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Neural Network Modulation by Trauma as a Marker of Resilience

Differences Between Veterans With Posttraumatic Stress Disorder and Resilient Controls

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Importance: Posttraumatic stress disorder (PTSD) and resilience reflect 2 distinct outcomes after exposure to potentially traumatic events. The neural mechanisms underlying these different outcomes are not well understood.

Objective: To examine the effect of trauma on synchronous neural interactions for veterans with PTSD and resilient controls using magnetoencephalography.

Design: Participants underwent diagnostic interviews, a measure of exposure to potentially traumatic events, and magnetoencephalography.

Setting: US Department of Veterans Affairs medical center.

Participants: Eighty-six veterans with PTSD and 113 resilient control veterans recruited from a large Midwestern medical center.

Main Outcome Measures: Multiple regression analyses were performed to examine the effect of lifetime trauma on global and local synchronous neural interactions. In analyses examining the local synchronous neural interactions, the partial regression coefficient indicates the strength and direction of the effect of trauma on the syn-

chronous interactions between the 2 neural signals recorded by a pair of sensors. The partial regression coefficient, or slope, is the primary outcome measure for these analyses.

Results: Global synchronous neural interactions were significantly modulated downward with increasing lifetime trauma scores in resilient control veterans ($P = .003$) but not in veterans with PTSD ($P = .91$). This effect, which was primarily characterized by negative slopes (ie, decorrelations) in small neural networks, was strongest in the right superior temporal gyrus. Significant negative slopes were more common, stronger, and observed between sensors at shorter distances than positive slopes in both hemispheres ($P < .001$ for all) for controls but not for veterans with PTSD.

Conclusions: Neural modulation involving decorrelation of neural networks in the right superior temporal gyrus and, to a lesser extent, other areas distinguishes resilient veterans from those with PTSD and is postulated to have an important role in healthy response to trauma.

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POSTTRAUMATIC STRESS DISORDER (PTSD) is a complex psychiatric syndrome that develops in response to trauma exposure. Individuals with PTSD experience intrusive recollections or reexperiencing of the traumatic event, avoidance of trauma reminders, emotional numbing, and hyperarousal.¹ In addition, PTSD is associated with high rates of concomitant physical and mental health problems, increased health care use, and impairment in social and occupational functioning.²⁻⁵ Almost 7% of the general population⁶ and up to 30% of veterans^{7,8} meet lifetime criteria for PTSD. Indeed,

PTSD is one of the most common psychiatric disorders, representing a significant and costly public health concern.

Acute distress after trauma exposure is common; however, most people exposed to a potentially traumatic event (PTE) do not develop PTSD. Epidemiological studies^{9,10} have found that between 60% and 90% of people in the United States report lifetime exposure to at least 1 PTE, yet only a fraction of them subsequently experience chronic distress in the form of PTSD or related disorders. In fact, resilience, or the ability to maintain healthy functioning in the face of adversity, represents the modal outcome after exposure to PTEs.¹¹⁻¹⁴

The discrepancy between trauma exposure and dysfunction has led to a growing interest in the heterogeneity of trauma responses and in individual differences that underlie response to PTEs.

A substantial body of research has focused on neurobiological processes that underlie individual differences in response to PTEs, particularly on neural mechanisms associated with PTSD. Studies¹⁵⁻¹⁸ have identified structural and functional differences in various areas of the brain associated with memory and emotional processing, including the amygdala, hippocampus, prefrontal cortex, anterior cingulate cortex, and other areas in individuals with PTSD compared with controls. However, various methodologic issues^{19,20} have hindered progress toward identification of biomarkers.

Recently, task-free magnetoencephalography (MEG) has been applied to the study of PTSD, providing compelling evidence for candidate biomarkers.²¹⁻²³ MEG is a noninvasive technique that detects magnetic fields above the surface of the head produced by postsynaptic potentials in the brain.²⁴ These highly replicable phenomena form the basis of synchronous neural interaction (SNI) biomarkers.²² Specifically, SNIs are zero-lag partial correlations in pairs of MEG time series and denote the strength and polarity (positive or negative) of neuronal interactions. Anomalies in SNIs as assessed by MEG differentiate psychiatric disorders from healthy brain functioning and can discriminate among various brain diseases.²¹⁻²³ From this research, a highly distinctive, unique PTSD SNI signature characterized by miscommunication of temporal and parietal and/or parieto-occipital right hemispheric areas with other brain areas has emerged.^{21,23} These findings, in addition to the growing research applying MEG to other psychiatric disorders,²⁵⁻²⁷ highlight the utility of MEG in identifying biomarkers of disease and underscore the potential for broader clinical applications of MEG.

