Male veterans with PTSD exhibit aberrant neural dynamics during working memory processing: an MEG study

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Background: Posttraumatic stress disorder (PTSD) is associated with executive functioning deficits, including disruptions in working memory. In this study, we examined the neural dynamics of working memory processing in veterans with PTSD and a matched healthy control sample using magnetoencephalography (MEG). **Methods:** Our sample of recent combat veterans with PTSD and demographically matched participants without PTSD completed a working memory task during a 306-sensor MEG recording. The MEG data were preprocessed and transformed into the time-frequency domain. Significant oscillatory brain responses were imaged using a beamforming approach to identify spatiotemporal dynamics. **Results:** Fifty-one men were included in our analyses: 27 combat veterans with PTSD and 24 controls. Across all participants, a dynamic wave of neural activity spread from posterior visual cortices to left frontotemporal regions during encoding, consistent with a verbal working memory task, and was sustained throughout maintenance. Differences related to PTSD emerged during early encoding, with patients exhibiting stronger α oscillatory responses than controls in the right inferior frontal gyrus (IFG). Differences spread to the right supramarginal and temporal cortices during later encoding where, along with the right IFG, they persisted throughout the maintenance period. **Limitations:** This study focused on men with combat-related PTSD using a verbal working memory task. Future studies should evaluate women and the impact of various traumatic experiences using diverse tasks. **Conclusion:** Posttraumatic stress disorder is associated with neurophysiological abnormalities during working memory encoding and maintenance. Veterans with PTSD engaged a bilateral network, including the inferior prefrontal cortices and supramarginal gyri. Right hemispheric neural activity likely reflects compensatory processing, as veterans with PTSD work to maintain accurate performance despite known cognitive deficits associated with the disorder.

Introduction

Posttraumatic stress disorder (PTSD) is a psychiatric disorder characterized by re-experiencing, avoidance, negative alterations in mood and cognition, and physiologic arousal symptoms, which may develop subsequent to a traumatic event (e.g., combat).^{1,2} The lifetime prevalence of PTSD in the United States is roughly 7%–9%;^{3,4} however, prevalence rates among recent combat veterans are estimated at 13%–22%.^{5,6} Previous studies have demonstrated that patients with PTSD experience deficits in memory, attention and executive functioning.^{7–9} More specifically, a recent meta-analysis of 60 neurocognitive studies comparing patients with PTSD to healthy controls (4108 participants) found the largest effect sizes reflecting deficiencies in the PTSD group for verbal learning, information processing speed and attention/working memory.¹⁰ The etiol-

ogy of these functional deficits is not entirely clear, but they do appear to be contributing factors to PTSD symptomatology.^{11,12}

Working memory is an essential component of information processing and is typically divided into 3 cognitive subprocesses: encoding, maintenance and retrieval.¹³ Studies using functional magnetic resonance imaging (fMRI) and positron emission tomography¹⁴ have identified the network architecture serving working memory processing in healthy adults. Critical brain regions include the prefrontal cortex, superior parietal lobule and adjacent areas, lateral occipital regions, cerebellum, and the left supramarginal gyrus and contiguous temporal regions.^{14,15} While such studies elucidate brain regions responsible for general working memory function, they rely on indirect measures of brain activity (e.g., local blood oxygenation), making it difficult to dissociate which areas are active during each phase of working memory.

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Brain imaging studies using methods with greater temporal specificity, such as electroencephalography (EEG) and magnetoencephalography (MEG), have begun to fill this void by characterizing the inherent dynamics of working memory processing (e.g., maintenance phase), and many of these studies have focused on neural oscillatory responses.^{16–26} Oscillatory analyses do not require that neural activity is phase-locked to the initial onset of the stimulus, which makes them ideal for studies of working memory and other higher-level tasks where neural responses are extended in time (i.e., seconds) and likely involve reverberative activity across the brain. Previous oscillatory studies of verbal working memory in healthy participants have shown widespread α desynchronizations in left hemispheric language regions during encoding and maintenance and robust increases in parieto-occipital α (i.e., synchronization) during maintenance.^{16,19,26} This latter, well-replicated finding, is the basis of an influential theory proposing that this parieto-occipital α activity reflects inhibition of the visual stream.^{16,17,22} Such inhibition would function to transiently protect working memory representations being retained in more anterior regions (e.g., Broca area) from being disturbed by incoming visual information.^{16,17,22} Several electrophysiological studies of working memory have also found θ oscillations, although reports of θ activity are far less common.^{18,19,21}

