

## ORIGINAL ARTICLE

# Behavioral self-regulation in pediatric bipolar disorder and healthy offspring of bipolar patients

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**Objectives:** This study investigated behavioral self-regulation problems using the Children's Hostility Inventory (CHI) in pediatric bipolar disorder (PBD), healthy offspring of bipolar disorder patients (HOBD), and healthy controls (HC) without previous history of psychiatric disorders.

**Methods:** The CHI was administered to 41 consecutive children and adolescents diagnosed with PBD, to 16 HOBD, and to 22 HC. The inventory assessed irritability, expression, hostility, and aggression and was completed by the children with the help of their mothers. Adolescents and their respective parents were interviewed separately using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL).

**Results:** All subscales of the CHI presented statistically significant differences, except for the subscale assessing feelings of suspicion. Pairwise comparisons revealed consistently significant differences between the PBD group and controls, indicating more self-regulation difficulties in the PBD group, represented by high levels of hostility and aggressive behavior. There were no significant differences between the PBD and HOBD groups.

**Conclusions:** Future studies should further investigate if such behavior is state-dependent or a trait of bipolar juvenile expression. Expression of hostility and irritability should be considered relevant targets in psychosocial approaches addressing this population.

**Keywords:** Pediatric bipolar disorder; self-regulation; hostility; bipolar offspring; irritability

## Introduction

Children and adolescents with pediatric bipolar disorder (PBD) often have a dysphoric mood characterized by short periods of intense lability and mood irritability, which tend to manifest as disruptive behaviors at home and at school.<sup>1</sup> Irritable mood can be defined as an elevated tendency to anger against peers and has been associated with poor academic performance, impaired interpersonal relationships, poor psychosocial functioning, increased risk for suicidality, and functional impairment in adulthood.<sup>1-4</sup> Mood irritability, intense lability, and disruptive behaviors characterize behavioral self-regulation problems and poor self-regulation interferes in a person's everyday functioning, interpersonal relationships, learning, and emotional development.<sup>5</sup>

It is important to consider that irritability is a symptom present in 15 disorders in the DSM-5 and a diagnostic criterion for multiple disorders in youth. It occurs in PBD

and depressive disorder, but also in anxiety disorders, attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), conduct disorder (CD), severe mood dysregulation (SMD), and autism. It is considered an externalizing symptom, but it is less related to future antisocial problems than to future depression, dysthymia, and generalized anxiety disorder (GAD).<sup>6-9</sup> Irritable and disruptive behaviors have various forms of presentation, from easy annoyance to aberrant responses to frustration (emotional response to blocked attainment) and/or aberrant "approach" responses to threat. Behavioral manifestations can be feelings of anger and temper outbursts.<sup>6,10</sup>

Difficulty with self-regulation can include many components, such as demonstrations of verbal hostility or even indirect forms of hostility, for example, throwing things or saying negative things about someone else behind their back. Negative attitudes are often also present, as well as feelings of resentment and distrust, leading to important difficulties with development of closer relationships and

intimacy (resentment and suspicion). Feelings of guilt may also arise in some people after disruptive behaviors.<sup>11</sup>

With respect to children and adolescents diagnosed with PBD, Doerfler et al.<sup>12</sup> found that youngsters diagnosed with PBD were more verbally aggressive and exhibited higher levels of reactive aggression than youngsters with ADHD without co-occurring PBD. Farchione et al.<sup>13</sup> showed that healthy offspring of parents with bipolar disorder (HOBD) had significantly higher total scores on the Children's Hostility Inventory (CHI) and its subscales than offspring of community controls. Aggression is also considered a potential marker for early-onset bipolar disorder (BD), with anger and irritability as possible prodromal symptoms.<sup>14</sup> Comorbid ADHD and psychotic symptomatology are associated with worse global functioning.<sup>15-17</sup>

Considering the heritability of BD type I and the hypothesis that irritability, aggression, and/or hostility may precede other symptoms in early-onset BD, it is reasonable to examine the extent and nature of these symptoms in HOBD. Furthermore, such symptoms characterize behavioral self-regulation problems that significantly impact psychosocial adaptation.<sup>18</sup>

The present study had three objectives. The first was to determine which hostility and irritability traits can differentiate PBD from healthy controls (HC). More specifically, to determine whether disruptive behaviors occur more prominently in children and adolescents suffering from PBD characterizing behavioral self-regulation problems. The second was to determine whether HOBD would exhibit higher traces of hostility compared to controls, presenting a greater risk of developing behavioral self-regulation problems. The third objective was to verify whether presence of comorbidity with ADHD or psychotic symptoms would be associated with worse self-regulation capacity.

