



Family history of alcohol use disorders among adults with panic disorder in the community

Renee D. Goodwin^{a,*}, Joshua D. Lipsitz^{b,d}, Katherine Keyes^{a,c}, Sandro Galea^a, Abby J. Fyer^{b,c}

^a Department of Epidemiology, Mailman School of Public Health, Columbia University, 722 West 168th Street, Rm 1505, New York, NY 10032, USA

^b Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY, USA

^c New York State Psychiatric Institute, New York, NY, USA

^d Ben Gurion University of the Negev, Beer Sheva, Israel

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ABSTRACT

Objective: Clinical studies suggest a familial association between panic disorder and alcohol use disorders but this relationship has not been examined in a representative community sample. The objective of this study is to examine the familial association between panic disorder and alcohol use disorders among adults in the community.

Method: Data were drawn from the NESARC, a nationally representative sample of over 43,000 adults in the United States. Rates of alcohol use disorders were examined using the family history method in first-degree relatives (FDRs) of adults with panic disorder. Analyses were adjusted for demographics, alcohol use disorders in the proband, and anxiety disorders in the FDRs.

Results: First-degree relatives of adults with panic disorder have significantly higher odds of alcohol use disorders, compared with FDRs of adults without panic disorder. These associations persist after adjusting for demographic characteristics, alcohol use disorders in the proband, and anxiety disorders in the FDR's.

Conclusions: Consistent with findings from clinical studies, this is the first population-based study to show a familial link between panic disorder and alcohol use disorders. This association appears independent of the influence of comorbidity of alcohol use disorders and anxiety disorders, suggesting a potential familial and/or genetic pathway. Future longitudinal studies will be needed to further understand the mechanism of this observed association.

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1. Introduction

In recent years, there has been growing interest in the comorbidity of anxiety disorders and alcohol use disorders. While it was once thought that alcohol and other substance use disorders were more commonly comorbid only with depression and other mood disorders, research has increasingly shown strong and significant links between anxiety disorders and alcohol use problems (Zimmermann et al., 2003; Abram et al., 2007; Moss et al., 2010). Panic disorder has emerged as an anxiety disorder strongly linked with alcohol use disorders; population-based studies have shown that over 37% of adults with panic disorder have lifetime alcohol abuse or dependence (Kessler et al., 2006), and several community and clinically-sampled studies have reported similar findings (e.g., Joyce et al., 1989; Jacobi et al., 2004).

The reason for the observed link between panic disorder and alcohol use disorders is not known. The three main possibilities include: alcohol use disorders lead to the onset of panic disorder; panic disorder leads to onset of alcohol use problems, possibly via self-medication, or that there are common risk factors for the co-occurrence of both alcohol use problems and panic disorder. One possibility is that the observed comorbidity of panic disorder and alcohol use problems results from a shared familial vulnerability to both panic disorder and alcohol use problems. Several family studies have found increased rates of alcohol use problems in the first-degree relatives of panic disorder (PD) probands as compared to controls (Noyes et al., 1978; Crowe et al., 1983; Maier et al., 1993a,b; Goldstein et al., 1994; Merikangas et al., 1994, 1998). As such, evidence consistently suggests a familial link between PD and alcohol use disorders. Yet, several methodological features of previous studies leave questions unanswered. Specifically, with few exceptions (Maier et al., 1993a,b; Katerndahl and Realini, 1999), the study designs of previous investigations have not considered the potentially confounding role of comorbid alcoholism in the PD

* Corresponding author. Tel.: +1 212 342 0422; fax: +1 212 342 5168.

E-mail address: rdg66@columbia.edu (R.D. Goodwin).

proband. As alcohol use disorders have a familial component, it therefore remains unclear whether the observed increases reflect a familial association between alcoholism and PD, or are attributable to proband alcohol comorbidity. In addition, all previous studies have examined these relationships in clinical and specifically recruited treatment samples. As such, it is not clear whether findings are generalizable to those with alcohol use disorders and panic disorder in the community. As rates of PD are higher among females in the community, and alcohol use disorders are more common among males, the degree to which these patterns are gender specific in terms of familial vulnerability is unclear as this has been difficult to examine in clinical samples due to smaller sample size.

Against this background, the goal of the current study is to investigate the familial association between PD and alcohol use disorders among adults in the community. First, the study will examine whether there are higher rates of alcohol use problems among first-degree relatives of adults with panic disorder as compared to relatives of non-PD controls. Second, the study will examine the degree to which the familial link between PD and alcohol use disorders is explained by comorbid mental disorders or demographic differences. Third, the study will examine whether the familial link between PD and alcohol use problems differs by gender, as a previous clinical study (e.g., Goodwin et al., 2006) found significantly higher rates of alcohol use disorders in males, but not females, of PD probands though the patterns were similar so it was unclear whether this is a meaningful sex difference or due to smaller sample size. Based on clinical findings (Noyes et al., 1978; Crowe et al., 1983; Maier et al., 1993a,b; Goldstein et al., 1994; Merikangas et al., 1994, 1998; Goodwin et al., 2006), we hypothesized that there would be an elevated risk of alcohol use disorders among first-degree relatives of adults with PD. We predicted that this link would persist after adjusting for both alcohol use disorders in the proband, and other comorbid mental disorders.

