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Intolerance of Uncertainty Mediates Reduced Reward Anticipation in Major Depressive Disorder

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Abstract

Background—Reduced reward sensitivity has long been considered a fundamental deficit of major depressive disorder (MDD). One way this deficit has been measured is by an asymmetry in electroencephalogram (EEG) activity between left and right frontal brain regions. MDD has been associated with a reduced frontal EEG asymmetry (i.e., decreased left relative to right) while anticipating reward. However, the mechanism (or mediator) of this association is unclear. The present study examined whether intolerance of uncertainty (IU) mediated the association between depression and reduced reward anticipation.

Methods—Data were obtained from a prior study reporting reduced frontal EEG asymmetry while anticipating reward in early-onset MDD. Participants included 156 individuals with early-onset MDD-only, panic disorder-only, both (comorbid), or controls. Frontal EEG asymmetry was recorded during an uncertain reward anticipation task. Participants completed a self-report measure of IU.

Results—All three psychopathology groups reported greater IU relative to controls. Across all participants, greater IU was associated with a reduced frontal EEG asymmetry. Furthermore, IU mediated the relationship between MDD and frontal EEG asymmetry and results remained significant after controlling for neuroticism, suggesting effects were not due to broad negative affectivity.

Limitations—MDD participants were limited to those with early-onset depression. Measures were collected cross-sectionally, precluding causal relationships.

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Conflict of Interest

The authors have no conflicts of interest to report.

Contributors

S.A.S. obtained funding for the present study. B.D.N. contributed to data collection and analysis. B.D.N., S.A.S., and G.H.P. contributed to manuscript preparation and subsequent revisions.

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Conclusions—IU mediated the relationship between MDD and reduced reward anticipation, independent of neuroticism. Explanations are provided regarding how IU may contribute to reduced reward anticipation in depression. Overall, IU appears to be an important mechanism for the association between depression and reduced reward anticipation.

Keywords

depression; intolerance of uncertainty; reward; anticipation; electroencephalography

Introduction

Reduced reward sensitivity has long been considered a fundamental deficit of major depressive disorder (MDD; Klein, 1987; Meehl, 1975) and numerous studies have reported this association using multiple methodologies (Foti and Hajcak, 2009; Henriques et al., 1994, 2000; Pizzagalli et al., 2009). In addition, research suggests that this deficit may be driven by reductions in reward anticipation (Sherdell et al., 2012). One way reward anticipation has been examined is by measuring the asymmetry in electroencephalogram (EEG) activity between left and right frontal brain regions (i.e., reduced left relative to right; Davidson et al., 2002). In separate investigations, Shankman and colleagues (2007, 2013) examined frontal EEG asymmetry in individuals with early-onset MDD, a subtype particularly characterized by deficits in reward anticipation (Klein et al., 2009), and non-MDD participants while they played a slot machine game designed to assess reward anticipation. In both studies early-onset MDD participants exhibited a reduced frontal EEG asymmetry while anticipating reward relative to non-MDD participants (and in Shankman et al. [2007], relative to those with late-onset MDD as well). Furthermore, Nelson and colleagues (2013) found that reduced frontal EEG asymmetry while anticipating reward was also associated with family history of depression (i.e., a risk factor) independent of participants' current depression, suggesting that it may be a potential biomarker for depression.

The specific mechanisms that contribute to reduced reward anticipation in depression are unclear. Intolerance of uncertainty (IU) is a personality construct that may mediate this association given that pending rewards are (in most experimental paradigms and real-world contexts) uncertain. IU is a cognitive bias that influences perceptions, interpretations, and responses to uncertain situations on a cognitive, behavioral, and emotional level (Dugas et al., 2004). Individuals with high IU find ambiguous situations stressful and function poorly under these circumstances. IU was originally conceptualized as a causal risk factor for the development and maintenance of several anxiety disorders (Dugas et al., 1998; Tolin et al., 2003), but more recently IU has also been related to depression (Carleton et al., 2012). These results have led some to suggest that IU may be a transdiagnostic construct underlying depression and anxiety (Boswell et al., 2013; Mahoney and McEvoy, 2012).

