Article

Deficits in Social Cognition and Response Flexibility in Pediatric Bipolar Disorder

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Objective: Little is known about neuropsychological and social-cognitive function in patients with pediatric bipolar disorder. Identification of specific deficits and strengths that characterize pediatric bipolar disorder would facilitate advances in diagnosis, treatment, and research on pathophysiology. The purpose of this study was to test the hypothesis that youths with bipolar disorder would perform more poorly than matched healthy comparison subjects on measures of social cognition, motor inhibition, and response flexibility.

Method: Forty outpatients with pediatric bipolar disorder and 22 comparison subjects (no differences in age, gender, and IQ) completed measures of social cognition (the pragmatic judgment subtest of the Comprehensive Assessment of Spoken Language, facial expression recognition subtests of the Diagnostic Analysis of Nonverbal Accuracy Scale, the oral expression subtest of the Test of Language Competence), inhibition and response flexibility (stop and stop-change tasks), and motor inhibition (continuous performance tasks).

Results: Pediatric bipolar disorder patients performed more poorly than comparison subjects on social-cognitive measures (pragmatic judgment of language, facial expression recognition) and on a task requiring response flexibility. These deficits were present in euthymic patients. Differences between patients and comparison subjects could not be attributed to comorbid attention deficit hyperactivity disorder.

Conclusions: Findings of impaired social cognition and response flexibility in youths with pediatric bipolar disorder suggest continuity between pediatric bipolar disorder and adult bipolar disorder. These findings provide a foundation for neurocognitive research designed to identify the neural mechanisms underlying these deficits.

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For adults with bipolar disorder, research has begun to delineate a neuropsychological and social-cognitive profile characterized by deficits in verbal memory and sustained attention (1–6) and by differences from healthy comparison subjects in facial expression processing (7–11). Less is known about neuropsychological and social-cognitive features of pediatric bipolar disorder. In particular, the delineation of trait markers of vulnerability, or potential endophenotypes, for pediatric bipolar disorder could facilitate diagnosis and treatment. Neuropsychological testing provides one means for identifying such markers, which can then be studied by using neuroimaging to identify dysfunction in neural circuitry. Based on preliminary data, clinical observation, and findings in adults, two sets of cognitive skills—social cognition and response flexibility (flexible alternation between motor inhibition and execution)—represent candidate neuropsychological correlates of narrow-phenotype pediatric bipolar disorder, in which the full DSM-IV criteria for bipolar disorder are met (12).

Social Cognition

Youths with pediatric bipolar disorder demonstrate marked social impairments (13), despite normal social functioning before illness onset (14). These impairments remain imprecisely characterized, however, and examination of social-cognitive skills may enhance understanding of the mechanisms underlying functional outcomes in pediatric bipolar disorder.

Children and adults with bipolar disorder perform differently from comparison subjects and individuals with other disorders on social-cognitive measures, particularly facial expression processing tasks (7, 8, 15). Symptomatic adults with bipolar disorder also have difficulty using contextual cues to infer others' mental states (3). Less research has focused on expressive aspects of social cognition; clinical observation of youths with pediatric bipolar disorder, however, suggests that language pragmatics (i.e., appropriate social use of verbal/nonverbal language) may be problematic.

This pattern of aberrant social-cognitive skill suggests dysfunction in neural structures thought to mediate social, emotional, and possibly pragmatic linguistic processing (16–18). These structures include the ventrolateral and medial prefrontal cortices and the amygdala (19–21), which exhibit structural and/or functional anomalies in bipolar disorder (22–27).

