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Attentional control abnormalities in posttraumatic stress disorder: Functional, behavioral, and structural correlates

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Abstract

Background: Attentional disruptions are common in PTSD, but findings across neuropsychological and neuroimaging studies have been variable. Few PTSD studies have investigated abnormalities in attention networks using a multi-modal imaging approach and attentional tasks that include emotionally-salient images. This study combined a behavioral task that included these images (emotional Stroop) with functional and structural neuroimaging (fMRI and diffusion tensor imaging; DTI) methods to comprehensively investigate attentional control abnormalities in a highly-traumatized civilian sample.

Methods: 48 traumatized women with and without PTSD received clinical assessments, fMRI and DTI. During fMRI, the Affective Stroop (AS), an attentional control task that includes emotionally-salient distractor images (trauma-relevant, positive, neutral) and variable task demands, was administered.

Results: In response to more difficult AS trials, participants with PTSD demonstrated lower activation in the dorsal and rostral anterior cingulate cortex and greater activation in the insula. This group also showed comparatively poorer performance on positive AS distractor trials, even after adjusting for trauma exposure. Performance on these trials inversely correlated with structural integrity of the cingulum bundle and uncinate fasciculus.

Conclusions: Even after adjusting for trauma exposure, participants with PTSD showed worse performance on an attentional control task in the context of emotional stimuli. They also showed

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Supplementary materials

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relatively lower cognitive control network activation and greater salience network activation. Fronto-parietal and fronto-limbic white matter connectivity corresponded with AS performance. Our findings indicate that attentional control impairments in PTSD are most evident in the context of emotional cues, and are related to decrements in function and structure of cognitive control and salience networks.

Keywords

Attention; PTSD; fMRI; DTI; Structure; Cognition; Stroop

1. Introduction

Attentional disruptions are frequently experienced by traumatized people, and are reflected in several posttraumatic stress disorder (PTSD) symptoms: intrusive recollections or flashbacks of the trauma, an impaired ability to concentrate on desired tasks, and hypervigilance for trauma-related cues. Attention comprises three different processes: alerting, orienting, and executive control (Petersen and Posner, 2012). Among these, executive or attentional control may be the most amenable to modification; it functions under conscious awareness, making it a frequent target of treatments (Badura-Brack et al., 2015). Attentional control includes the ability to maintain focus on a given task and disregard irrelevant information, a process that is critical to many daily life activities.

Evidence for diminished attentional control in PTSD has emerged from studies that used neuropsychological tasks, including the Stroop paradigm (Scott et al., 2015; Stroop, 1935). The existing PTSD neuropsychological studies employing the Stroop task show some evidence for diminished attentional control in PTSD populations (Lagarde et al., 2010) via poorer task performance, as indicated by a recent meta-analysis (Cisler et al., 2011). However, effect sizes have been relatively small ($d \sim .2$) (Cisler et al., 2011), and some studies have not found between-group effects at all (Kanagaratnam and Asbjornsen, 2007; Lagarde et al., 2010; Vasterling et al., 2002). One potential reason relates to variations in PTSD symptom clusters between the different samples in these studies—there is evidence that these symptom clusters are differentially related to attentional control deficits (Grisanzio et al., 2018), with fearful arousal symptoms corresponding most with cognitive control problems.

Problems with attentional control in the context of emotion are likely to be related to dysfunction in two distinct neural circuits (Petersen and Posner, 2012; Posner and Petersen, 1990). The cingulo-opercular network includes the anterior cingulate cortex (ACC) and insula as well as the amygdala, and supports error monitoring and salience detection (frequently termed “salience network”). The fronto-parietal network, which includes the dorsal ACC, dorsolateral prefrontal (DLPFC) and inferior parietal cortex, supports the implementation of executive control and adjustment of attentional strategy. Increased cingulo-opercular and decreased fronto-parietal network function appears to characterize anxious populations in general (Sylvester et al., 2012).

However, neuroimaging studies of attention in traumatized populations indicate more mixed findings, both in terms of neural network response and behavior (Block and Liberzon, 2016).

This may, in part, reflect methodological differences, including the types of stimuli employed in attentional control tasks (i.e., images vs words, trauma-relevant vs generally aversive stimuli), as well as heterogeneous samples. Studies using affective versions of the Stroop have indicated differential fronto-parietal and cingulo-opercular network activation in PTSD in response to emotional stimuli. One study of women with complex PTSD indicated higher dACC, dorsolateral prefrontal cortex (DLPFC), ventromedial prefrontal cortex (vmPFC) and anterior insula response to trauma-related words in civilians with complex PTSD on an emotional Stroop task, compared to both traumatized and healthy controls (Herzog et al., 2017). Participants with PTSD demonstrated poorer Stroop task performance, particularly when presented with trauma words. Using an image-based Affective Stroop (AS), Blair et al. (2007) observed decreased DLPFC activation in patients with PTSD in response to heightened task demands (Blair et al., 2007), but no significant differences in task performance were observed; aversive images used in the task were not trauma-specific. Building upon this work by examining the functional connectivity during this same task, White et al. (2015) observed that PTSD symptoms positively correlated with amygdala connectivity to the DLPFC and dACC in veterans in response to emotionally-valenced vs neutral images, particularly to trials with positive image distractors (White et al., 2015). The authors also found that PTSD symptoms correlated with increased functional connectivity between the amygdala, dACC and anterior insula (White et al., 2015). However, no group differences were observed in task performance, and their population did not meet clinical criteria for PTSD. Studies using other word or number-based emotional Stroop tasks have indicated higher dACC response (Bremner et al., 2004) but lower response in the rostral ACC (Bremner et al., 2004; Shin et al., 2001) in participants with PTSD versus controls; in these two studies, significant differences in task performance were not observed. These data indicate that salience network activation appears to be more consistently related to attentional control disruptions in PTSD, whereas the direction of fronto-parietal circuit involvement has been more variable. Only one such study observed significant differences in task performance (Herzog et al., 2017).

