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Gender-related influences of parental alcoholism on the prevalence of psychiatric illnesses: Analysis of the National Epidemiologic Survey on Alcohol and Related Conditions

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Abstract

Background—Offspring of individuals with alcoholism are at increased risk for psychiatric illness, but the effects of gender on this risk are not well known. In this study we tested the hypothesis that the gender of the parent with alcoholism and the gender of offspring affect the association between parental alcoholism and offspring psychiatric illness.

Method—We analyzed the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) data to examine the gender-specific prevalence of Axis I and Axis II disorders in 23,006 male and 17,368 female respondents with and without a history of paternal or maternal alcoholism. Adjusted odds-ratios were calculated for the disorders based on gender and presence of maternal or paternal alcoholism.

Results—Maternal or paternal alcoholism was associated with a higher prevalence of every disorder examined, regardless of the gender of offspring. Gender-related differences in prevalences were present in nearly all examined disorders and the association between parental alcoholism and offspring psychiatric disorders was significantly different in men and women. These differences included stronger associations in female offspring of men with alcoholism (alcohol abuse without dependence); in female offspring of women with alcoholism (mania, nicotine dependence, alcohol abuse, and schizoid personality disorder); in male offspring of men with alcoholism (mania); and in male offspring of women with alcoholism (panic disorder).

Conclusions—Interactions between gender and parental alcoholism were specific to certain disorders but varied in their effects, and in general female children of women with alcoholism appear at greatest risk for adult psychopathology.

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INTRODUCTION

The influences of parental alcoholism on health are wide-reaching and reflect both genetic and environmental factors (Grant, 2000). Because of the substantial number of children exposed to parental alcoholism and its deleterious effects, a substantial body of research has emerged examining the effects of parental alcoholism and factors mediating these effects. Findings include increased risk of drug and alcohol dependence (Chassin et al., 1999; Christoffersen and Soothill, 2003; Schuckit et al., 2000), and numerous psychosocial disadvantages (e.g. increased odds of being involved in violence, premature death, family separation, and unemployment (Christoffersen and Soothill, 2003)). Furthermore, there is substantial evidence that familial alcoholism is associated with (but perhaps not independently responsible for) increased risk of mood and anxiety disorders (Merikangas et al., 1998; Preuss et al., 2002).

One area of research that remains understudied and in many respects without clear results is the role of gender in the effects of parental alcoholism on offspring mental health. Expectations for such a role are perhaps high because of the clear gender differences in the prevalence of substance use disorders, as well as mood, anxiety, and other psychiatric disorders (Kessler et al., 1997). Studies that have considered the interaction between offspring gender and family or parental history of alcoholism on psychiatric morbidity have typically focused on substance use and/or a limited number of mood, anxiety, or personality disorders (Dawson and Grant, 1998; Sher et al., 1991; Winokur and Coryell, 1991). Furthermore, such studies have produced varied results, with some studies suggesting that women may be at relatively increased risk for some of the negative outcomes associated with a family history of alcoholism (Berkowitz and Perkins, 1988; Chassin et al., 1999; Chermack et al., 2000; Crum and Harris, 1996; Curran et al., 1999; Sher et al., 1991) and other studies suggesting that genetic factors in the transmission of alcoholism in particular may be relatively stronger in men than in women (Light et al., 1996; McGue et al., 1996) or no different between men and women (Heath et al., 1997; Kendler et al., 1995).

Other studies have considered the influences of parent gender or the concordance of parent and offspring gender. A large population-based study noted that maternal, compared to paternal, alcoholism is associated with significantly higher occurrences of nearly all the negative psychosocial outcomes measured (Christoffersen and Soothill, 2003). Smaller studies in adolescents and young adults suggest that female offspring of individuals with alcoholism are more likely to have internalizing symptoms or disorders than are male offspring (Berkowitz and Perkins, 1988; Chassin et al., 1999) and that the risk may be greater when the parent with alcoholism is male (Berkowitz and Perkins, 1988). Another population-based study (Dawson and Grant, 1998) found an interaction between offspring gender and gender of the parent with alcoholism (and same-gender relatives on that side) in alcohol dependence in the offspring. In particular, the influence of alcoholism in maternal female relatives on alcohol dependence alone was greater in women than in men, and the influence of alcoholism in paternal male relatives on primary alcohol dependence with secondary depression was greater in men than in women.

Because of the as yet limited work in this area, as well as varied study designs and study questions, it remains unclear what role gender may play in the association between parental alcoholism and a broad range of psychopathology in the adult children of alcoholics. To investigate, we analyzed data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) to examine the relevance of parental history of alcoholism and parent and offspring gender in the expression of a wide range of psychiatric illnesses. We hypothesized that parental history of alcoholism would increase the odds for psychiatric illness regardless of gender; that there would be significant differences between men and

women in the prevalence of psychiatric illnesses; and that the prevalence of these disorders would reflect significant interactions between parental history of alcoholism and gender. Due to the lack of available literature and inconsistency in previous studies, we did not have *a priori* hypotheses about the nature or direction of these interactions.

