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Overall functioning in offsprings of parents with bipolar disorder and its association with clinical and sociodemographic variables

Alfredo Licona-Martínez,[1] Lino Palacios-Cruz,[1] Miriam Feria-Aranda,[1] Patricia Zavaleta-Ramírez,[2] Alejandro Vargas-Soberanis,[1] Claudia Becerra-Palars,[3] Francisco de la Peña-Olvera[1]

Original article

SUMMARY

The presence of a psychiatric disorder in parents is associated with increased frequency of psychopathology in their offspring. Children of parents diagnosed with bipolar disorder (BD) are at greater risk and lower function. However, it has not yet been determined precisely which clinical and socio-demographic factors are associated with the presentation of psychiatric disorders in this group of children and adolescents at risk. Under this framework, the aim of this study was to determine the clinical and socio-demographic variables associated with a lower function. We recruited 61 children and adolescents with ages ranging from six to 17. All of them were the children of parents with BD who were patients at the National Institute of Psychiatry Ramón de la Fuente Muñiz. Clinical evaluation was developed by the *Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version* (K-SADS-PL), and the *Children´s Global Assessment Scale* (C-GAS) scale was used to establish overall functioning. Of the 61 children evaluated, 62.3% were female, the lowest function (defined by <81 points C-GAS) was found in 44.3% of females *vs.* 18% of males (χ^2=3.29, p<0.043). Comorbidity with Major Depressive Disorder, Attention Deficit Hyperactivity Disorder, or Oppositional Defiant Disorder conferred ten times greater risk of lower global function. Being female gives three times higher risk for a lower global function.

Conclusion

We found that the comorbid externalizing disorders and depression, as well as female gender characteristics are linked to lower function in children and adolescents of parents with BD.

Key words: Offspring, children, bipolar disorder, comorbidity, function.

RESUMEN

La presencia de un trastorno psiquiátrico en los padres se asocia con una mayor frecuencia de psicopatología en sus hijos. Así, los hijos de padres con diagnóstico de Trastorno Bipolar (TB) comparados con aquellos hijos de padres sin psicopatología tienen mayor riesgo de presentar distintos trastornos psiquiátricos, a edades más tempranas, así como disminución en su funcionamiento global, sin embargo aún no se han determinado con precisión cuáles son los factores clínicos y socio demográficos asociados a la presentación de trastornos psiquiátricos en este grupo de niños y adolescentes en riesgo. El objetivo del presente estudio fue determinar y comparar las variables clínicas y socio demográficas asociadas a un menor funcionamiento global en una muestra de niños y adolescentes hijos de padres con TB. Previo asentimiento y consentimiento informado se reclutaron 61 menores de entre seis y 17 años de edad, hijos de padres con TB que fueran pacientes de la Clínica de Trastornos Afectivos del Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz. El diagnóstico de los menores se estableció mediante entrevista clínica utilizando el K-SADS-PL, y con la escala C-GAS se determinó el funcionamiento global. De los 61 evaluados, 62.3% fueron mujeres, el menor funcionamiento (definido por una puntuación <81) se encontró en el 44.3% de las mujeres *vs.* el 18% de los hombres (χ^2=3.29, p<0.043). Al evaluar la comorbilidad se encontró que los sujetos con trastorno depresivo mayor (TDM), trastorno por déficit de atención con hiperactividad (TDAH) y trastorno negativista desafiante (TND) presentaron 10 veces mayor riesgo de cursar con menor funcionamiento global. Ser mujer confiere tres veces mayor riesgo para un menor funcionamiento.

Conclusión

Se encontró que la comorbilidad con trastornos externalizados y depresión, así como el género femenino, son las características vinculadas al menor funcionamiento global en hijos de padres con TB.

Palabras clave: Hijos, trastorno bipolar, comorbilidad, funcionamiento.

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[1] Adolescent Clinic, National Institute of Psychiatry Ramón de la Fuente Muñiz.
[2] Clinical Services, INPRFM.
[3] Affective Disorders Clinic, INPRFM.