Decrements in the structural integrity of these neural pathways may contribute to the altered responses previously observed. In studies of depression, poorer microstructure of the cingulum bundle has been associated with increased interference on a Stroop task (Keedwell et al., 2016). This white matter tract connects brain regions in the attentional control network (ACC and parietal cortex) and is also a primary route of communication between prefrontal and entorhinal cortices. Similar findings with respect to cingulum integrity and Stroop task performance have been observed in schizophrenia (Kubicki et al., 2009). Our earlier studies suggest that the cingulum as well as the uncinate fasciculus, a fronto-limbic tract that connects the amygdala and vmPFC, are specifically compromised in PTSD (Daniels et al., 2013; Fani et al., 2015, 2012a, 2016). These tracts have been associated with treatment outcome as well (Kennis et al., 2015). However, little is known about how the structure of these pathways affects attentional control in PTSD.

To our knowledge, no studies to date have used a multi-modal approach, combining behavioral data (Affective Stroop task performance) with structural and functional MRI data to comprehensively investigate the nature of attentional control abnormalities in PTSD. We measured responses of traumatized participants with and without PTSD on the affective

Stroop (administered during fMRI) to examine differences in attentional performance during neutral and emotional conditions, including both positive and trauma-relevant distractors in this task. We predicted that a PTSD diagnosis would be associated with poorer performance on the Affective Stroop (error rates and response times were used to assess attentional control), particularly in the presence of emotional stimuli. We expected decreased activation in the fronto-parietal/cognitive control network and increased cingulo-opercular/salience network activation in response to increased task demands. We hypothesized that poorer integrity of cingulum bundle (CB) and uncinate fasciculus (UF) pathways would be associated with poorer AS task performance in the presence of emotionally-valenced distractors. To assess for specificity of findings with respect to white matter, we included a third pathway, the medial forebrain bundle, in analyses. We conducted exploratory analyses to examine the relationships between task performance, neural response patterns and PTSD symptom dimensions.

2. Methods

2.1. Participants

A sample of 48 African-American women aged 22–61 ($M = 38.7$, $SD = 11.2$) was recruited from an NIH-funded study of attentional control in PTSD (MH101380) and received MRI. Individuals were approached in general medical clinics of a publicly-funded hospital serving low income individuals in inner-city Atlanta, Georgia. On average, nearly half of all participants had completed up to 12 years of schooling or the equivalent (GED), and had monthly incomes of less than \$1000. Only 39% of the sample was employed. Participant characteristics are further detailed in Table 1.

The eligibility criterion for participation in the current study included the ability to understand English (assessed by a study researcher) and willingness to provide informed consent. Participants were excluded if they had current neurological conditions or psychosis, as well as current psychotropic medication use. Participants were excluded from MRI on the basis of: claustrophobia; contra-indications to MRI scanning (e.g., metal implants); current bipolar disorder (as assessed with the MINI interview Sheehan et al., 1998); current substance or alcohol dependence or intoxication. Participants were given a urine drug test on the day of the scan and tested negative. Although handedness was not used as an inclusion/exclusion factor, a majority of participants were right handed ($n = 42$; 88%). After being enrolled in the study, one participant reported starting on psychotropic medications. Participants receiving MRI were asked to refrain from caffeine consumption on the day of the scan, given possible effects on BOLD signal and cognition, as shown previously (Koppelstaetter et al., 2010; Laurienti et al., 2002). The Institutional Review Board of Emory University and Grady Hospital Research Oversight Committee approved all study procedures.

2.2. MRI acquisition, image processing

Scanning was conducted on a research-dedicated Siemens 3-Tesla TIM-Trio scanner (12 channel head coil) at Emory University Hospital. Acquisition parameters and image pre-processing details are provided in the Supplement.

2.3. Clinical assessments

We administered the following assessments, detailed further in the Supplement. The Traumatic Events Inventory (TEI) was administered to measure lifetime trauma exposure. Given that the two diagnostic groups demonstrated significant differences in trauma exposure (see Table 1), overall TEI scores were submitted as covariates in statistical analyses. The Clinician Administered PTSD Scale (CAPS; DSMIV; administered to 18 participants) and DSM5 (administered to 30 participants; Blake et al., 1995, Weathers et al., 2017) was administered to determine presence or absence of PTSD. Based on the CAPS, 26 participants met criteria for PTSD, whereas 22 did not meet PTSD criteria (Controls); all had experienced trauma. The PTSD Symptom Scale (PSS; (Foa et al., 1993) was administered on the day of the MRI scan, and subscale scores (re-experiencing, avoidance, hyperarousal, anhedonia) were used for correlational analyses with MRI data, given their similar time of administration. Participants in the control group had low PSS scores, with a mode of 0, a median score of 2 and mean = 3.4 (SD = 4). As expected, participants in the PTSD group had clinically significant PSS scores, with a mode of 25, a median score of 25 and mean = 25.4 (SD = 11.3) and scores were had a relatively even distribution across the symptom clusters.

2.4. fMRI task: affective stroop

The Affective Stroop (AS) is a measure of attentional control that has been detailed in earlier studies (Blair et al., 2007, 2012b; White et al., 2015), further described in the Supplement. Participants rapidly identify, via button-press, the number of numbers in a given display (3, 4, 5, or 6) while ignoring distractor images (trauma-relevant, positive, and neutral scenes) that appear prior to and following each number stimulus (Fig. 1a and b). The distractor images are identical. In some of these trials, the number of numbers is inconsistent with the actual number displayed, posing a heightened cognitive challenge. In addition, the task includes trials with no cognitive demands (“view only” trials). Error rates and response times were recorded and analyzed.

