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ORIGINAL ARTICLE

Self-regulation in youth with bipolar disorder

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Objectives: To examine the composition of self-regulation in pediatric bipolar disorder (PBD) through the relationship between executive functions, emotion processing, and family environmental factors. **Methods:** 58 participants (36 with PBD and 22 controls), ages 12-17, were assessed using the Barratt Impulsiveness Scale (BIS), Conners' Continuous Performance Test (CPT-II), Wisconsin Cards Sorting Test (WCST), Computerized Neurocognitive Battery Emotion Recognition Test-Facial Emotion Recognition Test (PENNCNB ER-40), and Expressed Emotion Adjective Checklist Questionnaire (EEAC).

Results: Adolescents with PBD displayed significant deficits in all three spheres when compared to the control group. Emotion processing correlated negatively with inhibition and attention, and correlated positively with mental flexibility/working memory. Family environmental factors correlated negatively with mental flexibility/working memory and emotion processing, and positively with attention and inhibition. These correlations indicate that better inhibitory control, attention, and mental flexibility/ working memory are associated with greater emotion processing and a fitter family environment.

Conclusion: This study is the first to investigate all of the components of self-regulation deficits simultaneously in patients with PBD. Results suggest that self-regulation is essential for a comprehensive perspective of PBD and should be assessed in an integrative and multifaceted way. Understanding that self-regulation is impacted by the abovementioned factors should influence treatment and improve the functional impairments of daily life observed in this population.

Keywords: Pediatric bipolar disorder; self-regulation; executive functions; emotion processing; family environmental factors

Introduction

Pediatric bipolar disorder (PBD) is now recognized by the scientific and medical community. Over the past two decades, there has been substantial growth in research aiming to understand and characterize PBD.¹ Like adult bipolar disorder (BD), PBD is characterized by mood fluctuations between euphoria and depression; however, atypical presentations are more frequent than in adult BD. Euphoric symptoms can include elation, irritability, feelings of grandiosity, flight of ideas, racing thoughts, decreased need for sleep, decreased self-criticism, as well as heightened sexuality, speech pressure, distraction, and energy levels.^{2,3} On the other side of the spectrum, depressive symptoms can include anhedonia, difficulty concentrating, lack of energy, sadness, irritability, and sleep alterations.^{4,5}

Youth with PBD often present with important deficits in executive functions (EF) and emotion regulation (ER), and frequently live in households or family environments

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with higher levels of tension and conflicts.⁶⁻⁹ These factors can lead to shortfalls in self-regulation, which pertains to the ability to willingly plan and, as necessary, modulate one's behavior to an adaptive end.^{10,11} Studies measuring separate components of self-regulation have found young individuals with PBD to have important deficits in these abilities in comparison to their peers, which may lead to many of the functional and clinical difficulties experienced by this population.¹²⁻¹⁹

Despite substantial growth in research aiming to elucidate self-regulation in PBD, no cross-sectional or longitudinal study has managed to explore the topic in a multifaceted and integrative manner. Although there is no consensus regarding the best method to study selfregulation, recent studies in healthy individuals have already begun to explore the intricate relations between EF, emotion processing, and family environmental factors.¹¹

Studies in the general population have shown that successful self-regulation early in life can be predictive

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of higher academic achievement,^{20,21} intelligence quotient (IQ),²² and prosocial behaviors,²³ as well as the ability to sustain a job, earn and save money.²⁴ Overall, self-regulation includes behavioral and emotional regulation, which requires the individual to coordinate multiple aspects of top-down control, such as inhibitory control, attention, and working memory, which are components of EF,²⁵ as well as make use of internal tools to regulate emotional perceptions and expressions¹⁰ aiming at specific goals or outcomes.

EF play a substantial role in the development of selfregulation, with inhibitory control, working memory, and mental flexibility being considered key traits in the latest studies of self-regulation in the general population.²⁶ In the PBD population, the latest meta-analytical studies on cognitive impairments found important deficits in the aforementioned EF, as well as in other cognitive functions.^{7,27} Children and adolescents with PBD exhibit important neuropsychological deficits, which hinder academic achievement and psychosocial development.²⁸ Cognitive difficulties in the domains of memory, attention, and EF are often present during episodes of (hypo)mania and depression, and frequently interfere with the daily lives of this population.²⁹

Emotional processing is also an important component of self-regulation mechanisms and is often evaluated by facial emotional expressions tests. Children and adolescents with PBD display important deficits in recognizing, identifying, and discriminating emotional facial expressions.³⁰ Studies suggest that identification of sad,³¹ angry,³¹⁻³³ and happy faces,^{32,33} as well as the intensity of emotional expression,³⁴ are altered in this population. When compared to children suffering from general anxiety disorder (GAD), attention deficit hyperactivity disorder (ADHD), major depressive disorder (MDD), and conduct disorders, individuals with PBD exhibit worse overall performance in the identification of facial emotional expressions.³⁵

Parental behavior has also been shown to be directly associated with the development of ER capacity in children. Adequate parental ability to emotionally selfregulate has been associated with fewer emotional and behavioral issues in offspring.^{36,37} Parents' emotional expressions are the primary context in which young children learn the basic rules for expressing and understanding emotions. The variables that best discriminate families with PBD from controls are higher levels of negative expressed emotion, elevated conflict and tension, and decreased cohesion and organization in the family environment.6,38,39 Moreover, the adult BD literature shows that individuals with BD experienced traumatic events during childhood more often than healthy controls (63% versus only 33%).40-42 Early trauma has been associated with different clinical characteristics in individuals with BD, such as early onset, rapid cycling, number of episodes, suicidal ideation, and psychotic symptoms.42-45

