

Posttraumatic Stress Disorder-Related Differences in Neural Connectivity Among Female Trauma Survivors

Natalie C. Noble, Mohammad S.E. Sendi, Julia B. Merker, Samantha R. Linton, Theresa K. Webber, Russell T. Toll, Amit Etkin, Wei Wu, Kerry J. Ressler, and Antonia V. Seligowski

ABSTRACT

BACKGROUND: Posttraumatic stress disorder (PTSD) is a debilitating condition that disproportionately impacts females. Prior research indicates that males with PTSD exhibit hypoconnectivity of frontal brain regions measured with resting electroencephalography (EEG). In the current study, we examined functional connectivity among females with PTSD and trauma-exposed control females, as well as the impact of sex hormones.

METHODS: Participants included 61 females (mean age = 31.41 years, SD = 8.64) who endorsed criterion A trauma exposure. Resting-state EEG data were recorded for 5 minutes in the eyes-open position. Using a linear mixed-effects model, functional connectivity of the theta band (4–7 Hz) served as the response variable.

RESULTS: Compared with the control group, the PTSD group showed hyperconnectivity between visual brain regions and the rest of the cerebral cortex (false discovery rate–corrected p [p_{FDR}] < .05). Additionally, participants with PTSD demonstrated enhanced connectivity between the default mode network and frontoparietal control network compared with control participants (p_{FDR} < .05), as well as increased connectivity between the ventral attention network and the rest of the cerebral cortex (p_{FDR} < .05). Estradiol was associated with higher connectivity, while progesterone was associated with lower connectivity, but these associations did not survive correction.

CONCLUSIONS: The results are consistent with prior research indicating that PTSD is associated with altered connectivity in visual brain regions, which may reflect disrupted visual processing related to reexperiencing symptoms (e.g., intrusive memories). Our findings provide additional support for the relevance of the theta frequency range in PTSD given its role in fear learning and regulation processes.

<https://doi.org/10.1016/j.bpsgos.2025.100491>

Posttraumatic stress disorder (PTSD) is a debilitating condition that involves reexperiencing symptoms, avoidance of trauma reminders, negative changes in thinking and mood, and altered arousal following a traumatic event (1). Notably, PTSD is twice as common among female trauma survivors (2). Both magnetic resonance imaging (MRI) and electroencephalography (EEG) techniques have captured important insights into altered fear processing among individuals with PTSD, and recent studies have begun to shed light on sex-specific neural alterations in this population (3). Given that sex hormones (e.g., estradiol [E2]) are known to regulate certain neural processes (4,5), additional research is needed to characterize these effects in female trauma survivors. It is worth noting that many studies use the term women to refer to individuals whose biological sex is female but who may or may not identify as women. Consistent with National Institutes of Health recommendations, we consider sex as a biological variable (e.g., female, male) and gender as a social and cultural variable (e.g., woman, nonbinary) (6).

Numerous MRI-based studies have demonstrated that PTSD is associated with hypoactivity of frontal brain regions,

such as the ventromedial prefrontal cortex (vmPFC), during fear extinction (7,8) and Go/NoGo inhibition tasks (9). Additionally, resting-state MRI studies have captured reduced connectivity between the vmPFC and limbic structures involved in the fear response, such as the amygdala and hippocampus (10,11). As reviewed by Koch *et al.* (12), hypoactivation of the vmPFC among individuals with PTSD is thought to reflect diminished top-down regulation, or inhibition, of the fear response during nonthreatening situations. Consistent with clinical presentations of PTSD, unchecked activation of the amygdala is associated with hypervigilance and hyperarousal (13).

Several high-density EEG studies have now replicated MRI-based studies in PTSD. For example, a resting-state EEG study of civilians with PTSD demonstrated decreased functional connectivity of frontal brain regions within the beta and gamma frequency bands (14). Similarly, in their resting-state EEG study of male combat veterans with PTSD, Toll *et al.* (15) observed hypoconnectivity of the orbital and anterior middle frontal gyri—structures located in the frontal lobe.

These findings were detected with a novel analytical technique that involves source localization and orthogonalization of amplitude correlations. Importantly, the results were significant in the theta frequency band (4–7 Hz). Theta oscillations are thought to facilitate information transfer between key regions of the fear network, including the amygdala, vmPFC, and dorsomedial prefrontal cortex, thereby enabling individuals to successfully acquire a conditioned response to threatening stimuli (16,17). Additional EEG research has linked frontal-midline theta oscillations to inhibitory control in uncertain situations (18). Taken together, aberrant theta signals may result in impaired fear learning (16), as well as excessive or maladaptive responses to uncertainty, such as experiential avoidance (18), both of which constitute hallmark symptoms of PTSD.

