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Neural Correlates of Rumination in Posttraumatic Stress Disorder Before and After Cognitive Processing Therapy

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NEURAL CORRELATES OF RUMINATION IN POSTTRAUMATIC STRESS
DISORDER BEFORE AND AFTER COGNITIVE PROCESSING THERAPY

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Abstract

The utilization of functional magnetic resonance imaging (fMRI) techniques to examine biomarkers and neural activity patterns related to posttraumatic stress disorder (PTSD) has provided a way to investigate mechanisms that underlie the development, maintenance, and recovery from PTSD. Studying the neural correlates of individual differences related to transdiagnostic factors has the potential to provide clinically relevant information beyond that of diagnostic categories. Rumination is one such factor. Rumination, defined as repetitive, negative, self-focused thinking is considered to be a transdiagnostic factor that is associated with depression, anxiety, and PTSD. In individuals with PTSD, rumination serves as a cognitive avoidance factor that contributes to the maintenance of symptoms by interfering with the cognitive and emotional processing of the traumatic event and it may interfere with treatment engagement and outcome. Little is known regarding the neural correlates of rumination in individuals with PTSD. The current study examined self-reported rumination in women with PTSD. Functional MRI (fMRI) was used to investigate the neural substrates of rumination in treatment seeking women with PTSD and the relationship between change in rumination and change neural activity across treatment. The relationship between rumination and treatment outcome was also examined. Participants included 39 women with PTSD, 17 women with trauma exposure and no PTSD, and 18 healthy controls recruited through a university-based trauma clinic. Results found that women with PTSD experienced greater levels of ruminative thought than women in the trauma exposed no PTSD or healthy control groups ($F(2, 71) = 28.24, p < .001, \eta^2 = .443$). At the end of Cognitive Processing Therapy, participants had a significant decrease in the level of rumination that

they reported ($t(19) = 4.693$, p (*two tailed*) $< .001$, $d = 1.05$). The fMRI findings evidenced a significant relationship between self-reported rumination and areas related to emotion generation and control. Findings did not generally support a relationship between pretreatment self-reported rumination and treatment outcome. Further, the activation of brain regions related to pretreatment rumination did not predict treatment outcome.

Neural Correlates of Rumination in Posttraumatic Stress Disorder Before and
After Cognitive Processing Therapy

Advancement of neuroimaging techniques, such as functional magnetic resonance imaging (fMRI), provides an opportunity to examine neurobiological correlates associated with psychological disorders (Miller, Elbert, Sutton, & Heller, 2007). Neuroimaging research has examined biomarkers and neural activity patterns related to a variety of psychological disorders in hopes of understanding mechanisms of development, maintenance, and recovery from disorders (Etkin, 2012; Frewen, Dozois, & Lanius, 2008). Although neurobiological research initially focused on identifying mechanisms to improve pharmacological interventions, more recent research has examined neurobiological alterations associated with psychotherapy (Roffman, Marci, Glick, Dougherty, & Rauch, 2005). To date, a handful neuroimaging treatment studies have demonstrated observable changes in brain metabolism and activity as a result of psychotherapy, suggesting that successful therapy outcomes are associated with normalization of brain activity (i.e. Felmingham et al., 2007; Ritchey, Dolcos, Eddington, Strauman, & Cabeza, 2011). With the support of these initial findings, it has been proposed that neuroimaging provides clinically relevant information on neural predictors of treatment outcome, information on the biological mechanisms of change during treatment, and a greater understanding of how a particular treatment addresses symptoms at the neurobiological level. Furthermore, neuroimaging, specifically fMRI, research on psychotherapy provides the basis for individualized, augmented, or tailored treatment through examination of neural substrates related to psychological factors and treatment

response across a variety of psychotherapies (Etkin, Pittenger, Polan, & Kandel, 2005; Frewen et al., 2008; Roffman et al., 2005).

Functional MRI (fMRI) research on psychotherapy generally examines brain activity during resting state or disorder-specific scanning tasks before and after treatment (i.e. Felmingham et al., 2007; Peres et al., 2011). The focus of this research is to identify how dysfunctional neural activity associated with a specific disorder is altered through psychotherapy. This research has been helpful in identifying how psychotherapy alters brain functioning to promote recovery; however, it is only the first step in utilizing fMRI techniques to individualize treatment. Moving towards this goal, other researchers have examined whether activation in specific brain regions predict psychotherapy outcomes (i.e. Bryant et al., 2008; Siegle, Carter, & Thase, 2006), potentially identifying biomarkers of treatment resistance. This research provides a foundation for development of new or augmented treatments for individuals who have these biomarkers (Etkin et al., 2005; Roffman et al., 2005). However, scanning technology is expensive and it seems unlikely that neuroimaging will be a standard psychotherapy assessment tool in the near future. Therefore, it is important to establish the relationship between neural circuitry variations that underlie psychological constructs commonly measured in a typical clinical assessment.

Although examining neural correlates of disorder-related symptoms is helpful in understanding how treatment alters brain activation, other psychological constructs that contribute to heterogeneity within diagnoses has the potential to provide information on differential treatment outcome and variation among individuals who have the same diagnosis (Etkin et al., 2005; Frewen et al., 2008). Potential targets for investigation are

transdiagnostic factors, such as rumination (Siegle, 2008). These transdiagnostic factors are psychological constructs that span multiple disorders and underlie comorbidity of psychological disorders (Dozois, Seeds, & Collins, 2009; McLaughlin & Nolen-Hoeksema, 2011). Treatment that targets transdiagnostic factors results in improvement of both disorders (Dozois et al., 2009; Topper, Emmelkamp, & Ehring, 2010).

Furthermore, as stated above, transdiagnostic factors such as rumination, contribute to individual differences between individuals who have the same diagnoses (Jones, Siegle, & Thase, 2008; Siegle, Steinhauer, Thase, Stenger, & Carter, 2002). Investigating neural correlates of transdiagnostic factors before and after treatment has the potential to contribute to the body of knowledge on the neural circuitry of psychotherapy. The current study investigated the neural substrates of the transdiagnostic factor of rumination before and after cognitive processing therapy (CPT) for posttraumatic stress disorder (PTSD) in women who have experienced interpersonal trauma.

Posttraumatic Stress Disorder and Rumination

As defined by the DSM-IV-TR (American Psychiatric Association, 2000), PTSD requires an etiological traumatic event that “involved actual or threatened” death, injury, or threat to physical integrity. During or after the event an individual must respond with “intense fear, helplessness, or horror” (DSM-IV-TR, 2000, p. 47). After experiencing trauma, PTSD is diagnosed when an individual has at least one reexperiencing symptom, three avoidance symptoms, and two hyperarousal symptoms for over one month.

Reexperiencing symptoms include intrusive trauma-related thoughts, recurrent nightmares, flashbacks, emotional distress in response to reminders, and physiological reactivity in response to reminders. Avoidance symptoms consist of avoiding thoughts

and feelings related to the event, avoiding people, places, and activities related to the trauma, difficulty remembering aspects of the traumatic event, anhedonia, emotional numbing, and feeling as if life will be cut short. Finally, hyperarousal symptoms include difficulty sleeping, irritability or angry outbursts, difficulty concentrating, hypervigilance, and a heightened startle response.

PTSD has been associated with a wide range of traumatic events, including traffic accidents, combat exposure, and interpersonal violence such as abuse or assault (Breslau, 2009; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). Additionally, PTSD is linked to multiple comorbid disorders (Kessler, Chiu, Demler, & Walters, 2005; Kessler et al., 1995) and difficulties with identification, regulation, and processing emotions (Boden, Bonn-miller, Kashdan, Alvarez, & Gross, 2012; Ehring & Quack, 2010; Frewen, Pain, Dozois, & Lanius, 2006a; Lanius, Bluhm, & Frewen, 2011). There are many factors that contribute to or interact with PTSD leading to heterogeneity within the diagnostic category of PTSD (Frewen & Lanius, 2006; Lanius et al., 2011). For this reason, it is important to investigate how these individual differences are associated with the course of PTSD, its underlying neural circuitry, and the process of psychotherapy.

Rumination has been identified as a potential risk and maintenance factor in PTSD (Elwood, Hahn, Olatunji, & Williams, 2009; Michael, Halligan, Clark, & Ehlers, 2007). Rumination, defined as repetitive, negatively valenced, self-referential thinking about the past, was originally thought to be uniquely associated with depression (Nolen-Hoeksema, 1991; Papageorgiou & Wells, 2003). However, further research demonstrated that rumination and ruminative thinking styles spanned mood and anxiety disorders, suggesting that rumination was a transdiagnostic factor (Birrer & Michael,

2011; McLaughlin & Nolen-Hoeksema, 2011). In fact, research has consistently linked rumination and PTSD. Reported rumination in individuals shortly after the experience of a traumatic event predicts PTSD symptoms and severity in the future (Ehlers, Mayou, & Bryant, 1998; Ehring, Frank, & Ehlers, 2008; Kleim, Ehlers, & Glucksman, 2007), indicating that rumination is a vulnerability factor for the development of PTSD (Bomyea, Risbrough, & Lang, 2012). Further, a significant positive relationship has been observed between rumination and PTSD severity (Michael et al., 2007). Rumination also contributes to the maintenance of PTSD symptoms. Individuals with PTSD who tracked their experiences of rumination in a daily log, reported that rumination often triggered intrusive memories of the traumatic event (Birrer & Michael, 2011). Research suggests that there is a bidirectional relationship between rumination and intrusive thoughts. It appears that individuals engage in ruminative thinking to avoid intrusive thoughts; however, rumination often triggers intrusive thinking leading to the maintenance of reexperiencing symptoms (Ehlers & Clark, 2000; Michael et al., 2007).

Generally, individuals who endorse ruminative styles of thinking report that engagement in rumination is outside of their control. Rumination in individuals with PTSD is associated with increased negative affect and feelings of guilt, helplessness, and anger (Birrer & Michael, 2011). It has been proposed that rumination serves as a cognitive avoidance factor in PTSD (Ehlers & Clark, 2000; Michael et al., 2007). Ruminative thinking consumes an individual's attention preventing the individual in engaging in productive cognitive and emotional processing of the traumatic event (Echiverri, Jaeger, Chen, Moore, & Zoellner, 2011; Michael et al., 2007). The content of rumination in individuals with PTSD tends to focus on questions of "What if?" and

“Why?” (Michael et al., 2007; Speckens, Ehlers, Hackmann, Ruths, & Clark, 2007; Watkins, 2004). When individuals perseverate on these questions, they only attend to specific aspects of the traumatic event instead of working through the event in the larger context. Focusing on questions of “What if?” and “Why?” can prevent integration and accommodation of the trauma memory and processing of the emotions related to the event (Foa & Kozak, 1986; Resick, 2001).

Although rumination appears to be a risk and maintenance factor in PTSD (Bomyea et al., 2012; Elwood et al., 2009; Michael et al., 2007), it is likely that there is variation in the levels of ruminative thinking in which individuals with PTSD engage. In other words, despite the strong association between PTSD and rumination, the diagnosis of PTSD is not dependent on ruminative processes (DSM-IV-TR, 2000). Rather, the level of rumination individuals engage in may affect their experience of PTSD and contribute to individual differences. For example, in one study of veterans with symptoms of depression and PTSD, only those who reported higher levels of rumination were found to engage in risky behaviors (Borders, Mcandrew, Quigley, & Chandler, 2012). This suggests that it is important to investigate how individual differences in ruminative thinking contributes to the course of PTSD.

Rumination and Psychotherapy Protocols for PTSD

Individual differences in rumination likely affect the course of psychotherapy (Echiverri et al., 2011; Jones et al., 2008; Siegle, 2008). The two major evidenced based therapy protocols for PTSD are Prolonged Exposure (PE; Foa, Rothbaum, Riggs, & Murdock, 1991), derived from Emotional Processing Theory (Foa & Kozak, 1986; Rauch & Foa, 2006), and Cognitive Processing Therapy (CPT; Resick & Schnicke, 1992,

1993), based in the Social Cognitive Theory (Janoff-Bulman, 2002; McCann & Pearlman, 1990; Resick & Schnicke, 1993; Resick, 2001; Schnurr et al., 2007). Although both therapies are classified as cognitive behavioral therapies (CBTs), the protocol for PE is focused on exposures and the main component of CPT is cognitive therapy aimed at challenging cognitions (Resick, 2001). From a PE perspective, verbally processing the traumatic event through imaginal exposures, in a safe environment assists individuals to process the emotions related to the event and extinguish their overgeneralized fear response (Foa & Kozak, 1986; Rauch & Foa, 2006). A CPT therapist, however, focuses on the client's interpretation of the event and teaches skills to identify and challenge trauma related cognitive distortions (Resick & Schnicke, 1993; Resick, 2001). There is little research investigating how these treatments address rumination and how rumination interacts with these protocols in individuals with PTSD.

In a case study (Echiverri et al., 2011) on an individual receiving PE, the authors concluded that the client's high level of rumination interfered with engagement in the exposure process. The client's rumination served as an avoidance factor and increased her negative emotions surrounding the traumatic event. The authors additionally noted that the client's ruminative processes interfered with many aspects of the imaginal exposure including the dose of exposure, the processing of the event, and the exposure content. Although it is not possible to draw broad conclusions from a case study, the authors provide an illustration as to how rumination might affect exposure based psychotherapy. Since exposure based psychotherapy for PTSD relies on clients to engage in the process of confronting the traumatic event in detail in session with the

therapist, a cognitive avoidance factor such as rumination could impact the course of treatment.

