

Research report

Increased sensitivity to error during decision-making in bipolar disorder patients with acute mania

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Abstract

Background: Decision-making is a complex and important function for daily life that can be assessed quantitatively using a simple two-choice prediction task. Bipolar disorder (BD) patients are thought to show altered responsivity to positive and negative feedback. In this study we examined whether BD patients with psychotic mania show altered patterns of decision-making as a function of the frequency of incorrect predictions or error rate. **Methods:** Fourteen adult DSM-IV-diagnosed BD patients with psychotic mania and 14 normal comparison subjects (NC) were tested with a two-choice prediction task using three error rate conditions (20%, 50%, or 80%). **Results:** BD patients showed an increased sensitivity to error rate changes and switched more frequently at high error rates than NC subjects. In comparison, there were no differences between BD and NC subjects on the degree to which the response or stimulus during a previous trial predicts the current response. **Conclusions:** Decision-making in BD patients with psychotic mania appears to be highly sensitive to high error rates. Moreover, the patterns of responses appear distinct from what has been previously observed in acutely and chronically ill schizophrenia patients. The results of this study are informative as to the effects of errors on decision-making strategies in psychotic BD manic patients. © 2003 Elsevier B.V. All rights reserved.

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1. Introduction

Bipolar mania is often accompanied by prominent cognitive and behavioral problems, including difficulties in making appropriate decisions. Decision-making is a complex process that occurs whenever a person selects an action in the presence of either a known or uncertain outcome (Tversky and Kahneman, 1981). In

a simple two-choice prediction decision-making paradigm, subjects are asked to repeatedly predict the location of a stimulus on a computer screen. When asked to select between response alternatives subjects will generally select the action which is most likely associated with the “correct” outcome (Calfee and Atkinson, 1966; Goulet and Barclay, 1967; Ludvigson, 1966). This response selection behavior corresponds to the well-known matching law that has been observed in a large number of animal studies (Herrnstein, 1997). Several psychological models have been proposed to explain how response selection is related to reinforcement history, even in the presence of

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random reinforcement (Restle, 1966; Rose and Vitz, 1966). Central to these models is the notion that subjects maintain a representation of the history of “correct” versus “incorrect” decisions in short term storage and adjust their strategies accordingly. Therefore, the decision-making process is influenced in a complex manner by the history of success or failure of previous actions.

Dysfunctions in decision-making as assessed by the two-choice prediction task have been observed in patients with schizophrenia. Notably, schizophrenia patients alternate between sequences of responses that are either highly predictable (perseverative) and highly unpredictable response sequences (Paulus et al., 1996). Additionally, schizophrenia patients do not utilize stimulus information to the same extent as normal comparison subjects (NC) (Paulus et al., 1999). Paulus et al. (2002) have also found that response selection in schizophrenia patients was more influenced by the previous outcome and that schizophrenia patients showed different patterns of brain activation in response to decision-making tasks when compared to non-patients.

Recently, genetic studies have led to the recognition that there may be considerable overlap between schizophrenia and bipolar disorder (BD) (Kelsoe et al., 2001). At cross-section during the acute phase of their illness, it is often difficult to discriminate between BD and schizophrenia patients (Carlson and Goodwin, 1973; Tam et al., 1998). Similarly, during acute episodes of mania, patients with BD have been found to be indistinguishable from schizophrenia patients on a variety of information processing tasks (Saccuzzo and Braff, 1986; Serper, 1993; Strauss et al., 1987). Decision-making ability in bipolar manic patients, particularly when they are in a psychotic state, is an important area of study as the hallmark symptoms of mania include poor judgement, engagement in risky behavior, and impulsive decision-making that results in painful consequences (American Psychiatric Association, 1994).

This investigation examined whether the frequency of incorrect predictions, i.e. the error rate, has an increased influence on the number of different strategies underlying decision-making in patients with BD. Using a two-choice prediction task, the frequency of correct or incorrect predictions can be determined a priori by the experimenter, which allows the investi-

gator to examine how decision-making changes as a function of error rate.