IU has most often been examined in relation to biased processing of uncertain threat. For example, during periods of uncertain/ambiguous threat, IU has been shown to relate to threat perception (Bredemeier and Berenbaum, 2008; de Bruin et al., 2006), insula activation (Simmons et al., 2008), and startle responding (Nelson and Shankman, 2011). However, one

recent investigation suggests that IU may also play a role in the processing of uncertain reward. Luhmann and colleagues (2011) found that IU was associated with poorer decision making during a delayed probabilistic reward task. High IU individuals may therefore find *all* uncertain situations (both aversive and appetitive) unpleasant and stressful, and it is possible that IU may be a mechanism contributing to the association between depression and reduced reward anticipation.

The present study tested the hypothesis that IU would mediate the association between depression and reduced reward anticipation. Data were obtained from a prior study which showed that individuals with early-onset MDD exhibit a reduced frontal EEG asymmetry while anticipating reward (Shankman et al., 2013). The present study involved an independent set of analyses aimed at examining a potential mechanism of the association between depression and reduced reward anticipation. To determine the specificity of IU as a mediator, the present study also examined whether the effects of IU were maintained when neuroticism, a broader construct shown to have significant overlap with IU (Norton and Mehta, 2007), was included as a covariate.

The present study had three primary hypotheses. First, consistent with recent investigations (Carleton et al., 2012), we hypothesized that MDD participants would report greater IU relative to controls. Second, consistent with high IU individuals finding all uncertain situations unpleasant, we hypothesized that greater IU would be associated with a reduced frontal EEG asymmetry while anticipating reward. Finally, we hypothesized that IU would mediate the relationship between MDD and reduced frontal EEG asymmetry while anticipating reward, independent of neuroticism.

Methods

Participants

The sample was taken from Shankman et al. (2013) and consisted of 191 individuals with current MDD and no lifetime diagnosis of any anxiety disorder (i.e., MDD-only; $n = 40$), current panic disorder (PD) and no lifetime diagnosis of any depressive disorder (i.e., PD-only; $n = 28$), current MDD and PD (i.e., comorbid; $n = 58$) and controls without a history of Axis I psychopathology ($n = 65$). From those 191 participants, 156 completed a self-report measure of IU (discussed below), leaving a sample of 30 MDD-only, 22 PD-only, 50 comorbid, and 54 control participants. Depression and anxiety diagnosis was examined as two 2-level factors, Depression Status (Present vs. Absent) and Panic Status (Present vs. Absent), instead of one 4-level factor in order to examine main effects and interactions of MDD and PD diagnoses.

Participants were excluded from the study if they had a lifetime diagnosis of psychosis, bipolar disorder, or dementia; were unable to read or write English; had a history of head trauma with loss of consciousness; or were left-handed (as confirmed by the Edinburgh Inventory; range of laterality quotient: +20 to +100; Oldfield, 1971). Participants were recruited through clinics in the greater Chicago area and advertising in the community. The study was approved by the Institutional Review Board of the University of Illinois – Chicago and all participants provided written informed consent.

Diagnosis and Symptom Measures

All diagnoses were made via the Structured Clinical Interview for *DSM-IV-TR* (SCID; First et al., 2002). Depression severity was determined via the 24-item Hamilton Depression Scale (HAM-D; Hamilton, 1960). Anxiety severity was determined via the Beck Anxiety Inventory (BAI; Beck et al., 1988). Both depressed groups were required to have an age of onset of first affective disorder (dysthymia or MDD) before age 18,¹ because Shankman et al. (2007) found that only early (i.e., child or adolescent) and not adult onset depression was associated with a reduced frontal EEG asymmetry while anticipating reward. This inclusion criterion reduced the heterogeneity in the MDD groups (Klein, 2008). Participants in the PD-only and comorbid groups were allowed to meet criteria for additional current and past anxiety disorders. Additional current anxiety disorders included social anxiety disorder ($n = 13$), obsessive-compulsive disorder ($n = 6$), specific phobia ($n = 11$), and posttraumatic stress disorder ($n = 8$). Control participants were required to have no lifetime history of Axis I psychopathology, with the exception of a past diagnosis of alcohol or cannabis abuse (but not dependence, $n = 2$). Control participants were also required to have HAM-D and BAI scores less than 8.