MATERIALS and METHODS

Sample

Data for this study come from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC, Wave I), which is described elsewhere in greater detail (Grant et al., 2003; Grant et al., 2004). Briefly, the NESARC, conducted by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the Bureau of the Census, surveyed a nationally representative sample of non-institutionalized U.S. residents (citizens and non-citizens) aged 18 years and over. Respondents were identified using a multi-stage cluster sampling technique, and the sample was enhanced with members of group-living environments, such as dormitories, group homes, shelters, and facilities for housing workers. Jails, prisons, and hospitals were not included. The study over-sampled black and Hispanic households, as well as young adults aged 18 to 24 years, in order to have sufficient power to perform meaningful analyses focusing on these populations. Weights have been calculated to adjust standard errors for these over-samples, the cluster sampling technique, and non-response. The final sample consisted of 43,093 respondents, representing an 81% response rate. All respondents gave consent to participate. The current investigation utilized publicly accessible, de-identified data and was thus exempted from formal institutional review board review.

Measures

The Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM IV version (AUDADIS-IV), a structured diagnostic assessment tool, was administered by trained lay interviewers in the NESARC study. The AUDADIS-IV has demonstrated good reliability and validity for detecting psychiatric disorders in a community sample. The NESARC data set contains diagnostic variables derived from AUDADIS-IV algorithms and based on DSM-IV criteria. The data contain diagnostic variables for major depression, dysthymia, mania and hypomania, panic disorder with and without agoraphobia, social phobia, simple phobia, generalized anxiety disorder, alcohol abuse and dependence, drug abuse and dependence, and nicotine dependence. We used lifetime measures of these disorders with substance and illness-induced symptoms excluded. Seven DSM-IV Axis II disorders were also assessed with the AUDADIS-IV: antisocial, avoidant, dependent, histrionic, obsessive-compulsive, paranoid, and schizoid personality disorders. The AUDADIS-IV has shown good to excellent reliability in assessing psychiatric disorders in community samples (Grant et al. 1995).

Family history of alcoholism was assessed separately for mothers and fathers. The interviewer stated the following before asking for family history: “Now I would like to ask you some questions about whether any of your relatives, regardless of whether or not they are now living, have EVER been alcoholics or problem drinkers. By alcoholic or problem drinker, I mean a person who has physical or emotional problems because of drinking [PAUSE]; problems with a spouse, family, or friends because of drinking [PAUSE]; problems at work or school because of drinking [PAUSE]; problems with the police because of drinking-such as drunk driving [PAUSE]; or a person who seems to spend a lot of time drinking or being hungover. [Repeat definition frequently]” Subsequent to this introduction, respondents were asked “Has your blood or natural father (mother) been an alcoholic or

problem drinker at ANY time in his (her) life?" Responses were coded as Yes, No, and Don't Know, with the last type removed from data analyses.

Data Analysis

The primary research questions concerned the relationship between parental alcoholism and offspring psychiatric illness, with offspring grouped by the presence or absence of paternal and maternal alcoholism and stratified by gender. To investigate, we first examined the association between paternal and maternal alcoholism and sociodemographic variables - age, gender, race/ethnicity, education, employment status, annual household income, and whether offspring had grown up with both biological parents. This was done to identify possible confounding factors for multivariable models. Next, we calculated gender-specific, unadjusted, weighted rates of psychiatric disorders with two separate stratifications, first by the absence or presence of paternal alcoholism and second by the absence or presence of maternal alcoholism. Finally, we fit a series of logistic regression models where psychiatric disorders were the dependent variables of interest and gender, the absence or presence of parental alcoholism, and the interaction between gender and the absence or presence of parental alcoholism were the independent variables of interest, adjusting for previously identified potentially confounding factors. Models were fit separately for maternal and paternal history of alcoholism. Similar to other NESARC analyses (Grant et al, 2009), these began with grouping psychiatric disorders into two categories (Axis I and II, respectively). Only when a significant association was observed between these categories and family history did we pursue analysis of the sub-categories of Axis I (mood, anxiety, and substance use) and Axis II (clusters A. B and C) disorders. For sub-categories that showed significant associations, the relationships with specific constitutive disorders was examined. Because of the limited number of initial analyses (two each for paternal and maternal family history for men and women, respectively) that was each significant at $p<0.001$, we did not adjust our alpha level to account for the multiple subsequent comparisons. Data were analyzed using SUDAAN software (Research Triangle Institute, 2001) and the NESARC calculated weights.

RESULTS

The analysis sample consisted of 23,006 men and 17,368 women who provided responses regarding parental history of alcoholism. Chi-square analyses indicated differences with respect to paternal alcoholism and gender, education, employment and household of origin composition with male gender, a college degree, not working, and having grown up with both biological parents were associated with a lower frequency of paternal alcoholism in this sample. A similar pattern was observed with respect to maternal alcoholism, and additionally, race/ethnicity was implicated with maternal alcoholism less frequently acknowledged among Hispanic respondents (Table 1). Of these factors, several appeared particularly robust: having grown up with both biological parents (over 50% reduction); having a college degree (~30% reduction); and, in the case of maternal alcoholism, Hispanic ethnicity (43% reduction).

