



## Research paper

## Neural reactivity to reward and internalizing symptom dimensions

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## ABSTRACT

**Background:** Reduced reward responsiveness, measured via the event-related potential (ERP) component the reward positivity (RewP), has been linked to several internalizing psychopathologies (IPs). Specifically, prior studies suggest that a reduced RewP is robustly related to depression and to a lesser extent anxiety. No studies to date, however, have examined the relation between the RewP and IP symptom dimensions in a heterogeneous, clinically representative patient population that includes both depressed and/or anxious subjects. The primary aim of the current study was to examine the relation between the RewP and specific internalizing symptom dimensions among patients with a variety of IP diagnoses and symptoms.

**Methods:** A total of 80 treatment seeking adults from the community completed a battery of questionnaires assessing a range of IP symptoms and a well-validated reward processing task known to robustly elicit the RewP.

**Results:** A principal components analysis (PCA) on clinical assessments revealed two distinct factors that characterized the patient sample: affective distress/misery and fear-based anxiety. Results showed that within this sample, an attenuated RewP was associated with greater affective distress/misery based symptoms; however, the RewP was unrelated to fear-based anxiety symptoms.

**Conclusions:** The current findings suggest that patients with higher distress/misery symptoms are characterized by decreased responsivity to rewards at the physiological level, and that this response tendency distinguishes distress/misery symptoms from fear-based symptoms. The RewP may be one promising transdiagnostic biological target for intervention efforts for individuals with distress-based symptoms of psychopathology.

## 1. Introduction

Internalizing disorders, such as anxiety and depression, are highly comorbid and overlapping in symptoms (Kessler et al., 2005; Watson, 2005), and share many common biological and neurological underpinnings (e.g., Etkin, and Schatzberg, 2011; Tambs et al., 2009). Issues surrounding the categorical nature of internalizing psychopathologies (IPs) and overlap among them have been widely recognized (e.g., Regier et al., 2009; Sanislow et al., 2010). To address these matters, the Research Domain Criteria (RDoC) initiative was developed by the National Institute of Mental Health (NIMH) in order to promote the development of dimensional constructs that integrate elements of psychology and biology (Kozak and Cuthbert, 2016). Specifically, the RDoC initiative seeks to move toward a personalized medicine approach and find novel ways of classifying psychiatric disorders that are based on dimensions of observable behavior and neurobiological measures (Cuthbert and Insel, 2013).

Several IPs are characterized by deficits in reward and effort valuation, reward outcome, and decision-making processes (e.g., Craske et al., 2016). As a result, RDoC identified a number of reward-related biologically based constructs within the Positive Valence System, including initial responsiveness to reward attainment. To examine reward responsiveness at the psychophysiological level, researchers have utilized the event-related potential (ERP) component the reward positivity (RewP). The RewP, previously referred to as the feedback negativity, is maximal at frontocentral electrode sites approximately 250–350 ms following the receipt of a reward and reflects processing of positive feedback (e.g., monetary reward) versus breaking even or losing (for reviews, see Proudfit (2015) and Proudfit et al. (2015)). The RewP has demonstrated excellent psychometric properties (Bress et al., 2015a), and there is growing evidence that it is a valid measure of individual differences in reward processing, as it has been correlated with self-report reward sensitivity (Bress and Hajcak, 2013),

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positive emotionality (Kujawa et al., 2015), and activation in brain regions implicated in reward, such as the ventral striatum and medial prefrontal cortex (Carlson et al., 2011; Foti et al., 2011; Gehring, and Willoughby, 2002).

Notably, the RewP has consistently been linked to IPs. The most robust finding in the literature is the relationship between an attenuated RewP and depression. For instance, less differentiation between gains and losses (i.e., a reduced RewP) has been shown to be related to concurrent symptoms of depression among youth (Bress et al., 2015b) and adults (Foti and Hajcak, 2009), and also future depressive symptoms and diagnoses among youth in a prospective study (Nelson et al., *in press*). An attenuated RewP to gains has also been observed in preschoolers (Belden et al., 2016) and adults (Liu et al., 2014) with depression, and shown to prospectively predict future depressive symptoms and diagnoses in children and adolescents (Bress et al., 2013, 2015a).

Despite the common comorbidity between depression and anxiety (Kessler et al., 2005; Watson, 2005), fewer studies have examined the association between the RewP and anxiety, and findings have been less consistent relative to studies with depression. In one study of college undergraduates, a smaller RewP was associated with greater trait anxiety (Gu et al., 2010). Conversely, researchers failed to find a relation between the RewP and anxiety symptoms among children and adolescents (Bress et al., 2012; Bress et al., 2015b) and college undergraduates (Foti and Hajcak, 2009). In a study of children, however, youth with higher generalized anxiety symptoms exhibited an attenuated RewP to losses, whereas children with higher social anxiety symptoms in this study exhibited an enhanced RewP to gains (Kessel et al., 2015).

