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Can Risk-Taking Be an Endophenotype for Bipolar Disorder? A Study on Patients with Bipolar Disorder Type I and Their First-Degree Relatives

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Abstract

Risk-taking behavior and impulsivity are core features of bipolar disorder. Whether they are part of the inherited aspect of the illness is not clear. We aimed to evaluate risk-taking behavior as a potential endophenotype for bipolar disorders, and its relationship with impulsivity and illness features. The Balloon Analogue Risk Task (BART) and Barratt Impulsiveness Scale-11 (BIS-11) were used to assess risk-taking behavior and impulsivity respectively in 30 euthymic bipolar I patients (BD), their 25 asymptomatic first-degree relatives (BD-R), and 30 healthy controls (HC). The primary BART outcome measure was the behavioral adjustment score (number of pumps after trials where the balloon did not pop minus the number of pumps after trials where the balloon popped). BD ($p < .001$) and BD-R ($p = .001$) had similar and significantly lower adjustment scores than HC. Only BD scored significantly higher on BIS-11 total ($p = .01$) and motor ($p = .04$) subscales than HC. Neither the BART, nor impulsivity scores associated with illness features. A limitation of this study is medicated patients and a heterogeneous BD-R were included. Riskiness may be a candidate endophenotype for bipolar disorder as it appears independently from illness features, presents similarly in BD and BD-R groups and differs from impulsivity.

Keywords

Bipolar disorder; Risk-taking; Impulsive behavior; Endophenotype; First-degree relative; The Balloon Analogue Risk Task

INTRODUCTION

Increased risk-taking behavior is one of the more recognized symptoms of bipolar disorder and is included in the diagnostic criteria for mania (APA, 2000). Risk-taking is defined as engaging in behaviors with a high potential for harm or danger and simultaneous opportunity for reward (Leigh, 1999). The operational definitions of impulsivity and risk-taking behavior are not straightforward. Although risk-taking propensity seems to have similar features with impulsivity and the two are oftentimes difficult to be delineated within a particular behavior, they are not synonymous constructs. Risk-taking behavior is assumed to be a selected strategic response (Floden, Alexander, Kubu, Katz, & Stuss, 2008). It is a situationally determined behavior (Kreek, Nielsen, Butelman, & LaForge, 2005), whereas impulsivity reflects reduced control over behavior and appears upon evoking (Floden et al., 2008). Whether risk-taking results from a deficit in impulse control is in dispute (Kreek et al., 2005). In general, impulsivity refers to a predisposition and an overall pattern of behavior (Kreek et al., 2005).

Brain imaging data can be considered to be in line with the notion that impulsivity and risk-taking are two separate constructs. The role of the frontal lobe in impulsive behavior is explained in detail in an extensive review by Evenden (1999). Findings from an animal model of attention deficit hyperactivity disorder (ADHD), where impulsivity is a core symptom involved brain regions such as the nucleus accumbens and amygdala. As these regions are linked to reward, reinforcement, and decision making the authors concluded that the involvement of such locations may be critical to the expression of impulsivity (King, Tenney, Rossi, Colamussi, & Burdick, 2003). On the other hand, several recent studies have demonstrated specific anatomical and functional locations contributing significantly to the risk behavior in the Balloon Analogue Risk Task (BART), a computer-based and valid measure of risk-taking propensity. These locations include dorso-lateral frontal (Lighthall et al., 2011; Rao, Korczykowski, Pluta, Hoang, & Detre, 2008; Rao et al., 2010), ventral and dorsal striatal (Jentsch, Woods, Groman, & Seu, 2010; Rao et al., 2008) brain regions. Data suggest an association between striatal function and risk-taking in the BART.

Increasing levels of impulsivity in bipolar disorders are present across all states of the illness (Peluso et al., 2007; Swann, Dougherty, Poazzaglia, Pham, & Moeller, 2004; Swann, Pazzaglia, Nicholls, Dougherty, & Moeller, 2003). Literature on the relationship between impulsivity and clinical aspects of the illness is contradictory. Impulsivity was shown to be independent of symptom severity and mood episodes (Holmes et al., 2009; Swann, Lijffit, Lane, Steinberg, & Moeller, 2009), therefore, supporting the proposition that it is a core trait of bipolar disorder (Najt et al., 2007). More recently, impulsivity, especially rapid-response, is stated to be more severe with a highly recurrent course of illness (Swann, 2010).

