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SYMPOSIUM

Longitudinal effects of PTSD on memory functioning

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Abstract

Numerous studies have demonstrated explicit and working memory deficits related to posttraumatic stress disorder (PTSD), but few have addressed longitudinal changes in memory functioning. There is some evidence to suggest an interactive effect of PTSD and aging on verbal memory decline in Holocaust survivors (Yehuda et al., 2006). However, the longitudinal trajectory of neuropsychological functioning has not been investigated in Vietnam veterans, a younger but substantial population of aging trauma survivors. We administered tests of visual and verbal memory, and working memory to derive different dependent measures in veterans between the ages of 41 and 63, the majority of whom served in the Vietnam War. Twenty-five veterans with PTSD and 22 veterans without PTSD were assessed over two time points (mean age at follow-up = 54.0; mean inter-test interval = 34 months). The PTSD+ group, consisting of veterans with chronic, primarily combat-related PTSD, did not show a significant change in PTSD symptoms over time. Compared to veterans without PTSD, veterans with PTSD showed a greater decline in delayed facial recognition only, and this decline was extremely subtle. (*JINS*, 2009, *15*, 853–861.)

Keywords: Veterans, Neuropsychology, Verbal learning, Delayed memory, Immediate recall, Aging

INTRODUCTION

Many research studies have documented both explicit memory (Bremner et al., 1993, 1995; Bremner, Vermetten, Afzal, & Vythilingam, 2004; Elzinga & Bremner, 2002; Gilbertson, Gurvits, Lasko, Orr, & Pitman, 2001; Vasterling, Brailey, Constans, & Sutker, 1998; Yehuda et al., 1995; Yehuda, Golier, Halligan, & Harvey, 2004) and working memory deficits (Gilbertson et al. 2001; Uddo, Vasterling, Brailey, & Sutker, 1993; Vasterling et al., 2002) in patients with posttraumatic stress disorder (PTSD). However, these findings have not always been consistent, with some studies showing no differences between patients with and without PTSD (Pederson et al., 2004; Stein, Hanna, Vaerum, & Koverola, 1999; Stein, Kennedy, & Twamley, 2002; Zalewski, Thompson, & Gottesman, 1994).

In two studies of veterans, we have reported conflicting findings, as well. Our first study (Neylan et al., 2004) compared attention and memory performance in a sample of Vietnam combat veterans with and without PTSD. The 24 healthy, well-educated (with an average of over 15 years of education) veterans with PTSD, but without current depression or alcohol or drug abuse within the past five years, performed similarly on tests compared to the 23 comparison participants. We suggested that memory and attention deficits previously seen in participants with PTSD may in fact be attributable to alcohol or depression, as this study carefully controlled for those comorbid conditions. However, excluding participants with comorbid conditions altogether from PTSD studies threatens the generalizability of findings, as 24–84% of patients with PTSD also exhibit depressive and alcohol abuse disorders (Keane & Kaloupek, 1997). In our second study (Samuelson et al., 2006) we attempted to clarify the unique contribution of PTSD to neuropsychological functioning by comparing four groups of veterans with and without diagnoses of PTSD and alcohol abuse or dependence, while statistically controlling for comorbid depressive symptoms. In this large study of 130 veterans, we found a main effect of PTSD on verbal memory, working memory, attention, and processing speed performance; a main effect

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of alcohol on visual memory performance; and did not find a PTSD by alcohol interaction on neurocognitive performance. These findings provide more conclusive evidence that verbal memory and attention deficits are attributable to PTSD. It may be that the sample from our first study, consisting of highly educated, depression- and alcohol-free participants, was a highly functioning subset of patients with PTSD that is not representative of the population of patients, particularly veterans, with PTSD.

As these previous studies have been cross-sectional in design, less is understood about the progression of memory deficits and other aspects of neurocognitive functioning over time. To our knowledge, the only previous study examining neuropsychological functioning in PTSD longitudinally in older patients was conducted by Yehuda and colleagues (2006). Examining Holocaust survivors five years after an initial memory assessment, they found that Holocaust survivors with PTSD, with a mean age of 73 years at the second testing, showed a greater decline in paired associates learning, relative to Holocaust survivors without PTSD. In addition, there was a significant relationship between greater age and poorer paired associates learning performance, and these correlations were greater for the PTSD+ group than for the PTSD– group. Unexpectedly, both the PTSD+ and PTSD– groups in this sample showed an improvement in word-list learning, as measured by the California Verbal Learning Test (CVLT) five years after their initial assessment. Differences between Holocaust survivors with and without PTSD on the CVLT that were evident at baseline were no longer apparent at follow-up. CVLT improvement was negatively associated with PTSD symptom severity, but not with age. The authors concluded that the improved performance on the CVLT may be related to improvements in initial attention to the task that are likely associated with PTSD symptom improvement.

