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Facial Emotion Recognition and Mood Symptom Course in Young Adults with Childhood-Onset Bipolar Disorder

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Abstract

Facial emotion recognition deficits are common in bipolar disorder (BD) and associated with impairment. However, the relationship between facial emotion recognition and mood course is not well understood. This study examined facial emotion recognition and subsequent mood symptoms in young adults with childhood-onset BD vs. Typically-Developing Controls (TDCs). The sample included 116 young adults (ages 18-30, 58% Male, 78% White) with prospectively-verified childhood-onset BD (n=52) and TDCs (n=64). At baseline, participants completed a facial emotion recognition task (Diagnostic Analysis of Non-Verbal Accuracy-2) and clinical measures. Then, participants with BD completed mood symptom assessments every 6 months (M=8.7±5.2 months) over two years. Analyses included independent-samples t-tests

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Conflicts of Interest

Dr. Dickstein receives research support from NIMH and NARSAD. Dr. Yen receives research support from NIMH and NICCH. Ms. Hower receives honorarium from the U.S. Department of Defense and UCSD, and research support from NIMH. Dr. Hunt receives honoraria from Wiley Publishers and LPG, and research support from NIMH. Dr. Keller receives research support from NIMH and donor gifts from The John J. McDonnell and Margaret T. O'Brien Foundation. Dr. Radoeva receives research support from AACAP. Drs. MacPherson, Kudinova, and Kim, and Ms. Jenkins, Gilbert, Barthelemy, and DeYoung declare that they have no conflicts of interest.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The described studies were both approved by the Institutional Review Boards of Bradley Hospital and Brown University.

Informed Consent

Informed consent was obtained from all individual participants included in these studies.

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and mixed-effects regression models. Participants with BD made significantly more recognition errors for child expressions than TDCs. There were no significant between-group differences for recognition errors for adult expressions, or errors for specific child or adult emotional expressions. Participants had moderate baseline mood symptoms. Significant time-by-facial emotion recognition interactions revealed more recognition errors for child emotional expressions predicted lower baseline mania and stable/consistent trajectory; fewer recognition errors for child expressions predicted higher baseline mania and decreasing trajectory. In addition, more recognition errors for adult sad expressions predicted stable/consistent depression trajectory and decreasing mania; fewer recognition errors for adult sad expressions predicted decreasing depression trajectory and stable/consistent mania. Effects remained when controlling for baseline demographics and clinical variables. Facial emotion recognition may be an important brain/behavior mechanism, prognostic indicator, and intervention target for childhood-onset BD, which endures into young adulthood and is associated with mood trajectory.

Keywords

bipolar disorder; face processing; emotion recognition; prediction; child; young adult

Introduction

Bipolar disorder (BD) is a major public health concern and ranked among the top four most burdensome problems worldwide in young people ages 10-24 [1]. BD affects 3.9% of youth [2], often persists into adulthood [3,4], and is associated with psychosocial impairment [5,6], poor quality of life [7], high rates of comorbidity and psychiatric medication usage [8], and suicidality [9]. Neurocognitive deficits are also common in BD, including impairment in facial emotion recognition [10-12]. Facial expressions offer important social information, and the ability to identify, interpret, and respond appropriately to human emotional expressions is critical to interpersonal functioning [13]. Such difficulties may contribute to psychosocial deficits observed in BD [5,6]. While impaired facial emotion recognition has been documented in samples of children and adults with BD [10-12], and proposed as a potential endophenotype [14,15], little is known about facial emotion recognition in childhood-onset BD (i.e., onset prior to age 18) across the developmental transition to young adulthood, and potential associations with mood symptom trajectory.

A substantial body of literature has documented deficits in facial emotion recognition at both a behavioral and neural level in child and adult BD samples. Adults with BD show deficits in facial emotion recognition compared to typically-developing controls (TDCs) when euthymic and symptomatic [10,11]. Similar deficits have been observed in first-degree relatives of adults with BD [14,15]. In addition, these deficits are associated with psychosocial dysfunction and poor quality of life [10,11]. Studies have also documented impairment in facial emotion recognition in children with BD [16-20] and at risk for BD [16] compared to TDCs and other diagnostic groups. Some studies have found this impairment in facial emotion recognition to be specific to child expressions [17,20], while the adult literature demonstrates more broad and generalized impairments in facial emotion

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recognition deficits [10,11]. In addition, facial emotion recognition deficits are correlated with psychosocial impairment in children with BD [18].

Functional magnetic resonance imaging (fMRI) investigations have also found that adults with BD have alterations in brain regions during facial emotion recognition tasks, including the amygdala, prefrontal cortex, and striatum [12]. Similarly, fMRI studies have shown alterations in prefrontal, limbic, and striatal functioning for children with BD while completing facial emotion recognition tasks [12]. However, no studies have examined the relationship between facial emotion recognition deficits and subsequent symptom trajectory in childhood-onset BD across development. Such data could inform age-related mechanisms, illness progression processes, and areas for intervention.