Maternal and paternal alcoholism and prevalence of Axis I and II disorders

Both maternal (Table 2) and paternal (Table 3) alcoholism were associated with significantly higher prevalences of every axis I and axis II disorder examined compared to those without such a parental history. Prevalence of any axis I disorder was 73% higher (67.93% versus 39.22%) in the maternal alcoholism group (versus no maternal alcoholism) and 63% higher (59.07% versus 36.32%) in the paternal alcohol group (versus no paternal alcoholism). Prevalence of any axis II disorder was 138% higher (32.32% versus 13.57%) in

the maternal alcoholism group and 103% higher (24.58% versus 12.13%) in the paternal alcohol group.

Gender differences in the prevalence of Axis I and II disorders by parental alcoholism status

Gender differences in the prevalence of these major psychiatric illnesses were also present (Tables 2 and 3). Among subjects without a maternal history of alcoholism or without a paternal history of alcoholism, comparisons across gender indicated similar patterns: female gender was associated with a higher prevalence of any mood disorder and any anxiety disorder. Within these categories, female gender was associated with major depression, dysthymia and each one of the specific anxiety disorders. Male gender was associated with a higher prevalence of any axis I disorder and any axis II disorder. Within the Axis I disorders, male gender was associated with conduct disorder, and pathological gambling, and any substance use disorder, and within this cluster, men were more likely than women to report each substance use disorder assessed. Within the personality disorders, men were more likely to report a cluster B personality disorder, particularly antisocial personality disorder.

Many of these same gender differences were also present among subjects with a maternal or paternal history of alcoholism. Among persons with a maternal history of alcoholism, however, there were no gender differences in the prevalence estimates of panic disorder, nicotine dependence, pathological gambling, or avoidant, dependent, or paranoid personality disorders (Table 2). Similarly, among those with a paternal history of alcoholism, there were no gender differences in the prevalence of pathological gambling or dependent or paranoid personality disorders (Table 3). In contrast, an increased prevalence of schizoid personality disorder in women was seen only among subjects with a maternal history of alcoholism (Table 2).

Adjusted odds ratios for psychopathology by parental history and gender of offspring are presented in Table 4. In women, paternal alcoholism was associated with increased odds for any axis I and any axis II disorder, and for every individual disorder examined except dependent personality disorder; maternal alcoholism was associated with increased odds for any axis I and any axis II disorder, and for every disorder except hypomania, panic disorder, and pathological gambling. Similarly in men, paternal alcoholism was associated with increased odds for any axis I and any axis II disorder, and every individual axis I and axis II disorder except pathological gambling and dependent personality disorder. Maternal alcoholism in men was associated with increased odds for any axis I and any axis II disorder, and for many individual disorders but not mania, hypomania, panic disorder with agoraphobia, social phobia, pathological gambling, nicotine dependence, dependent personality disorder, or schizoid personality disorder.

Interactions between maternal or paternal alcoholism and gender

Interactions between parental history of alcoholism and offspring gender were present in any axis I disorder, any substance use disorder, 4 of the individual axis I disorders (mania, panic disorder, nicotine dependence, alcohol abuse), and schizoid personality disorder (Table 4). These interactions varied based on the gender of the parent, the gender of the offspring, and the particular disorders. The finding of a significant gender-by-paternal history of alcoholism for any Axis I disorder was explained by a stronger association between paternal alcoholism and Axis I pathology in male offspring as compared to female offspring. The disorder showing the most statistically significant contribution related to this effect was mania. However, maternal history of alcoholism was associated with significantly stronger odds of mania in women than in men. Thus, although parental history of alcoholism

increased the odds of mania in male and female offspring, in the findings indicate a gender influence of parental alcoholism in association with mania in same-gender parent-offspring pairs.

A similar same-gender pattern was observed for substance use disorders, and particularly for nicotine dependence and alcohol abuse, and schizoid personality disorder in association with maternal alcoholism. In these cases, odds were significantly elevated in female offspring of women with alcoholism where as men either showed no association or a less robust association for the indicated disorder. A different pattern was observed for panic disorder: maternal history of alcoholism was associated with significantly higher odds for the disorder in men than in women. Analogously, a paternal history of alcoholism was more robustly associated with alcohol abuse in women as compared to men.

DISCUSSION

A family history of alcoholism previously has been associated with higher rates of drug and alcohol use disorders, other psychiatric disorders, and personality variables associated with psychiatric disorders and social maladjustment (Chassin et al., 1999; Christoffersen and Soothill, 2003; Grant, 2000; Merikangas et al., 1998; Preuss et al., 2002; Schuckit et al., 2000). Gender differences in the prevalence of psychiatric illness have also been shown. In particular, gender differences in some of the disorders considered here have been described previously in the NESARC data set without the consideration of parental history of alcoholism (Compton et al., 2005; Grant et al., 2004; Grant et al., 2005a; Grant et al., 2005b; Hasin et al., 2005; Petry et al., 2005). We found that paternal and maternal histories of alcoholism were each associated with higher rates of every psychiatric disorder examined, and that gender differences in the rates of these disorders in the absence of paternal or maternal alcoholism followed expected patterns.

