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Treatment-naive Active Alcoholics Have Greater Psychiatric Comorbidity than Normal Controls but less than Treated Abstinent Alcoholics

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Abstract

Background—Most alcoholism research in the U.S. uses convenience samples of treated alcoholics. The findings from treated samples have traditionally been applied to all alcoholics, including the 75% of alcoholics who are untreated. Improper generalization from select samples to an entire population is called ‘Berkson's fallacy’. We compared untreated versus treated alcoholics, in order to ascertain whether both groups belonged to the same population with regard to psychiatric comorbidity.

Methods—We measured psychiatric comorbidity in active treatment-naive alcoholics (TNA; n=86) versus non-alcoholic controls (NAC; n=118) and versus treated long-term abstinent alcoholics (TAA; n=52). We examined lifetime and current diagnoses, lifetime symptom counts, and psychological measures in the anxiety, mood and externalizing disorder domains.

Results—TNA did not differ from NAC in psychiatric diagnosis rates, were abnormal compared to NAC on all psychological measures, had more externalizing symptoms than NAC, and showed a strong trend for men to have more symptoms in the mood and anxiety domains. TAA compared to TNA had higher diagnosis rates (all domains), symptom counts (all domains), and psychological measures of deviance proneness, but were comparable to TNA on anxiety and mood psychological measures.

Conclusions—The abnormal thinking (psychological measures) in TNA (versus NAC) does not extend to behavior (symptoms) to the degree that it does in TAA. These results underline the importance of the use of subdiagnostic measures of psychiatric comorbidity in studies of alcoholics. The finding of lesser comorbidity in TNA versus TAA confirms the presence of Berkson's fallacy in generalizing from treated samples to all alcoholics.

Keywords

alcoholism; Berkson's fallacy; subdiagnostic psychiatric measures; classification of alcoholics; treated alcoholics; untreated alcoholics

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1. Introduction

In 2005, we showed that treated alcoholics are not simply former untreated alcoholics observed later in the progress of their disease. Treated alcoholics are a different population than untreated alcoholics; they drink more even at the beginning of their first heavy use of alcohol (Fein and Landman, 2005). This suggests more severe alcoholism in the treated alcoholics. This finding has far-reaching implications for two reasons: 1) it confirms the presence of Berkson's fallacy in the field of alcoholism research, and 2) it adds significant information to the current effort to classify alcoholics into clinically meaningful subgroups.

Most alcoholism research uses convenience samples of alcoholics in treatment, or shortly after treatment. Improper generalization from select samples to an entire population is called ‘Berkson's fallacy’; an example would be generalization from the 25% of alcoholics who have received treatment (Dawson et al., 2005) to the 75% of alcoholics who have not. (See Fein and Landman, 2005 for a history of Berkson's fallacy and examples in biomedical and psychiatric research.) In addition to alcoholism severity, findings on any measures of the antecedents or consequences of alcohol dependence that may be associated with levels of alcohol use (e.g., preexisting comorbid psychopathologic characteristics or exacerbation of comorbid psychopathologic characteristics) also may not extend from treated samples of alcoholics to untreated alcoholics in the general population.

Efforts to classify alcoholics into clinically meaningful subtypes began as far back as the nineteenth century (Babor et al., 1992; Babor and Lauerman, 1986; Babor and Meyer, 1986). Between then and now, there have been many attempts to derive a system of classification of alcoholics (Babor et al., 1992; Jellinek, 1960). As our understanding of the disease of alcoholism improved, typologies were discarded or expanded and refined (Babor et al., 1992; Hesselbrock et al., 1984; Morey et al., 1984; Moss et al., 2007; Penick et al., 1999; Schuckit, 1985; Sigvardsson et al., 1996). Penick, et. al., in a 1999 comparison of 11 typologies of alcohol-dependent individuals, concluded that the most powerful way of classifying alcoholics would require simultaneous consideration of at least two general dimensions: alcoholism severity and psychiatric comorbidity (Penick et al., 1999). A review of the literature shows that externalizing psychiatric disorders, chiefly anti-social personality disorder (ASPD), are considered by most to be the central psychiatric diagnoses in the classification of alcoholics, especially in severe alcoholism (although anxiety and mood disorders also play a role) (Cook et al., 1994; Epstein et al., 2002; Grant et al., 2004a; Grant et al., 2004c; Hauser and Rybakowski, 1997; Hesselbrock and Hesselbrock, 2006; Kessler et al., 1997; Moss et al., 2007; Penick et al., 1999; Sigvardsson et al., 1996; Windle and Scheidt, 2004).