Thus, this innovative study exploring the components of self-regulation in patients with PBD could contribute to understanding the mechanisms that underlie the important self-regulation deficits found in this population, as 21

well as cast light upon new pathways of care and prevention. Hence, we investigated the association between EF (inhibitory control, attention, and mental flexibility/working memory), emotion processing (facial emotional recognition), and family environmental factors (familial EEAC). We hypothesized that adolescents with PBD would perform worse than healthy controls in EF, emotional processing, and family environmental factors. We also hypothesized that better inhibitory control, attention, and mental flexibility/working memory would be associated with both greater emotional processing and a fitter family environment, and that greater emotional processing would be associated with a fitter family environment and vice versa.

Methods

Participants

The study included 36 patients with PBD and 22 healthy controls (total n=58). Patients with PBD were recruited from the outpatient clinic of the Bipolar Disorder Research Program (Programa de Transtorno Bipolar [PROMAN]) of the Instituto de Psiquiatria, Faculdade de Medicina, Universidade de São Paulo, while healthy controls were recruited from the local community by advertisements on radio, television, and the written press. Inclusion criteria for the PBD group (n=36) were age 12 to 18 years, $IQ \ge$ 70, and a diagnosis of PBD according to DSM-IV requirements. For controls (n=22), the inclusion criteria were age 12 to 18 years, $IQ \ge 70$, no axis I psychiatric diagnosis, and no parents with BD or any other psychiatric diagnosis. Exclusion criteria for both groups included the presence of clinical disorders with repercussions on the central nervous system, including neurological disorders.

Instruments

For patients with PBD, clinical variables were collected through the Kiddie-Sads Present and Lifetime Version (K-SADS-PL),⁴⁶ Children's Depression Rating Scale-Revised (CDRS-R),⁴⁷ and Young Mania Rating Scale (YMRS).⁴⁸ Both groups were assessed using the K-SADS-PL,⁴⁶ to investigate the presence or absence of psychiatric conditions; the Wechsler Abbreviated Scale of Intelligence (WASI)⁴⁹; and a structured baseline interview for demographic and clinical assessments.

Both groups underwent the same protocol to assess EF, emotion processing, and family environmental factors. EF were assessed using the Barratt Impulsiveness Scale (BIS-11),⁵⁰ Conners' Continuous Performance Test (CPT-II),⁵¹ and Wisconsin Cards Sorting Test (WSCT).⁵² Emotion processing was assessed using the Emotion Recognition Test-Facial Emotion Recognition Test-Facial Emotion Recognition Test (PENNCNB ER-40) component of the University of Pennsylvania Computerized Neurocognitive Battery. Family environmental factors were assessed in both groups using the Expressed Emotion Adjective Checklist Questionnaire (EEAC).⁵³

Statistical analysis

Statistical analysis was performed using the R statistical package, version 4.0.2. For numeric variables (such as age and IQ), the comparison between groups employed Student's *t* tests or Mann-Whitney tests for binary hypothesis testing, depending on verification of the assumption of residual normality, and an analysis of covariance (ANCOVA) in order to control for confounding variables. For the categorial variables (such as gender, socioeconomic status, and PBD type), contingency tables were constructed, and the chi-square or Fisher's exact test was performed. Statistical significance was accepted at p-values ≤ 0.05 .

Initially, we performed a principal component analysis to condense the variables of the facial recognition tests (PENNCNB ER-40), EEAC, WCST, and CPT. Subsequently, we calculated Pearson's productmoment correlation coefficients between the new components generated, including the entire sample, in order to attain a correlation coefficient between EF, emotion processing, and family environmental factors.

To group the variables into unique scores for each component (EF, emotions, and family environmental factors), when necessary, we reversed the signs of the factor loads of variables that presented opposite signs within the same component. Thus, the components must be read from the following perspective: for family environment (measured as EEAC), impulsivity (BIS), and attention (CPT-II), the higher the score, the worse the subject's performance; for emotions (PENNCNB ER40) and mental flexibility/working memory (WCST), the higher the score, the better the subject's performance (Table 1).

Ethics statement

All subjects gave written informed consent, and the study protocol was approved by the institutional ethics committee on human research under protocol number 64719.

Results

The study evaluated 58 participants in total, 36 with PBD and 22 controls. The PBD group consisted of 24 female (66.67%) patients and the control group consisted of six female (27.27%) participants (p = 0.004). The control group also presented significantly higher means for IQ (mean = 104.86, SD = 9.46 vs. 96.00, SD = 14.75; p = 0.007) and years of education (mean = 8.82, SD = 3.22vs. mean = 6.72, SD = 3.01; p = 0.015). There was no statistically significant difference in age or socioeconomic level between the two groups. The mean age of onset in patients with PBD included in this study was 8.81 years (SD = 3.54), 52.78% had PBD type I, 61.11% had comorbid ADHD, and 27.78% had psychosis. Regarding the patients' mood at the time of assessments. 35,48% were euthymic, 3.23% depressed, 25.81% hypomanic, 22.58% manic, and 12.9% were in a mixed state. Regarding the YMRS and CDRS-R scales, results for the PBD group were, respectively, mean = 10.10, SD = 6.74 and mean = 28.32, SD = 12.26.

