Psychiatry Research 215 (2014) 95–100

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Reward sensitivity and anger in euthymic bipolar disorder

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ARTICLE INFO

Article history:
Received 17 February 2013
Received in revised form
19 October 2013
Accepted 22 October 2013
Available online 30 October 2013

Keywords:
Bipolar
Reinforcement sensitivity theory
BAS hypersensitivity model ultimatum game

ABSTRACT

According to the hypersensitive behavioral approach system (BAS) model of bipolar disorder (BP), hypersensitivity of the BAS is a trait that should be present even in the euthymic state. This would be expected to result in increased anger and reward sensitivity, both of which are related to the approach system. This study examined these predictions through the use of tasks that assess different aspects of the BAS: reward sensitivity, anger and impulsivity. These characteristics were assessed using the probabilistic classification task (PCT), ultimatum game (UG) and single key impulsivity paradigm (SKIP), respectively. Participants were euthymic adult bipolar disorder patients (BP; $N=40$) and healthy controls (HC; $N=41$). In the UG, all participants showed the standard pattern of rejecting overtly unfair offers and accepting clearly fair offers; however, BPs rejected more of the moderately unfair offers than did HCs. BP and HC participants did not differ on their ability to learn, but did show different patterns of learning from reward and punishment. Learning for reward and punishment were negatively correlated in the BP group, suggesting that individuals could learn well either from reward or punishment, but not both. No correlation was found between these forms of learning in the HC group. BP patients show signs of their disorder even in the euthymic state, as seen by the dysbalance between reward and punishment learning and their residual anger in the UG.

1. Introduction

One model of bipolar (BP) disorder (Depue et al., 1989), proposes that it involves a hypersensitive behavioral approach system (Depue and Iacono, 1989; Urosevic et al., 2008). This model is consistent with some studies which have used structural and functional neuroimaging of BP patients (Strakowski et al., 1999; Noga et al., 2001; Almeida et al., 2010). The current study examines three behavioral manifestations of the model—reward sensitivity, anger and impulsivity—in euthymic BP patients and matched controls.

Since 1989, when Depue suggested that BP patients suffer from a hyper-sensitive behavioral approach system, which he termed the behavioral facilitation system (Depue et al., 1989), there has been a considerable amount of research in this field. Depue proposed that several major systems in the brain direct and motivate behavioral responses to significant stimuli (Depue et al., 1989). Gray and others suggested the reinforcement sensitivity theory (RST) as a framework for investigating motivated behavior. According to RST (Gray and McNaughton, 2000) there are three behavioral systems which organize human behavior. The first is the behavioral approach system (BAS), which is responsible for organizing behavior directed towards appetitive stimuli, is sensitive to stimuli that signal reward and the relief from punishment and is responsible for initiation of motor responses, positive affect, reward motivation and anger (Harmon-Jones and Allen, 1998; Depue and Collins, 1999). The BAS has been correlated to the activation of mesolimbic and mesocortical dopamine pathways in the brain, including the source of the projections in the ventral tegmental area, and the terminal regions of these projections in the nucleus accumbens and the orbitofrontal cortex, anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex (DLPFC) (Depue and Iacono, 1989; Depue and Collins, 1999; Berns et al., 2001). The second system, the fight flight freeze system (FFFS) is responsible for organizing behavior in response to aversive stimuli; it copes with an explicit danger that can be avoided or escaped. The third system, the behavioral inhibition system (BIS) is dominant during goal conflict resolution, including conflicts between: approach and avoidance (fight or flight), approach-approach or avoidance-avoidance.

According to the BAS hypersensitivity model, individuals with BP disorder are subject to extreme fluctuations in activation and deactivation of this system. This will result in exaggerated approach to rewarding stimuli when activated, alternating with indifference to reward, when deactivated. This would lead to hypomanic/manic and depressive symptoms, respectively (Depue et al., 1989). High

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0165-1781/$ - see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.psychres.2013.10.028

BAS scores have been correlated with bipolar symptoms (Alloy et al., 2006, 2008), and euthymic BP patients have been shown to score higher than healthy controls (Alloy et al., 2008) on the Barrat Impulsivity Scale (Barrett et al., 1996).