The primary goal of this study was to examine if the longitudinal memory decline found in older Holocaust survivors is also observed in a middle-aged sample of veterans. Secondary goals were to explore the effects of age on longitudinal changes in memory performance, and to examine the relationship between change in PTSD severity and change in memory performance. These studies were performed on a sample of veterans between the ages of 41 and 63, who were tested over two time periods ranging from two to five years.

METHOD

Participants

The sample consisted of 47 male veterans (25 PTSD+ and 22 PTSD–) who had previously participated in one of two earlier studies in which we examined neuroimaging and neuropsychological correlates of PTSD (Neylan et al., 2004; Samuelson et al., 2006). The study protocols and consent forms were approved by the Committee on Human Research at the University of California, San Francisco. At the time of the original studies, participants had given consent to be recontacted about future studies. Veterans were contacted after a minimum of two years had passed since the completion of the first assessment. The mean inter-test interval was 34 months (*SD* = 7.1), with a range of 24 to 60 months. At the time of the follow-up assessment, veterans ranged in age from 41 to 63, with a mean of 54.4 (*SD* = 5.6). One hundred and seventy-five veterans participated in baseline testing, and we attempted to contact 83 of these veterans between two and five years later. Recruitment priority was given to participants who were over the age of 50, although some veterans under the age of 50 also participated. Of the 83 contacted, 11 had moved, 4 had died, we were unable to reach 9, 1 had reported a cocaine relapse, which was an exclusion criterion for the present study, 1 reported a change in medical status that deemed him medically unsafe to participate in a neuroimaging study, and 3 declined to participate, resulting in a final sample of 54 veterans who participated in the longitudinal study. Of those 54, 3 did not complete the assessment, 1 was excluded because of cocaine abuse, 2 were excluded for positive toxicology screens on the day of neuropsychological assessment, and 1 was excluded from data analysis because of his young age, as the focus of these analyses was on middle-aged veterans over the age of 40.

Measures

Structured diagnostic interviews

Diagnoses of PTSD at baseline and follow-up were made by a clinical psychologist using the Clinician Administered PTSD Scale (CAPS; Blake et al., 1995). The Structured Clinical Interview for DSM-IV Diagnosis (SCID; First, Spitzer, Williams, & Gibbon, 1996) was used to diagnose comorbid and exclusionary conditions.

Symptom Checklist 90-R

Participants completed the Symptom Checklist–90-R (SCL-90; Derogatis, 1994), a clinical rating scale of psychiatric symptomatology. Of interest in the current study was the depression subscale score, which consists of 13 items of depressive symptomatology.

Lifetime Drinking History

We obtained lifetime alcohol use histories on all of the participants using the Lifetime Drinking History questionnaire (LDH; Skinner & Sheu, 1982).

Neuropsychological variables

All participants were administered a test battery at both time points. To assess verbal memory and learning, we used two variables from the California Verbal Learning Test (CVLT; Delis, Freeland, Kramer, & Kaplan, 1988). The CVLT measures recall of word lists over a number of trials. Total Trials 1–5 score provides a measure of verbal learning. Participants are then presented with an interference word list, asked to recall the initial word list (short-delay free recall), and then asked to recall the initial word list after 20 minutes

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(long-delay free recall). The Retention score is a percent change score which is derived from subtracting the short-delay free recall score from the long-delay recall score and dividing by the short-delay recall score. That variable, used in this study, is thus less influenced by the examinee's immediate recall scores, allowing for a more accurate measure of memory retrieval.

