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Original research

Psychiatric comorbidity in Mexican adolescents with a diagnosis of eating disorders its relationship with the body mass index

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Abstract: (1) Background: The prevalence of comorbid psychiatric disorders among the patients with mental disorders is higher than general population. The aim of this study was to estimate the prevalence of comorbid psychiatric disorders among a Mexican adolescent sample diagnosed with eating disorders; (2) Methods: Only Mexican adolescents diagnosed with eating disorders were included in the study. The diagnoses were using the DSM-5 criteria. Adolescents with ages between 12 to 17 years were included. The psychiatric comorbidities were evaluated using MINI-kid and QEWP-R. In addition, the z-score values calculated from BMI; (3) Results: The mean age was 14.08±1.7 years old. In our Mexican sample the diagnoses more frequently were bulimia nervosa (55.61%). We found that 89% of the Mexican adolescents with eating disorders had another psychiatric comorbidity. Major depressive disorder (52.40%) and suicide risk (40%) were the most prevalent comorbidity; (4) Conclusions: Our results showed that bulimia nervosa is the most frequently diagnoses in Mexican adolescent and the suicide and major depressive disorder are the principal comorbidities. This emphasizes the importance that clinicians take into consideration the presence of psychiatric comorbidities to achieve an integrative treatment for patients with ED.

Keywords: Psychiatric comorbidity; Mexican population; Eating disorders

1. Introduction

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Eating disorders (ED) are multifactorial psychiatric disorders (anorexia nervosa, bulimia nervosa and binge eating disorder), characterized by alterations of the eating patterns and body weight perceptions [1, 2]. ED are a public health problem. The prevalence of eating disorders among female adolescent population is 0.3%-2.05% and 0.1%-0.8% for male population [3]. For Mexican population the prevalence for adolescent population for anorexia nervosa (AN) is 0.3% and for bulimia nervosa (BN) is 0.9% [4].

One focus of attention has been centered in the increased of mortality among patients with ED in comparison with the general population [5]. In this sense, an association between ED with the manifestation of other psychiatric disorders (comorbidity) has been reported to be a possible risk factor for the increase on the mortality rates in these patients [6]. Different psychiatric disorders as comorbidities (alcohol use disorder, substance use disorder, depression and personality disorders) have been associated with ED [5].

Additionally, neurobiological circuits of phenotypical traits (impulsivity) have been postulated to regulate food intake and body mass index (BMI), assembling a complex relation between psychiatric disorders and metabolism. In this sense, patients with obesity could demonstrate disruptive feeding behavior that leads to physical and functional impairment in diseases like bipolar disorder [7], schizophrenia [8] and attention-deficit/hyperactivity disorder (ADHD) [9].

However, in Mexican population and furthermore in adolescents, there is limited information about the prevalence of comorbid psychiatric conditions among adolescent patients with ED. The aim of this study was to report as preliminary results the prevalence of comorbid psychiatric disorders among a sample of Mexican adolescent diagnosed with ED, as well as to see if the comorbidities had relation with the obesity that they presented.

2. Materials and Methods

2.1 Study population

The recruitment of the sample was in the children´s psychiatric hospital "Dr. Juan N. Navarro" in Mexico City. The psychiatric hospital is one of the national reference institutions for children and adolescent attention on psychiatric disorders. As inclusion criteria, the patients were recruited from different services, like emergency room and outpatient clinic. A psychiatrist specialized in eating-disorders evaluated and diagnosed the patients. The diagnosis where based on the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) criteria [10]. In addition, the Spanish versions of the Mini International Neuropsychiatric Interview for Children and Adolescent (MINI-kid) [11, 12] and Questionnaire on Eating and Weight Pattern-Revised (QEWP-R) [13, 14], were applied to explored other psychiatric comorbidities and eating related patterns. Only adolescents with ages between 12 to 17 years were included. Also, to be included parents and grandparents had to be Mexicans.

The subjects were excluded from the study if missing data was found on the questionnaires or, if the parents´ participants (or tutors) withdrew their consent for participation in the study.