2. Method

2.1. Subjects

The participants in this study consisted of 14 subjects with a DSM-IV diagnosis of Bipolar Disorder, Manic with Psychotic Features (BD) (nine males, five females) and 14 NC subjects (six males, eight females). Only BD subjects who were able to verbally demonstrate that they understood the nature of the study and its associated risks and benefits were considered for inclusion. The BD subjects were diagnosed using DSM-IV criteria for BD, as determined by the use of the Structured Clinical Interview for DSM-IV (SCID-IV) (First et al., 1994). We previously established a 98% agreement for determining Axis I diagnoses using the SCID (Perry et al., 2001). There were no significant differences between subject groups for age [BD mean age = 36.5 years, NC mean age = 32.4 years, $t(26) = 0.95$, n.s.] or years of education [BD mean education = 14.3 years, NC mean education = 14.0 years, $t(26) = 0.39$, $P = 0.70$]. Subjects were excluded if they were determined to have an additional Axis I diagnosis or met DSM-IV criteria for substance abuse or dependence within the past 6 months, had a positive result on urine toxicology screen, an unstable medical condition, a history of a neurological disorder (e.g. a head injury with loss of consciousness), or were treated in the past with electroconvulsive therapy (ECT). All patients were tested within 96 hours of being admitted to the Neuropsychiatry and Behavioral Medicine Unit at the University of California San Diego-Medical Center, while in an acute psychotic state.

The NC subjects underwent screening interviews to rule out Axis I and II disorders, neurological illness or head trauma, exposure to psychoactive medication, or drug abuse. Subjects were excluded if they had a positive result on a urine toxicology screen.

2.2. Procedure

After a complete description of the study was given to the subjects, written informed consent was

obtained. The study protocol and consent forms were reviewed and approved by the UCSD Human Subjects Committee. BD patients were assessed with the Young Mania Rating Scale (YMRS; Young et al., 1978). Average YMRS score was 21.9 (S.D.=6.3). All but two of the BD subjects were prescribed psychotropic medication at the time of testing. The two not-medicated subjects were tested on the paradigm before the initiation of psychotropic treatment. Of the remaining 12 subjects, four were prescribed a mood stabilizer alone, and eight were prescribed a combination of a mood stabilizer and an anti-psychotic agent. The most common mood stabilizing medication prescribed was divalproex ($n=8$, mean daily dose = 1625 mg, S.D. = 443.2) and the most common anti-psychotic medication prescribed was risperidone ($n=5$, mean daily dose = 3 mg, S.D. = 1). Prior to initiation of treatment in the hospital, the BD subjects had not been taking medications, or had been taking medications at sub-therapeutic doses.

All subjects were administered the Vocabulary subtest from the Wechsler Adult Intelligence Scale-revised (WAIS-R) (Wechsler, 1981) to assess their premorbid level of verbal intellectual functioning. BD subjects had significantly lower WAIS-R scaled scores (mean = 8.9, S.D. = 2.6) than NC subjects (mean = 11.6, S.D. = 1.5) [$t(26) = 3.48$, $P = 0.002$].

Subjects were next administered the two-choice prediction task. The two-choice prediction task has been described in detail in previous articles (Paulus et al., 1997). Briefly, a house flanked by a person to the left and right is shown on a computer screen. The subject is instructed to “predict” whether a car will be shown on the left or right side of the computer screen and to press a left or right button so that the person on the screen can meet up with a car. After the subject has made a response, the car is presented for 300 ms on the far left or right side. Unbeknownst to the subject, a computer program, which takes the response of the subject into account, determines a-priori whether a response will be “correct” or “incorrect”. The two-choice prediction task was divided into three trial-blocks. During the first trial-block, which consisted of 128 trials, the computer program assured that 50% of all responses were “correct” (50% error rate), during the second trial-block corresponding to the next 64 trials 20% of all responses “correctly predicted” the

location of the car (80% error rate), and during the third trial-block, which comprised the next 64 trials, 80% of all responses were “correct” predictions (20% error rate). The basic variables are the subject’s response, the location of the car, and the latency to select a response, i.e. the time from the beginning of the trial to the button press. The subjects were given an opportunity to practice the task before the onset of data collection. The task was self-paced, i.e. there was no time limit for subjects’ responses to each trial. All subjects received the different trial blocks (50% vs. 80% vs. 20% error rate) in the same order.

