Neural Correlates of the Classic Color and Emotional Stroop in Women with Abuse-Related Posttraumatic Stress Disorder

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Background: *The anterior cingulate and medial prefrontal cortex play an important role in the inhibition of responses, as measured by the Stroop task, as well as in emotional regulation. Dysfunction of the anterior cingulate/medial prefrontal cortex has been implicated in posttraumatic stress disorder (PTSD). The purpose of this study was to use the Stroop task as a probe of anterior cingulate function in PTSD.*

Methods: *Women with early childhood sexual abuse-related PTSD (n = 12) and women with abuse but without PTSD (n = 9) underwent positron emission tomographic measurement of cerebral blood flow during exposure to control, color Stroop, and emotional Stroop conditions.*

Results: *Women with abuse with PTSD (but not abused non-PTSD women) had a relative decrease in anterior cingulate blood flow during exposure to the emotional (but not color) classic Stroop task. During the color Stroop there were also relatively greater increases in blood flow in non-PTSD compared with PTSD women in right visual association cortex, cuneus, and right inferior parietal lobule.*

Conclusions: *These findings add further evidence for dysfunction of a network of brain regions, including anterior cingulate and visual and parietal cortex, in abuse-related PTSD.*

Key Words: Posttraumatic stress disorder, Stroop, emotion, fear, amygdala, hippocampus, anxiety

Posttraumatic stress disorder (PTSD) is an important cause of morbidity that affects 10% of women in this country at some time in their lives and is twice as common in women as in men (Kessler et al 1995). Childhood sexual abuse, which affects 16% of women sometime before their 18th birthday (McCauley et al 1997), is the most common cause of PTSD in women (Kessler et al 1995). Little is known, however, about the long-term biological consequences of childhood abuse.

Exposure to uncontrollable stress has been used as an animal model for mood and anxiety disorders (Charney et al 2000). A variety of models of stress have been used, including exposure to electric shock, forced swim, and maternal deprivation. These stressors have in common a physical threat to life and have parallels to traumatic stressors, defined by DSM-IV as a threat to self or other associated with intense fear, horror, or helplessness. Animal studies in which these types of stressors were used provided evidence that brain regions involved in memory are sensitive to stress (Bremner 2002; McEwen et al 1992; Sapolsky 1996). These stressors result in structural changes in the brain region involved in new learning and memory (Gould et al 1998; Sapolsky 1996), with associated deficits in memory function (Diamond et al 1996).

The medial prefrontal cortex has also been implicated in the stress response and emotional regulation. Medial prefrontal cortex in the human consists of several related areas, including orbitofrontal cortex, anterior cingulate (Brodmann area [BA] 25—subcallosal gyrus, and BA 32), and anterior prefrontal cortex (BA 9) (Devinsky et al 1995; Vogt et al 1992). In the famous case of Phineas Gage, a physical injury resulted in damage to this part of the brain that was associated with deficits in emotional regulation, specifically problems inhibiting behavior, and social inappropriateness (Damasio et al 1994). Lesions of the medial prefrontal cortex in animals resulted in a failure of inhibition of amygdala function (Morgan and LeDoux 1995; Morgan et al 1993). Given the role of the amygdala in fear responding (Davis 1992; LeDoux 1993), these findings led to the hypothesis that medial prefrontal cortex mediates extinction of fear responses, and by extension dysfunction in this region might underlie the pathologic emotions associated with abuse-related PTSD.

Neuroimaging studies in PTSD are consistent with dysfunction of medial prefrontal cortex/anterior cingulate. Symptom provocation studies with personalized traumatic scripts, traumatic slides and sounds, and noradrenergic challenge have found decreased medial prefrontal cortical/anterior cingulate function (Bremner 1998; Bremner et al 1997, 1999a, 1999b; Lanius et al 2001; Rauch et al 1997; Shin et al 1999). Other brain areas implicated include parietal cortex, hippocampus (Bremner et al 1997; Bremner et al 1999a), temporal cortex (Bremner et al 1997, 1999a, 1999b), posterior cingulate (Bremner et al 1999a, 1999b; Lanius et al 2001), motor cortex (Bremner et al 1999a, 1999b), anteromedial prefrontal cortex (Zubieta et al 1999), middle/inferior frontal gyrus, cerebellum (Bremner et al 1999a, 1999b; Rauch et al 1996; Shin et al 1999, 1997), and amygdala (Rauch et al 2000).

The Stroop paradigm has been used as a tool in research related to PTSD (Stroop 1935). In the Stroop task, naming the color of a word with an incongruent semantic context (e.g., naming the color of the word "red" written in the color yellow) results in a delay in naming relative to naming semantically congruent words. Several hypotheses have been developed for this effect, including inhibition of the tendency to say the name rather than the color, engagement in two parallel processes, and distraction of attention (McNally et al 1993). A variant of the classic color Stroop, called the "Counting Stroop" (Whalen et al

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1998), which involves counting the number of color and emotional words that appear on a screen, has been developed for use with functional magnetic resonance imaging to avoid the problem with head motion associated with verbalization in the classic color Stroop. Different types of "emotional Stroop" tasks have also been developed for application to patients with PTSD, for instance asking subjects to name the color of the word "rape." Delay in naming of emotional words has been hypothesized to a diversion of attention toward traumatic as opposed to neutral material in individuals who have been sensitized to specific emotional stimuli through a history of traumatization (McNally et al 1996), in addition to other factors that apply to the delay in color naming outlined above.