Correspondence: Dr. Francisco de la Peña-Olvera. National Institute of Psychiatry Ramón de la Fuente Muñiz. Calz. México-Xochimilco 101, San Lorenzo Huipulco, Tlalpan, 14370. Mexico City. E-mail: adolesc@imp.edu.mx

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INTRODUCTION

The presence of a psychiatric disorder in parents is associated with a greater frequency of presentation in their children.[1] It has been seen that the presence of an affective disorder in parents increases the risk of a similar disorder occurring in their children.[2] Specifically, children of parents with bipolar disorder (BD) have a four times greater risk of developing an affective disorder, and are 2.7 times more likely to develop any psychiatric disorder, than children of parents without a psychiatric disorder.[3] Furthermore, it has been reported that, independent of the family burden of BD, stressful events increase the risk of presenting an emotional disorder during the course of a lifetime in children whose parents have BD.[4]

The interaction of genetic and environmental factors (gene-environmental interaction) is involved in the development of psychopathology in this high-risk group, given that it is not just the genetic burden conferred by the disorder itself that affects them, but also factors such as marital conflict, quality of childhood, and periods of parents' absence during hospitalizations, among others.[5]

Birmaher et al. have reported that children of patients with BD have 13.4 times more risk of developing BD than children of healthy parents, as well as 5.2 times greater risk of developing any emotional disorder, and 2.3 times greater risk of any anxiety disorder. The same authors made the first report on pre-school children, who had eight times more tendency towards ADHD throughout their lives, especially in children over four years of age, and greater frequency of depressive symptoms and sub-threshold manias. These results were adjusted for psychopathology in one or both parents.[6,7] Hirshfeld at al. reported a raised frequency of anxiety disorders in children of parents with BD, including Separation Anxiety Disorder or Generalized Anxiety Disorder, concluding that anxiety disorders could be a probable indicator of risk for the development of BD in children of parents with BD.[8]

Global functioning is a latent variable that seeks to determine the set of functionality in different areas of a person, involving various areas such as weekly routine, social and academic repertoire, personal tendencies (such as reactions to frustrating, hopeful, or self-control situations) and motivational tendencies (such as general biological state and intellectual function).[9] It has been reported that good premorbid global function in children of parents with BD is a predicting factor for their successful treatment.[10]

Other research shows that the total level of function in adolescent children of a father or mother with BD does not differ from that of adolescents of the general population,[11] while two more investigations describe the opposite. One reports that children of parents with BD definitely present a lower level of global functioning,[12] and the other concludes that children of parents with BD present lower psychosocial functioning overall, which appears to be attributable as much to the parents' condition as to the child's own psychopathology.[13]

In a study that assessed chronic and acute stressful events in a sample of children of parents with BD, it was reported that these patients experienced greater difficulties in different areas of inter-personal function even when controlled by an associated affective disorder, and it was very common that these patients could present moderate to severe stress in inter-personal areas.[14]

Revising the bibliography in Mexico and discussing the prevalence of patients with BD as information to take into consideration shows that recent studies report 2.0 for BD and 0.9 for BD II. In previous years, it was reported that 2% of school-age patients had presented with depression, with an average of seven episodes throughout their life, compared with three episodes of depression in adult life.[15,16]

As such, the first study that assessed psychopathology in children of patients with BD in Mexico showed that the majority of children of parents with BD had presented with some sort of psychiatric disorder during the course of their lives, with a moderate interference in their global function.[17]

Based on the above, there is controversy around the clinical and socio-demographic factors linked to lower global functioning in children of parents with BD. This inconsistency in the results could be attributable to methodological differences, the type of informants, assessment times, the origin and size of the samples, and the fact that some assessors had knowledge of the parental diagnosis.[18]

The primary objective of this research was to determine the clinical and socio-demographic variables associated with a lower present global function in children of parents with BD.

MATERIAL AND METHODS

Participants

The sample consisted of 61 subjects and the inclusion criteria were: children and adolescents between six and 17 years of age, biological children of a father or mother with BD who were outpatients of the Affective Disorders Clinic (CTA) at the National Institute of Psychiatry Ramón de la Fuente Muñiz (INPRFM). The father or mother met diagnostic criteria for BD I and BD II established by a certified psychiatrist, in accordance with the Revised Text of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). The children agreed to participate under the informed approval and consent of the father and/or mother.

Instruments

Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version (*K-SADS-PL*). This is a semi-structured interview that makes it possible to transversally and longitudinally assess the psychopathology of children and adolescents, as well as alterations in both global function (though the C-GAS) and specific diagnoses. It also provides information on the history of development, family history, and pathology of the subject.