Compared with the wealth of neuroimaging work aimed at identifying neural correlates of PTSD, research on the neurobiology of resilience has been lacking, although there is a burgeoning emphasis on neurobiological underpinnings of healthy outcomes after exposure to PTEs. Essentially, resilience is conceptualized as flexibility of psychological and physiologic systems in successfully adapting to stressors.²⁸⁻³² Research among healthy participants has demonstrated that neural activation differs among those who are high vs low in trait resilience, with highly resilient people flexibly responding to situational demands.³³ In addition, a novel prospective study^{34,35} examining neural sequelae of combat stress among combat-exposed soldiers without PTSD found that amygdala activity increased from predeployment to post-deployment but returned to baseline at follow-up 1½ years later, again highlighting the link between plasticity and resilience.

As a whole, the literature reviewed provides evidence that neural changes are associated with response to PTEs regardless of whether outcomes reflect healthy resilience or pathologic functioning. What remains unclear is the exact nature of those changes. To begin to address this issue, we used MEG to examine dynamic neural functioning among veterans characterized by

Table. Demographic Characteristics of Study Participants

Characteristic	PTSD	Control
Sex, No. ^a		
Male	77	111
Female	9	2
Age, mean (SD)	53.45 (14.00)	59.37 (13.22)
[range], y ^b	[22-83]	[25-92]
Era, No. (%) ^c		
OEF/OIF	18 (15.9)	25 (29.1)
Vietnam War	75 (66.4)	52 (60.5)
Gulf War	4 (3.5)	5 (5.8)
Korean War	4 (3.5)	1 (1.2)
WWII	2 (1.8)	1 (1.2)
Other	10 (8.9)	2 (2.3)

Abbreviations: OEF/OIF, Operation Enduring Freedom/Operation Iraqi Freedom; PTSD, posttraumatic stress disorder; WWII, World War II.

^aχ² test, *P* = .004.

^b*t* test, *P* = .003.

^cKolmogorov-Smirnov test, *P* = .60.

current PTSD (PTSD group) or resilience (control group). Specifically, in light of substantial evidence that trauma exposure itself influences brain functioning,^{17,35-37} the effects of lifetime PTEs on the mean whole-brain SNI (ie, global SNI [GSNI]) and the synchrony of individual sensor pairs (ie, local SNI [LSNI]) were evaluated. Consistent with models of resilience emphasizing plasticity, the control group was expected to exhibit neural flexibility or adaptation to PTEs. Specifically, it was anticipated that lifetime exposure to PTEs would modulate SNIs for the healthy control participants but not the PTSD group.

METHODS

PARTICIPANTS

A total of 199 US veterans (113 controls and 86 veterans with PTSD) participated in the study as paid volunteers (**Table**). Veterans with current Axis I disorders, history of traumatic brain injury, cardiac pacemakers or other imbedded ferrous metal (due to magnetic effects on MEG), serious chronic pain, or other central nervous system disorders (eg, Parkinson disease, dementia, and cerebral vascular accidents) were excluded from this study. Veterans who met eligibility criteria underwent diagnostic interviews, the Edinburgh Handedness Inventory,³⁸ and MEG. The study protocol was approved by the institutional review board at the Minneapolis Veterans Affairs Medical Center, and participants provided written informed consent before the study.

DIAGNOSTIC MEASURES

We assessed PTSD using the Clinician-Administered PTSD Scale for DSM-IV (CAPS³⁹) or the Structured Clinical Interview for DSM-IV-TR (SCID⁴⁰) PTSD module. The CAPS provides a continuous measure of symptom severity; to categorize participants in regard to PTSD status, the CAPS symptom scores were converted to dichotomous scores using the SCID Symptom Calibration (SXCAL) method.⁴¹ The SXCAL method provides empirically derived cut points for determining the presence or absence of PTSD symptoms. According to the rule, a symptom is considered present if the CAPS score meets or exceeds the em-

pirically derived cut point. The SXCAL scoring rule minimizes false-positive and false-negative results and is the preferred scoring method for the CAPS when differential diagnosis is the goal.⁴¹ When diagnosing PTSD in the present study, emotional responses other than intense fear, helplessness, or horror were accepted for criterion A2, consistent with the mounting research demonstrating wide-ranging reactions to trauma.⁴²⁻⁴⁴ The PTSD diagnoses were linked to a variety of traumatic events, including combat (82.6%), military noncombat (7.0%), sexual assault (5.9%), childhood abuse (1.2%), and other events (3.3%). Most of the PTSD group (72.9%) were prescribed psychotropic medications at the time of the study. Lifetime history of non-PTSD Axis I diagnoses were evaluated with the SCID⁴⁰ using DSM-IV-TR criteria. None of the individuals included in the present analyses met criteria for any current Axis I diagnosis other than PTSD.

Lifetime trauma exposure was assessed with the Deployment Risk and Resilience Inventory (DRRI⁴⁵). The DRRI is a suite of 14 scales that assess deployment-related factors in addition to predeployment and postdeployment factors that are implicated in risk for distress and resiliency. The psychometric properties of these scales have been detailed in prior studies.^{45,46} Three scales totaling 47 items were included in the present study: predeployment stressors, combat experiences, and postdeployment stressors. The 47 dichotomously scored items were summed to provide an index of lifetime exposure to PTEs. To account for a few missing items, a corrected trauma score (items endorsed of items possible) was computed and used in all subsequent analyses. As a result of this conversion, trauma scores ranged from 0 to 1.

