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Research report

Burden of maternal bipolar disorder on at-risk offspring: A controlled study on family planning and maternal care

Doris Hupfeld Moreno [a,*], Danielle Soares Bio [a], Sandra Petresco [a], Denise Petresco [a], Elisa Kijner Gutt [b], Márcio Gerhardt Soeiro-de-Souza [a], Ricardo Alberto Moreno [a]

[a] Mood Disorders Unit, Department and Institute of Psychiatry, Clinical Hospital, School of Medicine, University of Sao Paulo, Brazil
[b] Department and Institute of Psychiatry, Clinical Hospital, School of Medicine, University of Sao Paulo, Brazil

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ABSTRACT

Introduction: Bipolar disorder (BD) is a highly incapacitating disease typically associated with high rates of familial dysfunction. Despite recent literature suggesting that maternal care is an important environmental factor in the development of behavioral disorders, it is unclear how much maternal care is dysfunctional in BD subjects.
Objective: The objective of this study was to characterize maternal care in DSM-IV/SCID diagnosed BD type I subjects compared to healthy controls with (PD) and without (NPD) other psychiatric diagnoses.
Materials and methods: Thirty-four BD mothers and 106 controls underwent an interview about family planning and maternal care, obstetrical complications, and mother–child interactions. K-SADS-PL questions about violence exposure were used to ascertain domestic violence and physical/sexual abuse.
Results: BD mothers were less likely to have stable unions (45.5%; $p<0.01$) or to live with the biological father of their children (33.3%; $p<0.01$), but had higher educational level and higher rates of social security use/retirement. They also had fewer children and used less contraceptive methods than controls. Children of BD women had higher rates of neonatal anoxia, and reported more physical abuse (16.1%; $p=0.02$) than offspring of NPD mothers. Due to BD mothers' symptoms, 33.3% of offspring suffered physical and/or psychological abuse.
Limitations: Post hoc analysis, and the use of questions as a surrogate of symptoms as opposed to validated instruments.
Conclusion: This is one of few reports confirming that maternal care given by BD women is dysfunctional. BD psychopathology can lead to poor maternal care and both should be considered important environmental risk factors in BD, suggesting that BD psychoeducation should include maternal care orientation.

1. Introduction

There is a significant body of experimental evidence pointing to the importance of maternal influence on subsequent performance both in terms of physiological functions and behavior of offspring (Ressler and Anderson, 1973; Denenberg, 1999; Ottinger and Tanabe, 1969). Importantly, the nature of mother–offspring interaction influences gene expression and the development of behavioral responses in the offspring, which remain stable from early development to later stages of life (Weaver et al., 2004; Weaver, 2007; Zhang et al., 2010; Pinkernelle et al., 2009; van Hasselt et al., 2012). Essentially, environmental adversity alters mother–offspring interactions and these effects provide a basis for phenotypic plasticity. The role of biological predisposition and heritability in the development of mood disorders is universally accepted, although the influence of environmental risk factors, particularly at the family level, is also of relevance, decreasing or increasing biological risk. Psychiatric disorders affecting parents may impact the care devoted to their children, whom have been mostly investigated for depression. On the other hand, to the best of our knowledge, there are no studies characterizing maternal care in Bipolar disorder (BD), although it is a highly incapacitating mood disorder strongly influenced by environmental factors. Characterizing maternal care dysfunctions in BD would help reinforce its role as an environmental factor and incorporate maternal care orientation for BD women of reproductive age into psychoeducational guidelines. Furthermore, this characterization would open up new fields of research investigating how maternal care interacts with genetics in the development of BD.

Previous studies investigating maternal care characterization and how maternal symptomatology affects offspring have predominantly focused on depressive disorder. In two recent reviews, Dix and Meunier (2009) and Ritchie and Villebrun (2009) highlighted the as yet poorly understood influence of

* Correspondence to: Rua Dr. Ovídeo Pires de Campos, 785, CEAPESQ 3rd Floor, North Wing, Room 12, 05403-010 São Paulo, Brazil.
Tel./fax: +55 112661 6648.
E-mail address: dorismoreno@uol.com.br (D.H. Moreno).