While previous studies have informed basic processes in working memory, they generally focused on neural dynamics in normative samples, and to our knowledge no MEG study conducted to date has examined working memory function in patients with PTSD. However, several MEG studies have examined patients with PTSD during the resting state or during other cognitive tasks, and these studies have shown critical connectivity and/or oscillatory aberrations associated with the disorder.^{27–32} The primary goal of the present study was to characterize the oscillatory dynamics that underlie working memory encoding and maintenance and to identify potential aberrations associated with PTSD by comparing the neural activity observed in veterans with PTSD to that of healthy participants. Our selection of a verbal working memory task was based on meta-analytic findings of stronger verbal than visual memory effects in individuals with PTSD³³ and is consistent with new meta-analytic findings of larger effects for verbal learning/memory than for nonverbal learning/memory as well as for verbal learning over delayed recall, which may link these differences to verbal encoding deficits.¹⁰ We hypothesized that veterans with PTSD would show aberrant α activity in the posterior cortices of the left hemisphere during early encoding, which would spread to include the left prefrontal cortex and supramarginal gyrus later in the time course. Moreover, we hypothesized that patients with PTSD would more strongly use homologue language regions in the right hemisphere than controls and that this activity would reflect compensatory processes to maintain adequate performance. Such findings would be consistent with greater processing demands during working memory encoding and maintenance in participants with PTSD than in those without PTSD.

Methods

Participants

We recruited male combat veterans with PTSD and male controls without PTSD, some of whom were combat veterans, to participate in this study. All participants were recruited from the community using television commercials, flyers and/or social media, and all veterans had served in recent conflicts in Iraq or Afghanistan with their warzone service occurring between 2003 and 2014. We established the PTSD diagnosis using the Clinician Administered PTSD Scale (CAPS³⁴) in conjunction with the Life Events Checklist³⁴ and the original CAPS F1/I2 rule.³⁵ Veterans were further assessed using the Mini-International Neuropsychiatric Interview (M.I.N.I.³⁶) to rule out psychiatric diagnoses other than PTSD and concurrent anxiety or depression better explained by PTSD. Individuals eligible for participation in the control group were combat veterans without PTSD and nonveterans with no diagnosed psychiatric/neurological disorders or history of major trauma. The combat-exposed veterans without PTSD were assessed using the CAPS and M.I.N.I. to rule out PTSD and other psychiatric disorders. The combined sample of control participants was matched to those with PTSD on age, sex, education, race and handedness. Exclusion criteria were any other medical diagnosis affecting central nervous system (CNS) function (e.g., HIV/AIDS), known brain neoplasm or lesion, history of significant head trauma, current substance dependence and ferromagnetic implants. We obtained written informed consent, following the guidelines of the Institutional Review Boards of Creighton University and the University of Nebraska Medical Center, who approved the study protocols.

Working memory task

During the MEG recordings, participants were seated in a nonmagnetic chair and instructed to fixate on a centrally presented crosshair. A 19 × 13 cm grid (width × height) containing 6 letters was then presented for 2000 ms. The letters then disappeared and the empty grid remained on the screen for 3000 ms until a single “probe” letter appeared in the cell above the crosshair for 900 ms. Participants responded as to whether the probe was 1 of the 6 letters in the encoding set using their index fingers. Each trial lasted 6900 ms, including a 1000 ms prestimulus period (Appendix 1, available at jpn.ca). Each participant completed 128 trials; 50% of trials were probe-positive (i.e., the probe appeared in the encoding set).

MEG data acquisition

With an acquisition bandwidth of 0.1–330 Hz, neuromagnetic responses were sampled continuously at 1 kHz using an Elekta MEG system with 306 magnetic sensors. Using MaxFilter version 2.2 (Elekta), MEG data from each participant were individually corrected for head movement and subjected to noise reduction using the signal space separation method with a temporal extension (tSSS³⁷).