In 2007, Moss et. al, using data from the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) reported that co-occurring psychiatric problems were associated with severity of alcoholism and entering into treatment, and that ‘help-seeking’ (i.e., treatment) remains relatively rare. They also concluded that the NESARC data suggest that a majority of people with alcoholism were not represented in the samples previously used to define alcoholism subtypes (Berkson's fallacy). Moss and colleagues went on to suggest a typology of 5 subtypes of (both treated and untreated) alcoholics. The discriminating features were ASPD, age of onset of alcohol dependence (AD), multigenerational familial AD, endorsement of specific alcohol dependence criteria, comorbid substance use disorders, comorbid mood and/or anxiety disorders, and consumption patterns as the most probable identifiers of subgroups of alcoholics. These conclusions are, of course, limited by the types of data collected by the NESARC (i.e., for psychiatric data, only disorders that reached criteria for diagnosis).

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In 2007, we reported on the prevalence of psychiatric disorders (Di Sclafani et al., 2007) and measures of subdiagnostic psychiatric illness (Fein et al., 2007) (measures of the psychological substrate of psychiatric disorders and psychiatric symptom counts, whether or not they met criteria for a diagnosis) in the mood, anxiety and externalizing disorder domains in a sample of (primarily treated) long-term abstinent alcoholics compared to age and gender-comparable controls. When we examined the psychiatric and psychological data, we found that long-term abstinent alcoholics had a much higher prevalence of psychiatric disorders than their non-alcoholic controls in all domains, but that the bulk of the difference between groups in psychiatric illness was subdiagnostic. In fact, even after removing individuals with (lifetime or current) diagnoses within each domain, there were still substantial differences between the groups on psychological measures and lifetime symptom counts, suggesting that examining diagnoses alone does not control for comorbid psychiatric problems in studies of alcoholism.

Since psychiatric problems are so often a major concomitant of alcohol dependence, and untreated alcoholics are so rarely examined in alcoholism research, the current study examined: 1) whether treatment-naive alcoholics are different from non-alcoholic controls in diagnostic and subdiagnostic comorbid psychiatric problems and, 2) if this difference exists, is it different in magnitude or type from the diagnostic and subdiagnostic psychiatric comorbidity exhibited by treated long-term abstinent alcoholics.

2. Methods

2.1 Participants

The two samples recruited for the current study consisted of treatment-naïve actively drinking alcohol-dependent individuals (TNA, 37 women and 49 men), and age and gender comparable non-alcoholic controls (30 women and 40 men). Both groups had comparable years of education. All participants were recruited from the community through restaurant and bar postings, newspaper advertisements, and a local internet site. TNA participants met DSM-IV (American Psychiatric Association, 2000) criteria for current alcohol dependence.

In prior published work (Di Sclafani et al., 2007; Fein et al., 2007), we recruited 52 long-term abstinent alcoholics. For the purpose of the current study, we are examining the 46 of those subjects who underwent treatment to achieve abstinence (Treated abstinent alcoholics, TAA; n = 46, 19 women and 27 men; Alcoholics Anonymous (AA) was considered treatment for this study, along with inpatient or outpatient treatment.) The TAA and their 48 age and gender comparable non-alcoholic controls were recruited from the community through postings at AA meeting sites, mailings, newspaper advertisements, a local Internet site, and subject referrals. All TAA met lifetime DSM-IV (American Psychiatric Association, 2000) criteria for alcohol dependence, and were abstinent from alcohol and all other psychoactive drugs (except caffeine and nicotine) for at least 6 months (mean abstinence 6.32 yrs).