Inaccurate identification of facial expressions in individuals with BD may contribute to psychosocial and interpersonal impairments [5,6]. For instance, inability to correctly identify, interpret, and respond to emotional expressions in interpersonal interactions may be perceived as off-putting, invalidating, or frustrating to recipients, potentially fostering strained relationships. In the context of peer interactions, this may result in a deterioration of friendships (e.g., via distancing/avoidance or conflict). Within familial interactions, this may lead to increased arguments, tension, or high levels of negative expressed emotion. Indeed, impairments in both peer relations and family functioning are common in BD across development [21] and predictive of worse mood course [22,23]. Studies that have investigated these questions to date have mostly focused on samples of youth with BD or adults with late adolescent/young adult-onset BD using clinical interviews and self-report questionnaires. As such, a variety of interpersonal skills and psychotherapeutic strategies have been developed to target these deficits [24].

However, no studies have used behavioral tasks to investigate the relationship between facial emotion recognition abilities and subsequent mood symptoms in *young adults with childhood-onset BD*. Emotion recognition deficits in adult expressions could contribute to impairment in peer/social and occupational functioning (e.g., with coworkers/superiors in the workplace). In contrast, emotion recognition deficits in child expressions could negatively impact family relationships (e.g., perceived invalidation by younger siblings, extended family, or their own offspring) and functioning in the context of interactions with other youth (e.g., in places of employment—if a teacher, camp counselor, etc.). Thus, better understanding of facial emotion recognition abilities and subsequent mood symptoms in young adults with childhood-onset BD could inform multi-level mechanisms contributing to psychosocial and interpersonal difficulties across developmental transitions. In turn, such information could inform novel and developmentally-sensitive interventions to augment existing psychotherapies and pharmacotherapies, such as cognitive remediation [25] via facial emotion recognition training paradigms [26].

The Course and Outcome of Bipolar Youth (COBY) study [3] offers an ideal means to address this gap in the literature and ascertain a sample of young adults with prospectively-verified childhood-onset BD, as this longitudinal study assessed and confirmed BD diagnoses during childhood and has continued to follow participants over time. Findings arising from the COBY study demonstrate impaired clinical trajectory and poor functional

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outcomes in youth with BD [3-6]. While prior research demonstrated that children and adults with childhood-onset BD-I (the latter using a subsample of the COBY study) had facial emotion recognition deficits vs. TDCs [27], analyses were limited to cross-sectional data.

The current study, which incorporated longitudinal data from the COBY study in addition to cross-sectional clinical and behavioral task data from a separate study, builds on prior findings by: 1) examining facial emotion recognition deficits via a behavioral task in young adults with childhood-onset BD; and 2) evaluating the relationship between these deficits and subsequent symptom course. We hypothesized that: 1) participants with BD would demonstrate impairment in facial emotion recognition compared to TDCs (i.e., greater facial emotion recognition errors in both child and adult faces); and 2) greater impairment in facial emotion recognition would predict worse trajectory of manic and depressive symptoms in participants with BD. Given a lack of research on this topic, specific hypotheses were not made regarding depressive vs. manic symptoms, adult vs. child faces, and specific emotion types, though these were analyzed in exploratory analyses.

Methods

Participants

The hospital and university human subjects' protection committee approved procedures for the current cross-sectional study, which was separate but complementary to the COBY study. Specifically, in the current study two groups of participants ages 18-30 were enrolled: 1) participants with childhood-onset BD who were originally enrolled in one site of the COBY study as children (ages 7-17) [3] and who later enrolled in the current study as adults (n=52); and 2) young adult TDCs (n=64) who were newly recruited via community advertising/outreach.

Inclusion criteria for participants with BD were: 1) ages 18–30; 2) English fluency; 3) childhood-onset BD diagnosis per COBY (prior to the age of 18); and 4) at least six months of COBY follow-up data as young adults. Participants met the *DSM-IV's* definition of BD-I (at least one manic episode) or BD-II (at least one hypomanic and one major depressive episode), or the COBY study's definition of BD-Not Otherwise Specified (NOS), operationalized as either elation plus two associated symptoms or irritability plus three associated symptoms, change in functioning, ≥ 4 hours within a 24-hour period, ≥ 4 cumulative lifetime days [3].

Inclusion criteria for TDCs were: 1) ages 18-30; 2) English fluency; and 3) no current/lifetime psychiatric illness or substance abuse/dependence in participants or first-degree relatives.

Exclusion criteria for BD and TDCs were: 1) full-scale intelligent quotient (IQ) < 70 on the Wechsler Abbreviated Scale of Intelligence (WASI) [28]; 2) autism spectrum disorder, learning disorders, or primary psychosis; and 3) medical/neurological conditions potentially mimicking/confounding psychiatric illness and BD diagnosis.

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Procedures

After written informed consent, young adult participants with BD and TDCs completed the Diagnostic Analysis of Non-Verbal Accuracy-2 (DANVA-2: a facial emotion recognition task) and clinical measures as part of their participation in the current cross-sectional study. For those with BD who continued to participate in the separate COBY study, we leveraged subsequent prospective longitudinal assessments of mood symptoms at 6-month intervals (M=8.7±5.2 months) for two years following the facial emotion recognition task. All participants received monetary compensation for completion of study procedures.

