

Running Head: PBD AND RECOGNITION OF EMOTION

Deficits in Emotion Recognition in Pediatric Bipolar Disorder: The Mediating Effects of Irritability

Stewart A. Shankman, Andrea C. Katz, Alessandra M. Passarotti, and Mani N. Pavuluri

University of Illinois at Chicago

Correspondence concerning this article should be addressed to Stewart A. Shankman

University of Illinois at Chicago 1007 W Harrison, room 1062D M/C 285 Chicago, IL 60607

Phone: (312) 355-3812 Fax: (312) 413-4122 Email: stewarts@uic.edu

Abstract

Background: Pediatric Bipolar Disorder (PBD) is a debilitating condition associated with impairment in many domains. Social functioning is one of the disorder's most notable areas of impairment and this deficit may be in part due to difficulties recognizing affect in others.

Methods: In the present study, medication naïve youth with PBD were compared to age-matched healthy controls on their ability to a) distinguish between categorical emotions, such as happiness, anger, and sadness on the Emotion Recognition Test (ER-40) and b) differentiate between levels of emotional intensity on an adapted version of the Penn Emotional Acuity Task (Chicago-PEAT).

Results: Results indicated that PBD youth misidentified sad, fearful, and neutral faces more often than controls, and PBD girls mislabeled 'very angry' faces more often than healthy girls. A mediation analyses indicated that these diagnostic group differences on emotion recognition were significantly mediated by irritability.

Limitations: The Chicago-PEAT only examined variations in emotional intensity for the emotions happy and anger. Additionally, all results are correlational; therefore causal inferences cannot be made.

Conclusions: Supporting previous literature, the present findings highlight the importance of emotion recognition deficits in PBD individuals. Additionally, the irritability associated with PBD may be an important mechanism of this deficit and may thus represent an important target for treatment.

Key words: pediatric bipolar disorder, facial recognition, emotion, irritability

Funding Body Agreements and Policies

This research was supported by National Institute of Mental Health grants R01MH081019, R01MH085639, RC1MH088462 and foundation grants from the American Foundation for Suicide Prevention, Marshall Reynolds Foundation, NARSAD Foundation, and DANA Foundation, all awarded to Mani N. Pavuluri. Therefore, if accepted for publication, this manuscript should be deposited in PubMed Central.

Conflict of Interest

All authors declare that they have no conflicts of interest to report.

Acknowledgements

We would like to thank Jacklynn Fitzgerald and Allison Lowes, who assisted with data preparation.

Contributors

Mani Pavuluri and Alessandra Passarotti designed the study and collected the behavioral data.

Stewart Shankman managed the literature searches, analyses, and wrote the manuscript.

Andrea Katz undertook the statistical analyses and wrote the first draft of the manuscript. All authors contributed to and approved the final manuscript.

Deficits in Emotion Recognition in Pediatric Bipolar Disorder: The Mediating Effects of Irritability

Pediatric bipolar disorder (PBD) is increasingly being recognized as a significant public health problem (Leibenluft, 2008; Pavuluri et al., 2005) as evidenced by the explosion of research on the disorder over the last 15-20 years (Carlson, 2011). Although there is still controversy regarding how PBD should be classified and distinguished from neighbor diagnostic disorders (e.g., adult onset bipolar disorder and severe ADHD; Geller et al., 2007), recent studies have shown it to be associated with a unique phenotype, pattern of familial psychopathologies, and underlying neurophysiology (Leibenluft, 2011; Rende et al., 2007; Rich et al., 2007).

Some of the most debilitating deficits in PBD are interpersonal. Compared to both healthy controls and youth with other psychopathologies, youth with PBD report having fewer friends, and often no friends (Geller et al., 2000) and are rated by their parents to have lower social competence, more social withdrawal and aggression towards others (Geller et al., 1998). These interpersonal deficits also relate to the poor family cohesion and functioning observed in these patients (Rademacher et al., 2007; Sullivan and Miklowitz, 2010) even during periods of euthymia (Schenkel, et al., 2008).

One of the putative mechanisms for these interpersonal deficits is deficient recognition of affect in others (Dickstein and Leibenluft, 2006; Pavuluri et al., 2005). Specifically, individuals with PBD may misinterpret or overlook social cues from facial expressions and this may ultimately result in interpersonal difficulties with peers and family members. Consistent with this hypothesis, numerous studies have shown that individuals with PBD make more errors in identifying facial expressions than controls and those with other psychopathologies (Guyer et al., 2007; McClure et al., 2003; 2005). However, studies of emotion recognition are unclear as to whether this deficit is for emotions in general or specific emotions, especially those with negative emotional valence (e.g., fear, sadness, anger etc). Thus, one of the primary aims of

this study is to examine which emotional expressions are particularly difficult to identify by patients with PBD.

A few studies have also found that the *intensity* of the facial emotional expression moderated whether or not individuals with PBD had difficulty identifying expressions. These studies, however, have yielded inconsistent findings. In a small study of PBD youth (N=11), McLure et al. (2003) found that PBD individuals had difficulty identifying low-intensity emotion expressions, but performed as well as controls and those with anxiety disorders on high-intensity emotional faces. On the other hand, Schenkel et al. (2007) found that individuals with PBD misinterpreted intensely happy and sad faces (specifically, viewing them as more moderate). These equivocal findings warranted our second aim of this study, to examine the role of intensity of emotional expression on PBD performance.

Mediators.

A final goal of this study is to identify mediators of emotion recognition deficits in PBD. Studies on emotional deficits in PBD have typically not explored potential mechanisms that may account for these emotional deficits. Identification of mediators is a particularly important goal in clinical research as it could help identify possible targets for intervention.