In females, PTSD has been associated with decreased vmPFC activity (19); disrupted vmPFC-amygdala connectivity (20); and decreased connectivity between the posterior cingulate cortex and the precuneus, vmPFC, hippocampus, and amygdala (21). Among these, the precuneus and posterior cingulate cortex are key components of the default mode network, which is typically active during introspective tasks such as self-reflection (22,23). In PTSD, decreased activation of the vmPFC is associated with impaired emotion regulation, while decreased connectivity between the vmPFC and amygdala is thought to contribute to a heightened fear response (20). Additionally, reduced activity and intrinsic connectivity of default mode brain regions may impair self-referential processing and the contextualization of traumatic memories (21). Taken together, these disruptions in neurocircuitry may translate to hallmark PTSD symptoms of hyperarousal (20), intrusion, dissociation, and avoidance (24).

One possible explanation for underlying neural differences between males and females with PTSD could be the fluctuation of sex hormones across the menstrual cycle. Evidence largely suggests that E2 plays a protective role against stress. For example, an MRI comparison of premenopausal females found that higher E2 levels were associated with significantly reduced activation of the hippocampus during an induction of psychosocial stress, suggesting that high E2 levels may dampen the stress response (4). Additionally, Graham and Milad (25) observed significantly worse extinction recall in women taking estrogen-inhibiting hormonal contraceptives compared with naturally cycling women. Extending this work, Bierwirth *et al.* (26) compared neural activity patterns among a healthy sample of males (low E2), females using hormonal contraceptives (low E2), and naturally cycling, midcycle females (high E2). Utilizing EEG and a fear-potentiated startle paradigm, the authors reported attenuated theta oscillations in the dorsal anterior cingulate cortex (DACC), as well as reduced physiological arousal, among females with high E2 levels during fear recall.

Results of research involving progesterone (Pg) and neural activity have been mixed. For example, some evidence suggests that during the midluteal phase (when Pg levels peak), females demonstrate a stronger connection between the default mode and the salience network, the network primarily responsible for shifting one's focus from introspective tasks to unexpected external stimuli (27). The authors proposed that heightened neural, endocrine, and physiological stress reactivity during the midluteal (elevated Pg) phase makes females

more vulnerable to negative memory bias, as well as affective and stress-related disorders. In contrast, Riddle *et al.* (5) observed that higher concentrations of Pg may be neuroprotective. Specifically, higher Pg levels were associated with increased amplitudes of theta oscillations in the frontoparietal network, the neural network primarily responsible for cognitive control processes. Additional neuroimaging research involving trauma-exposed samples is necessary to understand the complex interaction between PTSD and sex hormones, specifically in the theta frequency band.

In the current study, we examined resting functional connectivity among trauma-exposed females with and without PTSD. Based on prior research with male samples, we hypothesized that the PTSD group would demonstrate lower functional connectivity of frontal brain regions than the control group and that this difference would emerge for the theta frequency range (4–7 Hz). Given prior research that has demonstrated that low E2 levels are associated with worse PTSD severity and greater activation of the DACC, we also hypothesized that lower E2 levels would be associated with lower functional connectivity. We did not have a priori hypotheses about Pg given limited prior research in trauma and PTSD samples.

METHODS AND MATERIALS

Participants included 66 individuals assigned female at birth (mean age = 31.45 years, SD = 8.92) who endorsed DSM-5 criterion A trauma exposure. In terms of race, 4 (6.1%) participants identified as Asian or South Asian, 5 (7.6%) as Black or African American, and 53 (80.3%) as White; 4 participants (6.1%) indicated that their race was not listed or chose not to respond. Eight participants (12.3%) identified as being of Latino, Hispanic, or Spanish origin.

After they had provided informed consent, participants completed psychological measures and provided a blood sample, from which E2 and Pg were assayed. Approximately one half of the sample was naturally cycling/not on hormonal birth control ($n = 37$, 56.9%). Participants who were naturally cycling were asked to report the first day of their last menstrual period ($n = 23$ [62.2%] were in the follicular phase). Participants were then prepared for the EEG measurement. The institutional review board approved all study procedures, and participants received \$100 as compensation.

Psychological Measures

A demographics questionnaire was used to assess age, race/ethnicity, gender identity, marital status, education, employment, and income. Trauma exposure was measured with the Life Events Checklist (28), which is a self-report measure of 17 types of potentially traumatic events (e.g., natural disaster, sexual assault). PTSD was assessed with the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) (29).

Blood Sample

One blood draw of 44 mL was taken at the start of the visit. Blood samples were collected in EDTA tubes, wet iced immediately, centrifuged, and stored in a -80°C freezer. Serum was quantified for E2 (pg/mL) and Pg (ng/mL) levels using mass spectrometry. The assay for E2 has a lower limit of

detection of 1 pg/mL, an intra-assay coefficient of variation (CV) < 5%, and an interassay CV < 12%. The assay for Pg has a lower limit of detection of 0.05 ng/mL, an intra-assay CV < 9.3%, and an interassay CV < 10.8%.

EEG Data Acquisition

Resting-state data were recorded for 5 minutes in the eyes-open position using a 128-channel Electrical Geodesics saline EEG system, consistent with prior resting-state EEG research, including test-retest reliability studies (15,30–37). At a sampling rate of 1000 Hz, this duration yields approximately 300,000 data points per channel, capturing between 1200 and 2400 theta cycles (4–8 Hz). Participants were asked to remain still in order to minimize eye blinks and movements, and they were asked to look at a fixation cross. Landmark electrodes of the high-density geodesic montage were aligned to the standard 10-20 system. Data were collected at 1000 Hz with 0.1–100 Hz analog filtering, using Cz as a reference. Impedances were kept below 100 k Ω .