To assess short- and long-term visual memory, the Faces I, Faces II, Family Pictures I, and Family Pictures II subtests of the Wechsler Memory Scale–Third Edition (WMS-III; Wechsler, 1997a) were used. In the Faces I subtest, the participant is told to remember photographs of faces and then shown a series of faces and asked to identify if the face was one previously viewed. For the Family Pictures subtest, the participant is shown scenes with family members and asked to remember aspects of the scene. Whereas Faces is a test of recognition, Family Pictures is a test of recall, but low scores on both indicate memory deficits with visually presented material. For Faces II and Family Pictures II, participants are asked to identify or recall the faces or family pictures 30 minutes later. Few PTSD studies have examined facial recognition and contextual visual recall. We included these measures because most PTSD studies had not demonstrated a deficit in learning and recall of visuospatial information (e.g., Bremner et al., 1993; Vasterling et al., 2002; Zalewski et al., 1994) using measures such as the Continuous Visual Memory test and the Rey Osterreith Complex Figure Drawing Test.

To assess both verbal and visual-spatial working memory, veterans were administered the Digit Span and Spatial Span subtests of the WMS-III. In the Digit Span subtest, the participant is asked to repeat back a series of digits in the same sequence as the examiner presented, as well as the reverse order. In the Spatial Span subtest, the examiner taps cubes on a board in a specified sequence, and the participant must tap the blocks in the same sequence, as well as in reverse order.

Intellectual functioning

Participants were administered the Vocabulary subtest of the Wechsler Adult Intelligence Scale–Third Edition (WAIS-III; Wechsler, 1997b) at baseline as an estimate of intellectual functioning. The Vocabulary subtest is often used as a "hold" test from which estimates of premorbid functioning are derived in brain-injured populations (Lezak, Howieson, & Loring, 2004).

Procedures

At baseline, veterans with past but not current PTSD, or current subsyndromal PTSD, were not included in the study. At baseline and follow-up, exclusion criteria included history of head trauma, prolonged loss of consciousness (>10 min), and neurological disorder or systemic illness affecting central nervous system function. At baseline, participants were also excluded if the SCID revealed lifetime history of psychotic disorder or bipolar disorder, and drug abuse or dependence within the previous six months. At follow-up, three participants met one of the exclusionary diagnoses – two exhibiting psychotic symptoms and one exhibiting symptoms of bipolar disorder not otherwise specified. Data analyses were conducted both with and without these three participants to determine if group differences were driven by their inclusion. The pattern of findings remained the same, and these three participants did not represent outliers in terms of neuropsychological functioning, so their data were included in subsequent analyses.

A clinical psychologist administered the neuropsychological battery and the tests were administered in the same order for all participants. Participants were instructed to abstain from using alcoholic beverages and were breathalyzed before neuropsychological testing to verify absence of alcohol. Participants also had urinalysis for drug toxicology on the day of neuropsychological assessment. Data from two participants who had positive toxicology screens were excluded from analysis.

Data Analysis

To test the hypothesis of longitudinal change of memory function in PTSD, we first conducted paired *t* tests, separately for the PTSD+ and PTSD– participants, to determine if there were significant changes in memory performance from Time Point 1 to Time Point 2. Next, to examine if change in memory performance was different between the two groups, data from the repeated measures design were analyzed using random intercept linear mixed-effects regression models, with each primary neuropsychological variable as the outcome. Unlike analysis of variance (ANOVA), this method accurately models the intersubject differences in initial neuropsychological performance and the intrasubject correlation of the repeated measures (Hedeker & Gibbons, 2006). We tested for a group × time interaction. Furthermore, because Yehuda et al. (2006) reported longitudinal effects of age in an older population, we explored if the cognitive decline in PTSD was affected by age by testing for an age × group × time interaction in the longitudinal model. Finally, potentially confounding demographic variables (e.g., education) that were found to be different between the two groups were entered into each model as covariates. Within the mixed-effects regression model, we coded both group and time as 0 and 1, and centered age at its mean, in order to facilitate interpretation of coefficients and to minimize multicollinearity with regression terms (Aiken & West, 1991). To determine if memory performance change was related to PTSD symptom severity change, we conducted Pearson product correlations, correlating CAPS symptom change score with each memory measure change score. For all analyses, in order to control for multiple comparisons, we used a more conservative significance level of $p < .01$. All statistical tests were two-tailed.

