7-8-2015

Affectivity, Brain Structure and Function, and Treatment Outcomes in Cognitive Processing Therapy for Posttraumatic Stress Disorder

Wilson James Brown

University of Missouri-St. Louis, wilsonbrown@umsl.edu

Affectivity, Brain Structure and Function, and Treatment Outcomes in Cognitive
Processing Therapy for Posttraumatic Stress Disorder

Wilson J. Brown
M.A., Clinical Psychology, University of Missouri-St. Louis, 2011
B.S., Psychology: Neuroscience, Pennsylvania State University, 2008

A Dissertation Submitted to the Graduate School at the University of Missouri-St. Louis
in partial fulfillment of the requirements for the degree
Doctorate in Clinical Psychology
[June, 2015]

Advisory Committee

Steven E. Bruce, Ph.D.
Chairperson

Michael G. Griffin, Ph.D.

Kamila S. White, Ph.D.

Zoe D. Peterson, Ph.D.

Running Head: AFFECTIVITY, NEUROBIOLOGY, AND CPT

Affectivity, Brain Structure and Function, and Treatment Outcomes in Cognitive

Processing Therapy for Posttraumatic Stress Disorder

Wilson J. Brown, M.A.

University of Missouri, St. Louis

Dissertation

Submitted in Fulfillment

Of the Requirements for the Doctoral Program in Clinical Psychology

[Spring, 2015]

Abstract

Cognitive Processing Therapy (CPT) has been empirically validated as an efficacious treatment for Posttraumatic Stress Disorder (PTSD) (Resick, Nishith, Weaver, Astin, & Feuer, 2002; Cloitre, 2009). However, a deficiency of affect regulation skills may act as a barrier to the successful implementation of CPT in some cases, as CPT does not contain a module that directly addresses affectivity. The current study examined the relationship between affectivity and CPT by utilizing neuroimaging methodology to assess brain regions consistent with an affect regulation model of PTSD. Thirty-eight female interpersonal trauma survivors with PTSD received CPT, participating in assessment and scanning sessions at pre-treatment and post-treatment. The results indicated that CPT does indeed address affectivity over the course of treatment, with treatment completers reporting significantly greater positive affectivity (PA) and reduced negative affectivity (NA) post-treatment. Significant differences were also observed between the treatment completion and treatment dropout groups, such that individuals who dropped out of treatment exhibited lower levels of PA at pre-treatment. With regard to brain structure at pre-treatment, PA was found to exhibit a significant positive association with volume of the right medial frontal gyrus. The relationship between brain function and affectivity was also examined in treatment completers at pre- and post-treatment. The results and implications of this project are discussed.

Introduction

Posttraumatic Stress Disorder (PTSD) is a psychiatric condition that develops subsequent to the experience of a traumatic event involving "actual or threatened death, serious injury, or sexual violence" (DSM-5, American Psychiatric Association, 2013, p. 271). The course of PTSD is often chronic and debilitating, as evidenced by high rates of distress, diagnostic comorbidity, disability, and suicide. However, not all individuals exposed to a traumatic event will develop PTSD. Of the 81.7% of individuals who experience a traumatic event during their lifetime (Sledjeski, Speisman, & Dierker, 2008), only 15-25% of these individuals are estimated to meet diagnostic criteria for PTSD (Breslau et al., 1998; Kessler et al., 1995; Creamer, Burgess, & McFarlane, 2001). Thus, posttraumatic symptoms will remit with the passage of time for most trauma survivors. For others, PTSD symptoms persist, as lifetime prevalence rates range from 6.4-6.8% (Kessler, Chiu, Demler, Merikangas, & Walters, 2005; Pietrzak, Goldstein, Southwick, & Grant, 2011).

Psychotherapy is considered to be the first-line treatment option for the symptoms of PTSD, which include intrusion symptoms, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity (DSM-5, American Psychiatric Association, 2013). Specifically, cognitive processing therapy (CPT), a variant of cognitive behavioral therapy (CBT) for PTSD, has been empirically validated as an efficacious treatment (Resick, Nishith, Weaver, Astin, & Feuer, 2002; Cloitre, 2009). Empirical investigations have yielded data that CPT for PTSD is demonstrably more effective in providing clinically significant outcomes than treatment as usual or unstructured therapy modalities (Cloitre, 2009). In comparison to other forms of CBT for

PTSD, CPT exhibits equivalent efficacy in treating PTSD, and in contrast to prolonged exposure (PE), is additionally effective in reducing guilt related cognitions (Resick, Nishith, Weaver, Astin, & Feuer, 2002). Specific modules within CPT have demonstrated efficacy for treating PTSD as well. For example, Resick, Galovski, Uhlmansiek, et al. (2008) found that CPT, cognitive therapy, and exposure through written accounts each yielded significant symptom reductions in both PTSD and depressive symptomatology in a dismantling trial. The examination of such mechanisms has been an important step in the establishment of CPT as a preferred psychotherapy option for PTSD.

Common to variants of CBT, CPT addresses both cognitive and behavioral contributions to the manifestation of PTSD. CPT assumes PTSD to be a fear-based disorder that develops from maladaptive learning in response to exposure to threatening, traumatic stimuli (Lissek & Grillon, 2012). This exposure leads to a conditioned fear response thought responsible for PTSD symptoms. CPT recognizes that the formation of mental representations subsequent to a traumatic experience are comprised of feared stimuli, learned responses to the stimuli, and cognitive attributions about the event (Foa & Kozak, 1986; Resick & Schnicke, 1993). Processing the meaning attached to a trauma is considered to be integral to the resolution of the disorder.

However, there is an expansive body of literature that has established affect dysregulation as central to the conceptualization of PTSD, deemphasizing fear as the sole emotional component (Wolfsdorf & Zlotnick, 2001; Frewen & Lanius, 2006; Watson, O'Hara, & Stuart, 2008; Marshall-Berenz et al., 2011). This change in conceptualization is reflected by the expansion of symptom clusters from three to four in the diagnostic

criterion of PTSD in the recent iteration of the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition,* (DSM-5, American Psychiatric Association, 2013). The fourth symptom cluster, defined as "negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred" (American Psychiatric Association, 2013), is acknowledgment of the disruption of affective systems in PTSD. A deficiency of affect regulation skills may act as a barrier to the successful implementation of CPT in some cases, *as CPT does not contain a module that directly addresses affect dysregulation*. The consideration of affectivity can potentially address the limitations noted in the current CPT model.

Affectivity

According to Watson & Clark (1984), affectivity is comprised of a two factor-structure that includes negative affect (NA) and positive affect (PA). The term "affect" was adopted to classify the underlying factor structure of the general experience of mood (Watson & Tellegen, 1985). NA represents a dispositional mood dimension of subjective distress. The construct reflects extensive individual differences in self-concept and emotionality. The experience of NA is thought to subsume a variety of aversive mood states including anger, contempt, disgust, guilt, and nervousness (Watson, Clark, & Tellegen, 1988). NA is also associated with the pervasive experience of affective states of scorn, revulsion, self-dissatisfaction, a sense of rejection, and to a degree, sadness. However, at its inception, NA was considered to be unrelated to the emotion of fear (Watson & Clark, 1984). PA is defined as "pleasurable engagement with the environment" and encompasses the tendency to experience positive emotions and mood states (Watson, Clark, & Carey, 1988). PA has been considered an integral component to

the experience of depression, given that depressed individuals tend to report anhedonia and diminished positive mood and emotions (Watson, Clark, & Tellegen, 1988).

With consideration of the two-factor structure of mood, the experience of NA does not imply that an individual cannot experience positive mood or emotions and vice versa. In fact, there is an abundance of evidence that establishes NA and PA as orthogonal constructs (Watson & Tellegen, 1985; Watson, Clark, & Carey, 1988; Brown, Chorpita, & Barlow, 1998). Moreover, PA seems to be representative of an individual's level of engagement with the environment and less related to subjective levels of distress. This distinction between these two dimensions is important as it implies that both PA and NA are not simply reactive in nature. NA can still manifest in the presence of pleasurable engagement with the environment and the absence of any overt stressors (Watson & Clark, 1984).

The above conceptualization of affectivity characterizes the construct as containing both state and trait features. These characteristics are not mutually exclusive and coexist as a function of stimulus and time. For example, trait NA, often referred to as negative affectivity, represents the consistent, sustained experience of negative emotion and mood over time that occurs independent of specific cues. Conversely, state NA is an immediate emotional response that is temporally bound and related to a particular stimulus (Clark & Watson, 1991; Meriau et al., 2009). An individual's trait NA can interact with their temporal, state NA response to an immediate stressor in the environment. State NA is a natural part of the human emotional experience, but pervasive individual differences in mood and self-concept accounted for by negative affectivity can

exert a powerful influence over transient anxiety, under both neutral and stressful conditions.

The relationship between Negative Affectivity and PTSD

Symptoms within DSM-5 criterion D for PTSD include exaggerated negative beliefs and expectations, distorted cognitions that manifest notions of self-blame, and the persistent experience of a negative emotional state (e.g., fear, horror, anger, guilt or shame; American Psychiatric Association, 2013). These symptoms are characteristics of increased negative affectivity (NA). Generally speaking, NA acts as a predisposing factor for several types of anxiety disorder pathologies (Brown, Chorpita, & Barlow, 1998). PTSD, however, is unique in that it also requires the experience of a traumatic event to be diagnosed, a feature that accounts for the heterogeneous presentation of the disorder. Despite the often complex presentation of posttraumatic symptoms, NA has still been found to act as a predicting variable for the onset of PTSD (Frazier et al., 2011). For example, a study of NA in youths 17 months before the landfall of Hurricane Katrina found that preexisting NA significantly predicted the development of posttraumatic stress symptoms post-disaster (Weems et al., 2007). In a similar study, Souza and colleagues (2008) found that NA was a risk factor for the development of PTSD symptoms in United Nations peacekeepers in Haiti. They also demonstrated that NA interacts with intensively stressful situations to exacerbate PTSD symptoms, suggesting that individuals with greater NA may experience worsened posttraumatic reactions (Souza et al., 2008).

NA appears to be a pervasive risk factor for the development of PTSD, regardless of the type of trauma experienced. NA consistently predicts the development of PTSD in both men and women across different traumatic events, including a factory explosion and

physical assaults (Christiansen & Elklit, 2008). NA has also been found to predict PTSD symptoms in combat veterans who fought in Afghanistan (Rademaker et al., 2011) and Iraq (Ferrier-Auerbach et al., 2010). Brown and colleagues (2014) observed that self-reported NA was the strongest predictor of PTSD symptom severity and, specifically, re-experiencing symptoms in a sample of female interpersonal trauma survivors. Further evidence suggests that a disposition of high NA may interact with a traumatic event in such a way that predisposes an individual to the manifestation of PTSD (Pederson & Denollet, 2004).

The maintenance of PTSD symptoms is often explained as a function of avoidance by CPT (Resick & Schnicke, 1992). Indeed, it has been demonstrated that individuals experiencing high levels of trait NA exhibit the tendency to avoid threatening stimuli (Kunst, Bogaerts, & Winkel, 2011). Within the context of PTSD, high NA may cause an individual to avoid any reminder of the traumatic event. This notion is further supported by the fact that negative interpretations of intrusive memories and rumination, which are characteristics of high NA, exacerbate cognitive avoidance and depression symptom severity (Starr & Moulds, 2006). Additionally, acceptance of the traumatic event has been associated with non-pathological responses to trauma and decreased NA (Shallcross et al., 2010). High NA may impede subjective acceptance of a traumatic experience and instead facilitate further perseveration on the traumatic event. Perceptual consequences of high NA include negative self-concept and negative attentional bias, which likely influence notions of self-blame and inadequacy often experienced by survivors of traumatic events (Miller & Porter, 1983).

A factor analysis of cumulative PTSD symptoms yielded a moderate factor loading on a non-specific general distress component identified as NA (Watson, 2005). Additional findings have indicated that NA is primarily associated with the dysphoria factor of PTSD (Milanak & Berenbaum, 2009). NA has been found to predict PTSD symptom severity, such that higher levels of NA are associated with higher levels of PTSD cluster scores (Brown, Bruce, Buchholz, Mueller, Hu, & Sheline, 2014; Post, Zoellner, Youngstrom, & Feeny, 2011; Blanchard, Buckley, Hickling, & Taylor, 1998). The relationship between NA and the distress factor associated with PTSD is notable as it provides insight to symptom severity and conditions characterized by the pervasive experience of NA that are often comorbid with PTSD. For example, multiple studies have shown lifetime comorbidity rates of PTSD and Major Depressive Disorder (MDD) of approximately 50% and higher (King-Kallimanis, Gum, & Kohn, 2009; Nixon, Resick, & Nishith, 2004; Hankin, Spiro, Miller, & Kazis, 1999; Blanchard et al., 1998; Boudreaux et al., 1998; Kessler et al., 1995; Shore, Vollmer, & Tatum, 1989). PTSD also exhibits a 16.8% lifetime comorbidity rate with Generalized Anxiety Disorder (Kessler et al., 1995) and a 30.2% current comorbidity rate with Borderline Personality Disorder (Pagura et al., 2010). The substantial overlap of symptoms between these disorders is also proposed to be attributed to the common experience of NA (Clark & Watson, 1991; Mineka et al., 1998; Watson, 2005).

The relationship between Positive Affectivity and PTSD

Positive affect has rarely been examined within a PTSD conceptualization, despite DSM-5 diagnostic criteria for PTSD including symptoms of "markedly diminished interest or participation in significant activities" and "persistent inability to

experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings)" in criterion D, the affective symptom cluster (American Psychiatric Association, 2013, p. 272). However, a few studies have incorporated PA into their analyses regarding PTSD. One study demonstrated that women with PTSD reported fewer positive trait-descriptors as self-descriptive and experienced less positive affect in response to viewing pictures of themselves while listening to trait adjectives than women without PTSD (Frewen et al., 2011). Also, it has been reported that individuals with comorbid PTSD and MDD exhibit lower levels of PA than individuals solely diagnosed with PTSD, and this result is consistent with literature regarding the compounding effects of comorbid disorders (Post, Zoellner, Youngstrom, & Feeny, 2011).

Affect Regulation Theory and the psychopathology of PTSD

Healthy affect regulation is proposed to occur when an individual is able to utilize strategies prior to the full activation of their emotional response, like cognitive reappraisal (John & Gross, 2004). Cognitive reappraisal enhances the ability to construe a situation from multiple perspectives, subsequently altering the instinctual emotional response. Alternatively, research demonstrates that strategies accessed following the full activation of an emotional response, like expressive suppression, tend to be less successful in quelling negative affect (John & Gross, 2004). Simply stated, expressive suppression involves the effortful inhibition of an ongoing emotional response. The consistent usage of expressive suppression to manage emotions is thought to contribute to persistent affect dysregulation (John & Gross, 2004), as the concept is essentially a short-term avoidance strategy.

Affect dysregulation is defined as the "inability to adaptively manage or tolerate intense emotions" (Wolfsdorf & Zlotnick, 2001). This dysregulation can include the overwhelming or uncontrollable experience of anger, sadness, guilt, anxiety, or shame. Behavioral manifestations of affect dysregulation encompass angry or irritable outbursts, frequent interpersonal conflict, impulsive or risky behavior, self-injury, and suicidality (van der Kolk et al., 1996; Wolfsdorf & Zlotnick, 2001). There is evidence to suggest that affect dysregulation occurs subsequent to the experience of a traumatic event, regardless of whether the diagnostic criteria for PTSD are met (New, Fan, Murrough, et al., 2009; Dale, Carroll, Galen, et al., 2009). Also, when the diagnostic criteria for PTSD are met, affect dysregulation is typically experienced to varying degrees, regardless of trauma type (Ehring & Quack, 2010). While a traumatic event can bring about affect regulation difficulties, prior affect dysregulation can also be exacerbated by a trauma and increase risk for the development of PTSD (Cloitre et al., 2005; van der Kolk et al., 2005).

Indeed, convergent evidence indicates that individuals with PTSD experience substantial difficulty regulating affect. One study observed that veterans of combat trauma generally experience difficulty processing and regulating emotional stimuli (Wolf, Miller, & McKinney, 2009). Other research has found that traumatized individuals have increased difficulty with the ability to identify and label their own emotional states (i.e., alexithymia) as compared to non-traumatized controls (Cloitre, Scarvalone, & Difede, 1997; Monson et al., 2004; McLean, Toner, Jackson, Desrocher, & Stuckless, 2006). Traumatized individuals also exhibit a greater fear of negative emotions and more difficulty tolerating and regulating these emotions in comparison to non-traumatized control subjects (Briere & Rickards, 2007; Tull, Jakupcak, McFadden, & Roemer, 2007).

A study by van der Kolk and colleagues (1996) found a strong positive relationship between PTSD and affect dysregulation. This study also demonstrated that individuals with current PTSD tend to report more difficulties modulating affect than individuals with a history of PTSD or trauma-exposed control subjects without a history of PTSD. However, individuals with a history of PTSD also continued to report disruptions of affect as well compared to healthy controls, suggesting the persistence of affect dysregulation in the absence of current PTSD symptoms (van der Kolk et al., 1996).

Research regarding affect dysregulation and PTSD has led to the use of neuroimaging techniques as a neurobiological indicator of cognitive and emotional disruption. Many of the same brain areas implicated by the fear circuitry model of PTSD, including the amygdala, hippocampus, and medial prefrontal cortex (mPFC), demonstrate dysregulation in response to affective stimuli unrelated to feared reminders of the traumatic event. For example, in one study using Positron Emission Tomography (PET technology), individuals with PTSD exhibited decreased blood flow to the orbitofrontal cortex, anterior cingulate (ACC), mPFC, left hippocampus, and the fusiform gyrus during retrieval of emotionally valenced word pairs in comparison to healthy controls. Blood flow unexpectedly increased to the posterior cingulate, left inferior parietal cortex, and left middle frontal gyrus, suggesting a disruption of normal emotion regulation in this sample (Bremner et al., 2003).

Several recent functional magnetic resonance imaging (fMRI) studies corroborate findings in these brain regions in response to emotional stimuli. In addition to its function of perceiving threatening stimuli, the amygdala influences the generation of sustained emotional responses (Davis, 1992; Davis & Whalen, 2001; Liberzon et al., 1999), which

theoretically can be considered the "source" of dysregulated affect. Convergent evidence indicates that the amygdala is hyperresponsive to both emotional and threat-related stimuli in individuals with PTSD (Liberzon, Britton, & Phan, 2003; Armony, Corbo, Clement, & Brunet, 2005; Bryant et al., 2008). However, in comparison to other disorders of fear circuitry, hyperactivation of the amygdala was found more frequently in social anxiety disorder and specific phobia than in PTSD (Etkin & Wager, 2007). This finding suggests that fear circuitry is less integral to the conceptualization of PTSD than other disorders of fear.

The mPFC, a central component of fear circuitry, exhibits consistent hypoactivation in response to threat-related stimuli in individuals with PTSD (Britton et al., 2005). However, in response to emotional stimuli, the mPFC demonstrates hyperactivation coupled with hypoactivation of the ACC, representing another neural substrate of dysregulated affect within PTSD (Garfinkel & Liberzon, 2009). Findings regarding the ACC in individuals with PTSD indicate decreased activation in this area in response to script driven imagery symptom provocation. Consistent across both traumatic and non-traumatic emotional state paradigms, these results suggest that activation in this brain region is not specific to just traumatic stimuli (Lanius et al., 2001; Lanius, Hopper & Menon, 2003). Other studies report robust findings of decreased blood oxygenation level dependent (BOLD) signal in the ACC in response to nontraumatic emotional stimuli, further implicating dysregulated affect as a component of PTSD neurocircuitry (Hsu, Chong, Yang, & Yen, 2002; Shin et al., 2001). These findings make sense regarding dysregulated affect within PTSD, given that the ACC is believed to be important for cognitive control of emotion and the interpretation of emotionally relevant

stimuli (Bush, Luu, & Posner, 2000). Decreased activation in this area during a task involving emotion regulation may represent a biomarker for the negative perception of neutral emotional stimuli.

The insula, a vast cortical area that maintains connections with the amygdala, also appears to be contributing to dysregulated affect within PTSD. Among the several proposed functions of the insula, it is hypothesized to be important in the processing and experience of affect (Wager & Barret, 2004). Individuals with PTSD tend to exhibit increased insula activation in comparison to control subjects when presented with trauma script related imagery (Hopper, Frewen, van der Kolk, & Lanius, 2007).

Taken together, fMRI research studies on emotion regulation within PTSD suggest that fear circuitry alone is too simplistic to capture the complex emotional presentation of the disorder (Diekhof, Geier, Falkai, & Gruber, 2011). Additionally, brain regions implicated in PTSD pathology have also been found to be independently associated with the experience of affectivity. Affective inductions typically elicit the recruitment of the mPFC (Beauregard et al., 2001, 2004; Levesque et al., 2003; Kalisch et al., 2005; Matsumoto et al., 2006), the ACC (Ochsner, Bunge, Gross, & Gabrieli, 2002; Anderson & Phelps, 2002; Schaefer et al., 2002; Pissiota et al., 2003; Whittle, Allen, Lubman & Yucel, 2006; Banks, Eddy, Angstadt, Nathan, & Phan, 2007), the amygdala (Barrett, Bliss-Moreau, Duncan, Rauch, & Wright, 2007; Cremers et al., 2009), and the insula (Wager & Barret, 2004).

Similar to fMRI studies of PTSD and emotion regulation, magnetic resonance imaging (MRI) studies of PTSD have also identified structural abnormalities in areas thought to be important for the processing of emotion. In participants with PTSD,

decreased gray matter volumes have been observed in the ACC (Kasai et al., 2008;

Herringa et al., 2012), amygdala (Rogers et al., 2009), hippocampus (Karl et al., 2006;

Woon & Hedges, 2011; Zhang et al., 2012), insula (Chen et al., 2006; Kasai et al., 2008;

Herringa et al., 2012), and caudate nucleus (Herringa et al., 2012). Other structures such

as the hypothalamus (Herringa et al., 2012), thalamus, and globus pallidus have also

demonstrated decreased gray matter volumes in trauma exposed individuals (Shucard et

al., 2012). In contrast to fMRI findings, the relationship between affect dysregulation and

structural abnormalities within these areas has yet to be explored.

Affectivity and CPT

Generally speaking, cognitive and behavioral therapies require basic level

cognitive processes to be intact to facilitate treatment gains. Additionally, a considerable

amount of cognitive insight is often an important indicator of treatment effectiveness

(Beck, Baruch, Balter, Steer, & Warman, 2004; Holtforth, Castonguay, Boswell, Wilson,

et al., 2007). Elements of cognition and affect are integrally related (Duncan & Barrett,

2007; Forgas, 2008), as a mild to moderate presence of NA is posited to elicit adaptive

cognition functioning (Bless & Fiedler, 2006; Forgas, 2007). However, there is a

substantial amount of evidence suggesting that increasing amounts of NA actually disrupt

these preconditions for attention, processing, and memory, thus presenting an additional

challenge for CPT-oriented clinicians.

Attention

NA has been found to narrow the attentional field and induce distractibility

(Derryberry & Tucker, 1994; Fredrickson & Brannigan, 2005; Lazar, Kaplan, Sternberg,

& Lubow, 2012). Additional findings support this notion and suggest that NA moderates

selective attention, restricting focus to threatening stimuli and magnifying the inhibitive

effect of salient distracters (Frischen, Eastwood, & Smilek, 2008; Vermeulen, 2010). NA

also undermines the ability of these neural control processes to accurately determine task-

relevant information from distracters in the presence of affective stimuli (Melcher, Born,

& Gruber, 2011). A continuous focus on threatening stimuli can become reinforced by

the introduction of a traumatic event, forming a resistant attentional pattern and

manifesting avoidant behavioral strategies often observed in individuals diagnosed with

PTSD. A constricted focus on specific stimuli also interferes with initial information

processing, likely manifesting several types of cognitive distortions, including filtering,

overgeneralization, and polarized thinking. Moreover, high levels of NA could

potentially disrupt a client's ability to broaden their focus to consider beneficial cognitive

alternatives. In addition to a constrained focus, excessive NA can also influence the

detection of relevant stimuli in the current environment. For example, NA has been found

to facilitate inattention to relevant stimuli in the current context caused by excessive

worry, avoidance and rumination (Borkovec & Sharpless, 2004). These cognitive

processes are typically associated with the experience of NA and notoriously deplete

available cognitive resources (Derakshan & Eyesenck, 1998). Disengaging a client from

these ingrained processes may be quite challenging through the utilization of cognitive

techniques, considering the client's already exhausted cognitive system.

