxiety disorder symptom counts on the cDIS were summed in the diagnosis categories of social phobia, agoraphobia, panic disorder, PTSD, the number of PTSD traumatic events, obsessive disorder, and compulsive disorder.

2.2.3. Mood Disorder Domain Measures—Depression and hypomania were assessed using the Depression and Hypomania Scales of the Minnesota Multiphasic Personality Inventory-2 (MMPI-D and MMPI-H) (Hathaway and McKinley, 1989). Mood disorder symptoms on the cDIS were summed in the diagnosis categories of depression, depressive episodes, dysthymia, and mania.

2.2.4. Personality Disorder (Externalizing) Domain Measures—Deviance proneness was assessed using the Socialization Scale of the California Psychological Inventory (CPI-SS) (Gough, 1969), and the Psychopathic Deviate Scale of the MMPI-2 (MMPI-PD) (Hathaway and McKinley, 1989). Externalizing disorder symptoms on the cDIS were summed in the diagnosis categories of conduct disorder and antisocial personality disorder (ASPD).

2.2.5. Family Drinking Density—The Family History Drinking Questionnaire (Mann et al., 1985; Stoltenberg et al., 1998) was administered to assess the density of problem drinkers in the participant’s family. Participants were asked to rate the members of their family as being alcohol abstainers, alcohol users with no problem, problem drinkers, or unknown. Family Drinking Density was defined as the proportion of 1st degree relatives who were problem drinkers.

2.3. Alcohol Use Variables

Based upon participants’ responses on the lifetime drinking history questionnaire, alcohol use variables were defined. Alcohol Use refers to the number of months of alcohol consumption in the individual’s lifetime, while Peak Use refers to the number of months of peak alcohol use. Average (Avg) Dose is the average number of drinks per month during periods of alcohol

consumption over the subject's lifetime, while Peak Dose is the number of drinks per month during their period of peak alcohol consumption.

2.4. Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc., 2004). Comparisons were performed in each of the three psychiatric domains (anxiety, mood, and externalizing disorders). First, psychological measures and lifetime symptom counts were compared between LTAA and NC groups for all participants in each domain, and then again after excluding participants with a lifetime diagnosis in the psychiatric domain being examined (e.g., excluding LTAA and NC individuals with a lifetime mood disorder diagnosis for comparisons of mood psychological measures and mood disorder symptom counts). This second comparison addressed the question of whether excluding individuals with a lifetime psychiatric diagnosis removes differences between LTAA and NC in psychological measures and symptoms of the psychiatric domain being examined.

A third comparison was conducted, comparing LTAA and NC groups after removing all individuals with a current (i.e., last 12 months) psychiatric diagnosis in the psychiatric domain being examined. That comparison was only performed for psychological measures. We did not compare symptom counts when excluding individuals with current diagnoses, since in gathering the symptom count data using the cDIS, we could not distinguish between lifetime and current symptoms. Finally, we did not perform this analysis for the externalizing domain since no participants met diagnostic criteria for a current externalizing disorder.

Because statistical significance levels are affected by sample sizes, we computed the effect size 'd' (Cohen, 1988) for all comparisons to facilitate assessment of group differences when all participants were examined, when participants with lifetime diagnoses in the psychiatric domain were excluded, and when participants with a current diagnosis in the psychiatric domain were excluded. To determine whether effect sizes were affected by excluding participants who met criteria for a psychiatric diagnosis, we created a data set with only the reduced number of participants (i.e., only those participants not meeting criteria for lifetime mood disorder diagnosis) and concatenated that data set to the full data set of all participants, creating a variable called 'exclude' that was set to a value of 1 for the full data set, and a value of 2 for the diminished data set. We then examined the effect of the 'exclude' variable on the symptom counts and psychological measures, as well as the interaction effect of the 'exclude' variable and the grouping (i.e., LTAA vs. NC) variable. The main effect of 'exclude' measured the degree to which the dependent variables (symptom counts and psychological measures of a domain) were affected by excluding participants with psychiatric diagnoses (lifetime or current) within that domain. The interaction effect measured whether excluding participants with a diagnosis affected the magnitude of group differences on measures in each domain. These analyses were carried out using all measures in each domain in a multivariate analysis.