EEG Data Preprocessing

EEG data were preprocessed in MATLAB (version R2022b; MathWorks, Inc.) using custom scripts that built on the EEGLAB toolbox version 2020.0. This involved a fully automated artifact rejection pipeline that has been validated in our prior work (15) and minimizes bias from subjective manual artifact rejection. The preprocessing pipeline involved 1) resampling data to 250 Hz; 2) removal of 60 Hz AC line noise artifact; 3) removal of nonphysiological low-frequency data using a 0.01-Hz high-pass filter; 4) rejection of bad epochs by thresholding the magnitude of each epoch; 5) rejection of bad channels by thresholding spatial correlations among channels; 6) exclusion of participants with more than 25% bad channels; 7) estimation of EEG signals from bad channels from the adjacent channels through spherical spline interpolation; 8) independent component analysis to remove remaining artifacts, including scalp muscle artifact, ocular artifact, and electrocardiogram artifact; 9) re-referencing signals to the common average; and 10) filtering of signals to 4 frequency ranges: theta (4–7 Hz), alpha (8–12 Hz), beta (13–30 Hz), and low gamma (31–50 Hz). To further ensure the integrity of our processed data, all channel data were visually inspected to confirm the efficacy of the automated artifact rejection and correct any potential oversights, thereby combining the strengths of automated processes with expert review. To filter the data, we employed a Hamming windowed sinc finite impulse response filter, selecting the filter order through a heuristic approach. We implemented this filter using a toolbox developed by Widmann *et al.* (38) and used in the previous studies (15,39).

EEG Connectivity Processing

Following initial filtering, we conducted a detailed analysis of complex-valued time-series data from each vertex in the brain's source space. To ensure that the signals from each brain region were effectively isolated, we used orthogonalization for each vertex's analytical signal, thereby significantly reducing signal redundancy and interference and enhancing the specificity of our connectivity measurements. Source

localization was achieved using the Brainstorm toolbox, specifically using the OpenMEEG plugin to implement a boundary element model (40,41). For the source localization technique, we utilized minimum norm estimation, which excels in providing a spatially coherent distribution of neuronal activity by integrating depth weighting and regularization (42,43). This method proved particularly advantageous for our study, handling noise effectively and facilitating detailed spatial mapping in conjunction with our comprehensive head model. Subsequently, we calculated power envelopes from these orthogonalized time series and applied a logarithmic transformation to normalize the data distribution. Connectivity between regions was then assessed by calculating Pearson's correlation coefficients between the log-transformed power envelopes of each pair of vertices. These findings were contrasted with findings obtained from raw power envelopes derived from non-orthogonalized time series, which served as a methodological comparison to highlight the effectiveness of our orthogonalization and source localization approach.

We focused our connectivity analysis on 31 regions of interest (ROIs) within the Montreal Neurological Institute space. These regions included the left and right visual area 1, somatosensory cortex (SMC), inferior frontal junction, intraparietal sulcus (IPS), frontal eye fields, supplemental eye fields, angular gyrus (ANG), posterior middle frontal gyrus (PMFG), orbital gyrus, middle temporal gyrus (MTG), anterior MFG, insula, and supramarginal gyrus (SUP), as well as the posterior cingulate cortex, mPFC, and DACC. These regions were selected based on an independent parcellation from a previous study's analysis (16). This approach allowed us to ground our EEG ROIs in a well-established, functional MRI-based framework for major cortical connectivity networks, while adjusting for the lower resolution of EEG data. Then, we applied Fisher's z transformation to these correlations, a statistical method that normalizes data for better comparison and analysis.

Data Analysis

For each brain connectivity measurement, we identified the central data range using the 25th and 75th percentiles. Then, we calculated the interquartile range (IQR) and established outlier thresholds at 1.5 times the IQR above and below these percentiles (15,44). Data points outside these boundaries were marked as outliers and excluded from further analysis. Next, using a linear mixed-effects model, functional connectivity of the theta band (4–7 Hz) served as the response variable. The model included PTSD diagnosis as a categorical predictor and age, marital status, education, and income as covariates. A random intercept for each participant was also incorporated into the model; models did not include random slopes. p Values derived from this analysis were corrected using a single false discovery rate (FDR) adjustment across all ROIs using the Benjamini-Hochberg method (p_{FDR} , 465 comparisons < .05).

To explore the relationship between theta band power envelope connectivity and levels of E2 and Pg, we also used linear mixed-effects models. This analysis covaried for age, marital status, education level, and income. In all statistical evaluations, p values were adjusted using the Benjamini-Hochberg correction method to account for multiple comparisons. This adjustment was made across 465 comparisons,

with a significance threshold set at $p_{FDR} < .05$. All data analysis, including EEG processing, was conducted using MATLAB.