Cross-Sectional Measures

Facial emotion recognition.—Facial emotion recognition for participants with BD and TDCs was assessed using the DANVA-2 [29,30]. The DANVA-2 is a computerized task with separate subtests for child and adult facial emotional expressions. Each DANVA-2 subtest includes 24 standardized photographs (12 male, 12 female) displaying one of four facial emotions (angry, sad, fearful, happy). Faces were presented for two seconds, and participants chose which of four emotions listed was expressed in the photograph. Both DANVA-2 subtests have been standardized and demonstrate construct validity, internal reliability (α=.64-.81), and test-retest reliability for first graders through young adults [29,30]. In this study, all participants were completing the DANVA-2 for the first time. Primary outcome variables used in analyses included the sum of total recognition errors for child and adult emotional expressions separately (e.g., number of times an emotion was incorrectly identified). Exploratory outcome variables included the sum of recognition errors for each emotion type (angry, sad, fearful, happy) for child and adult expressions separately.

Demographic information.—Participants with BD and TDCs reported on their age, race, and whether they were taking psychiatric medications at the time of enrollment. Socioeconomic status (SES) was assessed via the Hollingshead Four-Factor Index [31], which incorporates information on education, occupation, sex, and marital status. Composite scores were computed by multiplying the Occupation scale value by a weight of 5 and the Education scale value by 3 and summing the products. Hollingshead Education scores range from 1 (less than seventh grade) to 7 (graduate professional training), and Hollingshead Occupation codes ranged from 1 (farm laborers/service workers) to 9 (higher executives and major professionals). Hollingshead Index raw scores range from 8 to 66, with higher scores reflecting higher SES.

Participants with BD and TDCs were also administered the WASI [28] by trained research assistants to measure IQ (M=100±15). Two subtests were used to measure IQ: Matrix Reasoning and Vocabulary. Higher scores indicate greater intellectual ability. The WASI is widely used to measure intellectual ability. This 2-subtest version of the WASI has also demonstrated good reliability (internal consistency .93-.94) and concurrent validity [28].

Psychiatric diagnoses.—Young adult participants' current and lifetime BD subtypes (BD-I, BD-II, BD-NOS) and other psychiatric diagnoses (number of comorbid conditions, ADHD, Any Anxiety Disorder, Substance Use Disorder) were evaluated in the current study using the Structured Clinical Interview for *DSM-IV* [32] for adults. Interviews

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were conducted by a board-certified child/adolescent psychiatrist or a licensed clinical psychologist with established inter-rater reliability (κ>.85). For those with BD who participated in the COBY study, in childhood, BD diagnoses were determined via the Schedule for Affective Disorders and Schizophrenia for School Age Children, Present and Lifetime Version (K-SADS) [33], with good inter-rater reliability (κ>.74). Given participants' initial participation in the COBY study, young adults' diagnoses of childhood-onset BD were prospectively confirmed (i.e., assessed/determined when participants were children, rather than recalling symptoms that occurred during childhood as adults, providing more accurate diagnoses assessed closer to initial onset incorporating both parent and child report). The average age of BD onset in the COBY study was *M*=9.3±3.9 years [8]. Given documented conversion rates of BD diagnoses and changing diagnostic makeup over development [3], for present analyses, focus was on current psychiatric diagnoses during the time of completion of the DANVA-2.

Global functioning.—To characterize global functioning at the time of completion of the DANVA-2, participants with BD were assessed via the clinician-administered Global Assessment of Functioning (GAF) [34] (scores range from 1-100; 100 indicates superior functioning). The GAF was completed during the same study visit as the DANVA-2, but was not administered to TDCs.

Longitudinal Measures

Mood symptoms.—Following aforementioned cross-sectional DANVA-2 and other measures, change in mood symptoms over two years for participants with BD was assessed using the semi-structured K-SADS Depression Rating Scale (KDRS) [35] and K-SADS Mania Rating Scale (KMRS) [36]. The COBY study has continued to use the KDRS and KMRS in their longitudinal assessments of participants with BD into adulthood to maintain measurement consistency, rather than shifting from child to adult measures (though the current study only used ratings in young adulthood assessed after completion of the DANVA-2) [4,37,38]. The 12-item KDRS and 13-item KMRS were used to assess depressive and manic symptoms, respectively, for the most symptomatic week in the month preceding follow-up assessments for the current study at baseline, 6-months, 12-months, 18-months, and 24-months. Items are Likert-style (6- or 7-point scales for KDRS; 5- or 6-point scales for KMRS) ranging from "none" to "extreme" with total scores ranging from 0 to 61 on the KDRS and 0 to 64 on the KMRS. Higher scores indicate greater severity. Scores of ≥ 17 on the KMRS and ≥ 16 on the KDRS indicate moderate severity. These scales have strong internal consistency (KDRS α=.72-.87; KMRS α=.94), inter-rater reliability (KDRS *r*=.72-.97; KMRS *r*=.97), and validity [35,36]. For current analyses, trajectory of mania and depression over two years following DANVA-2 were the primary longitudinal variables of interest.

