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Global–local visual processing in posttraumatic stress disorder

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Abstract

The purpose of this study was to examine a behavioral index of hemispheric asymmetry (i.e., visual hierarchical attention) in posttraumatic stress disorder (PTSD), a disorder characterized by anxiety and other emotional symptoms. A reaction time based, computerized, global–local visual paradigm was administered to 26 PTSD-diagnosed and 22 psychopathology-free right-handed, male Vietnam War zone veterans. Results indicated that PTSD-diagnosed veterans displayed slower reaction times to all targets than the no-mental disorders comparison sample. However, findings also revealed a Group × Target location interaction in which the PTSD group was slower than the no-disorders comparison sample to respond to local, but not global, targets. Moreover, relative global bias was greater among PTSD-diagnosed veterans than their no-diagnosis counterparts. Findings provide partial support for the hypothesis that PTSD may be associated with a functional cerebral asymmetry favoring the right hemisphere. (*JINS*, 2004, *10*, 709–718.)

Keywords: PTSD, Neuropsychology, Attention, Laterality, Asymmetry

INTRODUCTION

It has become increasingly evident that the diagnosis of posttraumatic stress disorder (PTSD) is associated with a host of neurobiological abnormalities, including neuroendocrine and neurotransmitter dysfunction (see Bremner et al., 1999; Vermetten & Bremner, 2002; Yehuda, 2000, for reviews), increased activation of limbic regions in response to symptom provocation and emotional stimuli (see Bremner, 2002; Grossman et al., 2002; Hull, 2002; Pitman et al., 2001, for reviews), morphometric abnormalities (see Bremner, 2002; Sapolsky, 2000, for reviews; Rauch et al., 2003; Yamasue et al., 2003), and neuropsychological impairment (e.g., Beers & DeBellis, 2002; Brandes et al., 2002; Bremner et al., 1993; Gilbertson et al., 2001; Golier et al., 2002; Jenkins et al., 1998; Sachinvala et al., 2000; Vasterling et al., 2002; Yehuda et al., 1995). Taken as a whole, findings generated by this literature suggest bilateral cerebral involvement. However, the degree to which neural abnormalities in PTSD occur to the same extent across the right and left cerebral hemispheres is less clear.

Functional and structural neuroimaging studies of PTSD have documented unilateral findings suggestive of cerebral asymmetries (e.g., Bremner et al., 2003; Shaw et al., 2002; Villarreal et al., 2002), albeit somewhat unreliably regarding the hemisphere involved (cf. Bremner et al., 1995). That is, although imaging studies generally suggested an asymmetry favoring the right hemisphere in PTSD, this finding has not been universal. Bolstering the neuroimaging literature, Metzger et al. (in press) used electrophysiological methods to examine cerebral asymmetry in PTSD and found that PTSD arousal symptoms were associated with increased right-sided parietal activation. Likewise, using a qualitative error analysis on a block design construction task, Vasterling et al. (2000) found that PTSD was associated with an error pattern suggestive of relative left hemisphere, as compared to right hemisphere, hypoactivation. Thus, although the literature points to an asymmetry in PTSD favoring the right hemisphere, gathering further evidence using convergent methodologies is warranted.

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An asymmetry in PTSD favoring the right hemisphere would be predicted by most neuropsychological theories of hemispheric specialization of emotion. PTSD is typically characterized by the absence of positive, approach emotions (e.g., happiness), and the presence of heightened arousal and negative, withdrawal emotions (e.g., anxiety) and behaviors (e.g., social isolation). Thus, theories purporting right hemisphere dominance of emotion (e.g., Borod et al., 1983), right hemisphere dominance for negative and withdrawal emotions and the left for positive and approach emotions (e.g., Davidson, 1993; 1998; Lee et al., 1993; Silberman & Weingartner, 1986), and right posterior activation for anxious arousal (e.g., Heller, 1993) would each predict relative right hemisphere activation or advantage in PTSD.

