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Comparative study of psychopathology in offspring of patients with bipolar disorder

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Original article

SUMMARY

Background

The offspring of patients with bipolar disorder (BD) constitute a high risk population for multiple psychiatric disorders that require an early systematic evaluation and longitudinal follow up.

Objective

To describe and compare the psychopathology profile in offspring of parents with BD versus offspring of non-BD parents from a community sample.

Material and methods

Parents were evaluated with the Mini International Diagnostic Interview (MINI). Based on the results of the interview, two groups were created: parents with or without BD. After such interview, offspring psychopathology evaluation was conducted with the Kiddie Schedule for Affective Disorders and Schizophrenia for School-age Children Present and Lifetime Version (K-SADS-PL). The functioning was evaluated with the Clinical Global Assessment Scale (C-GAS).

Results

90% of the BD parents' offspring has had a psychiatric disorder throughout life. Externalizing disorders were the most frequent (81%). BD parents' offspring showed higher risk for having an externalizing disorder (RM=4.44; IC=95%; 1.43-13.84) and for an attention-deficit hyperactivity disorder (RM=3.38; IC=95%; 1.18-8.93) and for an oppositional defiant disorder (RM=3.06; IC=95%; 1.05-8.93).

Conclusion

Bipolar parents' offspring have a higher prevalence for psychiatric disorders, especially in the externalized area. The longitudinal course of early onset psychopathology suggests that this population requires early diagnostic and treatment strategies to change the disabling paths of chronic disorders.

Key Words: Bipolar disorder, offspring, psychopathology.

RESUMEN

Antecedentes

Los hijos de padres con diagnóstico de trastorno bipolar constituyen una población de alto riesgo para la presentación de múltiples trastornos psiquiátricos que requieren una evaluación sistemática temprana y un seguimiento longitudinal.

Objetivo

Describir y comparar el perfil psicopatológico en hijos de padres con trastorno bipolar *versus* hijos de padres sin trastorno bipolar en una muestra comunitaria.

Material y métodos

La evaluación de la psicopatología en los padres se realizó con la Entrevista Mini International Diagnostic Interview (MINI). Con base en los resultados, se crearon los grupos de padres con y sin trastorno bipolar (TBP). Posterior a la misma, se realizó la valoración de psicopatología en sus hijos con el Kiddie Schedule for Affective Disorders and Schizophrenia for School-aged Children Present and Lifetime Version (K-SADS-PL) y el funcionamiento con la Escala de Funcionamiento Global en niños (C-GAS).

Resultados

El 90% de los hijos de padres con TBP ha presentado un trastorno psiquiátrico a lo largo de la vida; el grupo de trastornos externalizados fue el más frecuente (81%). Los hijos de padres con TBP mostraron mayor riesgo de presentar cualquier trastorno externalizado (RM=4.44; IC=95%; 1.43-13.84), mayor riesgo para trastorno por déficit de atención e hiperactividad (RM=3.38; IC=95%; 1.18-8.93) y trastorno negativista y desafiante (RM=3.06; IC=95%; 1.05-8.93).

Conclusión

Los hijos de padres con TBP presentan una alta prevalencia de trastornos psiquiátricos, especialmente en el área de los externalizados. El curso longitudinal de la psicopatología de inicio temprano sugiere que esta población requiere estrategias tempranas de diagnóstico y tratamiento para cambiar las trayectorias discapacitantes de los trastornos crónicos.

Palabras clave: Trastorno bipolar, hijos, psicopatología.