Intolerance of Uncertainty Scale—Participants completed the Intolerance of Uncertainty Scale (IUS; Freeston et al., 1994), a 27-item self-report questionnaire assessing the trait-like belief that uncertainty is unacceptable, reflects poorly on them, and leads to frustration, stress, and the inability to take action. Respondents rate each item on a five-point Likert scale ranging from 1 = ‘not at all characteristic of me’ to 5 = ‘entirely characteristic of me’, with higher scores representing greater IU. Several studies have reported that the original 27-item IUS contains some items that are worry or generalized anxiety disorder specific (Gentes & Ruscio, 2011) or redundant (Khawaja & McMahon, 2011). Carleton et al. (2007) conducted a factor analyses on the 27-item IUS and found a more parsimonious 12-item version that was highly correlated with the 27-item version, but had better psychometric properties. In addition, a confirmatory factor analysis of the 12-item version revealed two sub-factors: a 7-item Prospective IU factor assessing concerns/anxiety about future events and a 5-item Inhibitory IU factor assessing the degree to which uncertainty inhibits action or experience (see also McEvoy and Mahoney, 2011; Thibodeau et al., 2013). The present study utilized the 12-item Total IU scale and also separately examined the Prospective and Inhibitory IU subscales. Cronbach’s alpha for the Total, Prospective, and Inhibitory IU subscales was .90, .88, and .81, respectively.

Eysenck Personality Questionnaire—Participants also completed the Eysenck Personality Questionnaire (EPQ; Eysenck et al., 1985), a 100-item measure of neuroticism, extraversion, and psychoticism. Each item is answered with a dichotomous ‘Yes’ vs. ‘No’ response. The present study focused on the neuroticism scale, which assesses the tendency

¹MDD only and comorbid participants were required to meet criteria for current MDD, but were allowed to have a past history of MDD or dysthymia. Participants first affective disorder could have been MDD or dysthymia; therefore, in order to compare the MDD only and comorbid groups on when they first began to experience a mood disorder, we took the age of the earliest affective disorder (either MDD or dysthymia) rather than just the age of their first major depressive episode as this latter approach would ignore dysthymia.

to react to stress. Cronbach's alpha for the neuroticism scale was .93. One control participant did not complete the EPQ and was excluded from analyses.

Procedure

Participants were seated in an electrically shielded, sound-attenuated booth approximately 3.5-feet from a 19-inch computer monitor. See Shankman et al. (2013) for the slot task main effects and diagnostic group differences in frontal EEG asymmetry. The present study conducted analyses that were independent of those reported in Shankman et al.

Slot EEG Task and Physiological Recordings—A computerized slot machine paradigm previously used by Shankman et al. (2007) was used to assess reward anticipation. The task consisted of three reels of numbers and fruit, which spun simultaneously for 11-s and then landed on a result for 11-s. The task was designed to provide both 'anticipatory' (reels spinning) and 'consummatory' (viewing result) phases of reward processing. To start the reels spinning, participants pressed a button with both thumbs that pulled a lever on the computer screen. The task included 60 spins that were divided into two possible outcomes of 30 trials each – a reward condition in which participants won money if the reels landed on three fruits and a no incentive condition in which participants were ineligible to win money regardless of the outcome. The reward condition was designed to elicit reward anticipation while the no incentive condition served as a control for several aspects of the reward condition (e.g., visual input, anticipating an outcome). The amount of money that could be won during each reward trial ranged from \$0.50–\$3.00.

