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RESEARCH ARTICLE

Psychiatric disorders among offspring of patients with Bipolar and Borderline Personality Disorder

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Abstract

Objective: As part of a larger study investigating biological risk factors for bipolar disorder (BD) and borderline personality disorder (BPD), we investigated the prevalence of psychiatric diagnoses presented by young BD or BPD offspring. With respect to the scarcity of studies interested in psychiatric disorders among BPD offspring, we have chosen to report these results despite the small sample size for a prevalence study.

Method: We recruited 21 BD and 22 BPD offspring and 23 control subjects. All subjects were assessed with a structured interview.

Results: Our main finding suggests that BPD offspring present a higher rate of psychiatric disorders compared to BD offspring. Attention deficit and hyperactivity disorder was the most prevalent disorder.

Conclusion: Our results contribute to the evidence that offspring of patients with BPD, are at high risk with regard to their mental health and deserve both more research and special attention at the clinical level.

KEYWORDS

attention deficit and hyperactivity disorder, bipolar disorder, borderline personality disorder, diagnosis, high risk

*Nader Perroud and Camille Piguet are joint last authors.

1 | INTRODUCTION

Parental mental illness puts offspring at risk of developing psychiatric disorders. Evidence indicates that familial risk is important, with children of parents with any mental disorders have increased risk for a wide range of psychiatric disorders, not only for concordant disorders but also for nonconcordant ones, with a higher impact of having two rather than one affected parent (Dean et al., 2010). For bipolar disorder (BD) specifically, numerous studies have demonstrated an elevated risk of developing any psychiatric disorders among offspring. Lau et al. (2018) lead a meta-analysis and reported that compared to control offspring, BD offspring are nine times more likely to present a bipolar-spectrum disorder, almost two and a half times more likely to develop a non-BD affective disorder and over two times more likely to develop at least one anxiety disorder. They also found that high-risk offspring showed a significantly increased risk of other nonaffective psychopathologies, such as attention deficit hyperactivity disorder (ADHD), or any type of behavioral disorder and substance use disorder (SUDs). In another longitudinal study started in the Netherlands, the authors found that overall, 72% of the BD offspring developed a lifetime *DSM-IV axis I* disorder, in particular, 54% of the offspring group were diagnosed with a mood disorder, and 13% with a bipolar-spectrum disorders (Mesman, Nolen, Reichart, Wals, & Hillegers, 2013). A similarly designed study in Switzerland also showed elevated rates of mood disorders among offspring of BD proband (34.5%) as compared to offspring of parents with major depressive disorder (MDD; 25.5%) and to those of controls (12.6%; Vandeleur, Rothen, Castelao, & Vidal, 2012).

Far fewer studies evaluated psychic health in offspring of patients suffering from a borderline personality disorder (BPD). BPD is a complex disorder whose etiology is believed to be the result of gene–environment interactions, with early-life adversities playing a major role (Gunderson, Fruzzetti, Unruh, & Choi-Kain, 2018). Weiss et al. (1996) reported ADHD as being the most frequent disorder among a cohort of 21 offspring of mothers with BPD (in 43% of the BPD offspring sample). To our knowledge, this is one of the few studies that assessed current psychiatric diagnoses in BPD offspring. Other studies, often not recent, have described clinical symptoms or attachment style in BPD. One study assessed 23 children of mothers with BPD in comparison to three other groups, including children of mothers with no known disorders (Barnow, Spitzer, & Grabe, 2006). Their results showed significant differences between the BPD offspring group and control groups on the frequency of self-rated symptoms of anxiety/depression, emotional problems, and self-esteem. More recently, a qualitative survey explored mental health clinicians' opinions regarding the impact of a parental diagnosis of BPD on offspring (Bartsch, Roberts, Davies, & Proeve, 2015b). The most prominent issues reported in offspring of BPD patients by clinicians were behavioral problems, in particular exhibition of signs of impulsivity, self-harming behaviors, suicide attempts, and parentification. Eyden, Winsper, Wolke, Broome, and MacCallum, (2016) published a systematic review of parenting and outcomes experiences for offspring of mothers with borderline personality pathology. In their review, based on 33 studies, the authors reported that adverse outcomes for BPD offspring include BPD symptoms, internalizing (including depression) and externalizing problems, insecure attachment patterns, and emotional dysregulation. These authors suggested that vulnerability may be partly transmitted from mother to offspring via maladaptive parenting and maternal emotional dysfunction. However, their conclusions were limited by the low number of studies, studies' heterogeneity in methodology and construct definitions, as well as a paucity of clinical comparison groups.