Prior research used latent class growth analysis to identify four longitudinal mood trajectories in the COBY sample using 8 years of follow-up data [4]. In the current study, breakdown of prior mood trajectory classification included: 1) predominantly euthymic (*n*=3, 84.4% time euthymic, 5.8% of current sample); 2) moderately euthymic (*n*=19, 47.3% time euthymic, 36.5% of current sample); 3) ill with improving course (*n*=16, 42.8% time

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euthymic, 30.8% of current sample); and 4) predominantly ill (n=14, 11.5% time euthymic, 26.9% of current sample). These mood trajectory classes, which described participants' mood symptom course over 8 years mostly preceding participation in the current study, were used as covariates in analyses to control for historical mood trajectory (detailed below).

Analytic Strategy

Analyses were implemented in SPSS 25 with two-tailed comparisons and a p<.05 significance criterion. Descriptive statistics were calculated to characterize the sample, using independent-samples t-tests and chi-square analyses to compare BD vs. TDCs on demographics and facial emotion recognition.

To examine the relationship of facial emotion recognition with trajectory of mood symptoms in BD, we conducted two-level mixed-effects regression models (MRMs) with repeated measures at level one nested within participant at level two. Random effects for intercepts and slopes were modeled using unstructured covariance matrices and retained when significant. Conditional growth models included effects for Time (centered at baseline), Facial Emotion Recognition, and the Facial Emotion Recognition x Time interaction. Prior COBY mood trajectory latent class (predominantly ill vs. not) [4] and baseline mood symptoms (KDRS, KMRS) were included as covariates, to examine whether facial emotion recognition predicted subsequent symptom course above and beyond prior and existing mood symptoms. The prior COBY mood trajectory latent class (predominantly ill vs. not) was the main covariate of interest, to determine whether facial emotion recognition remained a significant predictor of subsequent symptom course even among those experiencing the most severe symptoms. Other COBY mood trajectory latent classes were analyzed in post-hoc analyses.

A step-up model building strategy was used to compute four final models: relationship of child facial emotion recognition with mania (1) and depression (2); and relationship of adult facial emotion recognition with mania (3) and depression (4). Total recognition errors (primary analyses) and recognition errors per emotion type (exploratory analyses: angry, sad, fearful, happy) for child and adult facial expressions on the DANVA-2 were examined as predictors of intercept and slope, with prospective, longitudinal KDRS depression and KMRS mania scores as dependent variables (completed after DANVA-2). Only significant predictors were retained in final models. Cohen's d effect sizes were also calculated. Post-hoc analyses simultaneously covaried for baseline demographics (age, race, SES, IQ) and clinical variables (BD age of onset, functioning, psychiatric medications, comorbidity, other COBY mood trajectory latent classes).

Results

Demographics and Between-Group Differences in Facial Emotion Recognition

The sample was composed of young adults with childhood-onset BD-I (n=34), BD-II (n=3), BD-NOS (n=15), and TDCs (n=64). The average age of the sample was 21.37±2.46 (58% Male, 78% Caucasian) and average IQ was 109.57±12.19. There were no significant differences in participants with BD vs. TDCs for age, sex, race, IQ, and SES (Table 1).

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Consistent with prior literature on adults with BD [39], participants with BD in the current sample reported high rates of current comorbidity and psychiatric medication use, impaired global functioning, and moderate levels of KDRS depressive and KMRS manic symptoms. Regarding facial emotion recognition, participants with BD made significantly more total recognition errors on child expressions than TDCs (Table 2). There were no significant differences for total errors on adult expressions, or errors on child or adult expressions for specific emotion types (exploratory variables: angry, sad, fearful, happy).

Relationship of Facial Emotion Recognition Ability with Mood Symptom Trajectory

Primary analyses: Facial emotion recognition for all child and adult expressions.—In MRMs covarying for baseline and prior mood symptoms, recognition errors for all child expressions were significantly predictive of baseline mania levels (intercept) [$F(176.65)=4.79$, $p=.03$, $d=0.61$] and mania trajectory (slope) [$F(178.42)=4.91$, $p=.03$, $d=0.61$] (Table 3). To illustrate this effect, median splits dichotomized lower versus higher recognition errors for all child expressions with mania (Figure 1). Those with higher total recognition errors for all child expressions demonstrated lower baseline mania and stable/consistently low mania trajectory over two years. In contrast, those with lower total recognition errors for all child expressions demonstrated higher baseline mania symptoms and improving/decreasing trajectory over two years.

Recognition errors for all child expressions were not significant for depression, and recognition errors for all adult expressions were not significant for mania or depression.

Exploratory analyses: Facial emotion recognition by emotion subtype.—In MRMs covarying for baseline and prior mood symptoms, recognition errors for adult sad expressions were significantly predictive of depression [$F(175.92)=7.71$, $p=.01$, $d=0.77$] and mania [$F(182.11)=9.05$, $p=.01$, $d=0.83$] trajectories (slope), but not baseline levels of depression and mania (intercept) (Table 4). To illustrate effects, median splits dichotomized lower versus higher recognition errors for adult sad expressions with depression (Figure 2) and mania (Figure 3) over time. Despite similar moderate depression levels at baseline, those with higher recognition errors for adult sad expressions demonstrated worse trajectory (stable/consistent depression symptoms) over two years than those with lower recognition errors for adult sad expressions, who showed improving/decreasing depression symptoms over time. In contrast, those with higher recognition errors for adult sad expressions demonstrated higher baseline mania symptoms that improved/decreased over two years, while those with lower recognition errors for adult sad expressions exhibited lower mania symptoms initially which remained stable/consistently low over time.

