INTRODUCTION

The idea that the hippocampus contributes to declarative memory is a marquee finding of human neuropsychology; thus, it is natural to hypothesize that if PTSD patients have smaller hippocampi, and impaired declarative memory, then the two must be related. After all, a very strong confirmatory example is supplied by senile dementia of the Alzheimer’s type (SDAT). Since the 1990s, numerous studies have reported significant correlations between hippocampal volume and declarative memory performances in SDAT (Laakso et al., 1995; Soininen et al., 1994) and also in minimally impaired elderly people (Convit et al., 1995; Zimmerman et al., 2008). Even a strongly disconfirmatory study, such as that of Marquis, which failed to find hippocampal volume and paragraph memory correlation in 108 older adults, many of whom progressed to dementia (Marquis et al., 2002), cannot dent our faith in the underlying relationship. The role of the hippocampus in memory, the histopathologically confirmed degeneration of that structure, combined with profound memory loss in SDAT, together constitute an unchallengeable framework. But unlike in SDAT, the memory impairments of PTSD are not profound. This is evidenced not only by the Brewin meta-analysis that found only a modest effect size for verbal memory (Brewin, Kleiner, Vasterling, & Field, 2007). Memory loss is not among the diagnostic criteria for PTSD (the C3 symptom is specific to the circumstances of trauma), is generally absent from self-report psychodiagnoses in this field, and is rarely, if ever, a focus of treatment. At the same time, hippocampal functionality has additional facets of potential relevance to PTSD. These include spatial/contextual processing (Bilkey, 2007; Fortin...
et al., 2008; Lang et al., 2009) and perhaps subservient to these, configural cue processing (Gilbertson et al., 2007). There is a danger that such alternative avenues for understanding the hippocampus in PTSD could be under-researched to the extent that a declarative memory framework is overvalued.

This article asks whether the framework that has been so successful in understanding SDAT should be applied to PTSD. In our view, strong tests of that framework are predicated on the presence of main effects of a PTSD diagnosis on both hippocampal structure and declarative memory performance. Employing these requirements, we have reviewed studies in the Karl meta-analysis of hippocampal findings in PTSD (Karl et al., 2006) and five studies published since then (Bonne et al., 2008; Bossini et al., 2008; Pavic et al., 2007; Tischler et al., 2006; Yehuda et al., 2007). Among those 26 studies, 16 reported a smaller hippocampal volume and declarative memory performances did not demonstrate effects of PTSD-positive and PTSD-negative groups (cf. Woodward, Kaloupek, Streeter, Martinez et al., 2006a; Woodward, Kaloupek, Streeter, Martinez et al., 2006b). Two subjects were excluded because of an imaging artifact that disrupted cortical sheet extraction, and two because of the loss of testing data. PTSD was diagnosed and its severity estimated using the Clinician-Administered PTSD Scale (CAPS, Blake et al., 1997). Assessments of mood status, psychosis and associated symptoms, alcohol and substance use disorders, and anxiety disorders were performed using the Structured Clinical Interview for the *DSM-IV* (First, Spitzer, Gibbon, & Williams, 1995). Also administered were the Combat Exposure Scale (Keane et al., 1989), Life Events Checklist (LEC, Blake et al., 2000), Mississippi Scale for Combat-related PTSD (MISS, Keane, Caddell, & Taylor, 1988), Beck Depression Inventory (BDI, Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), and Michigan Alcohol Screening Test – Short Form (SMAST, Selzer, 1971). Eighty-four subjects also underwent a structured interview to determine whether LEC-elicited trauma endorsements fulfilled PTSD Criterion A1 and A2 and when they occurred.

