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Impact of posttraumatic stress symptom dimensions on psychophysiological reactivity to threat and reward

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ABSTRACT

Posttraumatic stress symptoms (PTSS) are associated with significant distress and impairment. Research has therefore focused on identifying neurobehavioral deficits that contribute to the pathophysiology of PTSS. One issue that has contributed to difficulty in identifying these deficits is the highly heterogeneous nature of PTSS. PTSS is comprised of four, factor analytically distinct dimensions of symptoms – re-experiencing, avoidance, hyperarousal, and negative cognitions and mood. It is therefore unlikely that there is one single mechanism that accounts for all of PTSS and elucidating neurobehavioral deficits associated with specific PTSS symptom dimensions may better inform clinical prevention and intervention efforts. Within the broader internalizing disorder literature, two key constructs that contribute to psychopathology are aberrant neural reactivity to threat and reward. However, the literature linking PTSS to these deficits is mixed, suggesting that aberrant neural reactivity to threat or reward may be specific to certain PTSS dimensions. In a sample of 51 trauma-exposed adults with a range PTSS, the present study therefore examined how the four dimensions of PTSS uniquely relate to two well-validated event-related potential (ERP) neural indices of threat and reward reactivity – the error-related negativity (ERN) and reward-related positivity (RewP), respectively. Results indicated that hyperarousal symptoms were associated with enhanced ERN, and enhanced RewP. In contrast, negative cognitions and mood symptoms were uniquely associated with a more blunted RewP. These results indicate that certain PTSS symptom dimensions have unique relations with neural indicators of threat and reward reactivity and may therefore have distinct pathophysiologies.

1. Introduction

Trauma exposure is highly common, and posttraumatic stress disorder (PTSD) is associated with significant impairment and distress, even at the subthreshold level (Gadermann et al., 2012; Zlotnick et al., 2002). It is therefore important to identify neurobehavioral deficits that may contribute to the development and maintenance of posttraumatic stress symptoms (PTSS). However, this effort is complicated by the heterogeneity of PTSS, which is evidenced by the wealth of factor analytic studies that have found PTSS to consist of four qualitatively different dimensions of symptoms: (1) re-experiencing, (2) avoidance, (3) negative cognitions and mood, and (4) hyperarousal symptoms (clusters B, C, D, and E, respectively; e.g., Elklit and Shevlin, 2007; Yufik and Simms, 2010). Given this, there are likely multiple PTSS profiles that are characterized by distinct neurobehavioral deficits. Examining the neurobehavioral correlates of specific PTSS dimensions could therefore lead to the dissemination of more individualized treatment, a goal that is in line with the National Institute of Mental Health's (NIMH) Research Domain Criteria Initiative (RDoC; Cuthbert and Kozak, 2013).

Two neurobehavioral processes that may relate to specific PTSS dimensions are reactivity to threat and reward, as abnormalities in these processes have been implicated in the pathophysiology of

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various internalizing disorders that share core features with PTSS. For example, heightened defensive responding to threat is a core dysfunction implicated in panic disorder, a condition that shares elevated physiological arousal with the hyperarousal PTSS dimension (Gorka et al., In Press; Lieberman et al., 2016; Shankman et al., 2013). Meanwhile, blunted appetitive responding to reward has been evidenced in depression, a condition that shares anhedonia and low positive affect with the negative cognitions and mood PTSS dimension (Shankman et al., 2013). Of note is that heightened threat sensitivity has been found to be specific to panic and other fear disorders, relative to distress disorders such as depression (Gorka et al., In Press; Shankman et al., 2013). Likewise blunted reward sensitivity has been found to be specific to depression, relative to fear-based anxiety disorders (Shankman et al., 2013). Aberrant threat and reward responding therefore distinguishes distress and fear-based anxiety disorders. Given that PTSS includes unique symptom dimensions that overlap with both classes of disorders (Watson, 2005), it is possible that PTSS is characterized by aberrant threat *and* reward responding.

As might be expected given the heterogeneity of PTSS, there have been inconsistent findings regarding the association between post-traumatic stress and threat and reward responding. For instance, individuals with PTSD have been found to exhibit heightened (Grillon et al., 2009; Jovanovic et al., 2010; Morgan et al., 1995), comparable (Rabinak et al., 2013), and even blunted (Britton et al., 2005) defensive responding during the anticipation of threat, relative to individuals without PTSD. Likewise, PTSD has been associated with heightened (Myers et al., 2013), comparable (Casada and Roache, 2005; Van Rooij et al., 2015), blunted (Elman et al., 2009; Felmingham et al., 2014), appetitive responding to reward. These findings together highlight that PTSS, broadly and categorically defined is not necessarily characterized by aberrant threat and reward responding. However, specific subgroups or dimensions of PTSS may uniquely relate to blunted and/or enhanced threat and reward reactivity. In particular, blunted reward sensitivity may be specific to negative cognitions and mood PTSS given the abovementioned overlap in symptoms between depression and this PTSS dimension. In contrast, the overlap in symptoms between fear-based disorders and the hyperarousal PTSS dimension might suggest that heightened sensitivity to threat is specific to hyperarousal symptoms.