Regarding our primary hypothesis, an ANCOVA, controlling for gender and IQ, found that adolescents with PBD showed lower performance in several variables of EF, emotional processing, and family environmental factors, when compared to the control group. Regarding inhibitory control, there was a significant difference between groups ($p \le 0.001$). Individuals with PBD showed deficits in the domains of attention ($p \le 0.001$), motor ($p \le 0.001$), and planning (p = 0.015) on the Barratt Impulsiveness Scale (Table 2).

A principal components analysis was done to reduce the number of variables in each component, considering the sample size (n=58), and aiming to retain the largest amount of information possible for each component. The variables of each instrument were selected based on previous significant findings in the PBD literature. Therefore, a self-regulation model was constructed using the following variables. For EF, inhibitory control was assessed using planning, motor, and attentional impulsivity; attention was assessed using the CPT-II's hit reaction time SD, variability, omission, and perseverance

Table 1 Correlations between executive functions, emotion processing, and family environmental factors			
Х	Y	Correlation	p-value
Environmental factors [†] Environmental factors [†] Environmental factors [†] Environmental factors [†] Emotion processing [‡] Emotion processing [‡] Emotion processing [‡]	Mental flexibility/working memory [‡] Attention [†] Emotion processing [‡] Inhibitory control [†] Mental flexibility/working memory [‡] Attention [†] Inhibitory control [†]	-0.427* 0.449* -0.362* 0.343* 0.234 -0.289 -0.207	0.001* < 0.001* 0.007* 0.015* 0.078 0.033 0.136

Pearson's product-moment correlation.

Attention (Conners' Continuous Performance Test [CPT-II]) = reaction time, standard error, variability, omission and perseverance; emotions (University of Pennsylvania Computerized Neurocognitive Battery Emotion Recognition Test-Facial Emotion Recognition Test [PENNCNB ER40]) = recognition of faces with no emotion, sad faces, and faces with mild expressions; environment (Expressed Emotion Adjective Checklist Questionnaire [EEAC]) = offspring's negative emotion and mother's negative emotion; impulsivity (Barratt Impulsiveness Scale [BIS]) = planning, motor, and attention; mental flexibility/working memory (Wisconsin Cards Sorting Test [WCST]) = persevering errors, loss of set, total errors, correct answers and number of categories.

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*p ≤ 0.05.
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The higher the score, the worse the subject's performance.

[‡]The higher the score, the better the subject's performance.

Table 2 Inhibitory control: PBD vs. controls

BIS	PBD (n=36)	Controls (n=22)	p-value*	
Attention	22.45 (3.99)	17.75 (2.99)	0.001	
Motor	24.21 (6.54)	18.75 (4.36)	0.001	
Planning	28.73 (4.45)	25.55 (4.48)	0.015	
Total	75.39 (11.87)	62.05 (9.62)	< 0.001	

Data presented as mean (SD). Analysis of covariance (ANCOVA).

BIS = Barratt Impulsiveness Scale; PBD = pediatric bipolar disorder.

* Significant at $p \leq 0.05$.

Table 3 Attention: PBD vs. controls

CPT-II	PBD (n=36)	Controls (n=22)	p-value*
Omission	57.86 (25.45)	40.23 (14.63)	0.002
Commission	62.31 (27.97)	40.36 (31.36)	0.009
Reaction time	42.02 (31.90)	44.59 (25.28)	0.579
Reaction time SD	57.85 (31.85)	45.84 (25.15)	0.194
Variability	59.80 (32.75)	42.52 (28.13)	0.069
Attention	61.67 (23.60)	45.58 (24.08)	0.018
Response	52.28 (20.10)	40.91 (12.63)	0.013
Perseverance	57.50 (26.00)	40.46 (18.86)	0.005
Block change reaction time	49.58 (23.67)	45.47 (26.44)	0.552
Reaction time standard error block change	45.68 (26.57)	41.93 (22.85)	0.595
Reaction time interval between stimuli	59.06 (29.51)	44.97 (25.99)	0.078

Data presented as mean (SD). Analysis of covariance (ANCOVA).

CPT-II = Conners' Continuous Performance Test; PBD = pediatric bipolar disorder.

* Significant at $p \leq 0.05$.

Table 4 Mental flexibility: PBD vs. controls

WCST	PBD (n=36)	Controls (n=22)	p-value*
Categories	3.03 (1.28)	3.86 (1.21)	0.018
Errors	18.92 (7.12)	12.86 (7.19)	< 0.001
Perseverative errors	6.36 (4.58)	5.73 (3.56)	0.527
Correct responses	45.03 (7.15)	51.05 (7.13)	< 0.001
Loss of set	0.36 (0.80)	0.45 (0.96)	0.802

Data presented as mean (SD). Analysis of covariance (ANCOVA).

PBD = pediatric bipolar disorder; WCST = Wisconsin Cards Sorting Test.

* Significant at $p \leq 0.05$.

variables; and mental flexibility/working memory was assessed using the WCST's perseverative errors, loss of set, total errors, correct hits, and number of categories variables. Emotion processing was assessed using the PENNCNB ER-40 neutral and sad faces and faces with mild expressions. Lastly, family environmental factors were assessed using the negative EEAC for both child and mother. The proportion of variance (amount of information retained) for each component, after using the principal component analysis, was 79.5% for EF, 57.3% for emotion processing, and 83.1% for the family environmental factors.