Studies examining non-PTSD psychiatric clinical populations have provided evidence of functional hemispheric asymmetry in mental disorders such as depression (Bruder et al., 1997; Davidson, 1998; Heller & Nitschke, 1997; Keller et al., 2000; Kentgen et al., 2000; Tomarken & Keener, 1998); panic disorder (Reiman et al., 1984), and schizophrenic spectrum disorders (Carter et al., 1996; Ferman et al., 1999; Granholm et al., 2002). PTSD potentially offers additional insights into hemispheric asymmetries because of its unique etiological attributes and complex symptom presentation. Unlike other mental disorders, a necessary condition for PTSD diagnosis is the presence of an environmental event that was experienced as life-threatening or traumatic. Moreover, the traumatic experience results in an array of emotional states (e.g., fear, arousal, anger) thought to be related to survival benefits at the time of the trauma. Thus, neuropsychological abnormalities in PTSD may be viewed in the context of emotional evolution.

Although imaging and electrophysiological studies have begun to explore cerebral asymmetry in PTSD, with the exception of Vasterling et al. (2000), little attention has been devoted to examination of behavioral indices of cerebral asymmetry in PTSD. Such an approach offers a noninvasive means of documenting asymmetries, with the potential to provide convergent evidence to imaging and electrophysiological research. Additionally, functional methodologies offer the potential to detect relatively dynamic states that may not be reflected on measures such as brain volume, potentially providing a more sensitive measure of cerebral asymmetry. The purpose of this study was to examine functional cerebral asymmetry in PTSD using a behavioral paradigm.

Performance on a global-local visual hierarchical processing task was used to compare combat veterans diagnosed with PTSD to combat veterans without mental disorders. Lesion, split brain, behavioral visual field (see Robertson & Rafal, 2000, for a review), electrophysiological (e.g., Heinz et al., 1998), and functional imaging approaches (e.g., Fink et al.,1996; 1997; Hans et al., 2002; Martinez et al., 1997), have revealed (see Blanca & Alarcon, 2002, for a counterexample) that the right hemisphere tends to be specialized for global visual perception and the left hemisphere for componential analysis of stimulus elements, especially under conditions of response competition (e.g., Malinowski et al., 2002). A global–local visual attention paradigm allows examination of biases (i.e., relative advantages) in processing global *versus* local stimulus elements during response competition. Faster reaction times to targets located at the local, as compared to the global, level indicate local bias and relative left hemisphere advantage; faster reaction times to targets located at the global, as compared to the local, level reflect relative global bias and right hemisphere advantage.

Based on neuropsychological theories of hemispheric specialization of emotion, prior imaging research, and the results of two recent electrophysiological (Metzger et al., 2004) and behavioral (Vasterling et al., 2000) studies of cerebral asymmetry in PTSD suggesting a relative right hemisphere advantage, it was predicted that, as compared to combat veterans without mental disorders, study participants diagnosed with PTSD would show a relative global processing advantage.

METHODS

Research Participants

Participants were 26 PTSD-diagnosed and 22 psychopathology-free male Vietnam War zone veterans, recruited from newspaper advertisements, veterans' organization newsletters, flyers posted at a VA Medical Center and Veterans Resource Center, and mail-outs to participants in a PTSD outpatient clinic. The study was described as a research project targeting "human adjustment to various situations" encountered by Vietnam military veterans.

All participants were right-handed, as indicated by their scores on the Edinburgh Handedness Inventory (Oldfield, 1971). Volunteers were not included in the protocol if they reported a history of head trauma other than mild injury (i.e., loss of consciousness greater than 15 min or requiring medical care), central nervous system disease, or developmental problems suggestive of learning disorder or attention deficit hyperactivity disorder. If participants wore corrective lenses, they were asked to wear them during the session. All participants were asked about the clarity of the stimuli. Any participant who reported difficulty seeing the stimuli clearly was excluded. As assessed by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First et al., 1996), veterans with current (i.e., previous 6 months) diagnoses of alcohol or substance disorders, lifetime history of bipolar or psychotic disorders, or subthreshold manifestations of PTSD were also excluded from study participation. In addition, veterans in the no-mental disorders comparison sample were excluded if they met criteria for any lifetime Axis I disorder, excluding substance use disorders, even if currently asymptomatic. Finally, sample selection reflected an attempt to equate the two groups on the Wechsler Adult Intelligence Scale, Third Edition (WAIS–III; Wechsler, 1997) Vocabulary subtest as an estimate of intellectual potential.