Patients with PTSD have been found to color-name emotional words more slowly than other types of words, relative to control subjects. Vietnam combat veterans with PTSD, compared with combat veterans without PTSD, have been found to take longer to color-name "PTSD" words than specific obsessive-compulsive disorder–related words, positive words, and neutral words, and this delay was correlated with severity of PTSD symptomatology as measured by the Mississippi Scale (McNally et al 1990, 1993, 1996). Stroop interference has also been shown in patients with PTSD related to the trauma of rape (Cassiday et al 1992; Foa et al 1991) and motor vehicle accidents (Beck et al 2001; Bryant and Harvey 1995), in mixed-trauma groups (McNeil et al 1999), and in children with PTSD (Moradi et al 1999).

Increased anterior cingulate activation has been consistently shown during the Stroop interference condition (Pardo et al 1990; Peterson et al 1999; Whalen et al 1998). A study of combat-related PTSD in which the counting Stroop was used found a failure in anterior cingulate function during counting of emotional (but not color) words (Shin et al 2001). In patients with depression (George et al 1997) and schizophrenia (Carter et al 1997)—disorders also hypothesized to be related to anterior cingulate dysfunction—performance of the Stroop task is associated with a failure in anterior cingulate activation. No studies to date have measured neural correlates of the classic color Stroop task in PTSD (naming word color for semantically incongruous words). The purpose of the present study was therefore to use positron emission tomography (PET) in the examination of neural correlates of both color and emotional Stroop tasks in women with a history of childhood sexual abuse with and without the diagnosis of PTSD. We hypothesized that Stroop performance would be associated with a failure of anterior cingulate activation in abuse-related PTSD.

Methods and Materials

Subjects

Twenty-one physically healthy women with a history of childhood sexual abuse (rape, molestation, or attempted rape before the age of 18 years) participated in the study. Subjects included women with (n = 12) and without (n = 9) the diagnosis of current PTSD. All subjects were recruited through newspaper advertisement. The study was approved by a local investigational review board at Yale University School of Medicine. Diagnosis of PTSD was established with the Structured Clinical Interview for DSM-IV (SCID; First et al 1995). Subjects gave written informed consent for participation, were free of major medical illness on the basis of history and physical examination, laboratory testing, and electrocardiogram, and were not actively abusing substances or alcohol (past 6 months). Subjects were free of all medications for at least 4 weeks before the study. No subjects were taking psychotropic medication at the time of the study; however, subjects did not discontinue taking medication for the purposes of participating in the study. Subjects with medical or neurologic illness, comorbid psychotic disorders, retained metal, a history of head trauma, loss of consciousness, cerebral infectious disease, or dyslexia were excluded. There was no difference in age between the women with (37 ± 11 years [mean ± SD]) and without (35 ± 9 years) PTSD [$t(20) = 1.3$, $p = .76$]. There was no difference in years of education between women with (14 ± 2) and without (15 ± 3) PTSD [$t(20) = 1.5$, $p = .15$]. All subjects were right handed.

Psychometric Assessments

History of childhood abuse was assessed with the Early Trauma Inventory (ETI). The ETI is a 56-item, clinician-administered interview that assesses physical, emotional, and sexual abuse, as well as general traumatic events. The ETI has been demonstrated to be reliable and valid in the assessment of childhood trauma (Bremner et al 2000). All women had a history of childhood rape, molestation, or attempted rape as assessed by the ETI.

Of the women with abuse and current PTSD, 10 of 12 PTSD subjects (83%) fulfilled criteria for a past history of major depression and 3 of 12 (25%) for current major depression, as determined by the SCID interview. One patient (8%) had current and lifetime dysthymia. In no cases did depression precede the onset of trauma or PTSD. One patient (8%) fulfilled criteria for current and lifetime history of panic disorder without agoraphobia. Three PTSD subjects (25%) met current and lifetime criteria for generalized anxiety disorder and social phobia, and one for simple phobia (8%). Three PTSD subjects (25%) fulfilled criteria for a past history of alcohol dependence, one (8%) for a past history of polysubstance dependence, two (17%) for a past history of marihuana abuse or dependence, three (25%) for a past history of cocaine abuse or dependence, and one (8%) with a past history of opiate dependence or abuse. No PTSD subjects had a current history of alcohol or substance abuse or dependence.

Of nine abused women without PTSD, five (56%) fulfilled criteria for a past history of major depression, with no women having current major depression, as determined by the SCID interview. One subject (11%) had a past history of social phobia, and one subject (11%) had a past history of bulimia. Two women (22%) fulfilled criteria for a past history of alcohol dependence, three (33%) for a past history of polysubstance dependence. No non-PTSD subjects had a current history of alcohol or substance abuse or dependence.

Subjects underwent behavioral assessment at baseline and immediately after each of the PET conditions (described below), retrospectively assessed for the period of the condition. Assessments included the Subjective Units of Distress Scale, a widely used measure of distress in the cognitive behavioral treatment of PTSD (Meadows and Foa 1999), the Clinician-Administered Dissociative States Scale, a validated measure of dissociative state symptoms (Bremner et al 1998), the PTSD Symptom Scale, a measure of PTSD symptom level, as well as analogue scales of fear and anxiety (Bremner et al 1997).