Regarding attention, measured by the CPT-II, an ANCOVA controlling for gender and IQ found that individuals with PBD showed worst performance in the variables omission errors (p = 0.002), commission errors (p = 0.009), attention (p = 0.018), number of responses (p = 0.013), and perseverance (p = 0.005) (Table 3).

Regarding mental flexibility and working memory, an ANCOVA controlling for gender and IQ found that individuals with PBD performed significantly worse than controls in the variables categories (p = 0.018), errors (p \leq 0.001), and correct responses (p = 0.001) (Table 4).

Within the emotion processing component, an ANCOVA controlling for gender and IQ found that patients with PBD differed from controls, showing a significantly worse performance in four of the 12 variables of the PENNCB ER-40. Such significant differences occurred in the recognition of neutral (p = 0.029), sad (p = 0.003), and mild (p = 0.030) faces; subjects with PBD also took longer than controls to correctly recognize faces with happy expressions (p = 0.050) (Table 5).

In the family environmental factors component, patients with PBD differed significantly from the control group in all variables of the EEAC. Patients with PBD showed higher positive (p < 0.001) and negative (p < 0.001) EEAC, as well as a positive (p < 0.001) and negative (p < 0.001) parental EEAC (Table 6).

Regarding our secondary hypothesis, a Pearson correlation analysis – including the entire sample (n=58) – between EF (inhibitory control, attention, mental flexibility/working memory), emotion processing, and family

PENNCNB ER-40	PBD (n=36)	Controls (n=22)	p-value*
Angry	4.08 (1.32)	4.09 (1.41)	0.961
Fearful	6.72 (1.45)	7.14 (1.55)	0.133
Нарру	7.39 (0.93)	7.59 (0.67)	0.456
Neutral	6.33 (1.88)	6.95 (2.03)	0.029
Sad	5.86 (1.50)	6.86 (1.83)	0.003
Mild intensity	10.28 (2.29)	11.59 (1.99)	0.030
Extreme intensity	13.78 (1.51)	14.09 (1.87)	0.219
Angry (time)	2,396.47 (899.37)	2,473.66 (930.97)	0.791
Fearful (time)	2,389.36 (962.83)	2,296.14 (657.22)	0.974
Happy (time)	2,070.29 (634.85)	1,792.86 (416.81)	0.050
Neutral (time)	2,461.46 (1,276.96)	2,245.30 (977.67)	0.683
Sad (time)	2,642.36 (1,068.32)	2,037.89 (707.82)	0.066

Data presented as mean (SD). Analysis of covariance (ANCOVA).

PBD = pediatric bipolar disorder; PENNCNB ER-40 = Computerized Neurocognitive Battery Emotion Recognition Test-Facial Emotion Recognition Test.

* Significant at $p \leq 0.05$.

	PBD n=36	Control n=22	p-value*
Positive EEAC Offspring [†]	52.80 (11.71)	73.27 (9.31)	< 0.001
Negative EEAC Offspring [†]	47.00 (10.79)	20.68 (9.75)	< 0.001
Positive EEAC Parent [‡]	63.16 (10.22)	72.59 (9.04)	< 0.001
Negative EEAC Parent [‡]	33.34 (12.60)	20.82 (7.95)	< 0.001

Data presented as mean (SD).

EEAC = Expressed Emotion Adjective Checklist Questionnaire; PBD = pediatric bipolar disorder.

* Significant at $p \leq 0.05$.

[†] Student's *t* test.

[‡]Wilcoxon-Mann-Whitney test.

environmental factors found positive correlations of family environmental factors with attention (r = 0.449, $p \le 0.001$) and inhibitory control (r = 0.343, p = 0.015) and of emotion processing with mental flexibility/working memory (r = 0.234, p = 0.078), as well as negative correlations of family environmental factors with mental flexibility/working memory (r = -0.427, p = 0.001) and emotion processing (r = -0.362, p = 0.007) and of emotion processing with attention (r = -0.289, p = 0.033) and inhibitory control (r = -0.207, p = 0.136) (Table 1).

Discussion

Regarding our primary hypothesis, adolescents with PBD showed poorer overall performance than controls on several aspects of EF, emotion processing, and family environmental factors. These results are consistent with previous literature, which found that PBD individuals exhibit important cognitive and EF deficits^{7,27}; facial emotion recognition deficits^{30,34}; and belong to households/family environments with worse EEAC scores.^{6,54,55}

Regarding our secondary hypothesis, our results suggest a significant association between family environmental factors, EF (inhibitory control, attention, mental flexibility/working memory), and emotional processing. Studying these three domains from an integrative perspective allows for a more holistic approach toward self-regulation in youth, which can be crucial considering the implications of impaired self-regulation.^{19,20}

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The results indicate that higher negative EEAC in the family environment in which these adolescents belong to is associated with lower abilities in mental flexibility/ working memory, attention, inhibitory control, and emotion processing. This suggests that the quality of the family environment is directly related to the adolescents' ability to adapt to sudden changes in the family environment, exert self-control, inhibit unwanted behaviors, retain and mentally work with information, and respond to their own and others' emotions. Possible explanations for these associations include the way in which the offspring learn by imitating parental behaviors and how they perceive facial and verbal expressions of emotion in social interactions. Also, children in stressful home/family environments often struggle to effectively allocate attention to less relevant outside stimuli (school, sports, and friends), which may affect their academic performance and cognitive development.⁵⁶ Finally, anxiety related to stressful family dynamics and consequent sleep pattern instability may also affect the availability of cognitive resources in other demanding environments.