RESULTS

Demographic and Clinical Information

Demographic characteristics (age, ethnicity, and education), and clinical and background variables (CAPS, trauma

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history, time since trauma, LDH, and WAIS-III Vocabulary score) are summarized in Table 1. The two groups had comparable Vocabulary scores. The groups did not differ by age or ethnicity, but the PTSD+ group had fewer years of education than the PTSD– group. Because of the differences found between groups on education level, and the relationship frequently reported in the literature between education and memory performance (Lezak et al., 2004), this variable was entered as a covariate in all subsequent analyses.

Table 1. Demographic and clinical characteristics

	PTSD+ (n = 25)	PTSD– (n = 22)	Significant Differences t (p)
Age Time Point 1			
Range	38–60	39–60	
Mean (*SD*)	51.2 (5.5)	52.09 (5.6)	.548 (.587)
Age Time Point 2			
Range	41–63	42–62	
Mean (*SD*)	53.97 (5.6)	54.96 (5.7)	.600 (.551)
Inter-test Interval (months)			
Range	24–60	25–42	
Mean (*SD*)	35.4 (8.2)	32.41 (5.4)	−1.45 (.153)
Education			
Range	12–20	12–20	
Mean (*SD*)	14.52 (2.3)	16.41 (2.2)	2.86 (.006)
Ethnicity	65% Caucasian 31% African American 4% Native American	77% Caucasian 18% African American 5% Asian American	
CAPS Time Point 1			
Range	31–92	0–11	
Mean (*SD*)	61.04 (14.98)	1.72 (3.27)	−18.17 (.001)
CAPS Time Point 2			
Range	19–84	0–11	
Mean (*SD*)	53.32 (18.99)	1.50 (3.23)	−12.62 (.001)
SCL-90 Depression			
Time Point 1			
Range	.154–2.77	0–1.31	
Mean (*SD*)	1.58 (.72)	.30 (.36)	−7.29 (.001)
SCL-90 Depression			
Time Point 2			
Range	.154–2.85	0–1.00	
Mean (SD)	1.38 (.76)	.36 (.31)	−5.86 (.001)
WAIS-III Vocabulary			
Range	36–65	29–66	
Mean (*SD*)	52.96 (7.88)	54.77 (8.85)	.736 (.466)
LDH Drinks in Past Month,			
Time Point 2			
Range	0–84	0–90	
Mean (*SD*)	10.00 (19.97)	20.11 (28.1)	−1.43 (.16)
LDH Lifetime Drinks			
Range	1745–253646	0–116448	
Mean (*SD*)	54660 (70792)	24177 (32240)	−1.86 (.07)
Traumatic Event:			
Vietnam combat	80%	50%	
Gulf War combat	4%	0%	
Other military	16%	0%	
Non-military trauma	0%	27%	
None	0%	23%	
Time Since Trauma			
Range	14–38	11–45[a]	
Mean (SD)	31.23 (5.6)	33.46 (8.14)	.964 (.34)

Note. CAPS = Clinician Administered PTSD Scale; LDH = Lifetime Drinking History; WAIS-III = Wechsler Adult Intelligence Scale–Third Edition; SCL-90 = Symptom Checklist – 90 Item Version, Depression subscale

[a]n = 17 PTSD– participants who endured a traumatic experience.

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As expected, the PTSD+ group had a higher CAPS score at both time points, as well as higher SCL-90 Depression scale scores. Depression is so common among individuals with PTSD that it is often conceptualized as part of the PTSD psychopathology (Sutker, Uddo-Crane, & Allain, 1991), with some overlapping symptoms, and thus was not entered as a covariate into subsequent analyses. However, to determine if an increase in depressive symptoms at Time Point 2 was related to any change in memory performance, we correlated change in the SCL-90 Depression score with change in memory performance with all of the variables, and no correlations were significant, either with the whole sample, or separately by group.

The traumatic event assessed for the majority of participants was Vietnam combat; similarly, the average time elapsed since trauma was 32 years, with 70% of the sample experiencing the trauma between 30 and 35 years ago. The groups did not differ in alcohol consumed in the month prior to testing at Time Point 2, $t(45) = 1.43$, $p = .158$, and there was a trend for greater lifetime alcohol consumption in the PTSD+ group, as measured by the LDH, $t(45) = –1.86$, $p = .070$. This lack of significant difference between the two groups is likely a result of the fact that the veterans participated originally in either a study in which none of the participants had a history of alcohol abuse in the past five years (Neylan et al., 2004) or in a study that employed a four-group design consisting of veterans with and without PTSD and histories of alcohol abuse, in which the PTSD+ and PTSD– groups had similar alcohol abuse histories (Samuelson et al., 2006). To further examine the potential impact of drinking history on neuropsychological performance, correlations were conducted examining the relationships between lifetime alcohol consumption and neuropsychological variables, and no correlations were significant.