There are no known investigations of rumination in CPT; however, researchers have examined how rumination interacts with Cognitive Therapy (CT; Beck, Rush, Shaw, & Emery, 1979) for depression (Jones et al., 2008; Siegle, 2008). Since CT for depression focuses on assisting the client in challenging cognitive distortions and engaging in cognitive restructuring similar to CPT (A. T. Beck et al., 1979; J. S. Beck, 2011), research on CT and rumination provides a basis for examining the relationship of rumination and CPT. Some have suggested that CT focused on cognitive restructuring directs clients' attention to their thoughts in such a way that increases rumination. Additionally, it has been suggested that daily thought records utilized in CT as between session work encourage and maintain ruminative thought processes (Ehlers & Clark, 2008). Therefore, some researchers have suggested that rumination must be targeted through interventions aimed at the process of thinking instead of the content of thoughts (Speckens et al., 2007; Watkins, 2009; Watkins et al., 2011).

Although CBT interventions focused on the process of thinking, including mindfulness based interventions, have proven to reduce ruminative thinking and symptoms in individuals with depression (Manicavasagar, Perich, & Parker, 2012; Sipe & Eisendrath, 2012; Watkins et al., 2011); there is a dearth of research on rumination and psychotherapies that involve challenging and restructuring cognitions. The few studies that have examined the relationship between CT and rumination suggest that further research is warranted. In a study on adolescents who were taking SSRIs for depression, a reduction in the adolescents' ruminative thinking was observed after a CBT protocol that

included cognitive restructuring (Wilkinson & Goodyer, 2008). Another study that compared a CBT protocol with treatment as usual in adults with depression found that individuals with greater than three prior episodes of depression who were in the CBT group reported significantly fewer cognitive symptoms, such as rumination, compared to the treatment as usual group. The authors suggested that this finding indicated that CBT addresses ruminative thinking (Conradi, de Jonge, & Ormel, 2008). A third study examining the effects of CBT and mindfulness based cognitive therapy in individuals with depression evidenced decreases in rumination across both treatments (Manicavasagar et al., 2012). This initial research suggests that interventions that challenge and attempt to restructure cognitions decrease ruminative styles of thinking.

It is also possible that the relationship between psychotherapies and rumination is more complex than a particular treatment decreasing rumination in all individuals. A study on the effect of rumination on the course of CT for depression demonstrated that across the sample, individuals who had higher levels of pretreatment rumination and symptoms severity needed a longer course of treatment and had lower odds of remission. However, this same study found that of the individuals who had the most severe symptoms, those that had higher levels of rumination experienced faster symptom improvement and had a higher likelihood of remitting (Jones et al., 2008). Overall, it appears that psychotherapy protocols that include identifying cognitive distortions, challenging these distortions, and restructuring cognitions decrease ruminative thinking styles. Therefore, CPT is a candidate for further research on whether a cognitive-based, trauma-focused intervention decreases rumination in individuals with PTSD.

As psychotherapy research continues to examine the relationship between ruminative styles of thinking and psychological interventions, it is also important to investigate the neural mechanisms that underlie this relationship (Etkin et al., 2005; Frewen et al., 2008; Roffman et al., 2005). The majority of research on neural circuitry and PTSD has focused on comparing individuals with and without the disorder in order to identify the neural substrates of the disorder (i.e. Bruce et al., 2012; Shin et al., 2005). Although this research has provided the field with models of neural circuitry deficits related to PTSD, further research is needed to fully understand the wide range of clinical presentations (Frewen et al., 2008). As stated above, investigation of transdiagnostic factors has the potential to contribute to the body of knowledge on individual differences in individuals with PTSD. Examining the neural correlates of rumination in individuals with PTSD and how these regions change through psychotherapy could lead to identifying mechanisms related to recovery processes. Further, a relationship between regions related to rumination and treatment response may exist and could inform the development of tailored or augmented treatments (Etkin et al., 2005; Frewen et al., 2008; Roffman et al., 2005).

Neural Circuitry of Rumination in PTSD

Neural Circuitry Models of PTSD. No known fMRI studies have examined the neural substrates of rumination in PTSD; however, neural circuitry models of PTSD along with research on neural correlates of rumination in depression and healthy individuals provides a foundation for further research. Current neural circuitry models of PTSD assist in identifying brain regions that might overlap with those involved in rumination. One of the most prominent models used in PTSD research is the fear

circuitry model (S. L. Rauch, Shin, Whalen, & Pitman, 1998). The fear circuitry model posits that dysfunction of fear circuitry underlies the reexperiencing and hyperarousal symptoms of PTSD. The basic model focuses on the connections between the amygdala, ventral medial prefrontal cortex (vmPFC), and hippocampus.

The amygdala is associated with fear learning, emotion processing, and negative affect (for review see Davis & Whalen, 2001; Ledoux, 2000; Phelps & LeDoux, 2005). Functional MRI (fMRI) investigations have consistently observed amygdala activity during fear conditioning tasks in which participants learn to associate a threatening stimulus with a neutral stimulus (LaBar, Gatenby, Gore, Ledoux, & Phelps, 1998; Phelps, Delgado, Nearing, & LeDoux, 2004; Sehmeyer et al., 2009). The vmPFC is a larger area of the prefrontal cortex that includes the rostral anterior cingulate (rACC), medial prefrontal cortex (mPFC), subgenual anterior cingulate cortex (sgACC), and the orbito-frontal cortex (OFC; S. L. Rauch, Shin, & Phelps, 2006a). The vmPFC has direct connections to the amygdala and is thought to have top-down control over the amygdala in the presence of threatening stimuli (Phelps et al., 2004; S. L. Rauch, Shin, & Phelps, 2006b). The vmPFC is also associated with extinction or safety learning in which a neutral stimulus previously learned to be associated with a threat stimulus is relearned to be associated with safety (Milad et al., 2007; Phelps et al., 2004). Finally, the hippocampus is associated with contextual memory, implicating it in overgeneralized fear responses related to PTSD (Charney, Deutch, Krystal, Southwick, & Davis, 1993; Corcoran, Desmond, Frey, & Maren, 2005; LaBar & Phelps, 2005; Maren & Holt, 2000).

The fear circuitry model (S. L. Rauch et al., 2006a) posits that individuals with PTSD demonstrate greater amygdala reactivity and lower vmPFC activation in response

to fear stimuli (trauma reminders). The failure of the vmPFC to inhibit the amygdala contributes to an overgeneralized fear response in which individuals perceive safe stimuli as threatening (Charney, 2004; Haglund, Nestadt, Cooper, Southwick, & Charney, 2007). This overgeneralized fear response is associated with re-experiencing and hyperarousal symptoms of PTSD. Additionally, individuals with PTSD demonstrate hypo-responsivity of the hippocampus, which is associated with contextual memory. Impaired function of the hippocampus in PTSD leads to difficulty in the identification of safe contexts (Charney et al., 1993).

Given that rumination triggers re-experiencing symptoms and increases negative affect (Birrer & Michael, 2011), it is likely that rumination interacts with fear circuitry. Rumination in individuals with depression has been associated with greater activity in the sgACC which is considered part of the vmPFC (Cooney, Joormann, Eugène, Dennis, & Gotlib, 2010). This finding suggests that individuals with PTSD who have high levels of rumination show a pattern of neural activity that is not consistent with the fear circuitry model, specifically these individuals demonstrate hyper-responsivity of both the amygdala and the vmPFC. Although many fMRI investigations have provided support for the fear circuitry model in PTSD, there are inconsistent findings that demonstrate hyperactivity in areas of the PFC (Bruce et al., 2012). It is possible that these inconsistencies are related to individual differences in participants' tendencies towards a ruminative style.

The sole focus on fear in the fear circuitry model has drawn critics who have suggested that the fear circuitry model does not account for the variety of clinical presentations seen within the diagnostic category of PTSD (Etkin & Wager, 2007; Frewen & Lanius, 2006; Lanius et al., 2011), especially those individuals who

experienced repeated childhood interpersonal trauma. To account for other symptoms associated with PTSD such as emotional numbing, affect dysregulation, and abnormalities in self-referential processing, a social cognitive and affective neuroscience (SCAN) theory (Lanius et al., 2011) has been posited for individuals that experienced childhood interpersonal trauma over time. This theory focuses on neural mechanisms of awareness of self and emotions, regulation of emotions, and self-referential processing. Lanius and colleagues (2011) highlight common brain regions thought to underlie these constructs such as the amygdala, insula, ACC, and various areas of the mPFC including the vmPFC, and dorsomedial PFC. This theory provides a broader view of PTSD as a multifaceted disorder that varies in its clinical presentations. It does not discount the fear circuitry model, but rather considers deficits in fear circuitry as part of emotion dysregulation along with symptoms of overmodulated emotion such as emotion numbing and alexithymia.

Topics of research from a SCAN approach that are relevant to investigation of the neural substrates of rumination in PTSD include emotional awareness and self-referential thinking. As stated above, it has been proposed that rumination is a form of cognitive avoidance that interferes with cognitive and emotional processing (Echiverri et al., 2011; Ehlers & Clark, 2000). Rumination increases negative affect and engages individuals in repetitive self-referential thinking that inhibits the individual from integrating the traumatic event into their belief system (Ehlers & Clark, 2000; Michael et al., 2007). Related to the topic of emotional awareness, research suggests a connection between rumination and aspects of alexithymia, specifically, difficulty identifying emotions (Di Schiena, Luminet, & Philippot, 2011). This connection may be the result of rumination

interfering with individuals' ability to process emotions in the moment. Research on the neural correlates of alexithymia in individuals with PTSD shows that as individuals report greater levels of alexithymia, they have less activity in the vmPFC and anterior insula while listening to accounts of their trauma (Frewen et al., 2008). Also consistent with the SCAN approach, individuals with PTSD demonstrate hyporeactivity in regions associated with disturbances of self-referential processing including the mPFC and parts of the ACC (Lanius et al., 2011).

Neural Circuitry of Rumination. To understand how the neural substrates of rumination interact with the neural circuitry of PTSD, it is helpful to review fMRI research on the neural circuitry of rumination in depressed and healthy individuals. This research details brain regions directly related to ruminative thinking and how individual differences in rumination affect neural functioning in other cognitive or emotional tasks. Neural circuitry related to rumination has been investigated through the use of tasks to induce rumination within individuals (i.e. Cooney et al., 2010) or by assessing individuals' general level of ruminative thinking through self-reports and correlating these scores with brain activation (i.e. Ray et al., 2005).

Rumination induction tasks provide information on the neural processes directly related to rumination. By inducing rumination in the fMRI scanner, investigators can investigate brain regions that play a role in the active process of ruminative thinking. Since this research places individuals in a condition to trigger a specific type of thinking, less attention is paid to the individuals' habitual rumination level. Therefore, rumination induction tasks provide information on which areas of the brain are involved in ruminative thinking, but these tasks do not provide the best opportunity to examine the

effects of individual differences in habitual rumination. Conversely, self-reports provide a way to measure individuals' tendency to ruminate (Brinker & Dozois, 2009; Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). It would be assumed that individuals with higher rumination scores on self-reports would engage in rumination in their daily life more than individuals who obtained lower scores on rumination self-reports. Thus, assessing rumination with self-report provides information on individual differences in rumination, and investigators can observe how these individual differences might relate to neural responses to disorder-specific tasks or tasks of constructs such as cognitive control or emotion regulation (i.e. Ray et al., 2005; Siegle et al., 2002). Therefore, it is important to examine both rumination induction tasks and the neural correlates of self-report of habitual rumination to understand the neural mechanisms related to ruminative thinking.

Given the association between rumination and negative affect, the amygdala is hypothesized to play a role in ruminative thinking. Evidence of greater amygdala activation during rumination induction as compared to an abstract thinking condition in individuals with depression supports this hypothesis (Cooney et al., 2010). Further research has found that in individuals with and without depression, self-reported rumination across groups had a positive relationship with the length of amygdala response to negative words (Siegle et al., 2002). The findings from the above study provide evidence that individual differences in general or habitual ruminative styles of thinking can affect neural responses within a diagnostic category, adding to variation in clinical presentations. As stated above, many fMRI investigations of PTSD have demonstrated hyperresponsivity of the amygdala (Bryant, Felmingham, et al., 2008;

Bryant, Kemp, et al., 2008; Peres et al., 2011; Shin et al., 2005), suggesting that the amygdala is a brain region associated with both PTSD and ruminative thinking.

However, it is unknown if ruminative thinking in individuals with PTSD is correlated with amygdala activity. It is possible that ruminative thinking in PTSD triggers negative affect or intrusive thoughts that lead to fear responses that contribute to the activation of the amygdala.

In addition to the amygdala, the dorsolateral prefrontal cortex (dlPFC), medial prefrontal cortex (mPFC), and parts of the anterior cingulate cortex (ACC) have been identified as brain regions that underlie ruminative thinking (Cooney et al., 2010; Nolen-Hoeksema et al., 2008). The dlPFC, mPFC, and the subgenual anterior cingulate cortex (sgACC) have been implicated in self-referential thinking, and thus associated with rumination (Johnson et al., 2006). Individuals with and without depression evidence greater BOLD signals in the dlPFC during rumination induction tasks versus abstract thinking conditions. Additionally, when rumination induction tasks are contrasted with concrete thinking tasks individuals with depression are observed to have higher dlPFC signals during the rumination condition (Cooney et al., 2010). In the same study, individuals with depression had greater BOLD signals in the sgACC, considered part of the vmPFC, as compared to controls during the rumination versus distraction condition. The role of the sgACC along with the mPFC was supported by another study (Kross, Davidson, Weber, & Ochsner, 2009) that examined BOLD signals when healthy individuals engaged in ruminative thinking by focusing on their feelings while listening to negative autobiographical memories. Increased activation was observed in both the sgACC and the mPFC in the above task contrasted with an acceptance condition.

Therefore, the current fMRI research suggests that ruminative thinking is associated with relative hyperactivity in the amygdala, dlPFC, mPFC, and sgACC.