Research on risk-taking behavior in general and in bipolar disorder is minimal although it is often part of the clinical presentation of bipolar disorder. The BART has been applied to study risk-taking in clinical populations, including schizophrenia (Cheng, Tang, Li, Lau, & Lee, 2012), Parkinson's disease (Rao et al., 2010), and ADHD (Weafer, Milich, & Fillmore, 2011). In the ADHD study, although patients did not differ from controls in terms of risk-taking, there was a trend toward greater risk-taking on the BART and the quantity of alcohol consumption in the patient population (Weafer et al., 2011). On the contrary, patients with schizophrenia performed suboptimally on the BART which was related to a possible abnormal tendency to engage in safe actions rather than risky actions as determined by the Risky-Gains Task response rates (Cheng et al., 2012). In an attempt to conceptualize risk-taking propensity and impulsivity in bipolar disorder, Holmes et al. (2009) demonstrated a link between risk-taking and previous alcohol abuse in bipolar disorder, and showed that risk-taking propensity and impulsivity are separable constructs that tap distinct aspects of the bipolar phenotype.

Studies focusing on the neurobiology of impulsivity and risk-taking show that genetic variation may partially underlie these complex traits (Anokhin, Golosheykin, Grant, & Heath, 2009; Congdon & Canli, 2008). Coupled with the evidence that impulsivity and risk-taking are important features of bipolar disorder, a better understanding of the familial transmission of risk-taking and/or impulsivity has implications for identifying endophenotypes of the illness. To consider a feature as an endophenotype, it should be associated with the disease in that population, be heritable, and be independent from clinical state; additionally, the marker and the disorder should co-exist among family members (Gottesman & Gould, 2003). Endophenotypes can be useful in defining subtypes of the illness, and developing new approaches in treatment of bipolar disorder (Frantom, Allen, & Cross, 2008; Najt et al., 2007). Very few studies investigated impulsivity as an endophenotype of bipolar disorder (Chamberlain & Sahakian, 2007) and no study to date has focused on risk-taking behavior as an endophenotype of bipolar disorder.

The primary objective of this study was to assess risk-taking behavior in patients with bipolar disorder (BD) and their asymptomatic first-degree relatives (BD-R) in comparison to healthy control participants (HC) as a potential endophenotype. Our secondary objective was to investigate the relationship between risk-taking and impulsivity in the same population. Third, we aimed to investigate the relationship between clinical characteristics and risk-taking as well as impulsivity in the patient group. The Balloon Analogue Risk Task (BART) (Lejuez et al., 2002) and the Barratt Impulsiveness Scale-11 (BIS-11) (Patton; Stanford, & Barratt, 1995) were used for measuring risk-taking behavior and trait impulsivity, respectively. We hypothesized that individuals with bipolar disorder and their asymptomatic first-degree relatives would present a similar propensity for risk-taking behavior and that both groups would differ in risk-taking compared to the healthy controls. We anticipated an association between scores of riskiness on the BART and BIS-11 scores. We anticipated an association between a more severe course of illness and higher levels of risk-taking and impulsivity in the patient group.

METHODS

Participants

The study was carried out at the neurocognitive research laboratories of Department of Neuroscience and the bipolar disorders outpatient unit of Department of Psychiatry, Dokuz Eylul University. The study was approved by the Ethics Committee for Clinical Trials of Dokuz Eylul University Hospital which follows Helsinki criteria. Euthymic patients with a previously diagnosed bipolar type I disorder who were being followed at the bipolar outpatient unit were referred to the study by their physician. All living first-degree relatives (parents, siblings, children) of the enrolled patients were invited to participate in the study. Healthy volunteers were recruited through announcements at the university hospital and on the medical school campus. All participants provided written informed consent. Thirty consecutive euthymic patients with DSM-IV BD type-I who were found to be eligible were enrolled in the study. Due to either lack or unavailability of all first-degree relatives (parent, sibling, and children) in each individual patient any consented first-degree relative was included for the screening. Those who met the inclusion criteria were enrolled in the study. In this group there were 25 asymptomatic first-degree relatives three of whom (12%) were offspring, nine (36%) were parents, and 13 (52%) were siblings. Thirty sex-, age-, and educationally matched healthy controls with no personal or family history of psychiatric illness were included in the study.