DATA ACQUISITION

As described previously,^{22,23} individuals lay supine within the electromagnetically shielded chamber and fixated their eyes on a spot approximately 65 cm in front of them for 60 seconds. The MEG data were acquired using a 248-channel axial gradiometer system (Magnes 3600WH, 4-D Neuroimaging), band-pass filtered between 0.1 and 400 Hz, and sampled at 1017.25 Hz. Data with artifacts (eg, eye blinks and saturation) were eliminated from further analysis.

STATISTICAL ANALYSIS

Single-trial MEG data from all sensors underwent prewhitening^{47,48} using a (50,1,1) autoregressive integrated moving average model. The Matlab package (version 2011b; Mathworks) was used to fit the model and obtain innovations (ie, residuals). All possible pairwise zero-lag cross-correlations ($N = 30\,628$, given 248 sensors) were computed between the prewhitened MEG time series. Finally, the partial, full-rank, zero-lag cross-correlations PCC_{ij}^0 between the i and j sensors were computed for all sensor pairs (SNIs); thus, for any given pair of sensors (from a total of 248), the effects of the remaining 246 sensors were partialled out. The PCC_{ij}^0 was transformed to z_{ij}^0 using Fisher⁴⁹ z -transformation to normalize its distribution:

$$z_{ij}^0 = \frac{1}{2} \ln \frac{1 + PCC_{ij}^0}{1 - PCC_{ij}^0} \quad (1)$$

Standard statistical methods⁵⁰ were used to compare variables between groups and assess relations among variables. Statistical analyses were performed using the IBM SPSS statistical package (version 20; SPSS Inc) and the Intel Visual Fortran Compiler Professional Edition (version 11.1; Intel Corporation).

In this study, we sought to assess the effects of trauma on the strength of SNIs (ie, on how the intensity of trauma [as reflected in the value of the trauma score] might modulate the intensity of SNIs). Therefore, we used the absolute value of z_{ij}^0 for these analyses. We then defined 2 levels of SNIs, namely, GSNI and LSNI ($LSNI = |z_{ij}^0|$). The strength of GSNI for each participant was estimated as the mean $|z_{ij}^0|$:

$$GSNI = \frac{1}{N} \sum |z_{ij}^0| \quad (2)$$

where 30 628 is the number of sensor pairs. To assess the relations between GSNI and trauma score within each group (control and PTSD), a multiple linear regression was performed with GSNI as the dependent variable and trauma, sex, age, and handedness score as independent variables: where T , S , A , and H

$$GSNI = a + bT + cG + dA + fH + e \quad (3)$$

denote the participant's trauma score, sex, age, and handedness score, respectively; a , b , c , d , and f are regression coefficients; and e is an error term. The same analysis was performed for each hemisphere. In addition, the same kind of multiple linear regression analysis was performed for each pair of sensors to evaluate the effect of trauma on local synchrony (LSNI) ie, on individual $|z_{ij}^0|$:

$$LSNI = |z_{ij}^0| = a'_{ij} + b'_{ij}T + c'_{ij}G + d'_{ij}A + f'_{ij}H + e'_{ij} \quad (4)$$

RESULTS

TRAUMA SCORE

The frequency distributions of the trauma score for the PTSD and control groups are shown in **Figure 1**. The distributions can be seen to overlap broadly and are similar in range. However, the trauma score in the control group (mean [SEM], 0.179 [0.012]; median, 0.149; $n = 113$) was significantly smaller than that in the PTSD group (mean [SEM], 0.381 [0.016]; median, 0.37; $n = 86$) (Wilcoxon W test, $P < .001$).

GSNI VS TRAUMA SCORE

Figure 2 plots GSNI against trauma score for the control and PTSD groups. In the control group, GSNI decreased with increasing trauma score; this relation was highly significant (linear regression analysis, $P = .003$). In contrast, no significant relation was found in the PTSD group ($P = .91$). These results were obtained with GSNI as the dependent variable and trauma score as the sole independent variable. When the regression analysis was repeated with sex, age, and handedness as additional independent variables, the significance values obtained were similar ($P = .002$ for the control group and $P = .69$ for the PTSD group); sex, age, and handedness did not have a statistically significant effect in either group.