Research examining individual differences in habitual rumination has focused on processes of emotion regulation and cognitive control. Individuals with high levels of rumination demonstrate difficulty in disengaging from negative stimuli (Joormann, Dkane, & Gotlib, 2006). This impaired ability to detach from negative stimuli is associated with activity in the dlPFC. In an fMRI study, individuals who endorsed higher levels of rumination, as compared to those who reported less ruminative thinking, evidenced greater dlPFC activity during an emotional inhibition task, indicating that these individuals needed to recruit more resources to inhibit their responses to or disengage from negative stimuli (Vanderhasselt, Kühn, & De Raedt, 2011). In another task related to cognitive control, activation of the posterior parts of the dorsal anterior cingulate cortex (pdACC) was positively related to rumination scores in healthy individuals (Vanderhasselt et al., 2013).

Similar to the amygdala, research suggests that the mPFC and sgACC play a role in both ruminative thinking and PTSD. However, while theories suggest that the mPFC and sgACC are hyporesponsive in PTSD and fail to inhibit brain regions involved in emotion such as the amygdala and insula (Lanius et al., 2011; S. L. Rauch et al., 2006a), the mPFC and sgACC appear to have a positive relationship with ruminative thinking such that when ruminative thinking is induced, individuals demonstrate increased levels of activity in the mPFC and sgACC (Cooney et al., 2010). It is possible that ruminative thinking in individuals with PTSD is associated with a different pattern of neural activity. Although the dlPFC is not identified in the neural circuitry models for PTSD, research

has demonstrated differences in dlPFC activity between individuals with PTSD and controls during attentional bias tasks using emotional face stimuli (Fani et al., 2012). Specifically, individuals with PTSD had increased BOLD signals in the dlPFC in response to threat stimuli in a dot probe task when compared to controls. This suggests that individuals with PTSD need to recruit more resources to inhibit or disengage from the negative emotional stimuli similar to individuals with higher levels of ruminative thinking. It is possible that ruminative thinking is associated with increases in dlPFC activity during cognitive tasks in PTSD.

Neural Circuitry of PTSD and Rumination Related to Psychotherapy

Few fMRI studies have examined psychotherapy outcomes in PTSD and none of the investigations have examined how clinical factors correlate with functional alterations in the brain. Individuals who have experienced a significant reduction in PTSD symptomatology due to psychotherapy demonstrated decreased amygdala and increased vmPFC BOLD signals from their pre to posttreatment scans (Felmingham et al., 2007; Peres et al., 2011; Roy et al., 2010). These findings suggest that deficits in neural circuitry related to PTSD normalize with successful psychotherapy. Since studies on CT for depression have found decreased levels of self-reported rumination after treatment (Conradi et al., 2008; Manicavasagar et al., 2012; Wilkinson & Goodyer, 2008), it is possible that the decrease of rumination due to CT is reflected through changes in the underlying neural circuitry. This has yet to be researched.

In regards to rumination, fMRI investigations have examined pretreatment activity in brain regions associated with self-reported rumination to identify potential predictors of psychotherapy outcome. Low sustained sgACC and high sustained

amygdala reactivity in individuals with depression has been associated with recovery through CT for depression (Siegle, Carter, & Thase, 2006). In this same study these brain regions were correlated with rumination scores and not symptom severity, indicating that the sgACC and amygdala are linked to rumination, and the neural substrates of rumination are predictors of symptom improvement through psychotherapy (Siegle, Carter, & Thase, 2006). Additionally, during an induced state of sadness, activity in parts of the mPFC that were positively associated with participants' rumination scores, predicted relapse of depressive symptoms (Farb, Anderson, Bloch, & Segal, 2011). These findings suggest that areas associated with rumination predict poorer treatment outcome, suggesting that higher levels of rumination are related to treatment resistance and relapse.

The Current Study

The current study examined the neural correlates of self-reported rumination in individuals with PTSD before and after CPT. Trauma-exposed no PTSD (TEC) and healthy control (HC) groups provided comparison for self-reported rumination scores. This study is the first known fMRI investigation of the neural correlates of habitual ruminative thinking styles in individuals with PTSD. An emotion interference task was selected to collect imaging data since it requires cognitive control over negative affective stimuli. As stated above individuals who engage in rumination have difficulties disengaging from negative stimuli (Joormann et al., 2006) and therefore it seems likely that an emotion interference task would be sensitive to individual differences in habitual rumination.

The emotion interference task, described in more detail later, consisted of the presentation of two pairs of images. One pair was either fearful or neutral faces and the other pair was houses. Participants were prompted to attend to either the vertical or horizontal pair and they indicated whether the images in the pair match. The task had four conditions: attend fearful faces (AF), attend neutral faces (AN), ignore fearful faces (IF), and ignore neutral faces (IN). To investigate cognitive control over emotionally valenced stimuli, the conditions that include fearful faces (either attend or ignore) were contrasted with the respective neutral face condition. The AF condition examined how participants engage in a cognitive task (matching) while attending to emotional stimuli, while the IF condition investigated how participants engage in a cognitive task with neutral stimuli in the presence of emotional distractors. In all, this task provided an opportunity to examine cognitive control over emotional stimuli modulated by attention.

For the current study, fMRI was the most appropriate imaging method given its relative level of safety and fair temporal, spatial, and anatomical resolution (Huettel, Song, & McCarthy, 2009). While other imaging methods such as single-photon emission computed tomography (SPECT) or positron emission tomography (PET), require radioactive tracers; fMRI utilizes the paramagnetic differences between oxygenated and de-oxygenated hemoglobin to reveal changes in brain activity over time. The primary metric is referred to as blood oxygen level-dependent (BOLD) signal (Huettel et al., 2009; Miller et al., 2007).

Study Hypotheses

Pretreatment hypotheses. Given rumination is associated with the development and maintenance of PTSD, it was hypothesized that the PTSD group would endorse

higher levels of ruminative thinking on the RTS as compared to the TEC and HC groups. Second, it was hypothesized that within the PTSD group, RTS scores would be positively related to BOLD signals during the emotion conflict task in the amygdala, dlPFC, mPFC, and sgACC in the AF>AN, IF>IN, and IF>AF conditions.

Treatment hypotheses. Third, it was hypothesized that the subgroup of PTSD treatment completers would demonstrate a significant decrease in RTS scores after at least 12 sessions of CPT. Fourth, it was hypothesized that within the PTSD group, higher levels of pretreatment rumination as measured by the RTS would predict a higher level of posttreatment PTSD symptoms as measured by the PDS. Fifth, it was hypothesized that within the PTSD group, higher pretreatment RTS scores would predict treatment dropout. Sixth, it was predicted that within the PTSD treatment completers, RTS change scores would be related to significant changes in BOLD signals from pre to post treatment in the amygdala, dlPFC, mPFC, and sgACC.

Exploratory hypotheses. Since this was the first known investigation of the neural correlates of rumination in PTSD, exploratory whole brain analysis was performed for the pretreatment time point. Any regions correlated with rumination at pretreatment were examined at the posttreatment time point. Secondary analysis also examined the predictive nature of pretreatment neural activity in brain regions associated with rumination. To understand the potential for neural correlates of rumination in individuals with PTSD predicting response to CPT, exploratory analyses were conducted to see if BOLD signals of regions associated with rumination at pretreatment would predict less symptom reduction as measured by the PDS.

Methods

Participants

Seventy-four women were recruited into three groups, three groups: PTSD treatment (PTSD; N=39), trauma-exposed control (TEC; N=17), and healthy control (HC; N=18). All participants were female, right-handed, and between the ages of 18 and 55 years ($M = 32$, $SD = 10$). The mean years of education was 16 ($SD = 3$), and 47 women (64%) identified as White, 17 (23%) as African American, one (1%) as Hispanic, one (1%) as Asian, three (4%) as other, and five (7%) opted not to report. Participants in the PTSD and TEC groups reported experiencing at least one interpersonal traumatic event (index trauma), defined as physical or sexual abuse or assault. The age of trauma ranged from early childhood (five years old) to adulthood (47 years old) and included both single incidences of assault and chronic abuse. HC participants reported no history of any type of traumatic event.

Inclusion criteria for all participants included fluency in English, the capacity to understand the nature of the study and participate in the informed consent procedures. Exclusion criteria for all participants included current use of psychotropic medication or drugs affecting the central nervous system, drug or alcohol abuse within the past three months, active suicidal or homicidal ideation, and MRI contraindications such as metallic implants, implanted medical or electronic devices such as pacemakers, pregnancy, claustrophobia, and ferromagnetic foreign bodies. Additional exclusion criteria for all participants included current or lifetime history of schizophrenia or other psychotic disorder, bipolar disorder, and current primary obsessive compulsive disorder.

PTSD treatment group (PTSD). The PTSD group consisted of 39 women who identified their index trauma as an interpersonal traumatic event. The average age of participants was 31 years old ($SD = 9$ years). Participants had an average of 15 years of education ($SD = 2$ years). Within the PTSD group 21 women (54%) identified as White, 12 women (31%) identified as African American, one woman (2%) identified as Hispanic, two women (5%) identified as other, and three (8%) opted not to report race or ethnicity. All participants in the PTSD group met full DSM-IV-TR criteria for PTSD as measured by the Clinician Administered PTSD Scale (CAPS), and only women with CAPS scores of 45 or above were included in the analysis. Individuals with comorbid depression and anxiety disorders were included, although PTSD had to be their primary diagnosis. Additionally, all participants in the PTSD group were seeking treatment to reduce symptoms of PTSD and agreed to complete 12 sessions of CPT. Based on their participation in treatment, as outlined in the measures section, participants in the PTSD group were categorized into subgroups of treatment completers ($N = 20$) and treatment dropouts ($N = 19$).

Trauma-exposed control group (TEC). The TEC group included 17 women who reported experiencing a criterion A traumatic event but did not meet full criteria for PTSD during the past month. Participants were an average age of 31 years old ($SD = 9$ years), and they had an average of 15 years of education ($SD = 2$ years). Within the TEC group, 12 women (71%) identified as White, two women (12%) identified as African American, one woman (6%) identified as other, and two women (11%) opted not to report race or ethnicity. Individuals who endorsed previous treatment for trauma or a current or lifetime anxiety disorder were excluded from this group.

Healthy control group (HC). Eighteen women were in the HC group. HC participants did not meet criteria for any DSM-IV-TR diagnosis and reported that they had not experienced any criterion A events. The average age of the participants in this group was 33 years old ($SD = 11$), and they had an average of 17 years of education ($SD = 3$). Within the HC group, 14 women (78%) identified as White, three women (17%) identified as African American, and one woman (5%) identified as Asian.

Recruitment procedures. Recruitment was conducted through the Center for Trauma Recovery at the University of Missouri-St. Louis and Washington University Medical Center in St. Louis in accordance with the universities' Institutional Review Board. Recruitment procedures included placing study advertisements in regional newspapers and online websites. Flyers for the study were posted at local businesses and colleges. Potential participants completed an initial phone screen. Individuals who were not excluded by the screener completed an in-person assessment to determine eligibility and gather baseline data. All participants were compensated for the completion of the fMRI scans and free psychotherapy was provided for the PTSD group.

Measures

PTSD Treatment Completers. Participants in the PTSD group were identified as treatment completers if they finished at least 12 sessions of CPT or the therapist and client decided to end treatment early due to symptom remission. In addition to the completion of CPT, treatment completers also needed to attend the posttreatment assessment and fMRI scan. Treatment completers were considered responders to treatment if they lost their diagnosis and experienced at least a 50 percent decrease in their symptoms as measured by the CAPS. Participants from the PTSD group who

completed treatment, but did not lose their diagnosis or experience at least a 50 percent decrease in their symptoms were identified as nonresponders.

PTSD Treatment Dropout. Participants in the PTSD group were categorized as a member of treatment dropout group if they either never engaged in therapy after agreeing to treatment or if they stopped attending CPT before 12 sessions.

Demographics Questionnaire. Participants completed a demographic questionnaire at the time of their first MRI scan. The questionnaire included information on age, race/ethnicity, and level of education.

Ruminative Thought Style Questionnaire (RTS). Rumination was measured by the RTS (Brinker & Dozois, 2008). The RTS is a 20-item, single factor, self-report measure that assesses a global style of ruminative thinking. Although many rumination measures directly assess depressive rumination, the RTS was designed to examine rumination independent of emotional valence and temporal focus. Participants rated the degree to which each item described their thinking style on a Likert scale ranging from 1, “Not at all,” and 7, “Very well.” The psychometric properties of the RTS are good with coefficient alphas ranging from .87 to .92. Test-retest reliability was initially found to be $r = .80$ as measured by a readministration of the RTS two weeks after the initial administration. Another study in which participants were asked to complete the RTS six times over the course of three weeks found the test-retest reliability to be $r = .57$ between the first and sixth administrations. It was suggested that these findings demonstrate that the RTS is sensitive to changes in ruminative thought while measuring an underlying stable construct (Brinker & Dozois, 2008). Therefore, the RTS is an appropriate measure to identify changes in ruminative thought over time while accounting for the generally

stable construct of global rumination. PTSD participants completed the RTS at the pre and posttreatment assessments. TEC and HC participants completed the RTS at the initial assessment.

Clinician-Administered PTSD Scale (CAPS). The CAPS (Blake et al., 1990) is a semi-structured, clinician-administered interview used to assess symptoms of PTSD according to the DSM-IV-TR. The 25-item scale allows the assessor to rate participants on symptom frequency and symptom intensity. The frequency and intensity scales sum to create a total symptom score. The frequency scale ranges from zero, indicating the absence of a symptom, to four, indicating the symptom is experienced on a daily basis. Similarly, the intensity scale ranges from zero, no distress, to four, severe distress resulting from the symptom. To identify clinically significant symptoms a combined rating of at least 1 on frequency and at least 2 on intensity was used. Furthermore, if participants met full criteria for PTSD based on symptoms, they were only included in analysis if their total CAPS score was above a 45. The CAPS has good psychometric properties with coefficient alphas ranging from .64 to .88 and two to three day test-retest reliability of .86 to .95 (Weathers, Keane, & Davidson, 2001). All participants who endorsed a criterion A event (PTSD and TEC groups) were administered the CAPS to assess for current and lifetime PTSD. Additionally, the PTSD group completed the CAPS at posttreatment assessments to measure symptom levels two weeks prior to the posttreatment scan.