All participants (patients, first-degree relatives, and healthy controls) were interviewed using the Structured Clinical Interview for the DSM-IV-TR Axis I Disorders (SCID-I) (First, Spitzer, Gibbon, & Williams, 1996). SCID interviews were completed by three experienced psychiatry residents who were formally trained for structured interviews and rating scales as a part of their psychiatry training. Information on demographics, clinical characteristics and treatment history of the patients was registered by using the standardized registration program for bipolar disorders-Turkey (SKIP-TURK) forms by the same clinicians (Özdem et al., 2004).

To be included in the study, patients needed to be euthymic for at least 6 months with no subclinical symptoms, score 7 or less on the validated and reliable Turkish version of the Young Mania Rating Scale (YMRS) (Karadag, Oral, Yalcin, & Erten, 2002), and score 7 or less on the validated and reliable Turkish version of the 21-item Hamilton Depression Rating Scale (HAM-D 21) (Aydemir & Deveci, 2003). Scales were given by the same clinician who ran the structured interviews. Patients with history of any comorbid Axis I disorder, neurodegenerative disease, mental retardation, epilepsy, cerebral tumor, cerebrovascular disease, or head trauma were excluded. The same exclusion criteria applied to the first-degree relatives and healthy controls.

Assessment Instruments

The Balloon Analogue Risk Task is a computer-based measure of risk-taking propensity. It is designed to examine risk-taking behavior in similar to real-world situations, where taking risk is rewarded until a certain point, after which more riskiness results in poorer outcomes (Lejuez et al., 2002). As there is no specific and established behavioral test that has been

used to measure risk-taking behavior in bipolar disorder, the BART was the most appropriate choice of selection for the present study, although balloon popping may not generalize to most risk-taking behaviors. It is of note that the task includes other cognitive features such as learning, planning, and cognitive flexibility.

BIS-11 is a widely used self rating test which is considered to be a good reference for studying impulsivity and related properties in psychiatric illnesses. It measures three theoretical subtraits of impulsivity: motor impulsiveness, non-planning impulsiveness, and attentional impulsiveness (Patton et al., 1995).

A single investigator introduced BIS-11 and administered the BART to all participants. The BART and BIS-11 were given during one session and in the same order to each participant to provide standardization of the procedure across all participants.

The Balloon Analogue Risk Task (BART)—The BART is presented on a computer screen which includes a small simulated balloon accompanied by a balloon pump button, a “collect” button for stopping and getting points earned until that time (temporary bank) and an indicator presenting permanent points (permanent bank). The balloon inflates and the participant earns one point with each pump, and the task includes 30 trials. In each trial, the participant can stop pumping at any point and click on the collect button for transferring all points from the temporary bank to permanent bank. If the balloon explodes, the participant loses all collected points. Information on the balloons’ breakpoints is not given to the participants to allow for testing both participants’ initial responses to the task and changes in responding as they gain experience with the task contingencies.

Construct validity of the BART was provided by Lejuez et al. (2002). Reliability of the test has been established across a range of samples and testing conditions. Split-third reliability examination (i.e., comparing scores across the first block, middle, and third blocks of 10 balloons each), revealed strong reliability (> 0.7) (White, Lejuez, & de Wit, 2008). Its performance was shown to be stable across several days, with test–retest reliability correlation coefficients approximating 0.77 (White et al., 2008).

The permission to use the BART was provided from Dr. Lejuez and his team before starting the project. To run the task in Turkish, translation and back translation of the participant instructions and button contents were completed independently by two experienced team members who were in good command of English and Turkish. The process was completed in collaboration with the Lejuez group. Before beginning the task, all participants were given full information on the procedure and told they would receive a symbolic reward proportional to the total points they earned at the completion of the task. No practice was allowed before beginning the task.