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Deployment status was verified by review of military discharge records (DD-214s); and psychopathology categories were derived from SCID (First et al., 1996) diagnoses. All veterans assigned PTSD diagnoses reported the onset of PTSD symptoms to be during or shortly after their return from Vietnam. Of the 26 PTSD-diagnosed participants, 17 met criteria for a current comorbid mental disorder, including major depression ($n = 11$), dysthymia ($n = 2$), depressive disorder, not otherwise specified ($n = 1$), generalized anxiety disorder ($n = 3$), panic disorder ($n = 1$), social phobia ($n = 1$), and binge eating disorder ($n = 1$). Given that mood and anxiety disorders are sufficiently common among PTSD-diagnosed individuals that they may be conceptualized as subcomponents of PTSD psychopathology (Breslau et al., 2000; Sutker et al., 1991), study volunteers were not excluded on the basis of these comorbidities. At the time of testing, no veteran in the no-mental disorders group was taking psychotropic medications; 21 veterans in the PTSD group were taking at least one psychotropic medication, including antidepressants ($n = 18$), nonantihistamine anxiolytics ($n = 2$), sleep medication ($n = 11$); anticonvulsants ($n = 5$); and atypical antipsychotics ($n = 6$), representing common PTSD pharmacological treatment regimens.

Slightly more than half the participants were White (58.3%) with a mean age of 54.79 years ($SD = 4.22$ years). Veterans served an average of 13.34 months ($SD = 5.64$ months) in the Vietnam War zone, scored in the average range for age ($M = 10.69$; $SD = 2.40$) on the Vocabulary subtest of the WAIS–III, and used illicit drugs an average of 5.15 years ($SD = 8.92$ years). As shown in Table 1, PTSD-diagnosed and psychopathology-free veterans did not differ on these variables. Although the two groups did not differ on an estimate of native intellectual potential (i.e., Vocabulary), PTSD-diagnosed veterans reported completing fewer years of education than veterans without mental disorders (see Table 1). As expected from the high lifetime comorbidity rates of PTSD and alcohol-use disorders observed in Vietnam veterans (Kulka et al., 1990), veterans with current PTSD diagnoses were also more likely to meet criteria for past alcohol use disorders than veterans without current mental disorder diagnoses (see Table 1). However, as compared to the no disorder sample, veterans with PTSD diagnoses reported lower average daily alcohol consumption during the year prior to study enrollment, as measured by the Khavari Alcohol Test (Khavari & Farber, 1978) and reported more years of alcohol use. Both the overall sample ($M = 7.4$ ml, $SD = 12.4$ ml) and the two subsamples were well below the national daily average consumption of 25.1 ml of absolute alcohol as reported by the National Institute on Alcohol Abuse and Alcoholism (1993).

Materials and Measures

Psychopathology measures

Diagnosis of mental disorders was accomplished using the SCID (First et al., 1996). Severity of PTSD, depression, and state anxiety symptoms was measured by the PTSD Symptom Scale (Foa et al., 1993); the Beck Depression Inventory (Beck et al., 1988), and the State subscale of the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1970), respectively. Self-reported level of combat exposure was assessed using the Combat Exposure Scale (CES; Keane et al., 1989). Drug and alcohol use was assessed with the Khavari Alcohol Test (Khavari & Farber, 1978) and the Substance Use Disorders modules of the SCID. Positive and negative affect was measured by the Positive and Negative Affect Scale (PANAS; Watson et al., 1988).

Estimated intellectual potential

Participants were administered the Vocabulary subtest of the WAIS–III (Wechsler, 1997). Subtest data were first transformed from raw to scaled scores using age-appropriate norms.