Posttraumatic Stress Diagnostic Scale (PDS). The PDS (Foa, 1995) is a 49-item, four part, self-report used to measure the presence and severity of symptoms related to PTSD (DSM-IV-TR criteria). For the current study, only the final two parts of the

PDS were used to assess participants' experience of PTSD symptoms to the week prior to completing the PDS. The PDS has coefficient alphas ranging from .78 to .92 and test-retest reliability scores ranging from .77 to .85 (Foa, Cashman, Jaycox, & Perry, 1997). The PTSD and TEC groups completed the PDS at baseline assessments. The PTSD group also completed the PDS before each therapy session to track symptoms during the course of treatment and they completed it at the posttreatment assessment for a final measure of symptoms related to PTSD.

Beck Depression Inventory-II (BDI-II). The BDI-II (Beck, Steer, & Brown, 1996) is a 21-item self-report designed to assess symptoms related to depression based on the DSM-IV-TR criteria. Items are rated on a 4-point severity scale ranging from zero to three. Items are summed to compute total scores. Psychometrics are good with coefficient alphas of .91 (Beck, Steer, Ball, & Ranieri, 1996) and a test-retest reliability of .93 (Beck et al., 1996). All PTSD and TEC participants completed the BDI-II at the initial assessment to measure baseline levels of depressive symptoms. In addition, PTSD participants completed the BDI-II before each therapy session to assess their experience of depressive symptoms since the previous session. A final BDI-II was administered to PTSD individuals at the posttreatment assessment.

Structured Clinical Interview for DSM-IV-Patient Version (SCID-IV-P). The SCID (First, Spitzer, Gibbon, & Williams, 2002) is a semi-structured, diagnostic interview based on criteria from the DSM-IV-TR. At the initial assessment for the PTSD and TEC groups, trained graduate research assistants administered SCID modules to assess for current and lifetime Axis I disorders including: Mood, Psychotic, Anxiety, Somatoform, and Eating Disorders. All current and lifetime Axis I disorders assessed by

the SCID were documented. PTSD participants completed the SCID at the posttreatment assessment as well. At the posttreatment evaluation, assessors rated symptoms experienced by the participant for the two weeks prior to the administration to identify Axis-I disorders that the participants continued to endorse.

Procedures

Trained graduate research assistants obtain informed consent and administered baseline assessments measures including the CAPS, SCID, RTS, BDI-II, and PDS. During the baseline assessment, participants who met any exclusion criteria were informed that they were not eligible for the study. All eligible participants were scheduled for the baseline neuroimaging session within a month of the initial assessment at Washington University Medical Center. Trained research assistants conducted the neuroimaging assessments, informed participants of scanning procedures and provided participants with instruction for the tasks. The fMRI sessions took place over the course of an hour and a half and they were divided into three sections. First, structural scans were completed. Participants were asked to remain still and were provided with the option of listening to music. Then, a resting state task was completed in which participants were asked to clear their minds and focus all their attention on a projected cross-hair fixation point. The final task administered in the scanner was the emotion interference task. Participants were asked to indicate whether the images matched by pressing one of two buttons on a hand-held device (see Figure 1). Research assistants provided instructions for the scanner tasks before and during the scan, and participants completed practice trials with only neutral faces. Participants in the TEC and HC groups

were compensated after the baseline neuroimaging assessment and their participation was considered completed at that time.

Participants in the PTSD group were assigned a therapist and scheduled for session one of CPT following the completion of the neuroimaging assessment. Participants who completed treatment attend 12-14 sessions of CPT. Symptoms were tracked throughout the course of therapy through weekly pre-session administrations of the BDI-II and PDS. All therapists utilized the CPT protocol, and participants completed between session CPT assignments and worksheets. Therefore, all participants wrote two accounts of their index traumatic event, and they read the accounts aloud in session. Additional sessions were allowed if the therapist and supervisor deemed an extra session clinically appropriate. All therapists were doctoral students trained in CPT. Therapists attended weekly group supervision with the study director. Individual consultation was also provided by the study director on an as needed basis. All CPT sessions were videotaped and reviewed at random by the study director and in weekly supervision meetings.

After treatment concluded, participants completed a posttreatment clinical and neuroimaging assessment. Independent raters conducted the posttreatment assessments which included the same measures as the baseline assessment. Posttreatment assessments focused on the past two weeks to determine current diagnoses. Lifetime ratings were not assessed at the posttreatment. The posttreatment neuroimaging assessment was identical to the baseline assessment except for the omission of some structural scans. Participants in the PTSD group were compensated after the completion of the second neuroimaging assessment.

Imaging Methodology

fMRI Emotion Interference Task. Participants completed the emotion interference task after the structural and resting state scans. The emotion interference task presented stimuli in an event related design. Each event included the presentation of two pairs of images, one pair of faces (fearful or neutral) and one pair of houses (See Figure 1). One pair of images was aligned horizontally and the other was arranged vertically around a cross-hair fixation point. The images were adapted from Ekman's series. The pictures were black and white, and they were presented on a grey background. Ten fearful faces, 10 neutral faces, and 20 houses were used. Each of the four sequences included 52 trials for a total of 208 events. Participants were cued to attend to either the horizontal or vertical pair of stimuli, and they were asked to press buttons on button box to indicate whether the paired stimuli match. Stimuli were projected on a screen placed behind the scanner. Participants viewed the stimuli through a mirror placed on the head coil. All stimuli were presented using PsyScope on an iMac computer. Behavioral data were recorded using a PsyScope button box interfaced with a fiber-optic key press. Participants were handed the button box and asked to press the top button if the images were the same and the bottom button if the images were different.

Image acquisition. A Siemens 3T TrioTim MRI scanner (Siemens, Erlangen, Germany) at Washington University Medical School was used to collect imaging data. Scanning sessions included acquisition of localizer images, a high-resolution structural image (magnetization prepared rapid gradient echo [MPRAGE]), and functional images from the resting state and emotion interference tasks. Structural images were collected with 1 x 1 x 1 resolution using a sagittal three-dimensional (3-D) T1-weighted sequence

with repetition time (TR) of 2.4 s, time-to-echo (TE) of 3.16 ms, flip angle = 8°, and inversion time (TI) of 1000 ms. Functional images were acquired in runs using an asymmetric spin-echo echo-planar sequence (volume TR = 2.2 s [slice TR = 64.10 ms], TE = 27 ms, flip angle = 90° degrees, and field of view (FOV) of 256 cm). A single acquisition was composed of 36 transverse slices, 4 mm thick (no gap), and with an in-plane resolution of 4x4 mm. Each functional run started with three volume images followed by 180 acquisitions for the paradigm.

Quality assurance procedures related to the neuroimaging data included daily scanning of a phantom to ensure the consistency of the scanning environment. Additionally, the MRI technician conducted visual data inspections during scans to identify artifacts such as head movement. Finally, to confirm accuracy of the data, the imaging data were compared to the event timeline and visually examined for BOLD signals in the visual and motor cortices that indicate the event timeline and imaging data coincide.

Preprocessing of MRI data were completed using SPM12 and Matlab. The preprocessing included: 1) scaling whole-brain signal intensity to a fixed value, 2) removing the linear slope on a voxel-by-voxel basis to counteract effects of drift, 3) aligned to correct for head motion using a six-parameter rigid-body rotation and translation correction, 4) and then blurring the images with an 8mm FWHM Gaussian filter. The intra-modality registration algorithm provided a straightforward method for conducting quantitative group comparisons. While preserving the enhanced temporal resolution of fMRI. 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.

Results

Data Analysis Strategy

Data analyses examining demographic and clinical measure data were completed using IBM SPSS Statistics 22. A priori power calculations were conducted using G*Power 3.1. All neuroimaging data was analyzed using SPM8 (Wellcome Department of Cognitive Neurology, London, UK). Functional MRI (fMRI) data were preprocessed as described above. Three separate regions of interest (ROI) masks were created using Wake Forest PickAtlas in order to test hypotheses related to the amygdala, dlPFC, vmPFC, and the ACC. Anatomically defined regions based on automated anatomical labeling (aal; Tzourio-Mazoyer et al., 2002) in Wake Forest PickAtlas were used to construct the masks. The amygdala mask consisted of the right and left amygdala. The aal labels for regions included in the dlPFC mask were “Frontal_Mid_L” and “Frontal_Mid_R.” The vmPFC and ACC were combined in a single mask using the bilateral aal regions: “Frontal_Sup_Orb,” “Frontal_Mid_Orb,” and “Cingulum_Ant.” All masks were dilated by 1 voxel 3D.

First level within subject analysis included the application of the general linear model (GLM) to produce statistical maps and magnitude maps for each subject. In order to investigate specific conditions of the emotion interference task, three contrasts were created at the subject level. First, to isolate the effect of attending to fearful faces as compared to neutral faces during the matching task, the attend fear condition (AF) was contrasted with the attend neutral condition (AN; AF>AN). In this contrast, AN served

as a baseline and the AF condition was the effect of interest. The second contrast was the ignore fear condition (IF) compared to the ignore neutral condition (IN; IF>IN). This contrast allowed for examination of fear distractors compared to neutral distractors. Finally to examine the inhibition of fearful stimuli as compared to direct attention of fear stimuli, a contrast was created between the IF and AF conditions (IF>AF).

The three within subject contrasts, AF>AN, IF>IN, and IF>AF, were utilized for second level, group analysis. ROI masks were applied for the second level analyses. The group analysis utilized a liberal significance threshold of $p < .001$ uncorrected with a 5 voxel cluster threshold. Small volume corrections utilizing the ROI masks were conducted, and results that had peak voxels survive a significance threshold of $p < .05$ corrected for family wise error rate were highlighted in the results and discussion.

Hypothesis 1. The first hypothesis stated that the PTSD group would endorse higher levels of ruminative thinking on the RTS as compared to the TEC and HC groups. This hypothesis was tested through the use of a one way Analysis of Variance (ANOVA) to compare mean RTS scores across the PTSD, TEC, and HC groups. To determine statistical significance for the analysis, the threshold of $p < .05$ was used. Eta squared was calculated to describe the effect size of the ANOVA (Howell, 2007). To achieve power = .80 with an alpha threshold of $p < .05$ for a one-way ANOVA, a sample size of 66 participants across three groups is needed to detect a large effect (effect size of $f = .40$), and a sample size of 159 participants across three groups is needed to detect a medium effect (effect size of $f = .25$).

To control for symptom severity that may affect levels of rumination, an ANCOVA was conducted. Pretreatment PDS and BDI-II scores were entered into the

analysis as covariates. Group was the independent variable and RTS scores were the dependent variable. A significance level of $p < .05$ was used in the analysis. Eta squared was calculated to describe the effect size of the ANCOVA (Howell, 2007). To achieve power = .80 with an alpha threshold of $p < .05$ for a one-way ANCOVA with two covariates, a sample size of 64 participants across three groups is needed to detect a large effect (effect size of $f = .40$), and a sample size of 158 participants across three groups is needed to detect a medium effect (effect size of $f = .25$).

Hypothesis 2. The second hypothesis predicted that within the PTSD group, RTS scores would be positively related to BOLD signals during the emotion conflict task in the amygdala, dlPFC, mPFC, and sgACC in the AF>AN, IF>IN, and IF>AF conditions. This hypothesis was tested through multiple regressions conducted in SPM8 to examine the relationship between RTS scores and BOLD signals in the ROIs. Three separate multiple regressions were conducted to examine RTS scores as a predictor for BOLD signals in each of the three ROI masks. This process was repeated for each of the contrasts, AF>AN, IF>IN, and IF>AF in both the positive and negative directions. To statistically control for pretreatment PTSD and depressive symptomatology, each regression was run a second time with PDS and BDI-II scores entered as covariates in SPM8. A significance threshold of $p < .001$ uncorrected and a cluster threshold of 5 voxels was used, although results that withstood a more conservative significance threshold of $p < .05$ corrected for family-wise error (FWE) were highlighted. For a multiple regression with a single predictors to achieve power = .80 with an alpha level of $p < .05$ to detect a large effect size ($f^2 = .35$) a sample size of 25 participants is needed and to detect a medium effect size ($f^2 = .15$) a sample size of 55 participants is needed.

For a multiple regression with a three predictors to achieve power = .80 with an alpha level of $p < .05$ to detect a large effect size a sample size of 36 participants is needed and to detect a medium effect size a sample size of 77 participants is needed. Given this hypothesis was tested using imaging data, it is possible that this is not an accurate power estimate since imaging data includes analysis within subject (level 1) before group analysis (level 2) can be conducted. Peer reviewed manuscripts with similar methodology have sample sizes that range from 26-31 participants (Frewen, Pain, Dozois, & Lanius, 2006; Vanderhasselt et al., 2013; Vanderhasselt et al., 2012).

Treatment Analysis

Hypothesis 3. Third, it was hypothesized that the subgroup of PTSD treatment completers would demonstrate a significant decrease in RTS scores after at least 12 sessions of CPT. To test this hypothesis a paired t-test was conducted to compare the means of pre and posttreatment RTS scores. A p value less than .05 was used to determine significance. The effect size was calculated using Cohen's d (Howell, 2007). To achieve power = .80 with an alpha level of $p < .05$ for a two tailed paired t-test a sample size of 15 participants to detect a large effect ($d = .8$) or a sample size of 34 is needed to detect a medium effect (Cohen's $d = .5$).