**Participants**

All 95 final participants were combat veterans of the Vietnam or Persian Gulf wars. All were free of acute medical disease, current substance abuse/dependence (abstinent more than six months), central nervous system (CNS) disease, and psychosis. PTSD-positive (PTSD+) participants met criteria as a result of experiencing one or more military traumas, but some also experienced civilian traumas before or after their military service. PTSD-negative (PTSD−) participants had never met criteria for PTSD as a result of military or civilian trauma. Table 1 presents selected subsample means. Noteworthy among them, the combat exposure scale (CES), and CAPS scores indicate that the PTSD+ subsample was heavily combat-exposed and severely symptomatic. They were also severely dysphoric, as indexed by mean BDI scores greater than 20. Of the PTSD+ participants, 75% also met criteria for current major depressive disorder (MDD) versus 4% of PTSD− participants, while for lifetime MDD the corresponding rates were 85% and 22%. Among subjects with histories of alcohol abuse/dependence (ETOH), those with PTSD had begun drinking, on average, 4.7 years earlier than those without PTSD (20.7 vs. 25.4 years, respectively). Participants were maintained on their psychotropic medications. In line with their symptomatic status, 69% of the PTSD+ participants were taking

**METHODS**

**Screening and Psychiatric Assessment**

Participants provided written informed consent in accordance with the procedures of the Institutional Review Boards of Stanford University Medical School/VA Palo Alto HCS or Boston VA Medical Center and the McLean Hospital. Recruitment and screening of this sample at two sites was described in detail in a prior publication (Woodward, et al., 2006a; Woodward, Kaloupek, Streeter, Martinez et al., 2006b). Two subjects were excluded because of an imaging artifact that disrupted cortical sheet extraction, and two because of the loss of testing data. PTSD was diagnosed and its severity estimated using the Clinician-Administered PTSD Scale (CAPS, Blake et al., 1997). Assessments of mood status, psychosis and associated symptoms, alcohol and substance use disorders, and anxiety disorders were performed using the Structured Clinical Interview for the *DSM-IV* (First, Spitzer, Gibbon, & Williams, 1995). Also administered were the Combat Exposure Scale (Keane et al., 1989), Life Events Checklist (LEC, Blake et al., 2000), Mississippi Scale for Combat-related PTSD (MISS, Keane, Caddell, & Taylor, 1988), Beck Depression Inventory (BDI, Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), and Michigan Alcohol Screening Test – Short Form (SMAST, Selzer, 1971). Eighty-four subjects also underwent a structured interview to determine whether LEC-elicited trauma endorsements fulfilled PTSD Criterion A1 and A2 and when they occurred.

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psychotropic medications versus 11% of PTSD– participants. Forty-four percent of the PTSD+ participants, 44% were taking selective serotonin reuptake inhibitors versus only 4% of PTSD– participants. Twenty-one percent of PTSD+ participants were taking anticonvulsant/mood-stabilizing medications, whereas no PTSD– participants were taking medications from this class.

Procedures
Participants arrived at the laboratory at approximately 0800. Structured psychodiagnostic interviews, self-report psychometrics, and baseline memory and cognitive testing required approximately four hours including breaks. After lunch, participants were prepared for psychophysiological recording (electroencephalogram, electro-oculogram, facial electromyogram, electrocardiogram, abdominal respiration, electrodermal activity). They then underwent two administrations of the Trier Social Stress Test (TSST, Kirschbaum, Wolf, May, Wippich, & Hellhammer, 1996) separated by a 40-minute rest period. After each TSST, declarative memory was assessed and a brief “oddball” event-related potential protocol was administered. After the completion of laboratory testing, participants were transported to the magnetic resonance imaging (MRI) laboratories for neuroimaging.

Verbal declarative memory was assessed at baseline using the Logical Memory (LM) subtest of the Wechsler Memory Scale-III (WMS-III, Wechsler, 1997) and the Hopkins Verbal Learning Test (HVLT, Brandt, 1991). Visual declarative memory was assessed using the Rey-Osterrieth Complex Figure Test (ROCFT) (Osterrieth, 1944; Rey, 1941; Spreen & Strauss, 1991) and the Rey Visual Design Learning Test (RVDLT, see Spreen & Strauss, 1991). The baseline assessment also included administrations of the Vocabulary subtest (VOCAB) and Digit Symbol Substitution (DSS) subtest of the Wechsler Adult Intelligence Test-III (WAIS-III, Psychological Corporation, 1997). After each administration of the TSST, the HVLT and the RVDLT were repeated using equivalent forms.