A recent meta-analysis of ER in PBD showed that children and adolescents with PBD display impairments in ER when compared to controls.⁹ This is depicted in deficits in ER-related tasks, such as reward processing, reversal learning, facial emotion recognition, and attention in emotional contexts.⁵⁷⁻⁵⁹ Nevertheless, most of the tasks included in these studies combined only emotional and cognitive stimuli, pointing to an interface between these two domains. Our study showed the importance of

adding family environment to this analysis. Family environment influences important developmental milestones in the affective, cognitive, neurological, and social spheres, contributing to the development of the ability to self-regulate. Parenting style and experiences in the home/family environment have been shown to play an important role in offspring emotional development.^{56,60}

Research with abused and neglected children can help us better understand the role of extremely stressful family environments. A comprehensive systematic review of facial emotion recognition in maltreated children found that many of the deficits in emotion processing and recognition were related to stressful family environmental factors present in their families and home/family environments.⁶¹ The review showed that decisive factors for the process of ER in this population were not only the severity of the violence but also the age of onset of the abuse experienced by the child. Children that were victims of physical, sexual, and psychological abuse had a bias in the recognition of negative expressions such as anger and fear. 32,33,62 They also detected facial expressions of anger with less visual information than the children that did not suffer any abuse.^{61,63} Additionally, they were less accurate in processing positive and neutral images in adulthood in comparison to control groups, and more prone to be diagnosed with major depressive disorder.⁶¹ The excessive interpretation of the environmental cues as threatening or the incorrect readings of other facial expressions could be an adaptation to protect them from their hostile environment, but, unfortunately, could also interfere with their adjustment in a healthier environment and future social interactions.⁶¹ These findings suggests that traumatic experiences in childhood can negatively affect brain development, eventually leading to future psychopathology.61

Studies with healthy individuals also corroborate specific findings of our study. Young children learn the elementary rules of emotional understanding and expression in their household/family environment; therefore, parents' expressed emotions are directly related to the development of social and emotional skills in children.^{38,39} Affective flexibility was also found to be predictive of the individual's ability to use reappraisal as a strategy to diminish the intensity of sad emotions.⁶⁴ Johnson & Carver⁶⁵ found that emotional impulsivity is related to EF deficits, being mostly affected by inhibitory control difficulties. Hendricks & Buchanan found working memory to be associated with reduction in negative affect, while inhibitory control and mental flexibility helped predict aspects of emotional behavior and regulation.

Difficulties with ER in patients with PBD are further endorsed by anatomopathological substrates. PBD individuals, when compared to patients with ADHD, activated the neural circuitry of emotional processing more intensely than the working memory circuitry.^{15,16} These studies also found that both patients with PBD and those with ADHD had reduced cortical-subcortical activity under negative emotional circumstances, and elevated under positive emotional circumstances.^{15,16} Townsend & Altshuler⁶⁷ questioned whether ER and mood lability in both mania and depression could be related to disturbances in the frontal-limbic functional neuroanatomical networks.

Thus, our findings corroborate our hypothesis, suggesting that difficulties in self-regulation may rather be the tip of an iceberg of much deeper-rooted issues, including stressful home/family environments, cognitive impairments, and deficits in the ability to effectively read facial and vocal emotional cues, often leading to impaired social interactions and presenting as behavioral and emotional dysregulation. Relevant clinical implications of our findings include the importance of a multidisciplinary and context-oriented approach to the treatment of selfregulation issues in youth diagnosed with PBD. Focus, therefore, should not only be directed to the selfdysregulation symptoms reported by the parents, but also - and perhaps more importantly - to a more global perspective, which includes investigating and actively intervening in the family environment, while also assessing and rehabilitating cognitive and social abilities. A comprehensive understanding of ER in psychiatry is crucial, as pointed out by a meta-analytic review on ER strategies that highlighted how difficulties in ER and the use of maladaptive ER strategies are related to the maintenance of different psychiatric disorders.68 Recent studies have begun to show the results of cognitive behavioral therapy (CBT) for ER.^{69,70} Yang et al.⁶⁹ investigated the efficacy of 12 weeks of Mindfulness-Based Cognitive Therapy for Children (MBCT-C) on structural brain networks for mood-dysregulated youth with familial risk for BD and found that, after MBCT-C, disrupted topological properties in the mood-dysregulated group were significantly reduced. A pilot study by Scott & Mever⁷⁰ investigated the effects of Cognitive Behavioral Regulation Therapy (CBT-REG) for young people at high risk of PBD, with outcome data indicating that the intervention appears to demonstrate a relatively high benefit-to-risk ratio.

Although this is the first study to investigate SR as the association between EF, emotion processing, and family environmental factors in PBD, our results should be viewed with caution, considering several limitations, such as the small sample size (n=58); the cross-sectional design of the study; and the significant differences in IQ and sex between groups, for which we controlled by using ANCOVA. A larger sample size would have allowed us to conduct more complex statistical analyses, including different regressions and structural equation modeling (EQM), revealing associations rather than correlations, and would also have allowed us to employ corrections for multiple comparisons, such as a Bonferroni test.