There were no other significant associations of recognition errors for child or adult expressions by emotion subtype for depression or mania.

Post-Hoc Analyses: Effect of Additional Demographic and Clinical Variables—In post-hoc analyses, effects in MRMs for DANVA-2 predictors (recognition errors for all child emotional expressions and adult sad expressions) on KDRS depressive and KMRS manic symptom trajectories (slope) were maintained at significance or trend significance ($ps<.06$) when simultaneously controlling for baseline demographics (age, race, SES, IQ)

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and clinical variables (BD age of onset, functioning, psychiatric medications, comorbidity, other COBY mood trajectory latent classes) in step-up modeling, thereby demonstrating the robustness of findings.

Discussion

To our knowledge, this is the first study to examine the relationship between facial emotion recognition and subsequent mood symptoms in young adults with prospectively-verified childhood-onset BD. Young adults with childhood-onset BD experienced greater impairment in recognition for child emotional expressions vs. TDCs. However, there were no between-group differences for total errors on adult expressions or errors on any specific child or adult emotion subtype (angry, sad, fearful, happy). Furthermore, recognition errors for all child emotional expressions were predictive of subsequent mania, while recognition errors for adult sad expressions were predictive of subsequent mania and depression. Effects were maintained when controlling for baseline demographics, current and prior mood symptoms, and other clinical variables. Findings suggest that impaired facial emotion recognition may be an important brain/behavior mechanism, prognostic indicator, and intervention target for childhood-onset BD.

Results add to the literature on neuronal underpinnings of BD [40,41] and facial emotion recognition abilities in children [16-20] and adults with BD [10,11] by demonstrating that impairments are present in young adults with prospectively-verified childhood-onset BD. Compared to TDCs, impairments were present for child emotional expressions, but not for adult emotional expressions or specific emotion types. This is consistent with research in children with BD demonstrating impaired emotion recognition for child expressions, but not adult expressions [17,20]. This distinction has not been observed in late adolescent/young adult-onset BD. Thus, when integrating current study results with prior research, findings suggest that mechanisms involved in facial emotion recognition in BD may differ by age of onset, and therefore may be important to target across ages through a developmental lens.

Specifically, for BD in childhood, impaired facial emotion recognition in child expressions may contribute to psychosocial and peer difficulties (e.g., misinterpreting peer expressions may lead the recipient to feel frustrated and/or misunderstood, potentially resulting in avoidance/withdrawal or conflict) [5]. In young adulthood and later in life, this impairment could contribute to difficulties with family functioning, parenting, and psychosocial abilities (e.g., if young adults cannot accurately perceive children’s emotions correctly, this may lead children to feel invalidated, resulting in tension and/or resentment in the relationship) [6]. Thus, young adults with childhood-onset BD may benefit from psychoeducation on identification of emotions in young people, effective responding, and associated parenting strategies. Focus on these facial emotion recognition impairments and associated skills could help to enhance interpersonal and parent-child interactions and ameliorate some family risk factors common in BD (e.g., impaired family functioning [21]) associated with mood exacerbation (e.g., low adaptability and cohesion; high expressed emotion, conflict, and stress [23]), potentially facilitating more favorable outcomes. Such strategies are incorporated in evidence-based psychotherapies for children with BD [24], and may be applicable to young adults with childhood-onset BD though a parenting framework. As

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research has also demonstrated the promise of facial emotion recognition training in children with mood disturbance [26], similar applications of cognitive remediation may be applicable to adults with childhood-onset BD [25] as an augment to existing pharmacotherapies and psychotherapies to increase their efficacy.

Higher recognition errors for child expressions were also predictive of mania trajectory, which has implications for understanding the pathophysiology of childhood-onset BD and novel treatment development. Those with higher total recognition errors for child emotional expressions demonstrated lower baseline mania and stable/consistently low mania trajectory over two years. This is contrary to hypotheses and suggests that higher total recognition errors for child emotional expressions may serve a protective effect (e.g., potentially missing interpersonal/social cues that may be stress- or conflict-inducing, thereby not exacerbating mania, but rather contributing to mood stability). In contrast, those with lower total recognition errors for child emotional expressions demonstrated higher baseline mania and improving (decreasing) trajectory over two years (e.g., correctly identifying facial emotions may contribute to interpersonal stress and strain initially—as conflicts/issues identified must then be addressed—potentially exacerbating mania at first, though continued accurate identification may enhance these relationships and interpersonal functioning over time, contributing to improved symptoms). Though additional research is clearly needed to further explore these findings and speculative explanations, results suggest that there may be a multi-faceted relationship between facial emotion recognition and mania symptom course in young adults with childhood-onset BD, which warrants further investigation.

