Risk for Bipolar Disorder Is Associated With Face-Processing Deficits Across Emotions

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ABSTRACT

Objective: Youths with euthymic bipolar disorder (BD) have a deficit in face-emotion labeling that is present across multiple emotions. Recent research indicates that youths at familial risk for BD, but without a history of mood disorder, also have a deficit in face-emotion labeling, suggesting that such impairments may be an endophenotype for BD. It is unclear whether this deficit in at-risk youths is present across all emotions or if the impairment presents initially as an emotion-specific dysfunction that then generalizes to other emotions as the symptoms of BD become manifest. **Method:** Thirty-seven patients with pediatric BD, 25 unaffected children with a first-degree relative with BD, and 36 typically developing youths were administered the Emotional Expression Multimorph Task, a computerized behavioral task, which presents gradations of facial emotions from 100% neutrality to 100% emotional expression (happiness, surprise, fear, sadness, anger, and disgust). **Results:** Repeated-measures analysis of covariance revealed that, compared with the control youths, the patients and the at-risk youths required significantly more intense emotional information to identify and correctly label face emotions. The patients with BD and the at-risk youths did not differ from each other. Group-by-emotion interactions were not significant, indicating that the group effects did not differ based on the facial emotion. **Conclusions:** The youths at risk for BD demonstrate nonspecific deficits in face-emotion recognition, similar to patients with the illness. Further research is needed to determine whether such deficits meet all the criteria for an endophenotype. *J. Am. Acad. Child Adolesc. Psychiatry,* 2008;47(12):1455–1461. **Key Words:** bipolar disorder, endophenotype, face emotion labeling, at risk.

Despite evidence that bipolar disorder (BD) is highly heritable,[1–5] the exact genetic profile remains unknown. Endophenotypes are biological or neuropsychological markers intermediate between clinical phenotype and genotype.[6,7] The identification of risk-related genes for complex illnesses, such as BD, which involve intricate modes of transmission,[8–10] could be aided by the identification of endophenotypes.

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Youths with BD have deficits in face-emotion labeling,[11–14] which may serve as an endophenotype for BD. This possibility is suggested by data finding face-emotion labeling deficits to be heritable in at least some populations,[15,16] state independent in BD,[13,14] and relatively unique to BD compared with childhood depression, anxiety, and behavioral disorders.[17] Most significantly, nonaffected youths at risk for BD by virtue of having a first-degree relative with the illness but who themselves have no personal history of mood disorder, seem to have deficits in face-emotion labeling similar to those seen in bipolar probands.[18]

An outstanding question is whether face-emotion processing deficits in at-risk youths, like those in pediatric patients with BD, are present across all emotions.[14] Alternatively, face-emotion labeling abnormalities may present initially as a specific deficit in labeling a narrow set of emotions, which then generalize to others over time. The purpose of this study is to examine whether face-emotion labeling deficits in youths with a first-degree

relative with BD are specific to certain emotions, or whether they are present across all emotions. To that end, we used a task designed to detect deficits in labeling happiness, sadness, anger, fear, disgust, and surprise. Prior work in BD[13,14] demonstrates a generalized impairment in face-emotion labeling across these emotions. Thus, we a priori hypothesized that youths at risk for BD would similarly demonstrate deficits in face-emotion processing across all emotions presented.

METHOD

Subjects included pediatric patients with BD (n = 37), at-risk youths (n = 25), and typically developing children (n = 36). All participants, ages 7 to 18 years, were enrolled in an institutional review board–approved study at the National Institute of Mental Health (NIMH). Parents and youths gave written informed consent/assent. None of the participants were biologically related. Pediatric bipolar patients were recruited through advertisements to support groups and psychiatrists.

At-risk youths were included if they had a parent and/or sibling in an NIMH IRB–approved study, in which a semistructured interview confirmed a diagnosis of *DSM-IV*-TR BD (BDI or BDII). Parental BD diagnosis was determined using the Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders–Patient Edition[19] or the Diagnostic Interview for Genetic Studies.[20] Pediatric BD probands, at-risk youths, and controls were clinically assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime version.[21] Interviewers were masters- or doctoral-level clinicians with excellent interrater reliability ($\kappa > 0.9$).