Two sets of measures were obtained from the sequences of responses to assess whether (1) subjects exhibit response biases; and (2) the current response can be predicted by the previous response, the previous presentation of the stimulus, or the previous outcome of the prediction. First, response bias measures quantified whether subjects were more likely to select RIGHT versus LEFT or were more likely to SWITCH between responses than to STAY with the same response. Second, the mutual information function (MI) (Herzel and Grosse, 1995) quantifies the predictability of the current response by the previous response. Given two responses within the same time series that are separated by k intermediate responses, the MI can be computed by evaluating the joint probability of the 1st to the $N-k$ th response with the k th to the N th response. The variable k is known as the delay of the MI and corresponds to a particular temporal scale. Here we set $k=1$, i.e. we examined the effect of the previous response on the current response. In addition, the cross-mutual information (CMI) quantifies the predictability of the current response by the previous stimulus, i.e. whether the car was presented on the LEFT or RIGHT side on the previous trial. The CMI was calculated based on the entropy of the presentation of the first $N-1$ presentations of the car, $H_{c,0..N-1}$ and the 1st to the N th choice, $H_{1..N}$ via $I_1 = H_{c,0..N-1} + H_{1..N} - H_{c,0..N-1,1..N}$.

2.3. Statistical analysis

All statistical analyses were performed using SPSS. Mixed analyses of variance (ANOVA) were conducted, with subject group (BD vs. NC) as the between-subjects factor and error rate (20% vs. 50% vs. 80%) as the within-subjects factor.

3. Results

The first analysis examined whether basic response characteristics during the two-choice prediction task, i.e. the probability of choosing the LEFT or RIGHT response, differed across BD and NC subjects. All subjects selected the RIGHT versus LEFT response an equal number of times [probability of selecting the RIGHT response: BD=0.52, NC=0.51, $F(1,26)=0.002$, n.s.]. Next, the rate of switching responses was examined. The higher the error rate the greater the switching rate from the current response to the alternative response ($F=20.0$, $df=2,25$, $P<0.01$). Additionally there was a significant group-by-error rate interaction ($F=5.3$, $df=2, 25$, $P=0.01$) such that as the error rate increased to 80%, BD subjects increased their rate of switching more than NC subjects (see Fig. 1).

The third set of analysis examined whether the response selection by BD subjects was significantly more affected by the previous response (MI) or the previous stimulus (CMI). The degree to which the previous response or the previous stimulus predicted the current response differed significantly across error-rate conditions (MI: $F=7.6$, $df=2,25$, $P<0.01$; CMI: $F=9.4$, $df=2,25$, $P<0.01$). Specifically, both the previous response and the previous stimulus were

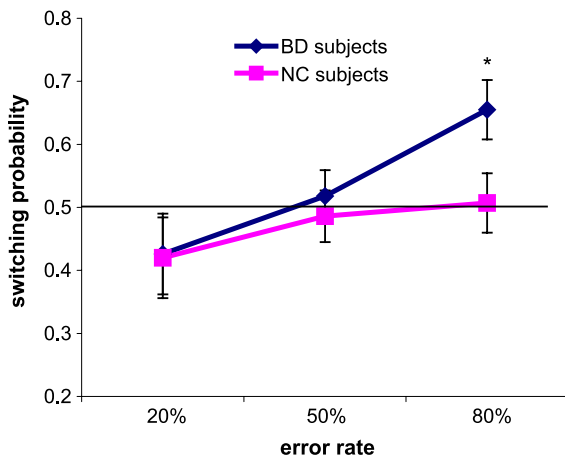


Fig. 1. Probability of switching (from LEFT to RIGHT or RIGHT to LEFT on consecutive trials) as a function of error rates (percentage of incorrect predictions) in subjects with BD with acute mania ($n=14$) and NC subjects ($n=14$). The horizontal line indicates chance level response switching.

more predictive of the current response during 20% error-rate relative to the 50% error-rate condition. The influence of the previous response or the previous stimulus was not different across groups (MI: $F=2.4$, $df=1,26$, n.s.; CMI: $F=3.1$, $df=1,26$, n.s.) nor was there a group by error-rate interaction (MI: $F=2.0$, $df=2,25$, n.s.; CMI: $F=1.1$, $df=2,25$, n.s.). Thus, BD subjects did not differ from NC subjects when selecting the current response in relation to the previous stimulus or response.