Given prior research demonstrating primarily right hemispheric SNI anomalies associated with PTSD,²¹ we conducted separate analyses for each hemisphere, which revealed a highly significant negative effect of trauma score on GSNI in the control group for both hemispheres ($P = .002$

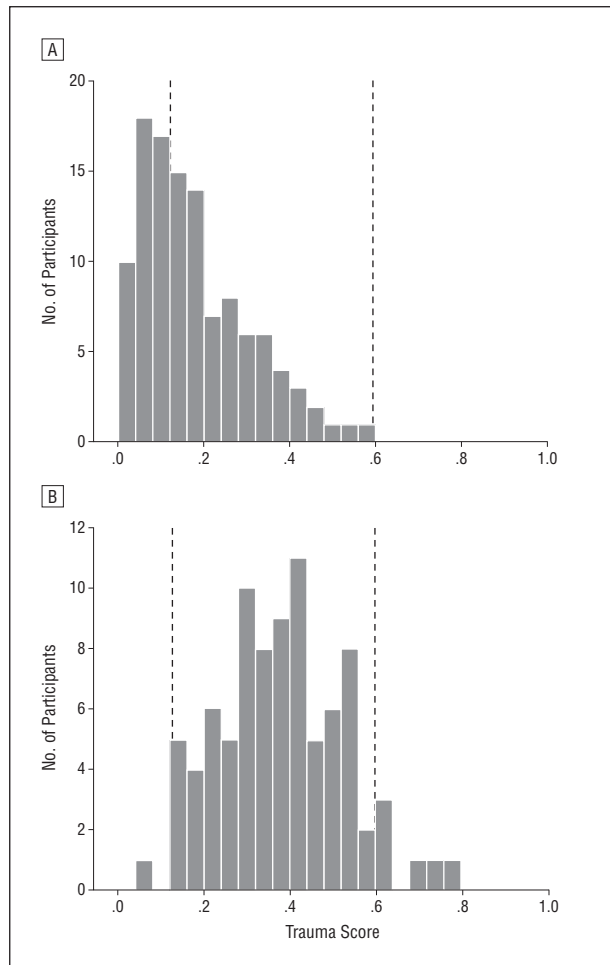


Figure 1. Frequency distributions of trauma scores. A, Control group (n = 113). B, Posttraumatic stress group (n = 86).

and $P = .001$ for the left and right hemispheres, respectively). However, the effect was significantly stronger for the right than the left hemisphere ($P < .001$, F test, analysis of variance of regression coefficients across groups). No statistically significant effect was observed in the PTSD group in either the left or the right hemisphere ($P = .66$ and $P = .90$, respectively). No significant effect was found for sex, age, or handedness in either hemisphere in either group. Practically identical results were obtained for both medicated and unmedicated participants.

Additional analyses were performed to determine the effect of the trauma distributions in the 2 groups (Figure 1) on the relations between GSNI and trauma. First, to account for the skewed trauma distribution in the control group, we calculated both parametric (Pearson) and non-parametric (Spearman) correlations between GSNI and trauma: these correlations were similar and highly statistically significant for the control group but nonsignificant for the PTSD group. Second, to address the different range of the trauma distributions in the 2 groups, we constrained the trauma range to be identical between the 2 groups (0.12-0.6) and performed the regression analysis again. We found the same kind of effects, namely, a strong negative effect of trauma on SNI in the control group ($P = .001$) and absence of an effect in the PTSD group ($P = .60$).

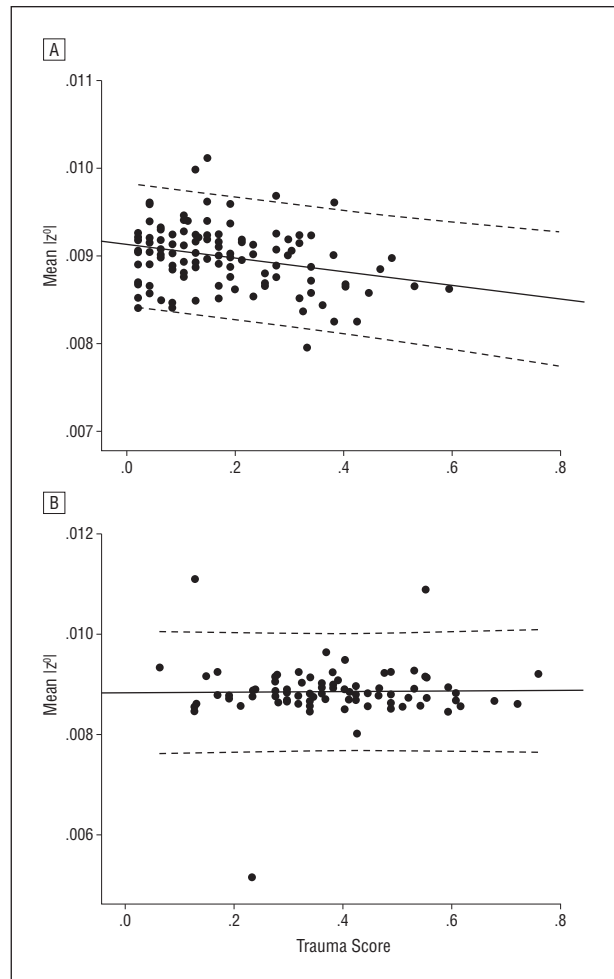


Figure 2. The mean absolute value of the zero-lag z-transformed correlation is plotted against trauma score. A, Control group. B, Posttraumatic stress group.