2.2 Ethical statement

All patients included were given verbal and written information related with the research objectives and procedures. The patients read and signed an informed assent; and informed consent was given by parents or tutors. The subjects were informed of anonymity, and they did not receive economical remuneration. This study was in accordance with the principles of the Helsinki declaration in 1975 and compliance with the code of ethic of

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the world medical association. The protocol was approved by the ethic and investigation committees of the Instituto Nacional de Medicina Genómica (INMEGEN) (approbation number: 06/2018/I) and the children´s psychiatric hospital "Dr. Juan N. Navarro".

2.3 Anthropometric measurements

The anthropometric measurements collected included weight and height as it has been previously reported [15]; the body mass index (BMI) was determined according the obesity task force criteria. One of the limitations of the use of BMI on children and adolescents is that this parameter could be influenced by the developing of the child. In order to make comparison between the BMI, we transformed this into Z-score (z-BMI) values (standard deviation) and age and sex-specific BMI percentiles (BMI percentiles), as previously reported [16, 17].

2.4 Statistical analysis

We reported the mean and standard deviations (s.d) for continuous variables, and frequencies and percentages for categorical variables. A X2 test was calculated to compare the prevalence of psychiatric comorbidities in our population in study with the reported prevalence on psychiatric disorders among adolescent Mexican population. The comparison data was obtained from Benjet C., et al [18]; this study is an epidemiologic survey of psychiatric disorders among Mexican adolescent population with a sample over 3 thousand subjects, it was carried out at the National Institute of Psychiatry "Ramon de la Fuente" (further citation as reference sample). Statistical analysis was performed with packages available in R software version 3.5.1 (https://CRAN.R-project.org) [19]. The significance level was set at $p < 0.05$.

3. Results

In the present study 187 adolescents diagnosed with eating disorders were included. There was a higher number of females in the sample compared to males [female 77% (n= 144); male 23% (n=43)]. The mean age was 14.08 (s.d ± 1.7) years old. Of the total of patients, 32 adolescents patients (17.11%) were diagnosed with anorexia nervosa, 104 patients (55.61%) with bulimia nervosa, and finally, 51 patients (27.27%) with binge eating disorder.

The BMI-for-age percentile was 74.26 ± 25.3, meanwhile the mean Z-score for the BMI was 0.8 ± 1. Based in growth charts, six patients (3.20%) were underweight; 93 patients (49.73%) had a normal-weight; 34 patients (18.18%) had overweight and 54 patients (28.87%) presented obesity. From the sample of patients with BN, almost 40% of the sample had overweight (20.19%) or obesity (23.08%). Whereas for the patients with BED, more than 70% of the individuals had overweight (23.53%) or obesity (56.86%).

3.1 Major depressive disorder was the most frequent psychiatric comorbidity

We observed that 89.30% (n=167) of the adolescents with ED had another psychiatric comorbidity. Patients diagnosed with BN or BED had the higher prevalence of any psychiatric comorbidity (BN 90.38% and BED 94.11%). At difference, patients with AN had a lower rate with 78.12% (n=25) prevalence of another psychiatric comorbidity.

The most prevalent comorbidity in individuals with ED were disorders related to mood alterations. Major depressive disorder was the most prevalent comorbidity with 52.40% of the sample presenting this. Noteworthy, over 40% of the adolescents with ED had suicide risk. In lesser prevalence was the dysthymic disorder with 22.45%. In relation to comorbidities related to anxiety disorders, generalized anxiety disorder was the most prevalent with 17.64%. However, a higher prevalence than anxiety-related disorders was seen related to development disorders, 20.85% of the patients with ED had attention-def-

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icit/hyperactivity disorder (ADHD). Finally, the less prevalent comorbidities in the patients with ED were oppositional defiant disorder (13.90%), psychotic disorders (6.95%) and substance use disorder (5.34%).

3.2 Prevalence of psychiatric disorders among patients with EDs is higher than the reference sample

We compared the prevalence of comorbid psychiatric disorders in patients with ED with the previous reported prevalence in the reference sample [18]. Of the 20 disorders compared between the ED sample and the reference sample, 11 disorders showed statistically significant differences. Almost all the disorders had a higher prevalence in the ED sample compared to the reference, except for specific phobia, where we found a reduction of 10% in prevalence in ED. Major depressive disorder was the disorder that show the higher difference between the ED sample and the reference, with almost an increase of 50%.