PET Imaging Methods

All subjects underwent PET scanning in conjunction with performance of the color and emotional Stroop tasks and control condition. The control condition consisted of naming the color of colored XXs that were presented randomly in the colors red,

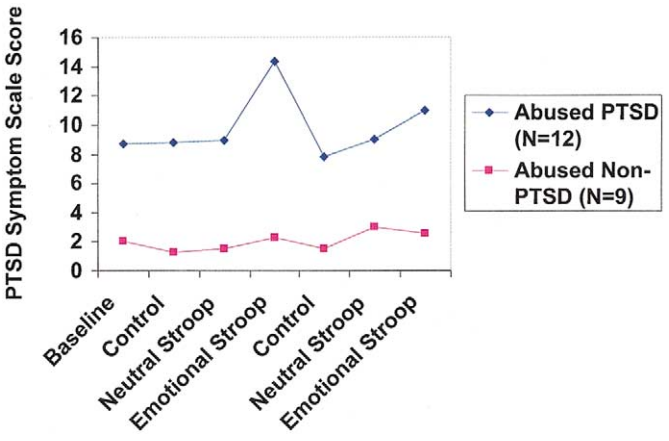

Figure 1. Posttraumatic stress disorder (PTSD) symptoms during color and emotional Stroop task. Subjects with PTSD had increased PTSD symptoms during all time points relative to abused women without PTSD, with the highest level of symptoms during the emotional Stroop task, which involved color naming of words like "rape" or "mutilate."

blue, green and yellow on a computer screen. The active color condition consisted of naming the color of colored words, in the colors red, blue, green, and yellow, when the semantic context of the word was a color name incongruous with the color (e.g., the word "red" spelled in the color yellow). The active emotional condition consisted of naming the color of words that were in the colors red, blue, green, and yellow, when the words were the emotional words, rape, bruise, weapon, and stench. These words were selected based on our prior studies showing that the words were associated with a high degree of emotional arousal (Bremner et al 2001). Although the color and emotional words were matched for syllable length, and all of the words are used frequently in the English language, it was not possible to find emotional words that are used as frequently in the English language as the very commonly used color words (Kucera and Francis 1967).

During the study period, assessments were also made of psychophysiologic factors, including the parameters of heart rate and blood pressure. The purpose of measuring heart rate and blood pressure was to have assessments of physiologic parameters related to the stress of the emotional and color Stroop tasks. Heart rate was measured continuously during the entire study period with a Polar Vantage heart rate recording device (Woodbury, New York). The Polar Vantage heart rate recording apparatus was moistened with water to facilitate recording and strapped around the subject's chest for direct measurement of heart rate. Heart-rate data were transmitted from the recording device to a Polar Vantage recording device worn as a wrist watch on the subject's wrist. After the study session, the data were downloaded to a personal computer for analysis. Heart rate over 5-sec intervals was compared during the interval of each task (described below) and during a baseline period 2–3 min before each of these sessions. Data were digitized for analysis on a personal computer. Mean heart rate was calculated for each baseline and task period, and the Δ of task minus baseline was compared between groups.

Each subject underwent six PET scans on a single day according to methods that have been described previously (Bremner et al 1999a, 1999b). Positron emission tomography imaging was performed on a Posicam PET camera (Positron Corporation, Houston, Texas) (in-plane resolution after filtering, 6 mm full width half maximum [FWHM]). Each subject was placed in the scanner with her head in a holder to minimize motion and positioned with the canthomeatal line parallel to an external laser light. An intravenous line was inserted for administration of $[^{15}0]H_20$. After positioning within the camera gantry, a transmission scan of the head was obtained with an external $^{67}Ga/^{68}Ge$ rod source, to correct emission data for attenuation due to overlying bone and soft tissue.

Subjects then underwent scanning during the control task and color and emotional Stroop tasks. Subjects were randomly assigned to a control-color-emotional-control-color-emotional or emotional-color-control-emotional-color-control order of scanning. Ten seconds before administration of $[^{15}0]H_20$, subjects received instructions for the performance of the task. Subjects were asked to name the color of the word and to proceed as quickly as they could through the list of words. Subjects then received a bolus injection of 30 mCi of $[^{15}0]H_20$ followed 10 sec later by a 60-sec PET scan acquisition. The onset of the PET scan acquisition was timed to correspond to the point of maximum rate of increase in uptake of tracer into the brain. Subjects were asked to stop naming the color of words after 60 sec, and the number of words correctly identified by color, representing the Stroop score, was recorded.

According to the logic of the study design, brain blood flow related to the act of identifying a color would be controlled for, and any differences in brain blood flow between the Stroop and the control condition would be secondary to the cognitive effort to inhibit the tendency to divert attention to the linguistic content rather than the color content of the presented stimulus. On the basis of prior imaging studies with the Stroop reviewed above, and on the hypothesis of anterior cingulate dysfunction in PTSD, we hypothesized an activation of the anterior cingulate with the Stroop in non-PTSD (but not PTSD) subjects. A similar logic applied for the emotional Stroop versus control contrast. For the emotional Stroop versus color Stroop contrast, both the process of identifying the color and ignoring the linguistic content of the words are controlled for, and differences in blood flow are specifically related to the attempt to ignore the emotional content of the words. On the basis of prior imaging studies demonstrating a role for the anterior cingulate in emotion reviewed above, and on the hypothesis of anterior cingulate dysfunction in PTSD, we hypothesized an activation of the anterior cingulate with the emotional Stroop in non-PTSD (but not PTSD) subjects.