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INTRODUCTION

Bipolar disorder (BD) is a disorder of mood of chronic, fluctuating course, with high rates of disability,[1] dysfunction,[2] psychiatric comorbidity[3] and suicide attempts,[4] which causes high health costs to society.[5]

Retrospective studies made in adults with BD have reported that 2O to 30% of cases started before 20 years of age;[6] however, most of them were not detected early. The delay in diagnosis occurred because before the onset of affective disorders there are other manifestations of psychopathology in childhood, such as antisocial personality disorder (ASPD) and attention deficit hyperactivity disorder (ADHD), which can hide the emotional and/or mood elevation patterns.[7-9]

Children of parents with BD are considered a high-risk group for developing such disorder, as indicated by studies showing that the likelihood of developing this disorder is 10%, when having an affected parent, and 40%, when both parents have it.[10] Also, studies on twins have shown that 70-80% of clinical manifestations are explained by genetic factors.[11]

The risk that this population faces is not only to develop BD, since studies report that 50% of BD parents' offspring meet criteria for at least one psychiatric disorder,[12-15] which shows a heterogeneous profile, but with higher rates of disruptive behavior disorders, anxiety and sleep disorders, as well as mood disorders, when compared to offspring of non-BD parents.[16-18]

Thus, compared with the general population, BD parents' offspring are 2.5 times more at risk to develop any psychiatric disorder and four times more at risk to have a mood disorder.[10] When considering a development perspective, studies in preschool children reported a prevalence eight times higher for the presence of ADHD, as well as an increased frequency of subthreshold manic and depressive symptoms, compared to children of parents without BD.[19] In adolescence there was an increase in prevalence of BD diagnosis (3-10%) and in a higher proportion for any mood disorder (40%).[20]

The study of this population is interesting because of health care, dysfunction and early psychopathology needs that have influence, in a heterotypic path, on other chronic and disabling disorders. This study is also important to design algorithms for early intervention and evaluate its outcome.

Objective

Describe and compare psychopathology in children and adolescents who are offspring of parents with BD *versus* offspring of non-BD parents from a community sample.

MATERIALS AND METHODS

Sampling

Parents with bipolar disorder. They were recruited through a clinic specialized in the diagnosis and treatment of mood disorders located at a third-level psychiatric hospital from October 2009 to July 2010. Patients with biological children ranging 6 to 18 years of age were invited to participate.

Parents diagnosed with BD secondary to substance use or medical cause and parents who during evaluation presented a psychiatric condition that prevented them to give their informed consent were excluded.

Parents without BD from the community. They were recruited from a private elementary and junior high school located near the geographical area in which the study was conducted. Parents were invited to take an informative course on anxiety disorders; then they were invited to participate in the study. All parents who voluntarily agreed to participate were included. Those who during the evaluation were diagnosed with BD and/or who had known first-degree relatives with this diagnosis were excluded.

Diagnostic interviews. For confirmation and/or diagnosis of parents, the *Mini International Neuropsychiatric Interview* (MINI) was used, adapted to Central and South America.[21] This is a structured diagnostic interview that assesses the major psychiatric disorders of Axis I according to the *DSM*–IV and the CIE-10. It has an inter-rater reliability of 0.67 to 0.95 for the different diagnostic categories. It was applied by a rater independent from the offspring assessments.

To assess psychopathology in children, the *Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version* (K-SADS-PL) was used. This is a semi-structured interview that assesses 46 psychiatric diagnoses in the present and throughout life. The inter-rater reliability has been reported between 0.66 and 1.0, depending on the diagnosis.[22] All raters were psychiatrists of children and adolescents who had the required training for the implementation of the instrument.

Psychosocial functioning was evaluated with the with the Clinical Global Assessment Scale (C-GAS), which is included in the last section of the K-SADS-PL. It consists of a score from 1 to 100, where the highest score corresponds to a better performance in academic, family and social areas.[22] For the evaluation of the Global Functioning variable, three categories were created: a) without dysfunction (GAF of 71-100); b) moderate dysfunction (GAF de 41-60), with interference in at least one area and/or in most social areas; and c) serious dysfunction (GAF 11-40), which included serious deterioration in the performance of different areas.

Likewise, the best current level of performance (last two weeks) was assessed, in the most severe episode in the past (MSEP), as well as the highest level of performance in the past (during last year).

Procedure

The protocol was submitted and approbed to the scientific and ethics committees of the institution where the study was conducted.

The informed consent from the parents and the assent from the children were obtained. The parents were assessed with the MINI, after which they were assigned to the BD or non-BD group of the community. In a second appointment the K-SADS-PL and the C-GAS were applied to their children.