The inclusion criteria for both the treatment-naïve and long-term abstinent studies non-alcoholic control samples were a lifetime drinking average of less than 30 drinks per month, no periods of drinking more than 60 drinks per month, and a negative lifetime history for alcohol abuse/dependence. There were no differences between the control groups in diagnosis rates (all p's > 0.53), nor in symptom counts or psychological measures (all p's > .400). Given the absence of cohort differences on the dependent variables, the two control groups were combined into a single non-alcoholic control group (NAC, n = 118) for subsequent analyses. Exclusion criteria for all groups were: 1) lifetime or current diagnosis of schizophrenia or schizophreniform disorder using the computerized Diagnostic Interview Schedule (c-DIS; (Robins et al., 1998), 2) history of drug abuse or dependence, 3) significant history of head trauma or cranial surgery, 4) history of significant neurological disease, 5) laboratory evidence of hepatic disease, or 6) clinical evidence of Wernicke-Korsakoff syndrome.

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2.2 Procedures

Procedures and assessments for all four groups were exactly the same. All individuals were fully informed of the study's procedures and aims, and signed a consent form prior to their participation. Participants completed four sessions that lasted between one and a half hours to three hours, and included clinical, neuropsychological, electrophysiological, and neuroimaging assessments. TNA and NAC were asked to abstain from consuming alcohol for at least 24 hours prior to any lab visit. A Breathalyzer (Intoximeters, Inc., St. Louis, MO) test was administered to all participants. A 0.00 alcohol concentration was required of all individuals in all sessions. Participants were compensated for time and travel expenses upon completion of each session. Individuals who completed the entire study were also given a completion bonus.

2.2.1 Alcohol Use Variables—Alcohol use variables were defined using the lifetime drinking history methodology (Sobell and Sobell, 1990; Sobell et al., 1988). Alcohol lifetime duration refers to the number of months of alcohol consumption in the individual's lifetime, while peak duration refers to the number of months of peak alcohol use. Alcohol lifetime dose is the average number of drinks per month 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. Age at which the participant took their first drink, and age and level at first heavy use of alcohol (defined as at least 80 drinks/mo for women and 100 drinks/mo for men) were also included as alcohol use variables, as was abstinence duration (for the TAA participants only).

2.2.2 Familial Drinking Density—The Family Drinking Questionnaire (Mann et al., 1985; Stoltenberg et al., 1998) was administered in the first session 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, or problem drinkers. Family Drinking Density was defined as the proportion of first-degree relatives who were problem drinkers.

2.2.3 Current and Lifetime Psychiatric Diagnoses, Symptoms, and Psychological Measure—The computerized Diagnostic Interview Schedule (c-DIS (Grant, et. al., 2004a; Grant, et. al., 2004b)) was administered to all participants by a research associate. We found it helpful to have the research associate ask the individual the c-DIS questions to avoid the participants' frustration with the c-DIS decision tree. In addition, this allowed the research associate to compare participants' answers to the c-DIS with their phone screen and other volunteered information. (We found this verification of information especially helpful in studies of individuals who were non-abstinent alcoholics.) The c-DIS generates a list of endorsed lifetime symptoms, and examines the symptoms to determine whether individuals met criteria for a lifetime diagnosis. The c-DIS assessed symptoms in the anxiety disorder domain of: Agoraphobia, Compulsive Disorder, Obsessive Disorder, Panic Disorder, Post-Traumatic Stress Disorder, and Social Phobia. In the mood disorder domain, the c-DIS assessed symptoms of : Dysthymia, Mania, and Major Depressive Disorder. In the externalizing disorder domain, the c-DIS assessed symptoms of Antisocial Personality Disorder, and Conduct Disorder (without ASPD). If criteria for a lifetime diagnosis were met, the c-DIS followed up with questions about whether criteria were met for a current diagnosis (one that existed in the prior 12 months). Although the c-DIS does determine current diagnoses, it does not yield currency information for individual symptoms. For the endorsed symptoms, we constructed three aggregate variables, encompassing symptoms of mood, anxiety, and externalizing disorders, respectively. In addition, we gathered psychological measures of mood, anxiety, and externalizing problems. The psychological scales used to assess the anxiety construct were the Reiss-Epstein Anxiety Sensitivity Index (ASI) (Reiss et al., 1986), and the