Image Processing and Data Analysis

Images were realigned to the first image in the scanning session with statistical parametric mapping (spm96; Friston et al 1991). The mean concentration of radioactivity in each scan was obtained as an area-weighted sum of the concentration of each slice and adjusted to the nominal value of 50 mL/min/100 g. The data were then rescaled and transformed into a common anatomic space (expressed in Talairach three-dimensional x, y, and z coordinates) for statistical analysis. After transformation, images were smoothed to 16 mm FWHM before statistical analysis. Regional cerebral blood flow was compared in Stroop and control conditions. Data were analyzed with spm96 (Friston et al 1991) with global blood flow considered as a confounding covariate with image data sets in which the values assigned to individual voxels correspond to t statistic. Statistical images were displayed with values of Z score units > 2.58 ($p < .005$) and clusters of more than 65 contingent significant voxels. A p value of .005 has been demonstrated to be associated with the most optimal minimization of type I and type II errors (Reiman et al

Table 1. Behavioral and Physiological Responses to Neutral and Emotional Stroop Task in Women with Abuse with and without PTSD

	Baseline	Control #1	Neutral #1	Emotional #1	Control #2	Neutral #2	Emotional #2	Time × Diagnosis Interaction F	p
Abused PTSD ($n = 12$)									
Diastolic blood pressure	75 (11)	79 (10)	77 (9)	79.8 (11)	81 (9)	79 (10)	79 (11)	.49	.81
Dissociative states (CADSS)	4 (6)	6 (8)	6 (7)	8 (10)	6.63 (8)	7 (10)	7 (9)	.49	.82
Anxiety (PASS)	5.90 (6)[a]	9.09 (8)[a]	8.9 (7)[a]	13.6 (12)[a]	12.7 (13)[a]	11.4 (11)[a]	10.8 (11)[a]	1.12	.35
Fear (analogue)	3.6 (3.4)	3.6 (3.8)	3.5 (3.4)	4.1 (4.1)	2.9 (2.9)	2.9 (3.1)	3.7 (3.6)[a]	1.36	.24
Subjective distress (SUDS)	.23 (.24)	.25 (.26)	.25 (.22)	.32 (.29)	.24 (.20)	.26 (.23)	.314 (.23)[a]	.97	.45
Abused Non-PTSD ($n = 9$)									
Diastolic blood pressure	72 (9)	74 (7)	73 (7)	75 (9)	73 (6)	74 (12)	75 (8)		
Dissociative states (CADSS)	0 (1)	0 (1)	1 (3)	2 (3)	0 (1)	1 (2)	1 (2)		
Anxiety (PASS)	0 (1)	1 (2)	3 (6)	3 (6)	2 (6)	3 (6)	2 (4)		
Fear (analogue)	1.4 (2.1)	1.0 (1.5)	1.6 (1.8)	1.8 (1.8)	2.0 (2.6)	1.5 (1.9)	1.1 (1.8)		
Subjective distress (SUDS)	.11 (.09)	.08 (.09)	.15 (.18)	.20 (.22)	.13 (.16)	.16 (.18)	.09 (.13)		

Data are expressed as mean (SD).

PTSD, posttraumatic stress disorder; CADSS, Clinician Administered Dissociative States Scale; PASS, Panic Attack Symptom Scale; Analogue, Analogue ratings for fear; SUDS, Subjective Units of Distress Scale.

[a]PTSD > non-PTSD by Duncan's multiple range test.

1997). Areas of activation were identified with standard stereotactic coordinates, according to the atlas of Talairach and Tournoux (1988).

Behavioral measures were analyzed with analysis of variance (ANOVA). For naming of Stroop words, the Δ of Stroop score between color Stroop and control and between emotional Stroop and control was determined. The Δ of these "baseline" corrected scores was then determined as baseline corrected color Stroop minus emotional Stroop. The rationale for examining the Δ of the color/emotional Stroop and control condition was to examine for specific Stroop effects controlling for reading speed, intelligence, and other nonspecific performance-related parameters.

Results

Color naming of colored words and color naming of emotional words both resulted in a lower number of correctly named words per session than in the control condition [82 ± 25 vs. 97 ± 21 vs. 103 ± 23, respectively; main effect for condition: $F(1,5) = 4.28$, $p = .04$; Duncan test: control > color and emotional, $p < .05$). Subjects with PTSD named fewer items across conditions [main effect for diagnosis: $F(1,5) = 3.96$, $p = .002$]. There was no interaction between diagnosis and condition. Abused PTSD compared with abused non-PTSD women showed a nonsignificant pattern of lower number of correctly named emotional versus color words as measured by the Δ between baseline adjusted emotional and color scores [−18.3 ± 17.3 vs. −13.7 ± 25.4, respectively; $t(19) = .47$, $p = .65$]. Posttraumatic stress disorder [$F(1,19) = 6.93$, $p = .01$] (Figure 1), anxiety [$F(1,19) = 7.27$, $p = .01$], distress [$F(1,19) = 3.08$, $p = .10$], fear [$F(1,19) = 3.28$, $p = .08$], and dissociative [$F(1,19) = 4.44$, $p = .04$] symptoms were greater at all time points in the PTSD subjects relative to control subjects. There was no interaction between time and diagnosis for any behavioral measure (Table 1). Heart rate was higher at all points in PTSD, both during the baseline periods and during the tasks, and heart rate increased in both PTSD and control subjects to an equal degree with all of the tasks (Figure 2).