Hypothesis 4. Fourth, it was hypothesized that within the PTSD group, higher levels of pretreatment rumination as measured by the RTS would predict a higher level of posttreatment PTSD symptoms as measured by the PDS. To test the fourth hypothesis a multiple regression was conducted to determine if there is a relationship between pretreatment RTS scores and posttreatment PDS scores. To control for the possible confounding factor of pretreatment symptom severity, a hierarchical multiple regression

was conducted. Pretreatment BDI-II and PDS scores were entered in the first step of the regression with RTS scores entered second to see if RTS scores predicted higher posttreatment PTSD symptoms after partialing out the variance related to posttraumatic and depressive symptomatology. *Adjusted R²* was used to report the variance that the predictor variables account for in the dependent variable given the small sample size (Meyers, Gamst, & Guarino, 2006). Cohen's *f²* was calculated to describe the effect size. For a multiple regression with a single predictors to achieve power = .80 with an alpha level of $p < .05$ to detect a large effect size ($f^2 = .35$) a sample size of 25 participants is needed and to detect a medium effect size ($f^2 = .15$) a sample size of 55 participants is needed. For a multiple regression with three predictors to achieve power = .80 with an alpha level of $p < .05$ to detect a large effect size a sample size of 36 participants is needed and to detect a medium effect size a sample size of 77 participants is needed.

Hypothesis 5. The fifth hypothesis stated that within the PTSD group, higher pretreatment RTS scores would predict treatment dropout. This hypothesis was tested through a logistic regression conducted with treatment dropout as a binary dependent variable and pretreatment RTS scores entered into the equation as a predictor variable. Given age was significantly different between treatment completers and dropouts, age was entered into the model in the first step for statistical control. To control for pretreatment PTSD and depressive symptoms a second analysis was conducted in which pretreatment PDS and BDI-II scores were entered into the first step of the regression and pretreatment RTS scores were entered in the second step. Odd ratios were used to describe the effect size. For a logistic regression with an odds ratio of 1.37 (calculated with probability of $H0 = .46$ and probability of $H1 = .54$), a sample size of 336

individuals was needed. It is of note that the sample size of the current study is greatly underpowered for this analysis. Therefore, the results must be interpreted cautiously.

Hypothesis 6. Sixth, it was predicted that within the PTSD treatment completers, RTS change scores would be related to significant changes in BOLD signals from pre to post treatment in the amygdala, dlPFC, mPFC, and sgACC. Multiple steps were taken to test this hypothesis. First, a paired t-test was conducted between pre and posttreatment scans using SPM8 to identify significant differences in mean BOLD signals within the ROI masks. Functional ROI masks were created for the five significant regions from the paired t-test. Parameter estimates from the paired t-test for each of these regions were extracted using Marsbar. The resulting parameter estimates represented pre and posttreatment BOLD signals. Posttreatment parameter estimates were subtracted from pretreatment values to create a change score. These values were entered into SPSS, and bivariate correlations were conducted between the parameter estimate change scores and RTS change scores. Effect sizes for the correlations were based on Cohen's guidelines (small, $r = .10$; medium, $r = .30$; large, $r = .50$). A sample size of 67 participants was to achieve 80% power with an alpha of $p < .05$ to detect a medium effect.

Exploratory Analysis

Whole brain analysis. Whole brain analysis was conducted in SPM8. For each of the three contrasts, AF>AN, IF>IN, and IF>AF, a multiple regression was run using pretreatment RTS scores as the predictor variable and BOLD signals across the whole brain as the dependent variable. To control for posttraumatic and depressive symptom severity a second regression was run with PDS and BDI-II scores entered as covariates into the model. For a multiple regression with a single predictor to achieve power = .80

with an alpha level of $p < .05$ to detect a large effect size ($f^2 = .35$) a sample size of 25 participants is needed and to detect a medium effect size ($f^2 = .15$) a sample size of 55 participants is needed. For a multiple regression with three predictors to achieve power = .80 with an alpha level of $p < .05$ to detect a large effect size a sample size of 36 participants is needed and to detect a medium effect size a sample size of 77 participants is needed. As stated above, it is possible that this is not an accurate power estimate since imaging data includes analysis within subject (level 1) before group analysis (level 2) can be conducted. Peer reviewed manuscripts with similar methodology have sample sizes that range from 26-31 participants (Frewen, Pain, Dozois, & Lanius, 2006; Vanderhasselt et al., 2013; Vanderhasselt et al., 2012).

Treatment predication. To understand the potential for neural correlates of rumination in individuals with PTSD predicting response to CPT, analyses were conducted to see if BOLD signals of regions associated with rumination at pretreatment would predict less symptom reduction as measured by the PDS. PDS changes scores were created by subtracting posttreatment scores from pretreatment scores. Functional ROI masks based on pretreatment results for each contrast (AF>AN, IF>IN, and IF>AF) were created using Wake Forest Pickatlas. To create these masks, a 10mm sphere was placed on the peak coordinate of the pretreatment findings. SPM8 was utilized to conduct a multiple regression between pretreatment BOLD signals in the ROI masks and PDS change scores for each contrast. To examine the direct relationship between BOLD signals in regions correlated with RTS scores and posttreatment symptoms, SPM8 was used to conduct multiple regressions between pretreatment BOLD signals within ROI masks and PDS posttreatment scores. For a multiple regression with a single predictors

to achieve power = .80 with an alpha level of $p < .05$ to detect a large effect size ($f^2 = .35$) a sample size of 25 participants is needed and to detect a medium effect size ($f^2 = .15$) a sample size of 55 participants is needed. Other research that examines regions of interest as potential predictors of treatment have sample sizes that range from 14 to 22 participants (Bryant, Felmingham, et al., 2008; Ritchey et al., 2011; Siegle et al., 2006).

Missing Data

Across all three groups, education level was not recorded for five participants who did not complete the demographics form. Given education was not a variable of interest to the main aims of the study, pairwise deletion was used for the five cases. One participant in the TEC group did not complete the BDI-II. Given the small sample size, pairwise deletion was used. The participant was not included in analyses in which the BDI-II scores were used, but other scores were used in the remaining analyses. The same method of pairwise deletion was used for a single missing posttreatment RTS score. Given the relatively small sample size, the participant was only included in analyses that did not utilize posttreatment or change RTS data.

The BDI-II was only administered to 10 of the 18 individuals in the HC group. The missing BDI-II data only affects the secondary analysis of the first hypothesis in which BDI-II scores were entered as a covariate. Given the large amount of missing data, the secondary analysis was conducted examining only the PTSD and TEC groups. Measures of PTSD symptoms (CAPS and PDS) were not administered to individuals within the HC group since all items are scored in relation to a criterion A traumatic event. The experience of a criterion A event would have excluded a participant from the HC group.

Data Screening

Preliminary data screening for univariate normality and outliers was conducted on the main pre and posttreatment variables for analysis including the RTS, CAPS, PDS, and BDI-II. Data screening procedures for specific hypotheses are discussed below.

For pretreatment data, skewness and kurtosis for all variables within each group were within the values of -1 and 1 with the exception of CAPs (kurtosis = -1.109, $SE = .741$) and BDI-II (kurtosis = -1.062, $SE = .741$) scores for the PTSD group and BDI-II (kurtosis = -1.360, $SE = 1.334$) scores for the HC group. However, given all pretreatment variables within each group met the criteria of skewness and kurtosis less than double the standard error (Meyers, Gamst, & Guarino, 2006), no transformations were conducted on pretreatment data. The Kolmogorov-Smirnov and Shapiro-Wilk tests of normality for all pretreatment variables in the PTSD, TEC, and HC groups were not significant ($p > .01$) suggesting that data were normally distributed. Boxplots were used to assess for outliers, and no univariate outliers were identified. Screening for posttreatment data is discussed below in respect to the relevant hypotheses.

Descriptive Statistics

Descriptive statistics were also examined for all demographic information and clinical measures across the three groups, PTSD, TEC, and HC (Table 1). To identify any significant difference in age or education across groups, two separate ANOVAs were conducted. No differences were found among the three groups for age ($F(2, 71) = .330, p = .720$); however, a significant difference in education was revealed across groups ($F(2, 67) = 5.036, p = .009$). Follow up analysis was conducted using Tukey HSD test. This analysis identified significant differences in the mean education between the HC group

and the PTSD group ($p = .015$) as well as the HC group and the TEC group ($p = .020$). In both comparisons, the HC group had a higher level of education than the PTSD and TEC groups. A chi-square test was conducted to identify any differences in race or ethnicity across groups. No significant differences were found ($\chi^2(10) = 10.45, p = .402$).

Out of the thirty-nine women in the PTSD group, 21 women completed a full course of CPT and 18 women dropped out of therapy. Descriptive statistics for each group were also examined for all demographic information and clinical measures (Table 2). Independent samples t-tests were conducted to identify possible differences in demographics and pretreatment clinical scores between the treatment completers and dropouts. Treatment completers were significantly older than treatment dropouts ($t(37) = -2.092, p < .045$), and no difference was found in education level between the two groups ($t(33) = -.947, p = .337$). Treatment completers also had significantly lower scores pretreatment on the PDS ($t(37) = 3.102, p = .004$) and BDI-II ($t(37) = 3.212, p = .003$). No differences were found between groups on the CAPS ($t(37) = -1.414, p = .166$) or RTS ($t(37) = -1.610, p = .116$).

The 21 women who completed treatment evidenced significant decreases in clinical measures including the CAPS, PDS, and BDI-II (see Table 3). The treatment completers were further categorized as responders or nonresponders (Table 4). There were 17 treatment responders who experienced at least a 50% decrease in symptoms across treatment and loss their PTSD diagnoses as measured by the CAPS. Four women were classified as nonresponders. Three of the nonresponders retained their PTSD diagnosis posttreatment. No significant differences were found between responders and nonresponders on demographic or pretreatment clinical variables (Table 4).

Pretreatment Analyses Results

Hypothesis 1. The first hypothesis predicted that the PTSD group would endorse higher levels of ruminative thinking on the RTS as compared to the TEC and HC groups. To test this hypothesis a one-way between subjects ANOVA was conducted to compare the mean pretreatment RTS scores among the PTSD, TEC, and HC groups. Special attention was paid to the assumption of homogeneity of variance given the difference in sample size across groups. A one-way ANOVA is generally robust to a departure from the assumption of homogeneity of variance except when sample sizes are unequal. To examine this a Levene's test of equality of error variances was conducted. Results were not significant ($p=.459$) indicating that there were no significant differences in the variances across groups. The ANOVA was significant ($F(2, 71) = 28.24, p < .001, \eta^2 = .443$) indicating that there was a difference in mean pretreatment RTS scores across groups. A Tukey HSD test indicated that the PTSD group had significantly higher pretreatment RTS than the TEC group ($p < .001$) and the HC group ($p < .001$). Pretreatment RTS scores between the TEC and HC groups were not significantly different ($p = .991$).

To control for pretreatment symptom severity, an ANCOVA was conducted. Only the PTSD and TEC groups were included in this analysis, since the HC group did not complete PDS self-reports and only ten individuals in the HC group completed BDIs. Additional screening was conducted in order to ensure that all assumptions for an ANCOVA were met. First, scatterplots were examined to confirm that the dependent variable had a linear relationship to the covariates. Next, homogeneity of variance in slopes was checked through examining possible interaction effects between the covariates

and the dependent variable. All interactions were nonsignificant. Pretreatment RTS scores were entered as the dependent variable, group (PTSD and TEC) was entered as the independent variable, and pretreatment PDS and BDI-II were entered as covariates. A Levene's test of equality of error variance was nonsignificant ($p = .917$). Therefore, the assumption of homogeneity of variance was met. The ANCOVA was significant ($F(1, 53) = 6.719, p = .012, \eta^2 = .110$) indicating that after controlling for pretreatment symptom severity, the PTSD group had significantly higher levels of rumination than the TEC group.

Hypothesis 2. Hypothesis 2 predicted that within the PTSD group RTS scores would be positively related to BOLD signals during the emotion conflict task in the amygdala, dlPFC, mPFC, and sgACC in the AF>AN, IF>IN, and IF>AF conditions.

AF>AN. A summary of results is presented in Table 5. For the AF>AN contrast no positive relationships were found between BOLD signals in the amygdala, dlPFC, mPFC, or ACC and RTS scores. No negative relationships were found between BOLD signals in the dlPFC and RTS scores. A negative relationship was found between RTS scores and the left amygdala BOLD signals ($p_{uncorr} < .001, p_{FWEcorr} = .082$), as well as RTS scores and the left ACC ($p_{uncorr} < .001, p_{FWEcorr} = .352$) and the left frontal medial orbital cortex ($p_{uncorr} < .001, p_{FWEcorr} = .466$). To control for symptom severity, PDS and BDI-II scores were entered as covariates to the model. No positive relationships were found between RTS scores and BOLD signals in any of the three ROI masks. The only significant negative relationship found after controlling for pretreatment posttraumatic stress and depressive symptoms was between RTS scores and the right frontal medial orbital cortex ($p_{uncorr} < .001, p_{FWEcorr} = .525$).

IF>IN. A summary of results is presented in Table 6. For the IF>IN contrast no positive relationships were found between RTS scores and BOLD signals in the amygdala, mPFC, or ACC. A positive relationship between RTS scores and BOLD signals in the right middle frontal gyrus (BA9; $p_{uncorr} < .001$, $p_{FWEcorr} = .279$) was found. No negative relationships were found between the RTS scores and BOLD signals in the amygdala, dlPFC, mPFC, or ACC. No positive or negative relationships were found between RTS scores and BOLD signals in any of the three ROI masks after controlling for pretreatment symptom severity.

IF>AF. A summary of results is presented in Table 7. For the IF>AF contrast no positive relationships were found between RTS scores and BOLD signals in the amygdala or ACC. Significant positive relationships were found between RTS scores and the left frontal middle gyrus (BA 8; $p_{uncorr} < .001$, $p_{FWEcorr} = .127$) and the left frontal inferior orbital cortex (BA 11; $p_{uncorr} < .001$, $p_{FWEcorr} = .317$). Additionally, results revealed that RTS scores positively predicted BOLD signals in a region in the right inferior orbital frontal cortex (BA 11; $p_{uncorr} < .001$, $p_{FWEcorr} = .004$; Figure 2). This finding survived a family wise error correction. This region remained significant ($p_{uncorr} < .001$, $p_{FWEcorr} = .019$) when the PDS and BDI-II were entered into the model as covariates. Finally RTS scores had a positive relationship to BOLD signals in the left inferior orbital frontal cortex (BA 11; $p_{uncorr} < .001$, $p_{FWEcorr} = .241$). No negative relationships were found between RTS scores and BOLD signals in any of the three ROI masks with or without covariates.