LSNI VS TRAUMA SCORE

The key measure in this analysis is the partial regression coefficient (slope for short) of LSNI vs trauma score (b_{ij} in equation 4 above), which indicates how the strength of the correlation between the 2 neural signals recorded by a pair of sensors changes with the trauma score. More specifically, the sign of the slope indicates the direction of change (eg, whether the absolute value of the correlation increases or decreases as the trauma score changes), whereas the absolute value of the slope indicates the strength of that effect. The results are illustrated in **Figure 3** and **Figure 4** for the negative and positive slopes, respectively. Each figure contains plots for the control and PTSD groups. The plots were generated as follows. First, a nominal threshold of $P < .01$ on the significance of the slope was applied to screen out weak effects. Second, the maximum absolute value of all slopes (MAXALL) was found and served to scale the plots. Third, for each sensor, the maximum absolute slope for a specific group-slope combination was found and the pair of sensors associated with it identified and plotted as a line connecting the 2 sensors. The color intensity of the line was scaled to MAXALL. In addition, a

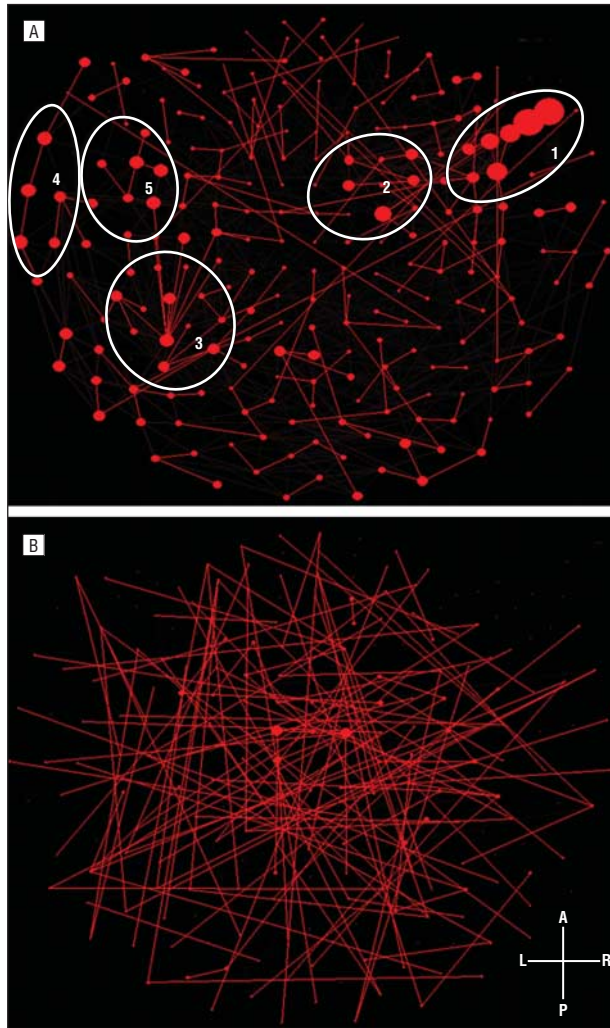


Figure 3. Two-dimensional sensor-space plots depicting the negative modulation of local synchronous neural interactions. A, Control group. B, Posttraumatic stress group. The radius of the ellipses and color intensity are proportional to the maximum trauma vs $|z_{ij}^0|$ slope for a specific sensor (of 247 possible). A indicates anterior; P, posterior; L, left; and R, right. Approximate location of cortical networks: 1, right superior temporal; 2, right inferior frontal; 3, left parietal; 4, left temporal; and 5, left inferior frontal.

filled ellipse was plotted at the location of the sensor such that its area and color intensity were scaled with respect to MAXALL. The same data for the negative modulation in the control group are illustrated using 2-dimensional and 3-dimensional contour plots in **Figure 5**.

The most marked effect is the modulation of the negative slopes in the control group (Figure 3 and Figure 5). Higher color intensity indicates stronger negative slopes and, hence, stronger decorrelation. The location of the strongest effect is at the right superior temporal gyrus, which means that the interactions of that node are most strongly decorrelated as a function of the trauma score. In stark contrast, no such decorrelation was observed in the PTSD group (Figure 3). Surprisingly, increases in positive slopes were much weaker than the negative slopes in the control group but practically nonexistent in the PTSD group (Figure 4). In summary, neural interactions, especially those involving the right superior tem-