Table 1. Study matrix coding the presence/absence of the features of a “strong test” of the proposition that hippocampal volume and declarative memory capacity are directly correlated in PTSD as they are in SDAT

<table>
<thead>
<tr>
<th></th>
<th>Smaller hippocampus</th>
<th>Relative declarative memory impairment</th>
<th>Hippocampal volume and declarative memory correlated</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bremner 1995</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Gurvits 1996</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bremner 1997</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Stein 1997</td>
<td>1</td>
<td>NR</td>
<td>0</td>
<td>memory results reported later</td>
</tr>
<tr>
<td>De Bellis 1999</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bonne 2001</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>De Bellis 2001</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Schuff 2001</td>
<td>0</td>
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<td>0</td>
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<tr>
<td>De Bellis 2002</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Fenemma-Notestine 2002</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Gilbertson 2002</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>tested implicit memory</td>
</tr>
<tr>
<td>Lindauer 2002</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
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<td>Villarreal 2002</td>
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<td>0</td>
<td></td>
</tr>
<tr>
<td>Bremner 2003</td>
<td>1</td>
<td>NR</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hedges 2003</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
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<td>Pederson 2004</td>
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<td>0</td>
<td>NR</td>
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<td>Shin 2004</td>
<td>1</td>
<td>0</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Wignal 2004</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Winter 2004</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
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<tr>
<td>Vythilingham 2005</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Tischler 2006/Yehuda 2007</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pavic 2007</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Bonne 2008</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Bossini 2008</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Weniger 2008</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>trauma-related DID</td>
</tr>
</tbody>
</table>

Note. Studies are those meta-analyzed in Karl et al (2006) plus five relevant studies published later. A “1” or a “0” indicates the proposition heading the column was tested, a “1” indicates a positive finding, a “0”, indicates a negative finding. NR indicates that the data were reportedly available for a test, but the test was not performed or was not reported. Weniger et al (2008) is included for completeness, but considered trauma-related dissociative identity disorder not PTSD.
Image Acquisition and Processing

Magnetic resonance (MR) images of subjects’ brains were acquired with 1.5T GE Signa II systems located near each study site (Diagnostic Radiology Center of Veterans Affairs, Palo Alto Health Care System and the Brain Imaging Center of McLean Hospital, Belmont, MA). Coronal images were acquired with a 3D spoiled-gradient recalled (SPGR) volumetric pulse sequence (TR = 35 ms, TE = 6 ms, flip angle = 45°, NEX = 1, matrix size = 256 × 192, field of view = 24 cm², slice thickness = 1.5–1.7 mm, slices = 124.)

This article considers brain structural indices obtained through two independent MR image analysis methods. Volumes of the hippocampus were obtained using manual tracing in accordance with the methods of the Stanford Psychiatry Neuroimaging Laboratory (Kates, Abrams, Kaufmann, Breiter, & Reiss, 1997; Reiss et al., 1998; Woodward, et al., 2006a). Image optimizations promoted accurate and reliable delineation of the hippocampal cross-sections on each slice. The anterior limit of the hippocampus was defined by the hippocampal sulcus or alveus, and the posterior limit by the fusion of the fornix with the splenium. Manual delineation was performed by a single rater (W.K.S.), trained to criterion within the Stanford Psychiatry Neuroimaging Laboratory, and blinded to participant identity and diagnosis. This processing protocol also produced various lobar tissue volume estimates via projection to and parcellation in Talairach space (Talairach & Tournoux, 1988). We have observed trends for these macro-volumes to be smaller in the PSTD+ participants with histories of ETOH. PTSD was strongly associated with mild reduction LM performance relative to those without PTSD, F(1, 92) = 4.27, p < .05, partial η² = 0.053, with lower VOCAB performance observed in participants with lifetime ETOH (ETOH+: F(1, 39) = 18.7, p < .001; ETOH–: F(1, 50) = 0.42, ns). VOCAB also exhibited a main effect of PTSD, F(1, 92) = 14.2, p < .001, partial η² = 0.136. The effect of ETOH was also significant, F(1, 90) = 5.07, ns, partial η² = 0.053, with lower VOCAB performance observed in participants with histories of ETOH. PTSD was strongly associated with lower DSS scores, F(1, 92) = 33.0, p < .001, partial η² = 0.268; however, unlike VOCAB, DSS exhibited no effect of ETOH and no interaction of PTSD and ETOH (Fs < 1). The size of the PTSD effect on DSS was similar in ETOH+ and ETOH– subgroups (partial η² = 0.275 vs. 0.285).