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maternal depressive symptoms on the psychological development of offspring. In addition to familial genetic factors, the impact of maternal and paternal depression as an environmental risk factor of depression on offspring were also investigated (Ritchie and Villebrun, 2009). Interactions among parental depression, the environment and depression in youth are complex and extend to the impacts of depressive psychopathology and physiopathology on offspring. Furthermore, cognitive, affective, and motivational processes, implicated as being responsible for the impact of depressive symptoms on parenting, were investigated in a review of 152 studies. The review sought to elucidate mechanisms that may lead depressive symptoms to impair adequate parenting (Dix and Meunier, 2009). The most extensively studied condition linking characteristics of maternal care with depressive symptoms in offspring was postpartum depression. However, even in children and adolescents, depressive symptoms undermine parenting in that they reduce child-oriented goals, weaken attention to child input, increase negative appraisals of children and parenting competence, activate low-positive and high-negative emotion, and increase positive evaluations of coercive parenting. Depressive mothers of infants up to 6-months old were reported to be more irritable and hostile, less engaged, and demonstrated less emotion and warmth; this depression compromises caregiving activities as a whole, including breastfeeding, sleep patterns, and healthcare (Field, 2010).

To date, this topic has been little studied in BD but it has been suggested that both episodes and residual symptoms affect maternal care toward offspring (Alloy et al., 2006), although there has been no clear characterization of maternal care deficits. A decreased level of care may, in turn, influence the psychological development of these children (Miklowitz and Johnson, 2009). In a controlled study, 12–18-month-old children of BD parents (at least one parent) were affected in several domains, namely: affect, adaptation to new situations, and prominent avoidance (Gaensbauer et al., 1984). Furthermore, BD families are more likely to be disorganized, have less cohesion and increased likelihood of arguing; on the other hand, children are more likely to show signs of poorly adaptive functioning in areas strongly determined by maternal care, and are more likely to display aggressive behavior. Hypomania or suicidal attempts among parents are strongly correlated with suicide ideation in their children. Finally, parental BD increases chance of BD in offspring, where this may be partially influenced by familial dysfunctions (Rocher et al., 2008). Nonetheless, few studies have accounted for the role of the familial environment and impaired maternal care in assessments of familial aggregation of BD. Most studies have focused either on high risk offspring (Mowbray et al., 2006; Goldstein et al., 2010) or did not account for the effects of parental psychopathology when investigating non-genetic risk factors, such as abuse or trauma, on the development of BD (Etain et al., 2008; Alvarez et al., 2011), as if these factors were independent of parental illness. Indeed, Chang et al. (2003) failed to correlate family environment alone with offspring psychopathology or vice-versa. In a controlled study on parenting style and family environment, parental communication style was more negative and less expressive, but only currently depressed children perceived family conflict and not asymptomatic offspring or controls (Vance et al., 2008). The studies of Miklowitz et al. (2003, 2004, 2006) found expressed emotions, assessed by measurements of criticism, rejection, hostility, and emotional over-involvement, to be common in families of BD and associated with increased risk of BD at adolescence.

Bipolar disorder can impact maternal care by interfering with parenting, but may also affect family planning, gestation, delivery, and breastfeeding. Even fertility rates were lower compared to levels for the general population, at least with respect to the first or second child, in a population-based study from Denmark (Laursen and Munk-Olsen, 2010). BD increased the risk of low birth-weight and pre-term births in a nation-wide Taiwanese study (Lee and Lin, 2010). Since both genetic predisposition and familial environment may influence onset of psychiatric conditions (Faraone et al., 2003; Wamboldt and Reiss, 2006), herein we conducted a case–control study of women with and without BD. The main objective of the present study was to identify sociodemographic, family planning, delivery and maternal care characteristics that may potentially affect the development of BD in children at risk. We hypothesized that compared to controls, BD have poorer maternal care.

