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Affective state and locus of control modulate the neural response to threat

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ABSTRACT

The ability to regulate the emotional response to threat is critical to healthy emotional function. However, the response to threat varies considerably from person-to-person. This variability may be partially explained by differences in emotional processes, such as locus of control and affective state, which vary across individuals. Although the basic neural circuitry that mediates the response to threat has been described, the impact individual differences in affective state and locus of control have on that response is not well characterized. Understanding how these factors influence the neural response to threat would provide new insight into processes that mediate emotional function. Therefore, the present study used a Pavlovian conditioning procedure to investigate the influence individual differences in locus of control, positive affect, and negative affect have on the brain and behavioral responses to predictable and unpredictable threats. Thirty-two healthy volunteers participated in a fear conditioning study in which predictable and unpredictable threats (i.e., unconditioned stimulus) were presented during functional magnetic resonance imaging (fMRI). Locus of control showed a linear relationship with learning-related ventromedial prefrontal cortex (PFC) activity such that the more external an individual's locus of control, the greater their differential response to predictable versus unpredictable threat. In addition, positive and negative affectivity showed a curvilinear relationship with dorsolateral PFC, dorsomedial PFC, and insula activity, such that those with high or low affectivity showed reduced regional activity compared to those with an intermediate level of affectivity. Further, activity within the PFC, as well as other regions including the amygdala, were linked with the peripheral emotional response as indexed by skin conductance and electromyography. The current findings demonstrate that the neural response to threat within brain regions that mediate the peripheral emotional response is modulated by an individual's affective state as well as their perceptions of an event's causality.

Introduction

The ability to effectively respond to threats in the environment is critical for healthy emotional function. The response to a threat, however, can vary depending on the circumstances in which the threat occurs. For example, an unpredictable threat elicits a larger emotional response than a predictable threat (Knight et al., 2011). The response to threat also varies considerably from one person to another and appears to be influenced by individual differences in emotion-related processes. For example, the emotional response to threat varies with aspects of anxiety (Grillon et al., 1993; Knight et al., 2011; Wood et al., 2012, 2013). Anxious behavior, however, is influenced by a number of characteristics that vary across individuals. For example, locus of control (i.e., the degree to which an individual believes events are internally versus externally controlled) and affective state (i.e., the degree to which an individual experiences positive and negative emotions in daily life) also vary from person-to-person and appear to influence anxious behavior (Chorpita and Barlow, 1998; Gros et al., 2007; Rotter, 1966; Watson et al., 1988). Therefore, individual differences in locus of control and affective state may also explain variability in the response to threat. However, there is limited prior research on whether inter-subject variability in locus of control, positive affect, and negative affect influences the neural processes that mediate expression of the emotional response. Thus, determining whether individual differences in these attributes influence the response to threat would provide important insight into emotion-related processes.

Pavlovian conditioning is a procedure often used to investigate emotional learning and memory processes. During Pavlovian fear conditioning, an originally innocuous cue (conditioned stimulus; CS) is typically paired with an innately aversive stimulus (unconditioned stimulus; UCS) that produces a reflexive response (unconditioned response; UCR). Repeated pairing of the CS and UCS then comes to elicit a conditioned response (CR) in anticipation of the UCS. Expression of a CR is typically used to index learning, while the UCR is often considered

Abbreviations: CS, conditioned stimulus; UCS, unconditioned stimulus; CS+, CS that predicts the UCS; CS−, CS that predicts the omission of the UCS; CS + UCS, UCS that follows the CS+; CR, conditioned response; UCR, unconditioned response; SCR, skin conductance response; PFC, prefrontal cortex; IPL, inferior parietal lobule; PCC, posterior cingulate cortex.

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an unlearned response. The UCR, however, also shows learning-related modulation. For instance, prior Pavlovian conditioning research has demonstrated learning-related changes in brain and behavioral responses to predictable compared to unpredictable threat (Baxter, 1966; Canli et al., 1992; Dunsmoor et al., 2008). These studies have demonstrated a diminished UCR once the CS–UCS relationship has been learned, a process known as conditioned UCR diminution (Dunsmoor et al., 2008; Kimmel, 1967; Knight et al., 2010, 2011; Wood et al., 2012). Thus, as the threat (i.e., the UCS) becomes predictable, the response to the threat (i.e., the UCR) is modulated (Bouton et al., 2001; Domjan, 2005; Wagner and Brandon, 1989). Interestingly, these studies have also found a relationship between UCR expression and negative affect indexed by the State-Trait Anxiety Inventory (STAI; Spielberger, 1983; Knight et al., 2011; Wood et al., 2012) suggesting that individual differences in emotional disposition modulate the response to threat. However, questions regarding whether the emotional response to threat also varies with locus of control and positive affect, independent of negative affect, remain unanswered.

Previous research has often taken a categorical approach to the study of anxious behavior. For example, clinical research has traditionally investigated groups with versus without anxiety disorders. This line of research has demonstrated important differences in both brain and behavior between patient and healthy control groups (Monk et al., 2006; Phan et al., 2005; Thayer et al., 1996; Zhao et al., 2007). Even in relatively healthy samples, prior work has often separated participants into “high” and “low” anxiety groups. These studies have typically found a larger emotional response in “high” compared to “low” anxiety participants (Cook et al., 1992; Grillon et al., 1993; Smith et al., 2005). This categorical division of “high” and “low” anxiety groups however may not fully capture subtleties in the degree to which individual differences in anxiety impact the emotional response.