Trials were presented in a pseudo-random order and there were never more than two consecutive trials of similar type or outcome. Participants began the game with \$2.00 and were told the specific condition (reward or no incentive) prior to each trial, but not the potential dollar amount in each reward condition. Importantly, participants did not know whether the reels would land on three fruits (a 'win') or would not land on three fruits (a 'non-win'), and the outcome of each trial ('win' vs. 'non-win') was uncertain. Unbeknownst to the participant, half of the trials in each condition landed on three fruits. Trials were divided into three blocks and participants were given their winnings (\$12.00) in cash at the end of the task.

EEG data were recorded from Ag/AgCl electrodes in a 64-channel stretch-lycra electrode cap. The ground electrode was at the frontal pole (AFZ) and the online reference was between CZ and CPZ. VEOG and HEOG electrodes monitored vertical and horizontal eye movements, respectively. Electrode impedances were under 5,000 ohms, and homologous sites (e.g., F3/F4) were within 1,500 ohms of each other. Data were recorded through a Neuroscan Synamp2 data acquisition system at a gain of 10K (5K for eye channels) with a bandpass of DC-200 Hz. Data were acquired at an A/D rate of 1,000 Hz. EEG data were re-referenced offline to the average data from left and right mastoids.

Physiological Data Processing—Details regarding physiological data processing are provided in Shankman et al. (2013). Briefly, EEG data while the reels were spinning (i.e., the 11-s 'anticipatory' phase) was segmented into consecutive 1.024-s epochs every 0.512 s (50% overlap). Power spectra were computed offline from EEG data by using a fast Fourier

transform. The average absolute alpha power was computed for each electrode site and then natural log transformed in order to normalize the data. For consistency with previous research (Bruder et al., 2005), the alpha band was defined as 7.81–12.70 Hz and used as an inverse measure of regional brain activity. Asymmetry scores were computed for the reward and no incentive conditions by subtracting power at left electrodes from power at homologous right electrodes (e.g., F8–F7), so that higher values reflected greater activity in left relative to right regions. Frontal EEG asymmetries between homologous electrode pairs (F3/4, F5/6, F7/8) were averaged together to create a composite frontal EEG asymmetry score. The composite EEG asymmetry scores were calculated because Shankman et al. (2013) found similar diagnostic group differences for all three recording sites. One PD-only participant was excluded due to excessive artifacts in electrodes of interest.

Data Analysis

Diagnostic group differences in symptom measures were examined using a two-way Depression Status (Present vs. Absent) X Panic Status (Present vs. Absent) between-subjects analysis of variance (ANOVA). Frontal EEG asymmetry during the no incentive control condition was not associated with individual differences in IU or neuroticism ($ps > .10$). Therefore, similar to previous investigations (Nelson et al., 2013; Shankman et al., 2013) response during the no incentive condition was subtracted from response during the reward condition (i.e., reward - no incentive) to control for the presentation of a stimulus. Standard regression and multiple regressions were conducted to examine the association between IU, neuroticism, and frontal EEG asymmetry. Psychiatric medication use (currently taking medication vs. not currently taking medication) was included as a covariate in all analyses.

To conduct mediational analyses we followed MacKinnon, Lockwood, and Williams's (2004) recommendations and used a nonparametric bootstrapping method. This approach has been shown to be statistically more powerful than other tests of mediation (MacKinnon et al., 2002). Specifically, we tested the proposed mediational model using the SPSS macro INDIRECT provided by Preacher and Hayes (2004), which provides a bootstrap estimate of the indirect effect between the independent variable and dependent variable, an estimated standard error, and 95% confidence intervals (CI) for the population value of the indirect effect. Confidence intervals for the indirect effect that do not include zero indicate a significant indirect effect at the $p < .05$ significance level. Analyses were conducted using 5,000 bootstrap samples. Prior to conducting mediational analyses, all variables were z-scored to produce standardized β weights.

