RESEARCH REPORT

Mood and disruptive behavior disorders and symptoms in the offspring of patients with bipolar I disorder

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The study aimed to ascertain the prevalence of mood and disruptive behavior disorders and symptoms in 35 children of 29 adult outpatients with a DSM-IV diagnosis of bipolar I disorder, compared with 33 children of 29 healthy adults, matched with patients on age, socioeconomic status and education. The offspring of bipolar patients had a 9.48 fold higher risk of receiving a psychiatric diagnosis. While only two children of patients with bipolar disorder were diagnosed with a mood disorder, 30.9% displayed mild depressed mood, compared with 8.8% of the controls, a statistically significant difference. The bipolar offspring also scored significantly higher on the hyperactivity and conduct problems subscales as well as the ADHD index of the Conners' Teacher Rating Scale. The disruptive behavior and mood symptoms observed in early life in the offspring of bipolar patients may indicate the need for early psychosocial intervention.

Key words: Childhood bipolar disorder, disruptive behavior disorder, attention-deficit/hyperactivity disorder, early psychosocial intervention

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Childhood bipolar disorder has not been diagnosed with any regularity until recently (1), although 59% of adults with bipolar I disorder recall having had their first mood symptoms as children or adolescents (2). The reliability and validity of the diagnosis of bipolar disorder in children and adolescents is a topic of considerable controversy. Leibenluft et al (3) suggested four phenotypes for juvenile mania: the narrow one (meeting the full DSM-IV diagnostic criteria, including duration and hallmark symptoms of mania); two intermediate ones (a clearly episodic illness failing to meet strict criteria for mania or hypomania either because the episodes are too short or because they lack the hallmark symptom of elevated mood); and the broad one (a chronic, nonepisodic illness lacking the hallmark symptoms of mania or hypomania but presenting severe irritability and hyperarousal). These criteria await validation.

Carlson and Weintraub (4) suggested that attention and behavioral problems in children of bipolar patients might predict the development of mood disorders in young adulthood. Indeed, a number of studies on children of people with bipolar disorder have shown an elevated risk for a wide range of psychopathology, including depressive, substance use, conduct, opposition defiant and anxiety disorders (5-9). None of these studies, however, distinguished between the offspring of patients with bipolar disorder I, II, or not otherwise specified (5).

The aim of the present study was to determine the prevalence of mood and disruptive behavior disorders and symptoms in the offspring of a sample of patients with bipolar I disorder in comparison with the offspring of matched healthy controls.

METHODS

The study was carried out in an adult mood disorders outpatient clinic. Forty-five families having one parent with bipolar I disorder and at least one child aged 7-18 years were invited to participate. The diagnosis of bipolar I disorder was made according to the DSM-IV and ascertained by the Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-CV, 10). Twenty-nine families agreed to take part in the study. The control group consisted of 29 healthy adults, matched with patients for age, socioeconomic and educational status, and their 33 children. They were randomly selected from the epidemiologic catchment area of Dokuz Eylül University Hospital. The absence of psychiatric disorders was verified by the SCID-CV. Families were excluded if the second parent in the case group and any parent in the control group received a psychiatric diagnosis. We excluded children with intellectual disability from both case and control groups. All parents gave informed consent for their children to participate in the study, and children gave assent.

Parents and children were interviewed using the Kiddie and Young Adult Schedule for Affective Disorders and Schizophrenia – Present State and Lifetime (WASH-U-KSADS, 11) to assess the presence of symptoms of bipolar disorder. The mania and depression sections of this instrument were translated into Turkish and back-translated to English. They were administered by two experienced clinicians to parents about their children and to children about themselves separately. Endorsement from both the child and the parents was required for an item to be rated as positive.

Parents completed the Turgay DSM-IV Scale (12) to assess the presence of attention-deficit/hyperactivity disorder (ADHD), opposition defiant disorder, and conduct disorder in their children. This is a parent report scale including all DSM-IV disrupting behavior disorders symptoms. Both parents' endorsement is required for an item to be rated as positive. Evidence supporting the instrument's reliability and validity in the Turkish population has been reported (12).

Teachers completed the Conners' Teacher Rating Scale (CTRS-28, 13) for the assessment of children's classroom behavior. This is a scale consisting of twenty-eight questions, grouped into four subscales: hyperactivity, conduct problems, inattention-passive and ADHD index. Raw scores for each subscale are transformed by age and sex into T scores. Evidence supporting the instrument's reliability and validity in a Turkish population has been published (14).

An ad-hoc form was used to collect information on educational, occupational and economic status of parents and on the illness of the bipolar parent.

Chi-square was used for categorical data and Mann Whitney-U test was used to analyse non-parametric data. Fisher's exact test was applied when necessary.

RESULTS

The case group consisted of 35 children (18 males and 17 females; mean age 12.2±3.3 years, range 7-17 years). The control group consisted of 33 children (22 males and 11 females; mean age 11.8±3.2 years, range 7-17 years).