In the presence of maternal or paternal alcoholism, however, the pattern of gender differences was altered. For example, odds of mania were significantly higher for sons of fathers with alcoholism, and daughters of mothers with alcoholism. For nicotine dependence and schizoid personality disorder, maternal history alone had a significantly stronger effect on female offspring than male offspring; while for alcohol abuse both paternal and maternal histories had a significantly stronger effect on female offspring. In only one disorder, panic disorder, did maternal history have a significantly stronger effect on male offspring.

The increased odds of alcohol abuse found in women compared to men with either a paternal or maternal history of alcoholism is supported by previously published work. Crum and Harris (1996) (Crum and Harris, 1996) studied a subset of the National Institute of Mental Health Epidemiologic Catchment Area Program data and found that the association between parental alcoholism and alcohol use disorders (abuse or dependence) was stronger in female offspring than in male offspring. In a large study of college freshmen, Sher et al. (1991) (Sher et al., 1991) examined gender by family history of alcoholism interactions and found a statistically greater effect of family history of alcoholism on offspring alcohol use disorders in women than in men. In a case-control study, Curran et al. (1999) (Curran et al., 1999) found that family history of alcoholism was a stronger predictor of symptoms of alcohol dependence in women.

Because the present study is a large, population-based study, we were able to examine alcohol abuse and alcohol dependence separately. This is of particular interest as twin studies, in contrast to the three studies mentioned in the previous paragraph, have shown that the inherited contribution to alcoholism in women is either no greater (Heath et al., 1997; Kendler et al., 1995) or is *less* than it is in men (McGue et al., 1996). We found no parental

history of alcoholism by gender interaction in the odds for alcohol dependence in this sample. However, in the subset of alcohol dependence without abuse (Hasin and Grant, 2004), maternal alcoholism interacted with offspring gender reflecting increased odds in women compared to men. Hence, in what may be two ends of the spectrum of alcohol use disorders, women appear to be disproportionately affected by alcoholism in their mothers.

The finding of increased odds of mania in daughters as compared to sons of alcoholic mothers and sons as compared to daughters of alcoholic fathers – compared to the opposite gender offspring - has not been previously reported to our knowledge, and additional research is required to explain what may mediate these findings. However, gender differences in the relationship between co-occurring alcoholism and bipolar disorder have previously been found (Helzer and Pryzbeck, 1988; Kessler et al., 1997; Regier et al., 1990), and some of these differences may relate to family history of alcoholism (Frye et al., 2003). Furthermore, Todd et al. (1996) (Todd et al., 1996) found in a study of families of children with major depression or bipolar disorder that maternal mood disorders and alcoholism were independently transmitted – i.e., maternal alcoholism itself did not increase the risk of mood disorders including bipolar disorder. Hence, the increased odds of mania in daughters of alcoholic mothers here is particularly noteworthy.

The increased odds of a disorder in offspring of the same gender as the alcoholic parent were also seen in nicotine dependence and schizoid personality disorder. In these cases, maternal alcoholism associated more strongly with the disorder in daughters. Indeed, sons of alcoholic mothers did not have increased odds of these disorders relative to sons of non-alcoholic mothers. Such a lack of effect of maternal alcoholism on male psychopathology was also evident for mania, suggesting that for these three conditions, the association between maternal alcoholism and psychopathology was limited to female offspring.

In general, the impact of maternal alcoholism on psychopathology was greater in female offspring than in male offspring. This not only was evident in the significant gender by maternal history of alcoholism interactions in mania, nicotine dependence, alcohol abuse and schizoid personality disorder, but also was suggested in the direction of the interactions that did not reach statistical significance. In particular, the odds ratios investigating the associations between maternal history of alcoholism and all of the other externalizing disorders (with the possible exception of pathological gambling, which may or may not represent an externalizing disorder) were non-significantly but consistently greater in female offspring than in male offspring. As externalization of emotions is more typically associated with men, this finding may indicate an effect of the relative absence of a female role model for daughters of alcoholic mothers. Such an interpretation is not inconsistent with prior findings. For example, Stanger and colleagues (Stanger et al. 2004) found that poor parental monitoring and inconsistent parental discipline led to more externalizing behavior in children - a scenario that could be relatively more likely to affect a daughter of an alcoholic mother. In addition, psychological traits in mothers and fathers interact differently with such traits in their children to influence internalizing and externalizing behavior. In particular, in the mother (but not the father) novelty seeking – a trait associated with substance misuse – may interact with harm avoidance in the child to promote externalizing behavior (Rettew et al. 2006).