Treatment Analysis Results

Hypothesis 3. The third hypothesis predicts that the subgroup of PTSD treatment completers would demonstrate a significant decrease in RTS scores after at least 12 sessions of CPT. To test this hypothesis a paired-sample t-test was conducted. A paired-sample t-test assumes that the differences between pre and posttreatment scores is normally distributed and does not include outliers. This assumption was checked using SPSS to create RTS change scores by subtracting posttreatment RTS scores from pretreatment RTS scores, and then the distribution was examined. Skewness and kurtosis for the RTS change score was between -1 and 1, indicating that there were no concerns with the shape of the distribution. The Kolmogorov-Smirnov and Shapiro-Wilk tests of normality were nonsignificant indicating that the data were normally distributed. No outliers were identified. The t-test was significant ($t(19) = 4.693, p$ (two tailed) $< .001, d = 1.05$) indicating that RTS scores significantly decreased over the course of CPT. The observed large effect size suggests that RTS scores decreased by approximately one standard deviation across treatment.

Hypothesis 4. Hypothesis 4 states that within the PTSD group, higher levels of pretreatment rumination as measured by the RTS would predict higher posttreatment PTSD symptoms by the PDS. Further, it was hypothesized that RTS would predict higher posttreatment PTSD symptoms after controlling for pretreatment symptom severity as measured by the PDS and BDI-II. Additional data screening was conducted before completing the analysis for this hypothesis. Univariate normality and outliers for pretreatment RTS, BDI-II, and PDS were already reviewed above. The distribution of posttreatment PDS scores was skewed (1.527, $SE = .501$) and had significant kurtosis

(2.006, $SE = .972$). One outlier was identified, and although the Kolmogorov-Smirnov test of normality was nonsignificant ($p = .048$), the Shapiro-Wilk test of normality suggested that the distribution of scores significantly deviated from the normal distribution ($p = .001$). Given the outlier was a nonresponder to treatment, it seemed that this score was important to include in the analyses. Therefore, a square root transformation was conducted using SPSS and univariate screening procedures were completed for the transformed posttreatment PDS scores. Skewness and kurtosis were both between -1 and 1, and the Kolmogorov-Smirnov and Shapiro-Wilk tests of normality were nonsignificant ($p > .200$, $p = .430$ respectively). No outliers were identified.

To identify possible multivariate outliers, Mahalanobis distance and Cook's D values were examined for both the combination of pretreatment RTS/transformed posttreatment PDS and pretreatment RTS, PDS, BDI-II/transformed posttreatment PDS. No outliers were observed. A scatter plot matrix of variables and residual plots indicated that all variables were linearly related. In the first regression analysis, pretreatment RTS scores were entered as the predictor variable and the transformed posttreatment PDS scores were entered as the dependent variable. The overall model was significant ($F(1, 19) = 5.200$, $p = .034$, $R^2_{adj.} = .17$, Cohen's $f^2 = .20$). The beta value ($\beta = .464$) indicated that RTS scores had a positive relationship with posttreatment PDS scores, and the *adjusted R²* suggests that RTS scores account for approximately 17% of the posttreatment PDS.

To control for pretreatment symptom severity, a hierarchical regression was conducted entering pretreatment PDS and BDI-II scores in the first step and RTS scores

in the second step. Transformed posttreatment PDS scores were entered as the dependent variable. Collinearity statistics were reviewed. Tolerance statistics were all above .01 and VIF statistics were all below 10 indicating no issues with multicollinearity. The first step of the model was significant ($F(2, 18) = 6.188, p = .009, R^2 \text{ adj.} = .342$, Cohen's $f^2 = .52$). Once the RTS was added to the model, the model remained significant ($F(3, 17) = 4.255, p = .021, R^2 \text{ adj.} = .328$, Cohen's $f^2 = -.02$); however, the decrease in the *adjusted* R^2 value indicates that the model with the RTS accounts for less of the variance in the dependent variable as compared to the first model. Therefore, when pretreatment symptom severity was accounted for, the data suggests that there is no significant relationship between the RTS and posttreatment symptoms as measured by the PDS.

Hypothesis 5. Hypothesis 5 states that within the PTSD group, higher pretreatment RTS scores would predict treatment dropout. Univariate data screening for the treatment completer and dropout groups was detailed above. Given women in the treatment completer group were significantly older than women in the dropout group, age was entered into the models in the first step to control for this difference between groups. Collinearity statistics were reviewed, and no problems with multicollinearity were noted. A logistic regression was conducted using treatment status (complete or dropout) as a binary dependent variable and age and RTS as predictor variables. To control for age, it was entered in the first step. RTS scores were entered at the second step. The overall model with age was significant ($\chi^2(2, N = 39) = 6.943, p = .031$); however, the block in which RTS scores were entered was not significant ($\chi^2(1, N = 39) = 2.903, p = .088$). Further, neither age ($p = .060$) nor RTS scores ($p = .108$) were found to be significant predictors of treatment dropout within this model. When pretreatment PDS and BDI-II

scores were entered into the first step of the model with age, the second block in which RTS was entered continued to be nonsignificant ($\chi^2(1, N = 39) = .045, p = .832$). None of the variables were significant predictors of treatment dropout.

Hypothesis 6. Hypothesis 6 predicts that within the PTSD treatment completers, RTS change scores would be related to significant changes in BOLD signals from pre to post treatment in the amygdala, dlPFC, mPFC, and sgACC. Paired t-tests were conducted to identify significant differences in BOLD signals from pre to post treatment for all three contrasts (AF>AN, IF>IN, and IF>AF). A liberal significance threshold of $p < .001$ uncorrected and extent threshold of 5 voxels for the purpose of region identification for the main analyses. Results of the paired t-test are found in Table 8. Marsbar was used to create a functional ROI mask for each significant voxel cluster, and parameter estimates were extracted from imaging data for use in SPSS. Change scores were created by subtracting pretreatment values from posttreatment values for the RTS and parameter estimates for all masked regions. Bivariate Pearson's correlations were conducted to examine the relationships between RTS change scores and the change scores of the parameter estimates. A single significant negative relationship was found between RTS change and the change in parameter estimates in the right superior frontal cortex (BA9; $x = 16, y = 42, z = 26$; Pearson's $r = -0.5, p = 0.25$) in the IF>AF contrast. Given the change scores for the parameter estimates included some negative values, results suggest that women who experienced a greater decrease in rumination had an increase in BOLD signals of the voxel cluster of the right superior frontal cortex. After controlling for pretreatment symptom severity by conducting a hierarchical multiple regression and entering PDS change scores in the first step, the relationship between RTS

change scores and parameter estimates for the cluster with peak voxel 16, 42, 26, is no longer significant.

Exploratory Analysis Results

Whole brain analysis. Given this is the first known investigation of the neural correlates of rumination in PTSD, pretreatment RTS scores were correlated with BOLD signals across the entire brain. A more conservative significance threshold of $p < .05$ corrected for family wise error was utilized to control for type I error since the analysis was exploratory. RTS scores predicted BOLD signals in the right inferior orbital frontal cortex (BA 11; peak coordinates 38, 40, -14, $t(37) = 5.62$, $p_{FWE} = .044$) in the IF>AF contrast. When PDS and BDI-II scores were entered into the model as covariates, the finding was no longer significant. No other significant relationships between RTS scores and BOLD signals were found in any of the three contrasts.

Treatment predication. To understand the potential for neural correlates of rumination in individuals with PTSD predicting response to CPT, analyses were conducted to see if BOLD signals of regions associated with rumination at pretreatment would predict less symptom reduction as measured by the PDS. Functional ROI masks were created for each contrast based on regions found to have significant relationships with RTS scores at pretreatment. The mask for AF>AN included three 10mm spheres placed on peak coordinates (-18, -6, -16; -6, 28, -8; and -6, 40, -10). The IF>IN mask was created with a single 10mm sphere placed on coordinate 42, 10, 40. The mask for the IF>AF contrast was created the same way using peak coordinates -30, 22, 48; 38, 40, -14; and -26, 34, -12. No significant relationships were found between pretreatment BOLD signals within the ROI masks and PDS change scores in any contrast. When

posttreatment PDS scores were used in the analysis instead of change scores, a positive relationship was found between pretreatment BOLD signals in the left inferior orbital frontal cortex (BA11; -22, 30, -12) and PDS posttreatment scores ($t(19) = 4.96$, $p_{FWE} = .022$, cluster size 15) in the group of 21 treatment completers for the IF>AF contrast. This finding suggests that greater pretreatment BOLD signals in part of the left inferior orbital cortex (positively associated with pretreatment rumination) predict higher levels of self-reported posttraumatic stress disorder after CPT.

Discussion

Results supported the first hypothesis. Women with PTSD endorsed higher levels of rumination than women in the TEC or HC groups. Even after symptom severity was controlled for, the PTSD group had higher levels of rumination as compared to the TEC group. This finding is consistent with the literature (Birrer & Michael, 2011; Michael et al., 2007), and suggests that rumination is associated with PTSD and not necessarily to the experience of trauma.

The second hypothesis was partially supported. Relationships between rumination and activation in regions of interest differed depending on the contrast examined. This finding suggests that the neural correlates of rumination in PTSD were influenced by attentional modulation of fear or emotion stimuli. Directing attention to fearful faces to indicate whether the images match as compared to attentional focus on neutral faces (AF>AN) resulted in negative relationships between RTS scores and the left amygdala, left ACC, and left medial orbital cortex (BA 10). These relationships were in the opposite direction as hypothesized, and this pattern of activation may indicate that the

women reporting higher levels of rumination demonstrated some emotional detachment or avoidance from the images of fearful faces.

Similar results were observed in prior research. During a task of cognitive reappraisal in which participants were presented with negative images and instructed to improve the image in their mind, a negative relationship was observed between self-reported rumination and the amygdala and midline cortical structures including the ACC and BA 10 (Ray et al., 2005). Although the findings of this prior study were in the context of down-regulating negative stimuli, it is possible that individuals with PTSD who report higher levels of rumination disengage from directly presented fearful images. To clarify, if rumination is a form of cognitive avoidance and a maladaptive emotion regulation strategy in PTSD (Ehlers & Clark, 2000), it is possible that when confronted with images of fearful faces, a particularly salient image for survivors of interpersonal trauma, these individuals avoid engaging with the full emotional content of the image.

It is notable that once pretreatment symptom severity was accounted for, the initial results for the AF>AN contrast did not survive. However, a negative relationship between RTS scores and the right medial orbital cortex (BA32) was found. It is possible that this finding underlies the same process as discussed above in which the negative relationship evidences a detachment or avoidance from the stimuli. Prior research has found that higher levels of self-reported dissociation or alexithymia are associated with lower BOLD signals in BA 32 during the presentation of a trauma script (Frewen, Pain, Dozois, & Lanius, 2006b; Mickleborough et al., 2011).

The next contrast examined was IF>IN. The ignore fear condition was the focus of this contrast. Participants attended to images of houses while ignoring images of

fearful faces. Given the threat bias associated with PTSD, the fearful faces serve as negative emotional stimuli that can provide interference in the overall task of determining if the house images match. Therefore, the IF>IN contrast examines inhibition of negative stimuli in comparison to inhibition of neutral stimuli. The only finding for the IF>IN contrast is a positive relationship between RTS scores and the right frontal middle gyrus or dlPFC (BA9). This finding did not remain significant when controlling for symptom severity. Even so, it is possible that the positive relationship between rumination and the voxel cluster in the dlPFC is a result of individuals with higher levels of rumination needing to recruit greater cognitive control circuitry to inhibit the negative stimuli. This is consistent with prior research that found a positive relationship between rumination and activity in the right dlPFC during disengaging from negative stimuli (Vanderhasselt et al., 2011).

As stated above the IF>IN contrast yielded no other significant findings. It is possible that the lack of significant relationships between RTS scores and the amygdala is a result of how BOLD signals were examined. Previous research (Siegle et al., 2006, 2002) indicated that greater reported rumination was associated with sustained processing in the amygdala rather than an increase in the magnitude of the BOLD signal. The short length of the inter-trial intervals in the current study prevented the analysis of the time course of amygdala reactivity. Therefore it is unknown if rumination would have been positively related to length of amygdala reactivity. Another explanation for the lack of findings in this particular contrast is the use of the ignore neutral faces condition as a baseline. Individuals with depression have been found to interpret neutral information as negative (Leppänen, Milders, Bell, Terriere, & Hietanen, 2004). It is possible that as

distractors, neutral images of faces are processed similarly to images of fearful faces in the clinical sample from the current study.

The final contrast examined, IF>AF, provided a way to investigate the neural substrates of rumination during inhibition of fearful stimuli as compared to directing attention to the negative images. Research on both healthy and depressed individuals suggests that rumination is associated with difficulty inhibiting or disengaging from negative stimuli (Vanderhasselt et al., 2013, 2011). Various fMRI studies on individual differences in rumination have found greater recruitment of regions related to cognitive control in individuals with higher levels of rumination, indicating inefficiency in neural processes of emotion inhibition in habitual ruminators (Vanderhasselt et al., 2013). This is consistent with the most robust finding of the current study. A positive relationship was found between rumination and a voxel cluster in the right inferior orbital frontal cortex (OFC; BA11) that survived family wise error, as well as the whole brain analysis.