Results

Diagnostic Group Differences

Table 1 displays demographics, clinical characteristics, and symptom measures across the different diagnostic groups. MDD-only, PD-only, and comorbid participants had greater Total IU, Prospective IU, and Inhibitory IU relative to controls. Comorbid participants had greater Inhibitory IU relative to PD-only participants. For neuroticism, comorbid and MDD-only participants had greater neuroticism relative to PD-only and control participants, and PD-only participants had greater neuroticism relative to control participants.

IU and Frontal EEG Asymmetry

As hypothesized, across all participants IU was inversely associated with frontal EEG asymmetry, $\beta = -.20$, $t(153) = -2.47$, $p < .05$, $d = -.40$. In other words, greater IU was associated with decreased anticipation to reward. Mediation analyses were conducted with Depression Status as the predictor, IU as the mediator, and frontal EEG asymmetry as the outcome (see Figure 1). Results indicated the mediation model was predictive of significant variance in frontal EEG asymmetry, $R^2 = .06$, $F = 4.85$, $p < .01$, $d = .36$. Depression Status was predictive of IU, $t(153) = 4.86$, $p < .001$, $d = .79$, and, in turn, IU was predictive of frontal EEG asymmetry, $t(153) = -2.42$, $p < .01$, $d = -.39$. Most importantly, analyses indicated that there was a significant indirect effect of Depression Status, mediated through IU, on frontal EEG asymmetry (95% CI: $-.16$ to $-.02$). Even though the hypothesized model had IU as the mediator and frontal EEG asymmetry as the outcome, when these two variables were switched (frontal EEG asymmetry as the mediator; IU as the outcome), the results indicated no indirect effect of Depression Status, mediated through frontal EEG asymmetry, on IU (95% CI: $-.09$ to $.04$).

Separate mediation models were conducted for the Prospective and Inhibitory IU subscales. Results indicated that Prospective IU (95% CI: $-.16$ to $-.02$) but not Inhibitory IU (95% CI: $-.12$ to $.04$) mediated the relationship between Depression Status and frontal EEG asymmetry. Lastly, when neuroticism was included as a covariate, Prospective IU continued to mediate the relationship between Depression Status and frontal EEG asymmetry (95% CI: $.01$ to $.13$).²

Discussion

The present study examined the association between depression, IU, and reward anticipation (measured via frontal EEG asymmetry). Results indicated that MDD was associated with greater IU relative to controls. Across all participants, IU was inversely associated with frontal EEG asymmetry while anticipating reward. Subscale analyses indicated that Prospective (and not Inhibitory) IU mediated the relationship between MDD and frontal EEG asymmetry while anticipating reward and this relationship remained significant after controlling for neuroticism. The present study suggests that IU may be an important mechanism that contributes to reduced reward anticipation in depression.

There are several potential explanations for how IU contributes to reduced reward anticipation in depression. At first glance it may be surprising that IU mediated the effect on reduced reward anticipation given that reduced reward processing reflects a deficit in a 'positively valenced' system and IU has typically been associated with 'negative valenced' responding (Bredemeier and Berenbaum, 2008; de Bruin et al., 2006; Nelson and Shankman, 2011; Simmons et al., 2008). However, IU has been posited to assess concerns about uncertain future events more broadly (McEvoy and Mahoney, 2011; Thibodeau et al., 2013). High IU individuals may therefore find *all* uncertain situations (both aversive and appetitive) intolerable and stressful. This explanation is consistent with research that has

²When analyses were conducted excluding PD-only participants, Prospective IU still mediated the relationship between Depression Status and frontal EEG asymmetry while controlling for neuroticism (95% confidence interval [CI]: $.01$ to $.03$).

demonstrated that acute stress reduces reward sensitivity (Berghorst et al., 2013; Bogdan and Pizzagalli, 2006). In the present study, while anticipating the outcome of the spinning slot machine reels, high IU participants may have found anticipating an uncertain rewarding outcome to be an unpleasant and aversive experience, which in turn elicited stress and contributed to decreased approach motivation.