2.5 fMRI data analysis

To examine blood-oxygen-level dependent (BOLD) signal change to task stimuli, a first-level, fixed-effects analysis was conducted. Onset times for each task condition were entered into a general linear model, convolved with a hemodynamic response function and linear contrasts between conditions were estimated. Subject-specific motion parameters were also included in the model as effects of non-interest. Given our interest in examining neural response and task performance under high vs low attentional demands, and in accordance with earlier studies using this task (Blair et al., 2012b; White et al., 2015), our primary analysis involved contrasting number incongruent versus number congruent trials. Events included the distractor and number stimuli. Since our primary objective was to examine differences in performance between PTSD and traumatized controls, between-group analyses were conducted at a whole brain, voxel-wise level, for this contrast. Where between-group differences in task performance were observed, we performed correlational analyses including all participants; PSS subscale scores were entered as subject-level regressors. Regions of interest included the ACC (dorsal and rostral), DLPFC, superior

parietal cortex, insula, and amygdala, similar to prior studies (White et al., 2018). Results were considered significant at a whole brain statistical threshold of $p < .001$, with cluster-level FWE correction at a threshold of $p < .05$ conducted with these a priori specified regions of interest, as recommended to account for error inflation due to multiple comparisons (Woo et al., 2014). Contrast parameters were extracted from clusters showing significant between-group differences and were used in analyses with behavioral data. To confirm that findings were within established networks of interest, we used Neurosynth (www.neurosynth.org; Yarkoni et al., 2011) to conduct a meta-analysis using cognitive control and salience network terms to identify regions consistently related to these networks.

2.6. DTI data processing and probabilistic tractography

To examine structural connectivity, probabilistic fiber tracking was conducted with PROBTRACKX implemented in FSL, detailed further in the Supplement. Masks of the CB and UF were created using the JHU White Matter Tractography Atlas (Mori et al., 2005) and used as an anatomical waypoint for these paths; a separate exclusion mask was created to eliminate the likelihood of pathways in irrelevant white matter tracts, gray matter regions and CSF. The medial forebrain bundle (MFB) was included in analyses to assess for specificity of findings. To create probabilistic streamlines for MFB pathways, we selected the nucleus accumbens and orbitofrontal cortex as seed regions using the Harvard-Oxford Subcortical Structural Atlas (http://www.cma.mgh.harvard.edu/fsl_atlas.html). Example probabilistic paths for the UF and CB are provided in Fig. 3c and d. Fractional anisotropy (FA) was used as our measure of tract integrity, given that earlier studies have indicated it to be a reliable assessment of microstructural integrity of white matter fibers (Fox et al., 2011). Data from 8 participants were discarded due to motion artifacts or unusable tracts (included anatomically unfeasible, deviated projections), leaving a sample size of 40; this sample of participants was used in all Affective Stroop and DTI data analyses. This sub-group of participants was also similar to the overall sample in terms of age ($M = 38.4$, $SD = 11.3$), PTSD symptoms (PSS total: $M = 16.1$, $SD = 14.1$), and trauma exposure (TEI lifetime trauma: $M = 4.7$, $SD = 2.6$).

2.7. Affective number stroop data analysis

Multivariate analyses of covariance were conducted to examine between-group differences in performance on cognitive measures (AS: error rate and response time) after accounting for the effects of trauma exposure (TEI), given between-group differences and associations found previously with test performance (Palmer et al., 1997); data were analyzed for the 40 participants with both fMRI and DTI data. PTSD diagnosis was the grouping variable, outcome variables included performance on the AS. Where group differences were observed, we also examined associations between PTSD symptom clusters and AS task performance in the entire sample. Finally, we examined correlations of task performance with structural connectivity of cingulum, uncinate fasciculus, and medial forebrain bundle pathways; using IBM SPSS version 24, partial correlations were conducted with mean FA values of all tracts and AS performance variables, controlling for trauma exposure (TEI), given its possible effects on white matter integrity (Fani et al., 2012a; Lebel et al., 2012; Ly et al., 2013; Wang et al., 2010). A threshold of $p < .05$, two-tailed, was used to define

statistical significance; Sidak correction was applied to adjust for error due to multiple comparisons ($p < .006$).

3. Results

3.1. Affective stroop task performance

3.1.1. PTSD vs controls—We examined effects of emotion and task condition on differences in accuracy and response time in the sample using two 3 (emotion: positive, trauma-relevant, neutral) \times 2 (task condition: number congruent, number incongruent) repeated measures ANCOVAs, with trauma exposure (TEI) as a covariate. We observed a significant emotion by task condition by TEI interaction ($F_{1,37} = 3.6$, $p = .04$), a significant emotion by diagnostic group interaction ($F_{1,37} = 5$, $p = .01$), as well as a significant emotion by task condition by diagnostic group interaction ($F_{1,37} = 4.1$, $p = .02$). Participants with PTSD demonstrated significantly poorer performance (more errors) on positive number congruent AS distractor trials (Cohen's $d = 0.65$). Controls had average error rates of approximately 4%, whereas participants with PTSD demonstrated average error rates of 9% (see Table 2). No other main effects or interactions were observed. With respect to response time, a main effect of task condition was observed ($F_{1,37} = 23$, $p < .001$), with slower response times observed in response to number incongruent trials. However, no other main effects or interactions were observed with respect to response time.