Next, the disorders that showed more differences in prevalence were suicide risk (increased of 31.89%), dysthymic disorder (increased of 21.96%), attention-deficit/hyperactivity disorder (increased of 19.26%) and generalized anxiety disorder (increased of 17.15%). We did not compare some comorbidities (adjustment disorder, psychotic disorder, TIC disorder and obsessive-compulsive disorder) for lack of information in the reference sample. The prevalence of comorbidities in our study sample and statistical results of the comparisons with the references are shown in Table 1.

Table 1. Comparison of psychiatric comorbidity prevalence in patients with eating disorders and reported prevalence in Mexican adolescent population.

Psychiatric comorbidity	***EDs*** ***n (%)***	**Reported prevalence n (%)** [a]	X^2	***p- value***
Major depressive disorder	98 (52.40)	144 (4.79)	**562.85**	**< 0.001**
Dysthymic disorder	42 (22.45)	15 (0.49)	**484.09**	**< 0.001**
Hypomanic disorder	3 (1.60)	75 (2.49)	0.58	0.620
Suicide risk	76 (40.64)	214 (8.75)	**176.84**	**< 0.001**
Panic disorder	9 (4.81)	48 (1.59)	**10.37**	**0.004**
Agoraphobia	9 (4.81)	108 (3.59)	0.43	0.500
Separation anxiety disorder	2 (1.06)	78 (2.59)	1.67	0.320
Social phobia	12 (6.41)	336 (11.18)	3.63	0.056
Specific phobia	19 (10.16)	628 (20.89)	**11.90**	**< 0.001**
Generalized anxiety disorder	33 (17.64)	15 (0.49)	349.50	**< 0.001**
Obsessive-compulsive disorder	3 (1.60)	-	-	-
Post-traumatic stress disorder	6 (3.20)	30 (0.99)	**7.71**	**0.010**

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Adjustment disorder	7 (3.74)	-	-	-
Alcohol use disorder	3 (1.60)	96 (3.19)	1.48	0.200
Substance use disorder (non-alcohol)	10 (5.34)	39 (1.29)	**19.10**	**< 0.001**
Conduct disorder	11 (5.88)	90 (2.99)	**3.89**	**0.040**
Oppositional defiant disorder	26 (13.90)	150 (4.99)	**25.15**	**< 0.001**
TIC disorder	4 (2.13)	-	-	-
Attention–deficit/hyperactivity disorder	39 (20.85) [b]	48 (1.59)	**239.05**	**< 0.001**
Psychotic disorder	13 (6.95)	-	-	-

Abbreviations: ED, eating disorders; X^2, Square Chi

Notes: Bold indicate significant statistical p-value <0.05; Fisher´s exact test was applied when values were <5

[a] Benjet, C., et al., Youth mental health in a populous city of the developing world: results from the Mexican Adolescent Mental Health Survey. J Child Psychol Psychiatry, 2009. 50(4): p. 386-95.

[b] Analysis between groups X^2= 6.13; p = 0.04

3.3 Attention-deficit/hyperactivity disorder prevalence was different between the diagnosis of ED and could modulate BMI

Further, we compared the differences in prevalence between the groups of ED diagnosis (i.e differences between AN, BN and BED). ADHD was the only comorbidity with significative difference between the groups (Table 2; Figure 1). Patients diagnosed with BED (31.37%) had the highest prevalence of ADHD, compared to BN (19.23%) and AN (9.38%). The comparison of prevalence stratified by ED diagnosis and statistical results of the comparisons are shown in Table 2.

Table 2. Comparison of psychiatric comorbidities in Mexican patients with eating disorders.