Results also suggest that impaired recognition for adult sad expressions may have implications for mood symptom trajectory. Despite similar depression levels at baseline, those with higher recognition errors for adult sad expressions demonstrated worse trajectory (stable/consistent depression symptoms) over two years than those with lower recognition errors, who showed improvement/decrease in depression. In contrast, those with higher recognition errors for adult sad expressions demonstrated higher baseline mania symptoms that improved/decreased over two years, while those with lower recognition errors for adult sad expressions exhibited lower mania symptoms initially which remained stable/consistently low. Though impairments in recognition of specific facial emotions vary across studies [10,11], findings align with prior work documenting impairment in recognition of adult sad expressions among adults [42-44] and children with BD [19]. Thus, psychoeducation and emotion recognition training for sadness in adults may offer a protective effect for depressive symptoms, but not necessarily for mania. However, as mania symptoms started off lower and remained low for those with lower recognition errors, it is possible that correct identification of adult sad faces is effective in helping to maintain already lower manic symptoms, though whether this translates into improving trajectory among those with higher baseline symptoms initially is unknown, and thus should be further researched. Alternatively, lower manic symptoms could also have been related to higher depressive symptoms.

Regarding *why* identification of adult sad expressions may be important for mood symptom course, it is possible that accurate perception of adult peers who are sad and/or distressed may foster empathy and closeness, thereby enhancing relationships (particularly in the

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context of sadness, arguably when social support may be needed the most). In turn, more positive/close relationships are associated with improved mood symptom course in BD [22]. Indeed, emotion recognition abilities are relevant to feeling empathy for others [45], and impairment in the ability to empathize is characteristic of many psychiatric conditions [46]. Therefore, focus on accurate identification of sadness in adults and teaching associated effective communication, responding, and relationship-building skills may be useful for young adults with childhood-onset BD.

Limitations

Findings should be interpreted within the context of limitations. First, the modest sample and small number of individuals with BD-II and BD-NOS limited power to examine between-group BD subtype differences. Second, although baseline and prior mood symptoms were controlled for in analyses, all possible demographic, clinical, and neurocognitive variables were not assessed, and therefore could not be included as covariates. Variables of interest that would be important to consider include psychotic symptoms, types of psychiatric medications, duration of BD, and number/type of mood episodes. Third, analyses were limited to two years of mood symptom data following the DANVA-2 to minimize missing data; thus, the relationship of facial emotion recognition with mood trajectory over a longer follow-up time is unknown. Fourth, only select emotions were measured on the DANVA-2 with limited number of trials (24 total); thus, differences in other expressions were not examined (disgust, guilt, shame), though may have implications for symptom course. Fifth, as only one cross-sectional assessment of facial emotion recognition was administered, followed by assessment of mood symptoms, the relationship between prospective course of facial emotion recognition and illness progression is unknown, and indeed, there is likely a bidirectional relationship between these constructs.

Future research should address these shortcomings by: 1) replicating findings in a larger, diverse sample with longer follow-up, TDC longitudinal comparison, and examination by BD subtypes; 2) measuring and accounting for additional demographic, clinical, and neurocognitive variables (especially psychotic symptoms, types of psychiatric medications, duration of BD, and number/type of mood episodes); 3) using a novel facial emotion recognition task to measure a broader array of emotions with more trials; and 4) assessing facial emotion recognition and mood concurrently over time and examining potential bidirectional relationships.

Conclusions

Results add to the literature on impaired facial emotion recognition in childhood-onset BD across the developmental transition to young adulthood. Facial emotion recognition impairments were associated with subsequent depressive and manic symptom course regardless of demographic and clinical factors. Thus, facial emotion recognition may be an enduring brain/behavior mechanism in childhood-onset BD with implications for prognosis. As such, consideration of facial emotion recognition impairments may be helpful in treatment development and planning for young adults with childhood-onset BD.

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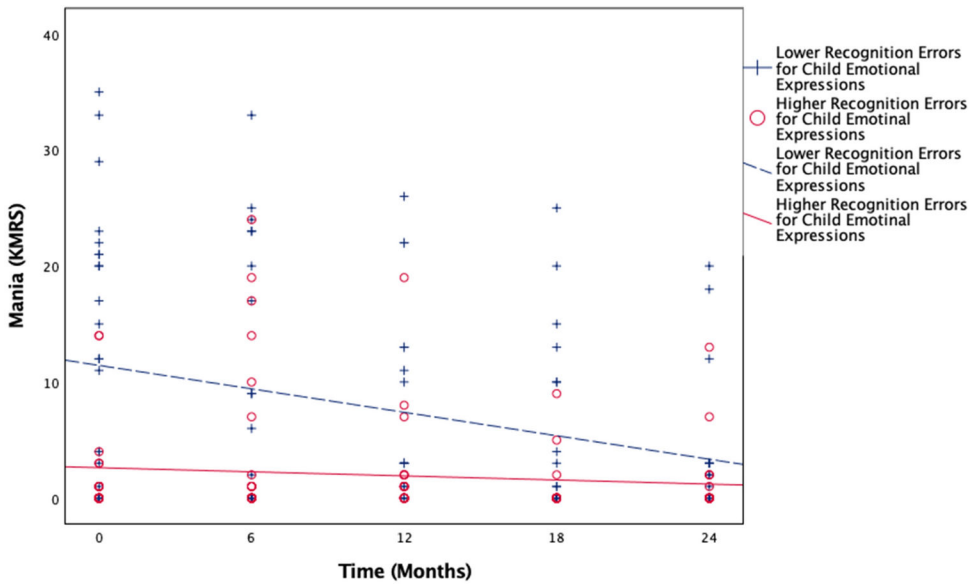

Fig. 1.