TABLE 1. Demographic and Clinical Characteristics of Patients and Healthy Comparison Subjects in a Study of Social Cognition and Response Flexibility in Pediatric Bipolar Disorder

Characteristic	Patients With Pediatric Bipolar (N=40)		Comparison Subjects (N=22)		Analysis		
	Mean	SD	Mean	SD	t	df	p
Age (years)	12.9	2.7	13.5	2.0	1.01	60	0.32
Wechsler Abbreviated Scale of Intelligence full-scale IQ	107.4	13.7	111.7	12.0	1.19	54	0.24
	N	%	N	%	χ^2	df	p
Gender					0.44	1	0.51
Male	22	55	14	64			
Female	18	45	8	36			
Bipolar diagnosis							
Bipolar I disorder	32	80					
Bipolar II disorder	8	20					
Comorbid diagnoses							
Current							
Attention deficit hyperactivity disorder (ADHD)	23	58					
Anxiety disorder	23	58					
Oppositional defiant disorder/conduct disorder	14	35					
Lifetime							
ADHD	28	70					
Anxiety disorder	26	65					
Oppositional defiant disorder/conduct disorder	16	40					
Current medications[a]							
None	6	15					
Atypical antipsychotic	22	55					
Lithium	15	24					
Anticonvulsant	29	73					
Antidepressant	12	30					
Stimulant	12	30					

[a] Most patients were taking multiple medications at the time of testing.

Inhibition and Response Flexibility

Studies demonstrate differences between individuals with bipolar disorder and comparison subjects on tasks involving motor inhibition or shifting. These measures require either simple inhibition of a prepotent response or substitution of an alternate response for an inhibited behavior. Although studies using continuous performance tasks have yielded consistent findings of discrimination deficits, they have provided mixed evidence of impaired inhibition in adults with symptomatic bipolar disorder (4, 28, 29) and no evidence of inhibitory deficits in adolescents with remitted bipolar disorder (30).

Research regarding inhibition with alternate responding, or response flexibility, in bipolar disorder is limited. However, performance on related measures involving reward-related response reversal or attentional set-shifting showed impairment in adults (29) and youths with bipolar disorder (31, 32). These findings suggest diminished flexibility in response to environmental contingencies.

Converging evidence from neuroimaging and lesion studies indicates that the inferior/ventrolateral prefrontal cortices modulate both motor inhibition and execution of alternative responses (33–35). In light of the structural and functional aberrations observed in the ventral prefrontal cortex in individuals with bipolar disorder (22–27), further characterization of both inhibition and response flexibility in pediatric bipolar disorder is warranted.

We hypothesized that patients with pediatric bipolar disorder would perform more poorly than comparison subjects on social-cognitive, inhibition, and response flexibility tasks. In addition, we explored the effects on patients' performance of current mood state and comorbid attention deficit hyperactivity disorder (ADHD). As noted earlier, we were particularly interested in identifying trait-related deficits.

Method

Subjects

Patients consisted of 40 youths who met the DSM-IV diagnostic criteria for pediatric bipolar disorder. Table 1 shows demographic data. Best-estimate diagnoses were based on data integrated from several sources, including separate child and parent interviews by clinicians with master's-level or higher-level credentials using the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (K-SADS-PL) (36), treating physicians' assessments, and medical records. Diagnoses were generated in consensus conferences that included all interviewers and were chaired by two psychiatrists (K.E.T., E.L.) with extensive experience assessing children with pediatric bipolar disorder. All children exhibited narrow phenotype pediatric bipolar disorder (each had experienced at least one hypomanic or manic episode that met the full DSM-IV duration criterion and included expansive, elevated mood) (12). Comorbid disorders were common (Table 1); 83% met the criteria for at least one addi-

TABLE 2. Scores on Measures of Social Cognition and Response Flexibility in Patients With Pediatric Bipolar Disorder and Healthy Comparison Subjects