The inferior (or ventral) OFC is considered part of the ventral medial prefrontal cortex (vmPFC). It has reciprocal connections with the amygdala (Croxson et al., 2005), and it has been implicated in processing negatively valenced information (E. T. Rolls, 2004). The OFC is associated with decision making, subjective valuation, and reward (see Edmund T. Rolls & Grabenhorst, 2008 for review). The OFC appears to be responsible for monitoring and updating emotional information and the value of stimuli over time. This temporal assessment of the context of information contributes to decision making and reward driven behaviors (Dolan, 2007; Edmund T. Rolls & Grabenhorst, 2008). Additionally, research has identified the right inferior OFC as a region that is recruited to assist in emotion interference resolution in working memory indicating that

activation in the right inferior OFC underlies the process of inhibiting emotional information within working memory by providing information on the context of the emotional information (Levens & Phelps, 2010). Furthermore, individuals with lesions in the right inferior OFC demonstrate increased emotion interference in a working memory task (Levens, Devinsky, & Phelps, 2011). This prior research suggests that the right inferior OFC contributes to the inhibition of emotional information. The current findings that women with PTSD who have higher levels of rumination have greater recruitment of the right inferior OFC during inhibition of negative stimuli suggests that greater rumination is associated with an inefficiency in emotional inhibition. Women with higher pretreatment rumination had more difficulty ignoring irrelevant negative stimuli while attempting to match the images of houses.

Other results for the IF>AF contrast were significant positive relationships between rumination and the left frontal middle gyrus or dlPFC (BA8) and the left inferior orbital cortex (BA11). These findings are consistent with the other results from this contrast, and suggest that more top-down control is needed in individuals with higher levels of rumination in order to inhibit negative stimuli.

Results for the third hypothesis suggested that CPT results in a significant decrease in rumination. Overall, women who completed treatment reported less rumination at the posttreatment assessment. The mechanism that underlies this decrease is unknown, however, it is possible that the cognitive strategies learned through CPT provided the women with a more efficient, healthier way to think about negative events in their life. An alternative possibility is that the decrease in rumination is related to symptom decrease through treatment; however, it is notable that participants in the PTSD

group had posttreatment rumination scores comparable to the initial rumination scores of the HC group.

The fourth hypothesis was also partially supported by the study. Pretreatment rumination scores predicted posttreatment PDS scores. Women with higher levels of rumination pretreatment reported greater PTSD symptoms posttreatment as compared to women with lower levels of pretreatment rumination. However, when pretreatment symptom severity was added into the model, the relationship between pretreatment RTS scores and posttreatment PDS scores was no longer significant indicating that rumination does not predict treatment outcome above initial symptom severity.

The fifth hypothesis was not supported. Individual differences in levels of rumination did not predict drop out from CPT. Multiple explanations exist for why a relationship between rumination and treatment dropout was not found. First, there may be multiple subgroups of individuals within the treatment dropout group. For example, individuals who dropout in the first few sessions of therapy could have vastly different reasons than individuals who dropout closer to the end of treatment. Practical life issues such as work and family commitments sometimes result in dropout from treatment creating another subgroup of individuals. The current study did not have a large enough sample to investigate the possible effects of rumination within subgroups of the treatment dropout group.

The sixth hypothesis was not supported. Results indicated that there was a negative relationship between the change in rumination and the change in BOLD signals pre to posttreatment in a voxel cluster of the superior frontal cortex (BA 9) in the IF>AF contrast. As discussed above, BA 9 is thought to contribute to cognitive control. This

region did not have a significant relationship to rumination pretreatment, but the results suggest that individuals who experienced a greater decrease in RTS scores, had increased reactivity in the voxel cluster of the right superior frontal cortex from pre to post treatment in IF>AF contrast. Although this finding did not remain significant when controlling for pretreatment symptom severity, it is possible that this finding demonstrates that a greater decrease in rumination scores across treatment leads to better recruitment of brain regions associated with cognitive control.

The exploratory analysis provided two findings of note. First, as discussed above, the whole brain analysis evidenced a significant positive relationship between rumination and the right inferior OFC (BA 11) in the IF>AF contrast. Although this relationship did not remain significant after controlling for pretreatment symptoms severity, it is of note that the same region was positively related to RTS scores in the ROI analysis even when pretreatment symptom severity was added into the model. The significance of the relationship was discussed above.

Finally, the exploratory analysis examining whether regions associated with pretreatment rumination would predict treatment outcome found that greater activity in a voxel cluster in the left inferior OFC (BA 11) predicted higher PDS scores posttreatment among responders and nonresponders. This suggests that greater left inferior OFC activity pretreatment leads to poorer symptom reduction across CPT. The inferior OFC (BA 11) is a region associated with facilitating control over emotional interference. A higher level of activity in this region possibly indicates an inefficiency in exerting cognitive control over emotional distractors. Through cognitive behavioral treatments such as CPT, it is thought that clients learn cognitive skills to manage emotions and

engage in balanced thinking (Resick & Schnicke, 1992, 1993), thereby increasing cognitive control. It is possible that the findings of the current study indicate that individuals with less ability to exert cognitive control over emotional information have greater difficulty either learning or utilizing the skills taught in CPT. Further hypothesis driven research is needed to understand what might drive the relationship between the left inferior OFC and posttreatment PDS scores.

Limitations and Future Directions

The current study was not without limitations. First, this study recruited only female participants with interpersonal trauma, and therefore these results might not generalize to men and other trauma types. The stimuli of fearful and neutral faces may be particularly salient to women with a history of interpersonal violence, also affecting possible generalizability. Given the main focus of the study was on neuroimaging, a smaller sample was recruited due to costs associated with fMRI scans. Therefore, many of the analyses using only clinical data were underpowered increasing the likelihood of a type II error. The small sample also made it difficult to examine treatment outcome as only four individuals were identified as treatment nonresponders.

Another limitation of the study was the use of a single measure of rumination. Rumination is a multifaceted construct that includes a variety of repetitive thought processes such as brooding and reflection (Mandell, Siegle, Shutt, Feldmiller, & Thase, 2014; Siegle, Moore, & Thase, 2004). Previous research has found that rumination is not a singular construct, but rather one that is comprised of different components. Although various measures of rumination appear to measure different, sometimes unrelated aspects of rumination; when these measures are used in aggregate, they measure a single

construct (Siegle et al., 2004). Therefore, future research should utilize a battery of rumination measures.

Despite these limitations, the current study provided new information on rumination in women with PTSD. Consistent with prior research, women with PTSD were found to have higher levels of rumination as compared to women who had a history of trauma and no PTSD as well as healthy controls even when symptom severity was considered. Future research is needed to understand why women with PTSD demonstrate higher levels of rumination. How might pretrauma rumination levels interact with the experience of trauma in the development of PTSD?

The current study also suggests that individual differences in levels of ruminative thought in women with PTSD are reflected in underlying neural circuitry, specifically the right inferior orbital cortex (BA11), when inhibiting fear stimuli. This region has been associated with the facilitation of control over the interference of emotional information suggesting that women with PTSD who report higher levels of rumination potentially have a more difficult time inhibiting distracting emotional information. Further, the current study found that greater pretreatment activation in the left inferior orbital cortex (BA 11) predicted higher levels of PTSD symptoms posttreatment. This potentially has implications for approaching treatment with individuals with higher levels of rumination. Future research is needed to understand the connection between the inferior orbital frontal cortex, rumination, and treatment for PTSD.

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Table 1.
Participant Demographics and Pretreatment Clinical Scores Divided by Group

	PTSD <i>N</i> = 39	Trauma Controls <i>N</i> = 17	Healthy Controls <i>N</i> = 18	Statistic	<i>p</i>	Effect Size
Age	<i>M</i> = 31.33 <i>SD</i> = 9.38	<i>M</i> = 31.24 <i>SD</i> = 9.32	<i>M</i> = 33.44 <i>SD</i> = 10.72	$F(71, 2) = .332$.719	$\eta^2 = .01$
Education	<i>M</i> = 15.37 <i>SD</i> = 2.30	<i>M</i> = 15.31 <i>SD</i> = 2.41	<i>M</i> = 17.44 <i>SD</i> = 2.96	$F(66, 2) = 4.619$.013*	$\eta^2 = .123$
Race/Ethnicity				$\chi^2 = 10.445$.402	$\Phi = .376$
White	21 (53.8%)	12 (70.6%)	14 (77.8%)			
African American	12 (30.8%)	2 (11.8%)	3 (16.7%)			
Hispanic	1 (2.6%)	0	0			
Asian	0	0	1 (5.5%)			
Other	2 (5.1%)	1 (5.8%)	0			
Unreported	3 (7.7%)	2 (11.8%)	0			
Pretreatment Clinical Measures						
CAPS	<i>M</i> = 73.05 <i>SD</i> = 15.89	<i>M</i> = 21.12 <i>SD</i> = 13.77	N/A N/A	$t(54) = 11.68$	< .001**	$d = 3.49$
PDS	<i>M</i> = 29.28 <i>SD</i> = 10.20	<i>M</i> = 9.94 <i>SD</i> = 8.46	N/A N/A	$t(54) = 6.85$	< .001**	$d = 2.06$
BDI-II	<i>M</i> = 25.97 <i>SD</i> = 10.65	<i>M</i> = 9.19 <i>SD</i> = 5.64	N/A N/A	$t(49)^a = 7.59$	< .001**	$d = 1.58$
RTS	<i>M</i> = 101.33 <i>SD</i> = 24.36	<i>M</i> = 60.35 <i>SD</i> = 23.84	<i>M</i> = 61.39 <i>SD</i> = 19.25	$F(2, 71) = 28.24$	< .001**	$\eta^2 = .443$

Note: * = $p < .05$, ** = $p < .001$, ^a indicates that equal variances were not assumed. CAPS = Clinician Administered PTSD Scale, PDS = Posttraumatic Stress Diagnostic Scale, BDI-II = Beck Depression Inventory II

Table 2.

Treatment Completers and Dropouts Demographics and Pretreatment Clinical Scores

	Completers <i>N</i> = 21	Dropouts <i>N</i> = 18	Statistic	<i>p</i>	Effect Size
Age	<i>M</i> = 34.00 <i>SD</i> = 11.25	<i>M</i> = 28.22 <i>SD</i> = 5.38	<i>t</i> (30) = 2.09 ^a	.045*	<i>d</i> = 0.51
Education	<i>M</i> = 15.70 <i>SD</i> = 1.72	<i>M</i> = 14.93 <i>SD</i> = 2.92	<i>t</i> (33) = .974	.337	<i>d</i> = 0.32
Race/Ethnicity					
White	13 (61.9%)	8 (44.4%)	$\chi^2 = .325$		$\Phi = .345$
African American	5 (23.8%)	7 (38.9%)			
Hispanic	0	1 (5.6%)			
Asian	0	0			
Other	2 (9.5%)	0			
Unreported	1 (4.8%)	2 (11.1%)			
Pretreatment Clinical Measures					
CAPS	<i>M</i> = 69.76 <i>SD</i> = 17.15	<i>M</i> = 76.89 <i>SD</i> = 13.78	<i>t</i> (37) = -1.41	.166	<i>d</i> = 0.46
PDS	<i>M</i> = 25.05 <i>SD</i> = 9.88	<i>M</i> = 34.22 <i>SD</i> = 8.34	<i>t</i> (37) = -3.10	.004*	<i>d</i> = 1.00
BDI-II	<i>M</i> = 21.43 <i>SD</i> = 9.82	<i>M</i> = 31.28 <i>SD</i> = 9.22	<i>t</i> (37) = -3.21	.003*	<i>d</i> = 1.03
RTS	<i>M</i> = 95.81 <i>SD</i> = 28.01	<i>M</i> = 107.78 <i>SD</i> = 17.94	<i>t</i> (34) = 1.61 ^a	.116	<i>d</i> = .51

Note: * = $p < .05$, ** = $p < .001$, ^a indicates that equal variances were not assumed. CAPS = Clinician Administered PTSD Scale, PDS = Posttraumatic Stress Diagnostic Scale, BDI-II = Beck Depression Inventory II

Table 3.
Treatment Completers (N = 21) Pre-Post Clinical Measures

	Pretreatment	Posttreatment	Statistic	<i>p</i>	Effect Size
CAPS	<i>M</i> = 69.76 <i>SD</i> = 17.15	<i>M</i> = 24.62 <i>SD</i> = 21.80	<i>t</i> (20) = 11.32	< .001**	<i>d</i> = 2.63
PDS	<i>M</i> = 25.05 <i>SD</i> = 9.88	<i>M</i> = 10.67 <i>SD</i> = 12.11	<i>t</i> (20) = 6.92	< .001**	<i>d</i> = 1.46
BDI-II	<i>M</i> = 21.43 <i>SD</i> = 9.82	<i>M</i> = 9.48 <i>SD</i> = 8.95	<i>t</i> (20) = 7.02	< .001**	<i>d</i> = 1.22
RTS ¹	<i>M</i> = 96.50 <i>SD</i> = 28.55	<i>M</i> = 63.05 <i>SD</i> = 28.55	<i>t</i> (19) = 4.69	< .001**	<i>d</i> = 1.05

Note: * = $p < .05$, ** = $p < .001$. CAPS = Clinician Administered PTSD Scale, PDS = Posttraumatic Stress Diagnostic Scale, BDI-II = Beck Depression Inventory II, ¹ $N = 20$ due to missing data

Table 4.
Responders and Nonresponders Demographics and Pretreatment Clinical Scores

	Responders N = 17	Nonresponders N = 4	Statistic	<i>p</i>	Effect Size
Age	<i>M</i> = 33.65 <i>SD</i> = 12.34	<i>M</i> = 35.50 <i>SD</i> = 5.20	<i>t</i> (12) = -.467 ^a	.648	<i>d</i> = .20
Education	<i>M</i> = 15.81 <i>SD</i> = 1.38	<i>M</i> = 15.25 <i>SD</i> = 2.99	<i>t</i> (18) = -.367	.736	<i>d</i> = .24
Race/Ethnicity					
White	10 (58.8%)	3 (75%)	N/A	N/A	
African American	4 (23.5%)	1 (25%)			
Hispanic	0	0			
Asian	0	0			
Other	2 (11.8%)	0			
Unreported	1 (5.9%)	0			
Pretreatment Clinical Measures					
CAPS	<i>M</i> = 68.00 <i>SD</i> = 14.62	<i>M</i> = 77.25 <i>SD</i> = 26.97	<i>t</i> (19) = .663	.549	<i>d</i> = .43
PDS	<i>M</i> = 23.29 <i>SD</i> = 9.15	<i>M</i> = 32.50 <i>SD</i> = 10.63	<i>t</i> (19) = 1.762	.094	<i>d</i> = .93
BDI-II	<i>M</i> = 20.06 <i>SD</i> = 8.83	<i>M</i> = 27.25 <i>SD</i> = 13.10	<i>t</i> (19) = 1.344	.195	<i>d</i> = .64
RTS	<i>M</i> = 92.29 <i>SD</i> = 28.94	<i>M</i> = 110.75 <i>SD</i> = 19.92	<i>t</i> (19) = 1.199	.245	<i>d</i> = .74

Note: * = $p < .05$; ** = $p < .001$; ^a indicates that equal variances were not assumed. CAPS = Clinician Administered PTSD Scale, PDS = Posttraumatic Stress Diagnostic Scale, BDI-II = Beck Depression Inventory II

Table 5.