RESULTS

See Table 1 for all sample descriptives. A total of 37 (56.9%) participants met diagnostic criteria for PTSD per CAPS-5. Compared with control participants, participants with PTSD demonstrated significantly increased theta band connectivity ($p_{FDR} < .05$) between visual brain regions and other areas of the cerebral cortex (Figure 1). Specifically, there was a notable increase in connectivity from the left visual brain regions to various key areas: the right supplementary eye fields, part of the dorsal attention network; the left ANG, associated with the default mode network; the left PMFG, and left MTG, all of which are components of the frontoparietal control network; and the left SUP, involved in the ventral attention network. Similarly, enhanced theta band connectivity was observed between the right visual region and left ANG and left SUP, in the PTSD group compared with the control group.

In addition, we noted increased theta band connectivity in the PTSD group compared with the control group between several additional brain regions. This includes heightened connectivity from the left SUP, which is a component of the ventral attention network, to various areas: the right IPS, part of the dorsal attention network; the posterior cingulate cortex and the right ANG, both associated with the default mode network; and the right SUP, also part of the ventral attention network.

As shown in Figure 2, higher E2 levels were associated with higher theta band connectivity in multiple brain regions. The most substantial correlation was observed between the left mPFC and the left IPS. Specifically, higher E2 levels were associated with stronger connectivity between the left SMC and the left ANG ($t_{43} = 3.42$, uncorrected $p = .001$). In all E2 analyses (including sensitivity analyses in the naturally cycling group), associations were no longer significant following FDR correction.

As shown in Figure 3, lower Pg levels were associated with higher theta band connectivity in multiple brain regions. Specifically, lower Pg levels were associated with stronger connectivity between the right SUP and the right ANG ($t_{19} = -2.70$, uncorrected $p = .016$). In all Pg analyses (including sensitivity analyses in the naturally cycling group), associations were no longer significant following FDR correction. In exploratory analyses, we examined associations between the Pg/E2 ratio and connectivity measures, and no significant observations were made.

DISCUSSION

Our findings provide additional support for the relevance of the theta frequency range in PTSD given its role in fear learning and regulation processes (17,45). We observed hyperconnectivity of frontal brain regions among our female sample, which is in contrast to prior research with male veterans (15), and we replicated prior work that has demonstrated altered visual connectivity among trauma-exposed populations (46–48). Furthermore, our results are consistent with prior research indicating that PTSD is associated with altered connectivity within and between the default mode network, ventral attention network, and frontoparietal control network (49). Our

Table 1. Demographic Characteristics of the Sample

| | Mean (SD) or <i>n</i> (%) |
|---|---------------------------|
| Race | |
| Asian or South Asian | 4 (6.1%) |
| Black | 5 (7.6%) |
| White | 53 (80.3%) |
| Not listed | 3 (4.5%) |
| Prefer not to respond | 1 (1.5%) |
| Ethnicity | |
| Non-Hispanic/Latina | 57 (87.7%) |
| Education | |
| High school or GED | 2 (3.1%) |
| College | 43 (66.2%) |
| Graduate/professional school | 20 (30.7%) |
| Marital Status | |
| Single | 48 (73.8%) |
| Married or equivalent | 10 (15.4%) |
| Divorced | 7 (10.8%) |
| Household Income | |
| ≤\$10,000 | 4 (6.2%) |
| \$10,000–\$24,999 | 8 (12.3%) |
| \$25,000–\$49,999 | 19 (29.2%) |
| \$50,000–\$74,999 | 13 (20.0%) |
| ≥\$75,000 | 19 (29.2%) |
| Prefer not to respond | 2 (3.1%) |
| PTSD | 37 (56.9%) |
| Naturally Cycling | 37 (56.9%) |
| Taking Hormonal Birth Control | 28 (42.4%) |
| Menstrual Cycle Phase^a | |
| Follicular | 23 (62.2%) |
| Luteal | 13 (35.1%) |
| Gender Identity | |
| Woman | 58 (89.2%) |
| Nonbinary | 6 (9.2%) |
| Gender queer | 1 (1.5%) |
| Trauma Exposure | |
| Natural disaster | 4 (6.1%) |
| Fire or explosion | 10 (15.2%) |
| Accident | 25 (37.9%) |
| Exposure to toxic substance | 12 (18.2%) |
| Physical assault | 8 (12.1%) |
| Sexual assault/unwanted sexual experience | 3 (4.5%) |
| Other | 2 (3.0%) |
| Prefer not to respond | 2 (3.0%) |
| Age, Years | 31.45 (8.92) |
| Estradiol, pg/mL | 94.39 (99.17) |
| Progesterone, ng/mL | 1.35 (2.67) |

PTSD was determined by clinical interview (CAPS-5), and trauma exposure was determined by self-report (LEC-5 experienced).

CAPS-5, Clinician-Administered PTSD Scale for DSM-5; GED, general educational development; LEC-5, Life Events Checklist for DSM-5; PTSD, posttraumatic stress disorder.

^aOnly available for participants who were naturally cycling; $n = 1$ missing.

results also suggest that E2 and Pg may have different associations with neural activity in trauma-exposed females, regardless of PTSD status.