3. Results

3.1. Demographic and Alcohol Use Variables

Table 1 presents demographic and alcohol use variables for all participants. The groups were similar in years of education, but did differ significantly in family drinking history, with the LTAA having a greater proportion of first-degree relatives who were problem drinkers ($F_{1,92} = 32.08$ $p < 0.001$). On average, the LTAA men drank 5.9 drinks per day and the LTAA women drank 4.3 drinks per day. NC drank an average of 0.2 drinks per day for men and women. LTAA had a peak alcohol dose that was almost twenty times the peak dose for NC. LTAA were abstinent from alcohol an average of 6.7 years.

3.2. Psychological Measure and Psychiatric Symptom Count Variables

Table 2 presents the average LTAA and NC values for psychological measures and psychiatric symptom counts in each psychiatric domain (anxiety, mood, and externalizing). Comparisons between LTAA and NC groups are shown for all study participants, after excluding participants with a lifetime psychiatric diagnosis in the psychiatric domain (i.e., only participants without a lifetime diagnosis examined), and after excluding participants with a current psychiatric diagnosis in the psychiatric domain (i.e., only participants without a current diagnosis examined). Figures 1–3 plot the mean of the difference between LTAA and NC groups on these measures, for the anxiety, mood, and externalizing domains, respectively. Confidence interval bars that do not cross the dashed line at zero indicate a significant difference between LTAA and NC groups on the measure being examined.

3.3. Anxiety Measures and Anxiety Disorder Symptoms

When examining all participants, LTAA had greater anxiety on all psychological measures of anxiety (all p 's < 0.01), and significantly greater symptom counts for social phobia, agoraphobia, panic disorder, PTSD, and PTSD traumatic events. The effect sizes for all anxiety measure variables varied from $d = 0.34$ to $d = 0.78$. After excluding participants with a lifetime anxiety disorder diagnosis, the number of symptoms and the magnitude of psychological abnormality were not significantly reduced (Wilks $\lambda_{10,155} = 0.920$, $p = 0.208$), nor was the difference between groups in these measures significantly affected (Wilks $\lambda_{10,155} = 0.967$, $p = 0.873$). Excluding participants with a current anxiety disorder diagnosis neither reduced the magnitude of psychological anxiety measures significantly, nor did it affect the difference between groups in these measures (both p 's = 0.755).

3.4. Mood Disorder Measures and Mood Disorder Symptoms

When examining all participants, LTAA had significantly greater depression and hypomania scale scores on the MMPI-2, and significantly higher symptom counts for all mood domain diagnostic categories examined. The effect sizes varied from $d = 0.50$ to $d = 0.84$. After excluding all participants with a lifetime mood diagnosis, the number of symptoms and the magnitude of psychological abnormality were greatly reduced (Wilks $\lambda_{6,136} = 0.829$, $p < 0.001$), but the difference between groups in these measures was not significantly affected (Wilks $\lambda_{6,136} = 0.976$, $p = 0.755$). Excluding participants with a current mood disorder diagnosis neither reduced the magnitude of psychological mood measures significantly, nor did it affect the difference between groups in these measures (both p 's > 0.345).

3.5. Deviance Proneness Measures and Externalizing Disorder Symptoms

When examining all participants, LTAA had significantly higher MMPI-PD scale scores than NC, significantly lower CPI-SS scores than NC, and significantly higher conduct disorder and antisocial personality disorder symptom counts than NC. In Figure 3, the CPI Socialization scale scores are plotted as the inverse of the difference between LTAA and NC so that greater deviance for all measures is plotted as positive. The effect sizes for the deviance proneness measures and the antisocial personality disorder symptom counts varied between 1.37 and 1.69 (absolute value), which was much greater than that for the mood or anxiety disorder measures of Figures 1 and 2. In Figure 3, this larger effect size is indicated by the greater degree to which the data (including its 95% confidence interval) is distant from the zero line in comparison to the measures in Figures 1 and 2. Excluding participants with a lifetime diagnosis of an externalizing disorder (13 LTAA and 4 NC) did not significantly affect the dependent variables or the group differences in the dependent variables (both p 's > 0.12).