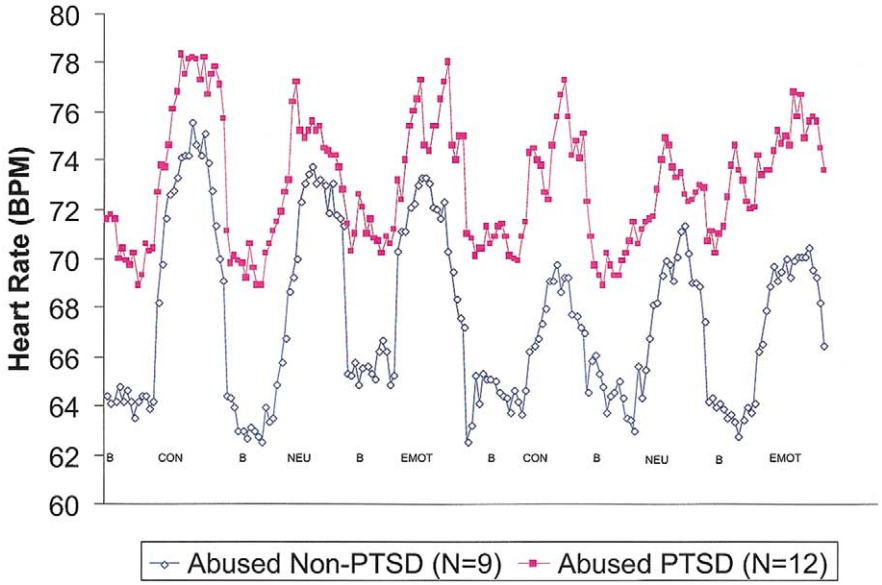

Figure 2. Heart rate response to color and emotional Stroop tasks. Individual symbols represent mean heart rate measured over 5-sec intervals during the period of tasks and intervening resting baseline periods. Posttraumatic stress disorder (PTSD) subjects had a higher heart rate at all time points relative to control subjects, both during the baseline periods between tasks (B) and during the control (CON), neutral color (NEU), and emotional Stroop (EMOT) conditions (see text for explanation). There was no difference in the Δ of task minus baseline between PTSD and control subjects for any of the conditions.

Table 2. Areas of Increased and Decreased Blood Flow with Neutral Stroop versus Control in Women with Childhood Abuse without PTSD

Increased Blood Flow					Decreased Blood Flow				
	Talairach Coordinates					Talairach Coordinates			
Z Score[a]	x	y	z	Brain Region	*Z* Score[a]	x	y	z	Brain Region
3.13[b]	−50	−42	−24	Cerebellum	3.06[b]	−12	54	−8	L anterior frontal cortex (10)
2.90[b]	10	32	2	Anterior cingulate (24,32)	2.90[b]	16	−88	6	Cuneus (17)
3.17[b]	50	−62	6	R middle temporal gyrus (37)					
3.13[b]	−50	−42	−24	L fusiform gyrus (36)					

Numbers in parentheses represent Brodmann's areas.
PTSD, posttraumatic stress disorder; L, left; R, right.
[a]*Z* score > 3.09, $p < .001$; *Z* score > 2.58, $p < .005$.
[b]Area of greatest activation in a contiguous cluster of activated voxels that extends over several brain regions.

Performance of the color Stroop compared with the control task resulted in a nonspecific increase in anterior cingulate blood flow in both PTSD and non-PTSD subjects. Direct comparison of the two groups showed no difference in activation between the two groups in anterior cingulate blood flow with the color Stroop. The emotional Stroop, when compared with the color Stroop, showed decreased blood flow in the PTSD (but not the non-PTSD) subjects in anterior cingulate. This difference was significant when the two groups were directly compared. When the emotional Stroop was compared with the control condition, the non-PTSD (but not PTSD) subjects showed increased blood flow in the anterior cingulate; this difference was not significant when the two groups were directly compared.

Other regions that showed increased activation in the non-PTSD subjects during the color Stroop when compared with the control condition included cerebellum, right middle temporal gyrus, and left fusiform gyrus, and a decrease in blood flow was seen in the left anterior frontal cortex and cuneus (Table 2). In the PTSD subjects, the color Stroop resulted in increased blood flow in cerebellum, left inferior and middle frontal gyrus, right superior temporal gyrus, cerebellum, right supplementary motor area, and right amygdala and in decreased blood flow in right visual association cortex, precuneus, and right inferior parietal lobule (Table 3; Figure 3). There were relatively greater increases in non-PTSD compared with abused PTSD women with the color Stroop in right visual association cortex, cuneus, and right inferior parietal lobule and relatively greater decreases in right superior temporal gyrus and orbitofrontal cortex (Table 4).