2. Materials and methods

2.1. Sample and procedures

This study entailed a post hoc analysis of a high-risk offspring investigation (Petresco et al., 2009). We identified 34 women with BD type I (mean age 38.2 ± 7.5 years) from the Mood Disorders Unit of the Institute of Psychiatry, Clinicas Hospital, School of Medicine, University of Sao Paulo, and 106 controls (mean age 39.7 ± 4.4 years) from the Obstetrics and Gynecology Clinics of the same hospital, 53 with mild to moderate psychiatric disorders (PD controls), and 53 with no mental disorders (NPD controls). Diagnoses were assigned according to the Structured Clinical Interview (SCID) (First et al., 1996). To be eligible for study inclusion, women had to have at least one child aged 6–18 years old. Children were assessed using the Kiddie Schedule for Affective and Schizophrenic disorders (K-SADS-PL) (Kaufman et al., 1997). Performance and functioning of the children were assessed using the Children Behavior Checklist (CBCL) (Achenbach and Dumenci, 2001). Violence exposure was ascertained using the K-SADS-PL/PTSD section asking about presence or absence of domestic violence, physical abuse and sexual abuse. To be eligible for study inclusion, BD subjects had to be in euthymia or partial remission according to DSM-IV criteria (DSM-IV 2000).

Sociodemographic characterization of the sample was done based on data from the *Brazilian Association of Research Institute* (ABEP). Details of the methods have been described elsewhere (Petresco et al., 2009).

As part of the original study, 35 questions were included in the assessment forms, in order to obtain information on family planning and maternal care, with special emphasis on reproductive planning, care during pregnancy, obstetrical complications (OC), and mother-child interactions. The questionnaire focused on the following variables: total number of pregnancies, abortions, prenatal care, use of contraceptives, medical problems during pregnancy (use of medications, acute psychiatric symptoms, psychiatric hospitalizations, accidents, physical violence, other diseases); type of delivery, and obstetrical complications (delayed delivery, premature delivery, neonatal anoxia, prolonged hospitalization of the children after maternal discharge). The assessment also verified whether children were breastfed and collected information on use of medication during this period (including BD medications). Most answers were of the "yes or no" type, with the exception of numerical type questions (number of offspring).

Information on type of household, primary person caring for the children, and whether women were in stable unions, was also collected. Finally, detailed information on type and quality of interactions between mother and child was obtained. We focused on whether children lived with the mother during acute episodes of the disease or exacerbations, as well as whether children suffered physical or psychological abuse. All these parameters were also assessed by "yes or no" type questions and when applicable, detailed information was obtained using an open

question format. The institutional ethics committee approved the study, and all patients signed the informed consent.

2.2. Statistical analysis

Statistical analyses were conducted with SPSS 14.0. Comparisons among the three groups (BD, PD, and NPD) (e.g. for demographic variables) was performed using one-way ANOVA. For univariate analyses, Student's-*t* test (for continuous variables) and Pearson's chi-square test (for categorical data) were used. To compare the groups while controlling for education, income, occupation and marital status, logistic regression (for dichotomous variables), linear regression (for continuous variables) and Poisson regression (for count data; e.g. number of offspring) were used. The significance level was set at 0.05 and all tests were two-tailed.

3. Results

Most BD women were in partial remission according to SCID (First et al., 1996) (64.1%), where 47.5% had attempted suicide at least once, and 15% at least twice. Mean duration of disease was 12.2 ($\pm$8.0) years and in 37.2% onset of disease was before the age of 18. Most had been hospitalized at least once, and 52.5% had psychotic symptoms during episodes. Comorbidities were frequent: anxiety disorders occurred in 34.9%, eating disorders in 13.9%, and substance-related disorders in 11.6%. Depressive (60.4%) or anxiety disorders (71.7%) were present in most PD controls, while few had eating disorders (7.5%) (Petresco et al., 2009).