Table 1. Sample characteristics

	PTSD ($n = 26$)		No mental disorders ($n = 22$)			
Variable	*M*,%	*SD*	*M*,%	*SD*	*F*, χ^2	*p*
% minority	50.00		31.81		1.62	.203
Age in years	54.58	4.31	55.05	4.19	0.14	.706
Vocabulary, age SS	10.19	2.61	11.27	2.02	2.50	.121
Education in years	12.77	2.16	14.45	1.50	9.49	.003
Months in Vietnam	14.27	5.41	12.41	5.92	1.27	.266
Average daily alcohol intake (oz.): past yr.	0.12	0.28	0.39	0.51	5.57	.023
% with past alcohol use disorder diagnosis	76.9		36.4		8.076	.005
Years of alcohol use	21.99	13.01	29.88	11.60	4.754	.034
Years of drug use	5.89	9.28	4.27	8.61	0.385	.538

Note. PTSD = posttraumatic stress disorder; SS = scaled score.

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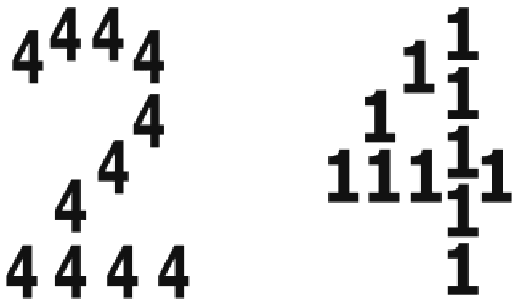


Fig. 1. Sample stimuli. In the figure on the left, the target (4) is at the local level; in the figure on the right, the target (4) is at the global level.

Global–local stimuli

Stimulus elements were modeled after Filoteo and his colleagues (Filoteo et al., 1992, 1995). Namely, eight global–local stimuli were created by hierarchical combination of the numerals, "1" and "2" (targets), and "3" and "4" (distractors). Large "1"s and "2"s composed of either smaller "3"s or "4"s formed 4 of the stimuli; large "3"s and "4"s composed of either smaller "1"s or "2"s formed the remaining four stimuli. Please see Figure 1 for a stimulus example. Stimuli were presented in black on a white background on a 17-inch Dell color monitor associated with a Dell XPS T600 desk-top computer.

It is generally believed that, all things being equal, processing of global features predominates local processing, especially in the initial stage of observation (Kimchi, 1992, p. 36). Because it was hypothesized that a relative global advantage would be associated with PTSD diagnosis, decisions regarding the stimulus size and distance from participants were made with the goal of maximizing local advantage, thereby avoiding a ceiling effect. Global–local stimuli presentation is most typically described in angles of visual subtension, which reflect a combination of distance from the eye to the stimuli and size of the stimuli. Based on the work of Carter et al. (1996), who demonstrated a consistent local advantage with cognitively-intact, psychopathology free normals, (1) participants placed their chins on a chin rest located approximately 295 mm from the computer screen and (2) stimuli were sized to subtend visual angles of approximately $6.6 \times 4.2^{\circ}$ at the global level and $1.2 \times 0.7^{\circ}$ at the local level. Using E-prime, v1.0, beta 5.0 (Schneider et al., 2002) to control presentation, each stimulus was repeated 16 times in a pseudorandom order (i.e., no more than three consecutive trials with the target in the same position), thus creating a total of 128 trials. Three possible pseudorandomized orders were created, one of which was assigned to each subject. Orders 1–3 were sequentially assigned to subjects and were yoked across groups.

Procedures

Following provision of written informed consent, demographic information and medical history were reviewed with participants. Participants were next administered the Edinburgh Handedness Inventory, psychopathology measures, and the WAIS–III Vocabulary subtest. Before beginning the actual task, participants were first given a set of 15 practice trials accompanied by trial-by-trial computer-generated corrective feedback ("correct" or "incorrect"). The experimenter repeated the instructions (see below) and responded to any questions, as needed. Upon completion of the practice trials, the experimenter then initiated the task. During the actual task, no corrective feedback was provided.

Each global–local trial began with a 500 ms fixation crosshair presented in the middle of the screen and an associated 500 ms warning tone, which was followed immediately by the stimulus. Because global–local advantage is thought to shift as stimulus duration is prolonged (Kimchi, 1992), stimuli were presented in the screen center for a controlled duration of 100 ms. To avoid a lateralized motor response, subjects were asked to press a key marked "1" with their left index finger if they observed "the number 1 in any form" and to press a key marked "2" with their right index finger if they observed "the number 2 in any form." They were further instructed to respond as quickly as they could without making mistakes. The trial ended with a response-initiated 1000 ms interstimulus interval.