## Methods

### *Participants*

We included 79 children and adolescents who were between 6 and 17 years old and presented an intelligence quotient (IQ)  $\geq 80$ . Exclusion criteria were presence of head injury with loss of consciousness, neurological disorders, any serious medical problems, or substance use disorder.

Participants were divided into three groups: 1) 41 children and adolescents with BD were recruited from a pediatric clinic run by the Programa de Transtorno Bipolar, Universidade de São Paulo (USP) and were included into the study if they fulfilled DSM-IV-R criteria for BD; 2) 16 healthy offspring of parents diagnosed with type I BD (HOBD) were included; and 3) 22 HC were recruited through advertisement and included if they had no personal or family history of any axis I DSM-IV diagnoses.

### *Clinical assessment*

Children and adolescents and their parent/legal guardian were interviewed separately using the Schedule for

Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL).<sup>19</sup> All interviews were reviewed by board certified child psychiatrists. Children and adolescents who presented clear manic or hypomanic episodes, but lacking the duration needed to be classified as BD I or BD II, were diagnosed as BD not otherwise specified.<sup>20</sup> All parents with reported type I BD had their diagnoses confirmed using the Structured Clinical Interview for DSM-IV-TR (SCID).<sup>21</sup>

Adolescents were evaluated using the Children's Depression Rating Scale-Revised (CDRS-R)<sup>22</sup> and the Young Mania Rating Scale (YMRS)<sup>23</sup> to rate the severity of depressive and manic symptoms, respectively. Overall impairment was measured using the Children's Global Assessment Scale (CGAS).<sup>24</sup> Socioeconomic status was assessed using the instrument Qualificação Socioeconômica e Demográfica das Classes da Escala Abipeme, Associação Brasileira dos Institutos de Pesquisa de Mercado (ABIPEME).<sup>25</sup> The Vocabulary and Matrix Reasoning subtests of the Wechsler Abbreviated Scale of Intelligence (WASI) were administered to estimate IQ.<sup>26</sup>

### *Inventory to assess hostility aspects*

We used the CHI, created and validated by Kazdin et al.<sup>11</sup> The CHI examines how children perceive their own aggression, hostility, and irritability. Four subscales are designed to measure aggression (Assaultiveness, Indirect Hostility, Negativism, and Verbal Hostility), which include items that reflect overt acts. Aggression is defined as overt acts in which aversive events (physical or verbal) are directed at others. Two subscales are designed to measure hostility (resentment and suspicion) and they include items reflecting internalized and covert characteristics. Hostility is defined as an attitudinal, perceptual, and affective component, which is not necessarily reflected in overt acts. Some items assess expression of irritability.<sup>11</sup> The guilt subscale is used infrequently because it does not relate consistently with aggression or hostility and has not presented a correlation with other items in adults' studies.<sup>11</sup> The CHI was translated into Portuguese by our research group with back translation by a bilingual researcher. The CHI was completed by the children themselves.

### *Statistical analysis*

Statistical analyses were performed using SPSS version 19 for Windows with the level of significance set at 0.05. The data assumption of normality was verified with the Kolmogorov-Smirnov test. Groups (PBD, HOBD, and HC) were compared using chi-square tests for categorical variables. The Mann-Whitney *U* test was used for variables with non-normal distribution and a Bonferroni correction was applied for multiple comparisons involving the eight CHI subscales ( $p > 0.005$ ). The Kruskal-Wallis test was employed for the three-group comparison (PBD, HOBD, and HC) and subsequent pairwise comparisons.

Finally, a linear regression was employed to investigate associations between age and hostility traits.

### Ethics statement

This study was approved by the ethics committee at the Faculdade de Medicina, USP. Parents or legal guardians provided written consent prior to participation, and assent was obtained from all subjects (CAPPesq, protocol no. 0459/09).

### Results

Groups did not differ in terms of age, sex, education, or socioeconomic level. Because there was a trend to significance in estimated IQ between HOBD and controls, we included IQ in the posterior analysis of covariance (ANCOVA) analyses as a confounding variable. However, it is important to consider that mean IQ was within the average range of performance in all three groups.

Table 1 presents demographic and clinical data and CHI measures.