3.1. Clinical and sociodemographic characteristics

All women with BD type I ($N=34$) were in outpatient care. Cases and controls were similar regarding age and race (Table 1). BD women were significantly less likely to be married (45.5%) or to be part of a stable union compared with PD (77.6%) and NPD (81.6%) controls, while 39.4% had never married. BD women had a higher educational level than PD ($p<0.01$) and NPD ($p=0.02$) controls, and greater familial income than PD controls ($p=0.03$). Rates of employment were similar across groups, but BD women were more likely to have received health benefits or be retired (26.5%) compared with NPD controls (4.1%) (Table 1).

3.2. Family planning

Regardless of group, less than 50% of women planned their pregnancy (Table 1). Groups did not differ with respect to past use of contraceptive methods (CCM) but chance of current use of CCM was 80% lower in BD than control subjects (Table 2); logistic regression showed that older women made less use of CCM. Women with BD had fewer children compared to both control groups ($p=0.01$), but the rate of aborting was similarly high across all groups (range 28.6–42.4%) (Table 1). During pregnancy, most women received prenatal care and a minority used medications, regardless of group. Rates of obstetric complications (OC) were the same among groups, except for neonatal anoxia, which risk was nine times greater (OR 9.17; IC 1.02–83.33) in BD subjects (16.7%; $n=5$) than NPD controls (2.1%; $n=1$) ($p=0.04$) (Table 2).

Most women breastfed their children equally in all groups, but only 8% of BD patients used medications during this period (Table 1). Type of delivery was comparable across groups.

3.3. Family attention and maternal care

Only a third of BD women lived with the biological father of their children ($p<0.01$), and 54.5% raised their children alone, whereas all lived with their offspring (Tables 1 and 2). The vast majority (97%) of the offspring of BD women lived with their mother during episodes. Of concern, was the fact that 33.3% of offspring were exposed to risks due to mother's symptoms, such as physical abuse and/or psychological abuse, while this was rare in PD controls ($p<0.01$) (Table 1). Finally, suicidal attempts in the presence of children occurred only in the BD group. Physical abuse reported by the children was more frequent in BD women (16.1%) than NPD controls (1.9%) ($p=0.046$) (Tables 1 and 2).

4. Discussion

To the best of our knowledge, only a few studies have characterized maternal care in BD, as well as reproductive planning in a controlled setting. Of concern, was the fact that BD mothers were less likely to live in stable unions or with the biological father of their children and that 33.3% of the offspring of BD mothers were at increased risk of physical and/or psychological abuse due to their mother's symptoms. Compared with NPD controls, children of BDI women had higher rates of neonatal anoxia and reported greater physical abuse.

Studying the burden of BD to the family is of fundamental importance. Indeed, this kind of familial environmental exposure should be considered a risk factor, together with the inherent biological predisposition, for incident BD in offspring. Our sample was homogeneous in terms of age and race, but women with BD were less likely to be married or to live with the biological father of the children. This may have contributed to increased exposure of children to maternal disease, since other caregivers were not sharing the household. A study on the prevalence and correlates of abuse in 446 bipolar youth, found that living in a non-intact family was a risk factor for physical and sexual abuse (Romero et al., 2009). Although women with BD tended to have greater schooling than controls, they were more likely to be retired or to receive social security support (26.5%), possibly another consequence of disease severity in our sample selected from a tertiary care center. Nevertheless, studies on 600 BD patients from the Depressive and Manic-Depressive Association (Hirschfeld et al., 2003), and 2308 individuals from the Stanley Center (Kupfer et al., 2002), reported even higher rates of unemployment (60–65%, respectively), while 40% of patients were retired or received social security, indicative of the burden of BD on global functioning.