Lejuez et al. (2002) used the total number of times balloons were pumped on trials where the balloon did not pop, (adjusted pumps for successful trials) as a measure of risk-taking. This approach does not account for the number of pumps on trials where the balloon that exploded (e.g., unsuccessful trials), and thus may not adequately model those trials where individuals adopt a risky strategy. For this reason, our primary dependent measure was the

average number of pumps after successful trials minus the average number of pumps after unsuccessful trials. We believe that this within subject “adjustment score” indexes change in behavior after a popped trial and reflects a behavioral adjustment in risk-taking behavior (i.e., the smaller the difference is, the poorer the adjustment). To assess riskiness in a broader sense, we used the total number of exploded balloons as a secondary outcome measure.

Barratt Impulsiveness Scale-11 (BIS-11)—The BIS-11 is a 30-item self-report measure of impulsivity. The BIS-11 items are measured on a 4-point Likert scale (1 = Rarely/Never; 2 = Occasionally; 3 = Often; 4 = Almost Always/Always). Some items are scored inversely to avoid response bias. The BIS-11 total score indicates level of impulsiveness.

The BIS-11 includes three sub-scales: (1) Attentional Impulsiveness (eight items; racing thoughts, impatience to cognitive complexity, concentration, and attention problems), (2) Motor Impulsiveness (11 items; fast reactions or restlessness), (3) Non-planning Impulsiveness (11 items; lack of future orientation) (Patton et al., 1995).

Cronbach's alpha for internal consistency of the original BIS-11 scores are as follows: for total score: 0.83, for attentional subscale score 0.74, for motor subscale score 0.59, and for non-planning score 0.72. These second order factors have consistently been found (Stanford et al., 2009) with test–retest reliability figures of $r = 0.72$, 0.61 , and 0.67 , respectively (Stanford et al., 2009).

Permission for using the BIS-11 was obtained from the contact person (Marijn Lijffijt, PhD) of the test before beginning the project. Translation and back translation were completed independently by two experienced team members with good command of English and Turkish. The process was completed in collaboration with Dr. Marijn Lijffijt. For validation, BIS-11 Turkish version was administered to a sample of 105 volunteers. Cronbach's alpha for internal consistency was 0.83 which shows the reliability of the Turkish version. This is consistent with the previously reported and acceptable internal consistencies (Cronbach's alpha) for other translated versions of BIS-11 total score (0.71–0.83) (Stanford et al., 2009).

Data Analysis

Statistical analyses were conducted using Statistical Package for Social Sciences 15.0. Before analyses, all variables were shown to conform to normality (Shapiro-Wilk test $p > .05$ for all variables). The adjustment score (average number of pumps after successful trials - average number of pumps after unsuccessful trials), the total number of exploded balloons on the BART (total, motor, non-planning, and attentional) were examined with a linear mixed model with group as a between-subjects factor and random family effects taken into account. Bonferroni test was used for all *post hoc* analyses.

To examine the relationship between impulsivity and riskiness in general, Pearson correlations were run between BIS-11 scores and the number of exploded balloons on the BART first for the entire sample ($n = 85$), and then individually for each group (BD, BD-R, and HC). Before running the correlation analysis, we performed a linear mixed model

analysis as explained above for BIS-11 scores to see whether the three groups differed in terms of impulsivity.

The difference in age and years of education between the three groups was assessed using one-way analysis of variance. Chi-square test was used to compare groups for sex. Regression analysis was used to examine the relationship between clinical characteristics of the patient group (duration of illness, number of months in euthymia, total number of past episodes, and number of hospitalizations) and the BART adjustment score, total number of exploded balloons on the BART as well as BIS-11 total score. In all tests, two-tailed p values $< .05$ were accepted as significant. Results in the manuscript are given as mean $\pm$ standard deviation (SD).