3.1.2. PTSD symptom clusters—In the group as a whole, a significant correlation was observed between PTSD hyperarousal symptoms and performance on neutral number incongruent distractor trials ($r = 0.36$, $p = .03$), with a marginally significant correlation observed with trauma-relevant number congruent trials ($r = 0.32$, $p = .05$). Anhedonic PTSD symptoms also correlated with performance on neutral number incongruent distractor trials ($r = 0.34$, $p = .03$) and trauma-relevant number congruent distractor trials ($r = 0.32$, $p = .05$).

Response times for all conditions were normally distributed in the sample, as indicated by Shapiro-Wilk tests (all $ps > .25$). Hyperarousal was significantly associated with longer response times on trauma-relevant number congruent ($r = 0.39$, $p = .02$), positive number congruent ($r = 0.34$, $p = .04$), trauma-relevant number incongruent ($r = 0.42$, $p = .01$), positive number incongruent ($r = 0.38$, $p = .02$) and neutral number incongruent ($r = 0.45$, $p < .01$) distractor trials. Anhedonic PTSD symptoms correlated with response time on traumarelevant number congruent ($r = 0.37$, $p = .02$), trauma-relevant number incongruent ($r = 0.43$, $p < .01$), positive number incongruent ($r = 0.35$, $p = .03$) and neutral number incongruent ($r = 0.42$, $p < .01$) distractor trials.

3.2. fMRI analyses

3.2.1. PTSD vs controls—In response to AS number incongruent vs number congruent trials (increased attentional demands), PTSD participants demonstrated lesser activation in the dorsal ACC (Brodmann Area; BA 32, $MNI_{x,y,z} = 9,23,34$; Table 3) and rostral ACC (BA 24, $MNI_{x,y,z} = 9,35,7$) as compared to controls; the dACC cluster fell within the cognitive control network as defined by Neurosynth. For this contrast, participants with PTSD demonstrated heightened response in the insula (BA 13, $MNI_{x,y,z} = -39,-37,22$). No other

significant between-group differences in activation were found at the $p < .001$ statistical threshold between groups for all contrast conditions.

3.2.2. PTSD symptom clusters—As planned, regression analyses were conducted with the AS condition that had yielded between-group performance differences: positive versus neutral images. In response to positive vs neutral images, re-experiencing symptoms were associated with greater dACC activation (Brodmann area 24; $MNI_{x,y,z} = 0,23,22$; Fig. 2a), whereas avoidance was positively correlated with activation in the parahippocampal gyrus ($MNI_{x,y,z} = 9, -10, -23$; Fig. 2b). Hyperarousal symptoms were not significantly correlated with activation in specified ROIs, but were positively correlated with activation in the uncus (BA 34, $MNI_{x,y,z} = 15, -7, -23$) and middle cingulate gyrus (BA 24, $MNI_{x,y,z} = 0,-19,34$; Fig. 2c). No significant patterns of activation were observed for correlations with anhedonic symptoms for this condition.

3.3. White matter analyses

After accounting for trauma exposure, uncinate fasciculus FA was negatively associated with errors on positive number congruent trials ($r = -0.44, p = .005$; Fig. 3a, c) and trauma-relevant number incongruent trials ($r = -0.46, p = .002$). These relationships remained significant after removing trauma covariates ($r = -0.44, p = .004$ for positive number congruent trials and $r = -0.46, p = .002$ for trauma-relevant number incongruent trials). Right cingulum FA was also negatively correlated with performance on positive number congruent trials ($r = -0.42, p = .01$) and neutral number incongruent trials ($r = -0.33, p = .04$); however, these findings did not survive Sidak correction. After removing trauma covariates, right cingulum FA remained negatively correlated with performance on positive number congruent trials ($r = -0.39, p = .01$; Fig. 3b, d) and trauma-relevant number incongruent trials ($r = -0.35, p = .03$). After controlling for depression symptoms (BDI total score), all $ps < .05$ but were not less than the Sidak-corrected threshold. No other significant associations were observed between white matter integrity and task performance. Participants with PTSD showed lower right cingulum FA as compared to controls ($F_{1,41} = 6.6, p = .01$), replicating our earlier findings (Fani et al., 2012a, 2016).

4. Discussion

We administered an attentional control task with variable attentional demands and both neutral and emotionally-salient distractor stimuli to examine the precise nature of attentional control abnormalities in PTSD. We investigated potential differences in performance and neural response, as well as white matter connectivity. Together, our data indicate abnormalities in cognitive control and salience networks in participants with PTSD. As compared to traumatized controls, we found that participants with PTSD demonstrated similar task performance in the context of neutral stimuli, but performed more poorly in the context of emotional AS distractor stimuli, as we had predicted. Specifically, those with PTSD made more errors on positive AS distractor trials and demonstrated lower activation in cognitive control (fronto-parietal) and higher activation in salience networks in the context of higher AS task demands. Further, task performance on these AS positive distractor trials was correlated with structural integrity of the cingulum bundle (CB), a primary fronto-

parietal white matter connection, and the uncinate fasciculus (UF), a fronto-limbic white matter fiber implicated in various social and emotional processes (Johnson et al., 2011; Zappala et al., 2012). Re-experiencing, avoidance, and hyperarousal symptom clusters were correlated with distinctly different patterns of BOLD activation to positive AS stimuli. Hyperarousal and anhedonic PTSD symptoms were associated with poorer performance on neutral and emotion AS trials.