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State and Trait Scales of the State-Trait Anxiety Inventory for Adults (STAI-S and STAI-T) (Spielberger, 1983). Mood was assessed using the Depression and Hypomania Scales of the Minnesota Multiphasic Personality Inventory-2 (MMPI-D and MMPI-H) (Hathaway and McKinley, 1989). The externalizing construct was assessed using the Socialization Scale of the California Psychological Inventory (CPI-SS) (Gough, 1969) and the Psychopathic Deviance Scale of the MMPI-2 (MMPI-PD) (Hathaway and McKinley, 1989).

2.3 Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc., 2004). TNA were compared to both NAC and TAA groups (using the chi-square test) on the prevalence rates of any DSM-IV lifetime diagnosis and any current psychiatric diagnosis. Only if this comparison was significant, did we test for differences between groups in the prevalence of diagnoses in the mood, anxiety, and externalizing disorder domains. Chi-square tests were continuity corrected (conservative). We performed analyses of variance (ANOVA) (with group and gender as fixed factors) on the number of symptoms across all domains, and separately in the mood, anxiety, and externalizing disorder domains. We then analyzed the seven psychological measures in the same manner. Finally, we used Spearman correlations (which are robust to bivariate normal distribution assumptions, and are resistant to the effects of outliers) to examine the association of alcohol use and family history measures with psychiatric symptom counts and psychological measures. We computed the effect size (percent of variance of the dependent variable accounted for by the independent variable) because it facilitates comparison of effects among dependent variables and between studies.

For the TAA sample, for the analysis of current diagnoses (last 12 months prevalence), we removed all TAA with less than 18 months of abstinence, so that diagnoses during the period of drinking and the first six months of abstinence would not be included. This resulted in the exclusion of 6 TAA for current diagnoses.

3. Results

3.1 Lifetime and Current Diagnoses

TNA compared to NAC did not show a higher prevalence of lifetime (59.3% versus 48.3%) nor current (22.1% versus 9.3%) psychiatric diagnoses (both p's > 0.12). Within the TNA sample, the family density of (1st degree relative) problem drinkers was higher in individuals with a lifetime psychiatric diagnosis ($t_{82.8} = -2.340$, $p < .02$), the duration of peak alcohol use was lower in individuals with a current psychiatric diagnosis ($t_{84} = .047$, $p < .05$), and the age at which individuals started drinking tended to be earlier in individuals with a lifetime externalizing diagnosis ($t_{83} = 1.883$, $p = .06$).

Compared to TAA, TNA have fewer lifetime psychiatric diagnoses (59.3% versus 91.3%, $\chi^2=13.3$, $p < 0.0001$), a trend toward fewer current psychiatric diagnoses (22.1% versus 39.1%, $\chi^2=3.5$, $p = 0.06$), fewer lifetime mood diagnoses (48.8% versus 71.7%, $\chi^2=5.5$, $p < 0.02$), fewer lifetime anxiety diagnoses (10.5% versus 37.0%, $\chi^2=11.7$, $p < 0.001$), and fewer current anxiety diagnoses (1.2% versus 19.6%, $\chi^2=12.0$, $p < 0.001$). There were no differences between groups in lifetime or current externalizing diagnoses (18.6% versus 28.3%, $\chi^2=1.2$, ns, and 5.84% versus 0.0%, $\chi^2=1.4$, ns)nor in current mood diagnoses (17.4% versus 30.46%, $\chi^2=2.24$, ns).