RESULTS

Demographic and Clinical Characteristics

Groups did not differ in terms of age, sex, or years of education (Table 1). In the patient group, the number of past episodes was 5.30 ± 3.84 (range, 1–21), duration of illness in years was 9.67 ± 7.76 (range, 1–41 years), euthymia duration (in months) was 23.62 ± 17.59 (range, 7–72 months), number of hospitalizations was 1.53 ± 2.06 (range, 0–11), and age of onset of illness was 25.77 ± 10.14 years (range, 13–57 years). Only one patient (3.3%) was medication free, nine (30.0%) were on monotherapy with either lithium ($n = 4$) or valproate ($n = 5$). Thirteen patients (43.3%) were on combination treatment with a mood stabilizer plus atypical antipsychotic. The remaining sample ($n = 7$; 16.3%) was on combination treatment with various medications. SCID-I interview of the BD-Rs and HCs confirmed that none of the participants in these groups had any Axis I diagnosis.

Risk-Taking Behavior (BART) Results

Linear mixed model analysis revealed significant group difference on the adjustment score ($F_{2,82} = 12.26$; $p < .001$). Post hoc Bonferroni analysis revealed that both patients (1.72 ± 1.70) and relatives (2.06 ± 2.34) had significantly lower adjustment scores than controls (4.31 ± 2.45) (patients vs. controls $p < .001$; relatives vs. controls $p = .001$). However, patients and relatives had similar adjustment scores ($p > .05$) (Table 2 and Fig. 1). Two sided power analysis for the difference between patients and healthy controls with an α (type I error) value of 0.05 revealed a power of 1.0. The effect size (Cohen's d : 1.22) for the provided difference was large by the criteria of Cohen (1977). The power of the difference between relatives and healthy controls was 0.91 with a corresponding large effect size (Cohen's d : 0.93) by the Cohen criteria.

Groups did not differ significantly in the total number of exploded balloons ($F_{2,82} = 0.14$; $p = .86$) (Table 2).

Impulsivity (BIS-11) Results

In the linear mixed model analysis groups differed significantly on the BIS-11 total ($F_{2,82} = 4.51$; $p = .01$) and motor impulsivity subscale scores ($F_{2,82} = 3.30$; $p = .04$). *Post hoc* analysis showed that patients had significantly higher BIS-11 total (59.90 ± 9.93) and motor

impulsivity scores (19.70 ± 4.26) compared to controls (52.90 ± 7.25 , and 17.30 ± 3.70 , respectively) ($p = .01$, power 0.88 and $p = .04$, power 0.65, respectively). Effect size of the difference between patients and controls for the BIS-11 total score (Cohen's d : 0.81) was large and for the motor impulsivity scores was medium (Cohen's d : 0.60) by the criteria of Cohen (1977). BD-Rs did not significantly differ from either BDs or HCs on BIS-11 total (57.40 ± 10.10) or motor impulsivity (18.24 ± 2.63) scores. Neither the non-planning ($F_{2,82} = 2.74$; $p = .07$), nor the attentional subscale scores ($F_{2,82} = 2.54$; $p = .09$) showed significant difference among the three groups (Table 3).

In the whole group ($n = 85$) the number of exploded balloons was significantly correlated with the BIS-11 total ($r = 0.37$; $p < .001$), attentional ($r = 0.28$; $p = .01$), motor ($r = 0.25$; $p = .02$), and non-planning ($r = 0.31$; $p = .004$) subscale scores. There was no correlation between adjustment scores and either the total BIS-11 scores or BIS-11 subscores in the entire group ($n = 85$) (Table 4). Only the control group ($n = 30$) showed a statistically significant medium correlation between adjustment and BIS-11 total ($r = 0.397$; $p = .030$) and BIS-11 motor impulsivity scores ($r = 0.436$; $p = .016$).

Relationship Between Clinical Features and Risk-taking and Impulsivity

Linear regression analysis showed that the BART adjustment score ($R = 0.317$), total number of exploded balloons on the BART ($R = 0.405$) and BIS-11 total score ($R = 0.113$) did not have any significant relationship with either duration of illness (p values for the BART adjustment score, total number of exploded balloons on the BART and BIS-11 total scores are 0.57, 0.07, 0.96, respectively) or duration of euthymia (p values for BART adjustment score, total number of exploded balloons on the BART and BIS-11 total scores are; 0.36, 0.77, 0.76, respectively), or total number of past episodes (p values for BART adjustment score, total number of exploded balloons on the BART and BIS-11 total scores are; 0.26, 0.31, 0.72, respectively) or number of hospitalizations (p values for BART adjustment score, total number of exploded balloons on the BART and BIS-11 total scores are; 0.77, 0.32, 0.71, respectively).