<u>Cognitive Processing</u>

　　　Individuals with high trait NA also tend to adopt an analytical cognitive style

when processing information (Bless & Schwarz, 1999; Vermeulen, Corneille, & Luminet,

2007). Fiedler's affect-cognition model (2001) suggests an association between NA and

an accommodative processing style, a rigid approach that typically preserves the initial interpretation of novel information. Cognitive models of PTSD often recognize overaccommodated thoughts as problematic (Sobel, Resick, & Rabalais, 2009), which can lead to perseveration. Combined with an attenuated focus, it is understandable how a systematic processing approach to overaccomodated cognitions might exacerbate rumination and increase the probability of cognitive distortions. The introduction of analytical cognitive skills to clients with high NA may appear redundant and invalidate their emotional experience further, given their pre-existing hyperfocus on their own thoughts. Ignored by excessive analysis, the unprocessed affect is likely to persist as a significant contributor to emotional distress.

Memory

Higher levels of NA enhance the recall ability of autobiographical memory (Forgas, 2010). However, the recall of such memories often exhibits emotional congruence. As such, high NA individuals tend to retrieve significantly more emotional memories with a negative valence than individuals low in NA (MacLeod & Campbell, 1992). Considering counterfactuals about past situations may be consistently difficult for these clients, as the negative aspects of a situation are more easily recalled per the availability heuristic. Individuals reporting higher levels of NA also tend to report increased rumination regarding recalled autobiographical memories (Kross, Davidson, Weber, & Ochsner, 2009). Thus, high NA individuals diagnosed with PTSD may tend to dwell extensively on their history of traumatic events, further exacerbating symptomatology and subjective distress. Giving an appropriate amount of consideration to the positive aspects of a situation may be particularly challenging for these clients

during CPT. NA also appears to tax working memory. Prior research has demonstrated that individuals high in NA possess less cognitive resources to complete a primary working memory task (Derakshan & Eyesenck, 1998; Richards, French, Keogh, & Carter, 2000). There have been mixed results regarding the relationship between NA and short-term memory, from which no definitive conclusions can be drawn (Shackman, Sarinopoulos, Maxwell, Pizzagalli, Davidson, & Lavric, 2006).

Interpretation

Higher order cognitive processes, like interpretation, judgment, executive decision-making, and reasoning are also subjected to the influence of NA (Blanchette & Richards, 2010). Individuals high in NA tend to interpret ambiguous or neutral stimuli as threatening and view themselves at greater risk for negative occurrences (Stopa & Clark, 2000; Huppert, Pasupuleti, Foa, & Mathews, 2007). This type of interpretative bias can be compounded by the experience of a traumatic event, which may explain the manifestation of certain types of PTSD symptoms, like sustained irritability, constant surveillance of the environment, increased sensitivity to stimuli, and excessive physiological arousal. NA also interferes with an individual's ability to formulate accurate judgments about ambiguous future events. Individuals high in NA tend to overestimate the likelihood of negative events in comparison to control subjects, and these results cannot be simply attributed to semantic priming (Constans, 2001; Forgas, 2006). This probability overestimation is problematic after the occurrence of a traumatic event, and may fuel resistance in CPT to discounting the possibility that such an event could ever happen again. Moreover, this increased personal experience of negative events certainly undermines examination of "realistic" probability. Individuals high in NA also

exhibit the propensity to engage in emotional reasoning which is often the basis of their judgments (Clore & Huntsinger, 2007). As noted by Blanchette & Richards (2010), pervasive NA likely results in deviations from accurate, realistic judgments.

Decision-making

Decision-making is similarly impacted by the experience of NA. Research on this topic has traditionally been conducted using paradigms where subjects choose between options that differ in risk and consequence. Individuals high in NA have been found to avoid aversive options in comparison to individuals low in NA (Maner & Gerend, 2007; Vastfjall, Peters, & Slovic, 2008). Since the potential exists for their already heightened NA to increase as a result of a risky decision, these individuals are likely to avoid such scenarios. Thus, a therapy client may decide that the potential evocation of state NA through exposure is undesirable and dangerous. The decision to avoid aversive options by high NA individuals may directly contribute to the avoidant symptom cluster in the presence of PTSD.

Reasoning

In addition to decision-making, deductive reasoning is also inhibited by persistent NA. A study of verbal reasoning concluded that high NA individuals exhibited more impairments of logic than individuals with low NA. The differences between these two groups were further exacerbated when task demands were increased (Derakshan & Eyesenck, 1998). As negative emotionality appears to disrupt rational thought, emotional reasoning (i.e., forming judgments based on feelings) should not be discounted altogether. Recent findings suggest that victims of sexual abuse exhibit advantages in reasoning regarding abuse-related content (Blanchette & Richards, 2010). Thus,

emotional reasoning demonstrates applicability in certain trauma-related contexts, despite being labeled as a cognitive distortion variant by CPT.

Cognitive Regulation of Emotion

The impact of NA on the cognitive regulation of emotion is a legitimate barrier to the application of CPT principles and may be amplified in individuals with PTSD. Indeed, NA has exhibited an inhibitive influence over cognitive control in response to affective priming using threat-related stimuli (Blair et al., 2007; Melcher et al., 2011; Melcher, Obst, Mann, Paulus, & Gruber, 2012). Other research demonstrates that NA promotes cognitive inhibition, particularly in the presence of emotionally loaded conditions like sadness (Ramon, Geva, & Goldstein, 2011). The cognitive inhibition resulting from elevations in NA further limits the self-regulation of emotions (Magno, 2010; Bradley et al., 2011). It had been previously thought that individual differences in affect may lead to different strategies of cognitive control, with the adoption of a reactive control strategy in the presence of chronic NA (Braver et al., 2007). However, an EEG study of brain activity during a neurocognitive task that assessed proactive and reactive cognitive control revealed that trait NA weakened both types of strategies (West, Choi, & Travers, 2010). Elevated levels of NA have also been found to interfere with performance on executive control tasks (Moritz et al., 2002). Cognitive control is an important component of CPT as clients are expected to react to intrusions of negative thoughts by simultaneously accessing realistic alternative cognitions. A failure to account for individual differences in NA may result in an unexpected attenuation of cognitive control, leaving a client frustrated when attempting to continuously respond to negative, self-critical cognitions.

With the consideration of the numerous elements of cognition disrupted by NA, it is not surprising that a greater frequency of cognitive errors is often associated with higher levels of NA (Fetterman & Robinson, 2011). Impairments in cognition resulting from affect dysregulation cannot simply be rectified by the rigid application of cognitive and behavioral techniques. As clients may already be experiencing doubts about their ability to effectively evaluate a situation or their own emotional experience, these strategies may be perceived as initially threatening and subsequently frustrating to clients with persistent NA. This has yet to be investigated in CPT for PTSD, however, leaving room for speculation. Evidence consistent with this notion demonstrates that individuals high in NA tend to be more introspective and dwell upon and magnify mistakes, frustrations, disappointments, and threats (Glaser et al., 2006). Cognitive impairments from NA could be complicated further in the presence of PTSD, as preexisting belief structures are often drastically altered by the experience of a traumatic event. Routine cognitive errors are likely to reinforce negative alterations in cognition caused by the traumatic event, including self-critical ruminations about control and self-efficacy. Moreover, further inhibition of higher order cognitive processes that typically regulate negative emotions is likely to increase the salience of emotional distress in client experiences. Clients with elevated NA ultimately need a way to regulate this distress to subsequently engage in effective cognitive restructuring or exposure techniques.

Although adults are assumed to have developed emotion regulation skills as a product of aging and emotional maturity (Linehan, 1993), the intense emotions associated with a traumatic event can disrupt this development, especially if the trauma occurs at an early age. Affect regulation skills are often among the first skills taught to children who

have experienced a traumatic event, and these skills are automatically introduced prior to

the use of cognitive restructuring or exposure techniques. The rationale for focusing on

affect regulation, as noted by Cohen, Mannarino, & Deblinger (2006), is that the

experience of trauma often coincides with the experience of painful negative emotions.

More often than not, these children fear that they will be overwhelmed by this emotional

experience, which directly influences avoidance. Affective expression and modulation

grants these children the ability to cope with these painful emotions without resorting to

avoidant strategies. Thus, this treatment model recognizes that affect dysregulation

represents a risk factor for the development of PTSD in the presence of a traumatic

experience and serves to maintain PTSD symptomatology. Over time, it can be assumed

that a portion of these children will develop healthy emotion regulation techniques that

act as a protective factor or cause their symptomatology to remit. Though, those who

never develop those skills may become adults who continue to struggle with complex

PTSD or possibly, chronic personality disorders associated with trauma. Granted, not all

cases of PTSD begin during childhood and adolescence. However, NA still acts as a risk

and maintenance factor for PTSD in adults. So, it can be assumed that not all adults who

have not experienced a traumatic event possess the capacity to efficiently cope with

dysregulated affect if a trauma occurs. It is more likely that some adult clients will

possess the same fear of painful emotions resulting from a traumatic experience, leading

to subsequent avoidance. This makes sense, as NA is negatively associated with an

individual's tendency to confront psychological stimuli and analyze their own thoughts,

feelings, and behaviors (Tull et al., 2007). Proceeding with CPT after considering the

presence or absence of affect regulation skills may provide more favorable treatment outcomes in adults with PTSD.

The Current Study

Published results from randomized controlled trials (RCT) of CPT generally demonstrate high rates of treatment completion amongst interpersonal trauma survivors (Nishith, Resick, & Griffin, 2002; Resick, Nishith, et al., 2002). The experience of interpersonal trauma (i.e., traumatic event in which an individual is assaulted or violated by another person that may be known or unknown to the trauma survivor) can manifest a myriad of emotions other than fear including guilt, sadness, shame, disgust, and anger (Lily & Valdez, 2012), component emotions of NA. Survivors of interpersonal trauma tend to experience more emotion dysregulation in comparison to survivors of other types of trauma (Ehring & Quack, 2010). It remains unknown if CPT principles sufficiently address psychological and neurobiological dimensions of affectivity in survivors of interpersonal trauma diagnosed with PTSD. Additionally, the question of whether affectivity impacts the application of CPT in this population has yet to be explored. While benefits of an affective module have been demonstrated within a CPT protocol for a small group of survivors of child sexual abuse (House, 2006), the conclusions that can be drawn from these findings about the need for an affective module in the larger population of interpersonal trauma survivors are limited. This study attempts to delineate the relationships between self-reported affectivity, neurobiological dimensions related to affect, and CPT treatment completion.

Hypotheses:

        The current study examined the relationship between affectivity and CPT, utilizing neuroimaging methodologies to assess affect regulation within interpersonal trauma survivors recruited from a community setting. Neuroimaging methodologies have demonstrated promise as an observational strategy to gauge affect regulation in research settings (Diekhof, Geier, Falkai, & Gruber, 2011).

1)   PA and NA will be significant clinical predictors of treatment completion, such that high NA and low PA will be associated with subjects that dropout from CPT.

2)   Gray matter volumes in regions of interest (ROI) associated with affect regulation will be significantly different between the treatment completion and treatment dropout group. Participants who dropped out of treatment are expected to have reduced gray matter volumes in comparison to the treatment completion group. These regions include the amygdala, ACC, prefrontal cortex, insula, and hippocampus (Figure 2).

3)   A correlational analysis will be performed to assess the relationship between self-reported affectivity and the volumes of ROIs. NA is expected to exhibit an inverse relationship with gray matter volumes, such that higher scores of NA predict reduced gray matter volumes. PA is expected to exhibit a positive relationship with gray matter volumes, such that lower scores of PA predict reduced gray matter volumes.

4)   Self-reported affectivity will significantly change across CPT. PA is hypothesized to increase and NA is hypothesized to decrease. Exploratory analyses will also be conducted within the treatment completion group to examine the potential effects of NA and PA on other treatment variables influenced by CPT.

5)   Brain activation in the aforementioned ROIs associated with affect regulation has been shown to normalize across CPT treatment (Bruce et al., in preparation). A multiple regression analysis will be performed to assess the influence of self-reported affectivity on such changes during the presentation of fearful faces within a task of implicit emotional conflict.

Method

Participants

The intent-to-treat (ITT) sample was comprised of 38 women, ages 18-55 ($M =$ 30.8 years, $SD =$9.2 years), recruited at the Center for Trauma Recovery (CTR), a multi-disciplinary center at the University of Missouri-St. Louis, and Washington University of St. Louis. The ITT sample was relatively diverse, with 60.5% of the participants identifying as Caucasian, 23.7% as African American, 2.6% as Hispanic, and 5.2% identifying as "Other." Race was not identified for three (7.9%) participants. The sample completed, on average, 15.3 years ($SD = 2.2$ years) of education. Of the women included in this sample, 24 (63.1%) completed the full Cognitive Processing Therapy (CPT) protocol, 9 (23.7%) received partial treatment but terminated therapy prior to completion, and 5 (13.2%) never returned for the first session of therapy after the initial assessment.

Participants who dropped out of treatment completed an average of 3.78 sessions ($SD =$ 2.49), with a range of 2 sessions to 8 sessions. The modal average was 2 sessions, with 5 of 9 participants dropping out after completing session 2, which happens to be the review of the impact statement in CPT.

Participants were included in the ITT group if they experienced an interpersonal trauma (i.e., physical or sexual assault, molestation, or intimate partner violence) in childhood or adulthood and met the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*; American Psychiatric Association, 1994) criteria for Posttraumatic Stress Disorder (PTSD) at the time of the initial assessment, with the interpersonal trauma reported as their criterion A event. All participants were at least one month post-trauma of their most recent traumatic event. Other comorbid conditions were permitted for this study as long at PTSD was the primary diagnosis. Approximately 44.7% ($N = 17$) of the ITT sample was diagnosed with at least one current comorbid Axis I condition, with 21.1% ($N = 8$) of the sample reporting multiple comorbid conditions. With regard to commonly reported comorbidities in the ITT group, 23.7% ($N = 9$) reported comorbid depression, 23.7% ($N = 9$) reported comorbid specific phobia, 15.8% ($N = 6$) reported comorbid social phobia, 10.5% ($N = 4$) reported comorbid panic disorder, 5.3% ($N = 2$) reported comorbid agoraphobia without a history of panic, and 5.3% ($N = 2$) reported comorbid obsessive-compulsive disorder.

Baseline data from the ITT sample was compared to that of a sample of healthy controls. The control sample was comprised of 15 women, ages 18-55 ($M = 33.4$ years, $SD = 11.4$ years), recruited at the same locations as the ITT sample. Approximately 86.7% of participants identified as Caucasian, and the remaining 13.3% identified as

African American. The control sample completed, on average, 17.3 years ($SD = 3.1$ years) of education. Regarding demographic variables, age was not significantly different ($F(1, 50) = 0.75$, $p = .39$, partial $\eta^2 = .02$) between the ITT and control groups. A chi-squared analysis also indicated that race was not significantly different (X^2 (3, $n = 50$) = 2.66, $p = .45$) between the two groups. However, there was a significant difference in years of education ($F(1, 47) = 6.19$, $p < .05$, partial $\eta^2 = .12$). On average, the control group had completed more years of education than the ITT group.

Exclusion criteria for the study included illiteracy, the inability to give informed consent or speak English, active suicidality, Axis II conditions, current alcohol or substance abuse disorder, schizophrenia or other psychotic disorder, bipolar disorder, current use of psychotropic prescription or nonprescription drugs or herbals (e.g. hypericum), primary neurological disorders, and MRI contraindications (e.g., foreign metallic implants, pacemaker). In addition, participants were excluded from the sample if they were involved in a currently abusive relationship or being stalked. Sample characteristics are presented in Table 1.

Measures

Clinician-Administered PTSD Scale (CAPS; Blake, 1995)

The CAPS is a clinician-administered, 30-item scale that assesses validity, severity, and improvement of PTSD symptoms as identified by the DSM-IV-TR over a time period of interest (e.g., past week, past month, lifetime). These symptoms are classified into three groups: re-experiencing (Criterion B), avoidance/numbing (Criterion C), and arousal (Criterion D). The 1-month and lifetime time periods for each individual symptom were assessed in the current study. The CAPS also contains separate 5-point

frequency and intensity rating scales (0-4) for each symptom. The CAPS has demonstrated high internal consistency (α's = .92 - .99; Blake, 1995) and is an accepted, valid measure of PTSD symptoms and diagnosis. Internal consistency for the CAPS was high in the current sample (α = .87).

Structured Clinical Interview for DSM-IV-Patient Version (SCID-IV-P; First, 1997)

The SCID-IV-P is a semi-structured diagnostic interview that is administered in both clinical and research settings. The interview is designed to assess all primary Axis I disorders and is often used as an essential diagnostic tool. In this study, the SCID assessed the presence of Axis I comorbidity with PTSD. Additionally, the psychotic screen of the SCID was used for participant selection and exclusion. Symptoms are rated using a categorical system derived from the diagnostic criterion of disorders as outlined by the DSM-IV-TR. The SCID possesses fair diagnostic reliability ($\kappa = 0.61\text{-}0.83$) (Lobbestael, Leurgans, & Arntz, 2011).

Positive and Negative Affect Schedule-Expanded Form (PANAS-X; Watson & Clark, 1994)

The PANAS-X, a 60-item self-report questionnaire, measures the two predominant dimensions of self-reported mood, PA and NA. Individual items are rated on a scale from 1 to 5, with higher scores indicating a greater extent of experiencing a particular feeling or emotion. Respondents are instructed to reference "the past few weeks" when endorsing items to identify consistent affective experiences. The PANAS-X displays excellent convergent and discriminant validity and exhibits high internal consistency (Cronbach's coefficient alpha) for both the PA subscale (α = .83-.90) and the NA subscale (α = .85-.90). High internal consistency was observed for both the NA (α = .86) and PA (α = .83) subscales in the current sample.

Posttraumatic Stress Diagnostic Scale (PDS; Foa, 1995; Foa, Cashman, Jaycox, & Perry, 1997)

The PDS is a brief screening and diagnostic instrument that assesses trauma history and the presence and severity of PTSD symptoms based on the DSM-IV-TR criteria. It is a clinically-oriented, 17-item self-report instrument designed for brief administration and scoring. The frequency of each symptom is rated on a scale of 0 to 3, with higher scores indicating a greater frequency of symptoms. The PDS is appropriate for a wide variety of traumatic events and demonstrates high internal consistency (Cronbach's coefficient alpha= .92) and test-retest reliability (kappa= .74 for PTSD diagnosis; kappa= .83 for total PDS score). Internal consistency for total PDS score was high in the current sample (α = .88).

Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996)

The BDI-II is a self-report measure designed to assess the subjective experience of current depressive symptoms. It contains 21 items that assess symptoms consistent with the DSM-IV diagnostic conceptualization of MDD. Each individual item is rated on a scale of 0 to 3, with higher scores indicating greater perceived severity of symptoms. The BDI-II has demonstrated robust reliability and validity in diverse outpatient samples (Cronbach's coefficient alpha= .91) (Beck et al., 1996). Internal consistency for the total BDI score was high in the current sample (α = .90).

Length of Battery

The length of the baseline assessment was approximately 150 to 180 minutes depending on the participant's trauma history and extent of Axis I psychopathology, with an additional 90 minutes to complete the neuroimaging assessment. The length of the final assessment battery was approximately 60 to 90 minutes, as lifetime trauma history

and psychopathology were already assessed. The final neuroimaging assessment was, again, approximately 90 minutes in length as the protocol is identical to that of the baseline scan.

<u>Training and Reliability of Interviewers</u>

Interviews were conducted by trained, experienced clinical graduate students. Interviewers remained in frequent contact with the Principal Investigators, Dr. Yvette Sheline and Dr. Steven Bruce, to maintain uniform assessment criteria and to resolve diagnostic and other rating issues. Interviewers typically met weekly with the Principal Investigators to review any new assessments conducted to maximize reliability. Data underwent a thorough clerical editing process before keyed into the database.

To achieve and maintain calibration among interviewers, all interviews were audiotaped. Audiotapes were randomly selected every 2 months and coded by independent reviewers. For each interviewer, the median reliability from the internal consistency coefficients for all possible pairs of interviews was calculated, allowing the identification of discordant interviewer ratings. All interviewer reliability analyses were above 0.80, the minimum reliability threshold established for quality control at the beginning of the study.

Image Acquisition

Cognitive fMRI studies generally yield blood oxygenated level-dependent (BOLD) responses that are small in magnitude and distributed across the brain. The change in BOLD signal as a result of affective inductions may be small in magnitude as well, presenting an additional technical challenge. To detect these small changes, fMRI methods optimized for high sensitivity to the BOLD fMRI signal with contiguous whole

brain coverage were utilized. These methods included the use of optimized voxel sizes and a custom echo planar imaging (EPI) pulse sequence that has approximately 20% higher signal-noise-ratio (SNR) than the vendor pulse sequence at equivalent acquisition settings.

All scanning was performed on the 3.0 T Siemens TRIO system at the Research Imaging Center of the Mallinckrodt Institute of Radiology at the Washington University Medical School. Each scanning session included acquisition of structural and functional data. Structural imaging was used for definitive atlas registration. A 3D T2-weighted turbo spin echo (TSE) variable flip angle (VFL) structural image was also used in the fMRI atlas registration procedure.

Functional Magnetic Resonance Imaging (fMRI)

The functional images were collected in runs using an asymmetric spin-echo sequence (TE = 27ms, FOV = 384 mm, flip angle = 90°) sensitive to BOLD contrast (T$_2$* weighting). Thirty-six contiguous, 4.0 mm thick slices were acquired parallel to the anterior-posterior commissure plane (4.0 mm approximately isotropic voxels) providing complete brain coverage. Each fMRI run included 180 volumes continuously acquired at a repetition time (TR) of 2.2 seconds.

Statistical Parametric Mapping software, version 12 (SPM12; Wellcome Department of Cognitive Neurology, London, UK) was used to prepare functional images for analysis. To account for head motion, images were aligned to a subject-specific mean fMRI image. Images were then slice time corrected to account for interslice temporal differences. Next, the coregistration of each subject's structural and functional image was performed. The coregistered structural images were segmented into gray matter, white

matter, cerebrospinal fluid, bone, soft tissue, and air/background using the New Segment

tool for SPM12 (Ashburner & Friston, 2005). MRI data was then normalized to standard

Montreal Neurological Institute (MNI) space utilizing deformation fields. Normalized

images were filtered with an 8mm full width at half maximum (FWHM) Gaussian kernel.

Movement outliers were identified using the Artifact Detection Tool (ART; Whitfield-

Gabrieli, 2011) software package. ROIs were specified a priori based on previous

literature regarding the neurobiological correlates of affectivity and emotion regulation in

PTSD (Figure 2). The Wake Forest University PickAtlas toolbox for SPM12 was utilized

to define these regions as specified by Tzourio-Mazoyer and colleagues (2002).

PsyScope Presentation

During the neuroimaging assessment, affective inductions were presented using

PsyScope on an iMac Macintosh computer. The images were projected onto a computer

screen behind the subject's head within the imaging chamber. The screen was viewed

using a mirror attached to the head coil positioned directly above the subject's face. A

fiber-optic, light-sensitive key press interfaced with the PsyScope button box was utilized

to record the subject's behavioral performance during the task.

Conflict Task Description

The conflict task involved implicit emotional conflict which can be used to

examine emotional dysregulation experienced by participants in response to emotional

stimuli. Prior to the conflict task, there was a 30 second period during which the

participant fixated their vision on a crosshair. After the fixation period, the affective

inductions were presented. The affective inductions were comprised of stimuli that

display four pictures, with two faces and two houses arranged in vertical and horizontal

pairs. All pictures were black and white photographs presented on a gray background

through a mirror taken from Paul Ekman's series adapted by D. Perrett, courtesy of John

Morris and colleagues. The task required the subject to match either faces or houses in

which flanking distracters were either faces or houses (Fales et al., 2008). Ten faces

displaying negative emotion, ten neutral faces, and 20 houses unfamiliar to the subjects

were used. In different sequences of trials, subjects were instructed to attend to either just

the horizontal or just the vertical pair of stimuli. Subjects then indicated whether these

stimuli were the same or different by pressing corresponding buttons with the right hand

while ignoring the other stimulus pair. All four sequences included 52 trials for a total of

208 events. Following the conflict task was another 30 seconds of crosshair fixation. Two

conditions within the conflict task were of particular interest in relation to the

manifestation of PTSD following an interpersonal trauma: the attention to fearful faces

(AF) and the ignoring of fearful faces (IF). Two comparison conditions were also

produced by the task: the attention to neutral faces (AN) and the ignoring of neutral faces

(IN)

Structural Magnetic Resonance Imaging

Structural MRI scans were collected from all participants during the baseline

assessment. The structural images were acquired with 1x1x1 voxel resolution using a

sagittal 3-D MPRAGE sequence (TE = 3.13 ms, FOV = 256 mm, flip angle = 8°, TI =

1000 ms) with T1-weighting. Each high-resolution structural image included 176 slices

continuously acquired at a repetition time (TR) of 2.4 seconds.