MEG coregistration

Prior to MEG recording, 4 coils were attached to the participant's head and localized, together with the 3 fiducial and scalp surface points, using a 3-dimensional digitizer (Fastrak 3SF0002, Polhemus). Once the participant was positioned for MEG recording, these coils were localized in reference to the sensors allowing all MEG measurements to be transformed into a common coordinate system. With this system, each participant's MEG data were coregistered with a structural MRI template brain before image reconstruction. To enhance accuracy, we used all scalp surface points (> 100) in the coregistration procedure.

MEG time-frequency transformation and statistics

The MEG preprocessing and imaging analysis pipeline used the Brain Electrical Source Analysis software (BESA v6.0) and was closely based on the methods reported in a previous study by our group.¹⁹ We divided the continuous magnetic time series into epochs of 6900 ms duration, with 0 ms being the onset of the encoding grid and the baseline being the -400 to 0 ms time bin. Cardio-artifacts were removed from the data using signal-space projection, which was accounted for during source reconstruction.³⁸ Epochs containing other artifacts that were not suppressed by tSSS (e.g., some eye blinks) were rejected based on a fixed threshold method supplemented with visual inspection. The final number of accepted epochs did not statistically differ between groups.

We transformed artifact-free epochs into the time-frequency domain using complex demodulation (resolution: 1.0 Hz, 50 ms³⁹), and the resulting data per sensor were averaged over trials to generate time-frequency plots of mean spectral density. These sensor-level data were then normalized by dividing the power value of each time-frequency bin by the respective bin's baseline power, which was calculated as the mean power during the -400 to 0 ms time period. To derive the time-frequency windows of interest for the source imaging analysis, we used a data-driven statistical analysis of the sensor-level spectrograms across the entire array of gradiometers. This statistical analysis involved a 2-stage procedure to control for type 1 error. Briefly, in stage 1, we performed 1-sample *t* tests on each data point, and the output spectrogram of *t* values was thresholded at $p < 0.05$ to identify time-frequency bins containing potentially significant oscillatory deviations. In stage 2, supra-threshold bins were clustered with neighbouring bins that were also above the threshold, and a cluster value was derived by summing the *t* values of all data points in the cluster. We then conducted non-parametric permutation testing to derive a distribution of cluster values, and the significance of the observed clusters were tested directly using this distribution.^{40,41} Based on these analyses, we selected time-frequency windows containing significant oscillatory events across all participants for imaging. Further details of this statistical approach are available elsewhere.¹⁹

MEG source imaging and statistics

Cortical networks were imaged through an extension of the linearly constrained minimum variance vector beamformer,^{42,43}

which uses spatial filters in the frequency domain to calculate source power for the whole brain volume. The single images are derived from the cross-spectral densities of all combinations of MEG gradiometers averaged over the time-frequency range of interest, and the solution of the forward problem for each location on a grid specified by input voxel space. Following convention, we computed noise-normalized, differential source power per voxel in each participant using active (task) and passive (baseline) periods of equal duration and bandwidth. Such images are typically referred to as pseudo *t* maps, with units (pseudo *t*) that reflect noise-normalized power differences per voxel. The resulting 3-dimensional maps of functional brain activity were $4.0 \times 4.0 \times 4.0$ mm resolution and were statistically evaluated using a mass univariate approach based on the general linear model. Briefly, we examined the effect of group using a random effects analysis for the time-frequency bins of interest. All statistical maps were displayed as a function of α level, thresholded at $p < 0.005$, and adjusted for multiple comparisons using a spatial extent threshold (cluster restriction 80 contiguous voxels) based on the theory of Gaussian random fields.

Results

Twenty-seven male combat veterans with PTSD and 24 male control participants without PTSD, 12 of whom were combat veterans, completed the study. No participants in the PTSD group were receiving psychotherapy, and 9 (33%) were on stable (no change for at least 6 mo) doses of medication (3 SSRIs, 3 benzodiazepines, 3 mood stabilizers). Across the sample, 46 participants were white (24 patients, 22 controls), 4 were Hispanic (2 patients, 2 controls) and 1 patient with PTSD was black. Two-tailed independent-samples *t* tests were used for all demographic, clinical and behavioural performance data. These results are reported in Table 1.