Several factors may explain this somewhat expected increased risk of psychopathological symptoms in children of BPD patients, from the genetic transmission to parent–child interaction, including known environmental factors such as child maltreatment or other trauma (Distel et al., 2008). Indeed, parents suffering from BPD may face more difficulty coping with children, putting them at increased risk of being exposed to early-life adversities and thus of developing psychopathological traits (Barnow et al., 2013; Eyden et al., 2016). In this perspective, Weiss et al. (1996) found increased rates of placement outside the family, sexual abuse and physical neglect in offspring of BPD parent compared to a group of offspring of mother suffering from depression or a group of offspring of mother suffering from Avoidant, Dependent, or Obsessive-compulsive personality disorder (former Cluster-C personality

disorder). Altogether, these studies seem to indicate the increased occurrence of psychiatric disorders, higher impulsivity, and a higher frequency of borderline symptomatology in offspring of BPD subjects compared to controls (White, Gunderson, Zanarini, & Hudson, 2003).

We know that BD and BPD are frequently comorbid and might share common cognitive traits and risk factors (Frías, Baltasar, & Birmaher, 2016). However, no former study has directly compared the prevalence of psychiatric disorders in BD and BPD offspring. Given the expected vulnerability of BPD offspring and similarities with BD offspring but the paucity of existing data in the literature, we decided to examine the actual prevalence of psychiatric disorders among offspring of parents with BD, with BPD or with no psychiatric disorder. We hypothesized that offspring with a parent diagnosed with either BD or BPD would be more likely to present a higher rate of lifetime psychiatric disorder than control subjects with no parent diagnosed with a psychiatric disorder. We also hypothesized that the prevalence of diagnoses would be qualitatively and quantitatively different between the two high-risk populations.

2 | METHODS

2.1 | Population

The clinical data in the present study were gathered as part of a larger project, assessing the vulnerability to BD and BPD also in terms of brain circuit and associated biomarkers (Berchio, Piguet, Gentsch et al., 2017; Berchio, Piguet, Michel et al., 2017). Our sample included 21 offspring with at least one parent with BD (BDOFF), 22 offspring with at least one parent with BPD (BPDOFF), and 23 controls subjects (CTRL). The offspring were between 15 and 25 years of age at inclusion. Proband parent were outpatients from the Geneva University Hospital (HUG), followed either in the Mood Disorder Unit (TH) for BD patients, or in the Emotional Dysregulation Unit (TRE) for BPD patients. BPD diagnostic in the proband was established with the Structured Clinical Interview for *DSM-IV axis II* personality disorders (*SCID-II*; First, Gibbon, Spitzer, & Benjamin, 1997) as part of the TRE standard evaluation. BD diagnostic in the proband was established with the Mini-International Neuropsychiatric Interview (MINI; Hergueta, Baker, & Dunbar, 1998) as part of the TH standard evaluation. Control subjects were matched for age, gender, laterality, and years of education, and were recruited through advertisements placed at the University of Geneva and on classified web sites. Inclusion criteria were age, no history of psychiatric or neurological treatment for the subjects, and no reported history of a psychiatric disorder for their parents, as assessed during the interview of the subject. All participants gave written informed consent before assessment. Offspring of BD and BPD patients were recruited after their parents gave formal consent to contact their children. The research was conducted according to the principles of the Declaration of Helsinki and was approved by the University of Geneva research ethics committee (CER 13–081).