Voxel-Based Morphometry version 8 (VBM8) toolbox (http://dbm.neuro.uni---

jena.de/vbm8/) within SPM12 was used to prepare structural images for analysis. Once

acquired, structural images were aligned to a subject-specific mean MRI image. Images

were then normalized to a template space and segmented into gray matter, white matter, and cerebrospinal fluid. A quality check was then conducted to ensure the accuracy of the segmentation and normalization procedures. Normalized images were filtered with a 12mm full width at half maximum (FWHM) Gaussian kernel. Similar to the functional analysis, ROIs included the amygdala, ACC, prefrontal cortex, insula and hippocampus. The Wake Forest University PickAtlas toolbox for SPM12 was utilized to define these regions as specified by Tzourio-Mazoyer and colleagues (2002).

Therapists and Treatment Overview

Therapists included four women and three men with master's degrees or doctorates in clinical psychology. All therapists were trained in the administration of cognitive behavioral therapy. The assignment of clients was balanced so that therapist caseloads would be relatively equal throughout the study. All therapy sessions were videotaped for review by the primary investigator. Monitoring of individual cases occurred at weekly group supervision sessions attended by all therapists and directed by the primary investigator.

After completion of the initial assessment, all participants were immediately assigned to a therapist for CPT. While some of the therapists also acted as interviewers for the study, participants were assigned to a separate individual for the treatment phase to eliminate assessor bias. Once participants completed treatment, they were, once again, evaluated by an independent assessor. Therapy consisted of 12 weekly sessions, each 60 minutes in length. Treatment was scheduled to be completed within 12 weeks, but additional sessions were allowed if needed to complete the protocol.

CPT

CPT was administered in accordance with the manual updated to include more coherent wording on all therapy worksheets (Resick & Schnicke, 1993; Resick, 2001). CPT facilitates the identification and challenging of cognitive distortions embedded within an individual's belief structure of the self, others, and the world. The experience of a traumatic event is believed to alter this belief structure, manifesting cognitive distortions that maintain PTSD symptoms. CPT is delivered in a highly structured format intended to standardize the administration of the protocol. Session 1 begins with psychoeducation about the nature and symptoms of PTSD, rationale for CPT, and the assignment of an impact statement which requires the client to subjectively describe the meaning of their trauma. During the second session, clients read and discuss their impact statement and are introduced to the connection between events, thoughts, and emotions. Session 3 introduces the trauma narrative, an assignment which requires the client to write a descriptive account of their traumatic experience. At the beginning of session 4, the client reads the account to the therapist. The remainder of the session is allotted to the identification and challenging of cognitive distortions within the account, allowing the client to process their trauma. Socratic questioning is also used within this session to challenge notions of self-blame. The client is asked to re-write their account with increased detail for the following session. This account is processed in sessions 5 and 6 as challenging and changing cognitive distortions becomes the focus of therapy. Clients are taught to recognize their negative automatic thoughts and identify recurrent core beliefs that manifest such thoughts.

Beginning with session 7, clients are challenged to generate balanced alternative thoughts in response to their dysfunctional cognitions. Session homework consists of

advanced worksheets designed to assist clients in practicing the development of these statements. Sessions 7 through 12 address overgeneralized core beliefs about topics including safety, trust, power/control, intimacy, and self-esteem. Clients are asked to rewrite their impact statement at the conclusion of session 11, and this impact statement is compared to their original statement in the final session. This exercise provides an excellent opportunity to review treatment progress and discuss topics on which the client might continue to work.

Procedure

During a brief telephone screen, a graduate research assistant explained the project to all potential participants. Eligible participants were then scheduled for the initial assessment. During the baseline assessment, informed consent was obtained, and participants were informed that eligibility for treatment would be determined. This assessment began with administration of the CAPS-I and the SCID-I to assess trauma history and current and lifetime psychopathology. Participants who met eligibility requirements were then administered a standardized trauma interview to assess variables relevant to the traumas experienced as well as any treatment history. Participants then completed other clinician-administered and self-report assessments. Within three days of the initial assessment battery, participants were scheduled for the neuroimaging portion of the study. Upon completion of the fMRI scan, participants were assigned to a therapist, and CPT was initiated. All participants were administered the full CPT protocol before the termination of therapy. Immediately following the completion of CPT, participants were scheduled for their follow-up assessment and scan. The follow-up assessment consisted of the same protocol as the baseline assessment, except that only current

psychopathology was assessed. The follow-up scan protocol was identical to the baseline

scan, as both scans included the affective induction and the collection of structural and

functional images. Data collection occurred between September 2009 and August 2013.

<center>Results</center>

Pre-treatment Clinical Variables

A one-way between-subjects ANOVA compared the mean scores of clinical

variables (i.e., BDI, PDS, PA, NA) between the ITT group and healthy control group. All

comparisons of clinical variables were statistically significant. BDI scores ($F(1, 46) =$

32.13, $p < .001$, partial $\eta^2 = .41$) were greater in the ITT group ($M = 24.26$, $SD = 11.00$)

than in healthy controls ($M = 4.20$, $SD = 3.16$). PDS scores ($F(1, 46) = 60.75$, $p < .001$,

partial $\eta^2 = .57$) were also greater in the ITT group ($M = 28.44$, $SD = 10.34$) than in

healthy controls ($M = 3.92$, $SD = 5.70$). Additionally, NA scores ($F(1, 51) = 35.73$, $p <$

$.001$, partial $\eta^2 = .41$) were greater in the ITT group ($M = 28.84$, $SD = 8.63$) in

comparison to healthy controls ($M = 14.93$, $SD = 3.94$). As expected, PA scores ($F(1, 51)$

$= 40.12$, $p < .001$, partial $\eta^2 = .44$) were significantly lower in the ITT group ($M = 23.68$,

$SD = 7.51$) than in healthy controls ($M = 37.87$, $SD = 6.90$).

Similarly, a series of one-way between-subjects ANOVAs were conducted to

compare the mean scores of clinical variables (i.e., BDI, PDS, PA, NA) at pre-treatment

between the treatment completion and treatment dropout groups. These analyses

specifically tested the hypothesis that NA scores would be higher and PA scores would

be lower in the treatment dropout group versus the treatment completion group. Results

only partially supported this hypothesis as NA scores ($F(1, 36) = 0.06$, $p = .812$, partial η^2

$= .002$) were not significantly different between the treatment completion group ($M =$

28.58, $SD = 8.90$) and treatment dropout group ($M = 29.29$, $SD = 8.43$). However, PA

scores ($F(1, 36) = 5.29$, $p < .05$, partial $\eta^2 = .13$) were significantly different between the groups, such that the treatment dropout group had lower scores ($M = 20.21$, $SD = 6.07$) than the treatment completion group ($M = 25.71$, $SD = 7.63$). BDI scores ($F(1, 36) = 7.02$, $p < .05$, partial $\eta^2 = .16$) were greater in the treatment dropout group ($M = 30.00$, $SD = 9.73$) than in the treatment completion group ($M = 20.92$, $SD = 10.45$). PDS scores ($F(1, 34) = 9.26$, $p < .01$, partial $\eta^2 = .21$) were also greater in the treatment dropout group ($M = 34.36$, $SD = 8.12$) than in treatment completers ($M = 24.68$, $SD = 9.96$). This observed difference in PDS scores, a self-report measure, was inconsistent with results from the CAPS, a clinician-administered measure, as CAPS scores ($F(1, 36) = 2.29$, $p = .14$, partial $\eta^2 = .06$) were not significantly different between the treatment dropout group ($M = 77.43$, $SD = 15.34$) and the treatment completion group ($M = 67.96$, $SD = 20.21$).

To further understand the differences between individuals who initially present for treatment, one-way between-subjects ANOVAs were utilized to examine the differences on clinical variables of interest between the treatment completion group, a treatment dropout group comprised of individuals who presented for at least one session of CPT, and a treatment dropout group comprised of individuals who expressed interest in treatment but never attended any sessions of CPT. NA scores were not significantly different ($F(2, 35) = 0.07$, $p = .93$, partial $\eta^2 = .04$) between the groups. PA scores, interestingly, were trending towards significance across the groups ($F(2, 35) = 2.86$, $p = .07$, partial $\eta^2 = .14$). Pair-wise comparisons (i.e., Tukey's HSD Procedure) were then utilized to examine this trend. While the mean difference between PA scores was not significantly different ($p = .12$) between the treatment completion ($M = 25.71$, $SD = 7.63$) and treatment dropout after attending groups ($M = 21.22$, $SD = 6.12$), the mean difference

between PA scores was significantly different ($p < .05$) between the treatment completion and dropout before attending groups ($M = 18.40$, $SD = 6.19$). The mean difference between PA scores of the treatment dropout after attending and treatment dropout before attending was not significant ($p = .48$).

With regard to specific symptom measures and presentation for treatment, BDI scores were significantly different across the groups ($F(2, 35) = 3.52$, $p < .05$, partial $\eta^2 = .17$). Similar to self-reported PA scores, BDI scores were significantly different ($p < .05$) between the treatment completion group ($M = 20.92$, $SD = 10.45$) and the dropout before attending group ($M = 31.60$, $SD = 5.22$). Unlike the PA analysis, a significant difference was also observed ($p < .05$) between the treatment completion group and the dropout after attending group ($M = 29.11$, $SD = 11.73$). BDI scores in the dropout before attending and after attending groups were not significantly different ($p = .67$). The same trend was present in the analysis of PDS scores. PDS scores were significantly different across the groups ($F(2, 33) = 4.83$, $p < .05$, partial $\eta^2 = .23$). In pair-wise comparisons of mean differences, PDS scores were significantly different ($p < .05$) between the treatment completion group ($M = 24.68$, $SD = 9.96$) and the dropout before attending group ($M = 36.80$, $SD = 6.30$). A significant difference was also observed ($p < .05$) between the treatment completion group and the dropout after attending group ($M = 33.00$, $SD = 9.03$). PDS scores in the dropout before attending and after attending groups were not significantly different ($p = .47$). CAPS scores were not significantly different across the three groups ($F(2, 35) = 1.46$, $p = .25$, partial $\eta^2 = .08$). Correlations of clinical variables assessed in the ITT sample at pre-treatment are presented in Table 2.

Post-treatment Clinical Variables

To test the hypothesis that CPT will reduce NA and increase PA, one-way within-subjects ANOVAs were used to compare changes in the mean scores of clinical variables from pre-treatment to post-treatment within treatment completers. Indeed, NA scores changed significantly across treatment ($F(1, 21) = 24.32$, $p < .001$, partial $\eta^2 = .54$) such that participants had lower scores post-treatment ($M = 18.96$, $SD = 7.97$) than at pre-treatment ($M = 28.55$, $SD = 9.19$). Additionally, CPT also significantly increased PA ($F(1, 21) = 14.21$, $p < .01$, partial $\eta^2 = .40$) from pre-treatment ($M = 25.91$, $SD = 7.12$) to post-treatment ($M = 31.36$, $SD = 7.97$). Thus, these results support the a priori hypothesis regarding the impact of CPT on affectivity. Other clinical variables also were significantly modified over the course of treatment. BDI scores were significantly reduced ($F(1, 22) = 46.93$, $p < .001$, partial $\eta^2 = .68$) from pre-treatment ($M = 20.70$, $SD = 10.63$) to post-treatment ($M = 9.00$, $SD = 8.61$). PDS scores were also significantly reduced ($F(1, 18) = 40.23$, $p < .001$, partial $\eta^2 = .69$) from pre-treatment ($M = 24.16$, $SD = 10.18$) to post-treatment ($M = 10.47$, $SD = 10.11$). Likewise, CAPS scores were significantly reduced ($F(1, 22) = 117.99$, $p < .001$, partial $\eta^2 = .84$) from pre-treatment ($M = 67.00$, $SD = 20.10$) to post-treatment ($M = 23.17$, $SD = 21.37$). These results are presented in Table 3. Correlations of clinical variables assessed in the ITT sample at post-treatment are presented in Table 4.

Exploratory analyses were also conducted within the treatment completion group to examine the potential effects of pre-treatment NA and PA on other treatment variables influenced by CPT. Dependent variables included the change scores from baseline to post-treatment assessment in self-reported BDI scores, PDS scores, and CAPS scores. Results indicated that baseline self-reported NA was significantly associated with

changes in PDS scores (F (1, 26) = 5.77 $p < .05$, R^2 adj =.15; β = .43, $p < .05$) and BDI

scores (F (1, 29) = 11.84 $p < .01$, R^2 adj =.27; β = .54, $p < .01$). Thus, greater change

scores on the BDI and PDS were observed in participants with higher NA at pre-

treatment. Baseline NA was not a significant predictor of changes in CAPS scores or PA

across treatment. Baseline PA was a significantly associated with changes in PDS scores

(F (1, 26) = 7.36 $p < .05$, R^2 adj =.22; β = -.47, $p < .05$), BDI scores (F (1, 29) = 8.71 $p <$

.01, R^2 adj =.20; β = -.48, $p < .01$), and NA (F (1, 29) = 6.14 $p < .05$, R^2 adj =.15; β = -

.42, $p < .05$) across CPT. As such, participants with lower PA scores at pre-treatment

experienced the greatest decreases across these clinical variables. PA was not

significantly associated with changes in CAPS scores across treatment.

Structural Magnetic Resonance Imaging

Group Analyses

To test the second hypothesis that gray matter volumes would be significantly

different between the treatment completion group and the treatment dropout group in

identified ROIs, between-group comparisons of gray matter volume were performed with

the VBM8 toolbox using the general linear model (Friston et al., 1994). Each comparison

generated two t-statistic maps that corresponded with opposing contrasts of gray matter

volume (i.e. increased and decreased volume). To correct for multiple comparisons

within identified ROIs, Monte Carlo simulations using 3dClusterSim based in AlphaSim

(Ward, 2000) were performed. As a result of 10,000 Monte Carlo simulations, Type I

error was maintained at $p = .05$ using a combined voxel and uncorrected significance

threshold of $k = 271$ and $p < .005$.

Comparison of the treatment completion and treatment dropout groups using VBM analyses indicated that gray matter volumes were not significantly different between the groups. However, a closer look at the entire treatment dropout group yielded significant results. When compared to the subjects that dropped out from treatment before attending a session, the treatment group demonstrated significantly greater gray matter volumes in the bilateral parahippocampal gyrus/entorhinal cortex (Figure 3). When compared to the subjects that dropped out of treatment after attending at least one session, the treatment group had significantly reduced gray matter volumes in the bilateral supplementary motor area, left postcentral and precentral gyrus, and bilateral calcarine (Figure 4). Group results are presented in Tables 5 and 6.

An exploratory analysis of structural gray matter differences between all PTSD participants and healthy controls surprisingly yielded no significant differences. Given the aforementioned significant differences in gray matter volumes between the PTSD treatment groups, comparisons were also performed between the various treatment groups (i.e., treatment completers, treatment dropouts, & treatment no-shows) and the healthy control group. Results indicated that treatment completers were not significantly different from healthy controls in terms of brain structure.

There were no significant differences in gray matter volumes between healthy control participants and participants who dropped out of treatment prior to attending a session as well. However, this was not the case for participants who dropped out of treatment after participating in therapy. Participants who dropped out of treatment after attending at least one session had increased gray matter volume in the left superior frontal

cortex, the right precuneus, and the left calcarine (Figure 5). Results from this comparison are presented in Table 7.

<u>Regression Analyses</u>

To test the third hypotheses regarding the relationships between affective dimensions and gray matter volumes in ROIs, a series of multiple regressions were also performed. The VBM8 toolbox subsequently generated two contrast maps corresponding with opposing relationships between gray matter volumes and the variable of interest (i.e., positive and negative association). Since the same ROI mask was used for the group analysis, Type I error was maintained at $p = .05$ using a combined voxel and uncorrected significance threshold of $k = 271$ and $p < .005$.

Within the PTSD treatment group, NA demonstrated a significant positive association with gray matter volume in the right parahippocampal gyrus. These results remained consistent after controlling for depression symptoms (i.e., BDI scores). PA was found to be positively associated with gray matter volume in the right middle frontal gyrus (Brodmann Area 10) and right precuneus (Figure 6). These results also remained consistent after controlling for depression symptoms. Regression analyses were not conducted within sub-groups of the PTSD treatment group, as an analysis of each group (i.e., treatment completers, treatment dropout before attending, treatment dropout after attending) would have been significantly underpowered because of their small sample sizes, respectively.

In comparison, NA was found to have an inverse relationship with gray matter in the bilateral superior medial frontal gyrus, bilateral middle cingulate, and bilateral medial frontal orbital gyrus in the healthy control group. PA demonstrated a significant positive

association with gray matter in the left postcentral gyrus in healthy controls as well

(Figure 7). Results from the regression analyses in both groups are presented in Table 8.

Functional Magnetic Resonance Imaging

In a subset of participants from the current sample, Bruce and colleagues (in

preparation) demonstrated that CPT treatment completers exhibit functional activation

patterns during the conflict task that appear more similar to that of control subjects

instead of individuals with PTSD, suggesting that CPT may normalize brain function

during this task. The final hypothesis of this project attempted to explore the relationships

between affectivity and brain activation in ROIs during the conflict task prior to the

application of CPT and how these relationships changed post-treatment. Multiple

regressions were performed between both affect variables and brain activation in ROIs

during the four main conditions of the conflict task (i.e., AF, IF, AN, IN). Similar to the

structural analyses, Monte Carlo simulations using 3dClusterSim based in AlphaSim

(Ward, 2000) were performed to correct for multiple comparisons within identified ROIs.

As a result of 10,000 Monte Carlo simulations, Type I error was maintained at $p = .05$

using a combined voxel of $k = 116$ and uncorrected significance threshold of $p < .005$.

Pre-treatment Results

During the AF condition at pre-treatment, significant inverse relationships were

observed between NA and activation in the left superior frontal gyrus and right calcarine,

such that as NA increases, activation in these areas decreases. During the AF condition,

PA demonstrated a significant positive association with activation in the left postcentral

gyrus (Figure 8). PA also exhibited a significant inverse relationship with activation in

the left parahippocampal gyrus during the IF condition (Figure 9) and the bilateral

parahippocampal gyrus during the IN condition (Figure 10). Further, a significant

positive relationship between PA and activation in a large cluster in the right inferior orbitofrontal cortex during the IN condition was observed. No significant results were observed in the AN condition at pre-treatment. These results are presented in Table 9.

Post-treatment Results

At post-treatment, all of the significant relationships between affectivity and activation in ROIs at pre-treatment were not significant. During the AN condition, NA was inversely associated with activation in the right superior frontal and right middle orbitofrontal cortices. Thus, as NA decreases, activation in these areas increases. A significant positive relationship between PA and the left superior frontal cortex was also observed during the AN condition (Figure 13). During the AF condition, PA was found to be inversely related to activation in the left postcentral gyrus, right precentral gyrus, left fusiform gyrus, and the right precuneus (Figure 11). As PA was found to significantly increase across the course of CPT, this result implies that greater PA is associated with reduced activation in these areas. A final analysis of the IF condition at post-treatment yielded a significant positive relationship between PA and the right middle frontal cortex (Figure 12). No significant results were observed in the IN condition at post-treatment. These results are presented in Table 10.

Discussion

Clinical Variables

The current project sought to examine the interactions between affectivity, brain structure and function, and CPT treatment outcomes in a sample of female interpersonal trauma survivors with PTSD. Analysis of pre-treatment clinical variables indicated that the ITT sample was highly symptomatic. In comparison to the healthy control group, the ITT sample in this study exhibited significantly higher levels of both PTSD and

depression symptoms. Consistent with this observation, the ITT sample also reported significantly increased NA and reduced PA. Of the participants enrolled in CPT ($N = 38$), approximately 63% ($N = 24$) completed treatment, 24% ($N = 9$) dropped out after receiving partial treatment, and 13% ($N = 5$) never attended a therapy session. These rates of CPT treatment completion mirror that of prior CPT trials in interpersonal trauma survivors with PTSD (72%; Galovski, Blain, Chappuis, & Fletcher, 2013).

Indeed, CPT was effective in reducing PTSD-related symptoms for completers, resulting in an average CAPS score reduction of approximately 44 points from pre-treatment ($M = 67.00$, $SD = 20.10$) to post-treatment ($M = 23.17$, $SD = 21.37$). Symptoms of self-reported depression were similarly reduced. It was initially hypothesized that CPT would also reduce self-reported NA and increase PA. The present findings support this hypothesis for both affective variables, as CPT resulted in large reductions (partial $\eta^2 = .54$) in NA and moderate increases (partial $\eta^2 = .40$) in PA. As such, it appears that CPT can address concerns of both general distress and difficulties in experiencing positive emotion in a majority of treatment-seeking individuals without a module that specifically targets either.

While CPT was useful for the majority of the PTSD sample, the treatment was unable to address the clinically significant concerns of 14 participants. Randomized controlled trials often explicitly focus on participants who complete treatment, and treatment dropout issues remain unexamined. In fact, treatment dropout is frequently explained as a function of logistical issues for clients (i.e., transportation, financial concerns). However, there is some evidence to suggest that clinically relevant variables like frequency of abuse experienced in childhood (Resick, Suvak, & Wells, 2014) and

pre-treatment symptoms of depression, guilt, and anger (Rizvi, Vogt, & Resick, 2009) are predictive of treatment completion.

With these limitations in mind, it was hypothesized that NA and PA would be significant predictors of CPT completion and dropout. This hypothesis was only partially supported, as pre-treatment NA was not significantly different between the treatment completion and treatment dropout groups. Pre-treatment levels of NA were associated with change scores across CPT in other self-report measures in the study including the PDS and BDI, which may reflect a relationship between current distress reported across all measures. Higher levels of NA were associated with greater changes in self-reported PTSD and depression symptoms. NA was not associated with changes on the CAPS or in PA.

PA was significantly different between the groups, such that participants who dropped out of treatment had lower levels of PA at pre-treatment. Further analysis of the dropout group yielded findings that the lowest levels of PA were observed in participants that never attended a therapy session. Thus, reduced PA at pre-treatment may represent an additional risk factor for CPT dropout. Similarly, the treatment dropout group also self-reported higher levels of both PTSD and depression symptoms than the treatment completion group. Interestingly, PTSD symptoms obtained through a clinician administered instrument were not different between the groups, suggesting that subjective perception of the severity of both PTSD and depression symptoms may be related to suboptimal treatment outcomes. Similar to NA, pre-treatment PA was also predictive of change across CPT on the PDS and BDI. PA was not associated with change in CAPS total score. Interestingly, PA was predictive of change in NA across treatment. Lower PA

was indicative of greater reductions in NA for participants who were retained in treatment. This finding suggests that the capacity to increase PA may be an effective means of reducing NA; but reducing NA may not necessarily result in increased PA.

The insignificant finding between NA and treatment dropout is surprising, given the literature that identifies a relationship between self-reported NA and PTSD symptom severity (Brown et al., 2014). While symptom severity seems to be associated with treatment completion in this sample, the experience of increased NA is a non-factor. While this finding may simply be a result of insufficient power to detect small differences related to the size of the current sample, it does have implications for the application of CPT in interpersonal survivors, especially with consideration of the positive finding for PA between the groups. Currently, there some evidence to suggest that the augmentation of CPT (House, 2006) with affect regulation modules to address heightened, dysregulated affect enhances treatment effectiveness. The initial application of such modules was an extension of the hypothesis that individuals with high levels of NA may be unwilling or unable to tolerate the brief exacerbations of negative emotion that often accompany exposure techniques. However, it may only be necessary to apply these modules to certain populations with affect regulation concerns, as affect regulation modules have only demonstrated effectiveness in survivors of childhood sexual abuse with PTSD (House, 2006; Wolfsdorf & Zlotnick, 2001). These modules have yet to be examined with other variants of trauma in conjunction with objective measures of affectivity. While the present sample did include participants with childhood sexual trauma, events experienced as interpersonal traumas were highly variable across participants. Future

directions of the current project include an analysis of self-reported affect by trauma type and subsequent treatment outcome.

The significant difference in PA between the treatment completion and treatment dropout group is intriguing, given inconsistent findings regarding the relationship between PA and PTSD symptoms. For example, Brown and colleagues (2014) observed that PA was not a predictor of PTSD symptom severity or individual PTSD symptom cluster scores in a group of female interpersonal trauma survivors with PTSD. This study was only one of few to examine PA within the context of PTSD, as PA was traditionally conceptualized as primary latent construct of depression. However, a comparative study found that PA accounted for a significant amount of variance amongst both PTSD total symptom severity and numbing symptoms, although NA was the most significant predictor in these models (Fetzner et al., 2012). It is important to recognize that previous research on the relationship between PA and PTSD symptoms was conducted within the context of the DSM-IV-TR conceptualization of PTSD, not the DSM-5 conceptualization that includes a new symptom cluster addressing changes in affect and cognition as posttraumatic sequelae. While results of the current analyses cannot determine the extent to which PA is related to PTSD symptoms, the observed findings are consistent with previous research linking lower levels of PA with greater symptoms of depression in individuals with PTSD (Post et al., 2011). Additionally, these results suggest that low levels of PA may represent a broad risk factor for treatment dropout regardless of the relationship with PTSD symptoms, particularly during the initial stages of a manualized treatment protocol that may not specifically address the enhancement of PA.