Differences Between Current Sample and Larger Cohort of Baseline Assessment Completers

To determine if the findings from this smaller sample were generalizable to the larger cohort from which it was drawn, we first determined if there were differences at the baseline assessment between the groups who did ($n = 47$) and did not ($n = 128$) complete the follow-up evaluation. These comparisons are reported in Table 2. There were significant differences between the groups on age, $t(173) = –3.51$, $p = .001$; education, $t(173) = –2.30$, $p = .02$; WAIS-III Vocabulary score, $t(173) = –2.04$, $p = .04$; and Digit Span score, $t(173) = –2.60$, $p = .01$.

Within Group Comparisons from Time Point 1 to Time Point 2 on PTSD and Depression Symptom Severity and Memory Performance

The groups were first examined separately to examine potential differences between Time Point 1 and Time Point 2 on memory performance, using eight neuropsychological variables: CVLT Total Score, CVLT Retention, Faces I (immediate) and II (delayed), Family Pictures I (immediate) and II (delayed), Digit Span, and Spatial Span. The PTSD+ group declined significantly over time on the two delayed visual memory variables: Faces II, paired $t(24) = 2.88$, $p = .008$, and Family Pictures II, paired $t(23) = 3.63$, $p = .001$. The PTSD– did not show significant decline or improvement on any measures. Neither group showed a significant change from Time Point 1 to Time Point 2 in total CAPS score or SCL-90 Depression subscale score.

Between and Within Group Comparisons from Time Point 1 to Time Point 2 on Memory Performance

Table 3 shows the means and standard deviations for each group at each time point, and the t statistics and p values comparing the two groups. There were no significant differences between the two groups at Time Point 1. As described earlier, 22 of the veterans originally participated in the baseline study in which we did not find memory differences between PTSD+ and PTSD– participants (Neylan et al., 2004), while 25 veterans participated in the study in which memory

Table 2. Statistical comparisons between participants from original sample who did and did not participate in follow-up assessment

	Did Not Participate $n = 128$	Current Study $n = 47$	Significant Differences t (p)
Age	46.6 (9.4)	51.7 (5.6)	–3.51 (.001)
Education	14.6 (2.1)	15.4 (2.5)	–2.30 (.02)
WAIS Vocabulary	50.3 (10.0)	53.7 (8.3)	–2.04 (.04)
Total CAPS	35.5 (34.2)	32.7 (31.2)	.488 (*ns*)
LDH Lifetime Drinks	37,852 (56,972)	42,610 (57,981)	–.514 (*ns*)
CVLT Total Learning	48.7 (10.7)	50.8 (9.4)	–1.12 (*ns*)
WAIS-III Digit Span	16.8 (4.2)	18.7 (4.5)	–2.60 (.01)
WMS-III Spatial Span	15.6 (3.3)	15.5 (2.6)	.268 (*ns*)
WMS-III Faces I	37.4 (4.6)	36.7 (4.6)	.838 (*ns*)
WMS-III Faces II	37.2 (4.2)	37.1 (4.3)	.142 (*ns*)
WMS-III Family Pictures I	41.0 (11.5)	39.3 (11.8)	.847 (*ns*)
WMS-III Family Pictures II	40.0 (10.5)	40.1 (11.2)	–.055 (*ns*)

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Table 3. Means and standard deviations of neuropsychological test performance