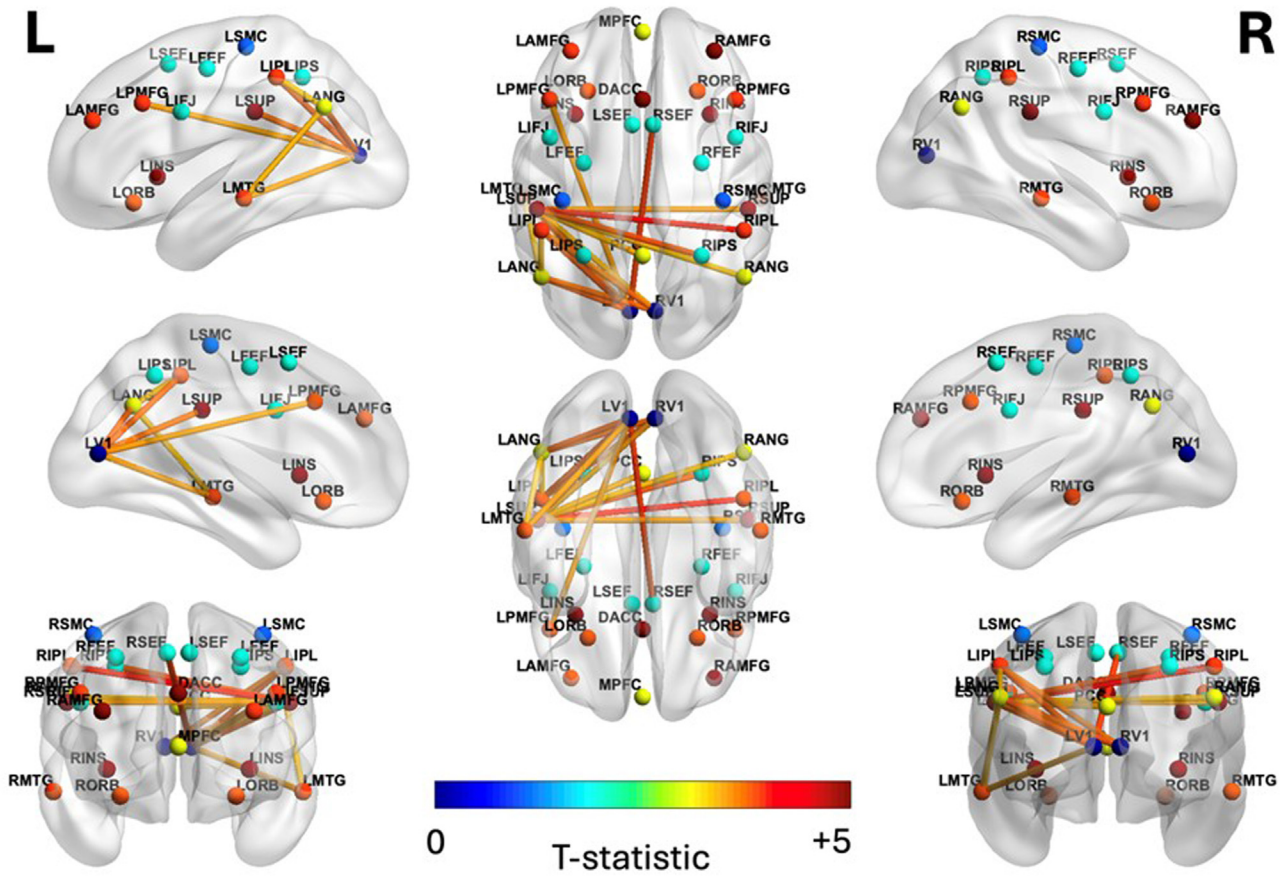


Figure 1. Theta band hyperconnectivity in posttraumatic stress disorder (PTSD). Thirty-one regions of interest were defined in the Montreal Neurological Institute space. We created linear mixed-effects models for the functional connectivity between 465 unique pairs of the 31 regions and diagnosis (i.e., trauma-exposed vs. PTSD) in the theta band, incorporating age, marital status, education, and income as covariates. A random intercept for each participant was also incorporated into the model. The *F* statistics of the models associated with each connectivity pair that survived after false discovery rate correction are shown from different views. The thickness and color of the edges represent the strength of the *F* value. The node colors represent the network to which the node belongs. AMFG, anterior middle frontal gyrus; ANG, angular gyrus; DACC, dorsal anterior cingulate cortex; FEF, frontal eye field; IFJ, inferior frontal junction; INS, insula; IPS, intraparietal sulcus; L, left; MPFC, medial prefrontal cortex; MTG, middle temporal gyrus; R, right; SEF, supplementary eye field; SMC, somatosensory cortex; SUP, supramarginal gyrus; V1, visual area 1 (primary visual cortex).