Furthermore, prior research suggests that PA may be much more than a latent construct of depression that warrants attention within the treatment of all emotional disorders. In fact, Brown and colleagues (1998) suggest that low PA may be feature and general diathesis of both mood and anxiety disorders after identifying a significant relationship between PA and social anxiety. Moreover, this relationship was similar in strength to the observed relationship in the same sample between PA and depression after accounting for variance in NA. Consistent with these findings, the current results suggest that more research is needed to determine the role of low PA in the conceptualization of emotional disorders, including PTSD.

The findings of the current study create a new dialogue in the application of manualized treatments for PTSD: what is the role of PA in client dropout amongst other viable explanations, including the common attribution to client logistical issues like financial or transportation concerns? The usefulness of this dialogue will not be found in efforts to determine which risk factor is most important but in the acknowledgement that addressing clinical variables such as low levels of PA or high levels of depression symptoms may indeed alter treatment completion trajectories. However, this recognition comes at the cost of scrutinizing the weaknesses of manualized protocols instead of dismissing treatment dropout as a product of individual client factors that cannot be addressed in therapy. Alterations to treatment plans including manualized protocols for individual clients that exhibit clinical indicators of dropout may indeed reduce treatment attrition rates. This is especially salient for empirically-based approaches for PTSD, like CPT and PE, which require clients to endure possible temporal increases in distress at the outset of therapy related to exposure techniques. Possible solutions include augmenting

current PTSD protocols with treatment components aimed at increasing PA, such as Behavioral Activation (BA; Jacobson et al., 1996), or creating and utilizing integrated protocols, such as Behavioral Activation and Therapeutic Exposure (BA-TE; Gros et al., 2012).

Structural Results

Within PTSD Treatment Group

The second hypothesis of this project proposed that gray matter reductions in ROIs theoretically linked with PTSD would be observed in the treatment dropout groups versus the treatment completion group. The results only partially supported this hypothesis, as gray matter volumes of the amygdala, insula, and ACC were not significantly different between the groups. While no significant differences were observed between the treatment completion group and the entire treatment dropout group, a closer look at the dropout group yielded interesting findings. Participants who never attended a therapy session exhibited significantly reduced gray matter in the bilateral parahippocampus and entorhinal cortex in comparison to completers. Results of the analysis between completers and treatment dropouts who attended at least one treatment session were also significant. Unexpectedly, treatment completers exhibited decreased gray matter volume in the bilateral supplementary motor area, left postcentral and precentral gyrus, and bilateral calcarine compared to those who dropped out after partial treatment.

Prior to the interpretation of these results, the non-significant results involving primary regions implicated in emotion regulation must be explored. The first possible explanation is that the analysis was underpowered. The entire clinical sample included 38

participants, comprised of 24 completers and 14 dropouts. An a priori analysis using

G*Power statistical software yielded results indicating that a sample size of 28 would be

required to detect large effects ($d = 1.00$) between two groups at a power ($1-\beta$) of 0.80.

However, only five participants dropped out of treatment after enrollment but before

attending a session, significantly limiting the power of these secondary analyses. While

the sample size of the treatment dropout before attending group could surely be

scrutinized as a limitation, the overall sample size of participants that were both enrolled

in treatment and administered an MRI scan is impressive for a neuroimaging study. The

analysis is also worthwhile, given that little is known about the minority of individuals

with PTSD for whom CPT is ineffective. The second possible explanation is that

differences in smaller brain regions may not have met the stringent multiple comparisons

threshold for significance, given the broad scope of regions examined in the current

analysis. The ROI mask for this study included all brain areas relevant to both emotion

regulation and PTSD, thus increasing the number of theoretical comparisons. It is

possible that a more focused analysis would yield significant findings in these regions.

     Nonetheless, it is worth noting that the areas identified with reduced gray matter

in treatment dropouts in this analysis (i.e., bilateral entorhinal cortex and

parahippocampal gyrus) have been implicated in theoretical models of PTSD. For

example, Sparta and colleagues (2014) found that inhibiting the projections from the

basolateral amygdala to the entorhinal cortex reduced freezing behavior in animals re-

exposed to a traumatic stimulus. When the pathway was not inhibited, the animals

continued to freeze in response to contextual re-exposure. The entorhinal cortex is also

thought to play a role in altered visual processing via the ventral stream of the visual

system in individuals with PTSD, who have been found to exhibit reduced activity in the entorhinal cortex during a picture-viewing task than trauma-exposed controls (Mueller-Pfeiffer et al., 2013). Reduced white matter integrity has also been reported in the cingulum, an area that connects the entorhinal cortex to the ACC in individuals with PTSD (Fani et al., 2012). Indeed, the entorhinal cortex may play an important role in emotion regulation, as documented projections include the hippocampus, insula, amygdala, and ACC (Canto, Wouterlood, & Witter, 2008). While only a paucity of research has examined the entorhinal cortex within the context of PTSD, several studies have observed reduced gray matter volume in the hippocampal gyrus of individuals with PTSD versus healthy controls (see Meng et al. [2014] for a review).

In consideration of the previous literature, the present findings suggest that gray matter volume in the entorhinal cortex and parahippocampus may not only differ between individuals with PTSD and healthy controls but also across individuals with PTSD. This observation is noteworthy as studies of VBM do not explicitly identify gray matter volume as a continuous variable. Generally speaking, group comparisons unintentionally imply dichotomous assumptions about brain volume (i.e., either reduced/increased or not). As such, within-group explorations of volumetric variations may have important practical implications. Results from the current project suggest that individuals with PTSD who exhibit the greatest reductions in volumes of these areas may be at risk for treatment dropout.

With regard to the observed results in gray matter volume between completers and therapy dropouts after partial attendance, the treatment group exhibited significantly reduced gray matter volumes in the bilateral supplementary motor area, left postcentral

and precentral gyrus, and bilateral calcarine. Volumetric findings in these areas are not

surprising, given that both functional and connectivity neuroimaging studies have

identified abnormal function in these regions in participants with PTSD. For example,

one study found that flashbacks appeared to be related to activity in the precentral gyrus

and supplementary motor area during a recognition task with personally relevant stimuli

in participants with PTSD (Whalley et al., 2013). Kennis and colleagues (2015) found

reduced connectivity between the ACC and precentral gyrus in veterans with PTSD

versus healthy controls. The precentral gyrus has also been linked to physiological

arousal (e.g., heart rate) (Barkay et al., 2012) and dysfunctional information processing

(Bae, Kim, Im, & Lee, 2011) in participants with PTSD. Another relevant study found

increased activity in the precentral gyrus and decreased activity in the left fusiform gyrus

and parahippocampal gyrus in PTSD participants in comparison with healthy controls

during an fMRI paradigm sequence of videos with a positive emotional valence (Jatzko et

al., 2006). The authors of this study suggest that the findings may be related to the

experience of emotional numbness in PTSD. In summary, increased activity in the

precentral gyrus in PTSD may relate to excessive cognitive regulation and subsequent

emotional numbing (Bremner et al., 1999; Shaw et al., 2002; Jatzko et al., 2006),

hyperarousal (Barkay et al., 2012), and flashbacks (Whalley et al., 2013).

     Similarly, the supplementary motor area has also been identified as salient to

PTSD in functional connectivity studies (Whalley et al., 2013; Shang et al., 2014).

Disruptions of this area are thought to be related to hyperarousal symptoms (Mueller-

Pfeiffer et al., 2014) and disruptions of working memory (Shaw et al., 2009). Abnormal

functioning of the calcarine has been associated with the negative interpretation of neutral

faces in patients with panic disorder (Petrowski et al., 2014), which suggests that a similar predisposition may be present in individuals with PTSD. Disruption of the calcarine may be particularly salient to interpersonal trauma survivors, given that other people can become feared stimuli depending on the nature of the experienced traumatic event (e.g., interpersonal trauma survivor fears all men following a sexual assault perpetrated by a man). There is a paucity of published functional findings regarding the postcentral gyrus in PTSD populations. Decreased response inhibition was found to be associated with activity in this area in veterans with PTSD (van Rooij et al., 2014).

While literature on the functional relationships of the areas identified as significantly different between treatment completers and dropouts after attending is abundant, reports of structural findings are not. A study by Lindemer and colleagues (2013) found a significant negative correlation between PTSD symptom severity and cortical thickness in the postcentral gyrus in veterans with PTSD, indicating that reduced gray matter is associated with increased severity of symptoms. As such, interpretation of the findings of the current study must be tempered with consideration of the lack of robust structural findings thus far.

Results from the current study begin to establish a basis for understanding structural abnormalities across individuals with PTSD and how this influences the application of treatment. The aforementioned functional studies can provide an elementary context for interpretation of the findings between the treatment completion group and individuals that subsequently dropped out of treatment after attending a session. With regard to these functional studies, it appears that the two groups may be predisposed to different responses to CPT that are associated with structural variations,

under the general assumption that increased functional activity of an area is related to neuronal proliferation and vice versa. For example, treatment completers exhibited reduced gray matter in the precentral gyrus, an area where increased activity is thought to be related to increased cognitive control. Thus, the application of CPT, which promotes healthy top-down regulation, may have been more amenable to treatment completers who were lacking such skills prior to treatment. Alternatively, treatment dropouts after attending the initial session may have already been over-engaged in the cognitive regulation of their emotions. Addressing "stuck points" and experiencing emotions associated with their traumatic memories may not have been as useful or appealing to this group for this reason.

The excessive cognitive regulation of emotion in treatment dropouts may have also been occurring in the presence of increased PTSD symptom severity and reduced PA, which were significantly different between the groups. However, previous research indicated that greater PTSD severity is associated with reduced cortical thickness of the postcentral gyrus (Lindemer et al., 2013). Treatment dropouts after attending exhibited increased volume in this area, despite their experience of more severe symptoms than their completer counterparts. The present results suggest that this result may not hold true within a PTSD group, given the extreme heterogeneity and variable symptom presentations of clinically significant PTSD. Future studies should examine the differences in symptom profiles of PTSD and how these differences may relate to observed variations in brain structures. These efforts may help clarify frequent inconsistencies observed in both structural and functional findings related to PTSD.

Between PTSD Treatment Groups and Healthy Controls

This project has been the first to examine gray matter abnormalities as an indicator of CPT treatment completion for PTSD. As such, the group results presented may be discordant with previous bodies of literature comparing a PTSD group to some sort of control group. Given the presence of a healthy control group in this study, group trends in gray matter volume were also explored between the entire PTSD group and healthy controls. Interestingly, there were no significant differences between the groups that survived the correction for multiple comparisons. However, this may result may have been a product of the heterogeneity previously observed within the PTSD treatment groups. Specific group comparisons were then conducted to see if this was the case. The results indicated that gray matter volumes within the PTSD treatment completion group were not significantly different from healthy controls. This finding suggests that gray matter abnormalities in general may impede the application of CPT. Individuals who do not exhibit these structural changes may be more amenable to CPT-based skills. The absence of gray matter abnormalities in this subset of individuals may be related to the specific aspects of individual traumatization and manifestation of pathology including trauma type, chronicity, symptom severity, or comorbid affective problems.

Whereas there were no significant differences in brain volume between participants who dropped out of treatment before attending a session and healthy controls, numerous significant differences in gray matter were observed between participants who dropped out of treatment after initially attending and the healthy control group. Treatment dropouts exhibited significantly increased gray matter in the left superior frontal cortex, right precuneus, and the left calcarine in comparison to the

control group. Of these areas, functional connectivity studies have indicated reduced

activity to the right precuneus in individuals with who experience early life stress (Philip

et al., 2013). Alternatively, increased activity to the right precuneus during functional

connectivity analyses has also been observed in natural disaster survivors with PTSD

(Wu et al., 2011; Yin et al., 2011). Reduced gray matter volumes have been observed in

the right precuneus in adolescents with PTSD as well (Ahmed et al., 2012). Increased

activity in the right precuneus in individuals with PTSD has been linked to a sensitivity to

stimuli encoded in emotional contexts (Whalley et al., 2009). A positron emission

tomography investigation found decreased activity in the right precuneus in individuals

who responded to pharmacotherapy for anxiety (Carey et al., 2004). Concordant with this

finding, the current project implicates the right precuneus as an area of interest for

treatment completion in PTSD.

The last significant finding of the analysis indicated increased gray matter volume

in the left superior frontal cortex in PTSD treatment dropouts versus healthy controls.

This finding is difficult to interpret, since it is a large region with numerous proposed

functions. Generally speaking, this area is thought to be important for the top-down

regulation of emotion. However, both increased (van Rooij et al., 2014) and decreased

(Wu et al., 2011) activation has been observed in the superior frontal gyrus of PTSD

participants in response to multiple tasks over several studies in comparison to healthy

controls. Studies of gray matter volumes are beginning to converge on similar

conclusions. For example, reduced gray matter volume was observed in the right superior

frontal gyrus in PTSD participants compared to trauma exposed controls (Li et al., 2014).

Qi and colleagues (2013) also suggest that cortical thinning in this region is associated

with increased PTSD symptom severity. However, the present findings appear inconsistent with this suggestion, as the PTSD treatment dropout group exhibited greater gray matter volume in this area relative to healthy controls.

Affectivity and Structural Findings

The final structural analysis of this project sought to examine the relationship between affectivity and emotional areas related to PTSD. NA demonstrated a significant positive association with gray matter in the right parahippocampus, even after controlling for BDI scores. As previously mentioned, the parahippocampus has been established as a brain region of interest in the study of PTSD. However, this was the only region with which NA was significantly associated. This result is intriguing, given the established relationship between NA and PTSD symptoms. One possible explanation is that self-reported NA does not represent a viable proxy for broad structural abnormalities associated with PTSD. This would infer measurement error with self-report as a method to assess symptoms. The issue could also be timing. Participants were reporting their experience of NA over the 'past few weeks.' Perhaps the subjective perception of current distress is not representative of structural changes that may occur over longer periods of time. As such future studies should not rule out the absence of such relationships, and functional imaging studies should explore whether or not NA influences temporal emotion regulation.

It was also predicted that PA would be inversely related to gray matter volume in areas related to emotion regulation. However, results indicated that PA was positively associated with volumes in the medial prefrontal cortex (mPFC; Brodmann Area 10) and right precuneus, and these relationships remained significant even after controlling for

symptoms of depression. The mPFC is generally implicated as an area important for the top-down regulation of emotion and is hypoactive in individuals with PTSD. These results suggest that, as PA increases, so does brain volume in this area. Treatment implications for this finding include the initial use of behavioral activation strategies at the outset of treatment for individuals with low PA to improve their overall regulation of distress. This implication also fits with the previous observation that PA was one of the clinical variables that was significantly different between treatment completers and dropouts. These results also suggest that individuals with PTSD may be better at reporting deficits in PA than excesses in NA, since PA may be a better proxy for structural alterations in this population.

Functional Results

Bruce and colleagues (in preparation) recently observed that CPT facilitates the normalization of emotional processing during the conflict task in participants treated for PTSD. The final hypothesis of this study examined how the relationship between affectivity and emotional processing during the conflict task changed from pre-treatment to post-treatment. Four primary conditions of the task were observed: AF, IF, AN, IN.

Pre-treatment Functional Results

When attention was oriented to fearful faces, self-reported NA was found to be inversely correlated with brain activation in the right calcarine and the left superior frontal cortex, such that increased NA prior to the administration of CPT is associated with decreased activation in these regions. PA was also positively associated with activation in the left postcentral gyrus during this condition. While ignoring fearful faces, PA was inversely associated with activation in the left parahippocampal gyrus.

Participants generally reported lower levels of PA at pre-treatment, which would infer greater activation in this area. The other significant findings at pre-treatment were between PA and activation during the ignoring of neutral faces condition. PA was found to be positively associated with activation in the right frontal inferior orbital cortex. In what appears to be a common finding to the ignore conditions, PA was also inversely associated with brain activation in the bilateral parahippocampal gyrus. No significant findings were observed within the attending to neutral faces condition.

It appears that decreased activation in the calcarine cortex is related to the abnormal processing of faces in some clinical populations. For example, Petrowski and colleagues (2014) found that patients with panic disorder and agoraphobia exhibited deactivation of this region in response to emotionally neutral faces in comparison to a healthy control group. While the current finding was observed within the attention to fearful faces condition, high levels of NA related to anxiety disorders and PTSD may imply a disruption of functioning in the calcarine. This disruption may be exaggerated when processing facial stimuli that are perceived as distressing, such as the fearful faces of the conflict task. Likewise, high levels of NA at pre-treatment were associated with reduced functioning in the left superior frontal cortex, an area thought responsible for domains of cognitive control.

The present findings also suggest that activity in the parahippocampal gyrus may be associated with abnormal processing of positive emotions when participants are tasked with ignoring both neutral and emotionally-valenced stimuli. Previous fMRI research using a paradigm to invoke positive emotional processing found that control subjects recruited the parahippocampal gyrus more so than the PTSD group (Jatzko et al., 2006).

The authors concluded that these findings may be related to emotional numbness in PTSD. The current results conflict with this previous finding in that lower positive affect was generally associated with increased activation of this area. However, the current paradigm does not explicitly invoke positive emotional processing. While the area may indeed be important for the processing of positive emotions, the area has also been implicated in episodic memory recall and flashbacks (Whalley et al., 2013) and assault exposure and PTSD symptom severity (Cisler et al., 2013). As such, fear processing may recruit this area in a different manner than positive emotion processing. Another interpretation is that increased activation of this area is associated with the normal processing of positive emotions, similar to the control sample in the Jatzko et al. (2006) study. Thus, while the sample reported generally low levels of PA, they continued to process positive emotions appropriately. As such, increased activation of this area may reflect a biomarker for resilience and treatment completion.

The final pre-treatment functional finding involved a positive association between PA and activation of the right frontal inferior orbital cortex. Low levels of PA at pre-treatment were thus associated with deactivation in this area during the ignoring of neutral faces condition. Previous research has identified emotional processing deficits in this region in individuals with PTSD, particularly during symptom provocation and exposure to traumatic reminders (Bremner, 1999). Another study observed increased spontaneous activity in the orbital cortex in veterans with PTSD in comparison to control subjects (Yan et al., 2013). Tarquis (2006) suggests that the orbital cortex plays an important role in the identification of fearful contexts and the anticipation of danger. The orbital frontal cortex projects to the limbic system and is thought to be important for

decision-making and the top-down regulation of emotion. The present findings imply that increasing PA may also influence the efficiency of conscious decision making and the regulation of emotional responses, particularly in the presence of trauma symptom provocation.

Post-treatment Functional Results

At post-treatment, participants reported significantly lower levels of NA and significantly greater levels of PA than at pre-treatment. This change reflected some interesting associations with brain activation during the conflict task after the completion of CPT. During the attention to fearful faces condition, self-reported PA was inversely associated with activation in the left postcentral gyrus, left fusiform, right precentral gyrus, and right precuneus. Higher scores of PA are thus indicative of lower activation in these regions in PTSD participants. Contrary to the pre-treatment findings during attention to fear, NA was not significantly associated with activation in any brain region. Significant findings were also observed during the attention to neutral faces condition. NA was found to be inversely associated with activation in the right middle orbitofrontal cortex and right superior frontal cortex. Lower scores at post-treatment are related to increased activation in these regions. PA was also found to be positively correlated with activation in the left superior frontal cortex such that higher scores are associated with increased activation in this area. During the ignoring of fearful faces condition, PA was significantly associated with increased activation in the right middle frontal cortex.

Some post-treatment relationships between brain activation and affectivity in CPT treatment completers are suggestive of normalized emotional processing. During the attention to fearful faces condition, higher PA scores were associated with lower

activation in the left postcentral gyrus, right precentral gyrus, left fusiform gyrus, and the right precuneus. With regard to these particular regions, previous research suggests that individuals with untreated PTSD exhibit greater activation in the left postcentral gyrus than healthy controls during a task of response inhibition (van Rooji et al., 2014). Similar results utilizing this task were observed in the precentral gyrus as well (Falconer et al., 2008). Concordant with these findings, decreased activation in these regions during the emotionally-valenced attention to fearful faces condition may reflect improvements in inhibitory control in the current sample. Increased activation of the fusiform during the viewing of fearful distractors has also been observed in untreated individuals with PTSD (Zhang et al., 2013). Greater PA in treatment completers was associated with decreased activation of the fusiform in the presence of fearful faces. Additionally, increased activity to the right precuneus during functional connectivity analyses was observed in natural disaster survivors with PTSD (Wu et al., 2011; Yin et al., 2011). Reduced activity in this area may be indicative of normalization of brain function in this region.

Perhaps the most interesting results from pre-treatment to post-treatment involve the relationship between activity in the left postcentral gyrus and PA. At pre-treatment, a positive association was observed such that low levels of PA were related to decreased activation in this region during the attention to fear condition. At post-treatment, the opposite relationship was observed, such that higher levels of PA were related to lower activation in this region. First and foremost, this was the only region to remain significantly associated with an affective dimension within the task across treatment. A study by van Rooji and colleagues (2014) found that reduced inhibition of the postcentral gyrus was associated with individuals with PTSD in comparison to trauma-exposed and

healthy controls during a task of reactive inhibition. Thus, increased activity in this region may represent a biomarker for dysregulation in reactive inhibition. As such, the present results suggest that activation remains reduced in this region from pre-treatment to post-treatment. It is possible that appropriate inhibition of this structure may act as a predictor of treatment completion, independent of the experience of PA.

During the presentation of the pre-treatment results, the superior frontal and middle frontal orbital cortices were discussed as areas important for inhibitory control. During the attention to fearful faces condition at pre-treatment, high NA was associated with deactivation in the left superior frontal cortex. Similarly, low PA was associated with deactivation in the middle frontal orbital cortex during the ignoring of fearful faces condition at pre-treatment. However, an increased BOLD response in these and related regions during the attention to neutral faces condition at post-treatment was observed as associated with lower scores of NA. While causality between NA and increased activation in these regions cannot be determined, it can be said with confidence that NA significantly decreased over the course of treatment. Changes in this self-reported dimension or changes in neurobiological emotion processing mechanisms as a result of CPT may reflect the improvements in emotional processing observed at post-treatment in this sample. As mentioned previously, increased activation of these areas is generally associated with the efficient top-down regulation of emotion.

Positive associations between PA and increased activation in the left superior frontal cortex during the attention to neutral faces condition and the right middle frontal cortex during the ignoring of fearful faces condition were also observed at post-treatment. These areas have several proposed functions within PTSD including non-conscious fear

processing (Bruce et al., 2012) and processing of positive emotional stimuli (Jatzko et al., 2014). Jatzko and colleagues (2014) reported increased activation in the superior frontal gyrus in PTSD participants relative to healthy controls during the processing of movie-induced positive emotions and suggest that this alteration in functioning may be related to emotional numbness in PTSD. The present findings differ from that presented by this previous study, as increased PA was associated with an increased bold response in that region, though not bilaterally, during both attention and ignore conditions. Taken together, the present study and the study by Jatzko and colleagues suggest a complex relationship between functioning of the superior frontal cortex and the experience of positive emotion in individuals with PTSD. While this area may indeed relate to emotional numbing in participants with PTSD, directionality is difficult to interpret, as few studies have examined the relationship between PA and this area as it relates to positive emotional processing.

There are several possible interpretations for the discrepancy between the Jatzko et al. study and the current project. First, the studies examined this region within the context of very different tasks: one elicited positive emotion processing, the other examined the relationship between self-reported PA and emotional processing during a task of affective induction. Another possible reason for the differences is that the current project only examined relationships between activation and affectivity in PTSD treatment completers who were also survivors of interpersonal trauma. As such, the present finding may only pertain to a specific sample of individuals. However, the analysis was necessary, as these relationships may provide insight to increasing the efficiency of CPT with interpersonal trauma survivors. Lastly, the relationship between the complex series

of regional interactions that constitute positive emotional processing and the task utilized by Jatzko et al. is questionable. Participants watched a well-known movie clip that may surely induce positive emotion, but does this clip actually go further and solicit positive emotional processing involving areas related to cognition in the prefrontal regions? Future research directions for the examination of this area involve understanding the specialized functions of the superior frontal gyrus as it relates to positive emotional processing and how these functions vary across different populations and experimental conditions.

Limitations

There are some limitations of the current project worth noting. The first limitation is the unequal number of subjects between the PTSD group and the healthy control group. Power of a between-group analysis is based on the size of the smaller group ($n = 15$), which may have limited the detection of significant group differences in this project. While this did not appear to be an issue with regard to self-reported clinical variables, insufficient power may have limited findings of the fMRI group analyses between PTSD participants and healthy controls. The second limitation is the relative homogeneity of the healthy control group. The healthy control group was significantly more educated and primarily composed of Caucasian participants in comparison to the PTSD group. While the racial composition of the groups was not significantly different, the PTSD group appears much more diverse than the control group. In addition, only within-group time 2 analyses were possible because the healthy control group did not receive a time 2 scan or assessment. As such, there was no comparison condition for time or treatment to the administration of CPT. However, the primary aim of this project was to examine the

interaction between affectivity and the administration of CPT, which was feasible using a within-subjects pre-treatment/post-treatment design.