2.2 | Procedure

Both offspring and controls were assessed by trained psychologists (A.-L. K., E. P., and P. C.). Participants younger than 18 years of age were assessed with the French version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Kaufman et al., 1997). Participants older than 18 years of age were assessed with the French version of the Diagnostic Interview for Genetic Studies (DIGS; Preisig et al., 1999). Although we were not able to directly interview the parents of the controls subjects, careful questioning was done with the participant regarding the medical history of his/her parents. The same goes for BDOFF and BPDOFF coparent, for which information regarding their mental health was only collected through their offspring's declarative statement during the inclusion interview. Among offspring and controls, as risk for BPD is not included in the DIGS/KSADS, it was evaluated with an in-house self-report screening questionnaire, including nine items referring each to one of the diagnostics criteria for BPD in *DSM-IV-TR* (Keizer, McQuillan & Bieler, 1999). The

answer to each item is binary (Yes or No). If the number of "Yes" answers is five or above, the subject is considered above the cutoff and at risk for BPD (Michalopoulos, 2015).

2.3 | Statistical analysis

Descriptive and analytic statistics were performed using STATA 13.0 software (Statacorp, 2013). Univariate comparisons between groups were conducted using the Pearson χ^2 test for the qualitative variable (gender), and one-way analysis of variance (ANOVA) for quantitative variables (age and year of education).

To compare the prevalence of each disorder among our groups, we conducted a one-way ANOVA with Tukey's post hoc comparisons. Statistical significance was accepted for $p < .05$.

3 | RESULTS

3.1 | Demography

As control subjects were matched with offspring subjects, all groups do not differ with respect to gender, age, and year of education. Descriptive data are reported in Table 1.

3.2 | Prevalence of psychiatric disorders

Seven (33.3%) BDOFF subjects, 16 (72.7%) BPDOFF subjects and two (8.7%) control subjects met criteria for at least one lifetime *DSM-IV-TR* diagnosis as reported in Table 2.

Subjects having a parent diagnosed with BPD are more likely than the other groups to develop at least one disorder before the age of 25. Whereas the BDOFF group showed a significantly higher rate of any psychiatric disorder in general, there was no significant difference with the control group for a specific disorder. On the contrary, offspring of parents diagnosed with BPD had significantly elevated rates, compared to controls, for the following disorders: substance use disorders, major depressive episode, anxiety disorders, and ADHD (see Table 2). For BPD, the numbers of subjects reporting five or more BPD symptoms is significantly higher in the BPDOFF group (See Table 2). With respectively, 19.0% and 54.3% of the BDOFF and BPDOFF suffering from ADHD, our results showed that ADHD is the most prevalent disorder in both BDOFF and BPDOFF groups. Our results also showed that BPDOFF presents more ADHD than BDOFF.

4 | DISCUSSION

Our study compared directly for the first time the offspring of BD and BPD to control subjects in terms of psychiatric disorders. We showed that 15–25-year-old offspring with at least one parent with BD or BPD are more at risk to present psychiatric disorders than controls, as hypothesized from the existing literature. Moreover, our results suggested that BPDOFF differ from BDOFF, presenting an elevated rate of psychopathology. In particular, symptoms of BPD and prevalence of ADHD were increased in BPDOFF. Here, we discuss first separately, findings in BDOFF, then BPDOFF, before drawing tentative conclusions given our small samples.

In the BDOFF group, 33.0% of the subjects were diagnosed with any type of disorders, significantly more than in the control group. However, this rate is lower than the one reported by Vandeleur et al. (2012), in another Swiss cohort, reporting a prevalence for any type of disorder of 61.9%, or the one from the Pittsburg cohort with a rate of 66.0% (Birmaher et al., 2009). Moreover, we did not find a significant difference between the BDOFF group and the control group regarding individual diagnosis (mood disorder, BD, anxiety, ADHD, or SUD). This is also in opposition with findings from epidemiological cohorts from different countries (Dutch, Canadian, or American [Axelson et al., 2015;