3.2 Lifetime Psychiatric Symptoms

(TNA versus NAC) Examining symptoms summed across the three psychiatric domains (Table 2), there were 50% more symptoms in the TNA group than NAC, and a strong trend toward a group by gender interaction, with the increase in symptom counts in TNA being larger in men

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than in women. There was no main effects of group for anxiety symptoms, , but a main effect of gender, with more anxiety symptoms in women, and a strong trend for a group by gender interaction, with increased anxiety symptoms in TNA being present primarily in men.. Within the mood domain, there were no main effects of group or gender, but a strong trend for a group by gender interaction, with increased mood symptoms in TNA being present primarily in men. There were 92% higher symptom counts in externalizing domain symptoms for TNA versus NAC, a main effect of gender (with 73% more externalizing symptoms in men than women), and no group by gender interaction.

(TNA versus TAA) Symptom counts were dramatically lower in TNA compared to TAA for total psychiatric symptoms (42% lower), mood (50% lower), anxiety (43% lower), and externalizing symptoms (30% lower).

3.3 Psychological measures of anxiety and mood disturbance, and deviance proneness

The TNA showed more anxiety, mood disturbance (both depressive and hypomanic), and deviance proneness on all measures compared to NAC (Table 2). These differences were all significant even after correcting for multiple comparisons (at an experiment-wise alpha = .05/7 = .007). There were no gender, or group by gender interactions, except for a trend for a group by gender interaction for the ASI, with the increase in anxiety sensitivity being greater in the TNA men versus women. Within the TNA group, the MMPI-D and MMPI-H scales were uncorrelated ($r = -0.115$, $p = 0.30$). On the psychological measures, the TAA and TNA groups did not differ on the mood or anxiety measures, but only differed on the deviance proneness measures, with the TAAs showing greater deviance proneness than the TNA group.

3.4 Association of symptom counts and psychological measures with alcohol use variables

Within TNA, an increased density of the family history of alcohol problems was associated with an earlier age of initiation of alcohol use, and more abnormal scores on all measures of externalizing illness. The number of externalizing symptoms was associated with higher lifetime and peak alcohol doses, and a higher dose at first heavy use, as well as with more abnormal scores on the socialization and psychopathic deviance scales. The number of mood symptoms was associated with a shorter peak alcohol use duration, a higher peak dose, more anxiety symptoms, and abnormal scores on the MMPI Depression scale, the CPI socialization Scale, the MMPI Pd scale, the ASI, and the STAI Trait and State (trend only) measures. The number of anxiety symptoms was associated with the anxiety psychological measures, abnormal scores on the CPI Socialization and MMPI Pd Scales, elevated MMPI Depression Scale scores and elevated mood symptom counts. This same pattern of associations among the psychological measures and symptom counts was also present in NAC, except that the correlations were slightly reduced since the range of scores on these measures in NAC was less than it was in the TNA sample.

4. Discussion

The core finding of this study is that TNA do not evidence more psychiatric diagnoses than NAC, but do evidence substantial psychological differences from NAC in the anxiety, mood, and externalizing domains. TNA showed a strong disposition for more anxiety, mood disturbance (both depressive and hypomanic), and deviance proneness on all psychological measures compared to NAC. The results for symptom counts were intermediate between the lack of findings on diagnosis rates and the strong findings on psychological tests. TNA had higher symptom counts than NAC for symptoms aggregated across all domains, for externalizing symptoms. For mood and anxiety symptoms, there was a trend for male TNA to have more symptoms than male NAC. In sum, with regard to psychiatric disorder in the anxiety, mood, and externalizing domains, we see psychological differences between TNA and NAC,

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smaller differences in psychiatric symptom counts, and no differences in actual psychiatric diagnosis rates. In other words, the observed psychological abnormality is attenuated with regard to manifestation in behavior (symptoms), seldom resulting in behavior that meets criteria for a psychiatric diagnosis.