Psychiatric comorbidity	**AN n=32 n (%)**	**BN n=104 n (%)**	**BED n=51 n (%)**	***X²***	***p-value***
Mood disorders	23 (71.88)	80 (76.92)	37 (72.55)	0.53	0.767
Major depressive disorder	14 (43.75)	55 (52.88)	29 (56.86)	1.37	0.502
Dysthymic disorder	8 (25.00)	21 (20.19)	13 (25.49)	0.69	0.706
Hypomanic disorder	0	3 (2.88)	0	2.43	0.745

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Suicide risk	9 (28.13)	47 (45.19)	20 (39.22)	3.01	0.221
Anxiety and stressor related disorders	9 (28.23)	33 (31.73)	23 (45.10)	3.44	0.178
Panic disorder	1 (3.13)	4 (3.85)	4 (7.84)	1.43	0.578
Agoraphobia	1 (3.13)	4 (3.85)	4 (7.84)	1.43	0.578
Separation anxiety disorder	1 (3.13)	1 (0.96)	0	1.84	0.387
Social phobia	2 (6.25)	6 (5.77)	4 (7.84)	0.24	0.917
Specific phobia	3 (9.38)	13 (12.50)	3 (5.88)	1.66	0.452
Generalized anxiety disorder	4 (12.50)	17 (16.35)	12 (23.53)	1.91	0.411
Obsessive-compulsive disorder	1 (3.13)	2 (1.92)	0	1.36	0.575
Post-traumatic stress disorder	1 (3.13)	2 (1.92)	3 (5.88)	1.72	0.381
Adjustment disorder	0	2 (1.92)	5 (9.80)	**7.39**	**0.042**
Substance-related and addictive disorders	0	9 (8.65)	2 (3.92)	3.79	0.178
Alcohol use disorder	0	3 (2.88)	0	2.43	0.745
Substance use disorder (non-alcohol)	0	8 (7.69)	2 (3.92)	3.14	0.232
Disruptive, Impulse-control and conduct disorders	2 (6.25)	18 (17.31)	10 (19.61)	2.88	0.228
Conduct disorder	1 (3.13)	7 (6.73)	3 (5.88)	0.57	0.913
Oppositional defiant disorder	2 (6.25)	16 (15.38)	8 (15.69)	1.89	0.454
Neurodevelopment disorders	3 (9.38)	21 (20.19)	16 (31.37)	**5.85**	**0.058**

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TIC disorder	1 (3.13)	1 (0.96)	2 (3.92)	1.61	0.284
Attention – Deficit / hyperactivity disorder	3 (9.38)	20 (19.23)	16 (31.37)	**6.13**	**0.046**
Psychotic disorder	1 (3.13)	8 (7.69)	4 (7.84)	0.87	0.791

Abbreviations: AN, anorexia nervosa; BN, bulimia nervosa; BED, binge eating disorder; X^2, Square Chi

Notes: Bold indicate significant statistical p-value <0.05; Fisher´s exact test was applied when values were <5

Psychotic disorder was considered as schizophrenia spectrum

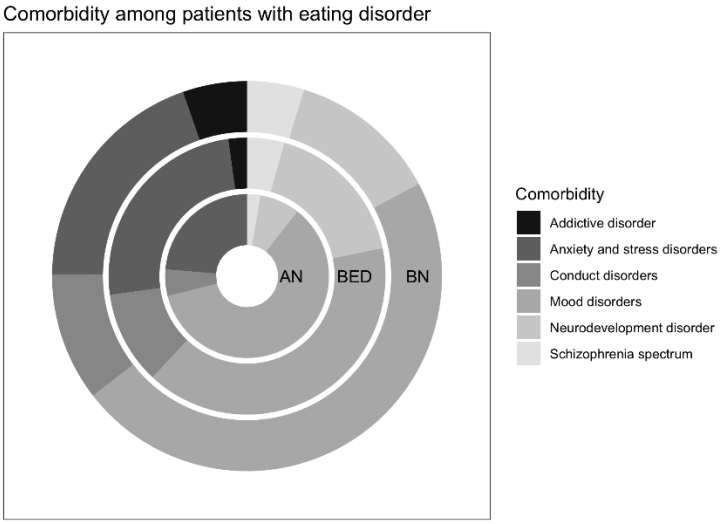

Figure 1. Comorbidity among patients with eating disorder.
Abbreviations: AN, anorexia nervosa; BN, bulimia nervosa; BED, binge eating disorder.