DISCUSSION

The primary finding of this study is that euthymic individuals with bipolar disorder and their asymptomatic first-degree relatives showed similar adjustment propensity in an experimentally probed risky condition. These two groups adjusted significantly less compared to healthy controls after the loss of a temporary gain on the BART. All participants reported reduced pumping after facing loss on the BART. However, the magnitude of this adjustment was similar in the patients and their relatives and it was significantly smaller compared to that of healthy controls. This magnitude difference in the behavioral change is what delineated healthy controls from patients as well as from their first-degree relatives. This may suggest a particular deficiency in learning behavior on a risk-taking construct by both patients and their first-degree relatives, suggesting that liability for bipolar disorder may be linked to a reduced ability to modulate risky activity in the face of negative consequences.

Early studies on risk-taking behavior by using or using the BART generally targeted populations with either nicotine (Lejuez et al., 2003; Lejuez, Aklín, Bornovalova, & Moolchan, 2005) or alcohol use (Skeel, Pilarski, Pytlak, & Neudecker, 2008) problems. To our knowledge, there is only one published study (Holmes et al., 2009) investigating risk-taking behavior with the BART in patients with BD in which a group of patients with prior history of alcohol abuse or dependence was compared to another group of bipolar patients without such a history. Our study is the first and only study where risk-taking behavior is investigated in a group of medicated patients who were otherwise homogeneous with regard to the illness subtype and state (all bipolar disorder type I, euthymic) and absence of present or past alcohol related problems. In the study by Holmes et al. (2009), only the group with past alcohol abuse/dependence showed impaired BART performance. These patients popped significantly more balloons than the bipolar patients with no prior alcohol related problems and failed to adjust their performance after popping balloons. Our euthymic patients who had no prior history of alcohol related problems did not differ from healthy controls in the number of exploded balloons which is similar to the non-alcohol group of the previous study. However, our patients still displayed significantly less adjustment on the BART than healthy controls, which contrasts with the finding of Holmes et al. (2009). This discrepancy may reflect differences in outcome measures (e.g., pumps after unsuccessful-pumps after successful trials) that had been used in these two studies. With our new outcome measure, we have been able to assess the behavioral change probed by a changing riskiness condition (pumps after unpopped trials vs. pumps after popped trials) instead of assessing a single measure (pumps only on successful trials). However, this new parameter seems to be more related to learning from past experience, presenting a new feature that has not much to do with risk-taking *per se*. It is also of note that we studied a homogeneous group of patients (all bipolar I and euthymic) in contrast to the study by Holmes et al. (2009), where both bipolar I and II patients in different states of the illness were included in assessments.

The significantly elevated BIS-11 total and motor subscale scores in BDs compared to HCs is consistent with previous studies (Swann, Anderson, Dougherty, and Moeller, 2001; Swann et al., 2003). However, there was no significant difference between relatives and either controls or patients on the BIS-11, despite the finding that they showed significantly lower adjustment than healthy controls (and similar adjustments to patients) on the BART. The fact that there was no significant difference between relatives and controls on the BIS-11 is important. Our finding suggests that diminished ability to adjust distinguishes relatives from healthy controls in contrast to self-reported impulsivity. A measure such as the BART may be able to pick up on an important endophenotype that would be missed by BIS-11, or, these two measures may be sensitive to two fundamentally different types of impulsivity.

In a previous study Jollant et al. (2007) found no correlation between impulsivity and decision-making performance in asymptomatic patients with bipolar disorder. In this study decision-making performance was tested using Iowa Gambling Task which relates to risk-taking in decision making and capitalizes on the learning of reward and punishment associations (Jollant et al., 2007). Christodoulou, Lewis, Ploubidis, and Frangou (2006) suggested that self-reported impulsivity as measured by BIS-11 may reflect rather specific

aspects of impulse control and decision-making but not necessarily of sustained attention in remitted patients with bipolar I disorder. Abovementioned findings and related arguments are indicative of a fact that a multi-faceted construct such as risk-taking warrants assessment using a multi-method, multi-informant approach.