The emotional Stroop compared with the color Stroop resulted in only a decrease in left inferior parietal lobule in the control subjects. In the PTSD subjects, the emotional Stroop resulted in increased blood flow in left precuneus, right cuneus, and right lingual gyrus and in decreased blood flow in left middle frontal gyrus, left inferior frontal gyrus, right anterior frontal cortex, cerebellum, insula, uncus, right hippocampal region, midbrain, and left superior temporal gyrus (Table 5; Figure 4). Abused non-PTSD women had greater increases in blood flow with the emotional Stroop compared with abused PTSD women in left insula, pons, cerebellum, and left middle frontal gyrus and relatively greater decreases in precuneus (Table 6).

The emotional Stroop compared with the control condition resulted in (in addition to increased blood flow in anterior cingulate) decreased flow in orbitofrontal cortex and right inferior parietal lobule in the control subjects. In the PTSD subjects, the emotional Stroop resulted in increased blood flow in left inferior frontal gyrus, cerebellum, hypothalamus, and subtha-

Table 3. Areas of Increased and Decreased Blood Flow with Neutral Stroop versus Control in Women with Childhood Abuse-Related PTSD

Increased Blood Flow					Decreased Blood Flow				
	Talairach Coordinates					Talairach Coordinates			
Z Score[a]	x	y	z	Brain Region	*Z* Score[a]	x	y	z	Brain Region
4.28[b]	−54	−42	−32	Cerebellum	3.61[b]	34	−78	28	R visual association cortex (19)
3.38	−46	−74	−30		3.52[b]	16	−76	6	
2.94	−42	−88	−12	Visual association cortex (19)	3.46[b]	16	−70	40	Precuneus (7)
3.90[b]	−24	14	−16	L inferior frontal gyrus (47)	3.41	18	−70	32	
2.88[b]	−44	22	24	L middle frontal gyrus (46)	3.27[b]	64	−30	24	R inferior parietal lobule (40)
3.82[b]	12	34	8	R anterior cingulate (24,32)					
3.65	8	28	30						
3.45[b]	50	18	−12	R superior temporal gyrus (38)					
3.40[b]	26	−88	−48	Cerebellum					
3.20	14	−86	−50						
3.17[b]	14	−12	50	R supplementary motor area (6)					
2.76[b]	28	0	−16	R amygdala					

Numbers in parentheses represent Brodmann's areas.
PTSD, posttraumatic stress disorder; L, left; R, right.
[a]*Z* score > 3.09, $p < .001$; *Z* score > 2.58, $p < .005$.
[b]Area of greatest activation in a contiguous cluster of activated voxels that extends over several brain regions (the *Z* scores without footnote symbols that appear below the noted *Z* scores).

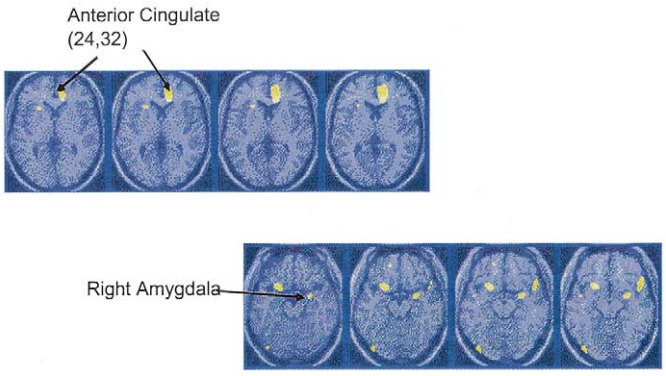

Figure 3. Statistical parametric map overlaid on a magnetic resonance imaging template of areas of significant activation during performance of the color Stroop task compared with the control condition in women with abuse and posttraumatic stress disorder. There was increased activation of the anterior cingulate as well as the right amygdala. Areas displayed in yellow are areas of activation at the level of *Z* score > 3.09 ($p < .001$). Abused women without PTSD also showed anterior cingulate activation (data not shown), which suggests that anterior cingulate activation with the color Stroop is nonspecifically seen in subjects with and without PTSD. Increased amygdala activation is felt to be related to the stress of performance of the task.

lamic area. There was decreased blood flow in the PTSD group in precuneus, right inferior parietal lobule, uncus, right hippocampal region, midbrain, and superior/middle temporal gyrus. Abused non-PTSD women compared with abused PTSD women had greater increases in blood flow with the emotional Stroop versus control condition in right hippocampus and right inferior temporal gyrus and relatively greater decreases in precuneus and posterior cingulate.

Discussion

Performance of the color Stroop task (color naming of semantically incongruent words) resulted in a nonspecific activation of the anterior cingulate (BA 24 and 32) in abused women both with and without PTSD. Comparison of the emotional Stroop with the color Stroop showed relatively lower blood flow response in the anterior cingulate in the abused PTSD compared with the abused non-PTSD women. These findings suggest that dysfunction of the anterior cingulate in PTSD is specific to the neural circuitry of processing of emotional stimuli and is not a nonspecific finding that can be elicited with a generic "anterior cingulate probe," such as the color Stroop task.