Scores for all CHI subscales except for the subscale assessing suspicion and guilt were statistically significantly higher in the PBD group. Pairwise comparisons revealed consistently significant differences between the PBD group and HOBD and controls. We conducted a secondary analysis solely including euthymic PBD individuals and these differences persisted, except for the indirect expression of hostility and negativism domains (Table 2).

We were also interested in some specific presentations of PBD, namely comorbidity with ADHD and presence of psychotic symptoms. Regarding CHI measurements, there were no significant differences between PBD with and without ADHD or between PBD with and without psychosis.

Finally, considering the role an individual's development plays in management of self-regulation, we conducted a linear regression analysis with age as the dependent

**Table 1** Sociodemographic and clinical measures for PBD, offspring, and HC subjects

Sociodemographic and clinical data	PBD (n=41)	HOBD (n=16)	HC (n=22)	p-value	P-values for pairwise comparisons
Age in years <sup>†</sup>	11.8 (3.2)	13.1 (3.0)	12.6 (3.3)	0.36	
Educational level <sup>†</sup>	6.5 (3.0)	8.3 (2.7)	7.7 (3.4)	0.10	
Estimated IQ <sup>†</sup>	98.5 (13.0)	93.4 (7.4)	102.2 (9.7)	0.06	Offspring > HC (0.019)
Gender <sup>‡</sup> (female/male) (n)	14/27	6/10	13/9	0.67	
Socioeconomic level <sup>‡</sup>					
A – 89 or +	3	1	3		
B – 59-88	20	6	15		
C – 35-58	12	8	4		
D – 20-34	4	0	0		
Comorbidities <sup>‡</sup> (n)					
PBD with ADHD	28				
PBD without ADHD	13				
PBD with psychosis	13				
PBD without psychosis	28				
Mood assessment <sup>‡</sup> (n [%])					
Euthymia	22 (53.6)				
Depression	2 (4.8)				
Mix	4 (9.7)				
Mania	10 (24.3)				
Hypomania	3 (7.6)				
Clinical assessment <sup>†</sup>					
CDRS	26.8 (12.5)				
YMRS	9.1 (6.9)				
CGI	4.0 (1.2)				
CGAS	52.8 (8.3)				
Suicide <sup>‡</sup> (n)					
Suicide attempt	6				
Suicidal ideation	35				
Bipolar diagnosis <sup>‡</sup> (n)					
SOE	21				
Type 1	18				
Type 2	2				

Data expressed as mean (SD), unless otherwise specified.

ADHD = attention deficit hyperactive disorder; CDRS = Children's Depression Rating Scale; CGAS = Children's Global Assessment Scale; CGI = Clinical Global Impressions Scale; HC = healthy controls; HOBD = healthy offspring of bipolar disorder patients; IQ = intelligence quotient; PBD = pediatric bipolar disorder; SOE = strength of evidence; YMRS = Young Mania Rating Scale.

<sup>†</sup> Student's *t* test; <sup>‡</sup> Chi-square test.

**Table 2** CHI scores for PBD, offspring, and HC subjects

Hostility scale <sup>†</sup>	PBD (n=41)	Offspring (n=16)	HC (n=22)	p-value	$\eta^2$ effect-size	P-values for pairwise comparisons
Assaultiveness	3.61 (1.70)	2.06 (1.12)	1.41 (1.40)	< <b>0.001</b>	0.29	PBD > HC (< 0.001) PBD > offspring (0.001)
Indirect expression of hostility	3.17 (1.24)	2.13 (1.31)	2.18 (1.10)	<b>0.002</b>	0.15	PBD > HC (0.004) PBD > offspring (0.004)
Irritability	3.10 (0.24)	1.49 (0.39)	2.01 (0.33)	<b>0.001</b>	0.17	PBD > HC (0.004) PBD > offspring (0.001)
Negativism	2.14 (1.25)	1.68 (0.94)	1.55 (0.80)	<b>0.001</b>	0.07	PBD > HC (0.024)
Resentment	2.02 (1.27)	1.31 (1.20)	0.90 (0.87)	<b>0.001</b>	0.14	PBD > HC (0.001) PBD > offspring (0.015)
Suspicion	2.39 (1.22)	1.94 (1.39)	1.81 (1.09)	0.175	-	-
Verbal hostility	3.53 (1.36)	2.18 (1.11)	2.40 (1.09)	< <b>0.001</b>	0.19	PBD > HC (0.001) PBD > offspring (0.001)
Guilt	2.12 (1.24)	1.38 (1.15)	1.41 (1.14)	<b>0.032</b>	0.08	PBD > HC (0.023) PBD > offspring (0.054)

Bold type denotes statistical significance. Data expressed as mean (SD).