In order to explore the effect that this comorbidity (i.e ED and ADHD) could have in the BMI in the adolescents, we compared the differences of the BMI between individuals with ED-ADHD and those that did not have ADHD. We made comparisons of z-BMI for the patients with BN and BED. The individuals with BED and ADHD have a higher prevalence of obesity, compared to individuals with BED without ADHD (p=0.0481) (Table 3). Even, individuals with BED and ADHD have higher z-BMI that those individuals with BN and ADHD (p=0.0009). (Figure 2).

Table 3. Comparisons between BMI diagnoses in patients with BN and BED with the presence or absence of ADHD in Mexican adolescent population.

	Bulimia nervosa	**Binge eating disorder**

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BMI diagnoses	No ADHD (n = 83)	ADHD (n = 20)	X^2; *p*-value	No ADHD (n = 35)	ADHD (n = 16)	X^2; *p*-value
Normal weight	45 (54.22)	13 (65.00)	1.07; 0.586	8 (22.86)	2 (12.50)	**6.00; 0.048**
Overweight	17 (20.48)	4 (20.00)		11 (31.43)	1 (6.25)	
Obesity	21 (25.30)	3 (15.00)		16 (45.71)	13 (81.25)	

Abbreviations: ADHD (attention-deficit/hyperactivity disorder), X2 (Chi square).
Note: Bold indicates p<0.05

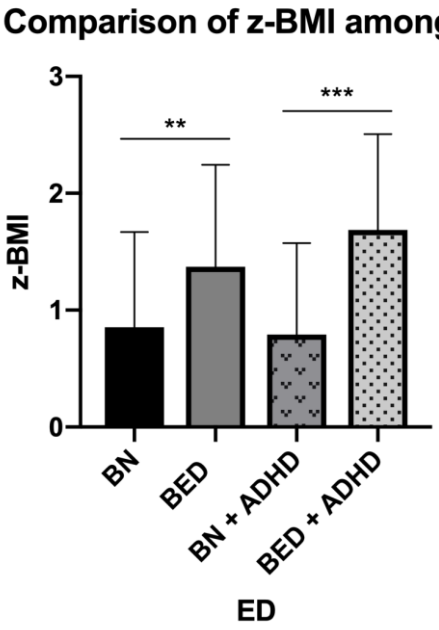

Figure 2. Comparison of z-BMI values among patients with ED and ED-ADHD
Abbreviations: ED, eating disorders; AN, anorexia nervosa; BN, bulimia nervosa; BED, binge eating disorder; ADHD, attention-deficit/hyperactivity disorder.
Notes: ** indicates p = 0.017; *** indicates p = 0.009

4. Discussion

In the present work, we performed an analysis of the prevalence of psychiatric comorbidities in adolescents' individuals diagnosed with eating disorders in a Mexican sample. In our sample, we found a high prevalence of mood disorders among patients with eating disorders. Our results are similar with previous studies, were an increased in mood disorders in patients with ED has been reported [20, 21]. Patients diagnosed with BED were found to have higher levels of comorbidity when compared with patients with AN or BN [21]. In this sense, criteria for the diagnosis of BED has been recently developed and the presence of comorbidity between this diagnostic group has been scarcely explored. These increase in the prevalence of other psychiatric comorbidities in patients with ED, could result in a negative impact on illness course and possible in treatment outcome

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[22]. Noteworthy, almost 40% of the individuals diagnosed with BN or BED presented suicide risk and the prevalence is even 30% higher that the reference sample.

The estimates of suicide risk in our population is in accordance with other reports, where an estimation with a range of 40 to 60% has been reported [23-25]. Suicide risk could be a marker of another suicide conducts, like suicide attempt or suicide completion [26]. This higher prevalence of suicide risk in the population with ED, has to be a point to considered in further analysis, due the high risk in mortality associated to suicide which could be even increased in adolescents diagnosed with ED. In this sense, a follow-up of the effect that these comorbidities could have on the development of the disorder has to be explored, but this analysis is outside of the aims of the present study.