MEG sensor-level analysis

Sensor level spectrograms were statistically examined using nonparametric permutation testing to derive the precise time-frequency bins for follow-up beamforming analyses. Results indicated a strong α desynchronization (9–16 Hz) that began shortly after onset of the encoding grid (~200 ms) and continued throughout the duration of the encoding phase and slightly into the maintenance period ($p < 0.001$, corrected). In addition, we detected a narrower α band (9–12 Hz) synchronization during the maintenance period, beginning about 2200 ms after the onset of the encoding grid and continuing until the retrieval phase ($p < 0.001$, corrected). These 2 oscillatory responses dominated the sensor-level spectrograms (Fig. 1). To interrogate the temporal dynamics, these significant oscillatory responses were divided into 12 nonoverlapping time windows of 400 ms duration (i.e., 200–600 ms, 600–1000 ms, 1000–1400 ms, 1400–1800 ms, 1800–2200 ms, 2200–2600 ms, 2600–3000 ms, 3000–3400 ms, 3400–3800 ms, 3800–4200 ms, 4200–4600 ms, 4600–5000 ms), and each window was imaged and statistically evaluated for group effects. The first 5 time windows (200–2200 ms) were imaged using the 9–16 Hz band and the remaining time windows were

imaged using the 9–12 Hz band. These precise time windows were chosen as they correspond to observed oscillatory dynamics (e.g., the 9–16 Hz response began at ~200 ms and concluded at ~2200 ms) and to our recent normative study.¹⁹

MEG beamforming analysis

We first performed a sanity check to evaluate whether it was reasonable to combine the combat veterans without PTSD ($n = 12$) with the nonveteran control participants ($n = 12$). This analysis revealed no statistical differences during the maintenance or encoding periods between these 2 control groups ($p > 0.005$). Thus, they were combined for the PTSD-related analyses.

We initially identified the neural dynamics serving working memory performance in each group. These data indicated a strong decrease (i.e., desynchronization) in 9–16 Hz α activity beginning early in the encoding phase in the bilateral occipital cortices and cerebellum, which rapidly spread to the left superior temporal regions and the supramarginal and inferior frontal gyri in each group (Fig. 2). Such decreases in α activity were sustained throughout the encoding and maintenance phases in the left frontotemporal cortices, although the frontal activity began to dissipate early in the maintenance phase and the superior temporal response weakened as retrieval approached. Generally, the spatiotemporal dynamics of left frontotemporal activity were

similar in patients with PTSD and controls, with the PTSD group having a stronger mean response from 1400–2600 ms in the left posterior temporal cortices that extended across a larger cortical region (Fig. 2). Both groups also had robust α increases (i.e., synchronization) in parieto-occipital cortices during the maintenance phase (Fig. 3), although these were moderately stronger and involved more cortical volume in the control group.

In regard to group differences, we found no significant effects in the left hemisphere during any time window. In contrast, patients with PTSD exhibited stronger decreases (i.e., greater desynchronization) in the right inferior frontal gyrus (IFG) in the 200–600 ms time bin ($p < 0.005$, corrected), which slightly dissipated below our corrected statistical threshold in the 600–1000 period (Fig. 4). Group differences re-emerged during the 1000–1400 ms period in the right IFG, supramarginal gyrus and superior and middle temporal gyri ($p < 0.005$, corrected). Group differences in the right superior and middle temporal gyri were sustained through the remainder of the encoding period and during the transition to maintenance (i.e., 1000–2200 ms; Fig. 4). Consistent with the encoding period, patients with PTSD exhibited significantly stronger decreases (i.e., greater a desynchronization) during maintenance in several right hemispheric cortical areas. Group differences emerged early in the right IFG and supramarginal regions (2200–2600 ms) and were largely sustained throughout the maintenance period

Table 1: Demographic, clinical and behavioural characteristics of study participants

Characteristic	Group; mean $\pm$ SD		Statistical test	p value
	PTSD	Control		
Age, yr	32.5 $\pm$ 7.12	30.6 $\pm$ 7.9	$t_{49} = 0.90$	0.37
Life events (LEC)*	42.78 $\pm$ 10.27	45.42 $\pm$ 11.97	$t_{37} = 0.70$	0.49
PTSD (CAPS)*	73.44 $\pm$ 16.88	21.17 $\pm$ 12.35	$t_{37} = 9.61$	< 0.001
Accuracy, % correct	81.62 $\pm$ 5.60	84.31 $\pm$ 6.32	$t_{49} = 1.67$	0.10
Reaction time, ms	624 $\pm$ 58	607 $\pm$ 53	$t_{49} = 1.02$	0.31

CAPS = Clinician Administered PTSD Scale; LEC = Life Events Checklist; PTSD = posttraumatic stress disorder; SD = standard deviation.