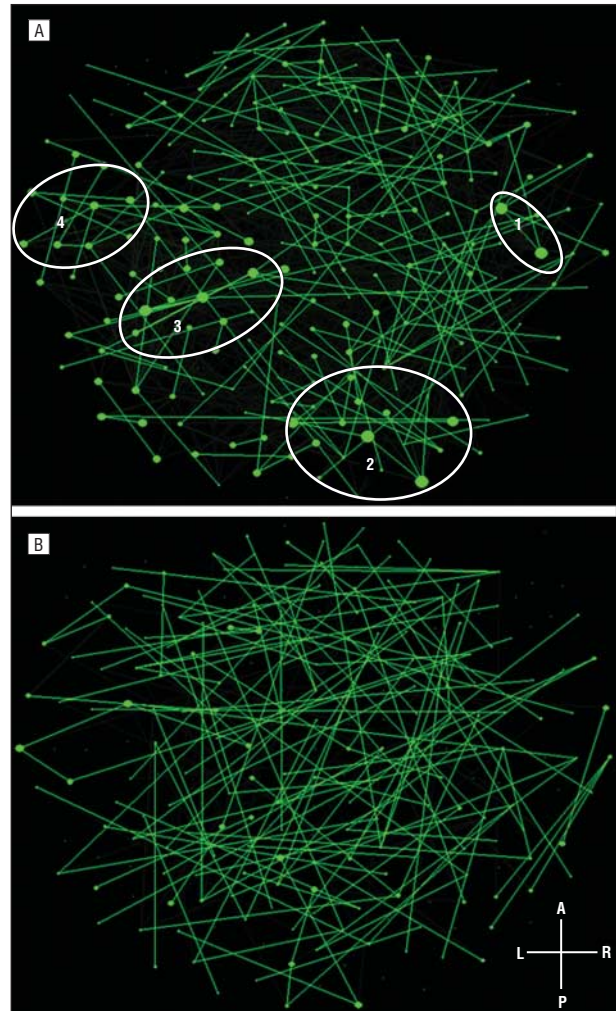


Figure 4. Two-dimensional sensor-space plots depicting the positive modulation of local synchronous neural interactions. A, Control group. B, Posttraumatic stress disorder group. The radius of the ellipses and color intensity are proportional to the maximum trauma vs $|z_{ij}^0|$ slope for a specific sensor (of 247 possible). A indicates anterior; P, posterior; L, left; and R, right. Approximate location of cortical networks: 1, right inferior parietal; 2, right occipital; 3, left parietal; and 4, left temporal.

poral gyrus, were decorrelated with increasing trauma exposure in the control group. Modulations of positive interactions were sparse in the control group, and modulation of either negative or positive interactions was practically absent in the PTSD group. Finally, the results of a detailed analysis of these findings demonstrated that relative to positive interactions, the intersensor distances for negative interactions were significantly smaller in the control group for both hemispheres and slightly smaller only in the right hemisphere for the PTSD group (**Figure 6**).

The results show a regional distribution of significant trauma effects in the control group. We tested the hypothesis that these effects could be accounted for by global factors that affect SNIs as follows. For each SNI, we performed 10 000 regressions in which the trauma score was the independent variable but the dependent variable was a correlation selected randomly from those unrelated to the particular SNI being tested. We then

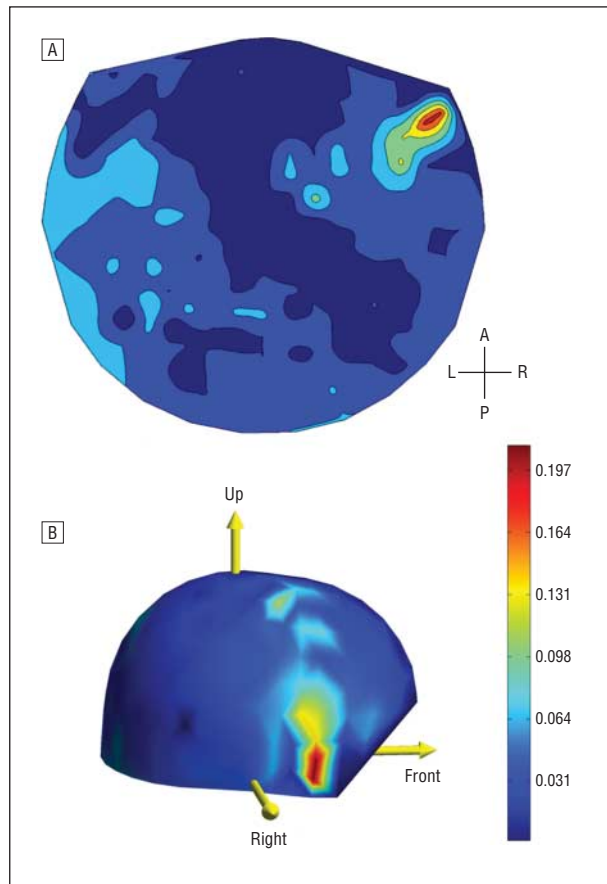


Figure 5. Two-dimensional and 3-dimensional contour plots. A, 2-Dimensional contour plot of color-coded negative trauma vs $|z|_i$ slopes interpolated linearly in sensor space in the control group. B, The same data are shown in a 3-dimensional surface plot using Delaunay triangulation of magnetoencephalography sensor coordinates. A indicates anterior; P, posterior; L, left; and R, right.

counted how many regressions yielded statistically significant slopes at the $P < .01$ level of significance: a large proportion of such significant regressions would indicate lack of regional specificity in the original findings. In contrast, we found that only 1.23% (well below the .05 significance level) of the 10 000 regressions yielded slopes significant at the $P < .01$ level. Therefore, the global hypothesis is rejected and the regional specificity of SNI modulation validated.