	PTSD+ Time Point 1 *M* (*SD*)	PTSD– Time Point 1 *M* (*SD*)	*t* (*p*)	PTSD+ Time Point 2 *M* (*SD*)	PTSD– Time Point 2 *M* (*SD*)	*t* (*p*)
CVLT Total	50.08 (9.5)	51.86 (9.7)	.632 (*ns*)	49.92 (9.1)	52.81 (9.7)	.844 (*ns*)
CVLT Retention [(Long Delay – Short Delay)/Short Delay]	.05 (.13)	.14 (.22)	1.88 (*ns*)	.08 (.14)	.06 (.20)	–.432 (*ns*)
WMS-III Digit Span	17.85 (4.2)	19.55 (4.6)	1.33 (*ns*)	16.65 (4.3)	20.23 (4.5)	2.81 (.01)
WMS-III Spatial Span	15.36 (2.6)	15.64 (2.7)	.334 (*ns*)	14.52 (3.2)	16.45 (3.3)	2.06 (.05)
WMS-III Faces I	36.77 (4.7)	36.64 (4.6)	1.31 (*ns*)	35.96 (4.4)	37.73 (5.0)	.591 (*ns*)
WMS-III Faces II	36.85 (3.7)	37.32 (4.9)	.377 (*ns*)	34.77 (4.2)	38.86 (5.5)	2.94 (.01)
WMS-III Family Pictures I	41.08 (11.4)	37.48 (12.3)	–1.04 (*ns*)	36.04 (12.6)	33.86 (10.8)	–.817 (*ns*)
WMS-III Family Pictures II	43.04 (10.2)	37.36 (11.7)	–1.18 (*ns*)	35.40 (13.9)	31.91 (11.2)	–.94 (*ns*)

Note. CVLT = California Verbal Learning Test, Children's Edition; WMS-III = Wechsler Memory Scale–Third Edition; *ns* = not significant.

differences were documented at baseline (Samuelson et al., 2006); by combining these two groups, differences were eliminated. Mixed-effects linear regression models were conducted examining differences in the two groups over time on memory performance, to examine potential group × time interactions, group × age × time interactions, and the contribution of education to memory performance. Education and age were entered into the model. The mixed-effects linear regression models revealed a greater decline in performance for the PTSD+ group compared to the PTSD– group on Faces II (see Table 4). There were nonsignificant trends for group × time interactions for greater decline in performance for the PTSD+ group on Digit Span (z = –2.02, p = .04) and Spatial Span (z = –2.17, p = .03). None of the analyses revealed a relationship between age and memory performance with any of the eight variables, and we failed to find significant group × age × time interactions for any of the memory variables.

We then conducted correlations to determine if memory performance change was related to CAPS change. None of the correlations were significant for any of the memory variables, either for the whole sample or separately by group. Additional analyses were conducted to elucidate the finding of a decline in Faces II performance for the PTSD+ group, in the absence of an age × group × time interaction. Surmising that the finding might be a result of the prolonged impact of PTSD on the brain, we correlated time since trauma exposure with Faces II performance at Time Point 2 for the PTSD+ group. This correlation was not significant, r = –.24, p = .29. In addition, we speculated that the decline in performance might result from differences between the groups on inter-test interval, although these differences were nonsignificant. Thus, we conducted a partial correlation correlating inter-test interval with change in Faces II performance, controlling for baseline Faces II performance, and the correlation was not significant, r = .181, p = .229. Finally, to determine if lifetime drink amount was related to Faces II performance at Time Point 2, we correlated these two variables and the correlation was not significant, r = –.194, p = .19.

Table 4. Mixed effects linear regression model predicting decline in delayed facial recognition

	Coefficient	*SE*	*z*	*p*
Faces II				
Group	.276	1.39	.20	.843
Age	–.349	.191	–1.83	.068
Education	.127	.284	.45	.656
Time	2.59	1.04	2.49	.013
Group ×Time	–4.98	1.41	–3.54	.000
Group × Age	.301	.279	1.08	.281
Age × Time	–.001	.185	–.01	.996
Group × Age × Time	.016	.272	.06	.952
Constant	35.00	4.79	7.31	.000

DISCUSSION

The major findings of this study are as follows. First, participants with PTSD showed a significant decline in measures of delayed visual recall and recognition during the 2–5 year interval of the study. Second, decline in delayed facial recognition was significantly greater for veterans with PTSD compared to veterans without PTSD. Third, veterans with PTSD did not demonstrate any improvement in PTSD symptom severity over time, and change in PTSD symptomatology was not associated with change in neurocognitive performance. Fourth, there was no effect of age on memory decline, suggesting that longitudinal decline in the PTSD+ group was not attributable to advancing age.