Design

The target was at the global level in half of the trials and at the local level in the other half. Thus, the design was a between-within mixed model with group (PTSD, no disorder) as the between subjects factor and target location (global level, local level) as the within-subjects factor.

Data Analysis

Global–local advantage was measured by reaction times (RT), which were logarithmically transformed to normalize their distribution. Faster response (i.e., smaller RT) to global targets reflects a global advantage, whereas faster response to local targets reflects a local advantage. To provide a measure of the relative advantage, or bias, between global and local processing, a bias score was calculated as: bias = log-transformed RT at local targets − log-transformed RT at global targets. Thus, positive bias scores indicate global processing advantage, and negative bias scores indicate a local processing advantage. Finally, accuracy was examined as a check to assure appropriate task completion.

Group comparisons of PTSD symptom severity, depression severity, state anxiety, and positive and negative affect were accomplished with a univariate analysis of variance approach. A single factor of group (i.e., PTSD, no mental disorders comparison sample) was examined.

As a manipulation check, accuracy data were subjected to analysis of variance (ANOVA) using the between-within design model (i.e., Group × Target location) described above. To address the primary study hypotheses, log-transformed RT data were subjected to analyses of covariance (ANCOVAs) using the same design model (i.e., Group × Target

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location) but including accuracy and Vocabulary as covariates to control for variance attributable to inaccurate responding and estimated native intellectual potential, respectively. (Education was also considered as a potential covariate in lieu of Vocabulary. However, because the covariate was not significant, $p = .248$, education was dropped from further consideration in subsequent analyses.) In addition, to examine relative global or local processing biases between groups, bias scores were subjected to one-way ANOVA with group as the between subjects variable. Analyses examining log-transformed RT data were repeated within the PTSD group using depression diagnoses (i.e., the presence or absence of major depressive disorder, dysthymia, or depressive disorder, not otherwise specified) as the between subjects factor.

To examine the relationships between global-local advantage and emotional, PTSD, and trauma exposure data, two-tailed Pearson correlations were conducted between bias scores and BDI, PANAS–Positive Affect, PANAS–Negative Affect, and PSS Symptom, and STAI scores. A Bonferroni adjustment, applied to correlations to control for Type 1 error in this variable grouping, set the threshold for significance at .01. To examine the impact of potential confounding variables, relationships between substance use variables, CES, estimated native intellectual potential (i.e., Vocabulary age SS scores), education, accuracy, and overall response time data were also examined with two-tailed Pearson correlations.

RESULTS

Group Comparison: PTSD and Emotional Distress

As expected, PTSD-diagnosed veterans reported more severe PTSD symptomatology, depression, state anxiety, and negative affect (*M*s = 32.46, 26.16, 52.11, 23.50, respectively; *SD*s = 8.44, 7.95, 8.81, 9.17, respectively) than veterans without mental disorders diagnoses (*M*s = 1.64, 4.73, 30.09, 11.41, respectively; *SD*s = 2.95, 4.53, 8.63, 10.67, respectively) on the PSS [$F(1,46) = 265.00$, $p < .001$], BDI [$F(1,46) = 124.32$, $p < .001$], STAI [$F(1,46) = 75.88$, $p < .001$], and PANAS–Negative Affect scales [$F(1,46) = 33.62$, $p < .001$], respectively, and less positive affect ($M = 25.08$, SD = 8.66) on the PANAS–Positive Affect scale than the no disorders comparison sample [$M = 31.55$, $SD = 8.38$; $F(1\,46) = 6.85$, $p = .012$].

Accuracy Comparisons

The 2 (group: PTSD, no mental disorders) × 2 (target location: global, local) ANOVA did not reveal significant main effects for group ($p = .472$) or target location ($p = .440$) or an interaction effect ($p = .095$). Mean accuracy scores reported by Group and Target Location can be found in Table 2.