There was a modest but significant correlation between the number of exploded balloons and the BIS-11 scores in the entire group ($n = 85$). However, no significant correlation between adjustment and BIS-11 scores was assessed in the same group. The dissociation between the number of popped balloons-BIS-11 score relationship *versus* adjustment score-BIS-11 score relationship may be generated by the difference between what the two BART measures actually represent. As the adjustment score used in this study intends to reveal more sophisticated parts of risk-taking behavior such as learning, and cognitive flexibility, correlation analysis may not accurately reflect its relation to the level of impulsivity as measured by BIS-11. Additionally, in a recent study where Ryan, Mackillop, and Carpenter (2013) investigated the relationship between impulsivity, risk-taking propensity and nicotine dependence among older adolescent smokers, greater risk-taking was found to be predictive of less nicotine dependence. The authors considered the finding as a further evidence that these neurobehavioral constructs are separable characteristics that may have unique contributions to smoking behavior. Our finding and the finding of the Ryan et al. study are in line with a recent meta-analysis where relationships among unidimensional impulsivity self-report and lab task conceptualizations indicated very little overlap in self-report and behavioral lab task constructs (Cyders & Coskunpinar, 2011). We found no relationship between clinical characteristics such as duration of illness, duration of euthymia, total number of past episodes, and number of hospitalizations, and either the total number of exploded balloons on the BART or the BIS-11 scores. These clinical features did not show any significant interaction with the adjustment behavior on the BART either. Previous studies comparing manic and euthymic patients found more commission errors during manic episodes (Bora, Vahip, & Akdeniz, 2006; Fleck, Shear, & Strakowski, 2005). Also high trait impulsivity was associated with a more severe course of illness and linked to a more severe suicide attempt history (Swann et al., 2005, 2009). On the other hand, other studies (Holmes et al., 2009; Swann et al., 2009) did not find a significant relationship between symptoms and impulsivity. However, unlike direct manic *versus* euthymic comparisons, these studies do not have sufficient variance of symptoms to show such an effect. The absence of a correlation between clinical features and impulsivity and adjustment scores in our study may be due to absence of patients in manic or depressive episodes. It is also worth noting that the state factors do not explain all impulsivity that is present in bipolar disorder, as there are also trait related aspects of impulsivity and risk-taking.

The main limitation of this study was that first-degree relatives group was heterogeneous and included parents, offspring and siblings. Having only the siblings would be ideal for studying any genetic predisposition. Despite this limitation, findings on the BART do reflect a familial risk-taking behavior pattern. As the impact of medication use on risk-taking and impulsivity is not established, having patients on various medications may be considered another limitation of the study. We suggest that working with drug free euthymic patients as well as medicated patients in large sample sizes would be beneficial to rule out the potential

effect of medication use on results. Similarly, assessment of specific effect of illness duration or length of euthymia would contribute to understanding how course of illness impacts risk-taking and/or impulsivity beyond the preexisting neurobiological infrastructure. Studies addressing these questions require larger patient populations to override the limitation of high variability in the course of illness as seen in the present study.

In conclusion, this is the first study showing evidence for decreased adjustment pattern in riskiness in a homogeneous group of euthymic bipolar I patients with no psychiatric or medical co-morbidities and in their asymptomatic family members in comparison to healthy controls. Our finding supports the idea that decreased adjustment pattern in riskiness may be a candidate endophenotype for bipolar disorder as it is present in the patient population (association to the given illness) in the asymptomatic first-degree relatives (co-existence among family members), and independent from clinical state (persists in the absence of symptoms) as defined by Gottesman and Gould (2003). Further studies on the underlying genetic make-up of risk-taking and related behavioral pattern in bipolar disorder will provide us with an answer for the question whether this trait is a true endophenotype.

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Fig. 1.

Adjustment patten in the three groups. Both BDs and BD-Rs show alike and less adjustment, therefore higher risk taking propensity compared to HCs. BD = patients with bipolar disorder; BD-R = first-degree relatives; HC = healthy controls.