Clinical severity did not affect family planning, since groups were similar with respect to use of contraceptives and planning pregnancy. In Brazilian women aged 15–49 years, use of contraceptives was common (51–58.7%) (Carlotto et al., 2008; Vieira et al., 2002), whereas in the United States 53.3–69.9% of women of reproductive age received some contraceptive service, either from a private doctor or publicly funded clinic (Frost, 2008).

Despite similarities in aspects of family planning, BD mothers had fewer children than psychiatric controls. Williams et al. (2007) reviewed data from research on fertility in mood disorders and found that in three out of the four studies, fertility rates were reduced in BD. Furthermore, in a controlled longitudinal population-based study in Denmark, BD patients also had lower fertility rates than other patients with non-psychotic disorders (Laursen and Munk-Olsen, 2010). These authors reported higher risk of abortions in BD patients compared with non-psychiatric controls. Nonetheless, no difference in abortion risk was found in the present study. Perhaps this is due to an abnormally high risk in all groups, since abortion rate for Brazil is 16.4% and 15% for the

Table 1
Sociodemographic, family planning, and nursing characteristics, as well as obstetric complications, familial environment and maternal care, in bipolar disorder (BD) mothers, compared to mothers without (NPD) and with other psychiatric diagnoses (PD), and violence exposure to the offspring, in a study of high-risk bipolar offspring.

	NPD	PD	BD	F	p
Age (mean)[a]	39.7 (5.7)	40.1 (4.5)	37.4 (8.1)	2.04	0.13
	n (%)	***n (%)***	***n (%)***		
Marital status[b]					**<0.01**
Married/cohabiting	40 (81.6)	38 (77.6)	15 (45.5)		
Separated/divorced/widowed	2 (4.1)	3 (6.1)	5 (15.2)		
Never married	7 (14.3)	8 (16.3)	13 (39.4)		
Ethnicity[b]					0.71
Caucasian	27 (50.9)	25 (47.2)	21 (61.8)		
Afro-descendant	8 (15.1)	7 (13.2)	4 (11.8)		
Mulatto	18 (34)	21 (39.6)	9 (26.5)		
Educational level[b]					**<0.01**
Iliterate	6 (12.2)	9 (18.4)	2 (6.1)		
High School	22 (44.9)	26 (53.1)	7 (21.2)		
College/University	21 (42.9)	14 (28.6)	24 (72.7)		
Employment status[b]					**0.03**
Employed	26 (53.1)	19 (40.4)	14 (41.2)		
Unemployed	21 (42.9)	23 (48.9)	11 (32.4)		
Social security/retired	2 (4.1)	5 (10.6)	9 (26.5)		
Familial income (%) (minimum wages)[b]					**0.07**
1–5	31 (64.6)	35 (72.9)	15 (45.5)		
6–10	15 (31.3)	11 (22.9)	13 (39.4)		
>10	2 (4.2)	2 (4.2)	5 (15.2)		
Family planning[b]					
Planned pregnancy	19 (38.8)	23 (48.9)	15 (45.5)		0.60
Used contraceptive methods	45 (91.8)	44 (89.8)	26 (78.8)		0.18
Actual use of CCM	37 (77.1)	35 (72.9)	15 (46.9)		**0.01**
Offspring (*n*)[c]	2.5 ± 1.5	2.4 ± 1.3	1.8 ± 0.9		**0.01**
Women aborting	16 (32.7)	14 (28.6)	14 (42.4)		0.42
Pregnancy[b]					
Pre-natal care	47 (97.9)	46 (97.9)	29 (96.7)		0.93
Took psychotropic medications	1 (2.1)	4 (8.5)	4 (13.8)		0.15
Trouble during pregnancy	10 (20.8)	18 (38.3)	11 (36.7)		0.14
Delivery[b]					
Trouble during delivery	19 (39.6)	15 (32.6)	9 (30)		0.64
Premature delivery	4 (8.5)	9 (19.6)	2 (6.7)		0.15
Neonatal anoxia	1 (2.1)	4 (8.7)	5 (16.7)		0.07
Type of delivery[b]					0.45
Normal	16 (33.3)	21 (44.7)	10 (33.3)		
Cesarean	27 (56.3)	25 (53.2)	18 (60)		
Forceps	5 (10.4)	1 (2.1)	2 (6.7)		
Breastfeeding[b]					
Breastfed baby	44 (91.7)	37 (80.4)	24 (80)		0.23
Took psychotropic medications	3 (7.7)	4 (11.4)	2 (8)		0.84
Familial environment and maternal care[b]					
Child lives with father	34 (69.4)	36 (73.5)	11 (33.3)		**<0.01**
Child lives with mother	48 (100)	46 (97.9)	33 (100)		0.42
Mother needed alternative caregiver	24 (49)	25 (52.1)	23 (69.7)		0.15
Child lived with mother during episodes		9 (23.1)	32 (97)		**<0.01**
Child at risk due to symptoms of mother		1 (2.6)	11 (33.3)		**<0.01**
Violence exposure of child[b]					
Domestic violence	7 (13.2)	7 (13.5)	8 (25.8)		0.25
Physical abuse	1 (1.9)	2 (3.8)	5 (16.1)		**0.02**
Sexual abuse	1 (1.9)	4 (7.7)	1 (3.2)		0.33