Limitations and Conclusions

The cross-sectional nature of this study does not allow psychological, environmental, or genetic effects related to parental alcoholism to be distinguished, and more research is necessary to explain the current findings with respect to these factors. Several additional limitations of these data should be acknowledged. One limitation is that the data do not allow us to examine the relative ages of onset of parental alcoholism and offspring

psychopathology. It is also possible that parental alcoholism had a greater effect on advancing the onset of psychiatric illness in offspring, artificially increasing prevalence rates in younger respondents with a parental history. This potential bias would have been reduced, however, by adjusting for age in multivariable models. The reliance on offspring to both diagnose and recall their parents' alcoholism is another limitation. For example, a reporting bias wherein daughters of alcoholic mothers recall differently than sons of alcoholic mothers could have occurred – leading to the apparent relationship between maternal alcoholism and mania, nicotine dependence, and schizoid personality disorder in female offspring. Such a bias would have likely been present in previous studies as well, and the effect of maternal alcoholism on rates of panic disorder in sons argues against this as a systematic issue.

Another limitation is that the models employed in this analysis did not adjust for possible psychiatric co-morbidity in parents. Hence it is possible that the effects seen in some disorders may have been mediated through an interaction between parental alcoholism and a co-morbid disorder or by the co-morbid disorder itself. Indeed, comprehensive measures of family histories of psychiatric disorders were not used in the current study, and this absence represents a limitation given the frequent co-occurrence of substance-related and non-substance related psychiatric disorders (e.g. Grella et a. 2009). Another limitation is that the existing data may not allow for a clear distinction to be made between substance-induced and primary psychiatric symptoms in. Nevertheless, the findings suggest that it could be beneficial to identify daughters of women with alcohol use disorders through screening, and that intervention based on the expectation of a predilection toward externalizing disorders may be particularly helpful. Specifically, when intervention in the parent is possible, it has been observed that interventions aimed at strengthening parent-child relations may be less effective than those aimed at reducing parent substance use (Burstein et al. 2006), and reducing parent substance use may be more important for interfering with the generational transmission of externalizing behavior than is any particular parenting practice (Bailey et al. 2009).

Despite the limitations of the present study, the results strongly implicate gender in the relationship between parental alcoholism and some psychiatric illnesses. Although these results do not identify mechanisms for the observed effects, elucidation of specific genetic and environmental factors (including co-occurring mental illness in parents, *in utero* exposure to alcohol, etc.) contributing to risk of psychiatric illness has significant prevention and treatment implications.

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Table 1

Socio-demographic characteristics of the NESARC sample, by family history

	Paternal History of Alcoholism						Maternal History of Alcoholism					
	Positive		Negative				Positive		Negative			
Characteristic	**n**	**%**	**n**	**%**	**Chiχ2**	**p**	**n**	**%**	**n**	**%**	**Chiχ2**	**p**
Gender												
Male	3175	18.21	14193	81.79	30.67	<0.0001	1331	5.01	21675	94.99	11.73	0.0011
Female	4874	21.19	18132	78.81			789	6.07	16579	93.93		
Education												
Less than high school	1482	22.45	5676	77.55	79.46	<0.0001	365	5.93	6793	94.07	21.14	0.0004
High school graduate	2471	21.09	9223	78.91			596	5.44	11098	94.56		
Some college	2569	21.35	9339	78.65			721	6.31	11187	93.69		
College or higher	1527	14.74	8087	85.26			438	4.59	9176	95.41		
Employment												
Full time	4412	20.44	16558	79.56	14.22	0.0016	1152	5.68	19818	94.32	8.64	0.0173
Part time	848	20.5	3133	79.5			249	6.6	3732	93.4		
Not working	2789	18.54	12634	81.46			719	5.08	14704	94.92		
Marital Status												
Married	4160	19.62	16766	80.38	4.21	0.1303	1059	5.42	19867	94.58	3.31	0.1995
Previously married	2033	20.69	8307	79.31			554	6.05	9786	93.95		
Never married	1856	19.4	7252	80.6			507	5.58	8601	94.42		
Race/ethnicity												
White/other	4975	19.7	20179	80.3	2.09	0.3577	1492	5.94	23662	94.06	25.46	<0.0001
Black	1419	19.25	5975	80.75			377	5.17	7017	94.83		
Hispanic	1655	20.67	6171	79.33			251	3.35	7575	96.65		
Grew up with 2 biological parents												
Yes	5836	16.86	28148	83.14	155.9	<0.0001	1420	4.35	32564	95.65	96.9	<0.0001
No	2213	35.4	4177	64.6			700	12.11	5690	87.89		

Ns represent actual number of respondents in each category; % indicate weighted percentages

Table 2

Prevalence rates of psychiatric disorders for those with and without maternal history of alcoholism, by proband gender

