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Research paper

Categorical and dimensional psychopathology in Dutch and US offspring of parents with bipolar disorder: A preliminary cross-national comparison ☆

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ABSTRACT

Objective: Accumulating evidence suggests cross-national differences in adults with bipolar disorder (BD), but also in the susceptibility of their offspring (bipolar offspring). This study aims to explore and clarify cross-national variation in the prevalence of categorical and dimensional psychopathology between bipolar offspring in the US and The Netherlands.
Methods: We compared levels of psychopathology in offspring of the Pittsburgh Bipolar Offspring Study ($n=224$) and the Dutch Bipolar Offspring Study ($n=136$) (age 10–18). Categorical psychopathology was ascertained through interviews using the Schedule for Affective Disorders and Schizophrenia for School Age Children (K-SADS-PL), dimensional psychopathology by parental reports using the Child Behavior Checklist (CBCL).
Results: Higher rates of categorical psychopathology were observed in the US versus the Dutch samples (66% versus 44%). We found no differences in the overall prevalence of mood disorders, including BD-I or -II, but more comorbidity in mood disorders in US versus Dutch offspring (80% versus 34%). The strongest predictors of categorical psychopathology were maternal BD (OR: 1.72, $p<.05$), older age of the offspring (OR: 1.19, $p<.05$), and country of origin (US; OR: 2.17, $p<.001$). Regarding comorbidity, only country of origin (OR: 7.84, $p<.001$) was a significant predictor. In general, we found no differences in dimensional psychopathology based on CBCL reports.
Limitations: Preliminary measure of inter-site reliability.
Conclusions: We found cross-national differences in prevalence of categorical diagnoses of non-mood disorders in bipolar offspring, but not in mood disorder diagnoses nor in parent-reported dimensional psychopathology. Cross-national variation was only partially explained by between-sample differences. Cultural and methodological explanations for these findings warrant further study.

1. Background

Bipolar disorder (BD) is characterized by recurrent episodes of (hypo)mania and depression that affects on average 1.8% of youth across the world (Van Meter et al., 2011). Whereas prevalence of BD-I and -II in youth in the general population is not different between US and non-US countries (Van Meter et al., 2011), clinical

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studies have shown an increase in the "administrative" prevalence of outpatient visits and hospital admission rates of BD in youth in the United States (US) as compared to most other countries (Holtmann et al., 2010; James et al., 2014; Kozloff et al., 2010; Soutullo et al., 2005). Comparisons between US and European adult patients with BD have also shown higher prevalence, younger age of onset, more severe illnesses, and increased parental history of BD in the US (Bellivier et al., 2011; Post et al., 2008, 2014a, 2014b).

Numerous studies have consistently shown that offspring of adults with BD (hereafter referred to as bipolar offspring) are at increased risk to develop BD and other psychiatric disorders (Axelson et al., 2015; DelBello et al., 2001; Duffy et al., 2011; Hafeman et al., 2016; Mesman et al., 2013). Also among these offspring samples, the prevalence of BD and other psychiatric disorders and the age of onset of mood disorders varies significantly across studies and countries. The question is whether these cross-national variations are a real phenomenon or reflect demographic, illness (e.g. parental- or offspring characteristics), methodological (e.g. recruitment method, assessment instruments, information source, age at assessment) or cultural factors and differences (Carlson and Klein, 2014; Duffy et al., 2011; James et al., 2014; Merikangas et al., 2011; Soutullo et al., 2005). Thus far, cross-national variability in psychopathology among bipolar offspring has not been well studied. Recently, a first attempt on this issue was carried out by Post et al. (2016). In this study, BD adults completed a detailed questionnaire about their own illness and their offspring's psychopathology (US: $n=365$, Europe $n=132$). Although based only on parent reports, the authors documented higher rates of psychopathology among US offspring in comparison to European offspring. This difference remained significant even when controlling for several prognostic factors including parental illness characteristics, childhood trauma and family history of psychiatric diagnoses. A better understanding of these cross-national differences is important for the interpretation of the scientific literature, and of course, development of effective mental health policies.