Significant differences are presented in bold ($p < 0.05$).

[a] ANOVA.
[b] Pearson chi-square.
[c] Kruskal–Wallis.

State of São Paulo, much lower figures than the 42.4% reported among BD women, or 32.7% and 28.6% in NPD and PD controls, respectively (Cecatti et al., 2010).

Neonatal anoxia was more common in the offspring of BD mothers (16.7%), and our rates were similar to those reported by Goldstein et al. (2010) (7.9–11.3%), in a high-risk offspring study without normal controls from the Pittsburgh Bipolar Offspring Study (BIOS) comparing non-bipolar and bipolar offspring, respectively. However, in a controlled BD high risk study on obstetrical complications, Singh et al. (2007) reported greater total and prenatal OC in at risk children, but not on infant scores. Given that only a small number of women with BD used medications

Table 2
Odds-ratios of family planning, obstetrical complications, familial environment and maternal care, as well as violence exposure reported by the child, controlled for education, income, occupation and marital status, in a study of high-risk bipolar offspring comparing bipolar disorder I (BDI) women with psychiatric (PD) and non-psychiatric controls (NPD).

	BDI × NPD			BDI × PD		
	OR	***p***	**95% CI**	**OR**	***p***	**95% CI**
Family planning						
Actual use of CCM[a]	0.17	**0.002**	0.06–0.52	0.21	**0.004**	0.07–0.61
Offspring (*n*) [b]	0.71	**0.032**	0.52–0.97	0.72	**0.038**	0.52–0.98
Obstetrical complications[a]						
Neonatal anoxia	9.17	**0.048**	1.02–83.33	1.95	0.352	0.48–7.94
Familial environment and maternal care[a]						
Child lives with father	0.18	**0.002**	0.52–0.06	0.17	**0.001**	0.06–0.50
Lived with mother during episodes	–	–	–	125	< **0.001**	15.38–1000
Child exposed to risk during episodes	–	–	–	16.67	**0.008**	2.11–142.86
Violence exposure of child[a]						
Physical abuse	9.43	**0.046**	1.04–83.33	4.29	0.095	0.76–23.81

CCM, contraceptive methods.

[a] Logistic regression.
[b] Poisson regression.

during pregnancy (13.8%) and breast-feeding (8%), the impact of discontinuation of BD medication during these periods of life should be taken into account (Sajatovic et al., 2007), considering that the puerperium can be regarded as a vulnerable BD period (Yonkers et al., 2004). Similarly low rates of psychotropic medication use during breastfeeding were also found in the BIOS sample study (around 11%) (Goldstein et al., 2010).