TABLE 1 Demographic Characteristics of BDOFF, BPDOFF, and CTRL

	BDOFF		BPDOFF		CTRL	
	(*N* = 21)		(*N* = 22)		(*N* = 23)	
	n	%	*n*	%	*n*	%
Gender						
Man	9	42.9	10	45.5	10	43.5
Mother with disorder	9	42.9	22	100	–	–
Father with disorder	12	57.1	0	–	–	–
Marital status						
Single	20	95.2	22	100	23	100
Married	1	4.8	0	–	0	–
Socioprofessional category						
Active	2	9.5	3	13.6	2	8.7
Unemployed	0	–	3	13.6	2	8.7
Students	19	90.5	16	72.8	19	82.6
	m	*SD*	m	*SD*	m	*SD*
Age (years)	19.4	3.1	20.2	3.7	20.0	3.1
Year of education	13.6	2.6	12.9	3.2	13.8	3.1

Abbreviations: BDOFF, offspring with at least one parent with bipolar disorder diagnostic; BPDOFF, offspring with at least one parent with borderline personality disorder diagnostic; CTRL, control subjects.

TABLE 2 Lifetime prevalence of psychiatric disorders among BDOFF, BPDOFF, and CTRL and group comparison

	OFFBD N = 21		OFFBPD N = 22		CTRL N = 23					
	n	%	*n*	%	*n*	%	*F* (df = 14)	*p* value	Post hoc A = OFFBD; B = OFFBPD; C = CTRL	Summary statistic R^2
Total substance misuse	3	14.3	6	27.3	1	4.3	1.36	.048*	C = A; A = B; C < B	0.082
Lifetime major depression	3	14.3	9	40.6	1	4.3	2.68	.007*	C = A < B	0.472
Bipolar disorder	1	4.8	1	4.5	0	–	0.54	.588	C = A = B	0.016
At risks of BPD	5	23.8	8	36.4	1	4.3	5.4	<.001*	C < A = B	0.597
Anxiety disorder	3	14.3	7	31.8	1	4.3	3.29	.044*	C = A < B	0.095
ADHD	4	19.0	12	54.5	1	4.3	2.32	.015*	C = A; A = B; C < B	0.389
Eating disorder	2	9.5	0	–	0	–	0.99	.477	C = B = A	0.232
Disorder of any type	7	33.3	16	72.7	2	8.7	3.13	.001*	C = A < B	0.462

Abbreviations: ADHD, attention deficit and hyperactivity disorder; BDOFF, offspring with at least one parent with bipolar disorder diagnostic; BPD, borderline personality disorder; BPDOFF, offspring with at least one parent with borderline personality disorder diagnostic; CTRL, control subjects.

*$p < .05$.

Duffy et al., 2014; Mesman et al., 2013]). Our results for ADHD prevalence were also lower than in the US cohort (Axelson et al., 2015) but higher than in the Dutch or Swiss cohort (Mesman et al., 2013; Vandeleur et al., 2012). Our BDOFF group seems therefore rather "healthy" despite a slight increase in the level of psychopathological traits overall. Several factors might contribute to explain the relatively low rates of psychiatric disorders in our BDOFF group. First, the small sample size might explain that differences between BD patient's offspring and control subjects did not reach a significant level for any given disorder for lack of statistical power. Second, given that offspring were recruited for the purpose of a wider study including EEG and MRI assessment, it is possible that we are facing a selection bias with relatively "high-functioning" offspring, interested in scientific work. Third, we might also hypothesize that the proband who gave their consent to contact their offspring were the most secure about their offspring's well-being. Although all these factors might partially explain our lower rates of psychiatric disorders in BDOFF compared to the existing literature, they certainly do not explain all the reported main result of the difference between BDOFF and BPDOFF, recruited by the same method.