Future studies, including larger samples and longitudinal designs, should aim at developing novel psychotherapeutic and rehabilitation approaches focused on a more global approach to improve self-regulation, by working simultaneously with all the components shown to be significant in the present study, including improving dynamics in the family environment and rehabilitating cognitive and social skills. Future studies should also aim to assess the correspondence between the deficits in EF found through neuropsychological testing with validated scales of executive functioning in daily life, as this would 26

be the most ecological way to detect nuances in these deficits.

The results of the present study suggest that, in patients with PBD, the development of SR ability is impacted by factors related to EF, emotion processing, and family environment. Thus, the construction of a solid and efficient self-regulatory ability would be contingent on the presence of satisfactory EF skills (inhibitory control, attention/working memory, mental flexibility), adequate emotion processing, and a favorable family environment.

Although incipient, results from this study are promising enough to highlight the importance of studying the development of self-regulation in PBD individuals, through the association between the abovementioned components. These findings bring much-needed attention to individuals with PBD in a complex, multifaceted, and integrated way. Treatment aiming to improve the adaptability and self-regulation of patients with PBD should study these young individuals from a developmental and integrative standpoint, encompassing the different factors presented in this study. Further research is needed in order to better understand how EF, emotion processing, and family environmental factors relate to each other and to the development of self-regulation in PBD, as well as how the treatment of these specific issues could help improve the difficulties in self-regulation found in this population.

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Disclosure

The authors report no conflicts of interest.

References

- 1 Goldstein BI, Birmaher B, Carlson GA, DelBello MP, Findling RL, Fristad M, et al. The International Society for Bipolar Disorders Task Force report on pediatric bipolar disorder: knowledge to date and directions for future research. Bipolar Disord. 2017;19:524-43.
- 2 Axelson DA, Birmaher B, Findling RL, Fristad MA, Kowatch RA, Youngstrom EA, et al. Concerns regarding the inclusion of temper dysregulation disorder with dysphoria in the diagnostic and statistical manual of mental disorders, fifth edition. J Clin Psychiatry. 2011; 72:1257-62.
- 3 Carlson GA, Klein DN. How to understand divergent views on bipolar disorder in youth. Annu Rev Clin Psychol. 2014;10:529-51.
- 4 Kleinman A, Caetano SC. Diagnostic challenges in youth with bipolar disorder. Curr Treat Options Psych. 2016;3:365-74.
- 5 Gomes BC, Kleinman A, Carvalho AF, Pereira TC, Gurgel AP, Lafer B, et al. Quality of life in youth with bipolar disorder and unaffected offspring of parents with bipolar disorder. J Affect Disord. 2016;202:53-7.
- 6 Nader EG, Kleinman A, Gomes BC, Bruscagin C, Santos B, Nicoletti M, et al. Negative expressed emotion best discriminates families with bipolar disorder children. J Affect Disord. 2013;148:418-23.

- 7 Frías A, Palma C, Farriols N. Neurocognitive impairments among youth with pediatric bipolar disorder: a systematic review of neuropsychological research. J Affect Disord. 2014;166:297-306.
- 8 Millman ZB, Weintraub MJ, Miklowitz DJ. Expressed emotion, emotional distress, and individual and familial history of affective disorder among parents of adolescents with bipolar disorder. Psychiatry Res. 2018;270:656-60.
- 9 Khafif TC, Rotenberg LS, Nascimento C, Beraldi GH, Lafer B. Emotion regulation in pediatric bipolar disorder: a meta-analysis of published studies. J Affective Disorders. 2021;285:86-96.
- 10 Gross JJ, Thompson RA. Emotion regulation: conceptual foundations. In: Gross JJ, editor. Handbook of emotion regulation. New York: The Guilford Press; 2007. p. 3-24.
- 11 Barkley RA. Attention-deficit/hyperactivity disorder, self-regulation, and executive functioning. In: Vohs KD, Baumeister RF, editors. Handbook of self-regulation: research, theory and applications. New York: The Guilford Press; 2011. p. 551-63.
- 12 Rich BA, Schmajuk M, Perez-Edgar KE, Pine DS, Fox NA, Leibenluft E. The impact of reward, punishment, and frustration on attention in pediatric bipolar disorder. Biol Psychiatry. 2005;58:532-9.
- 13 Nelson EE, Vinton DT, Berghorst L, Towbin KE, Hommer RE, Dickstein DP, et al. Brain systems underlying response flexibility in healthy and bipolar adolescents: an event-related fMRI study. Bipolar Disord. 2007;9:810-9.
- 14 Pavuluri MN, O'Connor MM, Harral EM, Sweeney JA. An fMRI study of the interface between affective and cognitive neural circuitry in pediatric bipolar disorder. Psychiatry Res. 2008;162:244-55.
- 15 Passarotti AM, Sweeney JA, Pavuluri MN. Differential engagement of cognitive and affective neural systems in pediatric bipolar disorder and attention deficit hyperactivity disorder. J Int Neuropsychol Soc. 2010;16:106-17.
- 16 Passarotti AM, Sweeney JA, Pavuluri MN. Emotion processing influences working memory circuits in pediatric bipolar disorder and attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2010;49:1064-80.
- 17 Passarotti AM, Ellis J, Wegbreit E, Stevens MC, Pavuluri MN. Reduced functional connectivity of prefrontal regions and amygdala within affect and working memory networks in pediatric bipolar disorder. Brain Connect. 2012;2:320-34.
- 18 Seymour KE, Kim KL, Cushman GK, Puzia ME, Weissman AB, Galvan T, et al. Affective processing bias in youth with primary bipolar disorder or primary attention-deficit/hyperactivity disorder. Eur Child Adolesc Psychiatry. 2015;24:1349-59.
- 19 Hafeman D, Bebko G, Bertocci MA, Fournier JC, Chase HW, Bonar L, et al. Amygdala-prefrontal cortical functional connectivity during implicit emotion processing differentiates youth with bipolar spectrum from youth with externalizing disorders. J Affect Disord. 2017;208: 94-100.
- 20 Duckworth AL, Carlson SM. Self-regulation and school success. In: Sokol BW, Grouzet FME, Muller U, editors. Self-regulation and autonomy: social and developmental dimensions of human conduct. New York: Cambridge University Press; 2013. p. 208-30.
- 21 Mischel W. The marshmallow test: understanding self-control and how to master it. New York: Random House; 2014.
- 22 Duckworth AL, Seligman ME. Self-discipline outdoes IQ in predicting academic performance of adolescents. Psychol Sci. 2005;16(12): 939-44.
- 23 Eisenberg N, Valiente C, Spinrad TL, Liew J, Zhou Q, Losoya SH, et al. Longitudinal relations of children's effortful control, impulsivity, and negative emotionality to their externalizing, internalizing, and co-occurring behavior problems. Dev Psychol. 2009;45:988-1008.
- 24 Moffitt TE, Arseneault L, Belsky D, Dickson N, Hancox RJ, Harrington H, et al. A gradient of childhood self-control predicts health, wealth, and public safety. Proc Natl Acad Sci USA. 2011;108:2693-8.
- 25 Ponitz CEC, McClelland MM, Jewkes AM, Connor CM, Farris CL, Morrison FJ. Touch your toes! Developing a direct measure of behavioral regulation in early childhood. Early Child Res Q. 2008; 23:141-58.
- 26 Diamond A. Executive functions. Annu Rev Psychol. 2013;64:135-68.
- 27 Elias LR, Miskowiak KW, Vale AMO, Köhler CA, Kjærstad HL, Stubbs B, et al. Cognitive impairment in euthymic pediatric bipolar disorder: a systematic review and meta-analysis. J Am Acad Child Adolesc Psychiatry. 2017;56:286-96.

