Brief Report

Deficits on a Probabilistic Response-Reversal Task in Patients With Pediatric Bipolar Disorder

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Objective: Patients with bipolar disorder become hyperhedonic when manic and anhedonic when depressed; therefore, it is important to test whether patients with bipolar disorder show deficits on behavioral paradigms exploring reward/punishment mechanisms.

Method: A probabilistic response-reversal task was administered to 24 bipolar children and 25 comparison subjects.

Results: Patients made more errors during probabilistic reversal, took longer to learn the new reward object, and were less likely to meet the learning criterion.

Conclusions: Children with bipolar disorder may have a reversal learning deficit.

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Children and adults with bipolar disorder experience episodic hyperhedonia and anhedonia. These symptoms may indicate abnormalities in reward-processing circuitry (1). Probabilistic response-reversal tasks model behavioral adaptation to changing reward contingencies. Patients identify and learn the reward object in a repetitively presented pair of items, and then they re-identify the rewarded object after it has been switched to the other item in the pair.

Neuroimaging and lesion studies have implicated two interconnected inferior-frontal regions—the orbitofrontal and ventrolateral prefrontal cortices—both in the pathophysiology of bipolar disorder (2) and in the mediation of response reversal (3). In bipolar children, one study reported deficits on a nonprobabilistic response-reversal task (4). We used a probabilistic response-reversal task to further explore response-reversal deficits in pediatric bipolar disorder.

Method

Patients ages 6–17 years with bipolar disorder and age- and gender-matched comparison subjects were recruited into this study, which was approved by our institutional review board. The parents and the children gave written informed consent/assent.

The patients met DSM-IV criteria for bipolar disorder, with at least one episode of euphoric (hypo)mania meeting duration criteria. Exclusion criteria included an IQ <70, severe pervasive developmental disorder, and substance abuse within 3 months. Clinicians administered the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (5) diagnostic interview. The Young Mania Rating Scale (6), the Children's Depression Rating Scale (7), and parent Conners's attention deficit hyperactivity disorder (ADHD) inventories (8) were completed within 1 week of the task. The comparison subjects met three inclusion criteria: no psychopathology in the patients or their first-degree relatives, an IQ >70, medically healthy, and no use of medication.

The self-paced probabilistic response-reversal task (an unpublished measure by Budhani and Blair) was conducted on laptop computers. The subjects were told, "Find out which animal is usually correct and choose it every time, even if it is occasionally wrong. At some point, it may change so that the other animal is usually correct, in which case you should choose that one every time." Each trial required a selection to continue. Messages stating, "You have won/lost 100 points" were displayed contingent on responses. Six pairs were presented. One pair, shown for 40 trials, had one continuously rewarded stimulus (100:0 nonreversing pair). A second pair (100:0 reversing pair) was shown for 80 trials. During the first 40 trials (acquisition phase), one stimulus was rewarded each time it was selected. During the second 40 trials (reversed phase), the other stimulus was rewarded. In a third pair (80:20 nonreversing pair), shown for 40 trials, one stimulus was rewarded 80% of the time, and the other stimulus was rewarded 20% of the time. In a fourth pair (80:20 reversing pair), one stimulus was rewarded 80% of the time (and the other stimulus was rewarded 20% of the time) during the first 40 trials (acquisition phase), after which the two stimuli were shown for another 40 trials, but the probability of reward was reversed (reversed phase). No data were collected for initial and terminal "dummy pairs." Trial order alternated randomly between the two pairs.

We used t tests to compare the patients and the comparison subjects on the number of errors they made for each pair, the number of errors they made before learning the reward object (the criterion for learning was six consecutive correct), and the proportion of subjects meeting the learning criterion.

After a significant association was identified between WAIS performance IQ and task performance, analysis of covariance (ANCOVA) was used to control for performance IQ. Exploratory post hoc Pearson's correlations examined the association between the bipolar patients' performance and age, sex, and ADHD diagnosis. For 20 bipolar patients, correlations between the following ratings and performance were also calculated: IQ, Young Mania Rating Scale score, the Children's Depression Rating Scale score, Conners's ADHD inventory scores, and a DSM-IV ADHD rating scale score representing the number of ADHD criteria reported by the parent.

TABLE 1. Comparison of Performance on the Probabilistic Response-Reversal Task of Patients With Bipolar Disorder and Comparison Subjects[a]

Performance Variable[b]	Comparison Subjects (N=25) Mean	Comparison Subjects (N=25) SD	Patients With Bipolar Disorder (N=24) Mean	Patients With Bipolar Disorder (N=24) SD
100:0 nonreversing pair, acquisition phase				
Met criterion	1.00	—	1.00	—
Errors to meet criterion[c]	0.68	0.69	1.00	1.14
Total errors	0.84	0.90	1.42	1.82
100:0 reversing pair				
Acquisition phase				
Met criterion	1.00	—	1.00	—
Errors to meet criterion[c]	1.04	0.98	1.75	2.36
Total errors	1.24	1.64	2.33	2.41
Reversed phase				
Met criterion	1.00	—	1.00	—
Errors to meet criterion[c]	3.24	2.17	2.33	1.43
Total errors	3.68	2.56	3.12	2.17
80:20 nonreversing pair, acquisition phase				
Met criterion	0.96	0.20	1.00	—
Errors to meet criterion[c]	2.76	3.88	3.54	4.28
Total errors	4.88	5.09	5.92	4.46
80:20 reversing pair				
Acquisition phase				
Met criterion	1.00	—	1.00	—
Errors to meet criterion[c]	3.60	4.10	3.75	3.71
Total errors	4.88	5.04	5.88	4.77
Reversed phase				
Met criterion[d]	1.00	0.00	0.75	0.44
Errors to meet criterion[c,e]	5.92	4.25	10.50	8.11
Total errors[f]	7.44	5.44	14.13	6.70

[a] Significance was set at p<0.05.
[b] The proportion that met the criterion for learning the positive reward object in a pair by correctly choosing the correct stimuli six times consecutively.
[c] The number of errors committed before meeting the learning criterion of six consecutively correct trials.
[d] t=–2.77, df=23, p=0.01.
[e] t=2.46, df=34.4, p=0.02.
[f] t=3.84, df=47, p=0.004.