It assesses the presence of 46 different diagnoses on Axis I in accordance with the criteria of Versions III and IV of the DSM-IV, both at the current time and throughout one's life. Diagnoses are coded as definitive (more than 75% of diagnostic criteria), probable (≥75% of diagnostic criteria of a disorder and some functional deterioration), or absent.[19] In Mexico it was translated into Spanish and assessed for its inter-assessor confidence; kappa coefficients were reported of 0.91 for ADHD, 0.76 for MDD; 0.53 for Generalized Anxiety Disorder (GAD), 0.71 for ODD, 0.84 for any general internalized disorder, and 0.87 for any externalized disorder.[20]

Children´s Global Assessment Scale. This is an instrument to assess global or general function in subjects, scored by the clinician after conducting the K-SADS-PL interview. The C-GAS offers examples of functioning every ten points. The scale can be assessed from 1 to 100. 100 is reserved for those individuals who are not only exempt from psychopathology, but who also show features considered to show positive mental health such as superior functioning, raised interests, integrity, quality, etc., and a score of 1 shows ideas of death. A score of 0 is reserved for when there is insufficient information. *Higher function* is considered for a score above 81, while scores equal to or lower than 80 are considered to show *lower function* or a deterioration in global function. Finally, it should be noted that as the scores in the scale reduce, the interference is considered to go from moderate to severe, and scores below 30 are translated as an inability to function in most areas.[21] It has been demonstrated that translation into Spanish provides adequate validity and reliability (test-retest and inter-assessor), reporting an interclass coefficient of correlation of 0.61 to 0.91.[22]

Procedure

Outpatients in the CTA of the INPRFM who had a diagnosis of BD and who had biological children between six and 17 years of age were directly invited to form part of this project. Psycho-educational groups for patients with BD were participated in, where invitations were also made for patients to join in the research. Parents who accepted were given an explanation of what the research would consist of, and they were then given a Letter of Informed Consent for them to sign, along with a Letter of Approved Consent for the children and adolescents. Once they agreed to participate in the study, they proceeded to be assessed with the K-SADS-PL interview, as well as the C-GAS scale. The identified cases were cared for through the outpatients of the INPRFM Adolescent Clinic.

Once the assessments had been completed, the results were gathered and interpreted through a statistical analysis.

Statistical analysis

Measures of central tendency were used to describe the socio-demographic and clinical variables, and χ^2 was used to compare percentages. The odds ratios (ORs) were calculated for the risk association, and a multivariate analysis was made by means of logistical regression to predict the behavior of the clinical and socio-demographic variables as risk factors or protectors of global function. Statistical significance was established with $p<0.55$. Capture and analysis of information was carried out with the SPSS version 17.0 statistical package.

RESULTS

Demographic data

Some 61 children and adolescent offspring of patients with BD were interviewed. From the sample total, 62.3% were female and 37.7% male; 47.5% were school-age (six to 12 years of age), and 52.5% were adolescents (13 to 17 years of age). Some 59% were from two-parent families, and 41% were from single-parent families.

The details regarding clinical variables are shown in table 1.

Present global function

Analysis was made by gender, age group, and family type.

By gender, higher global function (defined by >81 points) was found in 19.7% of the males *vs*. 18% of females. Lower function (defined by ≤81 points) was found with a

Table 1. Percentage of diagnosis, median, and SD of the starting age of children of parents with BD

Diagnosis Axis I	% found N=61	Starting age X	Starting age SD
Disorder:			
• Major Depressive	21.3	10.56	2.506
• Generalized Anxiety	24.6	8.00	2.697
• Separation Anxiety	29.5	5.17	1.472
• Attention Deficit Hyperactivity	59.0	6.11	1.537
• Oppositional Defiant	49.2	7.60	1.897
Social phobia	13.1	7.20	2.049
Specific phobia	27.9	7.50	2.380

*SD=Standard deviation.

Table 2. Comparison of clinical variables in accordance to the level of present global function

Variable	Performance Higher* N(%)	Lower** N(%)	x_2	p
Disorder:				
• Major Depressive	1 (1.6)	12(19.7)	6.33	0.0090
• Generalized Anxiety	2 (3.3)	13(21.3)	5.03	0.0190
• Separation Anxiety	4 (6.6)	14(23.0)	2.60	0.6500
• Attention Deficit Hyperactivity	6 (9.8)	30(49.2)	16.55	0.0001
• Oppositional Defiant	4 (6.6)	26(42.6)	14.92	0.0001
Social phobia	2 (3.3)	6 (9.8)	0.63	0.2370
Specific phobia	2 (3.3)	15(24.6)	6.75	0.0070
History of abuse	7(11.5)	24(39.3)	6.13	0.0100

*Higher function: scores above 81 points on the C-GAS scale.
** Lower function: scores equal to or lower than 80 points on the C-GAS scale.

significant difference in 44.3% of the females *vs*. 18% of the males (χ^2=3.29, p<0.043).

In terms of age group, lower function was observed in 24.6% of school children and 37.7% of adolescents, with no statistically significant differences.

With respect to family type, single-parent families reported 13.1% with higher function and 27.9% with lower function, while two-parent families reported 24.6% higher function and 34.4% lower function, respectively.