When faced with higher attentional demands on the AS, the PTSD group demonstrated lower activation in the dorsal and rostral ACC, regions involved with regulation of response on attentional tasks. The dACC has been implicated in top-down control more generally, and rACC involvement appears to be more specific to emotional task conditions (Banich et al., 2009). Decreased dACC activation during affective attentional processing has been observed in anxious populations (Blair et al., 2012a), and lower dACC and rACC response have been linked to PTSD in meta-analyses (Etkin and Wager, 2007). The rACC is implicated in performance monitoring (Ridderinkhof et al., 2004)—during emotional Stroop task performance, this region is more active when attentional demands are increased (Etkin et al., 2006). In healthy individuals, increased rACC corresponds with the ability to successfully identify erroneous responding and improve subsequent performance (Ridderinkhof et al., 2004). Volume of the rACC (Bryant et al., 2008) and increased response in the rACC (Bremner et al., 2017; Peres et al., 2011) and dACC (Malejko et al., 2017) has also been associated with successful treatment of PTSD. Similar to prior Stroop studies (Bremner et al., 2004; Shin et al., 2001), our findings indicate that participants with PTSD demonstrated under-engagement of the rACC during emotional Stroop task performance—unlike these studies, we also observed a difference in task performance. Participants with PTSD performed more poorly than controls on AS trials that included positive images. In the context of conditions with higher attentional demands, they also demonstrated comparatively higher insula activation. Given the role of the insula in salience detection, and the frequent observation of insula hyper-activation in PTSD (Hughes and Shin, 2011), it is likely that activation on this salience network disrupted the appropriate function of fronto-parietal networks, precluding their ability to exert cognitive control successfully.

We were somewhat surprised to find that attentional performance was disrupted by positive, rather than trauma-relevant, distractor images in PTSD—however, studies of other traumatized populations have observed similar findings with respect to positive images, including one using the AS task (White et al., 2015). Emotionally-salient images, including those with positive valence, have been found to disrupt attention in anxious (Chen et al., 2012, 2014; Taylor et al., 2010) and traumatized populations, such as our own (Fani et al., 2011). Disruptions in cognitive control circuits have also been observed in children with PTSD in response to positive images (Jatzko et al., 2006). Increasingly, disrupted behavioral and neural response to appetitive stimuli are being observed as manifestations of PTSD (Nawijn et al., 2015). People with high/frequent exposure to past trauma and adversity may have a complex relationship with positive images—these scenes may be incongruous with the realities and expectations of this population, and as such, can disrupt attentional focus.

Poorer white matter connections extending from the ACC were likely to play a role in producing these attentional decrements—task performance on positive emotion distractor

poorer AS task performance, particularly on trauma-relevant and neutral trials. Given the other relationships observed between integrity of the UF, CB and AS task performance, it is possible that avoidance and hyperarousal clusters emerge as a result of abnormalities within salience and cognitive control networks. Traumatized people with more fearful arousal and avoidance symptoms may show attentional control deficits in the context of emotion, heightened limbic activation and under-activation in attention control regions. Other studies have observed specific associations between hyperarousal and attentional control deficits (Grisanzio et al., 2018). This could indicate that these specific clinical and cognitive features of PTSD (hyperarousal and attentional control deficits, both of which are transdiagnostic features) may have shared neural substrates.

Although participants with PTSD demonstrated poorer performance on emotion-related AS trials, they demonstrated relatively similar performance on neutral trials. These findings highlight the fact that PTSD-related deficits in attention may be most visible in emotional contexts, and similarly illustrate the value of using attentional tasks that incorporate emotional stimuli in research and clinical settings. Given that they can accommodate images, tasks such as the AS are most useful in PTSD studies and are both sensitive enough to detect attentional disruptions and equipped to identify the nature of these disruptions in various traumatized populations.

Our findings not only reveal specificity in attentional control dysfunction and PTSD symptoms, but also shed light on attractive targets for PTSD treatment. Greater ACC response at pre-treatment has been shown to predict treatment response (Malejko et al., 2017). As a hub of attention and salience networks, the ACC is an excellent target for neuromodulation. Cognitive control can be trained in PTSD, as has been shown recently in a study that observed improved performance after training with an affective working memory task (Schweizer et al., 2017; others have proposed the use of web-based cognitive training (Fine et al., 2018). Mindfulness-based treatments, which involve training attentional focus to a sensory stimulus while monitoring emotional states, has been shown to improve response in fronto-parietal attentional control networks; a recent study found increased DLPFC and dACC response, as well as improved AS performance, in participants who completed 6 weeks of mindfulness treatment compared to those who received an active control condition (Allen et al., 2012).

The limitations of this study include the fact that the majority of our sample had experienced multiple traumas, which can influence cognition, brain structure and function. However, PTSD-specific effects remained even after accounting for trauma exposure in statistical analyses. We also used two different versions of the CAPS to diagnose PTSD, which introduces a source of variance to the findings, and included one participant with psychotropic medication use, a factor that may influence results. Given our cross-sectional study design, we were also unable to determine the onset of attentional control abnormalities and their temporal relationship to trauma—this is worthy of examination in future prospective designs with more heterogenous and expansive sample sizes.