Results

Twenty-four euthymic (Children's Depression Rating Scale score: mean=27.9, SD=7.7; Young Mania Rating Scale score: mean=8.3, SD=5.7; comorbid ADHD: N=16, 67%) patients and 25 age- and gender-matched comparison subjects performed the task (age of bipolar subjects: mean=13.6 years, SD=2.6, age of comparison subjects: mean=14.5, SD=1.8; male bipolar subjects: N=14, 58.3%, male comparison subjects: N=12, 48.0%). The patients with bipolar disorder performed similarly to the comparison subjects on the acquisition phases (Table 1). However, in the 80:20 reversal phase (but not the 100:0 reversal), the patients made more errors overall, made more errors before meeting the learning criterion, and were less likely to meet the learning criterion (Table 1).

Gender, age, and Young Mania Rating Scale (N=20) and Children's Depression Rating Scale (N=20) scores of the bipolar patients did not correlate with performance. Scores on Conners's ADHD inventories negatively correlated (r=–0.52, N=20, p<0.02) with the likelihood of meeting the learning criterion. However, neither of the other two ADHD measures correlated with performance. Performance IQ correlated (r=–0.44, N=20, p<0.05) with errors before the subjects reached the learning criterion but not with other measures. In an ANCOVA controlling for performance IQ, errors made in reaching the learning criterion no longer differed between groups (F=3.44, df=1, 39, N=39, p=0.07), although the differences in total errors (F=8.98, df=1, 39, N=39, p=0.01) and the number of subjects meeting the learning criteria (F=5.20, df=1, 39, N=39, p=0.03) remained significant.

Discussion

On this probabilistic response-reversal task, euthymic children with bipolar disorder, relative to comparison subjects, made more errors and were less likely to learn the reward object in the 80:20 reversal phase. This suggests that bipolar children have difficulty adapting to changing reward contingencies. These findings are noteworthy, given prior data linking the functioning of two interconnected inferior-frontal regions—the orbitofrontal and ventrolateral prefrontal cortices—to both the pathophysiology of bipolar disorder and to response reversal.

Studies have implicated the orbitofrontal and ventrolateral prefrontal cortices in response reversal. Lesioned monkeys and humans with damage to the orbitofrontal and ventrolateral prefrontal cortices have shown impairment on tasks requiring behavioral adaptation to changing contingencies (9, 10). Lesion and neuroimaging studies have also implicated the orbitofrontal and ventrolateral prefrontal cortices in the pathophysiology of bipolar disorder. Lesions inducing mania occur primarily in limbic areas (11). Deficits in the orbitofrontal and ventrolateral prefrontal cortices were found in patients with bipolar disorder with functional magnetic resonance imaging (fMRI) (2).

Because response reversal deficits occur in psychopathy (unpublished measure by Budhani and Blair) and ADHD (12), they are not specific to bipolar disorder. Given the comorbidity between ADHD and bipolar disorder, we assessed ADHD in this study. Because one of three ADHD measures predicted response-reversal performance, ADHD symptoms may contribute to our findings.

Future research might address limitations in the current study. Considerable evidence identifies developmental changes in reward-related behaviors during the adolescent period. Although no association was found in this small study between age and response-reversal performance, future studies in larger groups should examine developmental changes in response reversal among both healthy children and children with bipolar disorder. Pediatric bipolar disorder may interfere with normal developmental changes in reward-related behaviors, as possibly detected by the response-reversal task. Furthermore, larger studies in both children and adults with bipolar disorder might examine the effects of other clinical characteristics on the

performance of response reversal. These characteristics include age at illness onset, medication use, family/genetic factors, and cycle duration/frequency. Finally, further insights on the function of the orbitofrontal and ventrolateral prefrontal cortices in both pediatric bipolar disorder and ADHD may arise through fMRI studies with the response-reversal task.

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Brief Report

The Internal Struggle Between the Wish to Die and the Wish to Live: A Risk Factor for Suicide

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Objective: This study attempted to assess whether an index of the difference between the wish to die and the wish to live constitutes a risk factor for suicide.

Method: A study group of 5,814 patients, including 44 who committed suicide (0.8%), were recruited from a psychiatric outpatient clinic. Structured diagnostic interviews and clinician ratings of the wish to live and wish to die were conducted. The outcome variable was the occurrence of suicide, as indicated on death certificates.

Results: A dichotomized index score of the difference between the wish to live and the wish to die yielded a hazard ratio of 6.51 for suicide. This index contributed a unique risk for suicide after the authors controlled for age, psychiatric hospitalization, suicide attempts, bipolar disorder, major depressive disorder, and unemployment status.

Conclusions: The difference between the wish to die versus the wish to live is a unique risk factor for suicide.

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Shneidman and Farberow (1) noted that the motivation to commit suicide is often complex and involves considerable ambivalence and that suicidal individuals often experience an internal struggle between wanting to live and wanting to die. To test this observation, Kovacs and Beck (2) administered separate measures of the wish to live and the wish to die to patients hospitalized after a suicide attempt. They found that when the wish to die was