



The uncertainty of errors: Intolerance of uncertainty is associated with error-related brain activity

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ABSTRACT

Errors are unpredictable events that have the potential to cause harm. The error-related negativity (ERN) is the electrophysiological index of errors and has been posited to reflect sensitivity to threat. Intolerance of uncertainty (IU) is the tendency to perceive uncertain events as threatening. In the present study, 61 participants completed a self-report measure of IU and a flanker task designed to elicit the ERN. Results indicated that IU subscales were associated with the ERN in opposite directions. Cognitive distress in the face of uncertainty (Prospective IU) was associated with a larger ERN and slower reaction time. Inhibition in response to uncertainty (Inhibitory IU) was associated with a smaller ERN and faster reaction time. This study suggests that sensitivity to the uncertainty of errors contributes to the magnitude of the ERN. Furthermore, these findings highlight the importance of considering the heterogeneity of anxiety phenotypes in relation to measures of threat sensitivity.

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1. Introduction

The predictability of threat is an important feature that impacts the ability to avoid or mitigate undesirable consequences (Grupe & Nitschke, 2013). Indeed, the anticipation of unpredictable, relative to predictable, threat has been shown to elicit greater self-reported anxiety (Nelson & Shankman, 2011), startle response (Grillon, Baas, Lissek, Smith, & Milstein, 2004), and insula activation (Shankman et al., 2014). Task-irrelevant unpredictability has also been shown to increase amygdala activation and attentional bias to threat (Herry et al., 2007). These findings support a growing literature suggesting that unpredictability can potentiate negative valence system activation.

To date, most research has examined the impact of unpredictability on emotional responses while anticipating exogenous threat (e.g., noises, pictures, shocks). In contrast, few studies have examined whether unpredictability is also important for the processing of endogenous threat. For example, errors are a form of endogenous threat that interrupt behavior in unpredictable ways, and therefore can place an individual in danger (Hajcak, 2012; Weinberg et al., in press). Indeed, error commission is followed by a cascade of defense system activation, including increased negative affect (Spunt, Lieberman, Cohen, & Eisenberger, 2012), startle response (Hajcak & Foti, 2008), skin conductance response (Hajcak,

McDonald, & Simons, 2004), and amygdala activation (Pourtois et al., 2010).

An electrophysiological index of errors is the error-related negativity (ERN), a negative deflection in the event-related potential (ERP) that occurs approximately 50 ms after the commission of an error (see Gehring, Liu, Orr, & Carp, 2012 for review). The ERN is larger in individuals with generalized anxiety disorder (GAD; Weinberg, Olvet, & Hajcak, 2010; Weinberg, Kotov & Proudfit, 2014), obsessive-compulsive disorder (OCD; Hajcak, Franklin, Foa & Simons, 2008), checking behaviors (Weinberg et al., in press; Weinberg et al., 2014), and pathological worry (Moser, Moran, Schroder, Donnellan, & Yeung, 2013). Moreover, the ERN has been shown to be enhanced when errors are perceived as more motivationally salient, such as when errors are punished with an aversive loud sound (Riesel, Weinberg, Endrass, Kathmann, & Hajcak, 2012) or monetary loss (Hajcak, Moser, Yeung, & Simons, 2005), and when individuals with social anxiety are socially evaluated (Barker, Troller-Renfree, Pine, & Fox, 2015). The ERN is also enhanced in individuals with a familial history (i.e., risk) of OCD (Riesel, Endrass, Kaufmann, & Kathmann, 2011), and has been shown to prospectively predict the onset of new anxiety disorders (Meyer, Hajcak, Torpey-Newman, Kujawa, & Klein, 2015). Together, these findings support the ERN as a potential transdiagnostic index of sensitivity to threat and risk for psychopathology (Proudfit, Inzlicht, & Mennin, 2013). However, given the inherent unpredictability of errors, the elevated defensive responding observed across anxiety disorders may reflect a heightened sensitivity to unpredictability (Proudfit et al., 2013).

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Intolerance of uncertainty (IU) is the tendency to perceive, interpret, and respond to ambiguous or uncertain events as threatening (Dugas, Schwartz, & Francis, 2004). IU was originally conceptualized as a cognitive trait that contributed to increased worry and the development of GAD (Dugas, Gosselin & Ladouceur, 2001; Dugas, Buhr & Ladouceur, 2004; Gentes & Ruscio, 2011). However, recent conceptualizations have characterized IU as a transdiagnostic factor of emotional disorders (Boswell, Thompson-Hollands, Farchione, & Barlow, 2013; Mahoney & McEvoy, 2012). IU consists of two related (but distinct) factors—Prospective IU and Inhibitory IU (Carleton, Norton, & Asmundson, 2007; Fergus, 2013; McEvoy & Mahoney, 2011). Prospective IU measures anxiety, cognitive distress, and the urge to act in the face of uncertainty. High Prospective IU has been particularly associated with pathological worry and checking behaviors (McEvoy & Mahoney, 2011, 2012), GAD (McEvoy & Mahoney, 2012), and OCD (McEvoy & Mahoney, 2012). Inhibitory IU measures avoidance, inhibition of action, and paralysis when faced with uncertainty. Inhibitory IU has been particularly associated with social anxiety (Carleton, Collimore, & Asmundson, 2010; Whiting et al., 2014), panic disorder with agoraphobia (Carleton et al., 2014), post-traumatic stress disorder (PTSD; Fetzner, Horswill, Boelen, & Carleton, 2013) and depression (Carleton et al., 2010; McEvoy & Mahoney, 2011).