The present study examined two potential mediators that are pervasive, impact daily life, and often require immediate intervention in PBD – executive dysfunction (i.e., cognitive problems related to strategic information processing, interference control, behavior control, decision-making and planning) and irritability (i.e., an emotional problem in which patients react with anger or frustration to internal or external stimuli). Numerous studies have shown that compared to both controls and those with other psychiatric conditions, individuals with PBD have deficits in several aspects of executive functioning (Pavuluri et al., 2006; 2009; Walshaw et al., 2010). Aspects of executive functioning could mediate emotion recognition in several ways. For example, difficulty in inhibiting distraction from external stimuli (i.e., interference control) could lead to problems identifying facial features that are critical for expression identification

(e.g., mouth, eyebrows). Similarly, ability to grasp, process and organize visual information may be difficult for individuals with PBD (Pavuluri et al., 2009).

Irritability is another potential mediator of emotional recognition deficits in PBD. Extreme irritability has been shown to be common in PBD, leading some to argue for its inclusion in the diagnostic criteria (Wozniak et al., 1995; Geller et al., 2002; Findling et al., 2001). Irritability may mediate deficits in emotion recognition, as irritability is associated with abnormal attention to emotional stimuli (Rich et al., 2005; 2007) and more generally, reduced ability to process environmental information (Bernat et al., 2007; Harmon-Jones et al., 1997).

In sum, there are three aims of the current study. First, we will compare PBD and controls on their ability to correctly identify a broad range of emotional facial expressions; based on the existing literature we predict that youth with PBD will not identify as many facial expressions, particularly negatively valenced ones, as healthy youth. Second, we will examine whether the intensity of the emotional expression impacts PBD individuals' ability to correctly identify emotional facial expressions; we hypothesize that youth with PBD will perform similarly to healthy youth when identifying more intensely emotional faces, but will not do as well with less intense facial expressions. Finally, we will examine whether executive functioning and/or irritability may mediate the emotional recognition deficits in PBD.

Methods

Participants

The sample consisted of 98 medication naïve children and adolescents with PBD and 104 healthy controls (age range: 8-17). Participants were recruited from clinics from the greater Chicago area and from community advertising. All PBD participants were currently experiencing a manic episode, and control participants were required to have no past or current diagnosis of any DSM-IV Axis I disorder. Consistent with the literature, 24% of those in the PBD group (24%) had a comorbid ADHD diagnosis (Arnold et al., 2011). PBD participants with and without ADHD did not differ significantly on performance in any of the tasks, so data from the two groups were

combined for all analyses. Verbal or written assent was provided by all youth in addition to the written informed consent by parents.

There were no significant differences between controls and PBD participants on age or ethnicity (see Table 1). There was a trend ($p=.06$) for a greater percentage of males in the PBD group compared to controls. Thus, gender was included as a between-subjects variable in all analyses. As was expected, the diagnostic groups also differed significantly from controls on the clinical variables examined.¹

Interview and Clinical Ratings. Each participant was interviewed with the Washington University Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS; Geller et al., 1994) to determine placement into diagnostic group. The K-SADS is a semi-structured diagnostic interview widely used to assess PBD and other psychopathologies in youth. Additionally, each participant was administered the Young Mania Rating Scale (YMRS; Young et al., 1978) and the Children's Depression Rating Scale—Revised (CDRS-R; Poznanski et al., 1985). One parent also completed the Child Mania Rating Scale—Parent Version (CMRS-P; Pavuluri et al., 2006). All clinical interviews and rating scales were completed by a master's or doctoral level rater, and our group has demonstrated high inter-rater reliability (kappas and reliability coefficients >0.96) for these measures in prior studies (Schenkel et al., 2007).

Affect Recognition Tasks. Affect recognition was assessed using two tasks from the Penn Neurocognitive Battery (PNB; Erwin et al., 1992): the Emotion Recognition Task (*ER-40*) and a variant of the Emotional Acuity Task (*Chicago-PEAT*). In the *ER-40*, participants viewed 40 adult faces and indicated by keypress if they thought the face was 'happy', 'sad', 'angry', 'fearful', or 'neutral'. This task was self-paced. The faces varied in gender and ethnicity, but each actor was used in the five valences. Accuracy scores were generated for each type of expression by dividing the total number of correct answers for each emotion by the total number of trials for that emotion. This yielded a percentage of correctly identified expressions for each valence.

In the *Chicago-PEAT*, participants viewed 40 faces of adults, adolescents and children ranging in intensity from very happy to very angry. In this self-paced task, participants decided if the face was ‘very happy’, ‘moderately happy’, ‘slightly happy’, ‘neutral’, ‘slightly angry’, ‘moderately angry’, or ‘very angry’. The original PEAT included faces ranging from very happy to very sad and did not include children’s faces. We chose to include children’s faces given the ages of the sample. Moreover, we included angry instead of sad faces for several reasons. First, anger plays a critical role in extant models of PBD (e.g., Geller et al., 2002). Second, those in the PBD group were all in a manic episode, a phase of the illness associated with irritability and intense angry outbursts. Third, we felt that it was important to compare happiness to anger as both relate to approach motivations (Harmon-Jones, 2008) and differ only on valence (positive vs. negative). In contrast, happiness and sadness differ on both valence and motivational direction (approach vs. withdrawal; Davidson et al., 2002), thus complicating interpretation of differences.

Performance on the *Chicago-PEAT* was measured with a correct valence score for each type of face shown. A percentage of the correctly identified valences of each type of face was calculated to examine overall performance. For example, the number of moderately happy faces correctly identified as happy (even if they were judged as very or slightly happy) was divided by the total number of moderately happy faces presented.