Previous research has described the high incidence of comorbid psychiatric mood, anxiety, and externalizing disorders in individuals diagnosed with a substance use disorder (Di Sclafani et al., 2007; Grant et al., 2004b; Grant et al., 2004c; Kessler et al., 1997). In our study of long-term abstinent alcoholics, in whom a lifetime psychiatric diagnosis was the norm, we demonstrated that the association between an alcohol use disorder and comorbid psychiatric illness also exists for sub-diagnostic symptom counts and for psychological abnormality in the mood, anxiety, and externalizing disorder domains. Those findings indicated that diagnostic status was insensitive as an indicator of comorbid pathology when compared to psychiatric symptom counts and measures of psychological abnormality. In that study, we showed that using only the tail of the symptomatology distribution (i.e., diagnoses) is insufficient to control for psychiatric comorbidity in alcoholics. The results of the current treatment-naive study offer additional support for this conclusion. Without examining sub-diagnostic measures, our findings suggest that the TNA sample is psychiatrically normal. However, the sub-diagnostic data present a very different picture, clearly establishing that the TNA subjects are abnormal compared to NAC in all domains.

The comparisons between the TNA and TAA studies show that these groups of alcoholics are different in regard to psychiatric comorbidity, and add even more support for the use of subdiagnostic measures. Intuitively, we hypothesized that the TAA would have less comorbidity, since they were so successful in maintaining long-term abstinence. However, the TAA compared to the TNA had more symptoms and more lifetime and current diagnoses in all three psychiatric domains. TAA also evidenced more deviance proneness than TNA. In contrast, on the mood and anxiety domain psychological measures, TAA and TNA were comparable. In other words, in the mood and anxiety domains, TNA showed comparable psychological substrate abnormality to TAA, but much less behavioral abnormality. If we had limited our analysis to diagnosis rates, only the lessened psychiatric mood and anxiety comorbidity in TNA versus TAA would have been observed, again missing the abnormal (but less than TAA) TNA symptom counts, and the nearly comparable psychological substrate abnormality in the two study samples.

The efforts to classify alcoholics into clinically meaningful subgroups were advanced by our prior finding that TNA are a different population than TAA with regard to alcoholism severity, having lower doses than TAA during the early period of heavy alcohol use (Fein & Landman, 2005). We now show that TNA evidence much less psychiatric comorbidity than TAA. This demonstrates that generalization regarding psychiatric comorbidity in alcoholics from studies of treated samples to the population of untreated alcoholics is unwarranted. Our results also affirm once more the very strong association between the externalizing disorders of alcoholism and ASPD. Symptoms of ASPD (e.g., impulsivity, low harm avoidance, boredom susceptibility/thrill and adventure seeking, poor learning from negative consequences, etc.), are very similar to the traits of addiction. In addition, 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; Brady and Sinha, 2005; Plotsky et al., 1995). In contrast, there is undersensitivation 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).

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There is considerable research showing that a high family density of alcoholism is strongly associated with a greater severity of both alcoholism and other externalizing psychiatric disorders (Babor, 1996; Babor et al., 1992; Hesselbrock and Hesselbrock, 2006; Moss et al., 2007; Penick et al., 1999). At present, it is unclear whether this association arises from strong genetic loading for both alcoholism and antisocial personality, or of a single, heritable, 'liability' for externalizing illness (Krueger et al., 2005). This hypothesized externalizing liability predisposes individuals to express externalizing pathology; whether in one or multiple disorders, and in varying degrees of severity. In a comparison of the fit of categorical and continuous models to the NESARC data (n = 43,093), Markon and Krueger (2005) showed that both the first and second best-fit models were continuous (such as symptoms) rather than categorical (such as diagnoses), confirming that continuous conceptions of externalizing liability (that are normally distributed) provided substantial gains in fit over categorical conceptions of externalizing liability. Our results support Krueger's hypothesis. Findings were much stronger using subdiagnostic measures rather than diagnoses. Moreover, a single, heritable, externalizing liability is consistent with the data from both TNA and TAA. In both samples, differences from NAC on externalizing symptom counts and psychological measures of deviance proneness were much larger than the results for comparable symptoms and measures in the mood and anxiety domains.