Neuroimaging studies have provided circumstantial support for the BAS hypersensitivity model. Structural imaging studies found that the size of the amygdala of BP patients, which was correlated to emotional behavior and reward (Baylis and Gaffan, 1991; Aggleton, 1993), is significantly larger than that of healthy subjects (Strakowski et al., 1999). It has also been suggested that caudate enlargement may indicate a predisposition to bipolar disorder: Noga et al. (2001) found that both affected and unaffected monozygotic twins discordant for bipolar disorder had larger left caudate nuclei compared to the healthy participants (Noga et al., 2001), which may be related to altered reward sensitivity. Functional imaging studies indicate that adult (Almeida et al., 2010) and pediatric (Pavuluri et al., 2009) BP patients have higher activity levels in the amygdala and lower activity levels in several frontal cortical regions involved in emotional regulation, such as the ventro-lateral prefrontal cortex (VLPFC), dorso-lateral prefrontal cortex (DLPFC) and anterior cingulate cortex (ACC).

Self-report measures of trait anger and aggression have been positively associated with self-report measures of BAS (Harmon-Jones, 2003). BP patients, when manic, have been found to be more aggressive than other psychiatric patients (Látalová, 2009), although no studies reporting aggressive behavior in euthymic bipolar patients were found.

This study examines the BAS hypersensitivity model of BP disorder via the use of behavioral tasks. Reward sensitivity was assessed by a probabilistic learning task (Bodi et al., 2009). This task was chosen because of its ability to differentiate learning motivated by reward and punishment. One of the most known reward-related tasks that was tested on BP patients is the Iowa Gambling Task (IGT) (Bechara et al., 1994). Some authors did find that BP patients in different mood states (manic, depressed or euthymic) chose a non-profitable learning strategy (i.e.—chose more cards from the risky deck), while others found that only acute (manic, hypomanic or depressed) BP patients showed impaired decision making in the IGT (Yechiam et al., 2008; Adida et al., 2011). A recent meta-analyses was unable to detect consistent group differences between BP and healthy controls on the IGT (Edge et al., 2012), and the suggestion that euthymic BP patients are impulsive remains unresolved. Both the PCT and IGT assess learning involving reward and punishment which is at first implicit, but may involve a more explicit form of learning as the session progresses. However, the probabilistic classification task (PCT) allows one to distinguish between learning from reward or punishment, whereas in the IGT, the participant must weigh both elements in each choice. Therefore, the PCT was assessed in the present study.

We assessed the response to subjectively unfair offers using the Ultimatum Game (UG) as described in Koenigs and Tranel (2007). The UG was chosen in order to assess euthymic BP patient's responses to subjectively unfair offers (i.e., less than 30%), as presented in previous studies (Pillutla and Murnighan, 1996; Koenigs and Tranel, 2007; Crockett et al., 2008). Responses to these offers were associated with anger, aggressive behavior and low serotonin levels (Pillutla and Murnighan, 1996; Sanfey et al., 2003; Crockett et al., 2008; Mehta and Beer, 2010).

Impulsivity was assessed using the single key impulsiveness paradigm (SKIP) (Dougherty et al., 2003). BP patients were shown to be more impulsive in this task (Swann et al., 2009a).

We hypothesized that euthymic BP patients would be more sensitive to reward, and hence, would show a steeper learning curve than healthy controls in the rewarded - but not the punished PCT. We hypothesized that BP patients will reject more 'unfair' offers than healthy controls. Lastly, BP patients were expected to be more impulsive, resulting in a higher rate of response in the SKIP, despite the loss of points which this entails.

Table 1
Demographic data for bipolar and control participants.