Significant differences were only observed between the percentages of males and females with lower global function. Details of the percentages for higher and lower function according to the clinical variables are shown in table 2.

Risk association

MDD, ADHD, and ODD showed an odds ratio (OR) greater than 10, and only Separation Anxiety Disorder and social phobia did not show significant ORs. Details are shown in table 3.

Table 3. Risk of presenting a lower function in presenting a psychiatric disorder

Variable	RM (IC 95%)	Value of p
Disorder:		
• Major Depressive	10.14 (1.22 - 84.38)	0.0090
• Generalized Anxiety	5.46 (1.10 - 26.98)	0.0190
• Separation Anxiety	2.77 (0.78 - 9.80)	0.6500
• Attention Deficit Hyperactivity	10.62 (3.15 - 35.78)	0.0001
• Oppositional Defiant	10.29 (2.87 - 36.90)	0.0001
Social phobia	1.96 (0.36 - 10.69)	0.2370
Specific phobia	6.84 (1.39 - 33.56)	0.0070
History of any kind of abuse	3.91 (1.29 - 11.84)	0.0100

Table 4. Model of logistical regression for the clinical variables and gender in relation to lower function

Variable	x_2 Wald	gl	Sig.	Exp(B)
Female gender	2.106	1	.147	3.559
Disorder:				
• Major Depressive	.014	1	.906	1.206
• Generalized Anxiety	.370	1	.543	2.226
• Attention Deficit Hyperactivity	3.618	1	.057	4.758
• Oppositional Defiant	5.768	1	.016	9.018
Specific phobia	1.629	1	.266	3.215
History of abuse	2.972	1	.202	2.593

Finally, a multivariate analysis was made which confirmed that the female gender has a risk three times greater of presenting lower global function, just as there is a greater risk for ADHD and ODD, details of which are shown in table 4.

DISCUSSION AND CONCLUSIONS

Internalized disorders, specifically MDD, GAD, and specific phobia, externalized disorders such as ADHD and ODD, as well as the female gender and a history of abuse were associated with lower global function. MDD, ADHD, and ODD are associated with more than ten times the risk of presenting with lower global function.

We found that the clinical variables such as MDD, GAD, ADHD, ODD, specific phobia, and a history of abuse have a higher frequency of presentation in the subjects assessed. In other research, these variables have been seen to be specifically associated with lower interpersonal function;[23] previous data agrees with what was reported in earlier investigations.[11]

In conclusion, children of patients with BD are a group at high risk of developing both affective as well as behavioral disorders.[24] This study did not find significant associations between the male gender and clinical variables such as ADHD, MDD, or ODD, and lower global function.

The ages for externalized disorders start in infancy, and those for internalized disorders start during adolescence.[25] Our findings confirm this information. The presence of ADHD and/or ODD show a greater association with higher global function, which differs from that previously described in the bibliography.[26] Another very interesting finding contrary to our expectations, and which is apparently being reported for the first time in samples of children of parents with BD, is the greater presentation of psychopathology in female patients. However, this is information that should be taken with caution given the characteristics of the sample used. Contrary to expectations, subjects coming from single-parent families did not present a lower global function in comparison to those from two-parent families; however, no conclusion could be drawn from the data obtained.

We had a raised report of a history of abuse (be it physical, psychological, or sexual) in participants in this investigation. It could be noted that the abuse could be secondary to problems inherent to the psychopathology of the parent, or to the psychopathology of the minor that they condition to have a low tolerance with open aggression. This also coincides with a previous presentation of any psychiatric disorder which has recently been commented on in medical literature.[27]

As such, we should consider that which has been known for years and which is still valid today, in that children of parents with a diagnosis of BD will generally have raised levels of psychopathology, as well as usually having earlier ages of presentation than the rest of the population.[28-30] It is therefore a priority to carry out follow-up with the aim of efficiently identifying psychiatric disorders the could be prevented and, above all, limiting their effect on the global function of the child or adolescent.

Limitations

The transversal design of this study does not allow for causality to be established, and it is not possible to carry out greater follow-up on the patients in terms of their diagnoses recording different temporal stability in each one, and even in the development of their own function, whether it be an improvement or a deterioration. A non-probabilistic sample type was used which means that the grade of representativity or external validity could be questionable, therefore future research should seek to expand the population to other institutions that care for patients with diagnoses of BD. One very important limitation is that the research did not have a control group. Finally, the assessments of diagnoses and global function were made over different periods of time, which could influence the different presentation of psychopathology in subjects who participated in this research.

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