It is likely that some of the TNA will eventually seek treatment (all treated alcoholics were at an earlier time TNA). We believe it is likely that the TNA with the most externalizing psychiatric symptoms, greatest dose, and most dense family histories of problem drinkers are, or will become, the type of alcoholic seen in the TAA study. The TAA had a greater family density of problem drinkers, higher alcohol dose, and more externalizing psychiatric symptoms than TNA.

There are caveats to this research. The decision to compare the two studies, treatment-naive versus treated alcoholics, was post-hoc. Therefore, the samples were not designed to be directly comparable. There are two major differences between the TNA and the TAA study; the TNA are still drinking (as opposed to the long-term abstinent alcoholics in the TAA study), and the TNA are younger than the TAA. (Each study had an age- and gender- comparable control group.) These factors do not invalidate the comparison of the studies because, with regard to drinking, we have already shown that these TNA and TAA come from different populations with regard to alcoholism severity. In addition, there were no correlation between abstinence duration and lifetime or current diagnoses in TAA (there is very strong evidence that psychiatric comorbidity in alcoholics does not arise from alcohol dependence, but is premorbid (Berman and Noble, 1995; Hesselbrock et al., 1991; Merikangas and Avenevoli, 2000; Nurnberger et al., 2004; Pihl and Peterson, 1991; Yoshino et al., 2000). Finally, if current drinking exacerbated psychiatric comorbidity, the bias in this study would be against our findings; that is, the TNA would be more psychologically disturbed. Vis-à-vis the difference in age between the TNA and TAA studies, the 'original' age and gender comparable control groups for each study were combined because there were no cohort differences between the control groups in any of the dependent measures. In addition, there were no associations between age and diagnoses, symptoms, or psychological measures in any of the groups.

Improvements could be made in this study regarding *1)* collection of information on current symptoms (the c-DIS does not yield information on current symptoms, although it does yield information on current diagnoses), *2)* collection of information regarding which symptoms were linked to alcohol-seeking, intoxication, or withdrawal, and which were present not in the context of alcohol-seeking, intoxication, or withdrawal (Collins and Schlenger, 1988; Hines and Straus, 2007), and *3)*the addition of an assessment of Borderline Personality Disorder in the externalizing domain. (Borderline Personality Disorder is often comorbid with alcohol use disorders (Bowden-Jones et al., 2004; Dom et al., 2006), and is strongly associated with

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impulsivity (Dowson et al., 2004) and disadvantageous decision-making (Bazanis et al., 2002; Bowden-Jones et al., 2004; Dom et al., 2006)).

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Table 1

Demographic and Alcohol Use Data

	Treated Long-Term Abstinent Alcoholics (TAA)		Treatment-Naïve Alcoholics (TNA)		Non-Alcoholic Controls (NAC)[a]	
	Men (n=27)	**Women (n=19)**	**Men (n=49)**	**Women (n=37)**	**Men (n=65)**	**Women (n=53)**
Demographics						
Age (years)	45 ± 7	48 ± 6	31 ± 8	31 ± 8	37 ± 9	40 ± 11
Years of Education	15 ± 2	16 ± 2	16 ± 2	16 ± 1	16 ± 2	16 ± 2
Family History Density[b]	.39 ± 2	.45 ± .3	.14 ± .2	.245 ± .291	.6 ± .8	.7 ± 1
Alcohol Use Variables						
Age First Drank	15 ± 3	17 ± 6	16 ± 2	16 ± 2	19 ± 4	20 ± 5
Age at First Heavy Use	21 ± 5	27 ± 8	22 ± 5	22 ± 6	N/A	N/A
Lifetime Duration (months)	263 ± 95	268 ± 109	183 ± 96	178 ± 87	175 ± 120	200 ± 143
Average Dose (per month)	179 ± 149	136 ± 83	100 ± 45	79 ± 89	7 ± 7	6 ± 6
Peak Duration (months)	62 ± 59	86 ± 69	53 ± 50	52 ± 54	61 ± 73	78 ± 93
Peak Dose (per month)	341 ± 258	290 ± 219	181 ± 121	152 ± 205	15 ± 15	14 ± 17
Abstinence (years)	6 ± 6	7 ± 6	N/A	N/A	N/A	N/A