Log-Transformed RT Comparisons

The 2 (group: PTSD, no mental disorders) × 2 (target location: global, local) ANCOVA revealed a main effect for group [$F(1,46) = 6.75$, $p = .013$] and a Group × Target interaction [$F(1,46) = 5.38$, $p = .025$]. Findings failed to reveal a significant main effect for target location ($p = .620$). As indicated in Figure 2, although PTSD-diagnosed veterans reacted more slowly to all targets than veterans without mental disorder diagnoses, the response time differential between the two groups was more pronounced for local targets. That is, whereas group differences (PTSD sample: $M = 2.84$, $SD = 0.12$; no-disorder sample: $M = 2.79$, $SD = 0.08$) in log-transformed RT to targets at the global level did not reach significance [$F(1,46) = 3.15$, $p = .083$], the PTSD sample ($M = 2.87$; $SD = 0.15$) was significantly slower in responding to local targets than was the no-mental disorder comparison sample [$M = 2.76$, $SD = 0.09$; $F(1,46) = 8.84$, $p = .005$].

There was a nonsignificant trend ($p = .088$) for PTSD-diagnosed veterans to respond more slowly to local as compared to global targets; whereas, log-transformed RT did not differ among veterans without mental disorders ($p = .112$). When log-transformed RTs were viewed as bias scores, group comparison revealed that PTSD-diagnosed veterans showed a relative global processing advantage ($M = .02$, $SD = .07$) as compared to their psychopathology-free counterparts ($M = -.02$, $SD = .06$), who showed a relative local processing advantage [$F(1,46) = 6.02$, $p = .018$].

Table 2. Mean accuracy scores by group and target location with standard deviations

	PTSD ($n = 26$)		No mental disorders ($n = 22$)	
Target location	*M*	*SD*	*M*	*SD*
Local level	59.96	7.19	62.91	1.11
Global level	61.08	3.30	59.91	8.89

Note. PTSD = posttraumatic stress disorder.

Correlational Analyses

Two-tailed Pearson correlations indicated that PSS [$r(47) = .39$, $p = .006$], PANAS–Negative Affect [$r(47) = .38$, $p =$

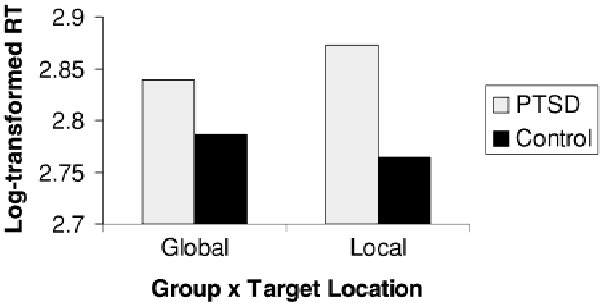


Fig. 2. Log-transformed reaction times for the PTSD and no-mental disorder control groups for targets at the local and global stimulus levels.

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.007], and STAI [$r(47) = .37$, $p = .010$] scores were positively correlated with bias scores, indicating that higher levels of PTSD severity, anxiety, and negative affect were associated with a greater tendency towards global advantage. Although the PANAS-Positive Affect score reached significance prior to Bonferroni correction [$r(47) = -.34$, $p = .019$], it did not reach significance at the Bonferroni-corrected level of significance ($p = .010$). BDI scores were not significantly correlated with bias scores ($p = .142$). To assure that inaccurate responding or generally slowed reaction time could not account for associations between PTSD and bias, zero-order correlations controlling for accuracy and overall response time were performed between PSS and bias scores. Findings revealed that the PSS [$r(44) = .32$, $p = .029$] continued to be positively correlated with bias scores, even after controlling for accuracy and overall response time.

There was no evidence of significant relationships between bias scores and estimated daily average alcohol consumption ($p = .271$), months of lifetime alcohol use ($p = .792$), months of non-alcohol drug use ($p = .267$), years of education ($p = .156$), or accuracy scores ($p = .545$). Correlations between bias scores and Vocabulary age scale ($p = .087$) and CES scores ($p = .053$) approached significance. Log-transformed reaction times collapsed across global and local target locations were positively associated with bias scores [$r(47) = .37$, $p = .010$].

Influence of Depression on Global–Local Performance

A mixed ANCOVA (Depression Status × Target Location) adjusted for Vocabulary performance and accuracy within the PTSD sample of log-transformed reaction times did not reveal significant main effects for either depression status ($p = .905$) or target location ($p = .236$), or a significant interaction effect ($p = .736$). Similarly, comparison of bias scores across depressed and nondepressed PTSD-diagnosed participants did not reveal a significant group difference ($p = .865$).