*Includes combat-exposed controls only.

Fig. 1: Oscillatory dynamics during working memory processing. Time-frequency spectrograms with time shown on the X axis and frequency (Hz) denoted on the Y axis. Percent power change was computed by dividing the mean power of each time-frequency bin by the respective bin's baseline power (–400 to 0 ms) and multiplying by 100. The colour legend is displayed to the right of each spectrogram and is identical for both. Data shown on the left represent a group-averaged peak sensor located near the left parieto-occipital cortex, whereas data shown on the right represent the same for a peak sensor near the right parieto-occipital cortex. Strong 9–16 Hz α desynchronization (i.e., decrease) was observed shortly after the encoding grid was presented, and this evolved into a narrower 9–12 Hz α synchronization (i.e., increase) during maintenance.

Fig. 2: Dynamics in left frontotemporal cortices. Group mean beamformer images (pseudo t) at 80% transparency for control participants (top) and veterans with posttraumatic stress disorder (PTSD; bottom) are displayed across all time bins spanning the encoding (blue labels) and maintenance (red labels) phases. A strong sustained decrease in α oscillatory activity was noted across both groups throughout most of the encoding and maintenance phases. This decrease began in posterior regions during early encoding, spread anteriorly to include left frontotemporal areas (including language-specific regions) during the latter half of encoding and the early maintenance period and then began to dissipate throughout the remainder of the maintenance phase.

Fig. 3: Parieto-occipital dynamics during maintenance. Group mean beamformer images (pseudo t) at 80% transparency for controls (top) and patients with posttraumatic stress disorder (PTSD; bottom) are displayed in the coronal orientation across the latter time bins of the maintenance period. Both groups exhibited strong α synchronizations with a right hemispheric bias throughout the later maintenance phase in the parieto-occipital cortices, which is broadly consistent with previous electrophysiological studies of working memory. Although this response was generally stronger in controls, this difference was not significant in any time bin. Interestingly, the amplitude of this response was significantly correlated with scores on the Clinician-Administered PTSD Scale, indicating that those with the most severe PTSD symptoms had the weakest parieto-occipital α synchronization during the maintenance phase.

($p < 0.005$, corrected; Fig. 5), especially in the right IFG. Late in the time course (4200–5000 ms), group differences also emerged in the right occipitotemporal notch, inferior and ventral temporal regions and right cerebellar cortices ($p < 0.005$, corrected; Fig. 5). Finally, controls exhibited stronger α synchronization in

parieto-occipital cortices throughout the maintenance period, but this difference did not survive our corrected statistical threshold in any time bin.

Spearman correlations were also conducted to link our neural measures with PTSD symptom severity. These

Fig. 4: Group differences in the right hemisphere during encoding. Significant group differences in 9–16 Hz α activity in the right hemisphere are shown across all time bins spanning the encoding (blue labels) and transition (white labels) phases. Patients with posttraumatic stress disorder (PTSD) exhibited a stronger α desynchronization than controls in the right inferior frontal gyrus (IFG) during the 200–600 ms time window ($p < 0.005$, corrected). This difference was slightly subthreshold in the 600–1000 ms window, and no other areas were significant. During the 1000–1400 ms period, α desynchronization was again stronger in patients with PTSD in the right IFG and the right supramarginal and the right superior and middle temporal gyri. The latter region was also significant in the 1400–2200 ms encoding and transition windows. All images are shown following radiological convention.