4. Discussion

There were four major findings in this study. First, there is greater psychiatric pathology in LTAA compared to NC. Second, the bulk of this difference is sub-diagnostic (i.e., falls short of criteria sufficient for a diagnosis). Third, excluding participants with a frank psychiatric diagnosis does not control for the differences between LTAA and NC groups in any of the three domains of psychiatric illness examined. Fourth, the difference in the presence and severity of psychiatric illness between LTAA and NC (whether individuals with a lifetime or current diagnosis are included or excluded in the comparison) is more than twice as large for antisocial personality disorder (ASPD) as it is for mood or anxiety disorders.

Previous research has described the high incidence of comorbid psychiatric mood, anxiety, and externalizing disorders in individuals diagnosed with a SUD (Di Sclafani, V., Finn, P., and Fein, G., Psychiatric Comorbidity in Long-Term Abstinent Alcoholics, submitted manuscript, June 2006; Grant et al., 2004a; Grant et al., 2004b; Kessler et al., 1997; Regier et al., 1990). The results presented here demonstrate that the association between an AUD (alcohol use disorder) and comorbid psychiatric illness also exists for sub-diagnostic symptomatology and psychological abnormality in the mood, anxiety, and externalizing disorder domains. Our findings indicate that the effect of diagnostic status on comorbid pathology is relatively minor, and that the predominance of the difference between LTAA and NC in psychiatric illness is carried by sub-diagnostic psychopathology. It is easy to see, then, that using only the tails of the symptomatology distribution (i.e., diagnoses) is insufficient to control for psychiatric comorbidity in SUDs.

The importance of sub-diagnostic psychopathology is starting to be acknowledged. Angst and colleagues (Angst et al., 2003), examined subthreshold bipolarity, evaluating bipolarity epidemiology and proposing criteria for minor bipolar disorders. Similarly, Hankin et al. (Hankin et al., 2005) examined the question of whether depression is best viewed as a continuum or a discrete category, performing a taxometric analysis of childhood and adolescent depression in a population-based sample. Other studies have proposed ways to conceptualize and account for the continuous, as opposed to threshold-defined, nature of psychopathology. Krueger and colleagues (Krueger et al., 2005; Markon and Krueger, 2005) investigated externalizing disorders, such as antisocial personality disorders and SUDs. They introduced a quantitative, model-based approach to comparing categorical and continuous conceptions of psychopathology, and applied this approach in an empirical study of patterns of comorbidity among externalizing disorders. They presented evidence that comorbidity among externalizing disorders is best modeled by an underlying normally distributed continuum of risk for multiple disorders within the externalizing spectrum.

Krueger et al.'s (Krueger et al., 2005) results support the concept of a single, heritable, externalizing 'liability.' As stated above, this externalizing liability is continuous (rather than discrete) in nature, and predisposes individuals to express externalizing pathology in varying degrees of severity. Substance use and antisocial behavior are important manifestations of an externalizing liability in an individual. The finding in the current sample is congruent with this concept; the difference between LTAA and NC is more than twice as large for ASPD as it is for mood or anxiety disorders.

The symptomatology of ASPD (impulsivity, low harm avoidance, boredom susceptibility / thrill and adventure seeking, poor learning from negative consequences, etc.) is very similar to the traits of addiction. Moreover, there is a different neural substrate for ASPD compared to mood and anxiety disorders. Mood and anxiety disorders are associated with a oversensitization of the Hypothalamic-Pituitary-Adrenal (HPA) axis resulting in

hypercortisolism (Arborelius et al., 1999; Plotsky et al., 1995). In contrast, there is undersensitization of the HPA axis (indicated by hypocortisolism) in ASPD, including substance abusers with ASPD (Deroche et al., 1997; King et al., 1990; Kosten et al., 2000; Moss et al., 1995; Vanyukov et al., 1993).

Markon and Krueger (Markon and Krueger, 2005) compared the fit of categorical and continuous models to the National Epidemiologic Survey on Alcohol and Related Conditions (n = 43,093). Both the first and second best-fit models were continuous rather than categorical, confirming that continuous conceptions of externalizing liability (that are normally distributed) provided substantial gains in fit over categorical conceptions of externalizing liability. In summary, this body of work is consistent with our findings of: 1) the greater power of continuous vs. categorical measures of comorbid psychopathology in distinguishing LTAA from NC, and 2) the stronger association of AUDs with ASPD vs. with mood and anxiety disorders.