Measures are reported mean ± standard deviation.

N/A: Not applicable

[a] The two studies involved different age groups; however, there were no differences whatsoever between the two original control groups on any of the dependent variables; therefore we combined the control groups into a single non-alcoholic control (NAC) group.

[b] Proportion of first degree relatives who are problem drinkers

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Table 2

Psychological Measures and Psychiatric Symptom Counts

	Treated Long-Term Abstinent Alcoholics (TAA)		Treatment-Naive Alcoholics (TNA)		Non-Alcoholic Controls (NAC)		Effects		
	Men (n=27)	Women (n=19)	Men (n=49)	Women (n=37)	Men (n=65)	Women (n=53)	TAA > NAC	TNA > NAC	TAA > TNA
Sum of all Symptoms[a]	47.0 ± 23.9	44.2 ± 19.5	28.3 ± 15.3	24.5 ± 15.0	15.0 ± 14.1	21.0 ± 17.0	***	**	***
Sum Internalizing Symptoms[b]	32.0 ± 22.8	33.1 ± 17.5	17.4 ± 13.2	17.2 ± 11.7	8.6 ± 11.4	17.9 ± 15.2			
Anxiety									
Symptoms	14.7 ± 13.2	14.2 ± 12.0	8.0 ± 7.0	8.6 ± 7.3	3.8 ± 5.0	8.5 ± 8.7	***		***
Measures									
ASI	20.5 ± 11.8	22.8 ± 13.5	20.6 ± 10.7	20.0 ± 9.6	13.1 ± 8.0	16.8 ± 11.2	**	**	
STAI-S	32.2 ± 11.0	31.4 ± 7.1	34.7 ± 9.2	35.8 ± 11.5	28.7 ± 9.3	28.3 ± 7.7		***	
STAI-T	23.2 ± 6.7	40.8 ± 20.0	41.3 ± 10.4	40.5 ± 9.4	34.1 ± 7.7	35.3 ± 9.7	***	***	
Mood									
Symptoms	17.4 ± 12.6	17.9 ± 13.9	9.5 ± 9.1	8.6 ± 6.8	4.9 ± 7.4	9.4 ± 8.9	***		***
Measures									
MMPI-D	21.9 ± 4.3	21.5 ± 3.8	19.0 ± 4.3	19.7 ± 5.3	16.5 ± 3.1	16.1 ± 3.5	***	**	
MMPI-H	20.1 ± 5.5	16.3 ± 4.2	19.1 ± 4.6	18.4 ± 5.1	16.1 ± 4.0	15.8 ± 4.2	**	***	
Sum Externalizing Symptoms	15.0 ± 8.0	11.1 ± 7.1	10.9 ± 8.0	7.3 ± 7.4	6.3 ± 6.1	3.1 ± 2.9	***	***	**
Measures									
CPI-SS	27.3 ± 5.8	30.6 ± 4.8	31.4 ± 4.4	31.1 ± 6.00	35.9 ± 4.4	37.2 ± 3.8	***	***	*
MMPI-PD	21.9 ± 4.3	21.5 ± 3.8	19.0 ± 4.3	19.7 ± 5.3	16.5 ± 3.1	16.1 ± 3.5	***	***	**

Effect is significant

[a] summed across anxiety, mood and externalizing domains

[b] mood + anxiety symptoms

* $p \leq 0.05$

** $p \leq 0.01$

*** $p \leq 0.001$