Measures for potential mediators

Executive Functioning. Executive functioning was assessed using the Behavior Rating Inventory of Executive Function (BRIEF) parent report form (Gioia et al., 2000). The BRIEF Parent Form is a self-report questionnaire that assesses parent’s perspective of their child’s executive functioning in home and school environments. The BRIEF provides a general measure of executive functioning (GEC), as well as two sub-domains within executive functioning: behavioral regulation index (BRI) and metacognitive index (MI). The BRIEF has

demonstrated good internal consistency and test-retest reliability, with the composite scores having higher reliability than individual area scores (all alphas in upper 0.80s; Gioia et al., 2000).

Irritability. Irritability was assessed using the Overt Aggression Scale—Modified for Outpatients (OAS-M; Coccaro et al., 1991). The OAS-M is a semi-structured interview that measures the frequency and severity of several categories of aggressive behavior and irritability. Global subjective irritability assesses the intensity and duration of externally directed *feelings* of irritability or anger, whether they are expressed or not. Global overt irritability, taps into the intensity of overt irritability, as evidenced by the child's *behavior*. The OAS-M has demonstrated adequate construct validity and internal consistency and is a standard measure of aggression and irritability in youth (Malone et al., 2000).

Data Analysis. To examine group differences on the *ER-40*, we conducted an emotion (Happy, Sad, Fearful, Angry, No Emotion) X diagnosis (PBD vs. Controls) mixed effects analysis of variance (ANOVA). Similarly, to examine group differences on the *Chicago-PEAT*, we conducted a valence (Happy vs. Angry) X intensity (Slightly, Moderately, Very) X diagnosis (PBD vs. controls) mixed effects analysis of variance (ANOVA). For both sets of analyses, accuracy was the dependent variable (see definitions above) and gender was included as a between subjects factor in all analyses. Because of the self-paced nature of the tasks, Reaction Time (RT) was not considered for analyses.

To test whether executive functioning and/or irritability mediated group differences, we used Preacher and Hayes' (2008) widely used analytic technique for testing mediation, an approach that has been shown to be more robust than other mediation techniques (e.g., Baron and Kenny, 1986).

Results

ER-40. For the *ER-40*, there were main effects of diagnosis ($F(1, 196) = 19.86, p < .01$) and valence ($F(4, 784) = 166.69, p < .001$). Across all conditions PBDs ($M = 0.74, SD = 0.15$) performed more poorly than HCs ($M = 0.81, SD = 0.16$), and both groups performed the best on

correctly identifying happy faces ($M = 0.96$ $SD = 0.12$) and the worst at identifying angry faces ($M = 0.55$ $SD = 0.19$), (see Figure 1).

These main effects were qualified by a significant interaction between emotion and diagnostic group $F(4, 784) = 166.69$, $p < .001$. Follow-up univariate ANOVAS comparing the two diagnostic groups on each level of emotion revealed that the PBD group correctly identified significantly fewer sad, fearful, and neutral faces than the HC group, $F(1, 196) = 7.94$, $F(1, 196) = 9.29$, $F(1, 196) = 18.39$, all p 's $< .01$. The two groups performed equally well on the happy faces and equally poorly on the angry faces (both p 's $> .29$). Additionally, there was a three-way interaction between emotion, diagnostic group, and gender, $F(4, 784) = 2.65$, $p < .05$, which was driven by the PBD boys' misidentification of neutral faces $F(1, 196) = 6.22$, $p < .05$ (see Fig. 1).

Chicago-PEAT. For the *Chicago-PEAT*, there were main effects for valence, $F(1, 198) = 30.38$, $p < .001$, diagnosis, $F(1, 198) = 10.59$, $p < .01$, and intensity $F(2, 396) = 265.76$, $p < .001$). These main effects reflected overall better identification for happy compared to angry faces (valence), better overall performance by controls than PBD individuals (diagnosis), and better overall recognition for 'very' intense compared to 'moderately' intense compared to 'slightly intense' (intensity). Additionally, there was a significant Valence X Intensity X Diagnosis X Gender 4-way interaction $F(2, 396) = 4.38$, $p < .05$. Follow-up analyses by gender revealed that this was driven by the PBD girls. Specifically, PBD girls were less likely to rate a very angry face as angry than their healthy counterparts $t(88) = 4.14$, $p < .01$ (see Fig. 2).

Mediation of group differences. Before looking at mediation, we conducted Gender (male vs. female) X Diagnosis (PBD vs. control) between-subjects ANOVAs for each of the proposed mediators to examine differences between groups. For all measures of executive functioning, there were main effects of diagnosis, such that those with PBD had more difficulties than controls (all p 's $< .01$), but no main effects for gender or gender by diagnosis interactions (all p 's $> .20$). For irritability, there was also a main effect of diagnosis such that youth with PBD had higher ratings than controls, $F(1, 193) = 430.82$, $p < .001$ and a main effect of gender, reflecting

higher ratings for girls than boys, $F(1, 193) = 5.56, p < .05$. These main effects were qualified by a gender by diagnosis interaction $F(1, 193) = 3.81, p = .05$. Follow-up analyses indicated that although boys and girls in the control group did not differ on irritability, $F(1, 101) = 0.12, n.s.$, girls with PBD had significantly higher irritability ratings than boys with PBD $F(1, 92) = 6.92, p < .05$.