Regression Results for PTSD Participant (N = 39) in the Negative Direction between RTS Scores and ROI Masks in the AF>AN Contrast

x, y, z	Region	Cluster	t	p FEW
No PDS or BDI-II scores				
-18, -6, -16	L Amygdala	7	3.65	0.082
-6, 28, -8	L Anterior Cingulum	7	3.87	0.352
-6, 40, -10	L Frontal Medial Orbital (BA 10)	5	3.70	0.466
PDS and BDI-II scores entered				
8, 38, -8	R Frontal Medial Orbital (BA 32)	5	3.64	0.525

Note. All results presented were determined significant at a $p < .001$ uncorrected and a cluster threshold of 5 voxels. Brodmann Areas (BA) are noted after the aal region label.

Table 6.

Regression Results for PTSD Participant (N = 39) in the Positive Direction between RTS Scores and ROI Masks in the IF>IN Contrast

x, y, z	Region	Cluster	t	p FEW
No PDS or BDI-II scores				
42, 10, 40	R Frontal Middle Gyrus (BA 9)	24	4.03	0.279

Note. All results presented were determined significant at a $p < .001$ uncorrected and a cluster threshold of 5 voxels. Brodmann Areas (BA) are noted after the aal region label.

Table 7.

Regression Results for PTSD Participant (N = 39) in the Positive Direction between RTS Scores and ROI Masks in the IF>AF Contrast

x, y, z	Region	Cluster	t	p FEW
No PDS or BDI-II scores				
-30, 22, 48	L Frontal Middle Gyrus (BA 8)	41	4.38	0.127
38, 40, -14	R Frontal Inferior Orbital (BA 11)	46	5.62	0.004
-26, 34, -12	L Frontal Inferior Orbital (BA 11)	6	3.83	0.317
PDS and BDI-II scores entered				
38, 38, -14	R Frontal Inferior Orbital (BA 11)	47	5.10	0.019
-26, 34, -12	L Frontal Inferior Orbital (BA 11)	10	3.61	0.241

Note. All results presented were determined significant at a $p < .001$ uncorrected and a cluster threshold of 5 voxels. Brodmann Areas (BA) are noted after the aal region label.

Table 8.

Results from Paired t-Tests Comparing Regions Before and After CPT

x, y, z	Direction	Region	Cluster	t	p FEW
AF>AN					
24, 64, 18	T1<T2	R Frontal Superior (BA 10)	5	4.12	.439
IF>IN					
8, 30, 12	T1>T2	R Anterior Cingulum	28	4.74	.190
IF>AF					
30, 26, 38	T1>T2	R Middle Frontal (BA8/BA9)	170	5.81	.034
-18, 24, 34	T1>T2	L Superior Frontal (BA9)	49	5.54	.055
10, 32, 12	T1>T2	R Anterior Cingulum	53	4.64	.191
16, 42, 26	T1>T2	R Superior Frontal (BA 9)	7	4.61	.200
-12, 36, -4	T1>T2	L Anterior Cingulum (BA 10)	10	4.15	.391
-6, 10, 32	T1>T2	L Middle Cingulate	10	3.97	.493

Note. All results presented were determined significant at a $p < .001$ uncorrected and a cluster threshold of 5 voxels. The direction is based on whether BOLD signals for the specified region are relatively greater at pretreatment (T1) or at posttreatment (T2). Brodmann Areas (BA) are noted after the aal region label.

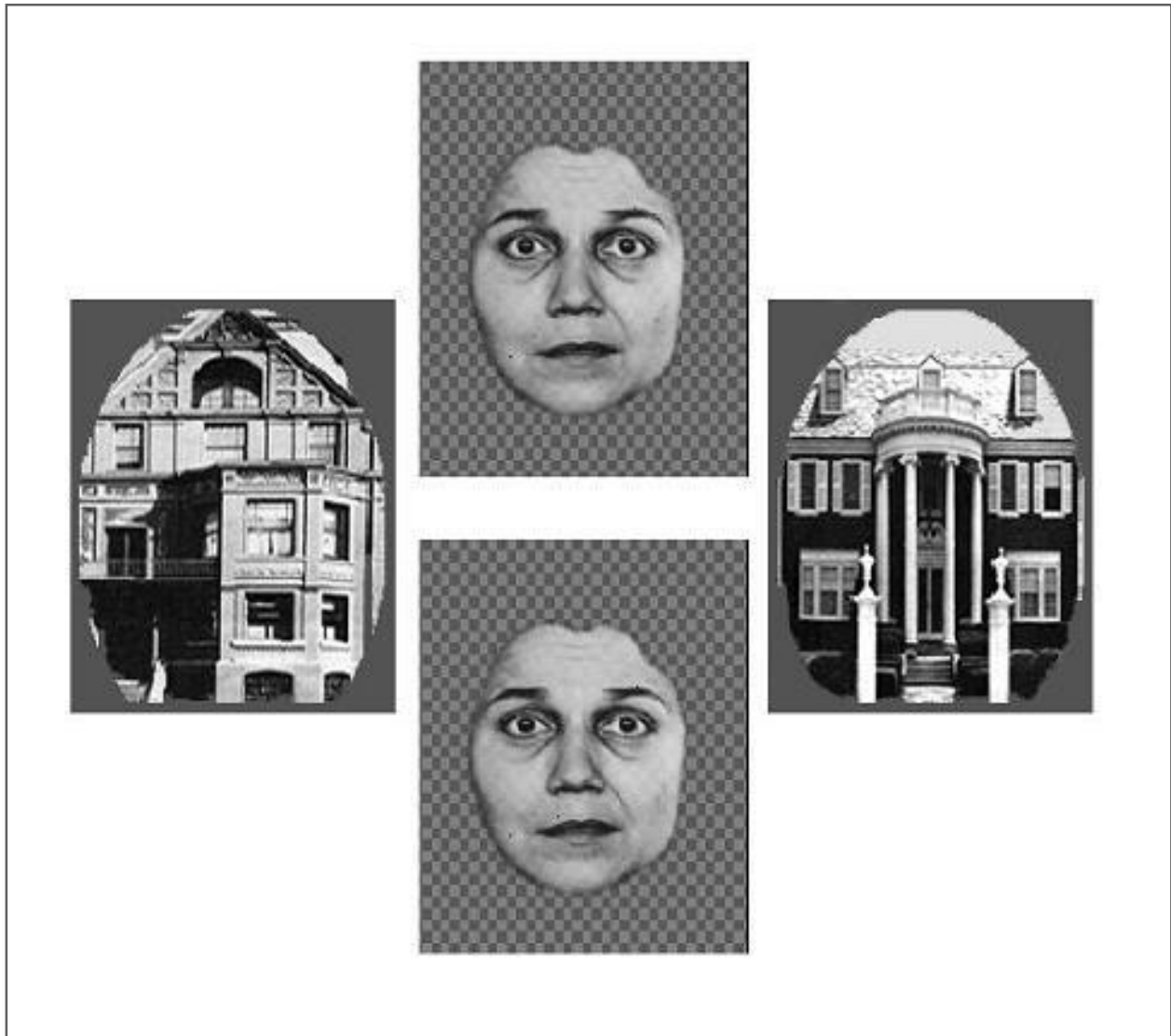


Figure 1. An example of a single trial from the emotion interference task. The images of neutral faces are aligned vertically while the images of houses are aligned vertically. In this particular trial, the participant would be cued to attend to the horizontal images.

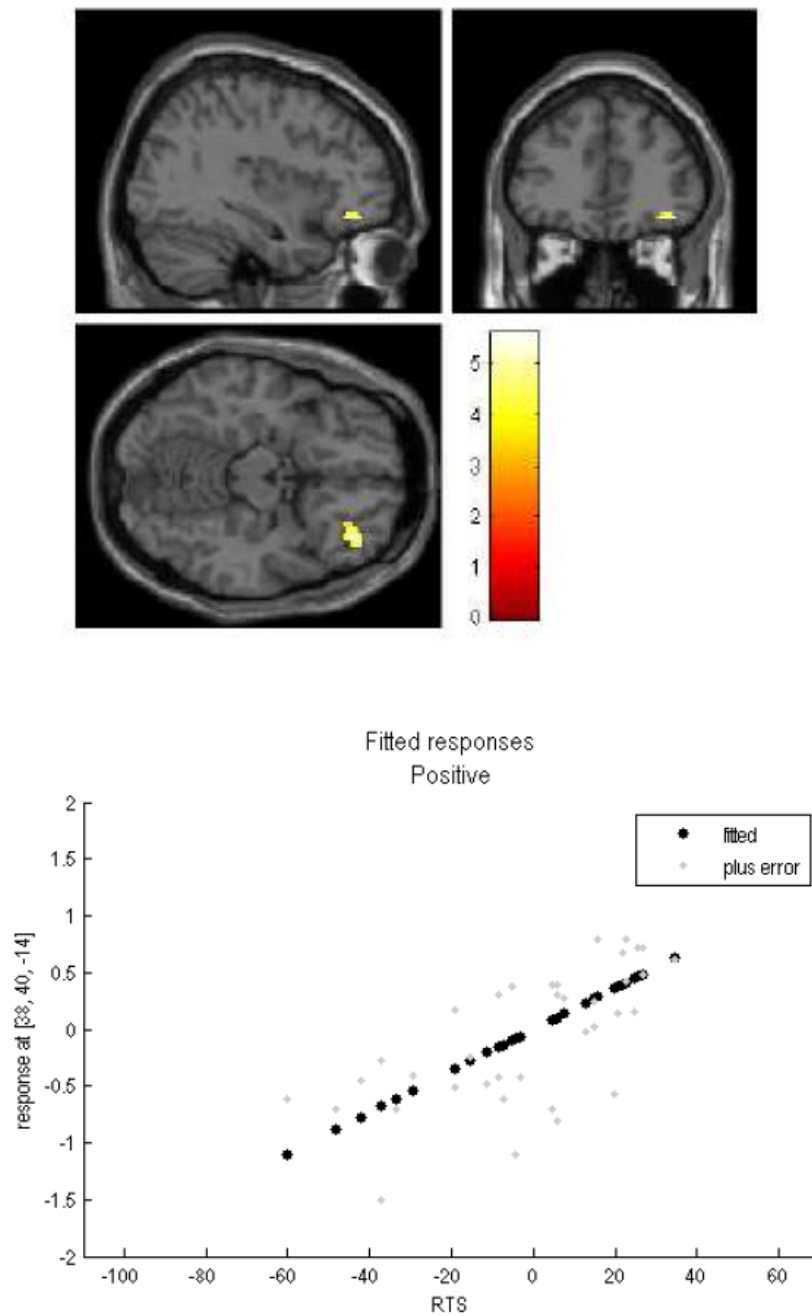


Figure 2. Image and graph of the significant relationship between RTS scores and the area of the right inferior orbital cortex (BA 11) in 39 women with PTSD before treatment in the IF>AF contrast. This contrast focuses on the condition in which participants ignored fear distractors as compared to when they attending to fearful faces.

Appendix

Ruminative Thought Style Questionnaire (RTS)

For each of the items below, please rate how well the item describes you. Participants are provided with a 7-point scale for each item, ranging from 1, “not at all,” to 7, “very well.”

1. I find that my mind often goes over things again and again.
2. When I have a problem, it will gnaw on my mind for a long time.
3. I find that some thoughts come to mind over and over throughout the day.
4. I can't stop thinking about some things.
5. When I am anticipating an interaction, I will imagine every possible scenario and conversation.
6. I tend to replay past events as I would have liked them to happen.
7. I find myself daydreaming about things I wish I had done.
8. When I feel I have had a bad interaction with someone, I tend to imagine various scenarios where I would have acted differently.
9. When trying to solve a complicated problem, I find that I just keep coming back to the beginning without ever finding a solution.
10. If there is an important event coming up, I think about it so much that I work myself up.
11. I have never been able to distract myself from unwanted thoughts.
12. Even if I think about a problem for hours, I still have a hard time coming to a clear understanding.
13. It is very difficult for me to come to a clear conclusion about some problems, no matter how much I think about it.
14. Sometimes I realize I have been sitting and thinking about something for hours.

15. When I am trying to work out a problem, it is like I have a long debate in my mind where I keep going over different points.
16. I like to sit and reminisce about pleasant events from the past.
17. When I am looking forward to an exciting event, thoughts of it interfere with what I am working on.
18. Sometimes even during a conversation, I find unrelated thoughts popping into my head.
19. When I have an important conversation coming up, I tend to go over it in my mind again and again.
20. If I have an important event coming up, I can't stop thinking about it.