Measure	Patients With Pediatric Bipolar Disorder			Comparison Subjects			Analysis	
	N	Mean	SD	N	Mean	SD	z	p
Comprehensive Assessment of Spoken Language pragmatic judgment subtest	34	98.9	13.5	18	113.5	9.9	4.04	0.0002
Diagnostic Analysis of Nonverbal Accuracy Scale								
Child facial expression subtest								
Errors	38	4.3	2.1	20	2.9	1.9	–2.50	0.01
Discriminability, by type of emotion								
Happy	38	0.88	0.09	20	0.81	0.12	–2.07	0.04
Sad	38	0.86	0.15	20	0.80	0.13	–1.83	0.07
Angry	38	0.80	0.14	20	0.65	0.20	–2.78	0.006
Fearful	38	0.81	0.17	20	0.76	0.16	–1.46	0.14
Adult facial expression subtest								
Errors	40	5.7	2.4	20	3.9	2.5	–2.94	0.003
Discriminability, by type of emotion								
Happy	40	0.82	0.08	20	0.77	0.15	–0.83	0.41
Sad	40	0.84	0.21	20	0.63	0.22	–3.62	0.0002
Angry	40	0.76	0.13	20	0.64	0.19	–2.43	0.02
Fearful	40	0.78	0.17	20	0.68	0.25	–1.45	0.15
AX Continuous Performance Test								
Response bias	33	0.30	0.16	22	0.35	0.19	–1.33	0.18
	N	Mean	SD	N	Mean	SD	t	p
Discriminability (hit rate minus false-alarm rate)	33	0.58	0.20	22	0.74	0.15	1.79	0.004
	N	Mean	SD	N	Mean	SD	z	p
Flanker Continuous Performance Test reaction time cost	33	–29.6	73.4	22	–45.8	39.9	–1.53	0.13
Identical Pairs Continuous Performance Test response bias	33	0.42	0.29	22	0.46	0.29	–0.98	0.33
	N	Mean	SD	N	Mean	SD	t	p
Stop task (stop signal reaction time)	38	250.6	71.1	22	216.5	62.9	–1.87	0.07
Stop-change task (change signal reaction time)	37	298.5	84.2	22	253.1	55.8	–2.49	0.02

[a] Significantly different from the comparison group ($p<0.05$, analysis of variance, followed by post hoc Tukey's honestly significant difference test for normally distributed variables; Kruskal-Wallis H test, followed by post hoc Wilcoxon tests, for nonnormally distributed variables).

tional current disorder, generally an anxiety disorder, ADHD, or oppositional defiant disorder. ADHD and oppositional defiant disorder diagnoses frequently overlapped. Of the 23 patients with ADHD, 48% (N=11) had comorbid oppositional defiant disorder; only three (12%) of the 14 youths with oppositional defiant disorder did not have current ADHD. Patients with severe pervasive developmental disorder, substance use within the past 3 months, or IQ <70 were excluded.

Mood state was assessed at the time of each task. Youths were classified as euthymic or symptomatic at each time point on the basis of parent/child summary scores on the Young Mania Rating Scale (37) and the Children's Depression Rating Scale (38). Symptomatic youths had Young Mania Rating Scale scores >12 and/or Children's Depression Rating Scale scores >40. For euthymic youths, Young Mania Rating Scale scores ranged from 0 to 11 (mean=3.7 to mean=5.4) and Children's Depression Rating Scale scores ranged from 18 to 40 (mean=22.9 to mean=26.1). For symptomatic youth, Young Mania Rating Scale scores ranged from 0 to 30 (mean=15.9 to mean=18.0) and Children's Depression Rating Scale scores ranged from 18 to 76 (mean=29.1 to mean=33.4). All but six patients were receiving medication (Table 1).

The comparison subjects consisted of 22 youths identified as diagnosis-free according to the K-SADS-PL (36). Comparison subjects were excluded if they or a first-degree relative met the criteria for any DSM-IV diagnosis (family history was ascertained by a clinical interview of the parent), if they reported substance use within the past 3 months, or if they had an IQ <70.

The groups did not differ in age or Wechsler Abbreviated Scale of Intelligence (39) IQ (Table 1). No group differences in gender were evident; however, because the male-to-female ratio in the two groups was unequal, we examined effects of gender on task performance. The results were significant for only one measure; for analyses of this measure, gender was covaried. The National Institute of Mental Health (NIMH) Institutional Review Board approved the study; each participant and a parent provided written informed consent/assent.

Procedures

Subjects completed testing during outpatient visits to NIMH. Verbal language tasks were administered by licensed psychologists; other tasks were administered by trained research assistants.

Measures

Social cognition. The pragmatic judgment subtest of the Comprehensive Assessment of Spoken Language (40) assesses awareness of appropriate language for varied social situations. Participants respond verbally to social vignettes that elicit polite interruptions, introductions, etc. The total standard score was the dependent variable.