COMMENT

The goal of the present study was to evaluate the effect of trauma exposure on correlated brain network activity assessed by SNI test in a task-free state. Specifically, we focused on 2 groups of veterans who differed in terms of functional outcomes after exposure to PTEs, namely, nonsymptomatic controls and veterans with current PTSD. We found notable differences between the 2 groups, amounting to systematic modulations in the control group but not the PTSD group. These results built on our previous study findings,^{21,23} which demonstrated robust differences in SNIs between healthy participants from the general population and veterans with PTSD.

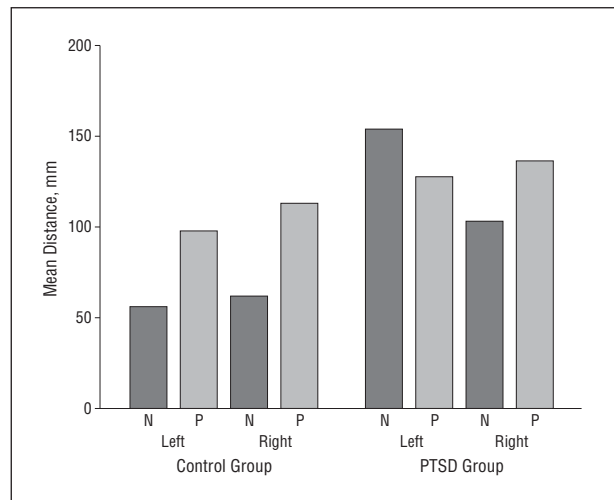


Figure 6. Mean intersensor distances by kind of effect, hemisphere, and group. N indicates negative slope; P, positive slope; PTSD, posttraumatic stress disorder. Control group (both hemispheres): N < P ($P < .001$); PTSD group (left hemisphere): N vs P ($P = .11$); PTSD group (right hemisphere): N < P ($P = .03$).

LIFETIME EXPOSURE TO PTEs

Prior research has highlighted the effect of cumulative trauma exposure on physical and psychological well-being and posited a dose-response relationship such that the likelihood of pathologic outcomes increases as trauma exposure increases.⁵¹ In the present study we evaluated lifetime exposure to PTEs among healthy veterans and those with PTSD. Consistent with dose-response models, the PTSD group endorsed significantly more exposure to PTEs than the control group. However, the distribution of trauma scores overlapped considerably between groups, underscoring the variability in individual responses to PTEs. One mechanism associated with this variability seems to be related to differences in neural modulation.

MODULATION OF GLOBAL AND LOCAL SNIs

The GSNI was significantly modulated downward with increasing lifetime trauma scores in resilient control veterans only. This effect, which was strongest in the right hemisphere, suggests that the ability of the brain to adapt in response to PTEs distinguishes resilient individuals from those with pathologic outcomes. It is interesting that increasing PTEs were associated with lower GSNI. Because this was observed in healthy controls, it can be interpreted as a neural mechanism of resilience to PTEs involving neural network decorrelation.

The LSNI analysis revealed notable differences between control and PTSD groups and further clarified the picture with respect to brain space and nature of the modulation, as follows. First, there was substantial modulation of LSNI in the control group but minimal in the PTSD group. Second, LSNI modulations in the controls were mostly negative (ie, decorrelations) and multifocal, with the most intense focus in the right superior temporal gyrus and with less involvement of other areas. Third, negative modulations involved closer areas than

positive modulations. These findings indicate that (1) the basic mechanism of adaptation to PTEs involves decorrelation of neural networks, (2) this decorrelation is distributed to specific networks, and (3) the size of the networks involved is relatively small.

NEURAL NETWORK DECORRELATION

The importance of neural network decorrelation in information processing has been pointed out by several investigators, mostly in the context of visual processing⁵²⁻⁵⁵ and neural network modeling.⁵⁶ In a way, network decorrelation can be regarded as a mechanism by which the network is “freed” from the hold of a particular input (eg, sensory stimulus or, in our case, trauma event) and becomes available for encoding new information. Regarding trauma exposure, it can be supposed that the information about the traumatic experience is transmitted successively to higher processing areas and is ultimately “deposited” in a memory engram. This neural processing and transmission of information always involves successive, partially overlapping neural networks. Gloor⁵⁷ advanced similar views with regard to experiences in general and speculated on the neural networks involved, based on data from neurosurgical operations. Similar considerations were discussed in a motor skill simulation study.⁵⁸ As an extension to trauma-related networks, LSNI lie at the level of the “encoding” network, and their downward modulation indicates a long-term effect of lifetime trauma exposure because PTEs were not necessarily recent in our control group. As a further analogy to other systems, the original trauma experience would “settle” as a “traumatic engram.” This would keep the memory of the event but would relieve the trauma-encoding network.