	Total [1]				Negative				Positive			
Diagnosis	**Negative**	**Positive**	**Chi_2**	**p**	**Males**	**Females**	**Chi_2**	**p**	**Males**	**Females**	**Chiχ2**	**p**
Any Axis I	**39.22**	**67.93**	**128.23**	**<0.0001**	**46.95**	**32.01**	**141.86**	**<0.0001**	**75.08**	**62.49**	**27.9**	**<0.0001**
Any Mood	**8.52**	**19.64**	**73.19**	**<0.0001**	**6.69**	**10.23**	**70.32**	**<0.0001**	**16.03**	**22.38**	**9.91**	**0.0026**
Major Depression	17.22	35.53	99.17	<0.0001	12.37	21.74	161.91	<0.0001	26.52	42.38	31.03	<0.0001
Dysthymia	4.4	13.05	59.86	<0.0001	3.22	5.49	56.08	<0.0001	9.2	15.97	15.66	0.0002
Mania	3.2	9.06	49.3	<0.0001	3.14	3.26	0.26	0.6093	7.8	10.03	2.33	0.1321
Hypomania	2.28	4.5	15.8	0.0002	2.41	2.16	1.79	0.1861	5.38	3.83	1.76	0.1898
Any Anxiety Disorder	**9.52**	**18.61**	**53.43**	**<0.0001**	**6.47**	**12.36**	**131.04**	**<0.0001**	**13.64**	**22.39**	**20.32**	**<0.0001**
Panic Disorder	4.15	8.36	25.88	<0.0001	2.66	5.55	75.66	<0.0001	7.47	9.04	0.93	0.3397
Panic + agoraphobia	1.02	3.09	21.81	<0.0001	0.66	1.34	26.64	<0.0001	1.99	3.93	4.85	0.0312
Social phobia	4.74	10.22	37.49	<0.0001	4.1	5.34	20.87	<0.0001	7.22	12.49	10.62	0.0018
Simple phobia	9.1	16.29	37.68	<0.0001	6.0	11.98	135.98	<0.0001	11.18	20.17	21.06	<0.0001
Generalized anxiety	4.23	9.85	44.19	<0.0001	2.96	5.42	69.34	<0.0001	6.66	12.27	14.24	<0.0001
Conduct disorder	4.02	14.29	71.12	<0.0001	6.15	2.03	111.83	<0.0001	20.67	9.45	27.18	<0.0001
Pathological gambling	0.39	0.87	5.43	0.0229	0.59	0.2	19.99	<0.0001	1.29	0.55	2.69	0.1058
Problem/path gambling	1.12	2.13	8.49	0.0049	1.7	0.59	41.92	<0.0001	2.7	1.7	1.76	0.1888
Any SUD	**36.69**	**64.79**	**124.8**	**<0.0001**	**47.32**	**26.79**	**166.63**	**<0.0001**	**73.7**	**58.02**	**36.91**	**<0.0001**
Nicotine Dependence	16.75	32.45	82.27	<0.0001	19.3	14.37	64.78	<0.0001	33.14	31.93	0.25	0.6193
Alcohol abuse	20.88	33.42	61.24	<0.0001	29.82	12.55	184.05	<0.0001	42.84	26.26	36.35	<0.0001
Alcohol dependence	11.34	29.34	105.1	<0.0001	16.1	6.9	155.21	<0.0001	38.9	22.07	37.48	<0.0001
Drug abuse	9.08	25.72	101.4	<0.0001	12.42	5.97	107.86	<0.0001	32.59	20.5	23.9	<0.0001
Drug dependence	2.14	9.27	52.89	<0.0001	2.79	1.54	32.21	<0.0001	11.67	7.45	6.9	0.0108
Any Axis II	**13.57**	**32.32**	**92.19**	**<0.0001**	**14.37**	**12.81**	**11.87**	**0.001**	**34.04**	**31.01**	**1.33**	**0.2539**
Any Cluster A	**5.61**	**15.06**	**60.43**	**<0.0001**	**5.44**	**5.76**	**1.1**	**0.2972**	**13.02**	**16.61**	**3.26**	**0.0755**
Paranoid	3.9	11.61	50.85	<0.0001	3.46	4.31	10.71	0.0017	9.89	12.91	2.77	0.1007
Schizoid	2.83	7.56	36.85	<0.0001	3.04	2.63	3.8	0.0555	5.75	8.93	4.42	0.0394
Any Cluster B	**4.28**	**15.36**	**74.7**	**<0.0001**	**5.84**	**2.84**	**90.99**	**<0.0001**	**21.1**	**11**	**21.1**	**<0.0001**

	Total [1]				Negative				Positive			
Diagnosis	**Negative**	**Positive**	**Chi_2**	**p**	**Males**	**Females**	**Chi_2**	**p**	**Males**	**Females**	**Chiχ2**	**p**
Antisocial	3.0	12.3	63.59	<0.0001	4.67	1.44	116.17	<0.0001	18.29	7.74	24.62	<0.0001
Histrionic	1.64	4.85	29.09	<0.0001	1.67	1.61	0.12	0.7304	5.51	4.34	0.98	0.325
Any Cluster C	**8.6**	**20.13**	**64.82**	**<0.0001**	**8.34**	**8.85**	**2.6**	**0.1117**	**19.42**	**20.67**	**0.27**	**0.6054**
Avoidant	2.12	5.76	26.27	<0.0001	1.73	2.49	14.38	0.0003	4.8	6.49	1.8	0.185
Dependent	0.44	1.34	7.33	0.0086	0.32	0.55	6.72	0.0118	1.01	1.59	0.78	0.3804
Obsessive-compulsive	7.3	17.04	55.87	<0.0001	7.35	7.26	0.08	0.7806	17.64	16.59	0.22	0.6425