DISCUSSION

This study examined a behavioral index of functional hemispheric asymmetry, global–local visual processing, in Vietnam War zone veterans diagnosed with PTSD. As compared to Vietnam War zone veterans without mental disorders diagnoses, PTSD-diagnosed veterans demonstrated a greater global processing advantage. Although veterans with PTSD responded more slowly to targets located at both global and local stimuli levels than veterans without mental disorders, findings revealed an interaction between diagnostic group and target level. When confronted with targets at the local, as compared to the global level, PTSD-diagnosed veterans responded more slowly. Conversely, the no-disorder comparison sample responded more quickly to targets at the local, as compared to global, level.

Taking into account studies using a broad array of methods that indicate that the right hemisphere tends to be specialized for global visual perception and the left hemisphere for componential analysis of stimulus elements (e.g., Fink et al., 1997; Hans et al., 2002; Heinz et al., 1998; Martinez et al., 1997), results of the present study suggest that PTSD diagnosis is associated with a functional asymmetry favoring the right hemisphere relative to the left. The association of PTSD diagnosis with a behavioral index of relative left hemisphere hypoactivation is consistent with previous research documenting left hemisphere-mediated visuospatial errors on a block design task in combat veterans diagnosed with PTSD (Vasterling et al., 2000) and right EEG alpha parietal activation among Vietnam-era nurses diagnosed with PTSD (Metzger et al., 2004). Results also support functional imaging studies indicating increased regional cerebral blood flow (rCBF) in the right hemisphere and decreased rCBF in the left hemisphere of PTSD patients during symptom provocation (e.g., Rauch et al., 1996; Shin et al., 1997).

The overall slowing displayed by veterans with PTSD is not wholly surprising and may be attributable to a number of factors including depressive comorbidity and medication side effects, which are both potentially associated with psychomotor slowing (Hickie et al., 1999; White et al., 1997). However, the interaction between diagnosis and target level is less readily explained by these sample characteristics. Correlational analyses did not reveal an association between depression and bias in this sample of military veterans, suggesting that the positive correlation between PTSD and global bias cannot be explained on the basis of comorbid depression alone. Similarly, when analyses were repeated among subsets of depressed and nondepressed PTSD-diagnosed veterans, no differences emerged between these two subsets on indices of reaction time to global or local stimuli. Although depression has been shown to be associated with relative hypoactivation of the anterior left hemisphere (e.g., Gotlib et al., 1998; Henriques & Davidson, 1990, 1991), studies examining posterior activation have suggested that depression is associated with hypoactivation of the right hemisphere, especially in the absence of comorbid anxiety or when depression was examined independently of anxiety symptoms (e.g., Bruder et al., 1997; Heller et al., 1995; Keller et al., 2000). These studies suggest that when anxiety and depression are comorbid, the asymmetry in depression resembles more closely that found in anxiety (cf. Metzger et al., 2004). Thus, it may be that, when accompanied by anxiety, depression-related posterior cerebral asymmetries are more closely aligned with those that characterize anxiety.

There were too few unmedicated PTSD-diagnosed veterans to conduct a meaningful subanalysis examining medication effects. Although it is possible that medications altered functional cerebral symmetry independently of their effects on symptomatology, past research has not revealed an association between psychoactive medications and other indices of functional hemispheric asymmetry in clinical samples of anxiety- and mood-disordered individuals (Jaeger et al.,

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1987; Keller et al., 2000), including those with PTSD diagnoses (Vasterling et al., 2000). In prospective studies examining the effects of antipsychotic medications on cerebral asymmetry in schizophrenia, findings revealed that medication usage was associated with left hemisphere advantage (Purdon & Flor-Henry, 2000; Purdon et al., 2001; Seidman et al., 1993), a finding opposite to the relative right hemisphere advantage documented in the present study. Thus, taken as a whole, the results of previous cross-sectional and prospective research examining the effects of medication on functional cerebral asymmetries suggest that the pattern of findings in the current study cannot be attributed to medications. Nonetheless, if feasible, it will be worthwhile for future research to examine the effects of medications commonly prescribed in PTSD on cerebral asymmetry.