CHI = Children's Hostility Inventory; HC = healthy controls; PBD = pediatric bipolar disorder.

<sup>†</sup>All measures were performed using analysis of covariance (ANCOVA) and were controlled for intelligence quotient (IQ).

variable. The results revealed an association between measures of verbal hostility and age ( $F[1.822]$ ;  $p = 0.021$ ) with  $R^2 = 0.296$  for the group of children with PBD.

## Discussion

Significant differences were found in hostility and irritability traits assessed by the CHI when PBD were compared with HOBPD and HC, suggesting serious behavior self-regulation problems in the PBD group.

In adult samples, overt irritability and psychomotor agitation appear to be markers for specific negative outcomes, risk of suicide attempts, and longer duration of episodes at admission measured in a subsyndromal bipolar mixed state.<sup>27</sup> Our sample of PBD was composed of children and adolescents with severe symptoms and presence of several emotional behaviors related to irritability, being, therefore, a sample at risk of problems in adult life.

However, there were no significant differences between HOBPD and controls in terms of aggressiveness (assaultiveness), hostility (verbal and indirect expression), irritability, negativism, resentment, or guilt. According to these data, the offspring group did not show a tendency to present self-regulation problems, which is not supported by literature, possibly due to our small sample size. For instance, Birmaher et al.<sup>18</sup> found significantly higher irritability on the Children's Affective Lability Scale (CALSL) in 257 non-BP offspring of BP parents when compared to 192 offspring of control parents. The HOBPD group did not exhibit significantly different responses in comparison to the control group, but they differed from the PBD group in almost all CHI variables, except negativism. The questions in this subsection refer to breaking down pre-established rules, reacting differently when you view the

other person as being bossy, and refusing to talk when you are upset with someone. Our data suggest that offspring and patients with PBD are usually more reactive when they feel upset.

Farchione et al.<sup>13</sup> used the same CHI scale to evaluate children of bipolar parents in a fairly large sample of 300 children and found that children of BD parents had significantly higher total CHI and subscale scores than children of healthy parents. After adjusting for demographic variables, three factors remained significant: total CHI by parent rating, irritability subscale by parent rating, and irritability by child self-report. The hostility subscale by parent rating became a trend. In their sample, children of BP parents were diagnosed with mood and anxiety disorders (24.3%), as well as ADHD (23.7%), ODD, and CD (17.3%). In our sample, offspring subjects did not meet criteria for any psychopathology that could explain significant differences in comparison with the control group. Furthermore, we had fewer individuals in the offspring group and the absence of a numerically balanced group could also explain these negative findings. Two other additional analyses were conducted with the aim of increasing our understanding about the group of children with bipolar parents.

In our study, euthymic PBD demonstrated presence of aggressive behaviors, defined as behaviors directed at another person with the intention of causing harm, such as injuring or hitting someone or punching their nose (questions of assaultiveness measure).<sup>8</sup> It is important to consider that these affirmations on the scale do not refer to occurrences at the current moment, but rather ask whether that behavior has occurred at least at some time in the past.

Euthymic PBD did not show significant differences in the measures of indirect expression of hostility and

negativism compared to non-euthymic PBD. Oppositional behavior and an aggressive object-directed reaction, such as breaking or throwing objects, knocking on doors, or having angry attacks were shown to be related to the symptomatology of BD in our study, suggesting that self-regulation difficulties can be considered a trait of the disorder, rather than a state, which seems to begin in infancy.

We investigated whether there were differences in the presence of comorbid ADHD or lifetime psychotic symptoms in terms of hostility expression. We expected that there would be greater expression of irritability in BP children with ADHD comorbidity, and increased hostility in BP children with lifetime psychotic symptoms, but comorbidity and psychotic symptomatology throughout life showed no impact on hostile or irritable behavior. The presence of BD is probably the key element related to hostility and irritability.