RESULTS

Cognition

WAIS VOCAB and DSS were compared over groups using analyses of covariance (ANCOVAs) covarying for age. VOCAB exhibited an interaction between PTSD and ETOH (F(1, 90) = 8.44, p < .01, partial η² = 0.086) related to the fact that the effect of PTSD (lower scores associated with PTSD) was only significant in participants with lifetime ETOH (ETOH+: F(1, 39) = 18.7, p < .001; ETOH–: F(1, 50) = 0.42, ns). VOCAB also exhibited a main effect of PTSD, F(1, 92) = 14.2, p < .001, partial η² = 0.136. The effect of ETOH was also significant, F(1, 90) = 5.07, ns, partial η² = 0.053, with lower VOCAB performance observed in participants with histories of ETOH. PTSD was strongly associated with lower DSS scores, F(1, 92) = 33.0, p < .001, partial η² = 0.268; however, unlike VOCAB, DSS exhibited no effect of ETOH and no interaction of PTSD and ETOH (Fs < 1). The size of the PTSD effect on DSS was similar in ETOH+ and ETOH– subgroups (partial η² = 0.275 vs. 0.285).

Regional Brain Volumes

The reader is directed to our prior publications for detailed presentations of the differences we have found between PTSD+ and PTSD– participants in this sample. In those studies, hippocampal tissue (gray + white) volume, parahippocampal cortical volume, and total cerebral cortical volume have all been shown to be smaller in the PTSD+ relative to the PTSD– participants (Woodward, et al., 2006a; Woodward et al., in press).

Memory

Table 2 presents means and standard deviations of the memory variables considered in this study. Baseline performance on the LM subtest of the WMS-III was analyzed for associations with PTSD and lifetime alcoholism (ETOH) using repeated-measures ANCOVA covarying for age and VOCAB. A within-subjects factor of recall trial contrasted immediate versus delayed recall. Participants with PTSD exhibited mildly reduced LM performance relative to those without PTSD, F(1, 89) = 4.27, p < .05, partial η² = 0.046. Although subjects’ performances declined nominally at recall, the
Recall trial did not approach significance ($F < 1$). Recall trial also did not interact with PTSD, ETOH, or their interaction. Similarly, neither ETOH, $F(1, 89) = 1.65$, $ns$, nor the PTSD $\times$ ETOH interaction ($F < 1$) influenced overall LM performance. Baseline performance on the ROCFT, analyzed in a similar fashion, exhibited the expected effect of trial [copy vs. recall: $F(1, 90) = 12.2$, $p < .001$], and a main effect of PTSD, $F(1, 89) = 6.9$, $p < .01$, partial $\eta^2 = 0.072$. There was no effect of ETOH and no interactions.