The decline in the PTSD+ group on measures of delayed visual recognition and recall (Faces II and Family Pictures II), and a greater decline in delayed facial recognition compared to the PTSD– group, are noteworthy in light of the multitude of cross-sectional studies that have not demonstrated visual memory impairments related to PTSD (see Danckwerts & Leathem, 2003, for a review). Besides our two earlier studies, which did not show differences between veterans with and without PTSD on Faces I or II (Neylan et al., 2004; Samuelson et al., 2006), only two other studies, to our knowledge, have examined facial recognition for

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emotionally neutral faces in patients with PTSD. The first study, conducted with sexual assault survivors (Islam-Zwart, Heath, & Vik, 2005), showed a positive correlation between PTSD severity and immediate, but not delayed, facial recognition. The authors surmised that hypervigilance may enhance attention for novel stimuli, particularly in sexual assault survivors who may be attuned to perceived threats of others, but that repeated exposure habituated the women to the stimuli. In an fMRI investigation of memory encoding, Dickie, Brunet, Akerib, and Armony (2008) found PTSD symptom severity to be correlated with reduced facial recognition performance in patients with a variety of trauma histories. In addition, higher CAPS scores were associated with reduced activity in the ventral medial prefrontal cortex (vmPFC), elicited when faces were forgotten by the participants. Coupled with our nonsignificant trend findings of working-memory decline in PTSD+ participants, also implicated in the PFC (Baddeley, 1986; Smith & Jonides, 1996), our results of facial recognition decline add to the growing body of literature linking PTSD to structural (Bremner et al., 2003; Geuze, Vermetten, Ruf, DeKloeet, & Westenberg, 2007) and neurobiological (Southwick, Rasmusson, Barron, & Arnsten, 2005) abnormalities in frontal regions.

Although we found a group × time interaction on Faces II performance, we did not find a group × age × time interaction on any of the neuropsychological variables, suggesting that the decline in performance is not a result of an interaction of PTSD and aging, or indicative of a linearly accelerated aging process for middle-aged veterans. In contrast, Yehuda et al. (2006) found a relationship between age and verbal memory performance that was greater for Holocaust survivors with PTSD than for survivors without PTSD, which was indicative of an age-accelerated decline for older patients with PTSD. Three important variable distinctions between the two samples are trauma type, education, and age. First, there may be additional risk factors associated with being a Holocaust survivor that contribute to the group × age interaction, that are not observed with veterans. Second, the present sample had high levels of education (almost 16 years) relative to the larger cohort of veterans from which they were drawn, and from the veteran population (Holder, 2007). In contrast, the Holocaust survivors from the Yehuda et al. sample had an average of 14 years of education. The cognitive reserve hypothesis has been confirmed in multiple studies documenting that higher education delays the onset of age-accelerated memory decline (e.g., Hall et al., 2007). It may be that age-accelerated declines would be evident in veterans with lower levels of education; this hypothesis should be examined in future longitudinal studies with veterans. Finally, the studies are examining cognitive decline in different age groups. With the present, middle-aged sample, we would not necessarily expect an interaction between age and PTSD, as memory decline typically begins after the age of 60 (Hultsch, Hertzog, Dixon, & Small, 1998). However, because some studies have also documented memory decline beginning in the 50s (Albert, Heller, & Milberg, 1987; Crook & West, 1990), the hypothesis was necessary to test with this age group. The absence of a group × age × time interaction is consistent with several studies of middle-aged and "young-old" (50s and 60s) patients with depression (Boone et al., 1994; Fossati, Coyette, Ergis, & Allilaire, 2002; Lyness, Eaton, & Schneider, 1994).

Findings of cognitive decline in patients with chronic PTSD may be associated with neuroanatomical changes in the PFC and hippocampus. For example, if PTSD is conceptualized as a sustained state of arousal, it is possible that prolonged abnormalities in the neurotransmitter systems associated with arousal in the PFC (e.g., noradrenergic and serotonin systems) could lead to a worsening over time in functioning in areas implicated in the PFC, including facial recognition and working memory. However, support for this hypothesis would likely be found through a relationship between time since trauma exposure and change in memory performance. We would expect veterans who have endured the consequences of trauma longer to show a greater effect of prolonged neurotransmitter dysfunction, and thus greater memory impairment. We failed to find this relationship, although this may be a result of the small sample size when examining the PTSD+ group separately, as well as the limited variability in the time since exposure variable, with 70% of our sample having experienced their trauma between 30 and 35 years prior to the follow-up assessment.