Fig. 5: Group differences in the right hemisphere during maintenance. Significant group differences in 9–12 Hz α activity in the right hemisphere during the maintenance phase are displayed across all time bins. Patients with posttraumatic stress disorder (PTSD) had significantly stronger α desynchronization in the right inferior frontal gyrus (IFG) relative to controls in all time bins ($p < 0.005$, corrected) except the 4200–4600 ms bin. Stronger desynchronizations were also found in the right supramarginal gyrus of patients with PTSD during most time windows, and this extended to the right inferior and ventral temporal region during the final time window ($p < 0.005$, corrected). Of note, a more medial slice is shown for the 3800–4200 ms bin, and 2 slices are shown for the final time window to illustrate the different brain regions where significant findings were detected. All images are shown following radiological convention.

data showed that CAPS scores correlated with the amplitude of activity in the peak group-difference voxel of the right supramarginal gyrus ($r_{39} = -0.43$, $p = 0.006$) and the parieto-occipital cortices ($r_{39} = -0.33$, $p = 0.042$), such that more severe PTSD was associated with greater desynchronization in the right supramarginal gyrus and weaker α synchronization in the parieto-occipital cortices, both of which support our key group difference findings. The CAPS scores were also marginally correlated with activity in the right IFG ($r_{39} = -0.28$, $p = 0.087$), such that more severe PTSD was associated with greater desynchronization.

Discussion

We evaluated the neural dynamics serving working memory processing in participants with and without PTSD using MEG. Our primary findings indicated that PTSD is associated with physiologic abnormalities during working memory, with the right supramarginal gyrus and inferior frontal regions being particularly affected. These neural abnormalities were relatively dynamic, as regional differences between groups varied with the time course. To our knowledge, this study represents the first MEG investigation of working memory processing in men with PTSD, and we describe each of its main findings and their implications in the sections that follow.

Brain networks serving working memory processing

Normative studies of the dynamics serving working memory processing have not been entirely consistent, but this is at least partially because of differences in task design, stimuli and/or focusing on different phases (e.g., maintenance or retrieval) and/or time windows (e.g., early or late).^{18,20,21,25} Nonetheless, our findings are congruent with those of previous studies, especially on the importance of α activity in working memory processing and the involvement of left-hemispheric language areas.^{18,20} Oscillatory activity in language areas has been a consistent finding across working memory studies that used language-related stimuli,^{18,44} especially those focusing on memory maintenance, and such activity is thought to reflect processing in Baddeley's so-called phonological loop.⁴⁵ In addition, verbal working memory tasks similar to ours have been shown in fMRI studies to activate cerebellar regions during encoding and maintenance operations.^{46,47} Our study broadly extends these data by revealing the temporal dynamics of working memory encoding, indicating that α oscillations emerge in the left supramarginal and prefrontal cortices by 600 ms following presentation of the encoding set, and that activity is largely sustained in these brain regions throughout the remaining encoding phase and into the maintenance phase. We propose that such sustained oscillatory activity in these brain regions reflects continuous processing in Baddeley's phonological loop and executive functioning, as participants are engaged in transforming the visual stimuli into a memory representation and then maintaining the representation through rehearsal.

Working memory encoding and maintenance deficits in veterans with PTSD

Potentially our most important findings were the group differences in α activity in the right IFG and supramarginal gyrus as well as the right superior and middle temporal gyri. These differences emerged in the 200–600 ms time window and continued throughout most of the encoding and maintenance phases. In addition, α activity in the right supramarginal gyrus and the parieto-occipital cortices were significantly inversely correlated with PTSD severity, strengthening our assertions about the importance of PTSD in these findings.

Based on previous neuroimaging studies, we originally hypothesized that there would be neurophysiological activity in the left prefrontal cortices^{48,49} and the supramarginal gyrus,⁵⁰ as these regions serve important roles for working memory processing. The left inferior frontal gyrus is within the prefrontal region and plays a primary role in language production, semantic and phonologic processing, being sometimes referred to as the Broca area.^{51–54} In contrast, the left supramarginal gyrus is important for language perception, processing and verbal working memory and includes the Wernicke area.⁵¹ Interestingly, in patients with PTSD, α activity in the right supramarginal and inferior frontal gyri were very similar to that observed in the left hemispheric homologue areas of both groups (i.e., strong desynchronization). Largely the same pattern emerged in the right superior and middle temporal gyri. We propose that such α desynchronizations in veterans with PTSD may indicate that these right hemispheric cortices are being strongly recruited to aid in task performance. Such a position is supported by our time course data, which indicate that these brain regions were temporally engaged in parallel. Conversely, while the patients with PTSD actively recruited right hemispheric language areas (demonstrated by α desynchronization), the healthy controls' right hemispheric language areas became less involved in task performance (demonstrated by no oscillatory changes or slight α synchronizations), which may reflect local inhibition or, at a minimum, idling cortex. The assertion that right frontotemporal desynchronization reflects a compensatory process is consistent with the observed α desynchronization in both groups in left hemispheric regions shown to be strongly activated during working memory performance by previous fMRI studies.^{14,15} Moreover, a combined EEG/fMRI study has supported the connection between α desynchronization and "activation" in the fMRI sense.⁵⁵ This interpretation also coincides with fMRI findings that older adults use bilateral inferior frontal gyri while performing a verbal working memory task similar to the one used in our study; young adult participants in this study recruited only the left inferior frontal gyrus.⁵⁶ Similarly, patients with post-stroke aphasia caused by damage to the left hemispheric language areas recruit right-sided homologue regions during language tasks,⁵⁷ and an fMRI