Performances on the HVLT and the RVDLT were analyzed using repeated-measures ANCOVAs, covarying for age and VOCAB. The within-subjects factor, session, had three levels contrasting baseline, post-TSST1, and post-TSST2 administrations. Thus, the session factor incorporated the impact of the TSST on subsequent verbal memory and visual declarative memory performances. For both, total learning and percent retention were analyzed separately. HVLT total learning exhibited a modest effect of PTSD, $F(1, 89) = 5.89$, $p < .05$, partial $\eta^2 = 0.062$. There was no effect of ETOH, $F(1, 89) = 1.63$, $ns$, partial $\eta^2 = 0.018$, and no PTSD $\times$ ETOH interaction, $F(1, 89) = 0.731$, $ns$, partial $\eta^2 = 0.008$. The effect of session was not significant, Wilks’ Lambda = 0.974, $F(2, 88) = 1.16$, $ns$. HVLT percent retention exhibited a significant interaction of PTSD, ETOH, and Session, Wilks’ Lambda = 0.900, $F(2, 88) = 4.89$, $p < .01$, partial $\eta^2 = 0.10$. Underlying this three-way interaction was a difference between PTSD+ and PTSD− subgroups as to the presence of an ETOH $\times$ Session interaction. This two-way interaction was significant only in PTSD+ participants, Wilks’ Lambda = 0.842, $F(2, 43) = 4.89$, $p < .01$, partial $\eta^2 = 0.158$, among whom HVLT percent retention diverged on the third (post-TSST2) trial as a function of ETOH. That is, for PTSD+/ETOH+ participants, HVLT retention dropped precipitously at post-TSST2 (96%, 91%, 82%, respectively), whereas for PTSD+/ETOH− participants, it improved relative to post-TSST1 (91%, 87%, 94%, respectively). There were no additional group effects or interactions influencing HVLT percent retention. RVDLT performances exhibited no significant main effects or interactions.

### Covariations Among Regional Brain Volumes and Memory Performances

Table 3 presents zero-order correlations between the regional brain volumes and memory performances considered in this study. Also included are HVLT and RVDLT total learning pre-/post-stress change scores. All variables exhibited normal distributions, supporting the use of parametric Pearson product-moment correlations. Review of bivariate plots confirmed that no correlation was artifactually amplified or attenuated by outliers or range restriction. By far, the strongest correlation was between PTSD and WM volume ($r = -0.45$, $p < .01$).

### Table 3: Raw means and standard deviations of memory performance variables

<table>
<thead>
<tr>
<th></th>
<th>PTSD+</th>
<th>ETOH</th>
<th>PTSD−</th>
<th>ETOH</th>
</tr>
</thead>
<tbody>
<tr>
<td>LM total learning</td>
<td>27.9</td>
<td>5.7</td>
<td>32.8</td>
<td>5.5</td>
</tr>
<tr>
<td>LM delayed recall</td>
<td>23.6</td>
<td>7.3</td>
<td>27.7</td>
<td>7.2</td>
</tr>
<tr>
<td>HVLT total learning</td>
<td>26.3</td>
<td>4.1</td>
<td>28.6</td>
<td>3.7</td>
</tr>
<tr>
<td>HVLT retention</td>
<td>0.92</td>
<td>0.12</td>
<td>0.93</td>
<td>0.13</td>
</tr>
<tr>
<td>ROCFT copy</td>
<td>60</td>
<td>7.3</td>
<td>63.4</td>
<td>7.5</td>
</tr>
<tr>
<td>ROCFT recall</td>
<td>30.6</td>
<td>13.3</td>
<td>36.9</td>
<td>10.9</td>
</tr>
<tr>
<td>RVDLT total learning</td>
<td>9.4</td>
<td>2.9</td>
<td>10.6</td>
<td>2.7</td>
</tr>
<tr>
<td>RVDLT retention</td>
<td>0.89</td>
<td>0.29</td>
<td>0.97</td>
<td>0.13</td>
</tr>
<tr>
<td>HVLT change (trial 2 - trial 1)</td>
<td>0.6</td>
<td>3.9</td>
<td>−0.2</td>
<td>4.1</td>
</tr>
<tr>
<td>RVDLT change (trial 2 - trial 1)</td>
<td>0.3</td>
<td>3.8</td>
<td>−0.3</td>
<td>3.7</td>
</tr>
</tbody>
</table>
### Table 4.
Pearson product-moment correlations between regional brain volumes implicated in declarative memory and memory performances computed over all 95 subjects.

