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Research report

Childhood maltreatment and the course of bipolar disorders among adults: Epidemiologic evidence of dose-response effects

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ABSTRACT

Background: Childhood maltreatment (CM) is highly prevalent among individuals with bipolar disorders (BP); however few studies have examined its potential role in the course and outcome of individuals with BP. We aim to examine the dose response relationship between the number of types of CM and the course of individuals with BP.

Methods: As part of the National Epidemiologic Survey on Alcohol and Related Conditions, 1600 adults who met lifetime *DSM-IV* criteria for BP-I ($n=1172$) and BP-II ($n=428$) were included. Individuals were evaluated using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-*DMS-IV* Version and data was analyzed lifetime and from Waves 1 and 2, approximately 3 years apart.

Results: Around half of individuals with BP had a history of at least one type of CM. Overall, there was a clear dose-response relationship between number of CM and severity of BP across several domains, including clinical characteristics, probability of treatment, lifetime prevalence of psychiatric comorbidity, incidence of anxiety disorders, substance use disorder, and nicotine dependence, and level of psychosocial functioning.

Limitations: The interviews were conducted by lay professional interviewers rather than clinicians, use of retrospective report to determine CM in individuals with BP, and not all respondents from Wave 1 were able to be interviewed in Wave 2.

Conclusions: The number of types of CM confers developmental differences in the course of BP with a worse course and outcome of BP. Early identification and treatment of CM are warranted to improve the course and outcome of individuals with BP.

1. Introduction

Bipolar disorder (BP) is a prevalent disabling disease with high morbidity rates that causes significant burden to patients, families and society (Begley et al., 2001; Gonzalez-Pinto et al., 2010; McIntyre and Konarski, 2004; Moreno et al., 2012). Recent research suggests that sexual, physical and emotional abuse and neglect frequently co-occur and confer increased risk for multiple psychiatric diagnoses including BP (Keyes et al., 2012; McLaughlin et al., 2010). Because childhood emotional, physical and sexual abuse are highly prevalent among individuals with BP (Brown et al., 2005; Leverich et al., 2002), an important question is whether childhood maltreatment (CM), beyond increasing the risk of BP, also worsens its course and prognosis. Another important question is whether there is a dose-response relationship. That is, are number of subtypes of CM associated with increasingly severe clinical characteristics?

A few clinical studies have examined the potential role of CM in the course and outcome of individuals with BP (Brown et al., 2005; Garno et al., 2005; Leverich et al., 2002, 2003; Post et al., 2003). For example, in a study of 100 adults with BP, a history of severe CM was found in approximately half of adults with BP, with multiple forms of abuse having occurred in about the third (Garno et al., 2005). In another clinical sample, CM was reported by 48.3% of 330 veterans with BP and found that individuals with physical and sexual abuse were more likely to have current post-traumatic stress disorder (PTSD) and lifetime diagnoses of panic disorder and alcohol use disorders (Brown et al., 2005). As part of the Stanley Foundation Bipolar Treatment Outcome Network with a sample of 631 adults with BP, a study found that those with childhood physical or sexual abuse had a history of earlier onset of BP, increased number of Axis I and II comorbid disorders, including a higher rate of suicide attempts (Leverich et al., 2002, 2003; Post

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et al., 2003). Furthermore, data from the National Comorbidity Survey Replication (NCS-R) indicate that a history of CM predict earlier onset and longer episode duration of BP (Green et al., 2010; McLaughlin et al., 2010).

We sought to build on those prior studies by examining whether findings of clinical samples extended to individuals with BP in the community. In prior cross-sectional studies using data from the National Epidemiological Survey on Alcohol and Related Conditions (NESARC), we found that sexual (Perez-Fuentes et al., 2013) and physical (Sugaya et al., 2012) abuse during childhood was associated with increased risk of having BP, with sexual abuse having stronger effect than physical abuse (OR=4.10 versus OR=3.58). Given the clinical relevance and potential prognostic implications of CM in adults with BP, we sought to examine the clinical characteristics, treatment, lifetime and incidence of psychiatry comorbidity, and functioning of adults with BP-I and BP-II using the NESARC. We hypothesized that among adults with BP there would be a dose response relationship between the number of types of CM and a broad range of variables including age of onset, duration of disorder, rates of comorbidity and rates of treatment seeking for BP.

2. Methods

2.1. Sample

The NESARC (Grant et al., 2003b, 2005a) is a longitudinal nationally representative survey whose target population is the civilian, non-institutionalized population of the 50 United States, age 18 and over. Data collection was supported by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and was conducted in two waves using face-to-face interviews. Wave 1 interviews (n=43,093) were conducted between 2001 and 2002 by professional interviewers who had an average of five years of experience working on Census and other health-related national surveys (Grant et al., 2003b). The current study utilized data from Wave 1 as well as Wave 2 interviews, which were conducted between 2004 and 2005 with 34,653 of the NESARC Wave 2 respondents (Grant et al., 2005a). After accounting for those ineligible for the Wave 2 interview, the response rate for Wave 2 was 86.7%. The mean interval between Wave 1 and Wave 2 interviews was 36.6 (SD=2.62) months. The research protocol, including informed consent procedures, received full human subjects review and approval from the U.S. Census Bureau and the U.S. Office of Management and Budget. Informed consent was obtained from all participants before beginning the interviews. Detailed descriptions of methodology, sampling, and weighting procedures can be found elsewhere (Grant et al., 2003b).