Other brain areas implicated in this study are consistent with prior functional imaging studies in abuse-related PTSD (Bremner et al 1995; Shin et al 1999). The color Stroop was associated with greater decreases in function in PTSD relative to control subjects in visual association cortex (BA 19), cuneus, and right inferior parietal lobule (BA 40) and with greater increases in right superior temporal gyrus (BA 38) and orbitofrontal cortex (BA 11). In addition to anterior cingulate, greater increases in blood flow were seen with the emotional Stroop in the abused non-PTSD compared with PTSD women in left insula, pons, cerebellum, and left middle frontal gyrus (BA 6) and relatively greater decreases in precuneus (BA 7) (Table 5).

The findings of the current study demonstrate alterations in a network of brain regions that have been implicated in previous studies of PTSD. Prior studies of PTSD used a variety of tasks, including script-driven imagery or exposure to traumatic slides and sounds, to activate specific memories associated with the traumatic event. In the current study, the stress of performing the Stroop under time pressure can be seen as a generic stressor; the emotional Stroop (involving exposure to trauma-specific words) involves the stress of the task as well as that of processing negative emotional information. As in prior PTSD studies, decreased function was seen in visual association cortex, cuneus, and inferior parietal lobule. Visual association cortex and cuneus are involved in making visual associations and processing visual imagery and memory. Altered function in these regions might represent a neural correlate of alterations in visual imagery in PTSD. Inferior parietal cortex is involved in spatial perception and processing. Alterations in this region might be related to changes in spatial processing related to the increased attention or fear response seen in PTSD patients when under stress. Other brain areas implicated in the current study include the insula, which plays a role in the fear response, and orbitofrontal cortex, which is involved in emotional and social processing. We found increased right amygdala activation with the color Stroop in PTSD, although the differences did not reach statistical significance when a direct comparison was made with non-PTSD subjects. The amygdala plays a critical role in the fear response and emotional processing, and increased amygdala activation might be related to the stress performance of the color Stroop. The absence of activation with the emotional–color Stroop contrast in PTSD suggests that increased amygdala activation is not associated with processing of emotional words in PTSD. This is consistent with prior studies that showed that external threat (but not internally generated emotion) is more consistently associated with amygdala activation in PTSD (Rauch et al 2000). The findings of the current study are also congruent with prior studies of PTSD in showing decreased function in anterior

Table 4. Areas of Greater Increased and Decreased Blood Flow with Neutral Stroop versus Control in Abused Women without PTSD compared with Women with PTSD

Increased Blood Flow					Decreased Blood Flow				
	Talairach Coordinates					Talairach Coordinates			
Z Score[a]	x	y	z	Brain Region	*Z* Score[a]	x	y	z	Brain Region
3.81[b]	50	−64	6	R visual association cortex (19)	2.98[b]	48	10	−12	R superior temporal gyrus (38)
2.90[b]	16	−74	32	Cuneus (19)	2.90[b]	−16	54	−12	Orbitofrontal (11)
2.89[b]	60	−36	32	R inferior parietal lobule (40)					

Numbers in parentheses represent Brodmann's areas.
PTSD, posttraumatic stress disorder; L, left; R, right.
[a]*Z* score > 3.09, $p < .001$; *Z* score > 2.58, $p < .005$.
[b]Area of greatest activation in a contiguous cluster of activated voxels that extends over several brain regions.

Table 5. Areas of Increased and Decreased Blood Flow with Emotional Stroop versus Neutral Stroop In Women with Childhood Abuse-Related PTSD

Increased Blood Flow					Decreased Blood Flow				
	Talairach Coordinates					Talairach Coordinates			
Z Score[a]	x	y	z	Brain Region	*Z* Score[a]	x	y	z	Brain Region
3.11[b]	12	−54	42	L precuneus (7)	4.27[b]	−46	22	24	L middle frontal gyrus (46)
2.72[b]	18	−80	8	R cuneus (17)	3.67	−24	14	−2	L putamen
2.66	16	−64	−6	R lingual Gyrus (17,18)	3.64	−42	24	4	L inferior frontal gyrus (45)
					3.52[b]	−32	4	56	L middle frontal gyrus (6)
					3.88[b]	−52	−40	−28	Cerebellum
					3.86[b]	−38	−12	2	Insula
					3.73[b]	26	−2	−28	Uncus
					3.12	42	−16	−18	R hippocampal region
					3.39[b]	4	−24	−22	Midbrain
					3.23[b]	24	−74	−30	Cerebellum
					2.62	22	−82	−46	
					3.14[b]	10	48	20	R anterior frontal cortex (9)
					3.07	6	30	32	R anterior cingulate (32)
					3.04	16	54	10	R anterior frontal cortex (10)
					3.78[b]	−64	−48	14	L superior temporal gyrus (22)

Numbers in parentheses represent Brodmann's areas.
PTSD, posttraumatic stress disorder; L, left; R, right.
[a]*Z* score > 3.09, $p < .001$; *Z* score > 2.58, $p < .005$.
[b]Area of greatest activation in a contiguous cluster of activated voxels that extends over several brain regions (the *Z* scores without footnote symbols that appear below the noted *Z* scores).

cingulate (Bremner et al 1999a, 1999b; Shin et al 2001). The findings suggest that an interrelated network of brain regions, which are involved in memory function, are dysfunctional in PTSD.