To examine potential mediators of the group differences observed, we used Preacher and Hayes' (2008) mediational analytic technique to explore whether executive functioning and/or irritability mediated the effect of diagnosis on the effects identified above - accuracy on 1) sad and 2) fearful trials on the *ER-40*, as well as 3) 'very angry' trials of the Chicago PEAT. Results showed that none of the executive functioning scores from the BRIEF were significant mediators of performance, as all of the confidence intervals contained zero. Irritability, on the other hand, emerged as a significant mediator of task performance for all three effects (see Figure 3). Specifically, irritability mediated (i.e., confidence intervals did not contain zero) the relationship between diagnosis and accuracy score for sad and fearful trials on the *ER-40*, as well as the relationship between diagnosis and correct valence score for the very angry trials on the *Chicago-PEAT*.

Discussion

The primary goal of this study was to identify deficits in emotional identification in the largest sample, to date, of medication naïve youths with PBD while also exploring potential mediators of these deficits. On the first task (*ER-40*; Erwin et al., 1992), individuals with PBD performed significantly worse than controls when identifying the discrete emotions of sad, fearful, and neutral. Interestingly, the two groups performed equally well on identifying happy faces and equally poorly on identifying angry faces. These findings support our first hypothesis and suggest that youth with bipolar disorder are no worse at correctly identifying happy faces than healthy controls and that their deficits are more apparent for negative valences – sad and fearful (but not anger). These results are consistent with other studies that have identified

emotion recognition deficits in PBD (de Almeida Rocca et al., 2009; McLure et al., 2003), but extend the literature by suggesting that the findings are specific to these negative emotions.

The most robust effect of diagnosis on accuracy in the *ER-40* was for neutral faces. This finding adds to the growing interest in psychopathology research on examining group differences on reactions to “non-emotional” stimuli (Leppanen et al., 2004; Nelson and Shankman, 2011) and within PBD, specifically. For example, Rich et al. (2006) found that compared to controls, youths with PBD perceived greater hostility in neutral faces and reported greater subjective fear while viewing them.

There are several explanations for why the groups did not differ on happy or angry faces on the *ER-40*. First, because PBD individuals were all in a manic phase of the illness, they may have been biased towards the happy faces (Elliott et al., 2004). However, studies in adult bipolar disorder have also failed to find effects for happy faces (Yurgelun-Todd et al., 2000). Second, the lack of effects for group may have been due to a ‘ceiling’ and ‘floor’ effect, respectively, as controls performed best on happy trials and worst on angry trials.

The results for the *Chicago-PEAT* helped address this latter explanation as it examined whether the groups differed on the accuracy of identifying angry and happy faces of *different intensities*. The PBD group did not exhibit deficits for any of the happy intensities, but, somewhat contrary to our hypotheses, they did differ from controls on the ‘very angry’ faces and this difference was moderated by gender. Specifically, PBD girls performed significantly worse at identifying ‘very angry’ faces compared to healthy girls. Taken together with the results from the *ER-40*, these results suggest that individuals with PBD have an intact ability to recognize happy emotional faces (regardless of the intensity of the happy expression).

The effects for ‘very angry’ on the *Chicago-PEAT* may have been specific to girls with PBD for several reasons. First, there may be a “threshold effect” of irritability that, when crossed, leads to an impaired ability to recognize very angry faces. As girls with PBD were more irritable than boys with PBD in the present sample, it is possible that girls were more likely

to “cross the threshold” and perform worse on the very angry trials of the PEAT. This concept has been put forth in other studies where girls have exhibited greater overall emotional intensity than boys (Silk et al., 2003).

Another possibility relates to the socialization of emotions. Studies show that throughout development, girls inhibit the expression and recognition of emotions considered to be socially unacceptable (like anger) and that this may be a result of socialization (Brody, 1985). Thus, the PBD girls may have misidentified the very angry faces on the PEAT due to cultural influences. On the other hand, this explanation does not address why healthy girls did not also misidentify very angry faces.

Irritability as a mediator. A particularly novel aspect of the study is that we examined potential mediators of these PBD deficits. Interestingly, the results suggest that irritability was a significant mediator of the relationship between diagnosis and performance on the *Chicago-PEAT* and *ER-40*. One interpretation of this effect is that youths with PBD may be too focused on their own feelings of irritability to correctly recognize the facial expressions of others. As recognition of emotional faces is closely related to the ability to empathize with others' emotional state (Besel and Yuile, 2010; Marissen et al., 2012), these results suggest that irritability may be a proximal factor in this critical interpersonal skill and potentially the overall interpersonal deficits observed in PBD (Geller et al., 2000). Additionally, while empathy has not been specifically examined in PBD, deficits in empathic responding have been observed in individuals with adult bipolar disorder (Cusi et al., 2010) even during a euthymic state (Shamay-Tsoory et al., 2009).

Strengths and Limitations

The study had several significant strengths including a large, carefully diagnosed sample of PBD youths, who were all un-medicated and in the same mood phase (i.e., manic). Additionally, key demographic characteristics were addressed in the design and/or analyses (e.g., matching on age, controlling for gender, IQ). The study, however, had a few limitations. First, the *Chicago-PEAT* only examined degrees of emotional intensity for happy and anger.

While these were the two emotions for which the groups did not differ on the *ER-40* (allowing for an analysis of whether intensity moderated these null effects), it is possible that there could be important group effects for different intensities of other emotions (e.g., sadness, fear). Second, all results were correlational and thus cannot elucidate upon the causal pathways of the results. Third, irritability was only assessed via self-report. It will therefore be important for future studies to examine other indicators of irritability, such as behavioral tasks that may assess this construct more directly.