In stark contrast to the control group, no or minimal SNI modulation was observed in the PTSD group. This finding implies that trauma-related networks are still in the trauma-encoding phase, a state that presumably leads to the PTSD maladaptation. This trauma-encoding phase parallels the fear structure that Foa and Kozak⁵⁹ proposed as the primary cognitive mechanism underlying anxiety disorders. In PTSD, harmless stimuli are incorrectly associated with threat, evoking arousal and maladaptive avoidance behaviors. With treatment, such as exposure therapy, this fear structure is activated and modified to incorporate new adaptive information about the likelihood of negative consequences that is, in turn, encoded, altering the fear structure. Such interventions may help free these networks from the trauma-encoding phase.

TRAUMA-RELATED NETWORKS

Neural network decorrelation as a function of PTE in healthy veterans involved most intensely the right superior temporal gyrus. An involvement of bilateral inferior frontal, left posterior parietal, and left temporal cortical networks was also observed at a lesser degree. Small-magnitude, positive PTE effects (ie, increased network correlation) were observed in the right inferior parietal, right occipital, left posterior parietal, and left temporal cortex. In addition, the mean intersensor distance in decorrelated networks was almost half of that ob-

served in networks with increased correlations (ie, positive trauma slopes). This was true for both hemispheres, and it means that trauma-related decorrelation affects interactions in close-by neural populations. Remarkably, intersensor distances were larger in both hemispheres in the PTSD group compared with the control group. These distances did not differ significantly between negative and positive modulations in the left hemisphere. In the right hemisphere, distances in decorrelated networks were smaller than those observed in the networks with positive slopes but to a lesser degree than the controls (Figure 6).

SUPERIOR TEMPORAL GYRUS OF THE RIGHT HEMISPHERE

The most intense trauma-related decorrelation was observed in the superior temporal gyrus. This is the same area that a previous MEG study²¹ found to be disturbed among individuals with PTSD. In fact, a growing number of studies have pointed to structural or functional abnormalities in the superior temporal gyrus in patients with PTSD.^{21,60-62} Although bilateral abnormalities have been cited in the literature, right hemispheric abnormalities predominate. Engdahl et al²¹ have previously speculated that abnormalities associated with the right superior temporal gyrus may be linked to the reexperiencing cluster of symptoms due to findings that electrical stimulation of that area elicits experiences akin to flashbacks.⁶³ Other research groups posit that abnormalities in the superior temporal gyrus of patients with PTSD are associated with dissociative phenomena.¹⁸ Although the present study provides further evidence of superior temporal gyrus abnormalities associated with PTSD, the specific nature of the relationship between superior temporal gyrus abnormalities and PTSD symptoms remains a topic of inquiry for future studies using MEG and complementary imaging techniques (eg, functional magnetic resonance imaging and diffusion tensor imaging).

LIMITATIONS

The present study extends prior work using MEG to study neural activity as it relates to PTSD²¹⁻²³; however, research applying MEG to the study of psychopathology is still in its infancy. In the absence of additional research demonstrating evidence of a distinct PTSD neural signature, inclusion of co-occurring disorders in the present study seemed imprudent. Consequently, these findings may not generalize to veterans who are diagnosed as having PTSD and other co-occurring psychiatric conditions. However, the current results, which continue to point to a PTSD neural signature defined by impaired functioning in the superior temporal gyrus for patients with PTSD, pave the way for future research aimed at identifying neural signatures of other psychiatric disorders both alone and co-occurring with PTSD.

In addition, the primary measure used to evaluate PTEs is not an index of trauma per se but rather a collection of dichotomously scored scales aimed at evaluating exposure to lifetime stressors and PTEs. Although such measures quantify PTEs, they fail to account for one's per-

ception of or reaction to a given event, both of which would be useful in establishing whether a person was actually traumatized. That is, exposure to a *potentially* traumatic event is not equivalent to traumatization. It is unlikely, however, that the neural differences seen in our study solely reflect whether traumatization occurred because several control participants reported events that met both criteria A1 (traumatic event) and A2 (extreme fear, helplessness, or horror) for PTSD but did not endorse other significant PTSD symptoms. On a related note, the DRRI and other related self-report-based measures inherently include a finite number of events and may not capture all PTEs that study participants experienced. That said, the DRRI subscales included in the present study capture a wide variety of life events that have been empirically found to affect health and psychological adjustment. Finally, the DRRI scales include events that do not meet criterion A1 for PTSD, raising the possibility that the effects are due to stressors rather than trauma per se. However, results were virtually identical when analyses were repeated with consensus-derived nontraumatic events excluded from the trauma score.

In conclusion, to our knowledge, this is the first MEG study examining how exposure to PTEs modulates neural activity among healthy veterans and those with PTSD. Overall, results suggest that neural modulation centered around the superior temporal gyrus distinguishes healthy from pathologic functioning. Moving forward, further research aimed at examining the specificity of these functional deficits to PTSD and evaluating changes in neural modulation as a function of treatment will be important in establishing the clinical utility of MEG.

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