Some findings regarding maternal care were striking. For example, thirty-three percent of BD mothers physically or psychologically abused their children due to psychopathology. However, most research on childhood abuse in BD focuses on offspring as opposed to parents. For instance, rates of 20.6% physical or sexual abuse were reported by children and adolescents (Romero et al., 2009), and by 47.5% of adults with severe mental illnesses (Alvarez et al., 2011). Factors related to abuse included non-intact family and first-degree family history of mood disorder, also found to be significant in our study (Romero et al., 2009). Children were also often exposed to BD symptoms and sometimes bore witness to suicide attempts. These findings are supported by other studies (Chang et al., 2003; Mowbray et al., 2006). We agree with Wamboldt and Reiss (2006), who suggested that this type of familial environment adds to biological predisposition, thereby increasing the vulnerability of these children to psychiatric illnesses.

Some authors suggest that women with psychiatric disorders suffer from increased surveillance of their skills as mothers, and may conceal their diseases, in fear of losing their rights as legal guardians (Nicholson et al., 1998). When mothers are symptomatic, these strategies may not work, and might become contradictory and ambivalent (Montgomery et al., 2006), as well as more permissive regarding their children's care. Symptomatic mothers also became less organized with mood fluctuations (Miklowitz and Johnson, 2009) and more often involved in conflicts (Chang et al., 2001, 2003). Taken together, this environment may affect children's social adjustment and performance at school (Lapalme et al., 1997; DelBello and Geller, 2001; Singh et al., 2007).

Symptoms of BD probably impact children differently as a function of their age and clinical baseline status. Indeed, the environment may not be dysfunctional at all. On the other hand, in a case–control study, Reichart et al. (2007) found that only children with BD felt that their BD parents had rejected them. Overall, parental rearing in families with a parent with BD was no more dysfunctional, as perceived by their offspring, than in families from the general population (Reichart et al., 2007).

The results of our study suggest that parental BD imposes a stressful environment during childhood, where stress has often been described as a risk factor for developing mood disorders (Duran et al., 2004; Ottinger and Tanabe, 1969). Nonetheless, scientific studies focusing on non-genetic determinants of BD family aggregation often fail to account for maternal psychopathology in the generation of stress (Etain et al., 2008). Birmaher et al. (2009) found that when both parents are affected, not only did the risk of BD in offspring increase dramatically (*OR*=3.6; 95% CI, 1.1–12.2), compared to only one affected parent, but physical and or sexual abuse also increased threefold. We speculate that the presence of physical and or sexual abuse might further increase this risk for BD.

An important limitation of this study was the use of questions as a surrogate of symptoms as opposed to using validated instruments, and the small sample size. We also failed to directly investigate obstetric complications, parental care, or family environment to better disentangle the influence of BD in children's development. With respect to possible recall bias, however, good agreement was found between OC reported by mothers and data from maternity records of the same subject (O'Callaghan et al., 1990). Finally, the study sample was enrolled at a tertiary care center, hampering generalization of findings for the general population. We have to assume, on the other hand, that obstetric and gynecologic controls from the same tertiary center received better pre and post natal care, but were more prone to OC, like spontaneous abortions and neonatal anoxia. Rates of abortions could have been falsely underestimated, and of neonatal anoxia overestimated in BD. The assessment of type of abortion (spontaneous or induced) would further clarify this topic. Nevertheless, it is important that future studies better investigate obstetrical complications, i.e. neonatal anoxia, in the pathophysiology of BD, and also consider parental psychopathology and its impact on parenting, as a risk factor for violence exposure.

5. Conclusion

Since recent studies have focused on the mutual influence of genetic and non-genetic exposures on the etiology of mental disorders, our findings call for deep reflections about the

influence of BD on violence, abuse and disorganization of the family, as well as a risk factor for BD in children mediated through parental psychopathology. Given that heritability influences BD prognosis, familial interventions may significantly decrease environmental stress thus reducing the risk of BD in vulnerable children.

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Conflict of interest

All authors declare that they have no conflicts of interest with respect to this study.

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