Performance during the two-choice prediction task quantified by response bias measures and MI functions was not significantly correlated with YMRS scores or WAIS-R Vocabulary scores for the BD subjects. There were no significant correlations between the choice task variables and either divalproex or risperidone doses.

4. Discussion

The primary focus of this investigation was to examine decision-making characteristics in BD patients with psychotic mania, specifically whether different error rates had an impact on response strategies in a two-choice prediction task. BD patients demonstrated more switching of responses at the high error rate condition, suggesting that decision-making behavior in these subjects is more sensitive to change as the probability of a successful outcome becomes uncertain and increasingly unlikely. Decision-making in BD has previously been studied with a computerized decision-making task where, similar to the two-choice prediction task, subjects must choose an outcome based on variably-related probabilities (Murphy et al., 2001; Rubinsztein et al., 2001). In the Murphy et al. (2001) study, manic patients displayed an increased tendency to choose the less probable of two possible outcomes relative to depressed patients and controls. This impairment was correlated with symptom severity scores such that increased severity of manic symptoms was associated with poorer decisions. Furthermore, detailed analysis of the “bets” that subjects were instructed to place on the accuracy of their decisions revealed that poor decision-making in the manic patients was more associated with impulsivity and lack of inhibition rather than just risk-taking behavior.

Decision-making is complex and involves several component processes, which are defined by the characteristics of the available options or the patterns of action selected. Among these processes are trend detection, risk-taking, and error processing. The current version of the two-choice prediction task was devised to probe the effects of errors on decision-making, i.e. whether subjects change their behavior more sensitively when they are frequently “correct” versus “incorrect”. In its current version this task does not address risk-taking (Bechara, 2001), which is the potential future harm that may arise from some action, or impulsivity (Evenden, 1999), which entails a premature response due to overwhelming initiation to act.

The response strategies of BD manic psychotic patients on the prediction task are distinct from what has been shown in schizophrenia patients. The selection of responses generated by schizophrenia patients appears to be more influenced by the previous response outcome when compared to normals (Paulus et al., 2002). In contrast, in the current study there were no group differences between BD patients and comparison subjects in the effect of either the previous response (MI function) or the previous stimulus (CMI) on response patterns.

The neuroanatomical network implicated in decision-making includes the dorsal anterior cingulate and the orbitomedial frontal cortex (Rubinsztein et al., 2001). Bipolar manic patients appear to have increased activation in the anterior cingulate relative to controls during a decision-making task and decreased relative activation in the orbitomedial frontal cortex. Orbital prefrontal cortex dysfunction, e.g. decreased activity in this area during word-generation tasks, has previously been observed in bipolar patients in a euthymic state (Blumberg et al., 1999). Additionally, patients with lesions in orbital frontal regions demonstrate poor strategies on decision-making tasks (Rogers et al., 1999). This and other imaging studies (Elliot et al., 2000) have led researchers to suggest that the orbitofrontal cortex is activated when subjects are faced with a decision and must take into account the likelihood of success or failure of the outcome (Rubinsztein et al., 2001). Psychotic manic BD patients may have difficulty with this complex problem-solving task, which involves a number of cognitive subroutines and requires careful ongoing evaluation of the effectiveness of current behavior.

Several caveats should be considered in interpreting the current results. As this was a naturalistic study, medications were not controlled for, and BD patients with psychotic mania were on a variety of anti-psychotic and mood-stabilizing medications. Additionally, BD patients had significantly lower verbal intellectual functioning scores than NC subjects. Although we did not find significant correlations between behavioral response measures and daily dosages of divalproex or risperidone or WAIS-R Vocabulary scores, subject numbers were too small to fully ascertain the potential impact of these variables on our findings. Furthermore, all of these subjects were psychotic at the time of their assessment, therefore, these results may not be generalizable to BD manic patients without psychosis.

In conclusion, BD patients with psychotic mania demonstrate increased sensitivity to error rates in that they switch responses more frequently than non-patients when error rates are high. This finding is suggestive of a decision-making strategy in BD subjects that differs from that previously seen in schizophrenia patients and is consistent with the notion that, especially in environments where a successful outcome is uncertain and unlikely, acutely manic patients show increased switching in decision-making. Our results add to the growing body of literature that has used behavioral and imaging tasks to explore reward-reinforcement systems in BD.

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