Patients with bipolar disorder met the criteria for "narrow phenotype" BD, with at least one full-duration hypomanic or manic episode characterized by abnormally elevated mood and at least three "B" mania symptoms.[22] At-risk subjects with anxiety disorders or attention-deficit/hyperactivity disorder (ADHD) were included to avoid studying an unusually psychopathologically resilient group. At-risk youths with current or past mood disorders were excluded because BD can manifest first as depression. Typically developing children were drawn from the community and had no lifetime psychiatric diagnoses, as determined by a Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime version interview with parent and child, and no first-degree relatives with a mood disorder. Psychopathology in first-degree relatives of typically developing youths was assessed via a telephone screening interview with a masters- or doctoral-level clinician.

Exclusion criteria for all of the subjects were as follows: IQ of less than 70, history of head trauma, neurological disorder, pervasive developmental disorder, unstable medical illness, or substance abuse/dependence. At-risk and typically developing youths were medication-free. Medicated patients with BD were included.

The Wechsler Abbreviated Scale of Intelligence[23] was administered to determine IQ. To evaluate mood state in patients and at-risk youths, clinicians with interrater reliability ($\kappa > 0.9$) administered the Children's Depression Rating Scale (CDRS)[24] and the Young Mania Rating Scale (YMRS).[25]

Subjects performed the computerized Emotional Expression Multimorph Task.[14,26] The face stimuli were taken from the empirically valid and reliable Pictures of Facial Affect Series.[27] During this task, the subjects viewed a virtual series of neutral faces, each of which morphed 39 times until it reached 100% intensity (Fig. 1). The subjects were told that the emotional expression would begin as neutral but would slowly change to reveal one of the six emotions: happiness, surprise, fear, sadness, anger, or disgust. The subjects were asked to press the "stop" button on the computer as soon as they were able to identify the facial expression. This stopped the morphing image, and the subjects were asked to identify one of the six emotional expressions listed on the screen. Upon selecting the emotion, the face would continue to morph through the remaining iterations. The subjects were told that they could change their emotional identification response at any time. When the face reached the final morph iteration (i.e., iteration 39, "morph 1," the full emotional expression), the subjects were asked to provide a final emotional identification response.

The response point along the 1 to 39 continua at which the subject stops the morphing process indicates the degree of facial intensity before the subject attempted to identify the emotion, with higher response points indicating better performance. There were two main dependent variables: number of morphs before the subject's first response (regardless of accuracy) and number of morphs before the subject's first correct response.

Data Analysis

Analyses of variance assessed group differences in age and IQ, and a χ^2 determined sex differences. Age differed significantly ($p \leq .01$), and IQ differed at a trend level (p = .09) among the groups (Table 1). Therefore, for primary analyses, repeated-measures analyses of covariance (ANCOVA) were performed, with group as the between-group factor and age and IQ as covariates.

Post hoc ANCOVAs, with age included as a covariate, compared at-risk children without an Axis I diagnosis and controls on the number of morphs before first response and number of morphs before first correct response. IQ was not included as a covariate in these analyses because it did not differ between these two groups (t = 0.40, p = .69). Cohen d effect sizes were calculated for task performance differences between the typically developing children and the entire at-risk sample (n = 25), and between the typically developing children and the subset of at-risk youths without a diagnosis (n = 18). Additional analyses in patients with BD used Pearson correlations and t tests to examine relations between performance and mood ratings, and between medication status and performance.

RESULTS

Analysis of variance revealed significant group differences for age ($p < .01$); at-risk youths were significantly younger than both the patients ($p < .01$) and the typically developing youths ($p < .01$), who did not differ from each other (p = .78). IQ differed among the groups at a trend level (p = .09). The patients had a significantly lower IQ than the typically developing youths (p = .03) but did not differ significantly from at-risk youths (p = .15). The typically developing and at-risk children's IQ scores did not differ from each other (p = .64). Sex did not significantly differ across groups.

Table 1 presents demographic and clinical data. Among patients with BD, 45.9% were euthymic (i.e.,