Other limitations concern the PTSD group. The group was comprised primarily of female interpersonal trauma survivors who received CPT. Results from this project may not generalize to males, individuals afflicted by other types of trauma, or individuals receiving another variant of trauma-focused therapy. As previously mentioned, power was also an issue when conducting within-group comparisons of participants with PTSD. Of the 38 participants originally enrolled in treatment, 24 successfully completed therapy and 14 participants did not. Examination of group differences between therapy completers and all therapy dropouts presented less of an issue than examining the completers in comparison to two distinct dropout groups: those who attended at least one session of CPT ($n = 9$) and those who dropped out before CPT began ($n = 5$). While power does not present an issue for significant differences that are detected, it does limit the ability of the analysis to detect smaller effects. Thus, the within-group PTSD analyses should be interpreted with caution. However, such an analysis was necessary to examine the impact of clinical and neurobiological dimensions on CPT treatment completion and was somewhat constrained by the relative success of CPT treatment completion (63%) in this sample. Additionally, all participants enrolled in the original ITT sample who dropped out of treatment were included in the dropout group, regardless of the circumstances surrounding their termination of services.

Limitations were also inherent to the design of the conflict task. During the experimental condition or affective induction, the task displays primarily fearful faces. While an argument could be made that these images likely invoke both fear circuitry and

affect dysregulation systems, the incorporation of other negative faces could serve as important comparison conditions. The task does indeed facilitate emotional processing and attentional resources, but it may have not been optimal for the examination of the broad-based emotional dimensions NA and PA. Additionally, the use of neutral faces as the comparison condition may have been confounded by the tendency for PTSD participants to interpret these faces negatively. Previous research on the viewing of neutral stimuli demonstrated that participants with depressive symptoms were more likely to perceive the stimuli as negative (Nejad et al., 2013).

A final limitation of note is the sensitivity of the ROI analyses in this project. Generally speaking, an ROI mask that specifies only a few brain regions is much more sensitive at detecting differences in those areas. However, given the multitude of brain regions implicated in both the fear circuitry and affect dysregulation models of PTSD that are of interest in this project, the ROI mask was quite broad, consequentially expanding the number of multiple comparisons in both the structural and functional analyses. As such, the error correction for multiple comparisons was quite stringent, requiring a particularly large voxel number to achieve statistical significance. With this constraint, it is possible that important differences in both brain structure and function in smaller brain regions were overlooked after failing to meet the significance criterion following the correction for multiple comparisons. Thus, ROIs that exhibited null findings in this project should not be dismissed as unimportant to affect regulation in individuals with PTSD.

Summary and Conclusions

CPT has demonstrated robust efficacy in the treatment of PTSD. While treatment dropout occurs, it is perceived to be inevitable in some cases and a result of individual client factors. An alternative hypothesis is that our evidenced-based treatments are not meeting the needs for clients with clinically significant impairment. The fact remains that some individuals drop out of treatment and remain symptomatic with suboptimal functioning. The next step in the development of established evidence-based approaches for PTSD is to examine this population with consideration of the active components of the treatment to improve treatment implementation and effectiveness. This can be done by examining the interaction between treatment implementation and individual client variables.

Of the many possible client variables of interest that may influence dropout (i.e., race, SES, marital status), those most affected by the treatment process are clinical variables and dimensions of functioning. The present study attempted to examine the interaction of self-reported latent constructs (i.e., affectivity) and neurobiological constructs within the application of CPT. While it was found that CPT can improve self-reported affectivity for individuals that remain in treatment, it appears that low PA in particular may represent a risk factor for dropout from CPT. Additionally, gray matter volume in some areas related to the top-down regulation of emotion was also found to be significantly different between the treatment completion and dropout groups. In conjunction, these results suggest that there is more work to be done in identifying clinically relevant client variables that influence the application of manualized treatments for PTSD. This research could provide the foundation for a clinical assessment protocol

that identifies individual risk factors for treatment adherence and dropout, allowing the subsequent treatment plan to be tailored for specific client needs. This may ultimately enhance the effectiveness of manualized treatments.

However, conducting an MRI scan on every treatment seeker is currently both impractical and expensive, which creates the demand for a means to approximate neurobiological structural and functional biomarkers of treatment. Exploration of clinical variables related to neurobiological dimensions is essential in this context. It is possible that within-group differences in gray matter may reflect differences in measurable clinical variables, including affectivity, individual PTSD symptom profiles, or symptom severity. Future analyses of this data will examine the relationships between other clinical variables of interest as they relate to variations in brain structure and function in this particular sample.

References

Ahmed, F., Spottiswoode, B.S., Carey, P.D., Stein, D.J., & Seedat, S. (2012). Relationship between neurocognition and regional brain volumes in traumatized adolescents with and   without posttraumatic stress disorder. *Neuropsychobiology*, *66*(3), 174.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders—text revision* (4th ed.). Washington, DC.

Anderson, A.K., & Phelps, E.A. (2002). Is the human amygdala critical for the subjective experience of emotion?: Evidence of intact dispositional affect in patients with amygdala lesions. *Journal of Cognitive Neuroscience, 14(5)*, 709-720.

Armony, J.L., Corbo, V., Clément, M.H., & Brunet, A. (2005). Amygdala response in patients with acute PTSD to masked and unmasked emotional facial expressions. *American Journal of Psychiatry*, 162(10), 1961-3.

Ashburner, J., & Friston, K.J. (2005). Unifiedsegmentation. *NeuroImage, 26*, 839–851.

Bae, K.Y., Kim, D.W., Im, C.H., & Lee, S.H. (2011). Source imaging of P300 auditory evoked potentials and clinical correlations in patients with posttraumatic stress disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *35*(8), 1908-1917.

Bagby, R.M., Ryder, A.G., Schuller, D.R., & Marshall, M.B. (2004). The Hamilton Depression Rating Scale: has the gold standard become a lead weight? *American Journal of Psychiatry, 161(12),* 2163–77.

Banks, S.J., Eddy, K.T., Angstadt, M., Nathan, P.J., & Phan, K.L. (2007). Amygdala-

frontal connectivity during emotion regulation. *Social Cognitive and Affective*

Neuroscience, 2(4), 303-312.

Barkay, G., Freedman, N., Lester, H., Louzoun, Y., Sapoznikov, D., Luckenbaugh, D.,

Shalev, A., Chisin, R., & Bonne, O. (2012). Brain activation and heart rate during

script-driven traumatic imagery in PTSD: Preliminary findings. *Psychiatry*

Research: Neuroimaging, *204*(2), 155-160.

Barrett, L.F., Bliss-Moreau, E., Duncan, S.L., Rauch, S.L., & Wright, C.I. (2007). The

amygdala and the experience of affect. *Social Cognitive and Affective*

Neuroscience, 2(2), 73-83.

Beauregard, M., Levesque, J., & Bourgouin, P. (2001). Neural correlates of conscious

self-regulation of emotion. *The Journal of Neuroscience, 21(18)*, 6993-7000.

Beck, A.T., Baruch, E., Balter, J.M., Steer, R.A., & Warman, D.M. (2004). A new

instrument for measuring insight: the Beck Cognitive Insight Scale.

Schizophrenia Research, 68(2-3), 319-329.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Beck Depression Inventory.* San

Antonio, TX: The Psychological Corporation.

Blair, K.S., Smith, B.W., Mitchell, D.G., Morton, J., Vythilingam, M., Pessoa, L.,

Fridberg, D., Zametkin, A., Sturman, D., Nelson, E.E., Drevets, W.C., Pine, D.S.,

Martin, A., & Blair, R.J. (2007). Modulation of emotion by cognition and

cognition by emotion. *NeuroImage*, 35, 430–440.

Blake, D.D., Weathers, F.W., Nagy, L.M., Kaloupek, D.G., et al. (1995). The
development of a Clinician-Administered PTSD Scale. *Journal of Traumatic Stress, 8(1)*, 75-90.

Blanchard, E.B., Buckley, T.C., Hickling, E.J., & Taylor, A.E. (1998). Posttraumatic
stress disorder and comorbid major depression: Is the correlation an illusion?
Journal of Anxiety Disorders, 12(1), 21-37.

Blanchette, I., & Richards, A. (2010). The influence of affect on higher level cognition: A
review of research on interpretation, judgement, decision making and reasoning.
Cognition & Emotion, 24 (4), 561-595.

Bless, H. & Fiedler, K. (2006). Mood and the regulation of information processing and
behavior. In J. P. Forgas (Ed.), *Hearts and minds: Affective influences on social
cognition and behaviour* (pp. 65–84). New York: Psychology Press.

Bless, H., & Schwarz, N. (1999). Sufficient and necessary conditions in dual process
models: The case of mood and information processing. In S. Chaiken and Y.
Trope (Eds.), *Dual process theories in social psychology* (pp. 423-440). New
York: Guilford.

Borkovec, T.D., & Sharpless, B. (2004). Generalized Anxiety Disorder: Bringing
cognitive behavioral therapy into the valued present. In S. Hayes, V. Follette, &
M. Linehan (Eds.), *New directions in behavior therapy (*pp. 209-242). New York:
Guilford Press.

Boudreaux, E., Kilpatrick, D.G., Resnick, H.S., Best, C.L., & Saunders, B.E. (1998).
Criminal victimization, posttraumatic stress disorder and comorbid

psychopathology among a community sample of women. *Journal of Traumatic Stress, 11(4)*, 665-678.

Bradley, B., DeFife, J. A., Guarnaccia, C., Phifer, J., Fani, N., Ressler, K. J., & Westen, D. (2011). Emotion dysregulation and negative affect: Association with psychiatric symptoms. *Journal of Clinical Psychiatry, 72,* 685–691.

Braver, T. S., Gray, J. R., & Burgess, G. C. (2007). Explaining many varieties in working memory variation: dual mechanisms of cognitive control. In A. Conway, C. Jarrold, M. J.Kane, A. Miyake, & J. Towse (Eds.), *Variation in Working Memory* (pp. 76-106). Oxford University Press.

Bremner, J.D. (1999). Alterations in brain structure and function associated with post-traumatic stress disorder. In *Seminars in clinical neuropsychiatry* (Vol. 4, No. 4, pp. 249-255).

Bremner, J.D., Staib, L.H., Kaloupek, D., Southwick, S.M., Soufer, R., & Charney, D.S. (1999). Neural correlates of exposure to traumatic pictures and sound in Vietnam combat veterans with and without posttraumatic stress disorder: a positron emission tomography study. *Biological psychiatry*, *45*(7), 806-816.

Bremner, J.D., Vythilingam, M., Vermetten, E., Southwick, S.M., McGlashan, T., Nazeer, A., Khan, S., Vaccarino, L.V., Soufer, R., Garg, P.K., Ng, C.K., Staib, L.H., Duncan, J.S., Charney, D.S. (2003). MRI and PET study of deficits in hippocampal structure and function in women with childhood sexual abuse and posttraumatic stress disorder. *American Journal of Psychiatry*, 160, 924–932.

Breslau, N., Kessler, R.C., Chilcoat, H.D., Schultz, L.R., Davis, G.C., & Andreski, P. (1998). Trauma and posttraumatic stress disorder in the community: The 1996 Detroit Area Survey of Trauma. *Archives of General Psychiatry,* 55(7), 626- 632.

Briere, J., & Rickards, S. (2007). Self-awareness, affect regulation, and relatedness: Differential sequels of childhood versus adult victimization experiences. *Journal of Nervous and Mental Disease, 195*, 497-503.

Britton, J. C., Phan, K. L., Taylor, S. F., Fig, L. M., & Liberzon, I. (2005). Corticolimbic bloodflow in posttraumatic stress disorder during script-driven imagery. *Biological Psychiatry*, 57, 832–840.

Brown, T.A., Chorpita, B.F., & Barlow, D.H. (1998). Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *Journal of Abnormal Psychology, 107(2)*, 179-192.

Brown, W.J., Bruce, S.E., Buchholz, K.R., Mueller, T., Hu, E., & Sheline, Y.I. (2014). Affective dispositions and PTSD symptom clusters in female interpersonal trauma survivors. *Journal of Interpersonal Violence.* DOI: 10.1177/0886260514555866.

Bryant, R.A., Felmingham, K., Kemp, A., Das, P., Hughes, G., Peduto, A., & Williams, L. (2008). Amygdala and ventral anterior cingulate activation predicts treatment response to cognitive behaviour therapy for post-traumatic stress disorder. *Psychological Medicine*, 38(4), 555-561.

Bryant, R.A., Kemp, A.H., Felmingham, K.L., Liddell, B., Olivieri, G., Peduto, A., Gordon, E., & Williams, L.M. (2008). Enhanced amygdala and medial

prefrontal activation during nonconscious processing of fear in posttraumatic

stress disorder: an fMRI study. *Human Brain Mapping*, 29(5), 517-23.

Bruce, S.E., Buchholz, K.R., Brown, W.J., Yan, L., Durbin, A., & Sheline, Y.I. (2013).

Altered emotional interference processing in the amygdala and insula in women

with post-traumatic stress disorder. *NeuroImage: Clinical*, *2*, 43-49.

Bush, G., Luu, P. & Posner, M.I. (2000). Cognitive and emotional influences in the

anterior cingulate cortex. *Trends in Cognitive Science,* 4(6), 215-222.

Canto, C. B., Wouterlood, F. G., & Witter, M. P. (2008). What does the anatomical

organization of the entorhinal cortex tell us? *Neural plasticity*, *2008*.

Carey, P.D., Warwick, J., Niehaus, D.J., Van der Linden, G., Van Heerden, B.B., Harvey,

B.H., Seedat, S., & Stein, D. J. (2004). Single photon emission computed

tomography (SPECT) of anxiety disorders before and after treatment with

citalopram. *BMC psychiatry*, *4*(1), 30.

Carhart-Harris, R.L., Wall, M.B., Erritzoe, D., Kaelen, M., Ferguson, B., De Meer, I.,

Tanner, M., Bloomfield, M., Williams, T.M., Bolstridge, M., Stewart, L., Morgan,

C.J.,Newbould, R.D., Feilding, A., Curran, H.V., & Nutt, D. J. (2014). The effect

of acutely administered MDMA on subjective and BOLD-fMRI responses to

favourite and worst autobiographical memories. *International Journal of

Neuropsychopharmacology*, *17*(4), 527-540.

Chen, S., Xia, W., Li, L., Liu, J., He, Z., Zhang, Z., Yan, L., Zhang, J., Hu, D. (2006).

Gray matter density reduction in the insula in fire survivors with posttraumatic

stress disorder: a voxelbased morphometric study. Psychiatry Research:

Neuroimaging 146, 65–72.

Christiansen, D.M., & Elklit, A. (2008). Risk factors predict post-traumatic stress disorder differently in men and women. *Annals of General Psychiatry, 7*, 24.

Cisler, J.M., Steele, J.S., Smitherman, S., Lenow, J.K., & Kilts, C.D. (2013). Neural processing correlates of assaultive violence exposure and PTSD symptoms during implicit threat processing: a network-level analysis among adolescent girls. *Psychiatry Research: Neuroimaging*, *214*(3), 238-246.

Clark, L.A., & Watson, D. (1991). Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. *Journal of Abnormal Psychology, 100(3)*, 316-336.

Cloitre, M. (2009). Effective psychotherapies for Posttraumatic Stress Disorder: A review and critique. *CNS Spectrums*, 14(Supplement 1), 32-43.

Cloitre, M., Miranda, R., Stovall-McClough, K. C., & Han, H. (2005). Beyond PTSD: Emotion regulation and interpersonal problems as predictors of functional impairment in survivors of childhood abuse. *Behavior Therapy* 36, 119-124.

Cloitre, M., Scarvalone, P., Difede, J. (1997). Posttraumatic stress disorder, self- and interpersonal dysfunction among sexually retraumatized women. *Journal of Traumatic Stress*, 10, 437–452.

Clore, G. L., & Huntsinger, J. R. (2007). How emotions inform judgment and regulate thought. *Trends in Cognitive Sciences*, 11, 393-399.

Cohen, J.A., Mannarino, A.P., & Deblinger, E. (2006). *Treating Trauma and Traumatic Grief in Children and Adolescents.* New York: Guilford Press.

Constans, J. I. (2001). Worry propensity and the perception of risk. *Behaviour Research and Therapy*, 39, 721_729.

Creamer, M.C., Burgess, P., & McFarlane, A.C. (2001). Post-traumatic stress disorder:

findings from the Australian National Survey of Mental Health and Well-being.

Psychological Medicine, 31(7),1237-1247.

Cremers, H.R., Demenescu, L.R., Aleman, A., Renken, R., van Tol, M., van der Wee,

N.J., Veltman, D.J., & Roelofs, K. (2009). Neuroticism modulates amygdala--

prefrontal connectivity in response to negative emotional facial expressions.

NeuroImage, 49(1),   963-970.

Dale, L.P., Carroll, L.E., Galen, G., Hayes, J.A., Webb, K.W., & Porges, S.W. (2009).

Abuse history is related to autonomic regulation to mild exercise and

psychological wellbeing. *Applied Psychophysiology and Biofeedback*, 34(4), 299-

308.

Daniels, J.K., Coupland, N.J., Hegadoren, K.M., Rowe, B.H., Densmore, M., Neufeld,

R.W., & Lanius, R. A. (2012). Neural and behavioral correlates of peritraumatic

dissociation in an acutely traumatized sample. *The Journal of clinical psychiatry*,

73(4), 420-426.

Dannlowski, U., Stuhrmann, A., Beutelmann, V., Zwanzger, P., Lenzen, T., Grotegerd,

D., Domschke, K., Hohoff, C., Ohrmann, P., Bauer, J., Lindner, C., Postert, C.,

Konrad, C., Arolt, V., Heindel, W., Suslow, T., & Kugel, H. (2012). Limbic scars:

 long-term consequences of childhood maltreatment revealed by functional and

structural magnetic resonance imaging. *Biological psychiatry*, *71*(4), 286-293.

Davis, M. (1992). The role of the amygdala in conditioned fear. In: *The amygdala:*

neurobiological aspects of emotion, memory and mental dysfunction (Aggleton

JP, ed), pp. 255–305. New York: Wiley.

Davis, M., & Whalen, P.J. (2001). The amygdala: vigilance and emotion. *Molecular Psychiatry*, 6(1), 13-34.

Derakshan, N., & Eysenck, M. W. (1998). Working memory capacity in high trait-anxious and repressor groups. *Cognition and Emotion*, 12, 697-713.

Derryberry, D., & Tucker, D. M. (1994). Motivating the focus of attention. In P. M. Niedenthal & S. Kitayama (Eds.), *The heart's eye: Emotional influences in perception and attention* (pp. 167–196). San Diego: Academic Press.

Desmond, J., & Glover, G. (2002) Estimating sample size in functional MRI (fMRI) neuroimaging studies: statistical power analyses. *Journal of Neuroscience Methods, 118(2),* 115-128.

Diekhof, E.K., Geier, K., Falkai, P., & Gruber, O. (2011). Fear is only as deep as the mind allows: a coordinate-based meta-analysis of neuroimaging studies on the regulation of negative affect. *Neuroimage*, 58(1), 275-85.

Duncan, S., & Barrett, L.F. (2007). Affect as a form of cognition: A neuro-biological analysis. *Cognition and Emotion*, 21, 1184-1211.

Ehring, T., & Quack, D. (2010). Emotion regulation difficulties in trauma survivors: the role of trauma type and PTSD symptom severity. *Behavior Therapy*, 41, 587–598.

Etkin, A., & Wager, T.D. (2007). Functional neuroimaging of anxiety: a meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *American Journal of Psychiatry*, 164, 1476–1488.

Falconer, E., Bryant, R., Felmingham, K.L., Kemp, A.H., Gordon, E., Peduto, A., Olivieri, G., & Williams, L.M. (2008). The neural networks of inhibitory control

in posttraumatic stress disorder. *Journal of psychiatry & neuroscience: JPN*, *33*(5), 413.

Fales, C.L., Barch, D.M., Rundle, M.M., Mintun, M.A., Snyder, A.Z., Cohen, J.D., Mathews, J., & Sheline, Y.I. (2008). Altered emotional interference processing in affective and cognitive-control brain circuitry in major depression. *Biological Psychiatry, 63(4)*, 377-384.

Fani, N., King, T.Z., Jovanovic, T., Glover, E.M., Bradley, B., Choi, K., Ely, T., Gutman, D.A., & Ressler, K. J. (2012). White matter integrity in highly traumatized adults with and without post-traumatic stress disorder. *Neuropsychopharmacology*, *37*(12), 2740-2746.

Ferrier-Auerbach, A., Erbes, C.R., Polusny, M.A., Rath, C.M., & Sponheim, S.R. (2010). Predictors of emotional distress reported by soldiers in the combat zone. *Journal of Psychiatric Research*, 44, 470-476.

Fetterman, A.K., & Robinson, M.D. (2011). Routine cognitive errors: a trait-like predictor of individual differences in anxiety and distress. *Cognition and Emotion,* 25(2), 244-264.

Fetzner, M. G., Collimore, K. C., Carleton, R. N., & Asmundson, G. J. (2012). Clarifying the relationship between AS dimensions and PTSD symptom clusters: are negative and positive affectivity theoretically relevant constructs?.*Cognitive behaviour therapy*, *41*(1), 15-25.

Fiedler, K. (2001). Affective influences on social information processing. In J.P. Forgas (Ed.), *The handbook of affect and social cognition* (pp. 163–185). Mahwah, NJ: Erlbaum.

First, M.B., & Gibbon, M. Hilsenroth, M.J. (Ed), & Segal, D.L. (Ed). (2004). The

    Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and the

    Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II).

    Comprehensive handbook of psychological assessment, Vol. 2: Personality

    assessment, 134-143. Hoboken, NJ, US: John Wiley & Sons Inc.

Foa, E. B. (1995). *Posttraumatic Stress Diagnostic Scale (manual).* Minneapolis, MN:

    National Computer Systems.

Foa, E. B., Cashman, L., Jaycox, L., & Perry, K. (1997). The validation of a self-report

    measure of posttraumatic stress disorder: The Posttraumatic Diagnostic Scale.

    Psychological Assessment, 9(4), 445–451.

Foa, E.B., Keane, T.M., & Friedman, M.J., eds. (2000). *Effective Treatments for PTSD:*

    Practice Guidelines from the International Society for Traumatic Stress Studies.

    New York, NY, US: Guilford Press.

Foa, E.B., & Kozak, M.J. (1986). Emotional processing of fear: Exposure to corrective

    information. *Psychological Bulletin,* 99, 20-35.

Forgas, J. P. (Ed.). (2006). Affect in social thinking and behavior. New York: Psychology

    Press.

Forgas, J. P. (2007). When sad is better than happy: Negative affect can improve the

    quality and effectiveness of persuasive messages and social influence strategies.

    Journal of Experimental Social Psychology, 43, 513–528.

Forgas, J. P. (2008). Affect and Cognition. *Perspectives on Psychological Science*, 3(2),

    94-101.

Forgas, J. P. (2010). Affect and global versus local processing: The processing benefits of negative affect for memory, judgments, and behavior. *Psychological Inquiry*, 21, 216-224.

Frazier, P., Keenan, N., Anders, S., Perera, S., Shallcross, S., & Hintz, S. (2011). Past, present, and future control and adjustment to stressful life events. *Journal of Personality and Social Psychology*, 100, 749-765.

Fredrickson, B. L., & Branigan, C. (2005). Positive emotions broaden the scope of attention and thought-action repertoires. *Cognition and Emotion*, 19, 313-332.

Frewen, P.A, Dozois, D.A., Neufeld, R.W., Densmore, M., Stevens, T.K., & Lanius, R.A. (2011). Self-referential processing in women with PTSD: Affective and neural response. *Psychological Trauma: Theory, Research, Practice and Policy, 3(4),* 318-328.

Frewen, P. A., & Lanius, R. A. (2006). Toward a psychobiology of posttraumatic self-dysregulation: reexperiencing, hyperarousal, dissociation, and emotional numbing. *Annals of the New York Academy of Sciences*, 1071, 110–124.

Frischen, A., Eastwood, J. D., & Smilek, D. (2008). Visual search for faces with emotional expressions. *Psychological Bulletin*, 134(5), 662-676.

Friston, K., Holmes, A., Worsley, K., Poline, J., Frith, C., & Frackowiak, R. (1994). Statistic parametric maps in functional imaging: A general linear approach. *Human Brain Mapping, 2*, 189–210.