Statistical Analysis

To describe the demographic and clinical variables, measures of central tendency were used. In turn, for categorical variables the χ^2 and Fisher's exact test were used when the number of observations was less than 5. Student's t-test was also used in continuous variables to compare percentages and means among the groups. 2x2 tables were used to estimate the odds ratio. Statistical significance was set at a value of $p<0.05$ (two-tailed). The analysis was performed using the statistical program IBM SPSS Statistics, version 20.

RESULTS

Socio-Demographic Characteristics

The sample included 62 children and adolescents: 31 children of parents with BD and 31 children of parents without BD. In the children of parents with BD, the average age was significantly higher than in the comparison group (12.2 [DE ± 3.55] *vs*. 10.1 [DE ± 1.55], t=-2.895, p=.006). The group of children of parents with BD had a significantly lower proportion of male participants (19 [61%] *vs*. 26 [84%], χ^2=.397, p=.046), while most of the children of parents without BD came from two-parent families (13 [42%] *vs*. 24 [77%], χ^2=8.11, p=0.04). When comparing whether they had received any drug treatment throughout life, there was no significant difference between groups (7 [22.58%] *vs*. 3 [9.7%], p=0.116) (Table 1).

Psychiatric diagnoses in children of parents with bipolar disorder *versus* children of parents without bipolar disorder

In order to reduce the probability of a type-II error for psychiatric disorders variable, in a first analysis was decided to group disorders in the following categories: any externalized disorder (ADHD, oppositional defiant disorder [ODD] and AD), any affective disorder (dysthymia, major depressive disorder and/or BD), any anxiety disorder (generalized anxiety, separation anxiety, social phobia, specific phobia, obsessive-compulsive disorder and posttraumatic stress) and any elimination disorder (enuresis and/or encopresis).

It was found that 90% of children of parents with BD and 87% of children of parents without BD had presented a psychiatric disorder throughout life (χ2=0.161, p=0.602). Children of parents with BD had a higher frequency for any externalized disorder than children of parents without BD (25 [80.6%] *vs*. 15 [48.4%], χ^2=7.045, p=0.008). No statistically significant differences between groups were found for the other categories (Figure 1).

In the analysis for each psychiatric diagnosis, children of parents with BD had a higher frequency of ADHD (22 [71%] *vs*. 13 [41.9%], χ^2=5.314, p=0.021) ODD (16 [51.6%] *vs*. 8 [25.8%], χ^2=4.351, p=.037, OR=3.06, IC=95%, 1.05-8.93) and a tendency for AD (4[13%] *vs*. 0 p=0.076). Two children of parents with BD (6.5%) had diagnosis of unspecified BD. The group of children of parents without BD had a higher frequency of social phobia (n=9 [29%] *vs*. n=2 [6.5%] *vs*. EF=0.043, p=.020).

Risk analysis by the odds ratio (OR) showed that the group of children of parents with BD faced a higher risk to

Table 1. Sociodemographic characteristics in children of parents with BD *vs*. children of parents without BD

	Children of parents with BD		Children of parents without BD		Statistical analysis		
Characteristics	Mean	S.D.	Mean	S.D.	Test	df	p
Age (years)	12.2	3.55	10.1	1.55	t	2.895	0.006
	N	**%**	**N**	**%**			
Male sexo	19	61.0	26	84.0	χ^2	0.397	0.046
Mestizos	31	100.0	31	100.0	NA	NA	NA
Two-parent family	13	42.0	24	77.0	χ^2	8.110	0.040
History of abuse*	16	52.0	9	9.0	χ^2	3.280	0.070
Pharmacological t&	7	23.0	3	10.0	FE	0.170	0.116

* Includes any physical, psychological and/or sexual abuse or negligence at some time in life.
& History for having received pharmacological treatment at some time in life.