These findings highlight the importance of investigating behaviors of aggression, hostility, irritability, negativity, resentment, and guilt in children with BPD. These symptoms can be treated with medication, but it is necessary to consider behavioral interventions that can help individuals to learn ways to manage their feelings and reactions. Some cognitive behavior-oriented psychotherapies have been designed specially to teach BPD children and adolescents to name their feelings and change their expression.<sup>28,29</sup>

The hallmark emotion of irritability and anger is thought to occupy a central position between internalizing and externalizing problems. Moreover, anger and fear together are regarded as part of a negative affect personality dimension that is a risk factor for internalizing problems. However, when anger appears separated from fear, it predicts aggressive behaviors. Particularly, irritability appears to be associated with hostile and disruptive problems.<sup>30</sup>

Brotman et al.<sup>31</sup> demonstrated that in comparison to healthy children, those presenting irritable traits showed deficient reward learning and higher sensitivity to reward receipt and omission, which have been associated with dysfunction in the prefrontal cortex, striatum, and amygdala. Moreover, children with irritable traits also presented difficulties in interpreting and labeling potential threats, which are also associated with prefrontal cortical and amygdala dysfunction. Lastly, it appears that irritable traits may affect and be affected by the child's environment, which suggests that changes may occur through environmental modification, such as parenting interventions.

It is considered that certain specific interventions can help develop better capacity for emotional regulation in children with PBD, such as multifamily psychoeducational psychotherapy, child and family-focused cognitive-behavioral therapy, and psychoeducational therapy.<sup>32-34</sup> Hostility and irritability measures should be considered as outcomes in future intervention studies regarding their potential as mediators of behavioral modification in this population.

The major limitations of the current study include its small sample size, mainly the number of offspring of BD parents, the absence of numerically balanced groups, and

the inclusion of symptomatic patients, although no previous studies have included euthymic individuals only, probably due to the unpredictable course of pediatric BD. Furthermore, we only employed one scale to evaluate behavioral self-regulation, which has not been validated for Brazilian subjects.

The PBD group demonstrated serious behavioral self-regulation problems, related to higher levels of hostility and irritability when compared with healthy offspring of BD parents and HC. PBD patients seem to be very reactive and have difficulty expressing assertive behavior. Presence of lifetime psychotic symptoms and comorbidity with ADHD were not associated with expression of behavioral aspects related to hostility and irritability in PBD. The self-regulation problems were shown to be related to BD symptomatology in our study and may thus be considered a trait of the disorder rather than a symptomatology dependent state. Future studies should investigate specific interventions focused on emotional self-regulation.

## Disclosure

The authors report no conflicts of interest.

## References

- 1 Kowatch RA, DelBello MP. Pediatric bipolar disorder: mood swings, irritability are cues to this diagnosis. *Curr Psychiatr*. 2003;2:40-7.
- 2 Leibenluft E, Stoddard J. The developmental psychopathology of irritability. *Dev Psychopathol*. 2013;25:1473-87.
- 3 Siegel RS, Freeman AJ, La Greca AM, Youngstrom EA. Peer relationship difficulties in adolescents with bipolar disorder. *Child Youth Care Forum*. 2015;44:355-75.
- 4 Best MW, Bowie CR, Naiberg MR, Newton DF, Goldstein BI. Neurocognition and psychosocial functioning in adolescents with bipolar disorder. *J Affect Disord*. 2017;207:406-12.
- 5 DeGangi GA. Pediatric disorders of regulation in affect and behavior: a therapist's guide to assessment and treatment. 2nd ed. New York: Routledge/Taylor & Francis Group; 2017.
- 6 Stringaris A. Irritability in children and adolescents: a challenge for DSM-5. *Eur Child Adolesc Psychiatry*. 2011;20:61-6.
- 7 Krieger FV, Leibenluft E, Stringaris A, Polanczyk GV. Irritability in children and adolescents: past concepts, current debates, and future opportunities. *Braz J Psychiatry*. 2013;35 Suppl 1:S32-9.
- 8 Leibenluft E. Irritability in children: what we know and what we need to learn. *World Psychiatry*. 2017;16:100-1.
- 9 Toohey MJ, DiGiuseppe R. Defining and measuring irritability: construct clarification and differentiation. *Clin Psychol Rev*. 2017;53:93-108.
- 10 Leibenluft E. Pediatric irritability: a systems neuroscience approach. *Trends Cogn Sci*. 2017;21:277-89.
- 11 Kazdin AE, Rodgers A, Colbus D, Siegel T. Children's Hostility Inventory: measurement of aggression and hostility in psychiatric inpatient children. *J Clin Child Adolesc Psychol*. 1987;16:320-28.
- 12 Doerfler LA, Connor DF, Toscano PF Jr. Aggression, ADHD symptoms, and dysphoria in children and adolescents diagnosed with bipolar disorder and ADHD. *J Affect Disord*. 2011;131:312-9.
- 13 Farchione TR, Birmaher B, Axelson D, Kalas C, Monk K, Ehmann M, et al. Aggression, hostility, and irritability in children at risk for bipolar disorder. *Bipolar Disord*. 2007;9:496-503.
- 14 Luby JL, Navsaria N. Pediatric bipolar disorder: evidence for prodromal states and early markers. *J Child Psychol Psychiatry*. 2010;51:459-71.
- 15 Glahn DC, Bearden CE, Barchi M, Barrett J, Reichenberg A, Bowden CL, et al. The neurocognitive signature of psychotic bipolar disorder. *Biol Psychiatry*. 2007;62:910-6.