Relationship of recognition errors for all child emotional expressions with mania symptoms over two years. Median splits dichotomized higher versus lower recognition errors for all child emotional expressions. KMRS=K-SADS Mania Rating Scale

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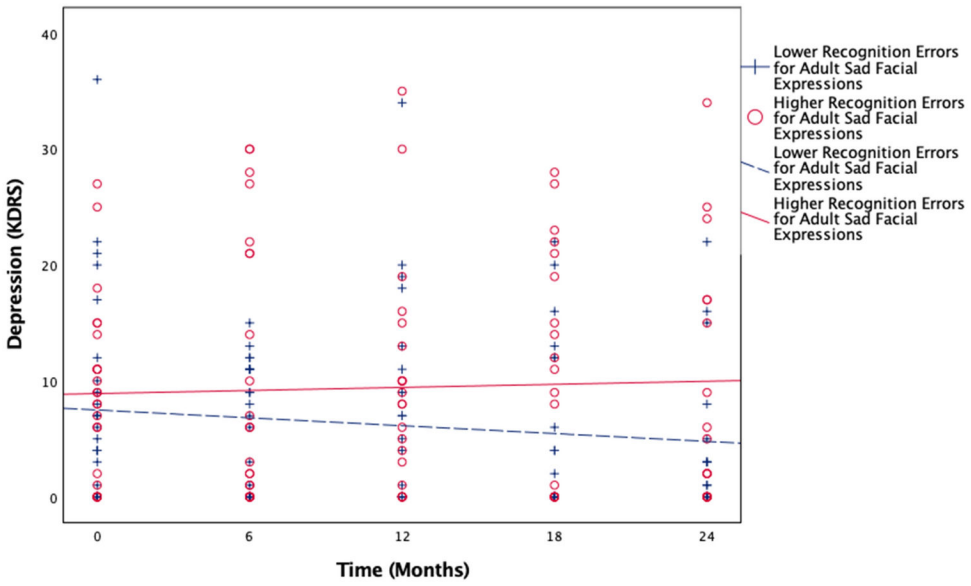

Fig. 2.

Relationship of recognition errors for adult sad expressions with depressive symptoms over two years. Median splits dichotomized higher versus lower recognition errors for adult sad expressions. KDRS=K-SADS Depression Rating Scale

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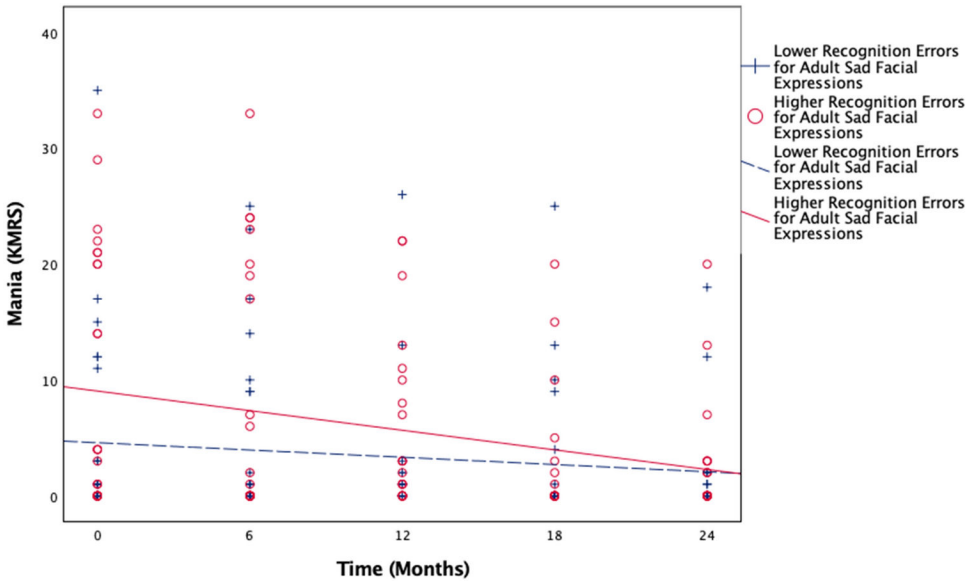

Fig. 3.