[1] Numbers in table represent column percentages

Table 3

Prevalence rates of psychiatric disorders for those with and without paternal history of alcoholism, by proband gender

	Total[1]				Negative				Positive			
Diagnosis	**Negative**	**Positive**	**Chi_2**	**p**	**Males**	**Females**	**Chi_2**	**p**	**Males**	**Females**	**Chi_2**	**p**
Any Axis I	**36.32**	**59.07**	**133.71**	**<0.0001**	**43.87**	**29.09**	**135.84**	**<0.0001**	**68.52**	**51.58**	**94.04**	**<0.0001**
Any Mood	**7.69**	**15.03**	**99.17**	**<0.0001**	**5.96**	**9.34**	**59.14**	**<0.0001**	**12.54**	**17**	**18.55**	**0.0001**
Major Depression	15.45	29.56	144.69	<0.0001	11.0	19.71	140.16	<0.0001	22.44	35.2	84.53	<0.0001
Dysthymia	3.92	8.77	90.96	<0.0001	2.81	4.98	50.92	<0.0001	6.7	10.41	21.47	<0.0001
Mania	2.63	7.18	91.21	<0.0001	2.45	2.79	2.26	0.1379	7.49	6.93	0.71	0.4038
Hypomania	1.99	14.06	41.42	<0.0001	2.11	1.88	1.45	0.2322	4.58	3.65	2.4	0.1261
Any Anxiety	**8.62**	**15.73**	**91.77**	**<0.0001**	**5.9**	**11.22**	**105.23**	**<0.0001**	**11.02**	**19.47**	**68.08**	**<0.0001**
Panic Disorder	3.74	7.01	60.93	<0.0001	2.49	4.94	57.92	<0.0001	4.74	8.82	27.14	<0.0001
Panic + agoraphobia	0.89	2.1	34.2	<0.0001	0.57	1.2	22.66	<0.0001	1.45	2.62	8.57	0.0047
Social phobia	4.25	8.28	70.93	<0.0001	3.7	4.78	14.44	0.0003	6.76	9.47	12.36	0.0008
Simple phobia	8.31	14.32	73.19	<0.0001	5.47	11.02	115.78	<0.0001	9.79	17.9	69.16	<0.0001
Generalized anxiety	3.77	7.72	74.48	<0.0001	2.56	4.92	58.26	<0.0001	5.78	9.25	24.41	<0.0001
Conduct disorder	3.32	9.77	107.37	<0.0001	5.1	1.61	97.17	<0.0001	14.87	5.74	73.42	<0.0001
Pathological gambling	0.32	0.78	10.35	0.002	0.52	0.13	20.81	<0.0001	1.08	0.55	3.51	0.0653
Problem/path gambling	0.98	2	22.46	<0.0001	1.46	0.51	30.67	<0.0001	3.03	1.18	17.74	0.0001
Any SUD	**33.69**	**56.79**	**147.16**	**<0.0001**	**44.18**	**23.66**	**163.06**	**<0.0001**	**68.67**	**47.37**	**116.72**	**<0.0001**
Nicotine dependence	14.66	29.66	150.69	<0.0001	17.1	12.32	61.24	<0.0001	32.97	27.04	19.68	<0.0001
Alcohol abuse	19.65	29.44	78.54	<0.0001	28.56	11.12	179.8	<0.0001	39.1	21.8	112.36	<0.0001
Alcohol dependence	9.66	23.21	146.81	<0.0001	13.83	5.67	127.07	<0.0001	32.54	15.83	106.71	<0.0001
Drug abuse	7.69	19.42	122.34	<0.0001	10.5	5.0	86.8	<0.0001	26.58	13.75	70.96	<0.0001
Drug dependence	1.62	6.25	90.52	<0.0001	2.05	1.21	14.92	0.0003	8.51	4.45	29.49	<0.0001
Any Axis II	**12.13**	**24.68**	**138.93**	**<0.0001**	**12.77**	**11.51**	**8.37**	**0.0052**	**26.98**	**22.86**	**11.11**	**0.0014**
Any Cluster A	**4.75**	**11.75**	**118.42**	**<0.0001**	**4.48**	**5.01**	**3.02**	**0.087**	**11.85**	**11.67**	**0.03**	**0.8536**
Paranoid	3.27	8.6	94.31	<0.0001	2.77	3.75	15.52	0.0002	8.31	8.83	0.4	0.5292
Schizoid	2.41	5.88	77.7	<0.0001	2.53	2.29	1.18	0.2806	6.1	5.7	0.3	0.5845
Any Cluster B	**3.59**	**10.23**	**109.84**	**<0.0001**	**4.81**	**2.42**	**63.51**	**<0.0001**	**14.64**	**6.73**	**65.19**	**<0.0001**