Two subtests from the Diagnostic Analysis of Nonverbal Accuracy Scale (41) were administered to evaluate identification of emotional facial expressions. Participants viewed standardized photographs of children (N=24) and adults (N=24) displaying high- and low-intensity expressions of happiness, sadness, anger,

Euthymic Pediatric Bipolar Disorder Patients			Symptomatic Pediatric Bipolar Disorder Patients		
N	Mean	SD	N	Mean	SD
20	98.1[a]	13.1	14	100.0[a]	14.5
23	4.3[a]	2.1	15	4.3[a]	2.3
24	5.5[a]	2.3	16	6.1[a]	3.1
16	0.30	0.18	17	0.29	0.14
N	Mean	SD	N	Mean	SD
16	0.56[a]	0.24	17	0.61	0.17
N	Mean	SD	N	Mean	SD
16	–38.9	70.1	17	–20.8	77.6
16	0.45	0.29	17	0.38	0.29
N	Mean	SD	N	Mean	SD
23	248.0	65.0	15	254.6	81.8
23	309.2[a]	88.4	14	280.9	76.5

or fear. After viewing each picture for 2 seconds, the participant identified which of the four expressions was displayed. For both the child and adult facial expression subtests, the total number of errors was the dependent variable. Post hoc analyses were also conducted to examine discriminability for each emotion. Discriminability (hit rate minus false-alarm rate) provides a measure of sensitivity in discriminating among expression types (42). Higher values indicate greater sensitivity.

To examine contributions of other aspects of expressive language to group differences in social cognition, we administered the oral expression subtest of the Test of Language Competence (43). This subtest requires participants to assemble verbal concepts into grammatically correct sentences; the total T score from this measure was covaried in analyses of social-cognitive variables.

Inhibition and response flexibility. Participants completed the stop and stop-change tasks (44, 45). Whereas the stop task indexes simple motor inhibition, the stop-change task measures ability to inhibit a prepotent response and substitute an alternative response. The stop task consists of go trials (participants are instructed to press "1" as quickly as possible when "X" appears or to press "2" when "O" appears) and stop trials (participants are instructed not to respond when the "X" or "O" appears followed by a change to a red background [the stop signal]). In the stop-change task, change trials were substituted for stop trials. In the change trials, subjects were instructed to press "3" rather than "1" or "2" when the background changed to blue (change signal) after the "X" or "O" appeared. On the first stop or change trial in a block, the signal appeared 250 msec after the "X" or "O." If the subject responded correctly, the next signal appeared 50 msec later, making inhibition more difficult. If the subject responded incorrectly, the next signal appeared 50 msec earlier, making inhibition easier. The timing of each subsequent "signal" trial was based on the previous trial of the same type.

The stop signal reaction time (speed of inhibition) and the change signal reaction time (speed of inhibition plus execution of an alternate response) were calculated by using an interpolation algorithm (45, 46). Stop signal reaction time and change signal reaction time served as dependent measures.

Motor inhibition. Indices from three continuous performance tasks served as measures of motor inhibition. The AX Continuous Performance Test requires participants to sustain attention while making conditional discriminations of targets and nontargets (47). Response bias, or failure to inhibit response to a nontargeted cue, served as the predictor variable. We also report data regarding a measure of discriminability, consistent with the literature on adult bipolar disorder.

The Flanker Continuous Performance Test is a test of selective attention that requires inhibition of a prepotent response when "incongruent" distractor stimuli appear (48, 49). The degree to which the presence of distractors during the incongruent trials impaired performance, relative to neutral trials (reaction time cost), served as the dependent variable.

The Identical Pairs Continuous Performance Test taxes both attention and working memory (50). Subjects are required to press a button whenever two identical stimuli appear consecutively within a sequence of rapidly flashed trials. The task includes 30 such target pairs; 29 "catch" trials, in which two successive stimuli are similar, but not identical; and 90 trials in which stimuli are randomly organized and dissimilar. Response bias, or failure to inhibit response to nontargeted cues, was the dependent variable.