There are caveats to our findings. We are not making any statements regarding causal relationships between psychiatric and substance abuse pathology. Our study is correlational only, and our sample size is limited. Finally, our symptom count measures are lifetime measures, and do not measure current symptoms. (The cDIS interview does not collect information on which symptoms are current unless criteria for a lifetime diagnosis are met. Measurement tools, such as the cDIS, reflect the prevailing paradigm and then reinforce that paradigm via the application of those tools.) We have now modified the cDIS interview so that in our future work we can tell if symptoms are current. We believe it is likely that the samples studied here would differ substantially on current symptom counts since there are large group differences (comparable in size to those on the lifetime symptom counts) in the psychological measures, which assess current psychological state.

We believe our findings are extremely important to the field of SUD research. An accurate picture of psychiatric illness comorbid to SUD will only emerge using continuous measures of psychiatric symptomatology, rather than the limited view provided by examining only symptomatology sufficient to meet criteria for diagnosis.

Acknowledgements

This work was supported by Grants AA11311 (GF) and AA13659 (GF), both from the National Institute of Alcoholism and Alcohol Abuse. We also express our appreciation to the NRI recruitment and assessment staff, and to each of our volunteer research participants.

References

- American Psychiatric Association. DSM-IV-R: Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Publishing, Inc.; Washington, DC: 2000.
- Angst J, Gamma A, Benazzi F, Ajdacic V, Eich D, Rossler W. Toward a redefinition of subthreshold bipolarity: epidemiology and proposed criteria for bipolar-II, minor bipolar disorders and hypomania. *J Affect Disord* 2003;73:133–146. [PubMed: 12507746]
- Arborelius L, Owens MJ, Plotsky PM, Nemeroff CB. The role of corticotropin-releasing factor in depression and anxiety disorders. *J Endocrinol* 1999;160:1–12. [PubMed: 9854171]
- Brady KT, Sinha R. Co-occurring mental and substance use disorders: the neurobiological effects of chronic stress. *Am J Psychiatry* 2005;162:1483–1493. [PubMed: 16055769]
- Cohen, J. Statistical Power Analysis for the Behavioral Sciences. 2. Lawrence Erlbaum Associates, Inc.; Hillsdale, NJ: 1988.
- Deroche V, Caine SB, Heyser CJ, Polis I, Koob GF, Gold LH. Differences in the liability to self-administer intravenous cocaine between C57BL/6 x SJL and BALB/cByJ mice. *Pharmacol Biochem Behav* 1997;57:429–440. [PubMed: 9218267]