Consistent with prior literature, the current findings indicated altered connectivity in visual brain regions for individuals with PTSD. One prior study of predominantly male veterans reported a relationship between greater reexperiencing symptoms and both increased visual-sensorimotor and decreased visual-frontoparietal functional connectivity (50). In our study, the right and left visual brain regions demonstrated increased connectivity with regions of the default mode network, frontoparietal control network, and ventral attention network, as well as with regions of the dorsal attention network for the left visual brain region only. These alterations may reflect the disrupted visual processing related to PTSD symptoms mentioned above, and reexperiencing in particular, which has recently been shown in acutely trauma-exposed individuals (46–48). Notably, PTSD is associated with heightened emotional arousal even at rest (i.e., without stress induction or an emotional visual stimulus), as evidenced by heightened amygdala and sympathetic nervous system activity

(e.g., heart rate) (10,51–53). Because one of the proposed mechanisms for this heightened arousal in PTSD is hypervigilance (e.g., constantly scanning one’s environment for threat), it follows that PTSD is associated with increased activity of brain regions involved in visuospatial processing. Further investigation is required to determine the precise nature of this relationship among females with PTSD.

Our results indicated greater connectivity between several brain regions for females with PTSD. Specifically, we observed increased connectivity within the ventral attention (i.e., salience) network as well as between the ventral attention network and various regions of the dorsal attention network, default mode network, and frontoparietal control (i.e., central executive) network. These findings are consistent with a prior study that observed a relationship between salience network connectivity and hyperarousal symptoms in PTSD, and it has been posited that individuals with PTSD are overly primed to detect salience (e.g., threat) in their environment (24). Although

based connectivity provide additional support for the role of theta in fear learning and regulation. Furthermore, our EEG-based connectivity findings of visual cortex alterations and enhanced visual sensitization in PTSD complement and validate prior MRI findings. Consistent with prior literature, our results may also suggest that higher relative E2 levels are associated with a protective effect, marked by greater neural connectivity and decreased PTSD symptomatology. Given that this association did not remain significant following correction for multiple comparisons, these findings require replication. Future studies are needed to compare these findings in larger mixed-sex samples.

ACKNOWLEDGMENTS AND DISCLOSURES

This work was supported by the National Institute of Mental Health (Grant Nos. K23MH125920 and K23MH125920-03W1 [to AVS]; T32MH125786 [to MSES]).

MSES receives consulting fees from NIJ Corp. AE reports equity and salary from Alto Neuroscience and equity in Akili Interactive. KJR serves on scientific advisory boards for Sage, Boehringer Ingelheim, Senseye, and the Brain Research Foundation and has received sponsored research support from Alto Neuroscience. All other authors report no biomedical financial interests or potential conflicts of interest.

ARTICLE INFORMATION

From the Department of Psychological Science, University of Vermont, Burlington, Vermont (NCN); Department of Psychiatry, Harvard Medical School, Boston, Massachusetts (MSES, SRL, KJR, AVS); Division of Depression and Anxiety Disorders, McLean Hospital, Belmont, Massachusetts (MSES, SRL, TKW, KJR); Department of Psychological, Newark & Brain Sciences, University of Delaware, Newark, Delaware (JBM); Department of Psychiatry, Center for Depression Research and Clinical Care, Peter O'Donnell Jr. Brain Institute, University of Texas Southwestern Medical Center, Dallas, Texas (RTT); Alto Neuroscience, Palo Alto, California (AE); Department of Psychiatry, Stanford University, Palo Alto, California (AE); Songjiang Hospital & Songjiang Research Institute, Shanghai Key Laboratory of Emotions and Affective Disorders, Shanghai Jiao Tong University School of Medicine, Shanghai, China (WW); and Department of Psychiatry, Massachusetts General Hospital, Boston, Massachusetts (AVS).

NCN and MSES are joint first authors.

Address correspondence to Antonia V. Seligowski, Ph.D., at aseligowski@mgh.harvard.edu.

Received Jul 31, 2024; revised Feb 27, 2025; accepted Mar 5, 2025.

Supplementary material cited in this article is available online at <https://doi.org/10.1016/j.bpsgos.2025.100491>