2. Method

2.1. Sample

The cross-sectional sample was drawn from participants in the 2001–2002 National Epidemiologic Survey of Alcohol and Related Conditions (NESARC), a nationally representative United States survey of 43,093 civilian non-institutionalized participants aged 18 and older. Details of the sampling frame are described elsewhere (Grant et al., 2003a,b, 2004a,b; Compton et al., 2004). The National Institute on Alcohol Abuse and Alcoholism (NIAAA) sponsored the study and supervised the fieldwork, conducted by the U.S. Bureau of the Census. Young adults, Hispanics, and African-Americans were over sampled, and the study achieved an overall response rate of 81%. To adjust for non-response and selection probability, the sample was weighted and adjusted to reflect the U.S. population from the 2000 Decennial Census in terms of age, race, sex, and ethnicity. The research protocol, including informed consent procedures, received full ethical review and approval from the U.S. Census Bureau and U.S. Office of Management and Budget.

2.2. Interviewers, training, and field quality control

Interviews were conducted by 1800 professional interviewers from the Census Bureau using computer-assisted software with built-in skip, logic, and consistency checks. All interviewers had experience with other national health-related surveys with an average of five years of experience, and were further trained for 10 days under the direction of NIAAA. Verification of the interviewer was conducted by regional supervisors who re-contacted a random 10% of all respondents for quality control purposes.

2.3. Measures

2.3.1. Alcohol dependence

The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-IV) (Grant et al., 2001), a state-of-the-art structured diagnostic interview, was administered to the NESARC participants. This instrument was specifically designed for experienced lay interviewers and was developed to advance measurement of substance use and mental disorders in large-scale surveys. The AUDADIS-IV used an extensive list of over 40 questions to assess alcohol abuse and dependence. Diagnoses were indicated according to the DSM-IV (American Psychiatric Association, 1994); at least 3 of 7 criteria are necessary for alcohol dependence. Withdrawal syndromes were also assessed according to DSM-IV criteria; the presence of at least 2 symptoms out of 8 plus distress is necessary for a withdrawal diagnosis. Time frames for diagnosis included the previous 12-month period and prior to the previous 12-month period, combined to create a 'lifetime' diagnosis.

The reliability and validity of alcohol dependence diagnosis has been extensively documented in the U.S. and abroad. The reliability of the alcohol dependence diagnosis has achieved a minimum kappa of 0.74 (Fyer et al., 1995; Swendsen et al., 1998; Katerndahl and Realini, 1999; Kushner et al., 2000). The validity of the diagnosis has been documented in numerous studies including the World Health Organization/National Institutes of Health Reliability and Validity Study and others (Hasin et al., 1997a,b,c,d; Canino et al., 1999; Hasin and Paykin, 1999; Hasin and Grant, 2004). Further, the symptom items have been validated using clinical reappraisals conducted by psychiatrists (Canino et al., 1999).

2.4. Panic disorder

An episode of PD was diagnosed when recurrent unexpected panic attacks occurred and at least one attack was followed by at least one month of persistent concern about having additional attacks, worry about the implications/consequences of the attacks, or a significant change in behavior related to the attacks. In the AUDADIS-IV, panic attacks were operationalized as discrete periods of intense fear/discomfort in which at least 4 of the 13 panic attack symptoms developed abruptly and reached a peak within 10 min.

2.5. Other psychiatric disorders

Dichotomous measures of lifetime any mood, any anxiety disorder, and any personality disorder were included as covariates in modeling (Grant et al., 2004a,b). Any mood disorder was coded as positive for individuals who met DSM-IV criteria for any of the following: major depression, dysthymia, mania, or hypomania. Anxiety disorders were included as separate covariates of: social phobia, specific phobia, or generalized anxiety disorder. Diagnoses of eight independently measured personality disorders were combined into one measure. The derivation and psychometric properties of these measures have been described elsewhere (Grant et al., 2004a,b, 2005, 2006).

2.6. Family history

Family history of alcohol problems included respondent report of any first-degree relative with an alcohol problem (i.e., parent or sibling). Participants were provided definitions of various examples of symptoms that are included in the alcohol and drug diagnostic criteria, and then asked whether relatives (in each category) had experienced the problem as described. The definitions read to respondents included observable manifestations, as these are most likely to be known to family informants and sensitivity is a key

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