- 28 Wozniak J, Petty CR, Schreck M, Moses A, Faraone SV, Biederman J. High level of persistence of pediatric bipolar-I disorder from childhood onto adolescent years: a four year prospective longitudinal follow-up study. J Psychiatr Res. 2011;45:1273-82.
- 29 Malhi GS, Ivanovski B, Hadzi-Pavlovic D, Mitchell PB, Vieta E, Sachdev P. Neuropsychological deficits and functional impairment in bipolar depression, hypomania and euthymia. Bipolar Disord. 2007;9:114-25.
- 30 Benito A, Lahera G, Herrera S, Muncharaz R, Benito G, Fernandez-Lira A, et al. Deficits in recognition, identification, and discrimination of facial emotions in patients with bipolar disorder. Braz J Psychiatry. 2013;35:435-8.
- 31 Shankman SA, Katz AC, Passarotti AM, Pavuluri MN. Deficits in emotion recognition in pediatric bipolar disorder: the mediating effects of irritability. J Affect Disord. 2013;144:134-140.
- 32 Bozorg B, Tehrani-Doost M, Shahrivar Z, Fata L, Mohamadzadeh A. Facial emotion recognition in adolescents with bipolar disorder. Iran J Psychiatry. 2014;9:20-4.
- 33 Lawlor-Savage L, Sponheim SR, Goghari VM. Impaired recognition of happy facial expressions in bipolar disorder. Acta Neuropsychiatr. 2014;26:253-9.
- 34 Rocca CCA, Heuvel EVD, Caetano SC, Lafer B. Facial emotion recognition in bipolar disorder: a critical review. Braz J Psychiatry. 2009;31:171-80.
- 35 Guyer AE, McClure EB, Adler AD, Brotman MA, Rich BA, Kimes AS, et al. Specificity of facial expression labeling deficits in childhood psychopathology. J Child Psychol Psychiatry. 2007;48:863-71.
- 36 Coleman PK, Karraker KH. Self-efficacy and parenting quality: findings and future applications. Dev Rev. 1997;18:47-85.
- 37 Karreman A, van Tuijl C, van Aken MAG, Deković M. The relation between parental personality and observed parenting: The moderating role of preschoolers' effortful control. Pers Individ Differ. 2008;44:723-34.
- 38 Halberstadt AG, Cassidy J, Stifter CA, Parke RD, Fox NA. Self-expressiveness within the family context: Psychometric support for a new measure. Psychol Assess. 1995;7:93-103.
- 39 Eisenberg N, Cumberland A, Spinrad TL. Parental socialization of emotion. Psychol Inq. 1998;9:241-73.
- 40 Etain B, Henry C, Bellivier F, Mathieu F, Leboyer M. Beyond genetics: childhood affective trauma in bipolar disorder. Bipolar Disord. 2008;10:867-76.
- 41 Etain B, Mathieu F, Henry C, Raust A, Roy I, Germain A, et al. Preferential association between childhood emotional abuse and bipolar disorder. J Trauma Stress. 2010;23:376-83.
- 42 Etain B, Aas M, Andreassen OA, Lorentzen S, Dieset I, Gard S, et al. Childhood trauma is associated with severe clinical characteristics of bipolar disorders. J Clin Psychiatry. 2013;74:991-8.
- 43 Garno JL, Goldberg JF, Ramirez PM, Ritzler BA. Impact of childhood abuse on the clinical course of bipolar disorder. Br J Psychiatry. 2005;186:121-5.
- 44 Upthegrove R, Chard C, Jones L, Gordon-Smith K, Forty L, Jones I, et al. Adverse childhood events and psychosis in bipolar affective disorder. Br J Psychiatry. 2015;206:191-7.
- 45 McIntyre RS, Soczynska JK, Mancini D, Lam C, Woldeyohannes HO, Moon S, et al. The relationship between childhood abuse and suicidality in adult bipolar disorder. Violence Vict. 2008;23:361-72.
- 46 Kaufman J, Birmaher B, Brent D, Rao U, Ryan N. Kiddie-Sadspresent and Lifetime version (K-SADS-PL) [Internet]. Pittsburgh: University of Pittsburgh; 1996. https://insideoutinstitute.org.au/ assets/kiddie%20sads%20present%20and%20lifetime%20version %20k%20sads%20pl.pdf
- 47 Poznanski E, Mokros HB, Grossman J, Freeman LN. Diagnostic criteria in childhood depression. Am J Psychiatry. 1985;142:1168-73.
- 48 Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry. 1978;133:429-35.