Group	Gender	N	Age	Education	Raven
BP	Female	18	40.56 (± 10.38)	13.22 (± 2.24)	40.39 (± 12.48)
BP	Male	22	43.45 (± 13.07)	13.73 (± 2.21)	43.82 (± 6.59)
HC	Female	18	37.11 (± 11.41)	13.44 (± 1.98)	45.50 (± 9.41)
HC	Male	23	40.30 (± 11.02)	13.57 (± 2.15)	43.30 (± 10.21)

2. Methods

2.1. Participants

Forty-seven patients, ranging in age from 18 to 65, were recruited from the ambulatory out-patient Mood Disorder Clinic at the Beer-Sheva Mental Health Center (Osher et al., 2010). All were known to have Bipolar I disorder as diagnosed by DSM-IV criteria based on the chart review and clinical interview, and had been fully euthymic for at least 1 month before inclusion. The patient group was carefully chosen by both a psychiatrist and a psychologist with a comprehensive knowledge of patient history. Axis II diagnosed patients were also excluded from this study. The control group consisted of 42 age and education (± 3 years) matched healthy controls recruited from the community by local advertisement. Exclusion criteria for both groups included a known Axis I diagnosis (except bipolar disorder for the patients group), current substance use disorder, known history of brain injury, or serious medical condition. Patients were also excluded if they had received electroconvulsive therapy (ECT) in the past year. Healthy controls were excluded for family history of bipolar disorder, diagnosis of any major mental illness or if taking psychotropic medications. Table 1 presents mean age, education and Raven Progressive Matrices scores of participants.

2.2. Instruments

2.2.1. Probabilistic classification task (PCT)

This was a computerized decision-making task, which tests the ability to implicitly learn a categorization rule based on either reward or on punishment. The participant does not know in advance which stimuli are associated with reward or punishment. In this task, the participant is asked to classify four unfamiliar stimuli to either category A or B; two stimuli are correlated to category A 80% of the time and two are correlated to category B 80% of the time. Two stimuli are associated with the punishment task (i.e., the participant loses points when choosing incorrectly and loses nothing if he chooses correctly) and the other two are associated with the reward task (i.e., the participant gains points when choosing correctly and gains nothing if he chooses incorrectly). The task has four blocks. In every block, each stimulus is presented 10 times in random order. Thus, each block consists of 20 reward trials and 20 punishment trials in a mixed order. Because the order is mixed, in the initial trials receiving feedback of 0 points is ambiguous as it can indicate a wrong response in the reward task or a correct response in the punishment task. The optimal answer, defined as the answer that fits the 80% probability was recorded. Thus the participant may learn from both reward (by gaining points) and punishment conditions (by losing points). To increase motivation, participants were promised a small monetary reward for achieving a high score (10 NIS, approximately $2.50).

2.2.2. Ultimatum game (UG)

This is a social decision making task that has been used in various formats to assess inter-personal interactions in negotiation-like settings. The single offer version of the task used in the present study was intentionally designed to compare the participants' responses to unfair offers in order to provoke angry (negative approach) emotions. In this task the participant decides whether to accept or reject an offer of a small amount of cash (10 NIS, approximately $2.50) offered by a fictitious partner whose face and name are presented to the participant. In fact, the offers were programmed by the computer. If the participant accepts the offer, each player receives the amount specified. If the participant declines the offer, neither player receives anything. Some of the offers were fair (4 or 5 NIS to the participant, leaving 6 or 5 NIS to the partner), some were biased in favor of the participant (8 NIS), and most were biased in the favor of the fictitious partner, in varying degrees of unfairness (leaving only 1, 2 or 3 NIS to the participant; (Crockett et al., 2008)). Participants were told in advance that they will receive actual cash at the end of the task, in proportion to the amount accumulated by offers accepted. This is a slight variation of the Koeings et al. procedure (Koenigs and Tranel, 2007).