The current findings are consistent with a prior study by Shin et al (2001), who showed a relative decrease in blood flow in anterior cingulate activation in combat-related PTSD. Similar to the current study, the Shin et al study showed decreased blood flow only for the emotional (combat) and not the color Stroop condition. Those authors used a "counting Stroop," which utilized the method of silently counting the number of times a word is seen in a particular color. This task might have important differences in the neural circuitry mediating the behavior, relative to the "classic" Stroop, which involves saying the color out loud while inhibiting the tendency to speak the word.

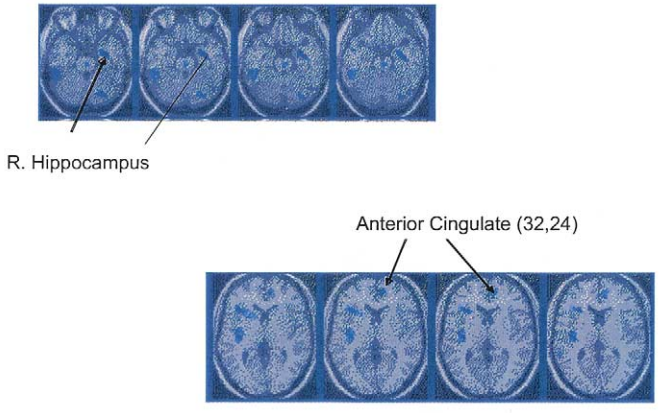

Figure 4. Statistical parametric map overlaid on a magnetic resonance imaging template of areas of decreased blood flow during emotional Stroop task in women with posttraumatic stress disorder (PTSD). Women with abuse-related PTSD showed decreased blood flow in anterior cingulate and right hippocampus. Areas displayed in blue are areas of decreased blood flow at the level of *Z* score > 3.09 ($p < .001$). There were greater decreases seen in the anterior cingulate in abused women with versus without PTSD during the emotional Stroop (data not shown).

Unlike prior studies, this study did not find a difference in response time to emotional versus color Stroop in PTSD versus control subjects. There was a pattern of difference in this direction, however, that might have been significant with a larger sample size. The findings suggest that differences in brain activation between the groups were not solely secondary to differences in performance of the tasks.

These findings, interpreted in conjunction with prior imaging studies in PTSD, suggest that deficits in anterior cingulate function are associated with PTSD. The neural circuitry of PTSD has been hypothesized to involve a variety of interconnected brain regions, including hippocampus, amygdala, thalamus, visual and parietal cortex, insula, and dorsolateral and medial prefrontal cortex (Bremner 2002; Pitman 2001). The medial prefrontal cortex has specifically been hypothesized to underlie the failure of emotional regulation and inability to turn off the fear response (through impairment of the ability to inhibit the amygdala) seen in PTSD subjects. The current study is consistent with a role for the anterior cingulate/medial prefrontal cortex area in the neural circuitry of PTSD.

Deficits in anterior cingulate function are not specific to PTSD. Prior studies in stress-related disorders such as depression in which the Stroop task was used have found deficits in anterior cingulate function (George et al 1997). The George et al (1997) study also showed anterior cingulate deficits with use of a "sad" type of emotional Stroop. Studies have also found deficits with the Stroop in schizophrenia (Carter et al 1997). We are not aware of any studies in non-PTSD anxiety disorders in which either the color Stroop or a variant of an emotional Stroop was used, thus we cannot comment on specificity within the anxiety disorders. The current study and the study by Shin et al (2001) of men with combat-related PTSD, however, only found deficits with the emotional Stroop. This suggests that PTSD might not

Table 6. Areas of Greater Increased and Decreased Blood Flow with Emotional Stroop versus Neutral In Abused Women without PTSD Compared with Abused Women with PTSD

Increased Blood Flow					Decreased Blood Flow				
	Talairach Coordinates					Talairach Coordinates			
Z Score[a]	x	y	z	Brain Region	*Z* Score[a]	x	y	z	Brain Region
3.18[b]	−38	−20	4	L insula	3.28[b]	14	−48	50	Precuneus (7)
2.92	−34	−8	−2		2.93[b]	−52	−14	−20	
2.69[b]	8	40	20	R anterior cingulate (32)					
3.33[b]	0	−24	−30	Pons					
2.93[b]	32	−80	−20	Cerebellum					
2.84[b]	−32	4	56	L middle frontal gyrus (6)					

Numbers in parentheses represent Brodmann's areas.
PTSD, posttraumatic stress disorder; L, left; R, right.
[a] Z score > 3.09, $p < .001$; Z score > 2.58, $p < .005$.
[b] Area of greatest activation in a contiguous cluster of activated voxels that extends over several brain regions (the Z scores without footnote symbols that appear below the noted Z scores).

be associated with nonspecific deficits in anterior cingulate function but rather that tasks that involve emotional circuits might be required to demonstrate this deficit in anterior cingulate function.

Some limitations of this study are worthy of mention. Measurement of Stroop performance used speed of response of correctly identified words and did not measure accuracy and speed separately. The current study used only a group of abused non-PTSD controls and did not include a group of nonabused non-PTSD women. This allowed us to examine only the effects of PTSD and not effects that might be related to childhood abuse in the absence of a psychiatric disorder. Additionally, the results are specific to childhood abuse–related PTSD in women and cannot be generalized to men with PTSD or to PTSD related to other traumas, such as combat. Future studies should measure neural correlates of the color and emotional Stroop in these other gender and population groups.

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