	Total[1]				Negative				Positive			
Diagnosis	**Negative**	**Positive**	**Chi_2**	**p**	**Males**	**Females**	**Chi_2**	**p**	**Males**	**Females**	**Chi_2**	**p**
Antisocial	2.42	7.97	99.72	<0.0001	3.77	1.13	92.34	<0.0001	14.48	4.41	73.34	<0.0001
Histrionic	1.42	3.44	46.3	<0.0001	1.4	1.44	0.08	0.781	3.94	3.03	3.39	0.07
Any Cluster C	**7.89**	**14.75**	**95.28**	**<0.0001**	**7.72**	**8.06**	**1.2**	**0.2783**	**14.19**	**15.2**	**0.87**	**0.3551**
Avoidant	1.78	4.54	70.84	<0.0001	1.46	2.08	11.15	0.0014	3.78	5.13	5.16	0.0265
Dependent	0.42	0.76	6.82	0.0112	0.26	0.57	9.54	0.003	0.76	0.75	0.001	0.9728
Obsessive-compulsive	6.76	12.26	72.14	<0.0001	6.9	6.63	0.8	0.3753	12.2	12.3	0.01	0.9129

[1]Numbers in table represent column percentages

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Table 4

Adjusted odds ratios for the association between maternal family history of alcoholism and psychopathology

	Males	Females	Interaction term	Males	Females	Interaction term
Diagnosis	**OR for present vs. absent paternal alcohol history**	**OR for present vs. absent paternal alcohol history**	**OR of association with paternal history in males vs. females**	**OR for present vs. absent maternal alcohol history**	**OR for present vs. absent maternal alcohol history**	**OR of association with maternal history in males vs. females**
Any Axis I	**2.47*****	**2.15*****	**1.15***	**2.02*****	**2.31*****	**0.88**
Any Mood Disorder	**1.89*****	**1.64*****	**1.16**	**1.71****	**1.78*****	**0.96**
Major Depression	2.06***	1.91***	1.07	1.63***	1.84***	0.88
Dysthymia	2.05***	1.83***	1.12	1.97***	2.36***	0.83
Mania	2.72***	1.99***	1.37*	1.37	2.1***	0.65*
Hypomania	1.92***	1.69***	1.13	1.46	1.22	1.19
Any Anxiety Disorder	**1.74*****	**1.69*****	**1.03**	**1.61****	**1.51****	**1.07**
Panic Disorder	1.61***	1.73***	0.93	2.19***	1.26	1.74*
Panic + agoraphobia	2.19**	1.84***	1.18	1.9	2.17***	0.87
Social phobia	1.73***	1.77***	0.98	1.26	1.85***	0.68
Simple phobia	1.7***	1.59***	1.07	1.42*	1.41***	1.01
Generalized anxiety	2.12***	1.74***	1.22	1.54*	1.83***	0.84
Conduct disorder	2.38***	2.52***	0.95	2.18***	2.72***	0.8
Pathological gambling	1.67	3.58***	0.47	1.51	1.43	1.06
Problem/path gambling	1.97***	1.97**	1.0	1.08	2.05**	0.53
Any SUD	**2.47*****	**2.37*****	**1.04**	**1.8*****	**2.36*****	**0.76***
Nicotine dependence	2.08***	2.13***	0.98	1.19	1.74***	0.68**
Alcohol abuse	1.51***	1.93***	0.78**	1.31**	1.71***	0.77*
Alcohol dependence	2.65***	2.46***	1.08	1.9***	2.32***	0.82
Drug abuse	2.56***	2.2***	1.16	1.85***	2.37***	0.78
Drug dependence	3.32***	2.55***	1.3	2.18***	2.77***	0.79

Diagnosis	Males	Females	Interaction term	Males	Females	Interaction term
	OR for present vs. absent paternal alcohol history	OR for present vs. absent paternal alcohol history	OR of association with paternal history in males vs. females	OR for present vs. absent maternal alcohol history	OR for present vs. absent maternal alcohol history	OR of association with maternal history in males vs. females
Any Axis II	**2.08*****	**1.84*****	**1.13**	**1.97*****	**2.12*****	**0.93**
Any Cluster A	**2.35*****	**1.97*****	**1.19**	**1.54****	**2.16*****	**0.71**
Paranoid	2.46***	1.9***	1.3	1.74**	2.14***	0.81
Schizoid	2.17***	1.99***	1.09	1.21	2.45***	0.5**
Any Cluster B	**2.49*****	**2.02*****	**1.23**	**2.36*****	**2.5*****	**0.95**
Antisocial	2.57***	2.59***	0.99	2.39***	2.98***	0.8
Histrionic	2.25***	1.65***	1.36	1.97***	1.82**	1.08
Any Cluster C	**1.7*****	**1.73*****	**0.98**	**1.92*****	**1.98*****	**0.97**
Avoidant	2.13***	2.06***	1.04	1.66*	1.75***	0.95
Dependent	2.13	0.9	2.37	1.65	2.31***	0.72
Obsessive-compulsive	1.64***	1.72***	0.95	2.05***	1.92***	1.07

* p<0.05,

** p<0.01,

*** p<0.0001