In conclusion, we found that PTSD was characterized by impaired attentional control in emotional contexts, and that these disruptions were associated with abnormal fronto-parietal

and fronto-limbic network function and structural integrity, as well as increased salience network activation. Our data show a mechanism through which attentional control problems may emerge in PTSD, and highlight the importance of using emotionally-salient tasks in PTSD assessment and intervention research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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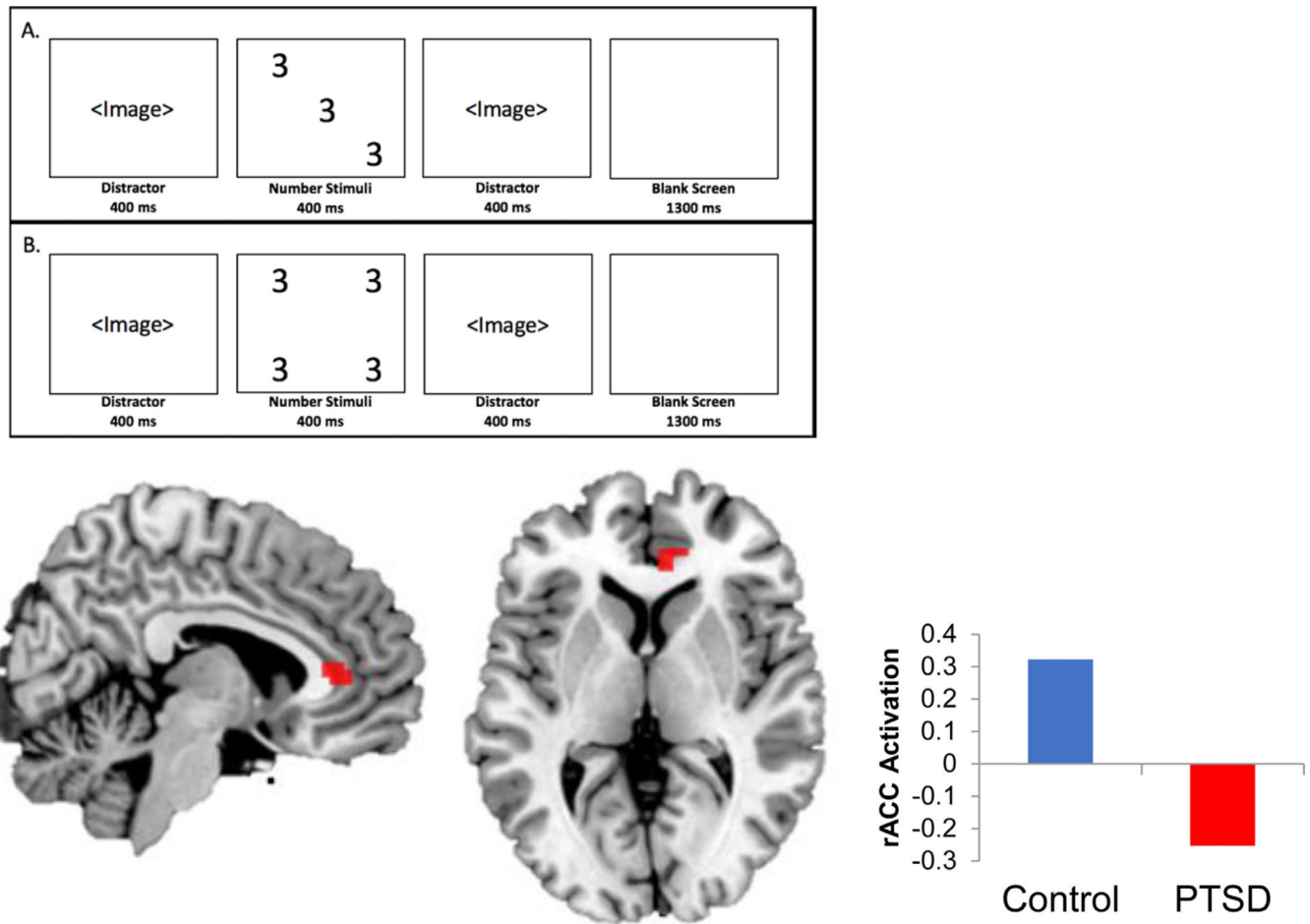


Fig. 1. Response to number incongruent (b) vs number congruent (a) Affective Stroop trials, voxelwise $p < .001$. Controls demonstrated higher activation in the dorsal and rostral ACC (shown in red, $MNI_{x,y,z} = 9,35,7$) in response to higher Affective Stroop task demands.