Conclusion

In summary, the results suggest that individuals with PBD have deficits in identifying sad, fearful and 'very intense' angry faces and that irritability may be an important mediator of these deficits. As correctly identifying the emotions of others is a key component of adaptive interpersonal functioning, one clinical implication of these results is that psychosocial interventions should address this deficit, perhaps by targeting the irritability observed in PBD. One way that irritability could be targeted is through mindfulness based therapy techniques that are beginning to be used with youths with PBD (West et al., 2009). These techniques encourage youths to bring their full attention to the present moment and to not judge their present state. This skill may decrease some of the arousal that comes with irritability (Specia et al., 2000), sever their connection to their own negative emotions, and thus allow for more pleasant, meaningful interactions with their peers and families.

Footnote

1. The groups also differed significantly on IQ (i.e., WASI; PsychCorp, 1999). Therefore, we conducted parallel analyses on a sample of these participants matched on IQ and obtained the same pattern of results. For ease of interpretation, only the results from the entire sample are reported here.

Table 1. Sample demographics and clinical characteristics

	PBD (n = 98)	HC (n = 104)	p-value
% Males	62%	49%	.059
White	54%	44%	.162
Comorbid ADHD	25%	---	---
Age (SD)	13.19 (2.26)	13.39 (1.76)	.491
IQ (SD)	100 (13.64)	112 (12.96)	.000
Mania Rating (SD)			
YMRS	23.00 (6.89)	2.50 (4.62)	.000
CMRS-P	21.93 (10.77)	3.63 (4.35)	.000
CDRS (SD)	39.89 (10.72)	20.74 (4.18)	.000
Executive Functioning (SD)			
BRI	64.55 (10.88)	34.80 (9.85)	.000
MI	102.26 (21.16)	63.38 (18.52)	.000
GEC	164.99 (33.91)	98.16 (27.25)	.000
Irritability			
Subjective	2.91 (1.00)	0.36 (0.77)	.000
Overall	2.88 (1.01)	0.34 (0.77)	.000

Note. Mania symptoms measured by Young Mania Rating Scale (YMRS) and Child Mania Rating Scale – Parent Version (CMRS-P). Depressive symptoms measured using Child Depression Rating Scale (CDRS). Executive function measured by Behavioral Regulation Index (BRI), Metacognition Index (MI), and Global Executive Composite (GEC) scores from the BRIEF.

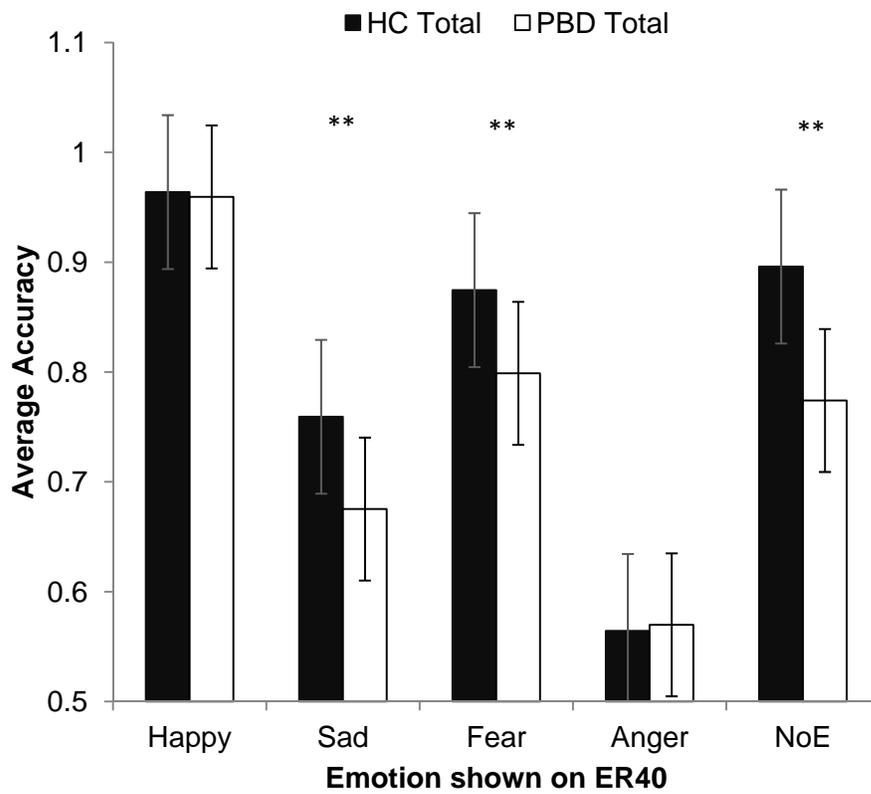


Fig. 1. Diagnostic group differences on accuracy scores on the *ER-40*. ** $p < .01$

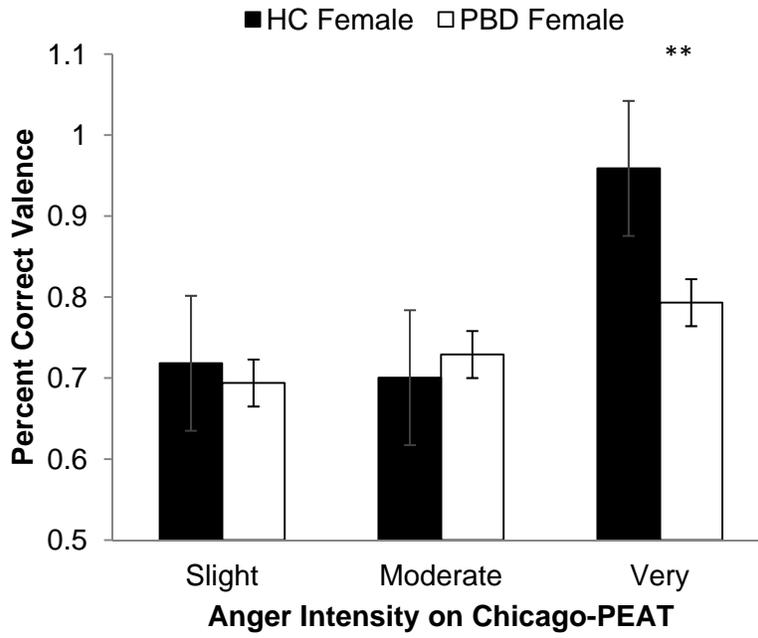


Fig. 2. Diagnostic group differences on valence accuracy on the *Chicago-PEAT* in females.