Our findings showed that almost 50% of the individuals diagnosed with ED, presented overweight or obesity, mainly patients with BN and BED. There is a close relationship between alteration of eating-patterns and changes in the modulation of BMI [27, 28]. Even when the mechanisms underlying this relationship is stilled under investigation, some hypothesis has been generated [29]. In this sense, one hypothesis suggested that alterations in body weight (i.e overweight or obesity) are processes influenced by a dysregulation on neurobiological circuits that control some behaviors, like impulsivity and reward sensitivity [30]. These alterations in the regulation of reward-impulsivity neurobiological circuits could lead to uncontrolled eating, those are the main points of discussion around this hypothesis. The regulations of these impulsivity-reward brain circuits have been mapped to brain areas like ventral tegmental area, lateral hypothalamus, prefrontal cortex, amygdala and hippocampus [31, 32]. Some findings had also reported alterations in these impulsivity-reward brain circuits in patients with ED, which could be a link between these complex traits [33-35]. Our results could be reinforcing this hypothesis (i.e alteration of impulsivity-reward brain circuits in ED diagnosed patients).

A relationship found between ADHD, BED and obesity. Similar results were found in childhood and adults, from other populations [36]. In this effect of ADHD and eating behavior, some results have point-out a genetic risk factor that could be modulating this relationship, the Fat-mass and obesity associated gene (FTO). FTO is known as a post genome-wide association study (GWAS) gene, this appellation was stablished because the association of FTO and BMI was discovered by a mean of a molecular technique known as GWAS [37]. In recent studies, genetic variants on FTO, principally the tag-SNP (rs9939609), has been stablished as genetic risk factor for ED and ADHD [38-40]. Another FTO gene polymorphism (rs1421085, in high correlation with rs9939609) has been associated with alterations on brain areas principally regulating impulsivity [41]. Also, FTO genetic variants (rs9939609), has been associated to alcohol dependence [42]. The possible relationship of FTO in ED-ADHD and impulsivity-reward alterations, remain undercover but is an interesting one to further explore [43]. Our study had some limitations, the patients recruited in our work, was considerably small in comparison with the reference sample. However, larger sample could asseverate the differences founded in our preliminary results.

5. Conclusions

In conclusion, we observed a high prevalence of depressive disorders and anxiety- and stressor-related disorders among adolescents' patients with eating disorders. Patients with eating disorders had higher prevalence of comorbidities in comparison with reference sample. Finally, patients with BED had higher prevalence of ADHD and this comorbidity could be impacting directly on BMI. This emphasizes the importance that clinicians take into consideration the presence of psychiatric comorbidities to achieve an integrative treatment for patients with ED.

Author Contributions: Conceptualization, IEJR, TBGC, CATZ, ES, NS and ADGM; methodology, DRR, JJMM, ARG, IEJR, TBGC, CATZ, ES, MLLN, NS and ADGM; software, DRR, JJMM, ARG,

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IEJR, TBGC, CATZ, ES, MLLN, NS and ADGM; validation, DRR, JJMM, ARG, IEJR, TBGC, CATZ, ES, MLLN, NS and ADGM; formal analysis, JJMM, TBGC, CATZ, ES, NS and ADGM; investigation, DRR, JJMM, ARG, IEJR, TBGC, CATZ, ES, MLLN, NS and ADGM; resources, DRR, JJMM, ARG, IEJR, TBGC, CATZ, ES, MLLN, NS and ADGM; data curation, DRR, JJMM, IEJR, TBGC, CATZ, MLLN, NS and ADGM; writing—original draft preparation, DRR, JJMM, ARG, IEJR, TBGC, CATZ, ES, MLLN, NS and ADGM; writing—review and editing, DRR, JJMM, TBGC, CATZ and ADGM; visualization, ARG, IEJR, TBGC, CATZ, ES, MLLN, NS and ADGM; supervision, DRR, JJMM, ARG, IEJR, TBGC, CATZ, ES, MLLN, NS and ADGM; project administration, DRR, JJMM, ARG, IEJR, TBGC, CATZ, ES, MLLN, NS and ADGM; funding acquisition, DRR, JJMM, ARG, IEJR, TBGC, CATZ, ES, MLLN, NS and ADGM. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Instituto Nacional de Medicina Genómica (INMEGEN) (approbation number: 06/2018/I) and the children´s psychiatric hospital "Dr. Juan N. Navarro".

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to the confidentiality of the data and the signing of the informed consent.

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Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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