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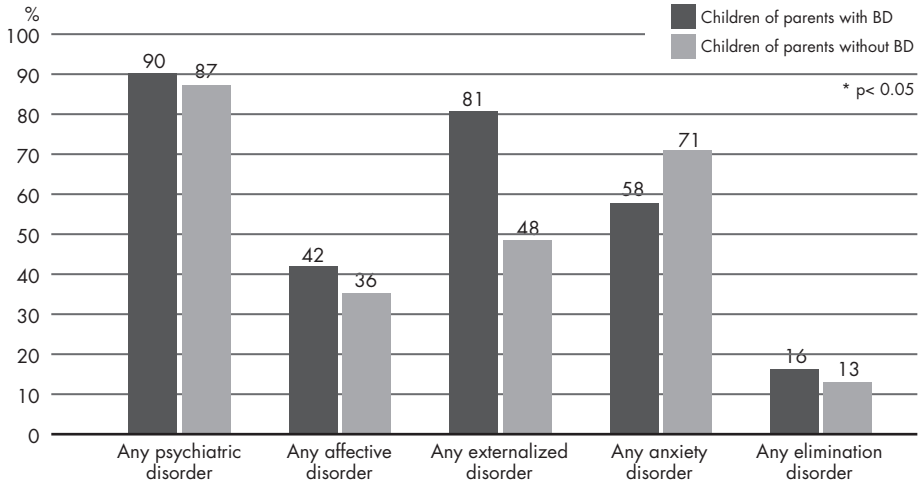

Figure 1. Comparison of diagnostic categories in children of parents with BD vs. children of parents without BD.

have any externalized disorder (R.M.=4.44, IC 95%, 1.43-13.84, p=.01), ADHD (R.M.=3.38, IC 95%, 1.18-8.93, p=0.04) and ODD (R.M.=3.07, IC 95%, 1.05-8.93, p=.06).

Overall functioning of children of parents with BD *versus* the community group

64.5% of children of parents with BD had moderate dysfunction in the current episode compared with 29% of children of parents without BD, which represented a statistically significant difference between groups (20 [64.5%] *vs.* 9 [29%] χ^2=.783, p=.005).

DISCUSSION

This study compared psychiatric disorders in children of parents with bipolar disorder treated in a third-level care

Table 2. Psychiatric diagnoses (*DSM*-IV) in children of parents with BD (n= 31) *vs.* children of parents without BD (n = 31)

	Children of parents with BD		Children of parents without BD		Statistical analysis		
Disorder	N	%	N	%	Test	df	p
Non-specified BD	2	6.5	0	0.0	EF	0.492	0.229
Major depression	5	16.1	2	6.5	EF	0.425	0.151
Generalized anxiety	2	6.5	6	19.4	EF	.255	0.130
Separation anxiety	11	35.5	9	29.0	χ^2	.295	0.587
Social phobia*	**2**	**6.5**	**9**	**29.0**	**FE**	**.043**	**0.020**
Specific phobia	11	32.3	16	51.6	χ^2	1.676	0.196
Obsessive-compulsive disorder	1	3.0	0	0.0	EF	1.000	0.313
Post-traumatic stress	0	0.0	1	3.0	EF	1.000	0.313
ADHD*	**22**	**71.0**	**13**	**42.0**	**χ^2**	**5314**	**0.021**
ODD*	**16**	**51.7**	**8**	**26.0**	**χ^2**	**4351**	**0.037**
ASPD**	4	13.0	0	0.0	EF	.238	0.076
Enuresis	3	10.0	5	16.0	EF	.707	0.449
Encopresis	1	3.2	0	0.0	EF	1.000	0.313
Anorexia nervosa	2	6.5	0	0.0	EF	.492	0.151
Bulimia	1	3.2	1	3.2	NA	NA	NA
Adjustment reactions							
• Disorder with depressed mood	5	16.0	5	16.0	EF	.425	0.151
• Anxiety disorder**	3	10.0	0	0.0	EF	.238	0.076

EF = Fisher's exact test.

hospital to children of parents without BD of the community. The results showed that both groups had a high rate of psychopathology. However, in the group of children of parents with BD, this rate was more than double that expected for the age group (90% of participants had a psychiatric disorder). This finding is relevant because it puts this population in a position of high risk to present any psychiatric disorder throughout life. Also, children of parents with BD constituted a group with a greater number of comorbid disorders (from three to seven diagnoses) and greater dysfunction, which ranks them as a different population in terms of severity when compared to children of parents without BD.