<table>
<thead>
<tr>
<th>Brain Volume</th>
<th>LM total learning</th>
<th>LM total retention</th>
<th>RVDLT total learning</th>
<th>RVDLT total retention</th>
<th>ROCFT learning</th>
<th>ROCFT recall</th>
<th>HVLT total learning</th>
<th>HVLT total recall</th>
<th>HVLT learning change</th>
<th>HVLT retention change</th>
<th>RVDLT learning change</th>
<th>RVDLT retention change</th>
<th>ROCFT learning change</th>
<th>ROCFT recall change</th>
<th>HVLT total learning change</th>
<th>HVLT total recall change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left hippocampal tissue volume</td>
<td>0.020</td>
<td>-0.073</td>
<td>0.093</td>
<td>0.207</td>
<td>0.152</td>
<td>0.152</td>
<td>0.091</td>
<td>-0.091</td>
<td>0.009</td>
<td>-0.120</td>
<td>0.091</td>
<td>0.091</td>
<td>0.024</td>
<td>0.075</td>
<td>0.012</td>
<td>0.009</td>
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<tr>
<td>Right hippocampal tissue volume</td>
<td>0.032</td>
<td>0.142</td>
<td>0.057</td>
<td>0.120</td>
<td>0.165</td>
<td>0.165</td>
<td>0.054</td>
<td>0.080</td>
<td>0.080</td>
<td>-0.099</td>
<td>0.068</td>
<td>0.048</td>
<td>0.032</td>
<td>0.048</td>
<td>0.009</td>
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<tr>
<td>Left parahippocampal gyrus</td>
<td>0.135</td>
<td>-0.014</td>
<td>0.032</td>
<td>0.137</td>
<td>0.095</td>
<td>0.095</td>
<td>0.021</td>
<td>0.032</td>
<td>0.021</td>
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<td>Right parahippocampal gyrus</td>
<td>0.192</td>
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<td>0.032</td>
<td>0.137</td>
<td>0.095</td>
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<td>0.003</td>
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<tr>
<td>Left hemisphere cortical volume</td>
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<td>0.077</td>
<td>0.083</td>
<td>0.159</td>
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<tr>
<td>Right hemisphere cortical volume</td>
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<td>0.159</td>
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<tr>
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<td>0.032</td>
<td>0.057</td>
<td>0.120</td>
<td>0.165</td>
<td>0.165</td>
<td>0.054</td>
<td>0.080</td>
<td>0.080</td>
<td>-0.099</td>
<td>0.068</td>
<td>0.048</td>
<td>0.032</td>
<td>0.048</td>
<td>0.009</td>
<td>0.009</td>
</tr>
<tr>
<td>Right parahippocampal cortex volume</td>
<td>0.032</td>
<td>0.142</td>
<td>0.057</td>
<td>0.120</td>
<td>0.165</td>
<td>0.165</td>
<td>0.054</td>
<td>0.080</td>
<td>0.080</td>
<td>-0.099</td>
<td>0.068</td>
<td>0.048</td>
<td>0.032</td>
<td>0.048</td>
<td>0.009</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Note: Some variables represent the ratio of a subvolume to a whole brain index in an effort to remove variance associated with body size. One, two, or three asterisks indicate nominal significance at \(p < 0.05, 0.01, \text{and} \ 0.001\), respectively. Boldface indicates correlations exceeding significance after Bonferroni correction for multiple comparisons (\(\alpha = 0.05/80 = 0.000625\)).
memory performances were given ample opportunity to mary, linear covariation between regional brain volumes and intelligence. Relationships between hippocampal volume performance, though in biologically plausible directions, were Correlations involving the verbal memory, such as LM per-
sample (cf. Andreasen et al., 1993; Woodward et al., in press).
was moderately correlated with total cortical volume in this
reported previously that verbal IQ, as estimated by VOCAB,
chance levels, given the number of tests performed. We have
only correlations with magnitudes comfortably exceeding
structural-functional relationships associating fi gure copy-
ing and regional brain volumes; nevertheless, these were the
the only correlations with magnitudes comfortably exceeding
chance levels, given the number of tests performed. We have
reported previously that verbal IQ, as estimated by VOCAB, was
moderately correlated with total cortical volume in this
sample (cf. Andreasen et al., 1993; Woodward et al., in press).
Correlations involving the verbal memory, such as LM per-
formance, though in biologically plausible directions, were
substantially smaller, and likely mediated in part by verbal
intelligence. Relationships between hippocampal volume and stressor effects on memory were wholly absent. In sum-
mary, linear covariation between regional brain volumes and
memory performances were given ample opportunity to emerge, but did not do so in a convincing fashion.