- 49 Weschler D. Weschler abbreviated scale of intelligence (WASI). New York: Harcourt Brace & Company; 1999.
- 50 Malloy-Diniz LF, Mattos P, Leite WB, Abreu N, Coutinho G, Paula JJ, et al. Translation and cultural adaptation of Barratt Impulsiveness Scale (BIS-11) for administration in Brazilian adults. J Bras Psiquiatr. 2010;59:99-105.
- 51 Conners CK, Staff MHS. Conners' continuous performance Test II (CPT II v. 5). New York: Multi-Health Syst Inc; 2000.
- 52 Berg EA. A simple objective technique for measuring flexibility in thinking. J Gen Psychol. 1948;39:15-22.
- 53 Friedmann MS, Goldstein MJ. Relatives' awareness of their own expressed emotion as measured by a self-report adjective checklist. Family Process. 1993;32:459-71.
- 54 Miklowitz DJ, Biuckians A, Richards JA. Early-onset bipolar disorder: a family treatment perspective. Dev Psychopathol. 2006;18: 1247-65.
- 55 Peris TS, Miklowitz DJ. Parental expressed emotion and youth psychopathology: new directions for an old construct. Child Psychiatry Hum Dev. 2015;46:863-73.
- 56 Repetti RL, Taylor SE, Seeman TE. Risky families: Family social environments and the mental and physical health of offspring. Psychol Bull. 2002;128:330-66.
- 57 Dickstein DP, Treland JE, Snow J, McClure EB, Mehta MS, Towbin KE, et al. Neuropsychological performance in pediatric bipolar disorder. Biol Psychiatry. 2004;55:32-9.
- 58 Dickstein DP, Leibenluft E. Emotion regulation in children and adolescents: boundaries between normalcy and bipolar disorder. Dev Psychopathol. 2006;18:1105-3.
- 59 McClure EB, Treland JE, Snow J, Schmajuk M, Dickstein DP, Towbin KE, et al. Deficits in social cognition and response flexibility in pediatric bipolar disorder. Am J Psychiatry. 2005;162:1644-51.
- 60 Bernier A, Carlson SM, Whipple N. From external regulation to selfregulation: Early parenting precursors of young children's executive functioning. Child Dev. 2010;81:326-39.
- 61 Assed MM, Khafif TC, Belizario GO, Fatorelli R, Rocca CCA, Serafim AP. Facial emotion recognition in maltreated children: a systematic review. J Child Fam Stud. 2020;29:1493-509.
- 62 Ferreira GCS, Crippa JA, Osório FL. Facial emotion processing and recognition among maltreated children: a systematic literature review. Front Psychol. 2014;5:1460.
- 63 Pollak SD, Sinha P. Effects of early experience on children's recognition of facial displays of emotion. Dev Psychol. 2002;38:784-91.
- 64 Malooly AM, Genet JJ, Siemer M. Individual differences in reappraisal effectiveness: the role of affective flexibility. Emotion. 2013;13: 302-13.
- 65 Johnson SL, Carver CS. Emotion-relevant impulsivity predicts sustained anger and aggression after remission in bipolar I disorder. J Affect Disord. 2016;189:169-75.
- 66 Hendricks MA, Buchanan TW. Individual differences in cognitive control processes and their relationship to emotion regulation. Cogn Emot. 2016;30:912-24.
- 67 Townsend J, Altshuler LL. Emotion processing and regulation in bipolar disorder: a review. Bipolar Disord. 2012;14:326-39.
- 68 Aldao A, Nolen-Hoeksema S, Schweizer S. Emotion-regulation strategies across psychopathology: A meta-analytic review. Clin Psychol Rev. 2010;30:217-37.
- 69 Scott J, Meyer TD. Brief research report: a pilot study of cognitive behavioral regulation therapy (CBT-REG) for young people at high risk of early transition to bipolar disorders. Front Psychiatry. 2021;11:616829.
- 70 Yang J, Lei D, Suo X, Tallman MJ, Qin K, Li W, et al. A preliminary study of the effects of mindfulness-based cognitive therapy on structural brain networks in mood-dysregulated youth with a familial risk for bipolar disorder. Early Interv Psychiatry. 2022;16:1011-9.