2.2. Measures

Sociodemographic measures included age, sex, race, marital status, education, employment status and personal income.

All diagnoses were made according to DSM-IV criteria using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-Version for DSM-IV (AUDADIS-IV), a valid, reliable, fully structured diagnostic interview designed for use by non clinician professional interviewers (Grant et al., 2001). Reliability of the BP-I diagnosis (κ=0.59) is fair and good for BP-II (κ=0.69) (Grant et al., 2005c), whereas the reliability is excellent for alcohol ($\kappa \geq 0.74$) and drug use disorders diagnoses ($\kappa \geq 0.79$) (Grant et al., 2004). The anxiety disorders included in the present study are panic disorder, social anxiety disorder, specific phobia, generalized anxiety disorder, and PTSD which have fair to good reliability (κ=0.42−0.52) (Grant et al., 2004). Attention deficit/hyperactivity disorder (ADHD) was assessed in the Wave 2 NESARC and the test–retest reliability was good (k=0.71) (Bernardi et al., 2012). Suicide attempts were assessed only in individuals, who reported having been sad, blue depressed or having a period that they did not care about things that they usually enjoyed for at least 2 weeks (Morcillo et al., 2010) In those cases, suicide attempt was assessed and computed for those who reported having attempted suicide during that period. Personality disorders assessed on a lifetime basis at Wave 1 and described in detail elsewhere (Compton et al., 2005; Grant et al., 2005b) included avoidant, dependent, obsessive–compulsive, paranoid, schizoid, schizotypal, narcissistic, borderline, histrionic, and antisocial, grouped in the present study into Clusters A, B, and C to increase statistical power and stability of the estimates. Test–retest reliabilities for AUDADIS-IV personality disorders diagnoses in the general population and clinical settings are fair to good (κ=0.40−0.77) (Canino et al., 1999b; Ruan et al., 2008).

We examined the lifetime clinical characteristics of BP (e.g., age of onset of BP, duration of BP, number of depressive and mania or hypomania episodes, suicidal attempts, psychosis) for individuals with BP with versus without different number of types of CM. In addition, we examined lifetime treatment patterns of individuals with BP (e.g., psychotherapy, medication, hospitalization and emergency room care) for major depressive (MDE) and mania or hypomania episodes and lifetime psychiatric comorbidities. Incidence of comorbid disorders was defined as developing a new disorder between Wave 1 and Wave 2. Psychosocial functioning was assessed at Wave 2 with the mental component summary, social functioning, role of emotional, and mental health of the 12-item Short Form Health Survey, version 2 (SF-12), a reliable and valid measure of disability used in population surveys (Ware et al., 2005).

2.3. Childhood maltreatment

CM was assessed in Wave 2. All questions about adverse childhood experiences are related to respondents' first 17 years of life. Questions were adapted from the Adverse Childhood Experiences study (Canino et al., 1999a; Grant et al., 1995, 2003a; Hasin et al., 1997; Ruan et al., 2008) and were originally part of an extensive battery of questions from the Conflict Tactics Scale (CTS) (Dong et al., 2003; Dube et al., 2003; Straus M, 1990) and the Childhood Trauma Questionnaire (CTQ) (Straus M, 1990; Straus, 1979). Response categories for most scale items were 1=never, 2=almost never, 3=sometimes, 4=fairly often, and 5=very often. Response category values were summed across items to generate scales. The emotional neglect items all required reverse coding. Childhood sexual abuse was defined by four questions developed by Wyatt (1985). All sexual abuse questions asked about sexual experiences with an adult or any other person and were restricted to behaviors that respondents did not want and were experienced when respondents were younger than 18 years old. The sexual abuse scale included questions about touching and fondling, touching in a sexual way, and attempting and actually having sexual intercourse (Perez-Fuentes et al., 2013). Physical abuse was defined by two questions from the CTS including the frequency of pushing, grabbing, shoving, slapping or hitting, and hitting so hard that respondents had marks or bruises or were injured were ascertained (Sugaya et al., 2012).

Emotional abuse was defined by three questions from the CTS. For emotional abuse, questions asked how often respondents' parents or caregivers living in their home: (1) swore at, insulted, or said very hurtful things to respondents; (2) threatened to hit or throw something at respondents but did not; and (3) acted in any other way that made respondents afraid that they would be physically hurt or injured (Ruan et al., 2008). For both emotional and physical neglect, sets of five CTQ items were used. Items assessing physical neglect included the frequency with which respondents: (1) were made to do chores too difficult or dangerous for someone their age; (2) were left alone or unsupervised