Yehuda et al. (2006) found that improved performance on the CVLT was associated with PTSD symptom improvement, but we did not replicate this finding. One reason for this discrepancy is that our participants did not show deficits in CVLT performance, or any other memory variables, at baseline, with both groups demonstrating unimpaired performance. Thus, we would not necessarily expect to see an improvement in CVLT performance (e.g.,, from average to above average performance) related to PTSD symptom improvement. In addition, in the Yehuda et al. sample, there was a significant improvement in PTSD symptom severity in the PTSD+ group, with 29% of the participants no longer holding a PTSD diagnosis at follow-up. Our sample consisted of veterans with chronic, primarily combat-related PTSD who did not show a significant improvement in PTSD symptoms over time. In fact, none of the participants' PTSD remitted, with all of the veterans sustaining diagnoses of either full or partial (two out of three symptom clusters) PTSD at follow-up.

In summary, although we found a decline over time in delayed facial recognition for veterans with PTSD compared to veterans without PTSD, the decline does not appear to result from an interaction of PTSD and advancing age, or neurotoxicity effect of PTSD, or any changes in symptom severity in the PTSD+ group. One possible explanation for this finding, which cannot be adequately answered with the present data, concerns the political climate during the time of follow-up testing. The veterans completed their follow-up assessments between November, 2001 and 2004, a challenging period in history for war veterans, who were likely reminded of their own war experiences following the World Trade Center attacks of 9/11 and the United States' subsequent

military involvement in Afghanistan and Iraq. As the visual memory functioning of veterans with PTSD declined during this period of time relative to performance pre-9/11, it is possible that this decline may be related to these triggers. Further research is needed to test the hypothesis of neuropsychological functioning change in veterans following current event triggers.

Several limitations of the current study should be noted. Sampling bias is often a problem in longitudinal studies, in which nonrandom attrition is amplified at follow-up. Compared to veterans who participated at baseline, veterans who participated at follow-up were more educated, had higher Vocabulary and Digit Span scores, and were older. Other studies have documented sampling bias in longitudinal studies in which nonparticipation at follow-up is related to having fewer years of education (Eaton, Anthony, Tepper, & Dryman, 1992; Jacomb, Jorm, Korten, Christensen, & Henderson, 2002) and lower IQ (Schaie, Labouvie, & Barrett, 1973; Jacomb et al., 2002). Studies of longitudinal neuropsychological functioning in particular can be biased when the sample is skewed toward the more educated and higher intellectual functioning participants. As the veterans in this study averaged almost 16 years of education and exhibited higher cognitive functioning than our initial sample, these findings might not be generalizable to the veteran population. In addition, differences in memory functioning between groups at both time points may have been harder to detect with this higher functioning sample, and as described earlier, findings of an age-accelerated decline may be harder to detect in a more highly educated sample. Finally, some of the nonsignificant trend findings, suggesting a decline in immediate facial recognition and working memory for veterans with PTSD, may have reached significance with subjects whose education levels and intellectual functioning were more representative of the veteran population.

Other sampling limitations of the study include the small sample size, with limited power to detect differences between groups. Approximately half of the veterans in this sample participated in a study where no memory differences were found between veterans with and without PTSD (Neylan et al., 2004). These participants constituted a sizeable subgroup of the full baseline sample for the current study, in large measure explaining why we did not find significant differences in the present sample on any memory variables at baseline. Findings of longitudinal decline may be more likely in a sample in which there were initial, cross-sectional differences. However, this limitation of our sample makes the findings of longitudinal decline in performance even more striking: These veterans, as a group, did not exhibit deficits in facial recognition at baseline, but showed an accelerated decline in performance over two to five years.

As Vietnam veterans are aging, there is a continued need to understand the ongoing impact of PTSD on neurocognitive functioning. Veterans Administration clinicians in particular will benefit from a better understanding of the links between PTSD, age, and memory, and can help their patients anticipate and prepare for changes in functioning. Areas for future research include studying Vietnam veterans into their 60s and 70s, to determine if there is an age-accelerated decline in an older sample similar to that seen in Holocaust survivors (Yehuda et al., 2006), and examining longitudinal decline in younger trauma survivors. Finally, longitudinal studies examining the trajectory of PTSD symptom change and neurocognitive change is needed to determine if neurocognitive impairment is yoked to PTSD, or if performance improves when PTSD remits.

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