Galovski, T. E., Blain, L. M., Chappuis, C., & Fletcher, T. (2013). Sex differences in recovery from PTSD in male and female interpersonal assault survivors. *Behaviour research and therapy*, *51*(6), 247-255.

Garfinkel, S.A., & Liberzon, I. (2009). Neurobiology of PTSD: A review of

neuroimaging findings. *Psychiatric Annals,* 39(6), 370-381.

Glaser, J., van Os, J., Portegijs, P. J. M., & Myin-Germeys, l. (2006). Childhood trauma

and emotional reactivity to daily life stressors in adult frequent attenders of

general practitioners. *Journal of Psychosomatic Research, 61,* 229-236.

Gros, D.F., Price, M., Strachan, M., Yuen, E.K., Milanak, M.E., & Acierno, R. (2012).

Behavioral Activation and Therapeutic Exposure (BA-TE): An investigation of

relative symptom changes in PTSD and depression during the course of integrated

behavioral activation, situational exposure, and imaginal exposure techniques.

Behavior Modification, 36, 580-599.

Grosse Holtforth, M., Castonguay, L. G., Boswell, J. F., Wilson, L. A., Kakouros, A. A.,

& Borkovec, T. D. (2007). Insight in Cognitive-Behavioral Therapy. In L. G.

Castonguay & C. E. Hill (Eds.), *Insight in psychotherapy* (pp. 57-80).

Washington: American Psychological Association.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery*

and Psychiatry. 23, 56-62.

Hamilton, M. (1967). Development of a rating scale for primary depressive illness.

British Journal of Social and Clinical Psychology, 6, 278-96.

Hankin, C.S., Spiro, A., Miller, D.R., & Kazis, L. (1999). Mental disorders and mental

health treatment among US Department of Veterans Affairs outpatients: The

Veterans Health Study. *American Journal of Psychiatry, 156*, 1924–1930.

Herringa R, Phillips M, Almeida J, Insana S, Germain A. (2012). Post-traumatic stress

symptoms correlate with smaller subgenual cingulate, caudate, and insula

volumes in unmedicated combat veterans. *Psychiatry Research: Neuroimaging,*
203(2), 139-145.

Hopper, J.W., Frewen, P.A., Sack, M., Lanius, R.A., & van der Kolk, B.A. (2007). The
responses to script-driven imagery scale (RSDI): assessment of state
posttraumatic symptoms for psychobiological and treatment research. *Journal of*
Psychopathology and Behavioral Assessment, 20, 249-268.

Hedges, D.W., Thatcher, G.W., Bennett, P.J., Sood, S., Paulson, D., Creem-Regehr, S.,
Brown, B.L., Allen, S., Johnson, J., Froelich, B., & Bigler, E. D. (2008). Brain
integrity and cerebral atrophy in Vietnam combat veterans with and without
posttraumatic stress disorder. *Neurocase*, *13*(5-6), 402-410.

Huppert, J. D., Pasupuleti, R. V., Foa, E. B., & Mathews, A. (2007). Interpretation biases
in social anxiety: Response generation, response selection, and self-appraisals.
Behaviour Research and Therapy, 45, 1505-1515.

Hsu C-C, Chong M-Y, Yang P, Yen C-F (2002). Posttraumatic Stress Disorder Among
Adolescent Earthquake Victims in Taiwan. *Journal of American Academy of*
Child & Adolescent Psychiatry, 41, 875–881.

Jacobson, N.S., Dobson, K.S., Truax, P.A., Addis, M.E., Koerner, K., Gollan, J.K.,
Gortner, E., & Prince, S.E. (1996). A component analysis of cognitive-behavioral
treatment for depression. *Journal of consulting and clinical psychology*, *64*(2),
295.

Jatzko, A., Schmitt, A., Demirakca, T., Weimer, E., & Braus, D.F. (2006). Disturbance in
the neural circuitry underlying positive emotional processing in post–traumatic

stress disorder (PTSD). *European archives of psychiatry and clinical neuroscience*, *256*(2), 112-114.

John, O.P., & Gross, J.J. (2004). Healthy and unhealthy emotion regulation: Personality processes, individual differences, and life span development. *Journal of Personality*, 72(6), 1301-1334.

Kalisch, R., Wiech, K., Critchley, H.D., Seymour, B., O'Doherty, J.P., Oakley, D.A., Allen, P., & Dolan, R.J. (2005). Anxiety Reduction through Detachment: Subjective, Physiological, and Neural Effects. *Journal of Cognitive Neuroscience, 17(6)*, 874-883.

Karl, A., Schaefer, M., Malta, L.S., Dorfel, D., Rohleder, N., Werner, A. (2006). A metaanalysis of structural brain abnormalities in PTSD. *Neuroscience and Biobehavioral Reviews, 30*, 1004–1031.

Kasai, K., Yamasue, H., Gilbertson, M.W., Shenton, M.E., Rauch, S.L., Pitman, R.K. (2008). Evidence for acquired pregenual anterior cingulate gray matter loss from a twin study of combat-related posttraumatic stress disorder. *Biological Psychiatry, 63*, 550–556.

Kennis, M., Rademaker, A.R., van Rooij, S.J., Kahn, R.S., & Geuze, E. (2015). Resting state functional connectivity of the anterior cingulate cortex in veterans with and without post-traumatic stress disorder. *Human brain mapping*, *36*(1), 99-109.

Kessler, R.C., Chiu, W.T., Demler, O., Merikangas, K. R., & Walters, E.E. (2005). Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Archives of General Psychiatry, 62*(6), 617-627.

Kessler, R.C., Sonnega, A., Bromet, E., Hughes, M., & Nelson, C.B. (1995).
Posttraumatic stress disorder in the National Comorbidity Survey. *Archives of General Psychiatry,* 52(12*)*, 1048-1060.

King-Kallimanis, B., Gum, A.M., & Kohn, R. (2009). Comorbidity of depressive and anxiety disorders for older Americans in the national comorbidity survey-replication. *The American Journal of Geriatric Psychiatry, 17(9*), 782-792.

Kross, E., Davidson, M., Weber, J., & Ochsner, K.N. (2009). Coping with emotions past: The neural bases of regulating affect associated with negative autobiographical memories. *Biological Psychiatry*, 65, 361-366.

Kunst, M. J. J., Bogaerts, S. and Winkel, F. W. (2011), Type D personality and posttraumatic stress disorder in victims of violence: a cross-sectional exploration. *Clinical Psychology & Psychotherapy*, 18, 13–22.

Lanius, R.A., Hopper, J.W., & Menon, R.S. (2003). Individual differences in a husband and wife who developed PTSD after a motor vehicle accident: a functional MRI case study. *American Journal of Psychiatry*, 160, 667–669.

Lanius, R.A., Williamson, P.C., Bluhm, R.L., Densmore, M., Boksman, K., Neufeld, R.W., Gati, J.S., & Menon, R.S. (2005). Functional connectivity of dissociative responses in posttraumatic stress disorder: a functional magnetic resonance imaging investigation. *Biological psychiatry*, *57*(8), 873-884.

Lanius, R. A., Williamson, P. C., Densmore, M., Boksman, K., Gupta, M. A., Neufeld, R.W., Gati, J.S., & Menon, R.S. (2001). Neural correlates of traumatic memories in posttraumatic stress disorder: A functionalMRI investigation. *American Journal of Psychiatry*, 158, 1920–1922.

Lazar, J., Kaplan, O., Sternberg, T., & Lubow, R.E. (2012). Positive and negative affect produce opposing task-irrelevant stimulus preexposure effects. *Emotion*, 12(3), 591-604.

Levesque, J., Fanny, E., Joanette, Y., Paquette, V., Mensour, B., Beaudoin, G., Leroux, J., Bourgouin, P., & Beauregard, M. (2003). Neural circuitry underlying voluntary suppression of sadness. *Biological Psychiatry, 53(6),* 502-510.

Li, L., Wu, M., Liao, Y., Ouyang, L., Du, M., Lei, D., Chen, L., Yao, L., Huang, X., & Gong, Q. (2014). Grey matter reduction associated with posttraumatic stress disorder and traumatic stress. *Neuroscience & Biobehavioral Reviews*, *43*, 163-172.

Liberzon, I., Britton, J. C., & Phan, K. L. (2003). Neural correlates of traumatic recall in posttraumatic stress disorder. *Stress*, 6(3), 151−156.

Liberzon, I., Taylor, S.F., Amdur, R., Jung, T.D., Chamberlain, K.R., Minoshima, S., Koeppe, R.A., & Fig, L.M. (1999). Brain activation in PTSD in response to trauma-related stimuli. *Biological Psychiatry,* 45, 817–826.

Lightsey Jr., O.R., Maxwell, D. A., Nash, T.M., Rarey, E.B., & McKinney, V.A. (2011). Self-control and self-efficacy for affect regulation as moderators of the negative affect- life satisfaction relationship. *Journal of Cognitive Psychotherapy*, 25(2), 142-154.

Lilly, M., & Valdez, C. (2012). Interpersonal trauma and PTSD: The roles of gender and a lifespan perspective in predicting risk. *Psychological Trauma: Theory, Research, Practice, and Policy*, 4, 140-144.

Lindemer, E.R., Salat, D.H., Leritz, E.C., McGlinchey, R.E., & Milberg, W.P. (2013). Reduced cortical thickness with increased lifetime burden of PTSD in OEF/OIF Veterans and the impact of comorbid TBI. *NeuroImage: Clinical*, *2*, 601-611.

Linehan, M.M. (1993). *Cognitive-Behavioral Treatment of Borderline Personality Disorder*. New York: Guilford.

Lissek S. & Grillon C. (2012). Conditioning models of PTSD. In J.G. Beck and D.M. Sloan (Eds.), *The Oxford handbook of traumatic disorders,* (pp. 175-190). New York, NY: Oxford University Press.

Lobbestael, J., Leurgans, M., & Arntz, A. (2011). Inter-rater reliability of the structured clinical interview for DSM-IV axis I disorders (SCID I) and axis II disorders (SCID II). *Clinical psychology & psychotherapy*, *18*(1), 75-79.

MacLeod, C. & Campbell, L. (1992). Memory accessibility and probability judgments: An experimental evaluation of the availability heuristic. *Journal of Personality and Social Psychology, 63,* 890-902.

Magno, C. (2010). Integrating negative affect measures in a measurement model: Assessing the function of negative affect as interference to self-regulation. *The International Journal of Educational and Psychological Assessment,* 4, 48-67.

Maner, J. K., & Gerend, M. A. (2007). Motivationally selective risk judgments: Do fear and curiosity boost the boons or the banes? *Organizational Behavior and Human Decision Processes*, 103, 256-267.

Marshall-Berenz, E.C., Morrison, J.A., Schumacher, J.A., & Coffey, S.F. (2011). Affect intensity and lability: the role of posttraumatic stress disorder symptoms in borderline personality disorder. *Depression and Anxiety*, 28(5), 393-399.

Matsumoto, A., Ichikawa, Y., Kanayama, N., Ohira, H., & Iidaka, T. (2006). Gamma band activity and its synchronization reflect the dysfunctional emotional processing in alexithymic persons. *Psychophysiology, 43(6),* 533-540.

Mazza, M., Tempesta, D., Pino, M.C., Nigri, A., Catalucci, A., Guadagni, V., Gallucci, M., Iaria, G., & Ferrara, M. (2014). Neural activity related to cognitive and emotional empathy in post-traumatic stress disorder. *Behavioural brain research*, *282,* 37-45.

McLean, L., Toner, B., Desroches M., Jackson J., & Stuckless, N. (2006). The relationship between childhood sexual abuse, complex posttraumatic stress disorder and alexithymia in two outpatient samples: Examination of women treated in community versus institutional clinics. *Journal of Child Sexual Abuse,* 15(3), 1-17.

Melcher, T., Born, C., & Gruber, O. (2011). How negative affect influences neural control processes underlying the resolution of cognitive interference: an event-related fMRI study. *Neuroscience Research*, 70(4), 415-27.

Melcher, T., Obst, K., Mann, A., Paulus, C., & Gruber, O. (2012). Antagonistic modulatory influences of negative affect on cognitive control: Reduced and enhanced interference resolution capability after the induction of fear and sadness. *Acta Psychologica*, 139(3), 507–514.

Meng, Y., Qiu, C., Zhu, H., Lama, S., Lui, S., Gong, Q., & Zhang, W. (2014). Anatomical deficits in adult posttraumatic stress disorder: a meta-analysis of voxel-based morphometry studies. *Behavioural brain research*, *270*, 307-315.

Meriau, K., Wartenburger, I., Kazzer, P., Prehn, K., Villringer, A., Van Der Meer, E., and

Heekeren, H.R. (2009). Insular activity during passive viewing of aversive stimuli

reflects individual differences in state negative affect. *Brain Cognition,* 69, 73–80.

Milanak, M. E. & Berenbaum, H. (2009). The Relationship between PTSD symptom

factors and emotion. *Journal of Traumatic Stress*, 22, 139-145.

Miller, D. T. and Porter, C. A. (1983), Self-Blame in Victims of Violence. *Journal of

Social Issues*, 39: 139–152.

Mineka, S., Watson, D., & Clark, L.A. (1998). Comorbidity of anxiety and unipolar

mood disorders. *Annual Review of Psychology, 49*, 377-412.

Monson, C.M., Price, J.L., Rodriguez, B.F., Ripley, M.P., & Warner, R.A. (2004).

Emotional deficits in military-related PTSD: An investigation of content and

process disturbances. *Journal of Traumatic Stress*, 17, 275–279.

Morey, R.A., Dolcos, F., Petty, C.M., Cooper, D.A., Hayes, J.P., LaBar, K.S., &

McCarthy, G. (2009). The role of trauma-related distractors on neural systems for

working memory and emotion processing in posttraumatic stress disorder.

Journal of psychiatric research, *43*(8), 809-817.

Moritz, S., Birkner, C., Kloss, M., Jahn, H., Hand, I., Haasen, C., & Krausz, M. (2002).

Executive functioning in obsessive-compulsive disorder, unipolar depression, and

schizophrenia. *Archives of Clinical Neuropsychology, 17*(5), 477-483.

Mueller-Pfeiffer, C., Schick, M., Schulte-Vels, T., O'Gorman, R., Michels, L., Martin-

Soelch, C., Blair, J., Rufer, M., Schnyder, U., Zeffiro, T., & Hasler, G. (2013).

Atypical visual processing in posttraumatic stress disorder. *NeuroImage:

Clinical*, *3*, 531-538.

Mueller-Pfeiffer, C., Zeffiro, T., O'Gorman, R., Michels, L., Baumann, P., Wood, N.,
Spring, J., Rufer, M., Pitman, R.K., & Orr, S. P. (2014). Cortical and cerebellar
modulation of autonomic responses to loud sounds. *Psychophysiology*, *51*(1), 60-
69.

Nejad, A. B., Fossati, P., & Lemogne, C. (2013). Self-referential processing, rumination,
and cortical midline structures in major depression. *Frontiers in human
neuroscience*, *7*.

New, A.S., Fan, J., Murrough, J.W., Liu, X., Liebman, R.E., Guise, K.G., Tang, C.Y., &
Charney, D.S. (2009). A functional magnetic resonance imaging study of
deliberate emotion regulation in resilience and posttraumatic stress disorder.
Biological Psychiatry, 66, 656–664.

Nishith, P., Resick, P. A., & Griffin, M. G. (2002). Pattern of change in prolonged
exposure and cognitive–processing therapy for female rape victims with
posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology, 70*,
880–886.

Nixon, R.D., Resick, P.A., & Nishith, P. (2004). An exploration of comorbid depression
among female victims of intimate partner violence with posttraumatic stress
disorder. *Journal of Affective Disorders, 82(2)*, 315-320.

Ochsner, K.N., Bunge, S.A., Gross, J.J., & Gabrieli, J.D. (2002). Rethinking feelings: An
fMRI study of the cognitive regulation of emotion. *Journal of Cognitive
Neuroscience, 14(8)*, 1215-1229.

Pagura, J., Stein, M.B., Bolton, J.M., Cox, B.J., Grant, B., & Sareen, J. (2010).

    Comorbidity of borderline personality disorder and posttraumatic stress disorder

    in the U.S. population. *Journal of Psychiatric Research*, 44, 1190-1198.

Pedersen, S.S. & Denollet, J. (2004). Validity of the Type D personality construct in

    Danish post-MI patients and healthy controls. *Journal of Psychosomatic*

    Research, 57, 265-272.

Petrowski, K., Wintermann, G., Smolka, M.N., Huebner, T., & Donix, M. (2014). The

    neural representation of emotionally neutral faces and places in patients with

    panic disorder with agoraphobia. *Journal of affective disorders*, *152*, 454-461.

Philip, N.S., Kuras, Y.I., Valentine, T.R., Sweet, L.H., Tyrka, A.R., Price, L.H., &

    Carpenter, L.L. (2013). Regional homogeneity and resting state functional

    connectivity: associations with exposure to early life stress. *Psychiatry Research:*

    Neuroimaging, *214*(3), 247-253.

Pietrzak, R.H., Goldstein, R.B., Southwick, S.M., & Grant, B.F. (2011). Personality

    disorders associated with full and partial posttraumatic stress disorder in the U.S.

    population: results from Wave 2 of the National Epidemiologic Survey on

    Alcohol and Related Conditions. *Journal of Psychiatry Research*, 45(5), 678-686.

Pissiota, A., Frans, O., Michelgard, A., Appel, L., Langstrom, B., Flaten, M.A., &

    Fredrikson, M. (2003). Amygdala and anterior cingulate cortex activation during

    affective startle modulation: A PET study of fear. *European Journal of*

    Neuroscience, 18(5), 1325-1331.

Post, L.M, Zoellner, L.A, Youngstrom, E., & Feeny, N.C. (2011). Understanding the

relationship between co-occurring PTSD and MDD: Symptom severity and

affect. *Journal of Anxiety Disorders*, 25, 1123–1130.

Qi, S., Mu, Y., Liu, K., Zhang, J., Huan, Y., Tan, Q., Shi, M., Wang, Q., Chen, Y., Wang,

H., Zhang, H., Zhang, X., Xiong, L., & Yin, H. (2013). Cortical inhibition deficits

in recent onset PTSD after a single prolonged trauma exposure. *NeuroImage:*

Clinical, *3*, 226-233.

Rademaker, A.R., van Zuiden, M., Vermetten, E., & Geuze, E. (2011). Type D

personality and the development of PTSD symptoms: a prospective study.

Journal of Abnormal Psychology, 120(2), 299-307.

Ramon, D., Geva, R.,& Goldstein, A. (2011). Trait and state negative affect interactions

moderate inhibitory control performance in emotionally loaded conditions.

Personality and Individual Differences, 51, 95-101.

Resick, P. A. (2001). *Cognitive Processing Therapy: Generic manual.* Unpublished

instrument, University of Missouri—St. Louis.

Resick, P.A., Galovski, T.E., Uhlmansiek, M.O., Scher, C.D., Clum, G.A., & Young-Xu,

Y. (2008). A randomized clinical trial to dismantle components of cognitive

processing therapy for posttraumatic stress disorder in female victims of

interpersonal violence. *Journal of Consulting and Clinical Psychology*, 76(2),

243-258.

Resick, P.A., Nishith, P., Weaver, T.L., Astin, M.C., & Feuer, C.A. (2002). A

comparison of cognitive-processing therapy with prolonged exposure and a

waiting condition for the treatment of chronic posttraumatic stress disorder in female rape victims. *Journal of Consulting and Clinical Psychology*, 70, 867-879.

Resick, P.A., & Schnicke, M.K. (1992). Cognitive processing therapy for sexual assault survivors. *Journal of Consulting and Clinical Psychology, 60*, 748-756.

Resick, P.A., & Schnicke, M.K. (1993). *Cognitive Processing Therapy for Rape Victims: A Treatment Manual.* Volume 4. Thousand Oaks, CA, US: Sage Publications, Inc.

Resick, P. A., Suvak, M. K., & Wells, S. Y. (2014). The impact of childhood abuse among women with assault-related PTSD receiving short-term cognitive–behavioral therapy. *Journal of traumatic stress*, *27*(5), 558-567.

Richards, A., French, C. C., Keogh, E., & Carter, C. (2000). Test anxiety, inferential reasoning and working memory load. *Anxiety, Stress, and Coping*, 13, 87-109.

Rizvi, S. L., Vogt, D. S., & Resick, P. A. (2009). Cognitive and affective predictors of treatment outcome in cognitive processing therapy and prolonged exposure for posttraumatic stress disorder. *Behaviour Research and Therapy*,*47*(9), 737-743.

Rogers, M.A., Yamasue, H., Abe, O., Yamada, H., Ohtani, T., Iwanami, A., Aoki, S., Kato, N., Kasai, K. (2009). Smaller amygdala volume and reduced anterior cingulate gray matter density associated with history of post-traumatic stress disorder. Psychiatry Research: *Neuroimaging 174*, 210–216.

Schaefer, S.M., Jackson, D.C., Davidson, R.J., Aguirre, G.K., Kimberg, D.Y., & Thompson-Schill, S.L. (2002). Modulation of amygdalar activity by the conscious regulation of negative emotion. *Journal of Cognitive Neuroscience, 14(6),* 913-921.

Shackman, A.J., Sarinopoulos, I., Maxwell, J.S., Pizzagalli, D.A., Lavric, A., & Davidson, R.J. (2006). Anxiety selectively disrupts visuospatial working memory. *Emotion*, 6, 40-61.

Shallcross, A. J., Troy, A. S., Boland, M., & Mauss, I. B. (2010). Let it be: accepting negative emotional experiences predicts decreased negative affect and depressive symptoms. *Behaviour Research and Therapy*, 48, 921–929.

Shang, J., Lui, S., Meng, Y., Zhu, H., Qiu, C., Gong, Q., Liao, W., & Zhang, W. (2014). Alterations in low-level perceptual networks related to clinical severity in PTSD after an earthquake: a resting-state fMRI study. *PloS one*, *9*(5), e96834.

Shaw, M.E., Moores, K.A., Clark, R.C., McFarlane, A.C., Strother, S.C., Bryant, R.A., Brown, G.C., & Taylor, J. D. (2009). Functional connectivity reveals inefficient working memory systems in post-traumatic stress disorder.*Psychiatry Research: Neuroimaging*, *172*(3), 235-241.

Shaw, M.E., Strother, S.C., McFarlane, A.C., Morris, P., Anderson, J., Clark, C.R., & Egan, G.F. (2002). Abnormal functional connectivity in posttraumatic stress disorder. *Neuroimage*, *15*(3), 661-674.

Shore, J. H., Vollmer, W. M., & Tatum, E. L. (1989). Community patters of posttraumatic stress disorders. *Journal of Nervous and Mental Disease*, 177, 681–685.

Shucard, J.L., Cox, J., Shucard, D.W., Fetter, H., Chung, C., Ramasamy, D., & Violanti, J. (2012). Symptoms of posttraumatic stress disorder are related to structural MRI and behavioral measures of affective stimulus processing in police officers. *Psychiatry Research*: *Neuroimaging*, *204,* 25-31.

Sledjeski, E.M., Speisman, B., & Dierker, L.C. (2008). Does number of lifetime traumas explain the relationship between PTSD and chronic medical conditions? Answers from the National Comorbidity Survey-Replication (NCS-R). *Journal of Behavioral Medicine,* 31(4), 341-349.

Sobel, A.A., Resick, P.A., & Rabalais, A.E. (2009). The effect of cognitive processing therapy on cognitions: impact statement coding. *Journal of Traumatic Stress*, 22(3), 205-11.

Souza, W.F., Figueira, I., Mendlowicz, M.V., Volchan, E., Mendonca-de-Souza, A.C., Duarte, A.F., Da Silva, A.M., Marques-Portella, C., Mari, J.J., & Coutinho, E. (2008). Negative affect predicts posttraumatic stress symptoms in Brazilian volunteer United Nations peacekeepers in Haiti. *Journal of Nervous and Mental Disease, 196(11),* 852-855.

Sparta, D. R., Smithuis, J., Stamatakis, A. M., Jennings, J. H., Kantak, P. A., Ung, R. L., & Stuber, G. D. (2014). Inhibition of projections from the basolateral amygdala to the entorhinal cortex disrupts the acquisition of contextual fear. *Frontiers in behavioral neuroscience*, *8*.

Starr, S., & Moulds, M. (2006). The role of negative interpretations of intrusive memories in depression. *Journal of Affective Disorders*, 93, 125–132.

Stopa, L., & Clark, D. M. (2000). Social phobia and interpretation of social events. *Behaviour Research and Therapy*, 38, 273_283.

Tarquis, N. (2006). Neurobiological hypothesis relating to connections between psychopathy and childhood maltreatment. *Encephale, 32*(3), 377-84.

Thomsen, D. K., Mehlson, M. Y., Viidik, A., Sommerland, B., & Zachariae, R. (2005). Age and gender differences in negative affect—Is there a role for emotion regulation? *Personality and Individual Differences*, 38, 1935–1946.