Therefore, more recent research has focused on differences between individuals, and has demonstrated that brain and behavioral data vary with indices of anxiety in a graded, rather than all or none, manner (Carre et al., 2013; Knight et al., 2011; Sehlmeyer et al., 2011; Wood et al., 2012). For example, functional magnetic resonance imaging (fMRI) research has shown graded changes in the blood-oxygen-level-dependent (BOLD) response that varies with the negative affect indexed by the STAI (Bishop et al., 2004, 2008; Wood et al., 2012; Vytal et al., 2014). Specifically, the BOLD response within prefrontal cortex (PFC), inferior parietal lobule (IPL), and amygdala often shows a linear relationship to STAI scores (Bishop, 2008; Etkin et al., 2004; Klumpp et al., 2011; Wood et al., 2012). Further, functional connectivity studies have found that the connectivity strength between areas that include the PFC and amygdala varies with STAI scores (Wheelock et al., 2014; Vytal et al., 2014). This prior work suggests that negative affect influences brain processes that mediate the emotional response. Prior research, however, has given limited attention to positive affect which varies independently of negative affect, and may also influence the emotional response (Brown et al., 1998; Gros et al., 2007). Thus, determining the impact of individual differences in positive and negative affectivity on BOLD fMRI and behavioral responses to threat may provide new insight into neural processes that mediate the emotional response.

Most prior work has focused on identifying linear relationships between the brain and behavior. However, non-linear brain–behavior relationships have also been observed. For example, prior emotion research has demonstrated a curvilinear relationship between emotional stimuli, psychophysiological responses, and the BOLD response (Bradley et al., 2001a, 2003; Lang et al., 1998; Wood et al., 2014). It is also well established that there is a curvilinear relationship between emotional arousal and many aspects of cognitive and behavioral performance (Dickman, 2002; Yerkes and Dodson, 1908). In addition, individuals with an “internal” locus of control show increased responses to uncontrollable threats and decreased responses to controllable threats, while those with an “external” locus of control show the opposite pattern (Bollini et al., 2004; Lundberg and Frankenhaeuser, 1978). Further, brain structure also varies with locus of control. For example, hippocampal volume increases as locus of control increases (Pruessner et al., 2005). This suggests that the fMRI signal response may also be influenced by an individual's locus of control. Taken together, these findings suggest that locus of control may also modulate brain and behavioral responses to threat. Thus, brain regions that mediate expression and regulation of emotion may show linear or non-linear relationships with locus of control and affective state.

The present study used a Pavlovian conditioning procedure to investigate the effect of individual differences in locus of control, positive affect, and negative affect on the emotional (i.e., brain and behavioral) response to predictable and unpredictable threats. Previous work has demonstrated differences in brain and behavioral responses to predictable and unpredictable threats (Dunsmoor et al., 2008; Knight et al., 2010, 2011; Wood et al., 2012). Individual differences in locus of control and affective state may influence learning-related changes in the brain and behavioral responses to threat. However, these differences may also impact the response to threat independent of learning. Therefore, the present study focused on both learning-related changes in the response to threat and the response to threat in general. Given the role of the amygdala, hippocampus, PFC, IPL, and insula in emotional processes, we hypothesized that the fMRI signal response would vary linearly or curvilinearly with locus of control, positive affect, and negative affect. Further, we hypothesized that learning-related changes in the neural response would vary (linearly and/or curvilinearly) with individual differences in locus of control, positive affect, and negative affect.

Methods

Participants

Thirty-six healthy participants were recruited from the Birmingham-Metropolitan area. All participants provided written informed consent as approved by the University of Alabama at Birmingham Institutional Review Board. Four participants were excluded from all analyses for issues affecting general data quality (e.g., failure to follow instructions, non-responsiveness, and excessive movement). Thus, 32 healthy participants were included in the final analyses (12 females, 20 males; 14 Caucasian, 18 African-American; age: $M = 18.84$, $SEM = 0.16$, range = 17–22 years).

Stimuli

CS (10 s duration) presentations consisted of two pure tones (700 Hz and 1300 Hz). One CS (CS+) co-terminated with the UCS (100-dB white noise, 0.5 s duration), while the other CS (CS−) was presented without the UCS. In addition, the UCS was also presented alone (UCS alone) on some trials. A total of 72 conditioning trials (18 s inter-trial interval) were presented across two fMRI scans (36 trials per scan; 12 CS+, 12 CS−, 12 UCS alone trials). Stimuli were presented in a pseudorandom order such that no more than two trials of any stimulus (CS+, CS−, and UCS alone) were presented consecutively. This study focused on brain and behavioral responses to the UCS (i.e., the threat) when it followed the CS+ (i.e., the CS + UCS) and when the UCS was presented alone (i.e., the UCS alone). Therefore, all analyses are related to trials in which a UCS was presented (i.e., CS + UCS and UCS alone). The response to the CS+ and CS− are important for understanding anticipatory processes that are not the focus of the present report, and will be presented separately.

Positive and Negative Affect Schedule

Participants completed the *Positive and Negative Affect Schedule* (PANAS; Watson et al., 1988). The PANAS is a self-report measure consisting of 20 questions related to positive and negative affect (10 questions assessing positive affect, 10 questions assessing