study of working memory in patients with PTSD and nontraumatized controls found that patients with PTSD abnormally recruit bilateral prefrontal areas, including the inferior frontal gyri, during working memory operations.⁵⁸ These prefrontal brain regions are critical for executive functioning and are known to have an important role in working memory performance and in compensatory processing in special populations.^{59–61}

Research using other tasks and imaging techniques has also documented abnormal activity in the right prefrontal cortices of patients with PTSD,^{8,48,49,62} and considerable research has demonstrated that symptoms of PTSD, such as cognitive control deficits, correlate with differences in prefrontal neural activity.^{7,63–65} A recent meta-analysis of neurocognitive functioning in PTSD also suggested that frontal regions are critical to the pathophysiology of PTSD, as the largest effect sizes were found for verbal learning, attention/working memory and speed of information processing.¹⁰ Our results concur with this view, providing important temporal and localization information suggesting that aberrations in working memory processing emerge within 200 ms after stimulus onset in the right prefrontal regions, spread to the right supramarginal and temporal cortices and largely continue throughout both the encoding and maintenance phases. Recruitment of these additional cortical areas may have enabled veterans with PTSD to achieve task performance nearly equivalent to controls, despite substantial evidence of verbal learning and working memory deficits in patients with PTSD. Working memory is an essential component of information processing and is vital for successful performance of complex cognitive feats, such as the formation and execution of future goals, the regulation of emotions, verbal communication (e.g., ability to carry on a conversation) and the ability to direct attention toward important tasks as well as shifting attention between tasks.¹³ Evidence of compensatory recruitment in the service of a working memory task in patients with PTSD may offer insight into concentration difficulties,^{1,2} impaired executive functioning^{7,9,12} and other neurocognitive disruptions^{8,10,11} associated with PTSD. Our findings suggest that PTSD severity may be associated with greater cognitive load when completing everyday tasks and contributes to various neuropsychiatric difficulties. Such neuropsychiatric difficulties become increasingly apparent under the cumulative cognitive demands that are necessary for life in the real world.⁶⁶

Limitations

Some limitations of this study include the focus on men and combat-related trauma and the emphasis on verbal working memory (i.e., not spatial). Future studies should evaluate women, different types of trauma and other working memory tasks. Future research evaluating potential influences of trauma exposure and medication influences on working memory may also further this line of research; however, a large meta-analysis found no significant effects of medication exclusion criteria or differences between trauma ex-

posed and no-trauma control groups on effect sizes distinguishing neurocognitive performance in patients with PTSD from that of controls.¹⁰

Conclusion

We evaluated the neural dynamics of working memory processing in a community sample of veterans with PTSD and matched controls. We found that veterans with PTSD exhibited abnormal α oscillatory activity in the right inferior frontal and supramarginal regions, as well as the right superior and middle temporal gyri throughout the time course of the encoding and maintenance phases. These findings are broadly consistent with known neurocognitive deficits in patients with PTSD, typically ascribed to dysfunction in frontolimbic circuitry;¹⁰ however, our results also provide time course information about the temporal nature of these disruptions, indicating that veterans with PTSD recruit additional cortical structures to aid in working memory processing almost immediately after stimulus onset, and evidence that these neural aberrations in the right supramarginal gyrus and the parieto-occipital cortices are associated with PTSD severity. The present study provides novel insight on the aberrant neural dynamics serving working memory processing in veterans with PTSD and provides a solid foundation for future studies in this area.

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