Tull, M.T., Jakupcak, M., McFadden, M.E., & Roemer, L. (2007). The role of negative affect intensity and the fear of emotions in posttraumatic stress symptom severity among victims of childhood interpersonal violence. *Journal of Nervous and Mental Disease, 195(7)*, 580-587.

Tzourio-Mazoyer N., Landeau, B., Papthanassiou, D., Crivello, F., Etard, O., Delcroix, N., et al. (2002). Automated anatomical labeling of activations in SPM using macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage, 15*, 273–89.

van der Kolk, B.A., Pelcovitz, D., Roth, S., Mandel, F.S., et al. (1996). Dissociation, somatization, and affect dysregulation: The complexity of adaption to trauma. *American Journal of Psychiatry, 153*, 83-93.

van der Kolk, B.A., Roth, S., Pelcovitz, D., Sunday, S., & Spinazzola, J. (2005). Disorders of extreme stress: The empirical foundation of a complex adaptation to trauma. *Journal of Traumatic Stress, 18,* 389-399.

van Rooij, S.J., Rademaker, A.R., Kennis, M., Vink, M., Kahn, R.S., & Geuze, E. (2014). Impaired right inferior frontal gyrus response to contextual cues in male veterans with PTSD during response inhibition. *Journal of psychiatry & neuroscience: JPN*, *39*(5), 330.

Vastfjall, D., Peters, E., & Slovic, P. (2008). Affect, risk perception and future optimism after the tsunami disaster. *Judgment and Decision Making*, 3, 64-72.

Vermeulen, N. (2010). Current positive and negative affective states modulate attention: An attentional blink study. *Personality and Individual Differences*, *49*, 542–545.

Vermeulen, N., Corneille, O., & Luminet, O. (2007). A mood moderation of the Extrinsic Affective Simon Task. *European Journal of Personality,* 21, 359-369.

Wager, T. D., & Feldman Barrett, L. (2004). From affect to control: Functional specialization of the insula in motivation and regulation. *Published online at Psychextra.*

Ward, B.D. (2000). Simultaneous inference for fMRI data. from http://afni.nimh.nih.gov/pub/dist/doc/manual/AlphaSim.pdf.

Watson, D. (2005). Rethinking the mood and anxiety disorders: A quantitative hierarchical model for DSM-V. *Journal of Abnormal Psychology, 114(4)*, 522-536.

Watson, D., & Clark, L.A. (1984). Negative affectivity: The disposition to experience aversive emotional states. *Psychological Bulletin, 96(3),* 465-490.

Watson, D., & Clark, L.A. (1994). *The PANAS-X: Manual for the positive and negative affect   schedule-expanded form*. University of Iowa: Psychology Publications.

Watson, D., Clark, L. A., & Carey, G. (1988). Positive and negative affectivity and their relation to anxiety and depressive disorders. *Journal of Abnormal Psychology, 97,* 346-353.

Watson, D., Clark, L.A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54(6),* 1063-1070.

Watson, D., O'Hara, M.W., & Stuart, S. (2008). Hierarchical structures of affect and psychopathology and their implications for the classification of emotional disorders. *Depression and Anxiety, 25,* 282-288.

Watson, D., & Tellegen, A. (1985). Toward a consensual structure of mood. *Psychological Bulletin, 98(2),* 219-235.

Weems, C.F., Pina, A.A., Costa, N.M., Watts, S.E., Taylor, L.K., & Cannon, M.F. (2007). Predisaster trait anxiety and negative affect predict posttraumatic stress in youths after Hurricane Katrina. *Journal of Consulting and Clinical Psychology, 75(1),* 154-159.

West, R., Choi, P., & Travers, S. (2010). The influence of negative affect on the neural correlates of proactive and reactive cognitive control. *International Journal of Psychophysiology, 76,* 107-117.

Whalley, M.G., Kroes, M.C., Huntley, Z., Rugg, M.D., Davis, S.W., & Brewin, C.R. (2013). An fMRI investigation of posttraumatic flashbacks. *Brain and cognition*, *81*(1), 151-159.

Whalley, M.G., Rugg, M.D., Smith, A.P., Dolan, R.J., & Brewin, C.R. (2009). Incidental retrieval of emotional contexts in post-traumatic stress disorder and depression: an fMRI study. *Brain and Cognition*, *69*(1), 98-107.

White, S.F., Costanzo, M.E., Blair, J.R., & Roy, M.J. (2015). PTSD symptom severity is associated with increased recruitment of top-down attentional control in a trauma-exposed sample. *NeuroImage: Clinical*, *7*, 19-27.

Whitfield-Gabrieli, S. (2011). *Artifact Detection Tools*. Boston, MA: Massachusetts Institute of Technology.

Whittle, S., Allen, N.B., Lubman, D.I., & Yucel, M. The neurobiological basis of temperament: Towards a better understanding of psychopathology. *Neuroscience & Biobehavioral Reviews, 30(4)*, 511-525.

Wolf, E.J., Miller, M.W., & McKinney, A.E. (2009). Emotional processing in PTSD: heightened negative emotionality to unpleasant photographic stimuli. *Journal of Nervous and Mental Disease*, 197(6), 419-26.

Wolfsdorf, B.A. & Zlotnick, C. (2001). Affect management in group therapy for women with posttraumatic stress disorder and histories of childhood sexual abuse. *Journal of Clinical Psychology*, 57(2), 169-181.

Woon, F., & Hedges, D.W. (2011), Gender does not moderate hippocampal volume deficits in adults with posttraumatic stress disorder: A meta-analysis. *Hippocampus, 21*, 243–252.

Wu, R.Z., Zhang, J.R., Qiu, C.J., Meng, Y.J., Zhu, H.R., Gong, Q.Y., Huang, X.Q., & Zhang, W. (2011). Study on resting-state default mode network in patients with

posttraumatic stress disorder after the earthquake. *Journal of Sichuan University: Medical science edition*, *42*(3), 397-400.

Yan, X., Brown, A.D., Lazar, M., Cressman, V.L., Henn-Haase, C., Neylan, T.C., Shalev, A., Wolkowitz, O.M., Hamilton, S.P., Yehuda, R., Sodickson, D.K., Weiner, M.W., & Marmar, C. R. (2013). Spontaneous brain activity in combat related PTSD. *Neuroscience letters*, *547*, 1-5.

Yin, Y., Jin, C., Hu, X., Duan, L., Li, Z., Song, M., Chen, H., Feng, B., Jiang, T., Jin, H., Wong, C., Gong, Q., & Li, L. (2011). Altered resting-state functional connectivity of thalamus in earthquake-induced posttraumatic stress disorder: a functional magnetic resonance imaging study. *Brain research*, *1411*, 98-107.

Zhang J, Tan Q, Yin H, Zhang X, Huan Y, Tang L, Wang H, Xu J, Li L. (2011). Decreased gray matter volume in the left hippocampus and bilateral calcarine cortex in coal mine flood disaster survivors with recent onset PTSD. *Psychiatry Research, 192(2)*, 84-90.

Zhang, J.N., Xiong, K.L., Qiu, M.G., Zhang, Y., Xie, B., Wang, J., Li, M., Chen, H., Zhang, Y., & Zhang, J. J. (2013). Negative emotional distraction on neural circuits for working memory in patients with posttraumatic stress disorder. *Brain research*, *1531*, 94-101.

Table 1. *Demographic characteristics of the PTSD and control participants at pre-treatment presented as Mean (standard deviation) or number (%).*

Characteristic	PTSD ($n = 38$)	Controls ($n = 15$)	F, X^2	p
Age (years)	30.78 (9.21)	33.40 (11.38)	0.750	0.391
Gender (female)	38 (100%)	15 (100%)	-	-
Race (AA, CAU)	9 (24%), 23 (61%)	2 (13%), 13 (87%)	2.658	0.447
Education (years)	15.32 (2.21)	17.27 (3.13)	6.190	0.016
Right Handed	38 (100%)	15 (100%)	-	-
BDI Total Score	24.26 (11.00)	4.20 (3.16)	32.126	<0.001
PDS Total Score	28.44 (10.34)	3.92 (5.70)	60.751	<0.001
NA Total Score	28.84 (8.63)	14.93 (3.94)	35.727	<0.001
PA Total Score	23.68 (7.51)	37.87 (6.90)	40.119	<0.001

Note: PTSD = Posttraumatic Stress Disorder, AA = African American, CAU = Caucasian, BDI = Beck Depression Inventory, PDS = Posttraumatic Diagnostic Scale, NA = Negative Affect, PA = Positive Affect

Table 2. *Pearson product-moment correlations between study variables at pre-treatment.*

	1	2	3	4	5	6	7
1.Negative Affect	-						
2.Positive Affect	-0.26	-					
3.CAPS Total Score	0.54**	-0.40ⱡ	-				
4.PDS Score	0.54**	-0.50*	0.62**	-			
5.BDI Score	0.57**	-0.60**	0.64**	0.84**	-		
6.Age	0.26	-0.16	0.13	0.23	0.13	-	
7.Education	0.17	0.08	0.09	-0.23	-0.24	0.14	-

ⱡ $p<0.05$ *$p<0.01$ **$p<0.001$

Table 3. *Pre-treatment and post-treatment clinical variables in PTSD treatment completers (n = 24)*

Characteristic	Pre-treatment	Post-treatment	F, X^2	p
CAPS Total Score	68.95 (20.95)	26.58 (22.03)	85.906	<0.001
BDI Total Score	21.11 (11.30)	9.84 (9.22)	36.591	<0.001
PDS Total Score	24.16 (10.18)	10.47 (10.11)	40.225	<0.001
NA Total Score	28.32 (9.85)	19.58 (8.11)	17.044	0.001
PA Total Score	25.00 (7.18)	30.16 (7.80)	9.863	0.006

Note: PTSD = Posttraumatic Stress Disorder, CAPS = Clinician Administered PTSD Scale, BDI = Beck Depression Inventory, PDS = Posttraumatic Diagnostic Scale, NA = Negative Affect, PA = Positive Affect

Table 4. *Pearson product-moment correlations between study variables at post-treatment.*

	1	2	3	4	5	6	7
1.Negative Affect	-						
2.Positive Affect	-0.30	-					
3.CAPS Total Score	0.80**	-0.39	-				
4.PDS Score	0.76**	-0.38	0.84**	-			
5.BDI Score	0.71**	-0.30	0.78**	0.78**	-		
6.Age	0.19	-0.21	0.32	0.23	0.22	-	
7.Education	0.01	0.43	-0.02	0.07	0.01	0.14	-

† $p<0.05$ *$p<0.01$ **$p<0.001$

Table 5: *Treatment Completers vs. Treatment Dropouts before Attending*

Region	MNI coordinate	Cluster size	Z	Direction
L parahippocampal gyrus L entorhinal cortex	(-24, -27, -26)	331	3.66	T > D
R entorhinal cortex R parahippocampal gyrus	(23, -12, -33)	369	3.34	T > D

Note: T = Treatment, D = Dropout, MNI = Montreal Neurological Institute, L = left, R = right.

Note: All structural analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 271 and an uncorrected p < .005.

Table 6*: Treatment Completers vs. Treatment Dropouts after Attending*

Region	MNI coordinate	Cluster size	Z	Direction
L supplementary motor area	(0, -1, 64)	761	3.80	T < D
R supplementary motor area	(2, -22, 61)			
L postcentral gyrus	(-21, -31, 58)	378	3.75	T < D
L precentral gyrus	(-29, -24, 57)			
R calcarine	(18, -67, -14)	1053	3.53	T < D
L calcarine	(0, -64, 15)			
R calcarine	(6, -70, 18)			

Note: T = Treatment, D = Dropout, MNI = Montreal Neurological Institute, L = left, R = right.

Note: All structural analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 271 and an uncorrected p < .005.

Table 7: *Dropout after Attending vs. Healthy Controls*

Region	MNI coordinate	Cluster size	Z	Direction
L superior frontal cortex	(-27, -9, 58)	273	3.79	D > C
R precuneus	(11, -69, 30)	2455	3.72	D > C
R superior occipital cortex	(21, -67, 32)			
L middle cingulate	(-12, -51, 32)			
L calcarine	(-8, -91, -9)	388	3.60	D > C
	(-11, -100, -2)			
	(-3, -96, 3)			

Note: D = Dropout, C = Controls, MNI = Montreal Neurological Institute, L = left, R = right.

Note: All structural analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 271 and an uncorrected p < .005.

Table 8: *Structural Regression Results*

Region	Group	MNI coordinate	Cluster size	Z	Variable	Direction
R parahippocampus	PTSD	(18, -3, -29)	428	3.63	NA	Positive
	PTSD	(20, -21, -24)				
R parahippocampus	PTSD	(21, -18, -27)	466	3.78	NA*	Positive
	PTSD	(26, 3, -33)				
	PTSD	(20, -3, -32)				
R middle frontal gyrus	PTSD	(41, 51, 4)	366	3.90	PA	Positive
R precuneus	PTSD	(3, -64, 37)	958	3.53	PA	Positive
	PTSD	(11, -60, 40)				
	PTSD	(6, -58, 30)				
R precuneus	PTSD	(45, 47, 3)	777	3.94	PA*	Positive
	PTSD	(8, -58, 28)				
	PTSD	(2, -61, 37)				
R superior medial frontal gyrus	Control	(11, 42, 36)	333	4.25	NA	Negative
R middle cingulate	Control	(6, 23, 39)				
	Control	(8, 33, 42)				
L middle cingulate	Control	(-3, -22, 45)	338	3.54	NA	Negative
	Control	(-12, -19, 45)				
L middle frontal gyrus	Control	(-26, 45, 33)	273	3.50	NA	Negative
L superior medial frontal gyrus	Control	(-9, 50, 27)				
L superior frontal gyrus	Control	(-17, 44, 30)				
L medial frontal orbital gyrus	Control	(-5, 60, -3)	375	3.28	NA	Negative
R medial frontal orbital gyrus	Control	(2, 47, -11)				
L postcentral gyrus	Control	(-51, -18, 37)	305	3.99	PA	Positive
	Control	(-51, -16, 30)				
	Control	(-47, -22, 51)				

Note: PTSD = Posttraumatic Stress Disorder, MNI = Montreal Neurological Institute, L = left, R = right, PA = Positive Affect, NA = Negative Affect.

* Denotes analysis that controlled for depression symptoms.

Note: All structural analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 271 and an uncorrected p < .005.

Table 9: *Pre-treatment fMRI Regression Results*

Region	Task Condition	MNI coordinate	Cluster size	Z	Variable	Direction
L superior frontal gyrus	AF	(-14, 42, 30)	189	3.54	NA	Negative
		(-16, 50, 26)				
		(-26, 54, 22)				
R calcarine	AF	(22, -62, 6)	180	3.48	NA	Negative
		(22, -72, 12)				
L postcentral gyrus	AF	(-18, -32, 70)	153	3.52	PA	Positive
		(-32, -38, 68)				
L parahippocampus	IF	(-22, -40, -8)	126	4.08	PA	Negative
R frontal inferior orbital	IN	(44, 36, -6)	338	4.35	PA	Positive
		(52, 24, -6)				
L parahippocampus	IN	(-28, -40, -8)	266	4.35	PA	Negative
		(-32, -44, -14)				
R parahippocampus	IN	(28, -38, -8)	128	3.67	PA	Negative

Note: MNI = Montreal Neurological Institute, L = left, R = right, PA = Positive Affect, NA = Negative Affect.

Note: All functional analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 116 and an uncorrected p < .005.

Table 10: *Post-treatment fMRI Regression Results*

Region	Task Condition	MNI coordinate	Cluster size	Z	Variable	Direction
R middle frontal orbital gyrus	AN	(36, 54, -12)	144	3.85	NA	Negative
		(26, 50, -12)				
R superior frontal gyrus	AN	(30, 46, 10)	119	3.37	NA	Negative
R middle frontal gyrus		(28, 50, 20)				
L superior frontal gyrus	AN	(-14, 42, 32)	161	3.69	PA	Positive
		(-10, 38, 40)				
L postcentral gyrus	AF	(-44, -22, 56)	310	4.38	PA	Negative
		(-56, -16, 42)				
		(-44, -22, 40)				
R precentral gyrus	AF	(28, -26, 70)	1174	4.15	PA	Negative
		(52, -8, 50)				
R middle cingulate		(8, -16, 42)				
L fusiform	AF	(-34, -30, -26)	314	3.81	PA	Negative
		(-32, -28, -18)				
L parahippocampus		(-24, -26, -24)				
R precuneus	AF	(10, -58, 56)	238	3.51	PA	Negative
L middle cingulate		(-2, -44, 52)				
L precuneus		(-10, -44, 64)				
R middle frontal gyrus	IF	(20, 54, 28)	155	3.58	PA	Positive
		(12, 54, 34)				

Note: MNI = Montreal Neurological Institute, L = left, R = right, PA = Positive Affect, NA = Negative Affect.

Note: All functional analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 116 and an uncorrected p < .005.