- Di Sclafani V, Finn P, Fein G. Psychiatric Comorbidity in Long-Term Abstinent Alcoholics. *Alcohol Clin Exp Res*. June;2006 Submitted
- Gough, HGPD. Manual for the California Psychological Inventory (So Scale). Consulting Psychological Press; Palo Alto, CA: 1969.
- Grant BF, Stinson FS, Dawson DA, Chou SP, Dufour MC, Compton W, Pickering RP, Kaplan K. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry* 2004a;61:807–816. [PubMed: 15289279]
- Grant BF, Stinson FS, Dawson DA, Chou SP, Ruan WJ, Pickering RP. Co-occurrence of 12-month alcohol and drug use disorders and personality disorders in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry* 2004b;61:361–368. [PubMed: 15066894]
- Hankin BL, Fraley RC, Lahey BB, Waldman ID. Is depression best viewed as a continuum or discrete category? A taxometric analysis of childhood and adolescent depression in a population-based sample. *J Abnorm Psychol* 2005;114:96–110. [PubMed: 15709816]
- Hasin DS, Grant BF. Major depression in 6050 former drinkers: association with past alcohol dependence. *Arch Gen Psychiatry* 2002;59:794–800. [PubMed: 12215078]
- Hathaway, S.; McKinley, J. MMPI-2: Minnesota Multiphasic Personality Inventory. The University of Minnesota Press; Minneapolis: 1989.
- Hirschfield, R.; Hasin, DS.; Keller, M.; Endicott, J.; Wunder, J. Depression and alcoholism: comorbidity in a longitudinal study. In: Maser, J.; Cloninger, C., editors. *Comorbidity of Mood and Anxiety Disorders*. American Psychiatric Press; Washington, DC: 1990. p. 293-304.
- Kessler RC, Nelson CB, McGonagle KA, Edlund MJ, Frank RG, Leaf PJ. The epidemiology of co-occurring addictive and mental disorders. *Am. J. Orthopsychiatry* 1996;66:17–31.
- 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. [PubMed: 9107147]
- King RJ, Jones J, Scheur JW, Curtis D, Zarcone VP. Plasma cortisol correlates of impulsivity and substance abuse. *Indiv Diff* 1990;11:287–291.
- Kosten TA, Miserendino MJ, Kehoe P. Enhanced acquisition of cocaine self-administration in adult rats with neonatal isolation stress experience. *Brain Res* 2000;875:44–50. [PubMed: 10967297]
- Krueger RF, Markon KE, Patrick CJ, Iacono WG. Externalizing psychopathology in adulthood: a dimensional-spectrum conceptualization and its implications for DSM-V. *J Abnorm Psychol* 2005;114:537–550. [PubMed: 16351376]
- Mann RE, Sobell LC, Sobell MB, Pavan D. Reliability of a family tree questionnaire for assessing family history of alcohol problems. *Drug Alcohol Depend* 1985;15:61–67. [PubMed: 4017879]
- Markon KE, Krueger RF. Categorical and continuous models of liability to externalizing disorders: a direct comparison in NESARC. *Arch Gen Psychiatry* 2005;62:1352–1359. [PubMed: 16330723]
- Merikangas KR, Mehta RL, Molnar BE, Walters EE, Swendsen JD, Aguilar-Gaziola S, Bijl R, Borges G, Caraveo-Anduaga JJ, DeWit DJ, Kolody B, Vega WA, Wittchen HU, Kessler RC. Comorbidity of substance use disorders with mood and anxiety disorders: results of the International Consortium in Psychiatric Epidemiology. *Addict Behav* 1998;23:893–907. [PubMed: 9801724]
- Merikangas KR, Zhang H, Avenevoli S, Acharyya S, Neuenschwander M, Angst J. Longitudinal trajectories of depression and anxiety in a prospective community study: the Zurich Cohort Study. *Arch Gen Psychiatry* 2003;60:993–1000. [PubMed: 14557144]
- Moss HB, Vanyukov MM, Martin CS. Salivary cortisol responses and the risk for substance abuse in prepubertal boys. *Biol Psychiatry* 1995;38:547–555. [PubMed: 8562667]
- Plotsky, PM.; Owens, MH.; Nemeroff, CB. Neuropeptide Alterations in Affective Disorders. In: Bloom, FE.; Kupfer, DJ., editors. *Psychopharmacology: the Fourth Generation of Progress*. Raven Press; New York: 1995. p. 971-981.
- Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *Jama* 1990;264:2511–2518. [PubMed: 2232018]

- Reiss S, Peterson RA, Gursky DM, McNally RJ. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. *Behav Res Ther* 1986;24:1–8. [PubMed: 3947307]
- Robins, LN.; Cottler, L.; Buckholz, K.; Compton, W. The Diagnostic Interview Schedule for DSM-IV. Washington University School of Medicine; St. Louis, MO: 1998.
- Skinner HA, Sheu WJ. Reliability of alcohol use indices. The Lifetime Drinking History and the MAST. *J Stud Alcohol* 1982;43:1157–1170. [PubMed: 7182675]
- Sobell LC, Sobell MB, Riley DM, Schuller R, Pavan DS, Cancilla A, Kladner F, Leo GI. The reliability of alcohol abusers' self-reports of drinking and life events that occurred in the distant past. *J Stud Alcohol* 1988;49:225–232. [PubMed: 3374136]
- Sobell LC, Sobell MB. Self-reports issues in alcohol abuse: State of the art and future directions. *Behaviorial Assessment* 1990;12:77–90.
- Spielberger, CD. State-Trait Anxiety Inventory for Adults: Form Y Review Set - Manual, Test, Scoring Key. Mind Garden, Inc.; Redwood City, CA: 1983.
- SPSS Inc. SPSS 13.0 for Windows. Chicago IL: SPSS Inc; 2004.
- Stoltenberg SF, Mudd SA, Blow FC, Hill EM. Evaluating measures of family history of alcoholism: density versus dichotomy. *Addiction* 1998;93:1511–1520. [PubMed: 9926555]
- Vanyukov MM, Moss HB, Plail JA, Blackson T, Mezzich AC, Tarter RE. Antisocial symptoms in preadolescent boys and in their parents: associations with cortisol. *Psychiatry Res* 1993;46:9–17. [PubMed: 8464960]