Statistical Analysis

Data for variables with significantly skewed distributions according to Shapiro-Wilk statistics were analyzed with nonparametric statistical tests. Data for normally distributed variables were examined by using parametric tests. We first performed Student's t tests or Mann-Whitney U tests for each target measure to identify significant differences between pediatric bipolar disorder patients and comparison subjects. To examine whether group differences on social-cognitive measures could be accounted for by general language competence, we followed the unprotected comparisons with a logistic regression analysis. Group (pediatric bipolar disorder group, comparison group) was the outcome variable, and the Comprehensive Assessment of Spoken Language pragmatic judgment score and Diagnostic Analysis of Nonverbal Accuracy Scale adult and child facial expression total error scores were the predictors. Test of Language Competence oral expression score was covaried.

To study effects of mood state, we conducted post hoc analyses of the variance of normally distributed variables between pediatric bipolar disorder patients (euthymic versus symptomatic) and comparison subjects, followed by pairwise comparisons with Tukey's honestly significant difference test where omnibus effects were significant. For nonnormally distributed variables, we conducted Kruskal-Wallis H tests, followed by post hoc Wilcoxon tests. We then used the previously described procedures to compare results on each measure for the healthy subjects with those for the pediatric bipolar disorder patients with and without current ADHD and with those for the pediatric bipolar disorder patients with and without current anxiety disorders. We set alpha at 0.05 for all tests.

TABLE 3. Logistic Regression Analysis of Social-Cognitive and General Linguistic Predictors of Diagnostic Group Status in Patients With Pediatric Bipolar Disorder and Healthy Comparison Subjects

Measure	z[a]	df	p	Odds Ratio	95% CI
Test of Language Competence oral expression subtest	3.33	1	0.07	0.67	0.43–1.03
Comprehensive Assessment of Spoken Language pragmatic judgment subtest	6.17	1	0.01	0.82	0.70–0.96
Diagnostic Analysis of Nonverbal Accuracy Scale					
Child facial expression subtest (errors)	2.17	1	0.14	1.80	0.82–3.96
Adult facial expression subtest (errors)	5.86	1	0.02	2.05	1.15–3.67
Constant	5.87	1	0.02		

[a] Wald criterion.

Because of time constraints or symptom severity during testing, not all participants completed every task.

Results

Social Cognition

The pediatric bipolar disorder group scored significantly lower than the comparison subjects on the Comprehensive Assessment of Spoken Language pragmatic judgment test ($p<0.001$) and made significantly more errors on the Diagnostic Analysis of Nonverbal Accuracy Scale child facial expression ($p=0.01$) and adult facial expression ($p<0.01$) subtests (Table 2). Scores on the Comprehensive Assessment of Spoken Language pragmatic judgment test and the Diagnostic Analysis of Nonverbal Accuracy Scale child and adult facial expression subtests were entered into a logistic regression model predicting group membership (pediatric bipolar disorder group, comparison group). Test of Language Competence oral expression score was covaried. The predictors, as a set, reliably distinguished between youths with pediatric bipolar disorder and healthy comparison subjects ($\chi^2=36.6$, df=4, N=49, $p<0.001$); 84% of the pediatric bipolar disorder group, 89% of the comparison group, and 86% of all participants were classified correctly (Table 3). According to the Wald criterion, only the Comprehensive Assessment of Spoken Language pragmatic judgment score ($z=6.17$, $p=0.01$) and the Diagnostic Analysis of Nonverbal Accuracy Scale adult facial expression total errors score ($z=5.86$, $p=0.02$) reliably predicted group status.

Post hoc Mann-Whitney U tests of discriminability scores for each emotion within each Diagnostic Analysis of Nonverbal Accuracy Scale subtest indicated that youths with pediatric bipolar disorder, relative to the comparison subjects, were less sensitive to happiness ($z=-2.07$, $p=0.04$) and anger ($z=-2.78$, $p<0.01$) in children and to sadness ($z=-3.62$, $p<0.001$) and anger ($z=-2.43$, $p=0.02$) in adults (Table 2).