When comparing by a diagnostic group, it was observed that there was a higher frequency of disorders of the externalizing spectrum for children of parents with BD who had 4.44 times greater risk of presenting any externalized condition; 3.38 and 3.07 times higher risk of ADHD and ODD, respectively. This finding is interesting because, although the total sample of children and adolescents was obtained from the community, in this study the frequency of externalized disorders in children of parents with BD was almost 15 times higher than the one reported in other studies with general population[23] and almost 50 times higher than the one reported in the national survey of adolescents.[24]

The results are also consistent with other international studies reporting high rates of disruptive behavior disorders and ADHD in children of parents with BD when compared to children of healthy parents[19] and/or with other psychopathology different than BD.[14] The relevance of the presence of ADHD in population at risk for developing BD has been shown with longitudinal follow-up, which report that the association of ADHD with conduct disorder and depressive episodes significantly increases the risk of a shift to mania in children and adolescents.[25]

For this reason, some authors have suggested that, in populations at risk, the ADHD may be a prodromal phase or an early manifestation of BD, according to the stage of development.[16,26] Another proposed hypothesis is that the BD and the ADHD share a biological substrate for the etiology of the disease.[26] However, cohort, genetic and neuroimaging studies are required to help clarifying this association. It is important that children and adolescents, included in this kind of studies, can be followed-up.

Moreover, mood disorders were more frequent in the group of children of parents with BD; however, there were no differences with the children of parents without BD. A likely explanation for the foregoing is that in this study the majority of those evaluated had not reached the age of greatest risk for the presence of affective disorders.[18,23] Children with symptoms of mood elevation did not meet the criterion of time according to the DSM-IV to confirm the diagnosis of TBP-I or II. However, research shows that these children can be diagnosed with an unspecified BD, which behavior is similar to the subtypes I and II in relation to the chronicity and dysfunction.[27] Some authors have modified the diagnostic criteria for pediatric BD considering the number of hours in which the symptoms of mood elevation are presented and during different days.[27] Yet, this diagnostic modality increases the prevalence of pediatric BD.

Anxiety disorders occurred more frequently in children of parents without BD. This finding was probably related to an increased sensitivity to parents' recognition of psychopathology when accepting that their children were assessed. Moreover, the results are consistent with studies of Mexican community samples where anxiety disorders are the most prevalent, but also the less disabling,[28] and finally a percentage of the sample from the school was referred by teachers, who may have detected a manifestation of abnormal behavior in a child and suggest his/her participation in the study.

Children of parents with BD had a lower overall level of functioning in the present, with impairment in at least one area in accordance with the C-GAS. Despite this, most of these children had received no therapeutic interventions and those who did have the history of medical treatment received the group of drugs more used, stimulants. The above suggests that externalizing symptoms were the main cause of dysfunction.

The interpretation of the results of this study involves some limitations because the psychiatric diagnosis could only be assessed in the participating parent. No information was obtained on the other biological parent. Also worthy of note is the difficulty in recruiting community parents without psychopathology, which has been reported in other studies with similar designs, where 50% of community parents have at least one psychiatric diagnosis.

Although the evaluators of children and adolescents were not blind to the diagnosis of parents, having used a semistructured interview validated in Mexican population and applied by qualified child and adolescent psychiatrists with experience in the use of interviews, as well as having included a comparison group, strengthens the results.

To our knowledge, this is the second report of psychopathology in Mexican children and adolescents considered as risk groups to present a bipolar disorder. Given that it replicates the results of studies conducted in this field in other parts of the world, this study can serve as a framework for developing subsequent studies, monitoring plans and management of special populations, as well as support for the implementation of screening programs in high-risk populations, as are the children of parents with any psychopathology attending psychiatric treatment.

CONCLUSIONS

This study reports psychopathology in children of patients with BD. The high frequency of psychiatric disorders found in this population, specifically for externalized disorders,

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entails a need for focusing on the clinical area the attention on prevention programs, diagnosis and/or early treatment for this high-risk group.

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