Relationship of recognition errors for adult sad expressions with mania symptoms over two years. Median splits dichotomized higher versus lower recognition errors for adult sad expressions. KMRS=K-SADS Mania Rating Scale

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Table 1

Demographics and Clinical Characteristics

Variables	Bipolar Disorder (*n*=52)	Typically-Developing Control (*n*=64)	Statistic χ^2/t	*p*
Demographics				
Age, *M*(*SD*)	20.89(2.70)	21.75(2.19)	−1.91	.06
Sex (Male), *n*(%)	31(60%)	36(56%)	0.13	.72
Race (Caucasian), *n*(%)	42(84%)	48(79%)	0.51	.48
Intelligence Quotient (IQ), *M*(*SD*)	107.44(12.25)	111.30(11.96)	−1.71	.09
Hollingshead Socioeconomic Status, *M*(*SD*)	26.50(11.92)	30.47(13.71)	−1.59	.11
Clinical Characteristics				
Age of Onset of Bipolar Disorder, *M*(*SD*)	9.48(3.21)			
COBY Prior Mood Trajectory (Predominantly Ill), *n*(%)	14(26.92%)			
Baseline KMRS Mania, *M*(*SD*)	26.33(10.19)			
Baseline KDRS Depression, *M*(*SD*)	17.63(9.28)			
Baseline Global Functioning, *M*(*SD*)	64.23(11.99)			
Any Baseline Psychiatric Medications (Yes), *n*(%)	22(43%)			
Current Comorbid Conditions, *M*(*SD*)	1.35(1.61)			
Current Attention-Deficit/Hyperactivity Disorder (Yes), *n*(%)	13(25%)			
Any Current Anxiety Disorder (Yes), *n*(%)	19(37%)			
Any Current Substance Use Disorder (Yes), *n*(%)	14(27%)			

Note. COBY=Course and Outcome of Bipolar Youth Study; COBY Prior Mood Trajectory (Predominantly Ill)=spent 11.5% time euthymic; KDRS=K-SADS Depression Rating Scale; KMRS=K-SADS Mania Rating Scale.

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Table 2

Facial Emotion Recognition Errors

Variables	Bipolar Disorder (*n*=52)	Typically-Developing Control (*n*=64)	Statistic *t*	*p*
Child Facial Recognition Errors				
Happy, *M*(*SD*)	0.25(0.44)	0.17(0.46)	0.93	.35
Angry, *M*(*SD*)	1.35(0.95)	1.08(0.80)	1.65	.10
Sad, *M*(*SD*)	0.37(0.63)	0.22(0.45)	1.46	.15
Fearful, *M*(*SD*)	0.92(0.99)	0.69(0.81)	1.41	.16
Total, *M*(*SD*)	2.90(1.86)	2.16(1.21)	2.61	.01
Adult Facial Recognition Errors				
Happy, *M*(*SD*)	0.44(0.70)	0.39(0.61)	0.43	.67
Angry, *M*(*SD*)	1.63(1.30)	1.28(1.02)	1.65	.10
Sad, *M*(*SD*)	1.42(1.07)	1.27(1.20)	0.74	.46
Fearful, *M*(*SD*)	1.63(1.12)	1.50(1.05)	0.67	.51
Total, *M*(*SD*)	5.13(2.27)	4.44(1.99)	1.76	.08

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Table 3

Final Mixed-Effects Regression Model Examining Relationship of Recognition Errors for All Child Emotional Expressions with KMRS Manic Symptom Trajectory

	Mania		
Effects	***B(SE)***	***95% CI***	***p***
Intercept	6.07(0.72)	4.65, 7.49	<.001
COBY Prior Mood Trajectory (Predominantly Ill)	2.74(0.97)	0.78, 4.69	.01
Baseline KMRS Mania	0.45(0.05)	0.35, 0.54	<.001
Time	−0.19(0.05)	−0.29, −0.10	<.001
Child Total Recognition Errors	−0.82(0.37)	−1.56, −0.08	.03
Child Total Recognition Errors x Time	0.06(0.03)	0.01, 0.11	.03

Note. KMRS=K-SADS Mania Rating Scale; COBY=Course and Outcome of Bipolar Youth Study; COBY Prior Mood Trajectory (Predominantly Ill)=spent 11.5% time euthymic.

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Table 4

Final Mixed-Effects Regression Models Examining Relationship of Recognition Errors for Adult Sad Expressions with KMRS Manic and KDRS Depressive Symptom Trajectory

	Depression			Mania		
Effects	***β (SE)***	***95% CI***	***p***	***B(SE)***	***95% CI***	***p***
Intercept	7.49(0.94)	5.63, 9.36	<.001	6.05(0.71)	4.64, 7.46	<.001
COBY Prior Mood Trajectory (Predominantly Ill)	2.61(1.44)	−0.29, 5.51	.08	2.82(0.97)	0.87, 4.78	.01
Baseline KDRS Depression	0.51(0.08)	0.35, 0.66	<.001	--	--	--
Baseline KMRS Mania	--	--	--	0.47(0.05)	0.38, 0.57	<.001
Time	−0.03(0.06)	−0.14, 0.08	.59	−0.19(0.05)	−0.29, −0.10	<.001
Adult Sad Recognition Errors	0.08(0.83)	−1.56, 1.72	.92	1.06(0.65)	−0.22, 2.35	.01
Adult Sad Recognition Errors x Time	0.16(0.06)	0.04, 0.27	.01	−0.14(0.05)	−0.24, −0.05	.01

Note. KDRS=K-SADS Depression Rating Scale; KMRS=K-SADS Mania Rating Scale; COBY=Course and Outcome of Bipolar Youth Study; COBY Prior Mood Trajectory (Predominantly Ill)=spent 11.5% time euthymic.

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