Research has indicated that total IU (Somerville et al., 2013) and the IU subscales are differentially associated with neural and psychophysiological indicators of sensitivity to unpredictability. For example, Prospective and Inhibitory IU have been associated with an enhanced and attenuated, respectively, startle reflex in anticipation of unpredictable (but not predictable) threat (Nelson, Liu, Sarapas, & Shankman, under review; Nelson & Shankman, 2011). Furthermore, Nelson, Kessel, Jackson, & Hajcak, (in press) recently demonstrated that Prospective and Inhibitory IU were also associated with enhanced and attenuated, respectively, ERP response to reward (i.e., the reward positivity; RewP). This pattern of findings suggests that Prospective IU may be associated with an enhanced psychophysiological response to motivationally-salient stimuli, while Inhibitory IU is associated with an attenuated response—particularly when there is an element of unpredictability. However, to date no study has examined the association between IU and the ERN.

The present study examined the relationship between individual differences in IU and error-related brain activity. Specifically, 61 participants completed the Intolerance of Uncertainty Scale (IUS; Freeston, Rhéaume, Letarte, Dugas, & Ladouceur, 1994) and a flanker task designed to elicit the ERN. As previously mentioned, several anxiety disorders (e.g., GAD, OCD) have been associated with both an enhanced ERN (Hajcak et al., 2008; Weinberg et al., 2010) and greater IU (Dugas, Buhr et al., 2004; Tolin, Abramowitz, Brigidi, & Foa, 2003). Furthermore, Prospective and Inhibitory IU have been associated with an enhanced and attenuated, respectively, startle response in anticipation of unpredictable threat (Nelson and Shankman, 2011; Nelson et al., under review). Therefore, we hypothesized that Prospective IU and Inhibitory IU would be associated with an enhanced and attenuated ERN, respectively.

2. Methods

2.1. Participants

The sample included 64 undergraduates who participated for course credit. Participants were college-aged ($M = 19.90$, $SD = 2.47$), 57.4% female, and ethnically/racially diverse, including 29.5% Caucasian, 13.1% Black, 14.8% Latino, 34.4% Asian, and 8.2% 'Other'. Exclusion criteria were an inability to read or write English or history of a neurological disorder. Informed consent was obtained

prior to participation and the research protocol was approved by the Stony Brook University Institutional Review Board.

2.2. Measures

2.2.1. Intolerance of uncertainty scale

The IUS (Freeston et al., 1994) is a 27-item self-report measure that assesses the degree to which individuals find uncertainty to be distressing and undesirable. Items are rated on a five-point Likert scale ranging from 1 (not at all characteristic of me) to 5 (entirely characteristic of me), with higher scores indicating greater IU. The present study utilized the psychometrically improved 12-item version of the IUS (Carleton et al., 2007), which includes two factor-analytically derived subscales of Prospective IU (7-items) and Inhibitory IU (5-items). Cronbach's alpha values for the IUS and its subscales in the current sample are shown in Table 1.

2.3. Flanker task

Participants completed a flanker task using Presentation software (Neurobehavioral Systems Inc., Albany, CA). On each trial, five horizontally aligned white arrowheads were presented for 200 ms. Participants indicated the direction of the central arrowhead with their right hand by clicking the left or right mouse button.¹ Half of the trials were compatible (e.g., «< or >>») and half were incompatible (e.g., «> or <<»); trial type was randomly determined. A variable inter-trial interval of 600–1000 ms followed the response. Participants completed a practice block containing 20 trials and the actual task consisted of 11 blocks of 30 trials (330 total trials).

2.4. EEG recording and processing

Continuous EEG was recorded using an elastic cap with 34 electrode sites placed according to the 10/20 system. Electrooculogram was recorded using four additional facial electrodes: three electrodes were placed around the right eye (one above, one below, and one on the outer canthus) and one electrode was placed on the outer canthus of the left eye. All electrodes were sintered Ag/AgCl electrodes. Data were recorded using the Active Two BioSemi system (BioSemi, Amsterdam, Netherlands). EEG was digitized with a sampling rate of 1024 Hz using a low-pass fifth order sinc filter with a half-power cutoff of 204.8 Hz. A common mode sense active electrode producing a monopolar (non-differential) channel was the recording reference.

EEG data were analyzed using Brain Vision Analyzer (Brain Products, Gilching, Germany). Data were referenced offline to the average of left and right mastoids, band-pass filtered from .1 to 30 Hz, and corrected for eye movement artifacts (Gratton, Coles, & Donchin, 1983). Response-locked epochs of 1500 ms were extracted, including a 500 ms pre-response interval. The 500–300 ms pre-response interval was used as the baseline (Weinberg et al., 2010). Epochs containing a voltage greater than 50 μ V between sample points, a voltage difference of 175 μ V within a 400 ms segment, or a maximum voltage difference of less than .50 μ V within 100 ms intervals were automatically rejected. Tri-

¹ All participants completed the Flanker task with their right hand; therefore, left-handed individuals used their non-dominant hand to key in responses during the task. In order to examine the possible impact of handedness on study results, we conducted additional analyses that excluded participants who were left-handed ($n = 6$), leaving a sample of 55 right-handed individuals for analysis. All results remained significant when the left-handed participants were excluded from analyses (all $ps < .05$).

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