** $p < .01$

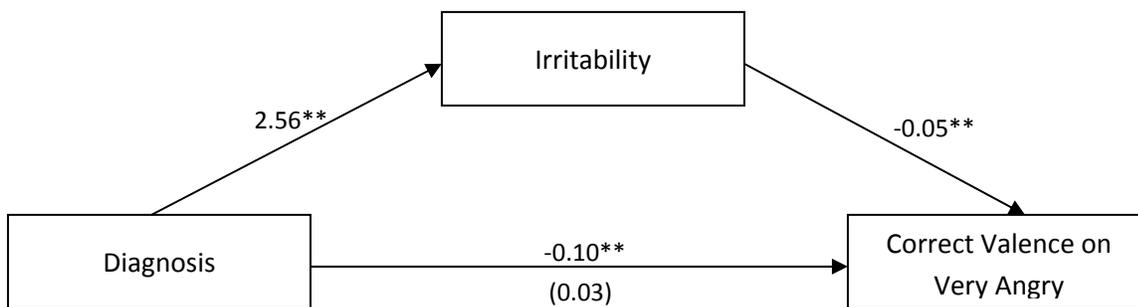
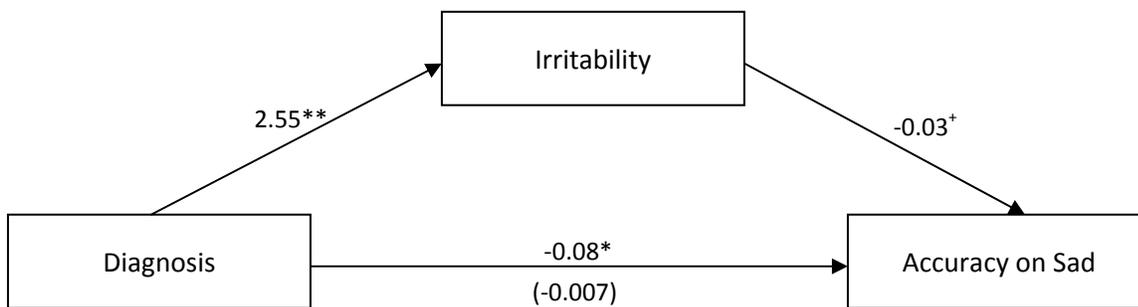
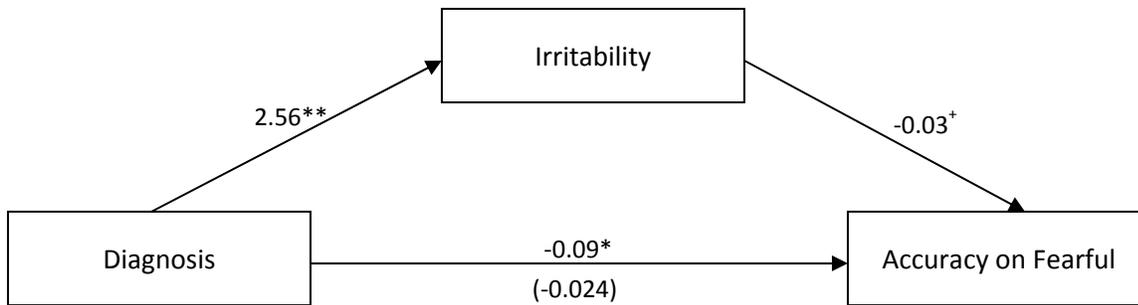


Fig. 3. Pictorial representation of irritability mediating the relationship between diagnosis and task performance on the fearful and sad trials of the *ER-40* and the very angry trials of the *Chicago-PEAT*. Path coefficients displayed for relationship between each variable.

** $p < .01$, * $p < .05$, + $p < .1$

References

- Arnold, L.E., Demeter, C., Mount, K., Frazier, T.W., Youngstrom, E.A., Fristad, M., Birmaher, B., Findling, R.L., Horwitz, S.M., Kowatch, R., Axelson, D.A., 2011. Pediatric bipolar spectrum disorder and ADHD: comparison and comorbidity in the LAMS clinical sample. *Bipolar Disord.* 13, 509-521.
- Baron, R.M., Kenny, D.A., 1986. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J. Pers. Soc. Psychol.* 51, 1173-1182.
- Bernat, E.M., Hall, J.R., Steffen, B.V., Patrick, C.J., 2007. Violent offending predicts p300 amplitude. *Int. J. Psychophysiol.* 62, 161-167.
- Besel, L.D.S., Yuille, J.C., 2010. Individual differences in empathy: the role of facial expression recognition. *Pers. Individ. Differ.* 49, 107-112.
- Brody, L.R., 1985. Gender differences in emotional development: a review of theories and research. *J. Pers.* 53, 102-150.
- Carlson, G.G., 2011. Diagnostic stability and bipolar disorder in youth. *J. Am. Acad. Child Adolesc. Psychiatry.* 50, 1202-1204.
- Coccaro, E.F., Harvey, P.D., Kupsaw-Lawrence, E., Herbert, J.L., Bernstein, D.P., 1991. Development of neuropharmacologically based behavioral assessments of impulsive aggressive behavior. *J. Neuropsychiatry Clin. Neurosci.* 3, s44-s51.
- Cusi, A., MacQueen, G.M., McKinnon, M.C., 2010. Altered self-report of empathic responding in patients with bipolar disorder. *Psychiatry Res.* 178, 354-358.
- Davidson, R.J., Lewis, D.A., Alloy, L.B., Amaral, D.G., Bush, G., Cohen, J.D., Drevets, W.C., Farah, M.J., Kagan, J., McClelland, J.L., Nolen-Hoeksema, S., Peterson, B. S., 2002. Neural and behavioral substrates of mood and mood regulation. *Biol. Psychiatry.* 52, 478-502.