Response Flexibility/Inhibition

The groups did not differ on inhibition measures, including the AX, Flanker, and Identical Pairs Continuous Performance Tests and stop signal reaction time ($p>0.05$) but did differ significantly on the AX Continuous Performance Test discriminability measure ($p=0.004$) (Table 2). The pediatric bipolar disorder group also had a significantly longer change signal reaction time than did the comparison subjects, whether gender was covaried ($p=0.03$) or not ($p=0.02$), suggesting a deficit in response flexibility.

Post Hoc Analyses: Mood State

Social-cognitive tasks. Exploratory Kruskal-Wallis H tests comparing the healthy subjects, the euthymic pediatric bipolar disorder patients, and the symptomatic pediatric bipolar disorder patients yielded significant omnibus differences among the three groups on the Comprehensive Assessment of Spoken Language pragmatic judgment test score ($p<0.001$) and the total errors scores on the Diagnostic Analysis of Nonverbal Accuracy Scale child facial expression ($p=0.02$) and adult facial expression ($p=0.02$) subtests (Table 2). Post hoc pairwise comparisons indicated that both pediatric bipolar disorder patient groups performed significantly more poorly than the healthy comparison subjects on all three measures ($p<0.05$).

Response-flexibility/inhibition tasks. Comparisons of the healthy subjects, euthymic pediatric bipolar disorder patients, and symptomatic pediatric bipolar disorder patients indicated significant omnibus differences on change signal reaction time, whether gender was covaried ($p=0.05$) or not ($p=0.02$), but not on any other motor inhibition measures (all $p>0.05$). Post hoc contrasts showed that only euthymic pediatric bipolar disorder patients performed more poorly than the healthy comparison subjects on change signal reaction time (gender covaried: $p<0.05$; no covariates: $p=0.01$).

Post Hoc Analyses: Comorbid Diagnoses

Exploratory comparisons indicated significant omnibus differences among the pediatric bipolar disorder patients with ADHD, the pediatric bipolar disorder patients without ADHD, and the comparison subjects on the social-cognitive measures (Comprehensive Assessment of Spoken Language pragmatic judgment: $\chi^2=16.72$, df=2, N=52, $p<0.001$; Diagnostic Analysis of Nonverbal Accuracy Scale adult facial expressions: $\chi^2=8.92$, df=2, N=60, $p=0.01$; Diagnostic Analysis of Nonverbal Accuracy Scale child facial expressions: $\chi^2=6.30$, df=2, N=58, $p=0.04$), but not on the inhibition/response flexibility measures (AX Continuous Performance Test response bias: $\chi^2=3.31$, df=2, N=55, $p=0.19$; Flanker Continuous Performance Test reaction time cost: $\chi^2=3.01$, df=2, N=55, $p=0.21$; Identical Pairs Continuous Performance Test response bias: $\chi^2=1.58$, df=2, N=55, $p=0.45$; stop signal reaction time: $F=1.55$, df=2, 59, $p=0.22$), except for change signal reaction time ($F=3.25$, df=2, 55,

p<0.05, with gender covaried). Post hoc comparisons indicated that the patients with and without ADHD performed worse than the comparison subjects on all three social-cognitive measures (p<0.05 for each comparison) and that the patients without ADHD had poorer change signal reaction time scores than the comparison subjects (p<0.05). There were no significant effects of current anxiety disorder on any measure (all p>0.05).

Discussion

Results indicate deficits in social cognition and motor flexibility in patients with narrow-phenotype pediatric bipolar disorder. Relative to comparison subjects of comparable age, gender, and IQ, youths with pediatric bipolar disorder performed more poorly on tasks involving facial emotion identification and formulation of socially appropriate responses to interpersonal situations. Indeed, performance on social-cognitive tasks correctly classified 86% of the study participants. Although the patients' motor inhibition was not clearly impaired, they showed deficient response flexibility when required both to inhibit a prepotent behavior and to execute an alternate response (the stop-change task). No group differences were attributable to comorbid ADHD.