REFERENCES

- American Psychiatric Association (1987): *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. Washington, DC: American Psychiatric Press.
- Kilpatrick DG, Resnick HS, Milanak ME, Miller MW, Keyes KM, Friedman MJ (2013): National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. *J Trauma Stress* 26:537–547.
- Eder-Moreau E, Zhu X, Fisch CT, Bergman M, Neria Y, Helpman L (2022): Neurobiological alterations in females with PTSD: A systematic review. *Front Psychiatry* 13:862476.
- Albert K, Pruessner J, Newhouse P (2015): Estradiol levels modulate brain activity and negative responses to psychosocial stress across the menstrual cycle. *Psychoneuroendocrinology* 59:14–24.
- Riddle J, Ahn S, McPherson T, Girdler S, Frohlich F (2020): Progesterone modulates theta oscillations in the frontal-parietal network. *Psychophysiology* 57:e13632.
- NIH Office of Research on Women's Health (ORWH): Sex & Gender. Available at: <https://orwh.od.nih.gov/>. Accessed July 22, 2024.
- Milad MR, Pitman RK, Ellis CB, Gold AL, Shin LM, Lasko NB, *et al.* (2009): Neurobiological basis of failure to recall extinction memory in posttraumatic stress disorder. *Biol Psychiatry* 66:1075–1082.
- Rougemont-Bücking A, Linnman C, Zeffiro TA, Zeidan MA, Lebron-Milad K, Rodriguez-Romaguera J, *et al.* (2011): Altered processing of contextual information during fear extinction in PTSD: An fMRI study. *CNS Neurosci Ther* 17:227–236.
- Falconer EM, Bryant R, Felmingham K, Kemp AH, Olivieri G, Peduto A, *et al.* (2006): 04-03 The neural networks of inhibitory control in post-traumatic stress disorder. *Acta Neuropsychiatr* 18: 323–323.
- Sripada RK, King AP, Garfinkel SN, Wang X, Sripada CS, Welsh RC, Liberzon I (2012): Altered resting-state amygdala functional connectivity in men with posttraumatic stress disorder. *J Psychiatry Neurosci* 37:241–249.
- Jin C, Qi R, Yin Y, Hu X, Duan L, Xu Q, *et al.* (2014): Abnormalities in whole-brain functional connectivity observed in treatment-naive post-traumatic stress disorder patients following an earthquake. *Psychol Med* 44:1927–1936.
- Koch SBJ, van Zuiden M, Nawijn L, Frijling JL, Veltman DJ, Olf M (2016): Aberrant resting-state brain activity in posttraumatic stress disorder: A meta-analysis and systematic review. *Depress Anxiety* 33:592–605.
- Rauch SL, Shin LM, Phelps EA (2006): Neurocircuitry models of posttraumatic stress disorder and extinction: Human neuroimaging research—Past, present, and future. *Biol Psychiatry* 60:376–382.
- Lee SH, Yoon S, Kim JI, Jin SH, Chung CK (2014): Functional connectivity of resting state EEG and symptom severity in patients with post-traumatic stress disorder. *Prog Neuropsychopharmacol Biol Psychiatry* 51:51–57.
- Toll RT, Wu W, Naparstek S, Zhang Y, Narayan M, Patenaude B, *et al.* (2020): An electroencephalography connectomic profile of post-traumatic stress disorder. *Am J Psychiatry* 177:233–243.
- Chen AC, Oathes DJ, Chang C, Bradley T, Zhou ZW, Williams LM, *et al.* (2013): Causal interactions between fronto-parietal central executive and default-mode networks in humans. *Proc Natl Acad Sci U S A* 110:19944–19949.
- Speri MFJ, Panitz C, Rosso IM, Dillon DG, Kumar P, Hermann A, *et al.* (2019): Fear extinction recall modulates human frontomedial theta and amygdala activity. *Cereb Cortex* 29:701–715.
- Cavanagh JF, Shackman AJ (2015): Frontal midline theta reflects anxiety and cognitive control: Meta-analytic evidence. *J Physiol Paris* 109:3–15.
- Jovanovic T, Ely T, Fani N, Glover EM, Gutman D, Tone EB, *et al.* (2013): Reduced neural activation during an inhibition task is associated with impaired fear inhibition in a traumatized civilian sample. *Cortex* 49:1884–1891.
- Stevens JS, Jovanovic T, Fani N, Ely TD, Glover EM, Bradley B, Ressler KJ (2013): Disrupted amygdala-prefrontal functional connectivity in civilian women with posttraumatic stress disorder. *J Psychiatr Res* 47:1469–1478.
- Bluhm RL, Williamson PC, Osuch EA, Frewen PA, Stevens TK, Boksman K, *et al.* (2009): Alterations in default network connectivity in posttraumatic stress disorder related to early-life trauma. *J Psychiatry Neurosci* 34:187–194.
- Aguilar DD, McNally JM (2022): Subcortical control of the default mode network: Role of the basal forebrain and implications for neuropsychiatric disorders. *Brain Res Bull* 185:129–139.
- Philippi CL, Koenigs M (2014): The neuropsychology of self-reflection in psychiatric illness. *J Psychiatr Res* 54:55–63.
- Akiki TJ, Averill CL, Abdallah CG (2017): A network-based neurobiological model of PTSD: Evidence from structural and functional neuroimaging studies. *Curr Psychiatry Rep* 19:81.
- Graham BM, Milad MR (2013): Blockade of estrogen by hormonal contraceptives impairs fear extinction in female rats and women. *Biol Psychiatry* 73:371–378.
- Bierwirth P, Speri MFJ, Antov MI, Stockhorst U (2021): Prefrontal theta oscillations are modulated by estradiol status during fear recall and