- Dickstein, D., Leibenluft, E., 2006. Emotion regulation in children and adolescents: boundaries between normalcy and bipolar disorder. *Dev. Psychopathol.* 18, 1105-1131.
- Elliott, R., Ogilvie, A., Rubinsztein, J.S., Calderon, G., Dolan, R.J., Sahakian, B.J., 2004. Abnormal ventral frontal response during performance of an affective go/no go task in patients with mania. *Biol. Psychiatry.* 55, 1163-1170.
- Erwin, R.J., Gur, R.C., Gur, R.E., Skolnick, B., Mawhinney-Hee, M., Smailis, J., 1992. Facial emotion discrimination: I. Task construction and behavioral findings in normal subjects. *Psychiatry Res.* 43, 231-240.
- Findling, R.L., Gracious, B.L., McNamara, N.K., Youngstrom, E.A., Demeter, C.A., Branicky, L.A., Calabrese, J.R., 2001. Rapid, continuous cycling and psychiatric co-morbidity in pediatric bipolar I disorder. *Bipolar. Disord.* 3, 202-210.
- Geller, B., Tillman, R., Bolhofner, K., 2007. Proposed definitions of bipolar I disorder episodes and daily rapid cycling phenomena in preschoolers, school-aged children, adolescents, and adults. *J. Child. Adolesc. Psychopharmacol.* 17, 217-222.
- Geller, B., Zimmerman, B., Williams, M., Del Bello, M.P., Bolhofner, K., Craney, J.L., Frazier, J., Beringer, L., Nickelsburg, M.J., 2002. DSM-IV mania symptoms in a prepubertal and early adolescent bipolar disorder phenotype compared to attention-deficit hyperactive and normal controls. *J. Child. Adolesc. Psychopharmacol.* 12, 11-25.
- Geller, B., Bolhofner, K., Craney, J.L., Williams, M., Del Bello, M.P., Gundersen, K., 2000. Psychosocial functioning in a prepubertal and early adolescent bipolar disorder phenotype. *J. Am. Acad. Child. Adolesc. Psychiatry.* 39, 1543-1548.
- Geller, B., Warner, K., Williams, M., Zimmerman, B., 1998. Prepubertal and young adolescent bipolarity versus ADHD: assessment and validity using the WASH-U-KSADS, CBCL and TRF. *J. Affect. Disord.* 51, 93-100.
- Geller, B., Zimmerman, B., Williams, M., Frazier, J., 1994. WASH-U-KSADS (Washington University at St. Louis Kiddie and Young Adult Schedule for Affective Disorders and

- Schizophrenia — Lifetime and Present Episode Version for DSM-IV). Washington University School of Medicine, St. Louis, MO.
- Gioia, G.A., Isquith, P.K., Guy, S.C., Kenworthy, L., 2000. Behavior Rating Inventory of Executive Function. Psychological Assessment Resources, Odessa, FL.
- Guyer, A.E., McClure, E.B., Adler, A.D., Brotman, M.A., Rich, B.A., Kimes, A.S., Leibenluft, E., 2007. Specificity of facial expression labeling deficits in childhood psychopathology. *J. Child. Psychol. Psychiatry.* 48, 863-871.
- Harmon-Jones, E., Peterson, C., Gable, P.A., Harmon-Jones, C., 2008. Anger and approach-avoidance motivation. In: Elliot, A.J. (Ed.), *Handbook of Approach and Avoidance Motivation.* Psychology Press, NY, pp. 399-413.
- Harmon-Jones, E., Barratt, E.S., Wigg, C., 1997. Impulsiveness, aggression, reading, and the P300 of the event-related potential. *Personality and Individual Differences,* 22, 439-445.
- Leibenluft, E., 2011. Severe mood dysregulation, irritability, and the diagnostic boundaries of bipolar disorder in youths. *Am. J. Psychiatry.* 168, 129-142.
- Leppänen, J.M., Milders, M., Bell, J.S., Terriere, E., Hietanen, J.K., 2004. Depression biases the recognition of emotionally neutral faces. *Psychiatry. Res.* 128, 123-133.
- Malone, R.P., Delaney, M.A., Leubbert, J.F., Carter J.C., Campbell, M., 2000. A double-blind placebo-controlled study of lithium in hospitalized aggressive children and adolescents with conduct disorder. *Arch. Gen. Psychiatry.* 57, 649-654.
- Marissen, M.A.E., Deen, M.L., Franken, I.H.A., 2012. Disturbed emotion recognition in patients with narcissistic personality disorder. *Psychiatry. Res.* in press.
- McClure, E.B., Pope, K., Hoberman, A.J., Pine, D.S., Leibenluft, E., 2003. Facial expression recognition in adolescents with mood and anxiety disorders. *Am. J. Psychiatry.* 160, 1172-1174.