To date, there have been a few studies that have attempted to explore how specific PTSS dimensions relate to threat and reward responding. Grupe et al. (2016) found that hyperarousal and re-experiencing symptoms positively predicted neural reactivity to threat; however, Jovanovic et al. (2010) reported no association between startle potentiation to threat and any specific PTSS dimension. With regard to reward, Felmingham et al. (2014) and Elman et al. (2009) reported a *negative* association between emotional numbing symptoms of avoidance (e.g., anhedonia and restricted positive affect) and neural reactivity to reward, whereas Contractor et al. (2013) reported a *positive* association between avoidance symptoms and self-reported motivation for reward.

Taken together, there is some prior evidence to suggest that distinct PTSS symptom clusters map onto distinct neurobehavioral deficits. However, several key questions remain. First, the studies noted above all used DSM-IV defined PTSS, which were significantly revised for DSM-5 and restructured from three, to four clusters (a change based on numerous factor-analyses of the PTSD symptom structure; Elklit and Shevlin, 2007; Yufik and Simms, 2010). Therefore, it is presently unknown how threat and reward responding relate to the four, DSM-5 PTSS clusters that are currently referred to in clinical settings and have better psychometric properties than the prior versions. Second, no studies to our knowledge have examined how specific PTSS clusters relate to threat and reward responding in the same sample. It is therefore difficult to draw conclusions about the specificity of these neurobehavioral deficits to any particular PTSS dimension. Moreover, investigations of this question to date have focused on individuals with full syndromal PTSD. Thus, the range of PTSS within each symptom dimension may have been restricted, which could limit the detection of associations between these neurobehavioral constructs and PTSS dimensions. Focusing on only those individuals who are full syndromal PTSD also ignores individuals who are subthreshold – a group that is known to display functional impairment (Gadermann et al., 2012; Zlotnick et al., 2002).

Although there are multiple ways to elicit and measure neural responding to threat and reward, event-related potential (ERP) components provide well-validated indices of threat and reward responding, and have strong psychometric properties (Bress et al., 2015; Meyer et al., 2013). In particular, the error-related negativity (ERN) is a frontocentrally maximal negative-going deflection in the ERP waveform that occurs between 0 and 100 ms after the commission an error, which is a motivationally salient event that signals the potential for harm (i.e., threat) and therefore engages the defensive motivational system to take corrective action (Weinberg et al., 2015a,b). Greater ERN is indicative of greater defensive responding to threat (Weinberg et al., 2015a,b), and has been associated with multiple anxiety disorders and high trait anxiety (e.g., Hajcak and Simons, 2002; Weinberg et al., 2010). The reward-related positivity (RewP) is a frontocentrally maximal positive-going deflection in the ERP waveform that occurs between 200 and 250 ms after the receipt of reward (Proudfit, 2015). Greater RewP is indicative of greater appetitive responding to reward (Proudfit, 2015), and a blunted RewP has been shown to be associated with major depressive disorder (MDD), and high levels of depressive symptoms (Liu et al., 2014; Proudfit 2015; Weinberg et al., 2015a,b).

Despite the utility of these ERPs for studying internalizing psychopathology, and the growing literature on ERPs in PTSS (e.g., Lobo et al., 2014, 2015; Wessa et al., 2005) little is known about the ERN and RewP in PTSS. No studies to our knowledge have examined the RewP in PTSD, and only three studies have examined the ERN in relation to PTSD and reported no difference in ERN between individuals with PTSD and controls (Gorka et al., 2016; Rabinak et al., 2013; Swick et al., 2015). However, none of these ERN studies examined how the ERN relates to specific PTSS dimensions. The present study therefore examined how the DSM-5, four clusters of PTSS – re-experiencing, avoidance, negative cognitions and mood, and hyperarousal – relate to the ERN and RewP in a sample of trauma-exposed individuals. PTSS was defined dimensionally rather than categorically, to include the full PTSS spectrum. All participants completed two well-validated tasks designed to elicit the ERN and RewP. We hypothesized that greater hyerparousal symptoms (Cluster E) would predict greater ERN. We predicted that other dimensions of PTSS would not relate to ERN. We also predicted that greater negative cognitions and mood (Cluster D) symptoms would predict blunted RewP, but that other dimensions of PTSS would not relate to RewP.

2. Methods

2.1. Participants

Participants were recruited from the community as a part of a larger investigation on affective and physiological abnormalities across internalizing psychopathology. A variety of advertisements were used to recruit a clinically representative patient population with a range of internalizing disorders and symptoms. In line with the aims of the larger study, participants were included if they