Figure 1

Conflict Task Depiction
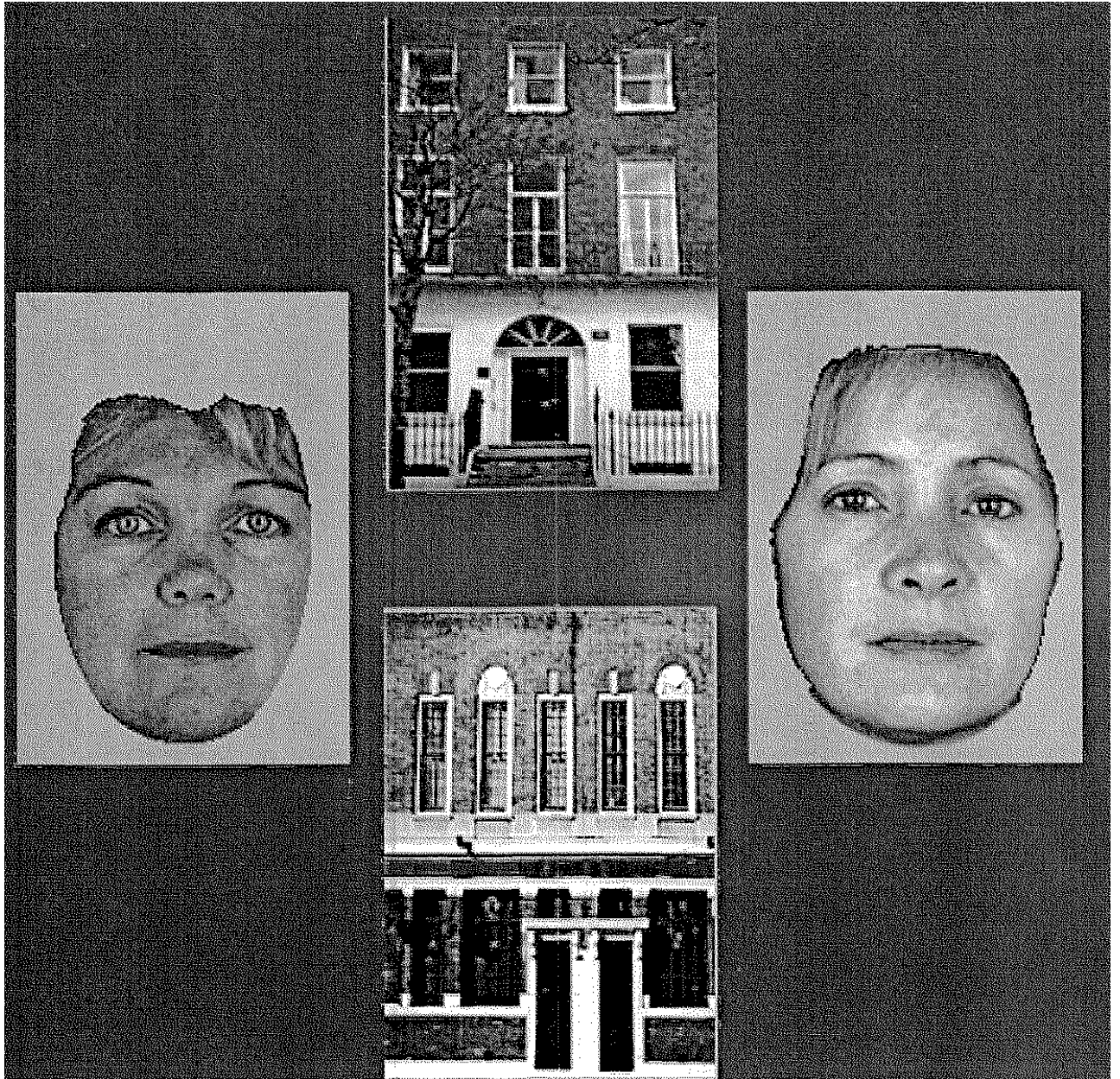
Figure 2

Region of Interest (ROI) Mask
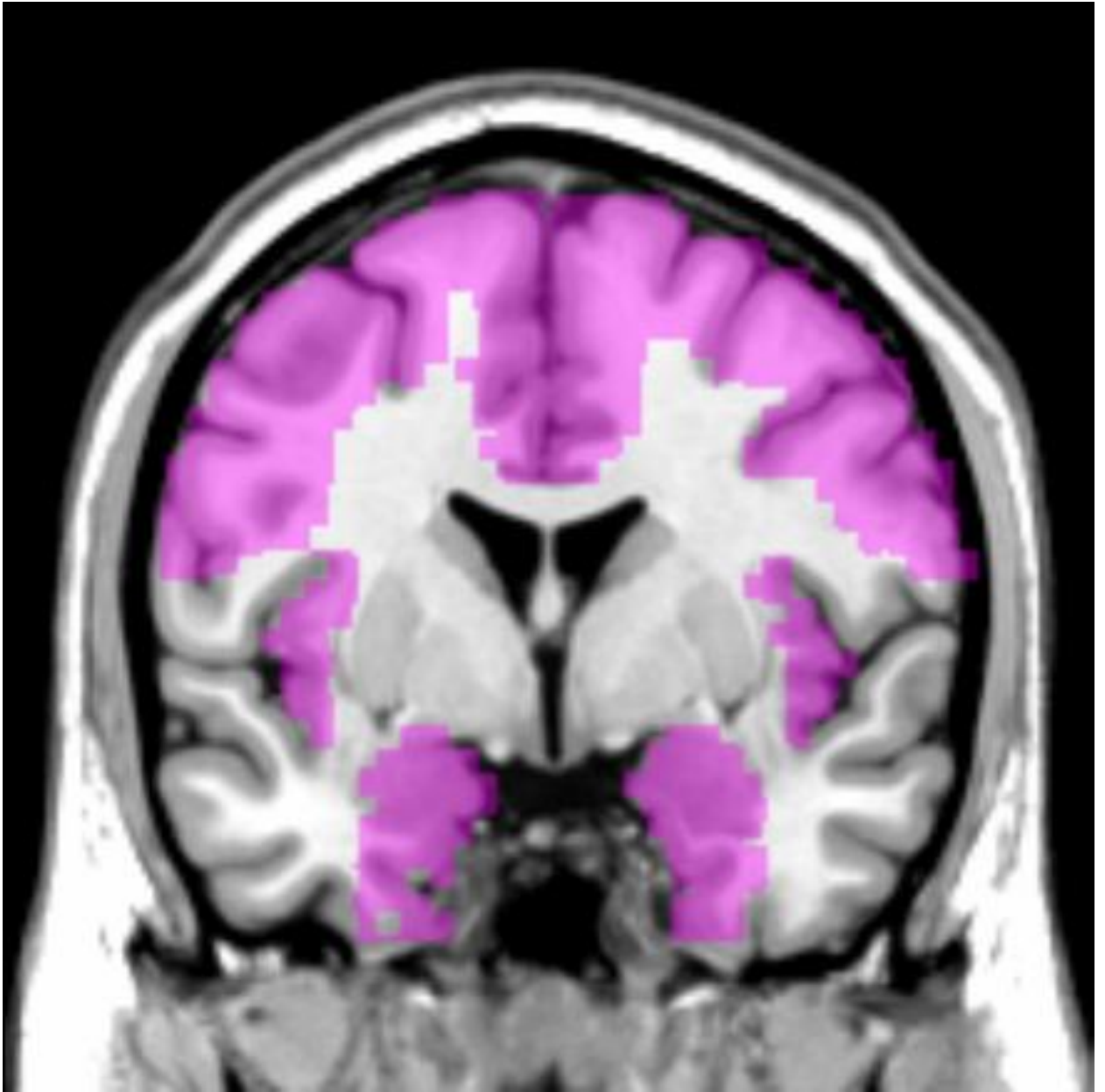
Figure 3

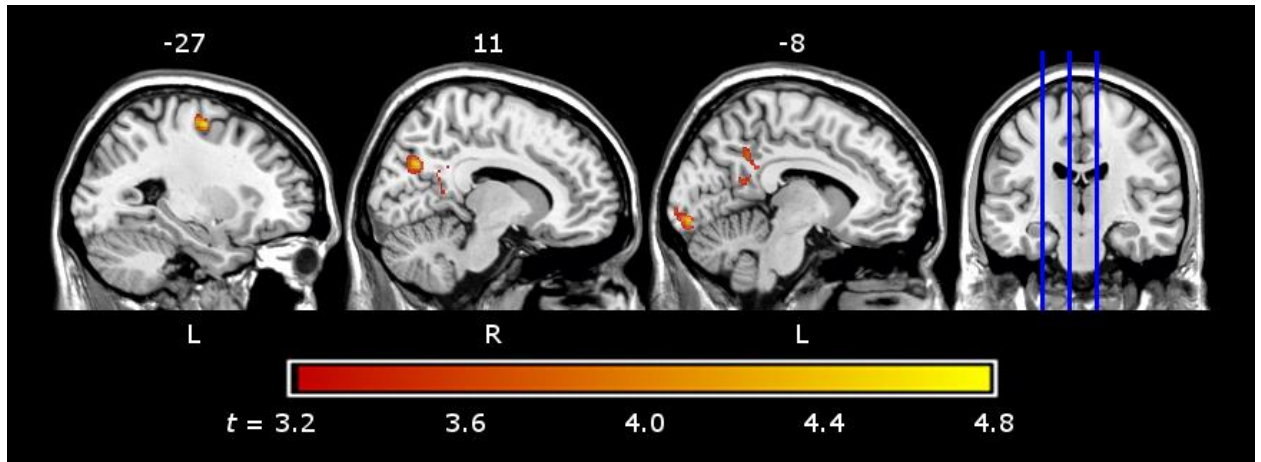*Gray Matter Differences between the Treatment Completion and No-show Groups*
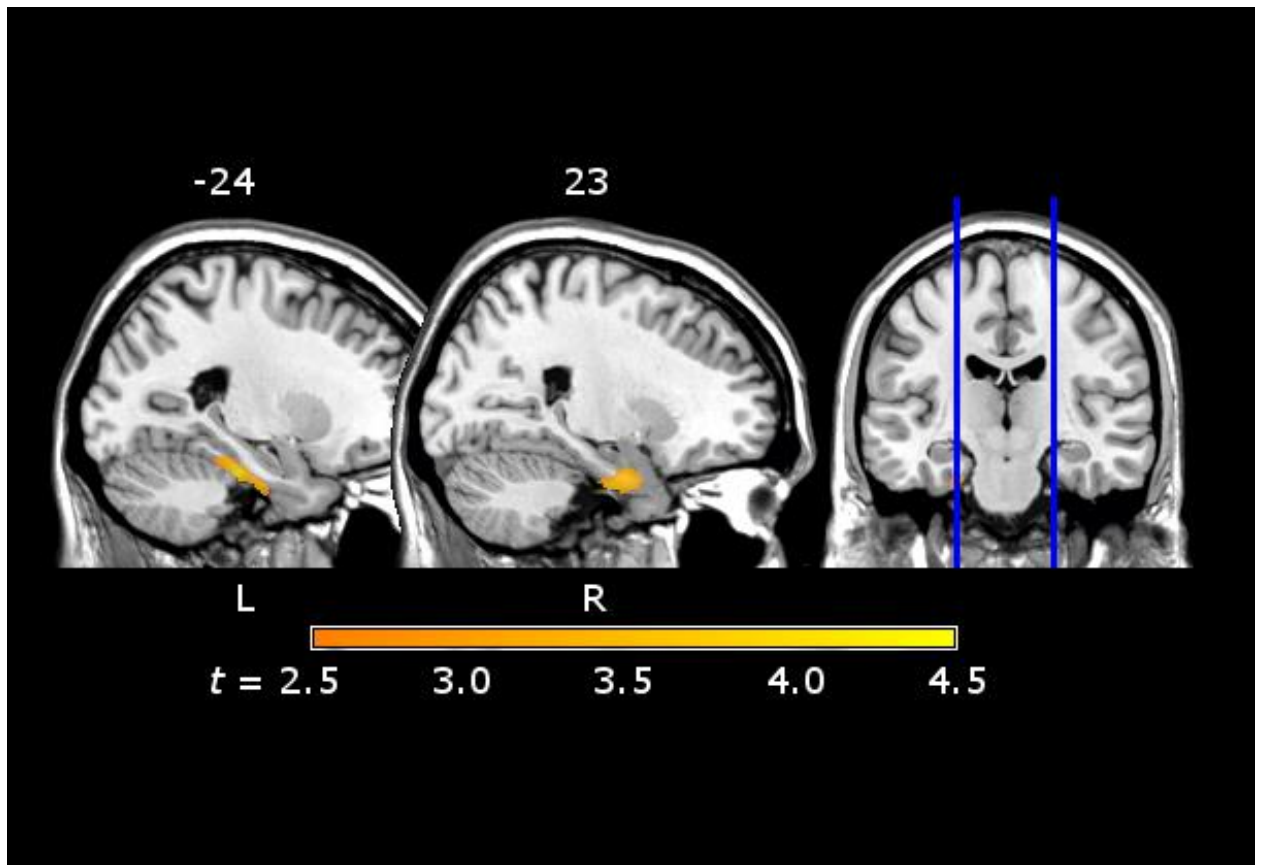
Note: L = left, R = right.

Note: Findings indicate greater volumes in treatment group.

Note: All structural analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 271 and an uncorrected p < .005.

Figure 4

Gray Matter Differences between the Treatment Completion and Dropout Groups
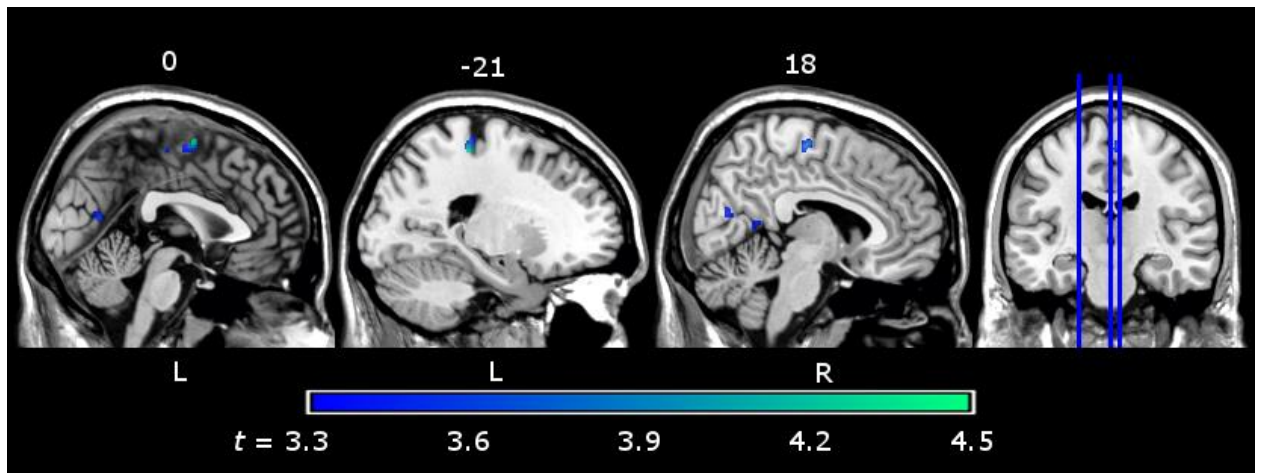
Note: L = left, R = right.

Note: Findings indicate reduced volumes in treatment group.

Note: All structural analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 271 and an uncorrected p < .005.

Figure 5

Gray Matter Differences between the Treatment Dropout and Control Groups

Note: L = left, R = right.

Note: Findings indicate greater volumes in treatment dropout group.

Note: All structural analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 271 and an uncorrected p < .005.

Figure 6

Association between Affectivity and Gray Matter Volume in PTSD Participants
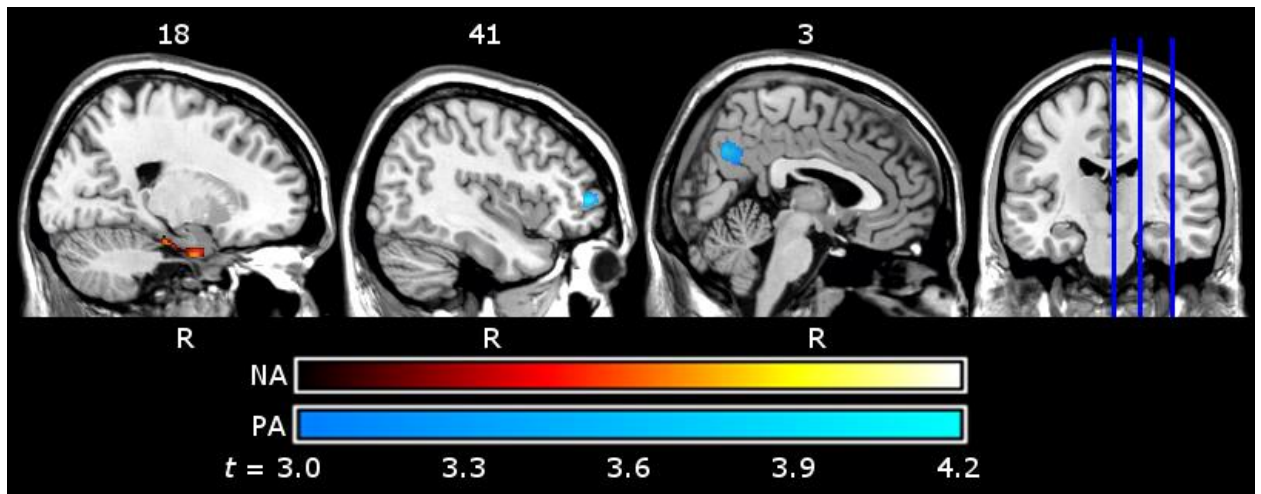
Note: L = left, R = right, PA = Positive Affect, NA = Negative Affect.

Note: All observed relationships represent positive associations.

Note: All structural analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 271 and an uncorrected p < .005.

Figure 7

Association between Affectivity and Gray Matter Volume in Control Participants
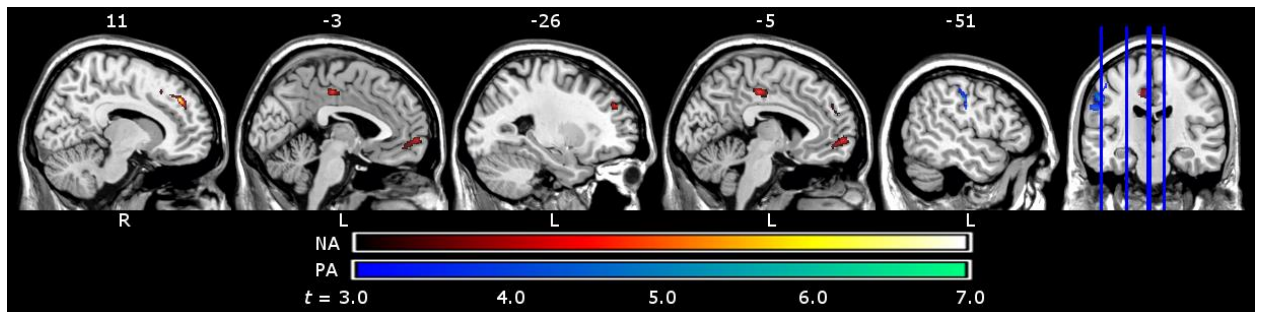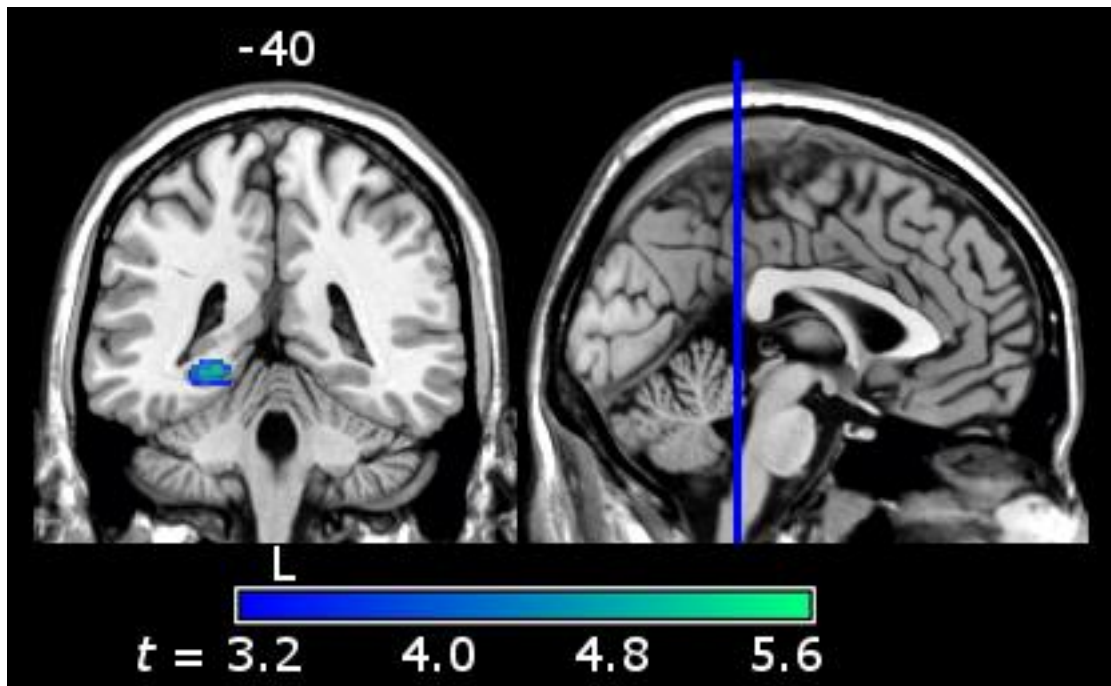

Note: L = left, R = right, PA = Positive Affect, NA = Negative Affect.

Note: Observed relationships with NA represent negative associations. Observed relationship with PA represents a positive association.

Note: All structural analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 271 and an uncorrected p < .005.

Figure 8

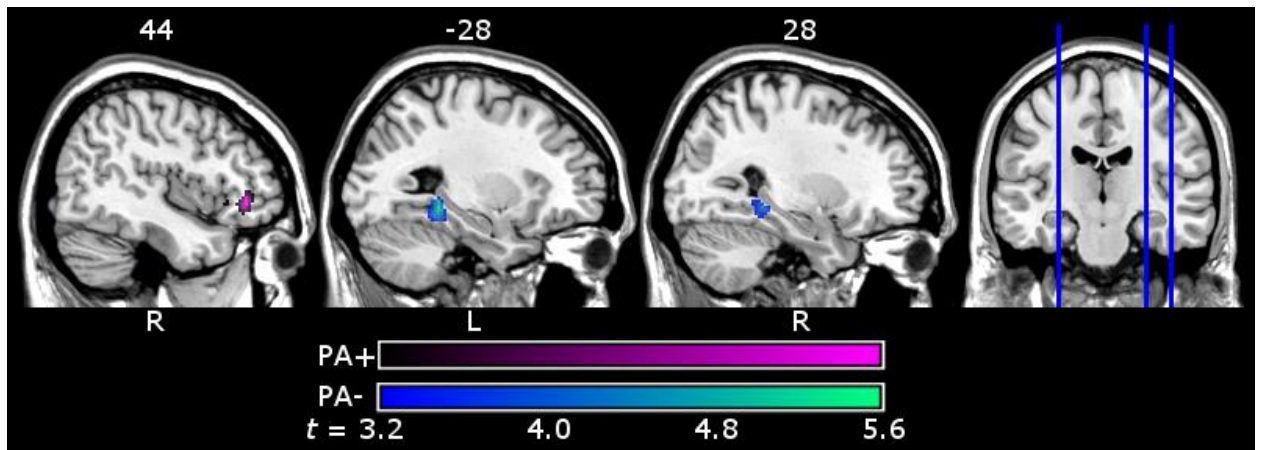*Pre-treatment Association between Affectivity and Activation during Attend Fear*

Condition
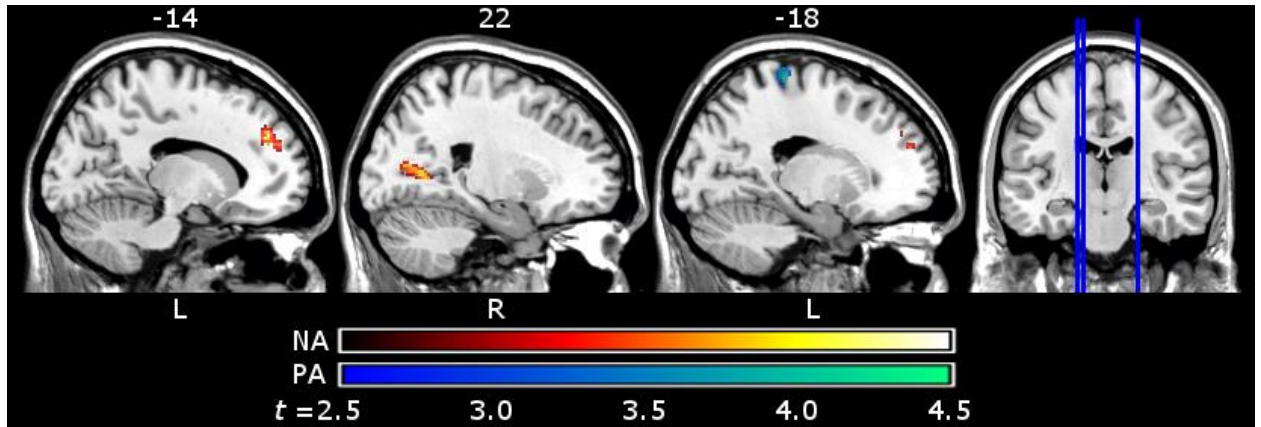
Note: L = left, R = right, PA = Positive Affect, NA = Negative Affect.

Note: Observed relationships with NA represent negative associations. Observed relationship with PA represents a positive association.

Note: All functional analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 116 and an uncorrected p < .005.

Figure 9

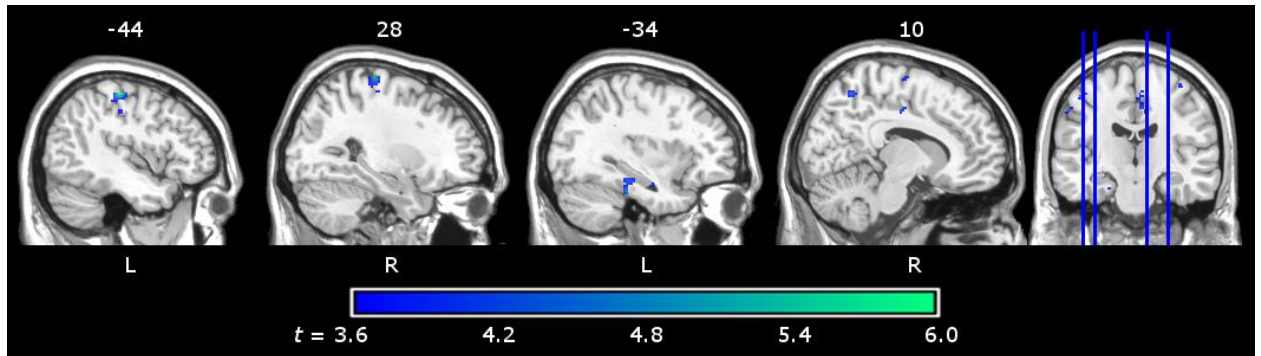*Pre-treatment Association between PA and Activation during Ignore Fear Condition*

Note: L = left, R = right.

Note: Observed relationship with PA represents a negative association.

Note: All functional analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 116 and an uncorrected p < .005.

Figure 10

Pre-treatment Association between PA and Activation during Ignore Neutral Condition

Note: L = left, R = right, (+) = Positive Relationship, (-) = Negative Relationship.

Note: All functional analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 116 and an uncorrected p < .005.

Figure 11

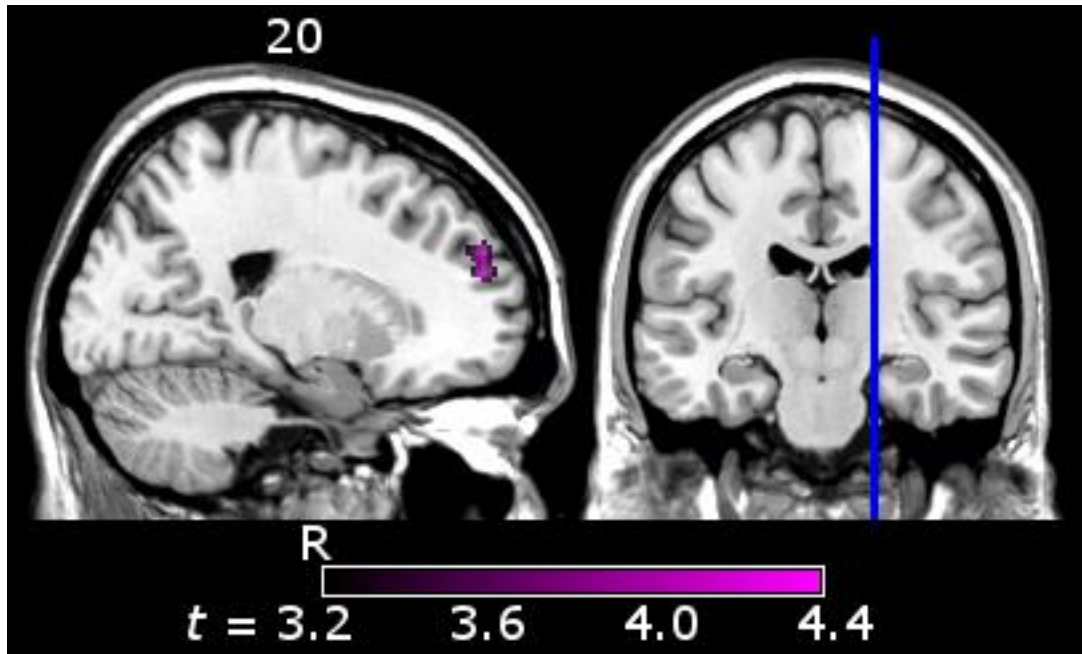*Post-treatment Association between PA and Activation during Attend Fear Condition*

Note: L = left, R = right.

Note: All observed relationships with PA represent negative associations.

Note: All functional analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 116 and an uncorrected p < .005.

Figure 12

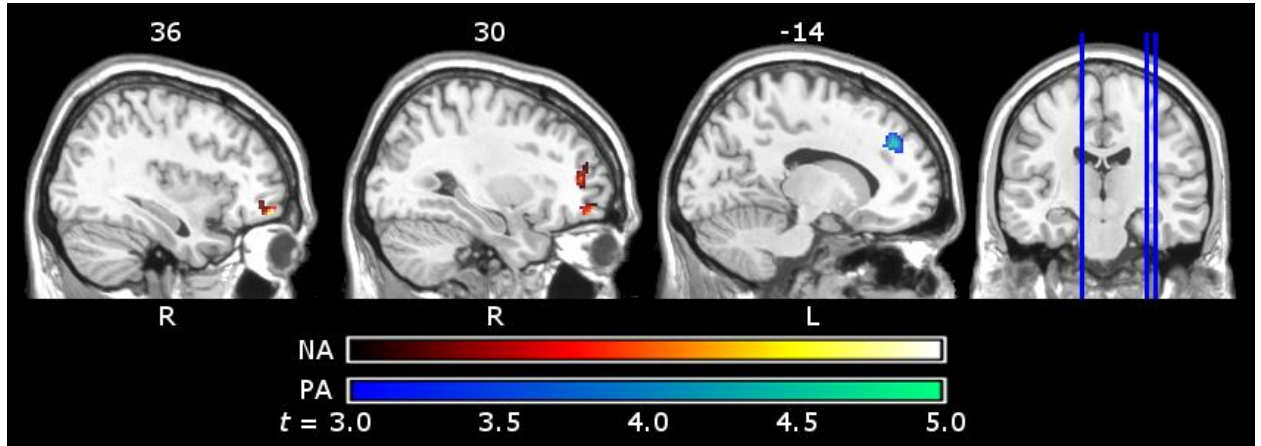*Post-treatment Association between PA and Activation during Ignore Fear Condition*

Note: R = right.

Note: Observed relationship with PA represents a positive association.

Note: All functional analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 116 and an uncorrected p < .005.

Figure 13

Post-treatment Association between Affectivity and Activation during Attend Neutral Condition

Note: L = left, R = right, PA = Positive Affect, NA = Negative Affect.

Note: Observed relationships with NA represent negative associations. Observed relationship with PA represents a positive association.

Note: All functional analyses were considered significant and corrected for multiple comparisons at a combined voxel extent threshold of k = 116 and an uncorrected p < .005.