Table 1

Demographic characteristics of the participants

Demographics	BD (<i>n</i> = 30)	BD-R (<i>n</i> = 25)	HC (<i>n</i> = 30)	Statistics
Sex				
Female <i>n</i> (%)	19 (63.3%)	17 (68.0%)	19 (63.3%)	$\chi^2 = 0.17$
Male <i>n</i> (%)	11 (36.7%)	8 (32.0%)	11 (36.7%)	$p = .92^a$
Age (years)				
Mean $\pm$ SD	35.50 $\pm$ 10.63	40.20 $\pm$ 13.41	35.73 $\pm$ 10.23	$F_{2,84} = 1.4$
Range	21–59	20–69	22–59	$p = .24^b$
Years of education				
Mean $\pm$ SD	12.50 $\pm$ 3.94	11.68 $\pm$ 3.44	12.63 $\pm$ 3.70	$F_{2,84} = 0.5$
				$p = .60^b$

BD = bipolar disorder; BD-R = bipolar disorder first-degree relatives; HC = healthy controls; SD = standard deviation.

^aChi-square test.^bOne-way analysis of variance.

Table 2

Balloon Analogue Risk Task (BART) scores of the participants

BART	BD (<i>n</i> = 30) Mean ± <i>SD</i>	BD-R (<i>n</i> = 25) Mean ± <i>SD</i>	HC (<i>n</i> = 30) Mean ± <i>SD</i>	Statistics	Effect size (Cohen's <i>d</i>)
Adjustment scores [*]	1.72 ± 1.70	2.06 ± 2.34	4.31 ± 2.45	$F_{2,82} = 12.26; p < .001^a$ <i>Post-hoc</i> analysis BD=BD-R; $p > .05^b$ BD < HC; $p < .001^b$ BD-R < HC; $p = .001^b$	1.22 0.93
Total no of exploded balloons	9.10 ± 4.05	8.52 ± 3.61	8.77 ± 4.13	$F_{2,82} = 0.14; P = .86^a$	

BD = bipolar disorder; BD-R5bipolar disorder first-degree relatives; HC = healthy controls; *SD* = standard deviation.^{*} Average number of pumping after successful trials - Average number of pumping after unsuccessful trials.^a Linear Mixed Model.^b Post-hoc Bonferroni test.

Table 3

Barratt Impulsiveness Scale (BIS-11) scores of the participants

BIS-11	BD (<i>n</i> = 30) Mean ± <i>SD</i>	BD-R (<i>n</i> = 25) Mean ± <i>SD</i>	HC (<i>n</i> = 30) Mean ± <i>SD</i>	Statistics	Effect size (Cohen's <i>d</i>)
Total	59.90 ± 9.93	57.40 ± 10.10	52.90 ± 7.25	$F_{2,82} = 4.51; p = .01^a$ <i>Post-hoc</i> analysis BD > HC; $p = .01^b$	0.81
Motor	19.70 ± 4.26	18.24 ± 2.63	17.30 ± 3.70	$F_{2,82} = 3.30; p = .04^a$ <i>Post-hoc</i> analysis BD > HC; $p = .04^b$	0.60
Non-planning	24.60 ± 5.05	24.60 ± 5.99	22.00 ± 3.54	$F_{2,82} = 2.74; p = .07^a$	
Attentional	15.60 ± 4.00	14.56 ± 3.55	13.60 ± 2.65	$F_{2,82} = 2.54; p = .09^a$	

Note. Statistical significance: *p* values < .05.

BD = bipolar disorder; BD-R = bipolar disorder first degree relatives; HC = healthy controls; SD = standard deviation.

^aLinear Mixed Model.

^b*Post-hoc* Bonferroni test.

Table 4Correlations between BART and BIS-11 scores in the entire group ($n = 85$)

BIS-11 score	BART Total no. of exploded balloons	BART Adjustment score
	$r(p)$	$r(p)$
Total	0.37 (<.001) *	0.91 (.40)
Attentional	0.28 (.01) *	0.48 (.66)
Motor	0.25 (.02) *	0.89 (.41)
Non-planning	0.31 (.004) *	0.73 (.50)

 r = Pearson correlation coefficient.

* Indicates statistical significance.