The patients all had "narrow-phenotype" pediatric bipolar disorder, which has a clinical presentation similar to that of adult bipolar disorder (12, 51). Like symptomatic adults with bipolar disorder, the patients in our study showed deficits in recognition of facial affect (9). The patients also showed significant deficits in expressive pragmatic language. Although adults with bipolar disorder have difficulty interpreting cues about others' mental states (3, 7, 9), little research has examined expressive language pragmatics in this population. Thus, although both children and adults with bipolar disorder have social-cognitive deficits, further study is needed to clarify these deficits and their continuity across development. Use of measures that can be implemented consistently across development would facilitate such research. In addition, comparison of performance across individuals with varied psychiatric disorders will be important to determine if the observed deficits are specific to bipolar disorder.

The results regarding response flexibility and inhibition showed some consistency with reports in the literature on adult bipolar disorder. In particular, the group differences on change signal reaction time, a measure of response flexibility, resemble reports in adult bipolar disorder and pediatric bipolar disorder of deficits on tasks that require both inhibition and flexible responding (29, 31). Also like other studies, our study showed no clear deficits on simple motor inhibition tasks (4, 28–30). Both the literature and our data suggest that, across the developmental spectrum of bipolar disorder, deficits may be more marked on tasks that pair inhibition and execution of alternative behaviors than on tasks that involve inhibition alone. This pattern of performance could reflect many factors, ranging from differences in task complexity to differences in neural mechanisms mediating the two task types.

The present study yields evidence of some behavioral continuity across narrow-phenotype pediatric bipolar disorder and adult bipolar disorder. An important next step will be to elucidate the neural mechanisms underlying social-cognitive and response-flexibility deficits in bipolar disorder. Evidence indicates that regions including the ventral prefrontal cortex and amygdala mediate facial affect processing and that the ventral prefrontal cortex and other prefrontal areas contribute to complex inhibitory functions (16, 18, 19, 33, 34, 52). Less is known about the neural mechanisms underlying pragmatic language, although research has implicated the frontal and temporal cortical regions (17). Given findings of structural and functional anomalies in the prefrontal cortex and amygdala in bipolar disorder (22–24, 26), neuroimaging studies implementing measures of social cognition and response flexibility in pediatric bipolar disorder patients are warranted. Optimally, such studies should include clinical comparison groups to evaluate the specificity of observed anomalies.

Our inclusion of euthymic and symptomatic pediatric bipolar disorder patients allowed us to examine performance in the context of both normal and clinically significant mood states. Both euthymic and symptomatic patients performed more poorly than comparison subjects on measures of expressive pragmatic language and facial expression identification. This pattern of findings raises the possibility that social-cognitive deficits may represent trait-based vulnerability markers and possibly endophenotypes for pediatric bipolar disorder. On a measure of response flexibility, the one other task where pediatric bipolar disorder patients exhibited deficits, only euthymic patients differed significantly from comparison subjects. This finding suggests that response-flexibility deficits may represent an additional trait vulnerability marker for pediatric bipolar disorder. However, the lack of difference between the symptomatic patients and the comparison subjects is puzzling. This negative finding, which may reflect type II error, requires further study. Replication in proband and high-risk groups, as well as longitudinal study of patients across both euthymic and symptomatic states, is warranted.

This study had several limitations. The number of subjects was relatively small, and most of the pediatric bipolar disorder patients were receiving medication. However, given that group differences were selective, it appears unlikely that they were entirely related to medication. Nonetheless, examination of social cognition and response inhibition/flexibility in unmedicated youths with bipolar disorder and in children at risk for bipolar disorder is indicated. In addition, direct comparison of youths with pediatric bipolar disorder and those with other disorders, particularly ADHD/oppositional defiant disorder and the broad phenotype of pediatric bipolar disorder (12), would

provide further evidence about the specificity of our findings. We are currently conducting studies to address these limitations.

In summary, our findings, along with those from other recent studies (31), begin to delineate a neuropsychological and social-cognitive profile for narrow-phenotype pediatric bipolar disorder. These results offer evidence of continuity between pediatric bipolar disorder and adult bipolar disorder, highlighting the need for further study using comparable measures in both populations. In addition, our findings of impairment among pediatric bipolar disorder patients on tasks involving pragmatic language, facial affect recognition, and response flexibility lay the groundwork for neurocognitive research aimed at elucidating neural mediators of these deficits.

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