Taken together, prior studies suggest that a reduced RewP is robustly related to depression. However, findings from studies with anxious populations tend to be less consistent, and there is some evidence that different types of anxiety disorders (i.e., social anxiety versus generalized anxiety) may yield a different RewP response (i.e., attenuated versus enhanced). One interpretation from these previous studies is that an attenuated RewP response may not distinguish depression from anxiety, *per se*, but rather distress-misery versus fear disorders. Specifically, in large samples of patients with comorbid IPs (Hettema et al., 2005; Slade and Watson, 2006; Vollebergh et al., 2001), co-occurrence of disorders is usually best explained by two factors, including distress-misery (i.e., depression, dysthymia, and generalized anxiety) and fear-based anxiety (i.e., panic disorder, social phobia, specific phobia). However, the majority of prior studies examining the RewP and IPs have either focused on single IP diagnostic groups (e.g., Liu et al., 2014) or undergraduate college samples (e.g., Foti and Hajcak, 2009; Gu et al., 2010) making it difficult to directly test whether the RewP is more strongly associated with distress-misery versus fear-based anxiety symptoms. In order to adequately test this question, it is necessary to include a large heterogeneous sample of patients with depressive and anxiety disorders and thus, variable distress and fear-based symptoms. This type of investigation will ultimately assist with the RDoC initiative of finding novel ways to classify psychiatric disorders based on neurological measures (i.e., RewP). Moreover, examining these relationships in a representative sample of comorbid and treatment-seeking patients will also advance current understandings of the RewP as a potential tool for informing prevention or intervention efforts.

Thus, the primary aim of the current study was to examine the relation between the RewP and specific internalizing symptom dimensions within a clinically representative patient population with a variety of IP diagnoses and symptoms. The study included treatment-seeking adults with one or more current IP diagnoses and a range of IP symptoms. We first sought to replicate the previously demonstrated two-factor model of internalizing psychopathologies (i.e., fear-based anxiety and distress-misery) in a treatment-seeking population utiliz-

ing a principal components analysis (PCA) on several well-validated self-report measures of IPs. Consistent with previous studies (e.g., Belden et al., 2016; Bress et al., 2013, 2015a, 2015b; Foti and Hajcak, 2009; Kessel et al., 2015; Liu et al., 2014), we hypothesized that less differentiation between gains and losses (i.e., the RewP) would be more strongly associated with symptoms of distress and misery, relative to fear-based symptoms of psychopathology. Specifically, we expected that there would be a negative relation between RewP and distress-misery symptoms, whereas there would be no relation between the RewP and fear-based symptoms of anxiety.

## 2. Materials and methods

### 2.1. Participants

The current study was funded by, and designed to be consistent with, the NIMH RDoC Initiative (RFA-MH-13-080). Thus, the study was comprised of a clinically representative patient population, with a full range of IPs and symptoms who consented to treatment with pharmacotherapy (selective serotonin reuptake inhibitors/SSRIs) or cognitive behavioral therapy (CBT). Participants were required to be between 18 and 65 and have a current full-threshold or sub-threshold DSM-5 depressive or anxiety disorder, report a total score of  $\geq 23$  on the Depression, Anxiety, and Stress Scale (DASS-21; Lovibond and Lovibond, 1995), and a Global Assessment of Functioning (GAF) score of  $\leq 60$ . Exclusionary criteria included an inability to provide consent and read and write in English, having a major active medical or neurological problem, a lifetime history of mania or psychosis, current obsessive-compulsive disorder (OCD), a current substance dependence, a history of an intellectual disability or pervasive developmental disorder, any contraindication to receiving SSRIs, being already engaged in psychiatric treatment (including medication), a history of traumatic brain injury, and being pregnant. All subjects were free of psychotropic/psychoactive medications and tested negative on a urine drug screen at the time of screening. The University of Illinois at Chicago Institutional Review Board approved the study, and informed consent was obtained from all participants.

Eighty-seven patients were enrolled in the study; however, seven were excluded due to poor quality EEG data, defined as having fewer than 15 artifact-free trials per condition. The final sample included eighty individuals. All data used in the current study were collected at baseline, prior to treatment.

### 2.2. Assessment of diagnoses

Lifetime Axis I diagnoses were assessed via the Structured Clinical Interview for DSM-5 Disorders (SCID-5; First et al., 2015) by trained research staff. After the evaluation, a consensus panel of at least 3 study staff/trained clinicians determined subjects' eligibility and if there were co-occurring disorders, the principal disorder warranting treatment was identified. Consistent with the RDoC strategy (Kozak and Cuthbert, 2016), individuals were not excluded for comorbid disorders but instead classified by their clinician-determined principal diagnosis, as determined by the most severe and impairing symptoms (see Table 1). Panic disorder (PD), social anxiety disorder (SAD), and post-traumatic stress disorder (PTSD) were coded as 'fear-based disorders' whereas major depressive disorder (MDD), dysthymia, and generalized anxiety disorder (GAD) were coded as 'distress/misery' disorders consistent with our prior studies (Gorka et al., *in press*).

### 2.3. Internalizing symptom measures

All participants completed a battery of standardized measures. By intention, some of the measures captured broad internalizing symptoms, whereas others were relatively specific to the principal disorders included in the sample.

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