Although this appears to be a relatively strong negative result, it is clearly not definitive. As always, sampling error
could have accounted for our failure to observe stronger re-
lationships between hippocampal volume, other regional
volumes, and memory performances. While the neuropa-
thology and memory loss characteristic of SDAT provide a
strong example, Sapolsky has noted that no clear links exist
between stress-related cellular adaptations in the hippocam-
pus and its gross volume (Sapolsky, 2000). Hippocampal
cell loss in SDAT is relatively generalized (Simic, Kostovic,
Winblad, & Bogdanovic, 1997). In contrast, stress-related
impacts on apical dendritic remodeling are specific to CA3,
while those on neurogenesis are specific to the dentate gyrus
(Gould & Tanapat, 1999). These structures each comprise
only a fraction of the hippocampal cross-section. If the im-
 pact of dentate atrophy on the volume of the hippocampus
was proportional, and the dentate contributed 20% of the
hippocampal cross-section, a halving of the dentate would
be required to produce only a 20% decrease in the parent
structure. It is also germane here that glucocorticoid-driven
depletion of mitochondria (Coburn-Litvak et al., 2004) and
synaptic numbers (Tata, Marciano, & Anderson, 2006) have
been observed in rat hippocampus in the absence of smaller
volume.

These considerations may guide us back to the common
finding that the declarative memory deficits of nonelderly
persons with PTSD are relatively modest (Brewin et al., 2007; cf. Golier, Harvey, Legge, & Yehuda, 2006; Yehuda, Golier, Tischler, Stavitsky, & Harvey, 2005). In this study, by
comparison, we observed an effect of PTSD on the WAIS
DSS subtest more than twice as large as those on LM or
HVLT. Samuelson also observed DSS performance (along
with Letter-Number Sequencing and Digit Span) to exhibit
strong effects of PTSD in the absence of significant effects
on LM (Samuelson et al., 2006). The origins of these asso-
ciations deserve further attention, and provide further support
for casting a wide net in our efforts to document the
neurocognitive deficits of PTSD. Findings from emotional
Stroop tasks (McNally, 1998; Metzger, Orr, Lasko, McNally,
& Pitman, 1997; Vythilingam et al., 2007) suggest that func-
tional cognitive impairments in PTSD may lie preferentially
at the interface with fear- and other trauma-related affects;
however, Stroop tasks test only word reading. Novel assess-
ments of the cognition-affect interface could borrow from
the PTSD literature methods for safely inducing mood states
and cognitive sets hardening back to the conditions of traum-
atzation. Although such procedures might pose challenges
to face-to-face neuropsychological assessment, they may be
compatible with computer-based assessments such as
the Automated Neuropsychological Assessment Metrics
cf. Vasterling et al., 2006).

In conclusion, a review of the existing literature relating
hippocampal volume to memory performance in PTSD, and
an extended re-examination of that relationship in a larger
sample, appear to be in agreement. The strong example of
SDAT may not be heuristic in this disorder, and alternative
perspectives on the function of the hippocampus and related
structures may be more revealing.

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