Among the bipolar offspring, 8 children (22.9%) received at least one lifetime DSM-IV diagnosis as compared to only one (3.0%) of the control children. Thus, the offspring of bipolar parents had a 9.48 fold higher risk for receiving a psychiatric diagnosis than the control group (OR = 9.48; 95% CI=1.07-21.5; p=0.028). Two children (5.7%) in the bipolar offspring group were diagnosed as having a mood disorder (one had bipolar I disorder and one cyclothymic disorder); three (8.6%) had a disruptive behavior disorder (two had ADHD and one oppositional defiant disorder), and three (8.6%) had another psychiatric disorder (one had enuresis and two separation anxiety disorder). One child from the control group received an oppositional defiant disorder diagnosis.

On the CTRS-28, the bipolar offspring scored significantly higher than the control group on the hyperactivity and conduct problems subscales as well as the ADHD index, but not on the inattentive-passive subscale (Table 1). On the WASH-U-KSADS, children of patients with bipolar disorder were more likely than the controls to present, at a mild severity level, depressed mood (30.9% vs. 8.8%; OR=7.88; 95% CI=2.24-29.11; p=0.0004), irritability and anger (23.5% vs. 5.9%; OR=6.44; 95% CI=1.64-27.37; p=0.004), and excessive or inappropriate guilt (17.6% vs. 1.5%; OR=18.3; 95% CI=2.16-404.7; p=0.002).

Table 1 Mean T scores on the Conners' Teacher Rating Scale (CTRS-28) subscales in the offspring of bipolar patients and matched healthy controls

Subscale	Cases	Controls	Z	p
Hyperactivity	50.28 ± 8.6	48.78 ± 3.8	2.53	0.012
Conduct problems	55.08 ± 8.8	48.84 ± 4.9	0.33	0.001
Inattention-passive	46.25 ± 5.4	43.93 ± 4.3	1.78	0.075
ADHD index	51.91 ± 12.1	47.18 ± 4.8	2.66	0.008

DISCUSSION

Our findings are consistent with previous data showing that children of bipolar patients are at increased risk for the development of psychiatric disorders, especially ADHD and mood disorders (5,9,15-17). Moreover, these children are more likely to display subsyndromal mood and disruptive behavior symptoms. Mild depression and emotional dysregulation may herald the development of the full bipolar syndrome in some children. A recent well-designed study reported that a family history of bipolar disorder is associated with an increased risk of subsyndromal bipolar disorders (cyclotaxia) and not just fully syndromal bipolar disorder (18).

Chang et al (9) reported psychiatric diagnoses and symptoms in a cohort of 60 bipolar offspring. They found that offspring who had bilineal pedigrees for mood disorders (bipolar disorder in one parent, bipolar disorder or unipolar depression in the other) had higher WASH-U-KSADS scores for irritability, depression, rejection sensitivity, and lack of mood reactivity (defined as mood regulation problems) than bipolar offspring with unilineal pedigrees. Because we excluded families in which both parents had a mood disorder, our study is not directly parallel to Chang et al's, but we did observe high rates of depression and irritability in our high-risk offspring.

Short-lived hypomanic episodes during early childhood have been reported to be more frequent than manic and mixed episodes among children at risk for bipolar disorder (5,19). A recent study found that "episodic irritability" in childhood was a better predictor of later mania than chronic irritability (20). Thus, mild, episodic symptoms of mania or depression, which were observed more frequently in our high-risk children, may be early signs of bipolarity.

ADHD may increase the risk for developing bipolar disorder, especially when the child is genetically at risk for bipolar disorder (5,21-25). Additionally, several studies have found that bipolar disorder and ADHD are often comorbid (22). Only a prospective follow-up of our sample would reveal whether bipolar offspring with hyperactivity and conduct problems are more likely to develop bipolar disorder, ADHD or simply ongoing subsyndromal mood dysregulation.

Our study had a small sample size and a large age range. It was cross-sectional in design and interviewers were not blind to parental diagnosis. Because it was not designed as a genetic study, and because the sample size was limited and detailed information on pedigrees was missing, we could not make a proper estimation of the patterns of inheritance. Thus, the symptoms observed in the offspring may have had environmental as well as genetic underpinnings. Some investigators have observed correlations between pathological family environments and severity of illness in bipolar offspring (25,26). Family environment may have a negative effect on the psychiatric status of offspring, or early mood instability could occur as a reaction to having a bipolar parent.

In conclusion, results from this study indicate that children of bipolar I patients may have a significantly higher rate of psychiatric symptoms at both the syndromal and subsyndromal level than do children of healthy controls. The children of people with bipolar disorder can be considered a risk group in which early diagnosis and intervention are important. Therefore, the disruptive behavior and mood symptoms observed in early life may indicate the need for early psychosocial intervention. Observing these children longitudinally may clarify the developmental pathways to bipolar disorder among children at risk.

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