High IU participants may have also engaged in maladaptive thinking patterns while anticipating reward. IU-depression and IU-anxiety associations has been shown to be mediated by different forms of repetitive thought, specifically worry and rumination, respectively (Yook et al., 2010). High IU participants may have engaged in rumination while anticipating a potential positive outcome (e.g., “I didn’t win last time, there is no way I’m going to win this time”). Alternatively, high IU participants may have engaged in excessive worry while anticipating reward. There is no consensus regarding the cognitive processes that are measured with frontal EEG asymmetry. However, worry (Hofmann et al., 2005) and rumination (Keune et al., 2011) have been found to be positively and negatively, respectively, associated with frontal EEG asymmetry. The present study found that IU was *negatively* associated with frontal EEG asymmetry while anticipating reward, which is more consistent with the previous finding for rumination (and not worry). Future research is needed to better understand the cognitive processes that underlie IU and frontal EEG asymmetry in depression.

Subscale analyses indicated that Prospective (but not Inhibitory) IU mediated the association between depression and reduced reward anticipation. These results are not particularly surprising, given that Prospective IU has been posited to index ‘cognitive’ concerns about future events, while Inhibitory IU represents ‘behavioral’ inhibition and/or avoidance (Carleton et al., 2007; McEvoy and Mahoney, 2011; Thibodeau et al., 2013). In the present study, participants completed a passive-viewing slot machine paradigm that required no behavioral response during the anticipatory phase. Even if high Inhibitory IU individuals found the uncertainty of the anticipatory phase unpleasant, there were few (if any) ways to inhibit ongoing behavior. Conversely, as previously discussed, high Prospective IU individuals may have engaged in maladaptive thinking patterns (e.g., rumination) that subsequently reduced reward anticipation.

The present study has implications for the conceptualization and treatment of not only depression, but perhaps internalizing disorders more broadly. Participants with MDD and/or PD reported greater IU relative to controls, and this is consistent with recent evidence supporting IU as a transdiagnostic construct underlying anxiety and depression (Boswell et al., 2013; Mahoney and McEvoy, 2012). This point is further supported by research indicating that treatments targeting IU are efficacious in reducing anxiety and depressive symptomatology (Robichaud, 2013; van der Heiden et al., 2012). Another implication concerns the potential importance of differentiating between IU and broader affective traits. Several theorists have emphasized shifting the focus of interventions to higher-order dimensions of personality, such as neuroticism (Barlow et al., in press), in the hopes of creating a more efficient approach toward treating emotional disorders. The present study suggests that IU (at least partially) provides a unique contribution to depression, and it is unclear whether a treatment targeting neuroticism will address this particular deficit. Future

research is needed to determine whether broad interventions can modify the impact of IU on reward anticipation.

The present study had several limitations that warrant consideration. First, MDD participants were limited to those with early-onset depression and results may not generalize to all types of depression (e.g., adult-onset depression). Second, depression, IU, and frontal EEG asymmetry while anticipating reward were all measured cross-sectionally, and causal relationships amongst these variables cannot be determined. Third, while MDD has been associated with a reduced frontal EEG asymmetry across numerous investigations (e.g., Shankman et al., 2007, 2013), it is still unclear what specific cognitive processes (e.g., rumination) are associated with frontal EEG asymmetry.