Importantly, an additional factor explaining the increased rate of psychiatric disorders in other BDOFF cohorts could be that the majority of studies in the field did not screen the BD proband for BPD when recruiting the offspring subjects. Since Fornaro et al. (2016) reported a 22% rate of BPD comorbidity among BD, we might expect that in BDOFF studies, a certain amount of BD parent was also suffering from BPD. When looking at the impact of BPD on offspring, we might hypothesize that a fraction of the results obtained in BD offspring studies might be imputed on BPD comorbidity. Given the comorbidity between BD and BPD, the reported rate of psychopathology in BD offspring could be inflated due to the underevaluation of BPD in proband. It indicates the need to screen for BPD in BD proband in epidemiological studies, as BPD seems to have an important impact on offspring psychopathology.

The main and newest finding in our study is the fact that in the BPDOFF group 73.0% of the subjects were diagnosed with at least one disorder of any type. This prevalence is significantly higher than the ones found for both BDOFF and controls groups. The rates of BPDOFF who experienced at least one major depressive episode in our cohort reached 40.0%, whereas in their review White et al. (2003) reported a prevalence which ranged from 4.6% to 31.2% for major depression disorder in relatives (and not exclusively offspring) of BPD proband. In the only study on BPDOFF reporting psychiatric disorders, authors found a significantly higher prevalence of diagnoses among BPDOFF than in a group of offspring with parents with other mental disorders; unfortunately, they did not report rates of specific disorders (Weiss et al., 1996). In a more recent study, BPDOFF reported significantly higher score on both the Youth Self-Report Anxiety/Depression subscales and on the Child Behavior Checklist Anxiety/Depression subscale than community controls and offspring of parents with other mental disorders (Barnow et al., 2006).

Regarding anxiety disorder, 31.8% of our sample had been diagnosed with an anxiety disorder. This is significantly higher compared to controls (4.3%), but not compared to BDOFF (14.3%). To our knowledge, no other study reported a prevalence of anxiety disorder among BPDOFF to compare our result with.

Interestingly, the most prevalent diagnosis among BPDOFF is ADHD, with a rate higher in this group than in BDOFF and CTRL groups. This 54.0% rate is more than twice the rate encountered within BDOFF (19.0%) and tenfold the prevalence in CTRL, leading to an elevated risk of ADHD in this population compared to BDOFF. Again, in the only study previously reporting the prevalence of diagnosis in BPDOFF, the rates of ADHD diagnosis among BPDOFF reached 43.0% (Weiss et al., 1996). The sample size in this study was about the same as in ours, however, the authors recruited BPD mothers from a previous study and reported that they had to the extent their inclusion criteria to lifetime-BPD symptoms as some mothers did not complete a full BPD diagnostic at inclusion time. Nevertheless, among the scarce literature dealing with the offspring of mothers with BPD, and although ADHD prevalence was rarely reported, impulsivity and inattention are a central concern often mentioned. Consistently with our findings, Barnow et al. (2006) reported a significantly elevated score for the Youth Self-Report Attention subscale in BPD proband's offspring compared to CTRL (although they showed no difference on the CBCL scale). Clinicians who took part in the Bartsch, Roberts, Davies, and Proeve (2015a) study commonly reported impulsivity as a BPDOFF feature.

Finally, a similar pattern as the one found for depression and anxiety disorders was found for substance use disorder. It was significantly more present among BPDOFF (27.3%) than among CTRL (4.3%), but again the difference with BDOFF (14.3%) did not reach the significance level. Among previous studies, only one reported the prevalence of alcohol use disorder, which reached 50.0% in the BPDOFF sample (Barnow et al., 2006).

To conclude, our results suggest that BPDOFF might be more at risk for any psychiatric disorder than both community control and BDOFF. Regarding specific diagnosis, compared to the control group, they might have an elevated risk of developing mood and anxiety disorders, ADHD, and substance use disorder. Compared to the BDOFF group, they seem to present an elevated risk of developing ADHD.

As this study is not primarily designed as an epidemiologic study, several limitations can be identified. First, we are very aware that the size of our sample is small, making this study a preview of further investigations to be made among BPDOFF. Second, by its design, our study is a picture at a given time, and a follow-up might show increased rate in all disorder assessed and bring our sample closer from the other cohorts. These factors might contribute to explain why differences between groups might be underestimated. However, given the striking difference in the prevalence of psychiatric disorders between BPD and BD offspring, we hypothesize that it would remain significant.