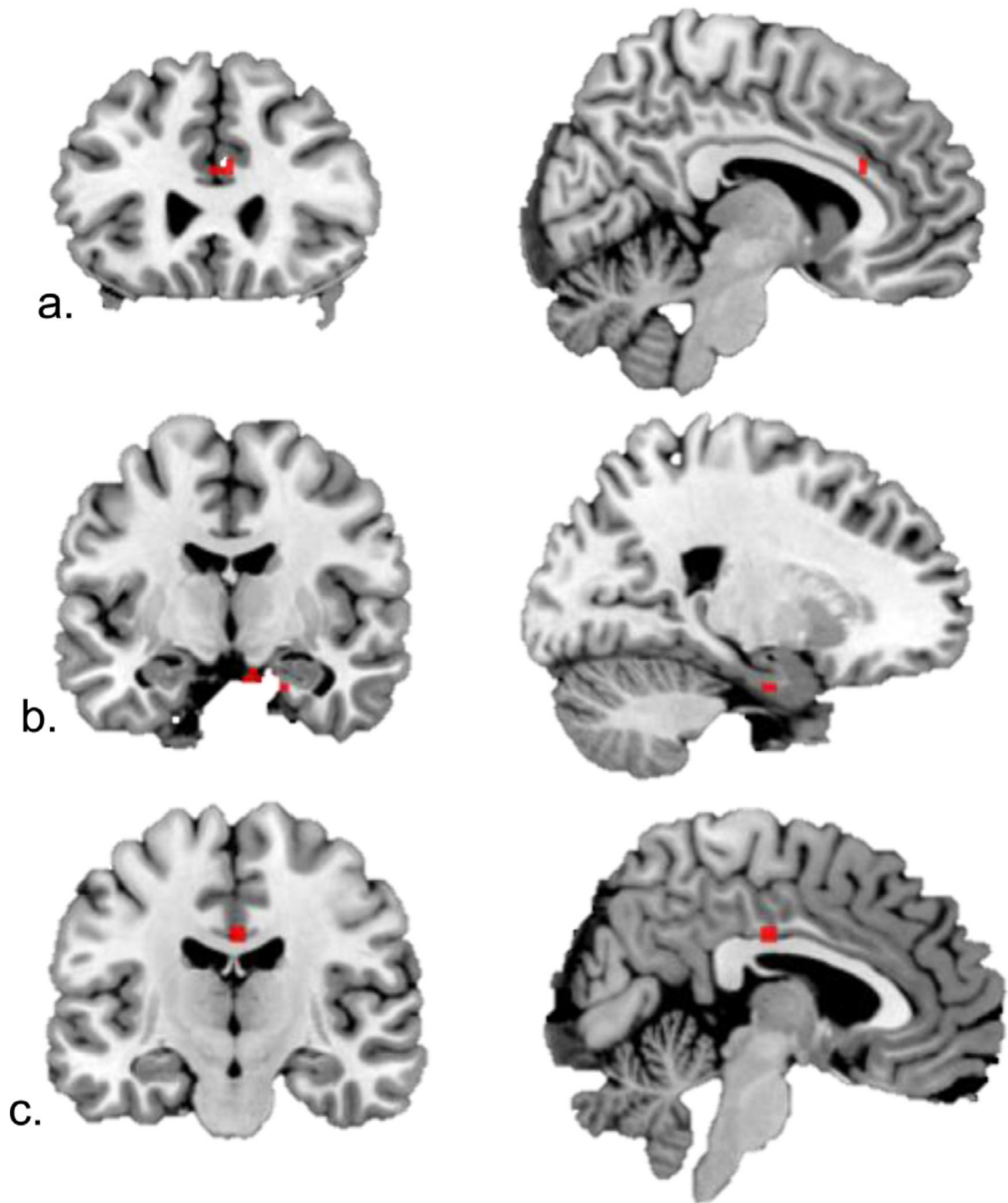


Fig. 2.

Correlations between PTSD symptom clusters and response to positive vs neutral Affective Stroop distractor trials, voxelwise $p < .001$. (a) Reexperiencing positively correlated with dACC ($MNI_{x,y,z} = 0,23,22$) activation. (b) Avoidance positively correlated with right parahippocampal gyrus ($MNI_{x,y,z} = 9,-10,-23$) activation. (c) Hyperarousal correlated with middle cingulate cortex ($MNI_{x,y,z} = 0,-19,34$) activation.