Additional research is needed to address these limitations and better understand the relationship between IU and reduced reward anticipation. For example, more studies are needed to determine whether IU is a mechanism of dysfunction across other disorders characterized by reduced reward anticipation, such as bipolar disorder (Singh et al., 2013), obsessive-compulsive disorder (Figeet al., 2011), and social phobia (Guyer et al., 2012). Future studies should also examine the association between IU and specific symptoms of depression (e.g., anhedonia) given the present study's finding of an association between IU and reduced reward anticipation during a laboratory task. Longitudinal studies are needed to determine the causal relationship between IU and reduced reward anticipation, and treatment studies may be helpful in determining whether increasing tolerance to uncertainty leads to improved reward anticipation. Finally, research is needed to better understand the specific cognitive mechanisms (e.g., rumination) contributing to the detrimental effects of IU on reduced reward anticipation.

In summary, the present study implicates IU as a potential mechanism for the association between depression and reduced reward anticipation. MDD participants reported greater IU relative to controls, and across all participants IU was negatively associated with frontal EEG asymmetry while anticipating reward. IU also mediated the relationship between depression and reward anticipation and results remained significant after controlling for neuroticism. These findings have potential clinical implications as IU treatments may improve reward anticipation deficits in depression, which has been posited to be central to the disorder (Pizzagalli et al., 2009; Sherdell et al., 2012) and is a predictor of poor response to treatment (McMakin et al., 2012).

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Figure 1.

Results of mediational analysis. Coefficients are standardized regression weights. Reward anticipation was measured via frontal EEG asymmetry while anticipating reward. Results indicated an indirect effect of Depression Status, mediated through Intolerance of Uncertainty, on Reward Anticipation (95% CI: $-.16$ to $-.02$). EEG = electroencephalography; * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 1

Participant Demographics, Clinical Characteristics, and Symptom Measures

	Control (<i>n</i> = 53)	MDD-only (<i>n</i> = 30)	PD-only (<i>n</i> = 21)	Comorbrids (<i>n</i> = 50)
Demographics				
Age (SD)	32.5(14.0)	30.1(12.4)	33.4(12.9)	35.7(11.3)
Sex (% female)	55.6%	70.0%	59.1%	68.0%
Race (% Caucasian)	42.6%	46.7%	40.9%	48.0%
Education (SD)	15.4(2.4)	14.5(1.9)	15.6(2.2)	14.8(2.4)
Clinical characteristics				
Currently taking psychiatric medication	0.0% _a	23.3% _b	27.3% _b	42.0% _b
GAF (SD)	89.7(6.7) _a	52.3(7.8) _b	58.9(9.7) _c	52.7(6.6) _b
Age of onset of first depressive disorder (SD)	-	13.4(3.4)	-	13.5(4.2)
Age of onset of first anxiety disorder (SD)	-	-	19.8(8.8)	15.7(9.3)
HRSD (SD)	1.5(1.8) _a	24.8(8.5) _b	9.3(7.6) _c	26.0(8.9) _b
BAI (SD)	1.7(2.1) _a	14.3(11.1) _b	15.8(12.7) _{b,c}	20.3(13.1) _c
Personality Questionnaires				
EPQ – Neuroticism (SD)	4.9(4.0) _a	16.6(4.1) _b	13.2(6.8) _c	16.9(4.5) _b
IUS – 12 Item				
Inhibitory IU (SD)	7.4(2.5) _a	11.7(5.3) _b	9.9(3.8) _{b,c}	12.5(4.6) _{b,d}
Prospective IU (SD)	15.4(5.1) _a	18.8(7.5) _b	19.6(6.2) _b	20.9(6.5) _b
Total IU (SD)	22.8(7.0) _a	30.5(11.8) _b	29.4(9.6) _b	33.4(10.4) _b

Note. Means or percentages with different subscripts across rows were significantly different in pairwise comparisons ($p < .05$, χ^2 test for categorical variables and Tukey's honestly significant difference test for continuous variables).

BAI = Beck Anxiety Inventory; EPQ = Eysenck Personality Questionnaire; GAF = Global Assessment of Functioning; HRSD = Hamilton Rating Scale for Depression; IUS = Intolerance of Uncertainty Scale; MDD = Major Depressive Disorder; PD = Panic Disorder; SD = Standard Deviation.