- McClure, E.B., Treland, J.E., Snow, J., Schmajuk, M., Dickstein, D.P., Towbin, K.E., Charney, D.S., Pine, D.S., Leibenluft, E., 2005. Deficits in social cognition and response flexibility in pediatric bipolar disorder. *Am. J. Psychiatry.* 162, 1644-1651.
- Nelson, B.D., Shankman, S.A., 2011. Does intolerance to uncertainty predict anticipatory startle response to uncertain threat? *Int. J. Psychophysiol.* 81, 107-115.
- Pavuluri, M.N., Henry, D.B., Bhargavi, D., Carbray, J.A., Birmaher, B., 2006. Child Mania Rating Scale: development, reliability, and validity. *J. Am. Acad. Child. Adolesc. Psychiatry.* 45, 550-560.
- Pavuluri, M.N., Birmaher, B., Naylor, M.W., 2005. Pediatric bipolar disorder: A review of the past 10 years. *J. Am. Acad. Child. Adolesc. Psychiatry.* 44, 846-871.
- Poznanski, E., Freeman, L., Mokros, H., 1985. Children's Depression Rating Scale—Revised. *Psychopharmacol. Bull.* 21, 979-989.
- Preacher, K.J., Hayes, A.F., 2008. Asymptotic and resampling methods for assessing and comparing indirect effects in multiple mediator models. *Behav. Res. Methods.* 40, 879-891.
- Rende, R., Birmaher, B., Axelson, D., Strober, M., Gill, M.K., Valeri, S., Chiappetta, L., Neal, R., Leonard, H., Hunt, J., Iyengar, S., Keller, M., 2007. Childhood-onset bipolar disorder: evidence for increased familial loading of psychiatric illness. *J. Am. Acad. Child. Adolesc. Psychiatry.* 46, 197-204.
- Rich, B.A., Schmajuk, M., Perez-Edgar, K.E., Pine, D.E., Fox, N.A., Leibenluft, E., 2005. The impact of reward, punishment, and frustration on attention in pediatric bipolar disorder. *Biol. Psychiatry.* 58, 532-539.
- Rich, B.A., Schmajuk, M., Perez-Edgar, K.E., Fox, N.A., Pine, D.E., Leibenluft, E., 2007. Different psychophysiological and behavioral responses elicited by frustration in pediatric bipolar disorder and severe mood dysregulation. *Am. J. Psychiatry.* 164, 309-3017.

- Rich, B.A., Vinton, D.T. Roberson-Nay, R., Hommer, R.E., Berghorst, L.H., McClure, E.B., Fromm, S.J., Pine, D.S., Leibenluft, E., 2006. Limbic hyperactivation during processing of neutral facial expressions in children with bipolar disorder. *Proc. Natl. Acad. Sci.* 103, 8900-8905.
- Rocca, C.C.A., Heuvel, D., Caetano, S.C., Lafer, B., 2009. Facial emotion recognition in bipolar disorder: A critical review. *Rev. Bras. Psiquiatr.* 31, 171-180.
- Schenkel, L.S., West, A.E., Harral, E.M., Patel, N.B. and Pavuluri, M.N., 2008. Parent-child interactions in pediatric bipolar disorder. *J. Clin. Psycholol.* 64, 422-437.
- Shamay-Tsoory, S., Harari, H., Szepsenwol, O., Levkovitz, Y., 2009. Neuropsychological evidence of impaired empathy in euthymic bipolar disorder. *J. Neuropsychiatry. Clin. Neurosci.* 21, 59-67.
- Silk, J.S., Steinberg, L., Morris, A.S., 2003. Adolescents' emotion regulation in daily life: Links to depressive symptoms and problem behavior. *Child. Dev.* 74, 1869-1880.
- Specia, M., Carlson, L.E., Goodey, E., Angen, M., 2000. A randomized, wait-list controlled clinical trial: the effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. *Psychosom. Med.* 62, 613-622.
- Sullivan, A.E., Miklowitz, D.J., 2010. Family functioning among adolescents with bipolar disorder. *J. Fam. Psychol.* 24, 60-67.
- Walshaw, P., Alloy, L., Sabb, F., 2010. Executive function in pediatric bipolar disorder and attention-deficit hyperactivity disorder: in search of distinct phenotypic profiles. *Neuropsychol. Rev.* 20, 103-120.
- Wechsler, D., 1999. Wechsler Abbreviated Scale of Intelligence. *Psychological Corporation.*
- West, A., Jacobs, R., Westerholm, R., Lee, A., Carbray, J., Heidenreich, J., Pavuluri, M., 2009. Child and family-focused cognitive-behavioral therapy for pediatric bipolar disorder: pilot study of group treatment format. *J. Can. Acad. Child. Adolesc. Psychiatry.* 18, 239-245.

Wozniak, J., Biederman, J., Kiely, K., Ablon, J.S., 1995. Mania-like symptoms suggestive of childhood-onset bipolar disorder in clinically referred children. *J. Am. Acad. Child. Adolesc. Psychiatry.* 34, 867-876.

Young, R.C., Biggs, J.T., Ziegler, V.E., Meyer, D.A., 1978. A rating scale for mania: reliability, validity and sensitivity. *Br. J. Psychiatry.* 133, 429-435.

Yurgelun-Todd, D.A., Gruber, S., Kanayama, G., Killgore, W.D.S., Baird, A.A., Young, A.D., 2000. fMRI during affect discrimination in bipolar affective disorder. *Bipolar. Disord.* 2, 237-248.