Figure 1.

Mean (and 95% CI) of the difference between LTAA and NC on anxiety disorder psychological measures and symptom counts, computed separately for: (a) all participants, (b) participants without a lifetime anxiety disorder diagnosis, and (c) participants without a current anxiety disorder diagnosis.

Figure 2.

Mean (and 95% CI) of the difference between LTAA and NC on mood disorder psychological measures and symptom counts, computed separately for: (a) all participants, (b) participants without a lifetime mood disorder diagnosis, and (c) participants without a current mood disorder diagnosis.

Figure 3.

Mean (and 95% CI) of the difference between LTAA and NC on measures of deviance proneness and externalizing disorder symptom counts, computed separately for: (a) all participants, and (b) participants without a lifetime externalizing disorder diagnosis. *CPI-SS values are plotted as the inverse of the difference between LTAA and NC so that greater deviance for all measures is plotted as positive.

Table 1

Demographic and Alcohol Use Measures

Variables	Long-Term Abstinent Alcoholics		Normal Controls		Group Effect Size ^a
	Male (n = 25)	Female (n = 23)	Male (n = 25)	Female (n = 23)	
Age	45.6 ± 7.0	48.1 ± 6.4	43.4 ± 6.3	48.0 ± 6.6	0.8
Yrs of Ed	15.5 ± 2.0	15.5 ± 2.4	16.3 ± 2.2	16.0 ± 1.9	2.5
Ethnicity ^b	1 AA, 22 C, 1 H, 1 B	23 C	2 AA, 15 C, 2 H, 1 B, 5 A	1 AA, 15 C, 2 H, 3 B, 2 A	
Proportion of 1 st Degree Relative Problem Drinkers	0.41 ± 0.25	0.45 ± 0.30	0.14 ± 0.22	0.17 ± 0.21	24.2 ^{c***}
Alcohol Use Variables					
Alcohol Use (months)	245.4 ± 88.8	268.1 ± 102.8	232.2 ± 130.3	294.0 ± 130.1	d
Avg Dose (drinks/mo)	176.3 ± 135.0	128.1 ± 79.1	6.9 ± 8.3	6.8 ± 7.6	d
Peak Use (months)	51.0 ± 30.9	92.1 ± 81.2	115.2 ± 154.9	113.8 ± 112.5	d
Peak Dose (drinks/mo)	361.8 ± 257.2	264.0 ± 202.8	15.1 ± 14.5	16.7 ± 22.4	d
Abstinence Duration (yrs)	6.9 ± 6.2	6.5 ± 5.6	N/A	N/A	d

^a Percent of variance of dependent variable accounted for by group membership^b AA = African American, C = Caucasian, H = Hispanic, B = Bi/Multiracial, A = Asian^c Before analysis, the proportions were first normalized using the arcsin transformation^d Statistical comparisons between groups on the alcohol use variables are not appropriate since amount of alcohol use was a selection criterion

Effect is significant:

* p ≤ 0.05

** p ≤ 0.01

*** p ≤ 0.001

Table 2

Psychological Measures and Psychiatric Symptom Counts

Variables	All Study Participants			Participants w/o Lifetime Diagnosis			Participants w/o Current Diagnosis		
	LTAA	NC	Effect Size ^d	LTAA	NC	Effect Size ^d	LTAA	NC	Effect Size ^d
Anxiety									
ASI	<i>n</i> = 48 20.4 ± 12.6	<i>n</i> = 48 13.7 ± 10.2	0.58**	<i>n</i> = 31 16.2 ± 10.2	<i>n</i> = 41 12.3 ± 8.3	0.42	<i>n</i> = 38 17.7 ± 11.5	<i>n</i> = 48 13.7 ± 10.2	0.37
STAI-S	32.2 ± 9.4	27.2 ± 8.8	0.55**	29.1 ± 7.0	27.6 ± 9.3	0.18	30.1 ± 7.3	27.2 ± 8.8	0.36
STAI-T	41.0 ± 10.6	33.4 ± 8.8	0.78***	36.6 ± 7.7	32.8 ± 8.9	0.46	38.0 ± 8.6	33.4 ± 8.8	0.53*
Social Phobia	4.2 ± 4.6	1.9 ± 2.8	0.59**	2.3 ± 3.2	1.2 ± 2.0	0.40	-	-	-
Agoraphobia	1.3 ± 2.5	0.4 ± 1.4	0.46*	0.6 ± 1.2	0.2 ± 1.1	0.34	-	-	-
Panic Disorder	5.9 ± 6.1	2.2 ± 3.6	0.73***	3.6 ± 4.3	1.3 ± 1.7	0.70***	-	-	-
PTSD	2.5 ± 2.7	0.7 ± 1.8	0.78***	1.1 ± 1.8	0.4 ± 1.2	0.46	-	-	-
PTSD Tr. Events	5.1 ± 2.5	3.8 ± 2.4	0.52*	4.5 ± 2.5	3.6 ± 2.4	0.37	-	-	-
Obsessive Disorder	0.3 ± 0.8	0.0 ± 0.2	0.35	0.2 ± 0.8	0.1 ± 0.2	0.25	-	-	-
Compulsive Disorder	0.7 ± 1.8	0.3 ± 0.8	0.34	0.4 ± 1.2	0.3 ± 0.9	0.11	-	-	-
Mood									
MMPI-D	<i>n</i> = 48 23.5 ± 7.1	<i>n</i> = 48 18.4 ± 4.6	0.84***	<i>n</i> = 20 21.6 ± 6.2	<i>n</i> = 29 17.7 ± 4.1	0.74*	<i>n</i> = 36 21.6 ± 5.9	<i>n</i> = 45 17.9 ± 3.8	0.75**
MMPI-H	18.3 ± 5.4	15.5 ± 3.9	0.50**	16.4 ± 5.5	15.3 ± 3.6	0.24	18.2 ± 5.7	15.5 ± 3.9	0.55*
Depression	13.1 ± 10.4	6.8 ± 8.3	0.68***	4.2 ± 5.4	0.8 ± 1.4	0.86*	-	-	-
Depressive Episodes	3.5 ± 6.1	1.1 ± 2.1	0.53*	1.2 ± 3.4	0.0 ± 0.2	0.48	-	-	-
Dysthymia	2.0 ± 3.9	0.2 ± 1.6	0.61**	0.8 ± 2.3	0.0 ± 0.0	0.50	-	-	-
Mania	1.4 ± 2.6	0.4 ± 1.4	0.50*	0.8 ± 1.9	0.3 ± 1.2	0.29	-	-	-
Externalizing									
CPI-SS	<i>n</i> = 48 28.1 ± 5.8	<i>n</i> = 48 36.3 ± 3.6	-1.60***	<i>n</i> = 35 28.8 ± 5.4	<i>n</i> = 44 36.5 ± 3.5	-1.60***	-	-	-
MMPI-PD	21.5 ± 4.3	16.4 ± 3.1	1.37***	21.3 ± 4.7	16.2 ± 3.1	1.29***	-	-	-
Conduct Disorder	3.8 ± 3.5	2.0 ± 2.7	0.60***	2.3 ± 2.3	1.3 ± 1.5	0.51*	-	-	-
ASPD	9.5 ± 5.7	2.6 ± 2.7	1.56***	8.5 ± 5.8	2.2 ± 2.3	1.43***	-	-	-

^d Effect size is difference between groups in within group standard deviation units

Measure scores are reported mean ± standard deviation

Effect is significant:

* $p \leq 0.05$

** $p \leq 0.01$

*** $p \leq 0.001$