In the present study we aimed to evaluate the cross-national differences in categorical and dimensional psychopathology in US and Dutch bipolar offspring in two large and well characterized bipolar offspring studies: the Pittsburgh Bipolar Offspring Study (BIOS) (Birmaher et al., 2009) and the Dutch Bipolar Offspring Study (DBOS) (Wals et al., 2001) using direct interviews and parental reports. Categorical and dimensional psychopathology were examined in offspring aged 10–18 years through the direct interview the Schedule for Affective Disorders and Schizophrenia for School Age Children (K-SADS-PL) (Kaufman et al., 1996) and parental reports using the Child Behavior Checklist (CBCL) (Achenbach, 1991) respectively. Based on the offspring study by Post et al. (2016), we hypothesized cross-national variation in categorical and dimensional psychopathology. These differences would be least partly explained by demographic, parental and methodological variables.

2. Methods

2.1. Subjects

The US sample is based on BIOS (Birmaher et al., 2009), a sample of 388 offspring, aged 6–18 years, of parents with a bipolar I or II disorder. Families were recruited through advertisement and adult outpatient clinics. Study design and recruitment procedures have been described in detail elsewhere (Birmaher et al., 2009). The Dutch sample is based on two ongoing prospective bipolar offspring cohort studies: the DBOS (Wals et al., 2001) and a new yet unpublished cohort: the Dutch Bipolar and Schizophrenia Offspring Study (DBSOS) (for detailed information see Addendum 1). The DBOS recruited 140 offspring, aged 12–21 years old, of parents with BD-I or -II, from 86 families between 1997 and 1999 (Wals et al., 2001). The DBSOS is recruiting bipolar and schizophrenia offspring, aged 10–16 years; all available bipolar offspring ($n=33$) recruited between 2010 and 2012 were included in the present study. Both Dutch studies recruited through the Dutch Association for Manic Depressives and Relatives and outpatient clinics for patients with BD in different regions of the Netherlands. The DBOS and DBSOS were combined in order to enlarge the Dutch sample and to optimize equality in age range between the US and Dutch sample (age 6–18 versus 10–21). Only offspring aged 10–18 years were selected to optimally compare the US and the Dutch samples. Exclusion criteria in offspring for both the US and two Dutch studies were a severe physical disease or handicap and an IQ < 70. Studies were approved by the institutional review board and written informed consent was obtained from parents and offspring (Wals et al., 2001). An overview of the sample selection is provided in Fig. 1.

3. Instruments

3.1. Parental psychopathology

In the US-sample, DSM-IV axis I disorders for all BD probands and 30% of the biological co-parents were directly ascertained through the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First, Spitzer, Gibbon and Williams, 1997). The psychopathology of the other biological co-parents was indirectly assessed using the Family History Research Diagnostic Criteria method (FH-RDC) (Andreasen et al., 1977) through the BD proband (Birmaher et al., 2009). Diagnoses were confirmed during diagnostic consensus conferences with a psychiatrist. In the DBOS, BD probands were directly evaluated using the International Diagnostic Checklists (IDCL) (Hiller et al., 1993) and diagnoses were confirmed by the treating psychiatrist or general practitioner. Biological co-parents were assessed by the FH-RDC directly, by phone interviews or through the bipolar proband. For the DBSOS, both the BD proband and biological co-parent were directly evaluated using the SCID-I. For the present analyses, both the US- and the Dutch samples, parental age of onset of the first mood episode of BD was classified as before age 19, between 19 and 25 years old or 26 years and older.

3.2. Categorical psychopathology in offspring

In both the US and the Dutch samples, all current (past 2 months) and past disorders in offspring were assessed using the Schedule for Affective Disorders and Schizophrenia for School Age Children Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997). Children and their parents were interviewed separately. Diagnoses were established in accordance with DSM-IV criteria (American Psychiatric Association, 1994). Although both samples were evaluated using the K-SADS-PL, there were minor differences in the implementation of the K-SADS-PL mood section. With regard to BD not otherwise specified (BD-NOS) and cyclothymia, the Dutch sample did not include BD-NOS, but included cyclothymia. The US sample included an operationalized BD-NOS criteria developed for the Course and Outcome of Bipolar Youth (COBY) study (Birmaher et al., 2006). Cyclothymia was subsumed under the BD-NOS category. Although BD-NOS and cyclothymia were not comparably assessed in both studies, all these offspring had mood symptoms with a considerable burden; thus it was decided not to exclude them from the analyses, and rather to