In their study Dean et al. (2010) clearly demonstrated that having two parents with a psychiatric diagnostics put offspring at a higher risk of psychiatric disorder. Therefore, another major limitation to our work is the lack of information regarding the coparent. As the only information, we had relied on the offspring report, we did not take this factor into consideration. The rather modest psychiatric disorder prevalence among our BDOFF group advocate for a small impact of the coparent mental health status. Regarding the BPDOFF, the question might be harder to address as BPD patient tend to report more chaotic relationships (Bouchard, Sabourin, Lussier, & Villeneuve, 2009). On the one hand, the coparent's presence/absence or mental health status might thus also contribute to the difference of prevalence of psychiatric disorders between BDOFF and BPDOFF, but on the other hand the differences found between our groups tend to show that even with one parent with a diagnosis of BPD the risk of psychiatric disorder is increased.

We also had three sets of siblings among our BDOFF group and three among the BPDOFF group. Looking at our sample sizes, we decided to take individuals as a primary unit of analysis although it would have been better to use families as the analyses unit. However, in studies in which both the child and the family were used as a unit of analysis, there is few if any difference in the results (Hammen et al., 1987; Weiss et al., 1996).

Finally, regarding the difference between BDOFF and BPDOFF, one major confound was the gender of the parent identified with a psychiatric disorder. Among the BPDOFF group, all the subjects were offspring of mothers with BPD whereas in the BDOFF group, diagnosed mother represent only 42.9% of the sample. Different studies showed that the mother diagnostic has more impact (Moreno et al., 2012), so along with the BPD diagnostic, the parent gender might also explain the higher rate of psychiatric disorder among BPDOFF.

As explained above, this study is part of a larger neuroimaging project, although our work is not an epidemiological study and cannot answer definitively the question of the rate of psychiatric disorders in offspring of BPD patients, it raises the concern that this population might be particularly vulnerable. It also demonstrates that both populations of offspring of BPD and BD patients might share some common vulnerability traits as inattention/impulsivity, but that they also differ in the severity of the psychopathological symptoms. Further studies on BDOFF should systematically screen for BPD in proband.

Even if the inclusion process might have contributed to undermining the prevalence of substances abuses among the offspring group and the high level of functional outcomes, it might also be important to notice that our cohorts are recruited almost 20 year after major cohorts such as the Pittsburg or the Dutch cohort. Over this period, awareness about mental illness and its impact on immediate relative rose, this might partially explain our lower rates of psychopathologies among BDOFF compare to literature. Another hypothesis that needs to be tested is that specialized care of proband might have a positive effect on offspring. Indeed, all proband were supported by professionals, which might undermine the impact of the disorder upon their relatives as Bartsch et al. (2015a, 2015b) identified therapeutic intervention on the parent as a protective factor for their offspring. Moreover, Bella

et al. (2011) demonstrated that the offspring of parents with BD exhibit impairments in psychosocial functioning, which appear largely attributable to proband parent functional impairment. As such, interventions to improve parental functioning, as well as early interventions to treat the child's psychopathology may help reduce the risk for long-term functional impairment in offspring.

To conclude, our results suggested that offspring with at least one parent diagnosed with BPD might be more at risk for psychiatric disorders than offspring with at least one parent diagnosed with BD. With ADHD being the most prevalent diagnostic among both groups, a specific vigilance should be aimed at the offspring of both BD and BPD patients regarding this disorder. Given the small sample size of our study, this finding clearly needs to be replicated in a large sample. Nevertheless, this study contributes to the body of evidence that children of mothers with BPD are exposed to a combination of risk factors and more likely to develop emotional and behavioral problems. This study, despite the small sample size, tends to underlines the utmost importance for preventive care and the necessity to evaluated offspring of severe mental disorders patients to decrease vulnerability.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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