Analyses also considered the potential effects of generalized slowing, accuracy, estimated native intellectual potential, and current and historical use of alcohol and non-alcohol illicit drugs on findings. There was no evidence that past or current use of alcohol or illicit drugs affected task performance, as correlational analyses failed to reveal an association between task performance and average daily alcohol use or number of years of past alcohol and drug use, and potential participants currently using illicit drugs were excluded. Participants were matched as closely as possible on Vocabulary performance; nonetheless, Vocabulary scores were positively correlated with bias scores. However, the introduction of Vocabulary and global-local task accuracy as covariates did not alter the pattern of results. Similarly, the correlation between PTSD severity and bias remained significant after controlling for log-transformed reaction time across target locations, suggesting that findings could not be explained on the basis of generalized slowing. In sum, none of these potentially confounding factors appeared to exert significant impact on study findings.

The study design incorporated a quasi-experimental, descriptive approach. Thus, although global–local processing was found to be associated with PTSD diagnosis, causal inferences must necessarily be regarded with caution. That is, it may be that relative hypoactivation of the left hemisphere and the emotional behavior associated with such functional asymmetry places individuals at greater risk for PTSD, or conversely, that trauma exposure alters the balance between right and left hemisphere neural activation in those individuals that develop PTSD. Recent twin research has indicated that there may be a genetic vulnerability for development of PTSD (Koenen et al., 2003), which may in some individuals be expressed as a neural (i.e., smaller hippocampal volume) component (Gilbertson et al., 2002). Documentation of left frontal hypoactivation in the children of mothers with major depressive disorder has provided evidence suggesting that, at least for major depression, functional cerebral asymmetry may be a vulnerability factor for subsequent psychopathology (Tomarken et al., 1994). However, it could also be reasoned that when confronted with life threatening events, a shift of attention to the global aspects of a situation (i.e., "the big picture") could serve an adaptive purpose, and that any changes in brain activity associated with global advantage continue long after the event ends in those individuals who develop PTSD. Findings among male participants in a study assessing memory for emotional information indicating that memory for central (i.e., global) but not peripheral (i.e., local) information from a story was greater under conditions of emotional arousal (Cahill & van Stegeren, 2003) provide partial support for this hypothesis. Thus, prospective research will be needed to examine the direction of causality more definitively.

Regardless of direction of causality, the findings are nonetheless in keeping with several current neuropsychological conceptualizations of emotion. Consistent with valence and approach-withdrawal hypotheses, which purport that the right hemisphere is specialized for negative emotions (Lee et al., 1993; Silberman & Weingartner, 1986) and withdrawal behaviors (Davidson, 1993), respectively, the constellation of symptoms associated with PTSD can be viewed as both negatively-valenced (e.g., anxiety) and withdrawal-oriented (e.g., avoidance and emotional detachment). Conversely, findings were not supportive of previous empirical (Basso et al., 1996; Derryberry & Reed, 1998) reports and theories (Tucker & Williamson, 1984) purporting that anxiety involves preferential activation within the left hemisphere. Hyperarousal symptoms (e.g., hypervigilance, exaggerated startle) characterize the clinical presentation of PTSD. Supporting the assertion of Heller and her colleagues (Heller, 1993; Heller et al., 1995), it may be that arousal-based anxiety symptoms such as many of those associated with PTSD are associated with increased right posterior activation. However, because this study used indirect measures of cerebral activation, replication using more direct indices of cerebral activation will be required.

In summary, results of this study add to the growing literature examining neurobiological alterations in PTSD and represent one of the first behavioral efforts to demonstrate functional cerebral asymmetry in relation to PTSD diagnosis. The inclusion of a combat-exposed comparison sample without mental disorders suggests that global advantage cannot be attributed to stress exposure alone. Future investigations directly comparing behavioral indices of hemispheric asymmetries to physiological indices of neural activation (e.g., functional imaging studies) and to morphometric indices of anatomic asymmetries will be particularly useful in depicting a more complete picture of neurobiological alterations associated with PTSD.

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