- 16 Arnold LE, Demeter C, Mount K, Frazier TW, Youngstrom EA, Fristad M, et al. Pediatric bipolar spectrum disorder and ADHD: comparison and comorbidity in the LAMS clinical sample. *Bipolar Disord*. 2011;13:509-21.
- 17 Diler RS. Pediatric bipolar disorders and ADHD. In: Daviss W, editor. *Moodiness in ADHD*. Cham: Springer; 2018.
- 18 Birmaher B, Goldstein BI, Axelson DA, Monk K, Hickey MB, Fan J, et al. Mood lability among offspring of parents with bipolar disorder and community controls. *Bipolar Disord*. 2013;15:253-63.
- 19 Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry*. 1997;36:980-8.
- 20 Birmaher B, Axelson D. Course and outcome of bipolar spectrum disorder in children and adolescents: a review of the existing literature. *Dev Psychopathol*. 2006;18:1023-35.
- 21 First MB, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM IV axis I disorders – patient edition (SCID/P, Version 2.0). New York: New York State Psychiatric Institute; 1995.
- 22 Poznanski EO, Mokros HB. Children's Depression Rating Scale – Revised (CDRS-R). Los Angeles: Western Psychological Services; 1996.
- 23 Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. *Br J Psychiatry*. 1978;133:429-35.
- 24 Shaffer D, Gould MS, Brasic J, Ambrosini P, Fisher P, Bird H, et al. A children's global assessment scale (CGAS). *Arch Gen Psychiatry*. 1983;40:1228-31.
- 25 Jannuzzi PM, Baeninger R. Qualificação socioeconômica e demográfica das classes da escala Abipeme. *Rev Admin*. 2008;31:82-90.
- 26 Wechsler D. Wechsler Abbreviated Scale of Intelligence (WASI). San Antonio: The Psychological Corporation/Harcourt Brace & Company; 1999.
- 27 Hunt JI, Case BG, Birmaher B, Stout RL, Dickstein DP, Yen S, et al. Irritability and elation in a large bipolar youth sample: relative symptom severity and clinical outcomes over 4 years. *J Clin Psychiatry*. 2013;74:110-7.
- 28 Feeny NC, Danielson CK, Schwartz L, Youngstrom EA, Findling RL. Cognitive-behavioral therapy for bipolar disorders in adolescents: a pilot study. *Bipolar Disord*. 2006;8:508-15.
- 29 Pavuluri MN, Graczyk PA, Henry DB, Carbray JA, Heidenreich J, Miklowitz DJ. Child- and family-focused cognitive-behavioral therapy for pediatric bipolar disorder: development and preliminary results. *J Am Acad Child Adolesc Psychiatry*. 2004;43:528-37.
- 30 Stringaris A, Cohen P, Pine DS, Leibenluft E. Adult outcomes of youth irritability: a 20-year prospective community-based study. *Am J Psychiatry*. 2009;166:1048-54.
- 31 Brotman MA, Kircanski K, Stringaris A, Pine DS, Leibenluft E. Irritability in Youths: A Translational Model. *Am J Psychiatry*. 2017;174:520-32.
- 32 Fristad MA, Verducci JS, Walters K, Young ME. Impact of multifamily psychoeducational psychotherapy in treating children aged 8 to 12 years with mood disorders. *Arch Gen Psychiatry*. 2009;66:1013-21.
- 33 West AE, Weinstein SM, Peters AT, Katz AC, Henry DB, Cruz RA, et al. Child- and family-focused cognitive-behavioral therapy for pediatric bipolar disorder: a randomized clinical trial. *J Am Acad Child Adolesc Psychiatry*. 2014;53:1168-78, 1178.e1.
- 34 Reinares M, Bonnín CM, Hidalgo-Mazzei D, Sánchez-Moreno J, Colom F, Vieta E. The role of family interventions in bipolar disorder: A systematic review. *Clin Psychol Rev*. 2016;43:47-57.