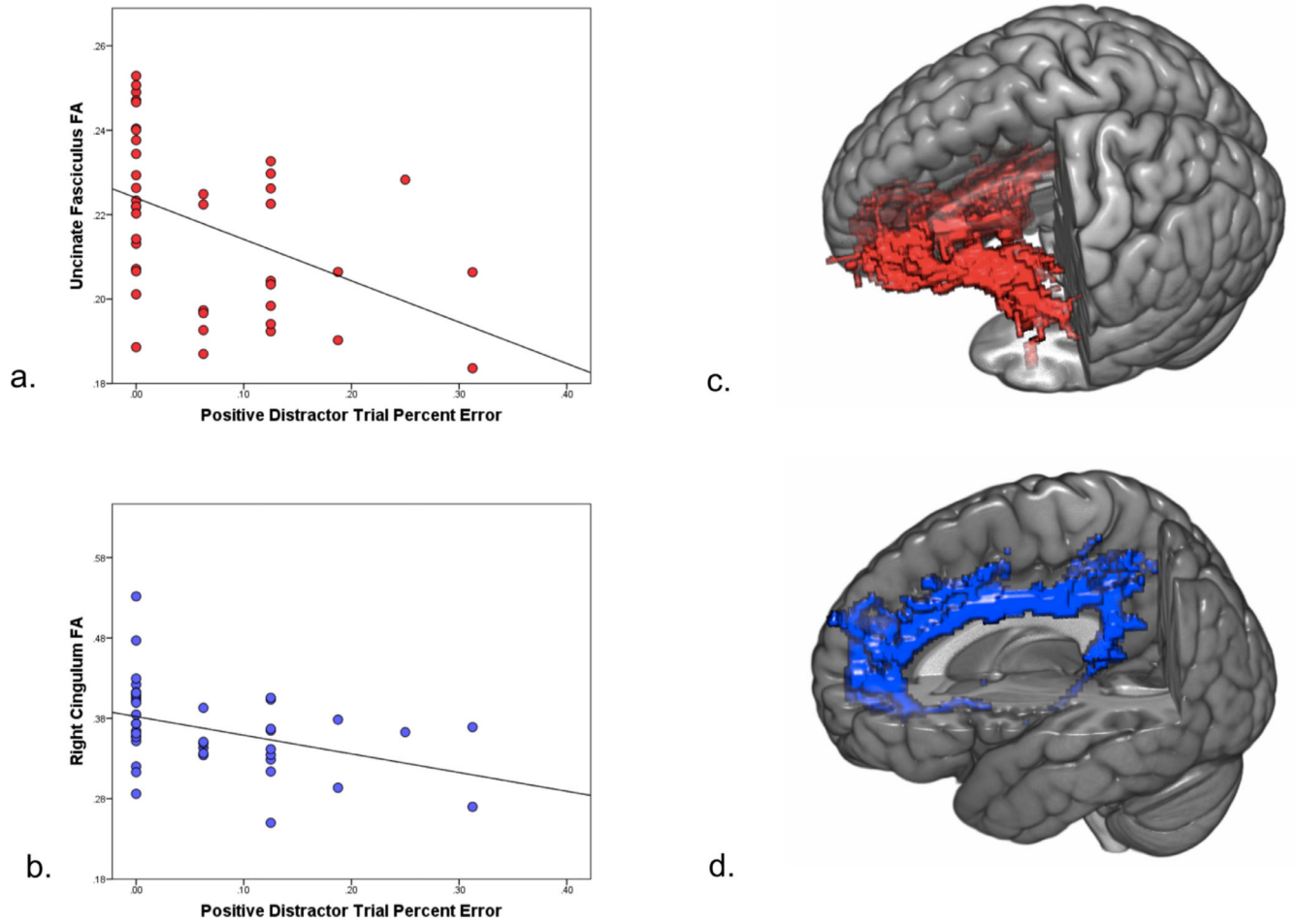


Fig. 3. White matter integrity and performance on positive Affective Stroop distractor trials in PTSD. Errors on positive number congruent distractor trials were inversely correlated with microstructure of the uncinate fasciculus (a) and right cingulum (b). Example probabilistic tracts of the uncinate fasciculus (c) and right cingulum (d).

Table 1

Demographic and clinical characteristics.

	Trauma controls (n = 22) Mean (SD)	PTSD (n = 26) Mean (SD)	F
Age	40.7 (9.9)	39.3 (12.8)	0.2
TEI lifetime trauma	2.4 (1.3)	4.2 (2.3)	11.1
TEI types of interpersonal trauma in adulthood	2.2 (1.6)	4.5 (2.3)	14.8*
			X ²
TEI childhood sexual, physical abuse endorsed	18%	53.8%	7.1*
PSS total score	3.1 (3.8)	25.4 (11.3)	77.9*
PSS re-experiencing	1 (1.2)	6.9 (3.9)	45.5*
PSS avoidance	0.5 (1)	4 (1.8)	64.6*
PSS hyperarousal	1 (1.6)	8.4 (3.7)	77*
PSS anhedonia	0.5 (0.7)	4.1 (3)	31.9*
BDI-II total score	6.5 (10.1)	20.8 (12.7)	21.6*
	No (%)	Yes (%)	X ²
Currently employed	50	70	2.7
Currently married or domestic partnership	27%	19%	2.8
	%		Fisher's exact test
Education			1.4
<12th grade	9.1	15.4	
High school graduate/GED	36.4	30.8	
Some college/tech school	36.4	42.3	
College graduate	9.1	3.8	
Graduate school	9.1	7.7	
Monthly income	%		7.3
\$0–249	0	15.4	
\$250–499	18.2	3.8	
\$500–999	31.8	46.2	
\$1000–1999	31.8	15.4	
\$2000 +	18.2	19.2	

TEI = Traumatic Events Inventory.

BDI-II = Beck Depression Inventory.

* $p < .01$.

Table 2

Affectivestroop performance.

	Controls (n = 22) Mean (SD)	PTSD (n = 26) Mean (SD)	F
Percent error			
Trial type			
Trauma-relevant, number congruent	8 (10.6)	11.8 (12.2)	1.2
Positive, number congruent	3.7 (8.3)	9.2 (8.6)	7.4*
Neutral, number congruent	6.3 (9.4)	8.4 (10.3)	0.4
Trauma-relevant, number incongruent	9.7 (10.9)	12.5 (13.1)	0.6
Positive, number incongruent	6.8 (9.2)	12.5 (15.3)	0.7
Neutral, number incongruent	6.2 (8.4)	11.5 (12.2)	1.9
Overall errors	6.9 (8.2)	11.5 (10)	1.6
Response time			
Trauma-relevant, number congruent	871.2 (160.6)	942.4 (147.4)	1.4
Positive, number congruent	856.1 (164.9)	926.4 (132.8)	1.9
Neutral, number congruent	861 (170.5)	914 (130)	1.2
Trauma-relevant, number incongruent	928.1 (157)	1010.5 (137.7)	2.1
Positive, number incongruent	906.7 (135.2)	996.7 (163.5)	2.3
Neutral, number incongruent	914.5 (139.2)	997.3 (143.7)	3.2
Overall response time	889.6 (148.6)	968.8 (135.9)	1.9

* $p < .05$.

Table 3

Anatomical locations of voxel-wide BOLD response to Affective Stroop distractor trials ($p < .001$, uncorrected).

	Brodmann area	x	y	z	Cluster size (mm ³)
Number incongruent vs number congruent trials					
<i>Trauma controls PTSD</i>					
Anterior Cingulate Gyrus (dACC)	32	9	23	34	8
Superior frontal gyrus	6	-6	29	58	12
Medial frontal gyrus	8	-6	41	40	6
Anterior cingulate gyrus (rACC)	24	9	35	7	7
<i>PTSD Trauma controls</i>					
Insula	13	-39	-37	22	5
		-33	-37	16	
Precuneus	7	15	-70	46	7
Positive vs Neutral trials					
PTSD Trauma controls					
Middle temporal gyrus	21	54	5	-23	7
PTSD Re-experiencing symptoms					
<i>Positive correlation</i>					
Middle temporal gyrus	21	54	2	-20	8
Midbrain		0	-13	-5	10
Anterior cingulate cortex (dACC)	24	0	23	22	7
PTSD avoidance symptoms					
<i>Positive correlation</i>					
Parahippocampal gyrus	34	9	-10	-23	33
Uncus	28	18	-7	-26	
Cerebellum		-24	-46	-11	8
Precentral gyrus	6	45	-13	28	8
Brainstem		0	-13	-5	5
Orbitofrontal gyrus	11	12	50	20	7
PTSD hyperarousal symptoms					
<i>Positive correlation</i>					
Middle cingulate cortex	24	0	-19	34	12
Uncus	34	15	-7	-23	8