- extinction recall. *Biol Psychiatry Cogn Neurosci Neuroimaging* 6:1071–1080.
27. Andreano JM, Touroutoglou A, Dickerson B, Barrett LF (2018): Hormonal cycles, brain network connectivity, and windows of vulnerability to affective disorder. *Trends Neurosci* 41:660–676.
 28. Weathers FW, Blake DD, Schnurr PP, Kaloupek DG, Marx BP, Keane TM (2013): The Life Events Checklist for DSM-5 (LEC-5). Available at: https://www.ptsd.va.gov/professional/assessment/documents/LEC5_Standard_Self-report.pdf. Accessed July 22, 2024.
 29. Weathers FW, Blake DD, Schnurr PP, Kaloupek DG, Marx BP, Keane TM (2013): The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5). Available at: <https://www.ptsd.va.gov/professional/assessment/adult-int/caps.asp>. Accessed July 22, 2024.
 30. Chae JH, Jeong J, Peterson BS, Kim DJ, Bahk WM, Jun TY, *et al.* (2004): Dimensional complexity of the EEG in patients with post-traumatic stress disorder. *Psychiatry Res* 131:79–89.
 31. Li Q, Coulson Theodorsen M, Konvalinka I, Eskelund K, Karstoft KI, Bo Andersen S, Andersen TS (2022): Resting-state EEG functional connectivity predicts post-traumatic stress disorder subtypes in veterans. *J Neural Eng* 19:1741–2552.
 32. Corsi-Cabrera M, Galindo-Vilchis L, del-Río-Portilla Y, Arce C, Ramos-Loyo J (2007): Within-subject reliability and inter-session stability of EEG power and coherent activity in women evaluated monthly over nine months. *Clin Neurophysiol* 118:9–21.
 33. Näpflin KJ, Wildi M, Sarnthein J (2007): Test-retest reliability of resting EEG spectra validates a statistical signature of persons. *Clin Neurophysiol* 118:2519–2524.
 34. Popov T, Tröndle M, Baranczuk-Turska Z, Pfeiffer C, Haufe S, Langer N (2023): Test-retest reliability of resting-state EEG in young and older adults. *Psychophysiology* 60:e14268.
 35. Choi J, Lim E, Park MG, Cha W (2020): Assessing the retest reliability of prefrontal EEG markers of brain rhythm slowing in the eyes-closed resting state. *Clin EEG Neurosci* 51:348–356.
 36. Carbone GA, Lo Presti A, Farina B, Adenzato M, Ardito RB, Imperatori C (2024): Resting-state EEG microstates predict mentalizing ability as assessed by the Reading the Mind in the Eyes test. *Int J Psychophysiol* 205:112440.
 37. Wang Y, Duan W, Dong D, Ding L, Lei X (2022): A test-retest resting, and cognitive state EEG dataset during multiple subject-driven states. *Sci Data* 9:566.
 38. Widmann A, Schröger E, Maess B (2015): Digital filter design for electrophysiological data—A practical approach. *J Neurosci Methods* 250:34–46.
 39. Zhang Y, Naparstek S, Gordon J, Watts M, Shpigel E, El-Said D, *et al.* (2023): Machine learning-based identification of a psychotherapy-predictive electroencephalographic signature in PTSD. *Nat Mental Health* 1:284–294.
 40. Kybic J, Clerc M, Abboud T, Faugeras O, Keriven R, Papadopoulos T (2005): A common formalism for the integral formulations of the forward EEG problem. *IEEE Trans Med Imaging* 24:12–28.
 41. Tadel F, Baillet S, Mosher JC, Pantazis D, Leahy RM (2011): Brainstorm: A user-friendly application for MEG/EEG Analysis. *Comp Intel Neurosci* 2011:879716.
 42. Gross J, Kujala J, Hamalainen M, Timmermann L, Schnitzler A, Salmelin R (2001): Dynamic imaging of coherent sources: Studying neural interactions in the human brain. *Proc Natl Acad Sci U S A* 98:694–699.
 43. Steinsträter O, Sillekens S, Junghoefer M, Burger M, Wolters CH (2010): Sensitivity of beamformer source analysis to deficiencies in forward modeling. *Hum Brain Mapp* 31:1907–1927.
 44. Kumaravel VP, Buiatti M, Parise E, Farella E (2022): Adaptable and robust EEG bad channel detection using local outlier factor (LOF). *Sensors (Basel)* 22:7314.
 45. Mueller EM, Panitz C, Hermann C, Pizzagalli DA (2014): Prefrontal oscillations during recall of conditioned and extinguished fear in humans. *J Neurosci* 34:7059–7066.
 46. Harnett NG, Finegold KE, Lebois LAM, van Rooij SJH, Ely TD, Murty VP, *et al.* (2022): Structural covariance of the ventral visual stream predicts posttraumatic intrusion and nightmare symptoms: A multivariate data fusion analysis. *Transl Psychiatry* 12:321.
 47. Harnett NG, Stevens JS, Fani N, van Rooij SJH, Ely TD, Michopoulos V, *et al.* (2022): Acute posttraumatic symptoms are associated with multimodal neuroimaging structural covariance patterns: A possible role for the neural substrates of visual processing in posttraumatic stress disorder. *Biol Psychiatry Cogn Neurosci Neuroimaging* 7:129–138.
 48. Rowland GE, Roeckner A, Ely TD, Lebois LAM, van Rooij SJH, Bruce SE, *et al.* (2023): Prior sexual trauma exposure impacts post-traumatic dysfunction and neural circuitry following a recent traumatic event in the Aurora study. *Biol Psychiatry Glob Open Sci* 3:705–715.
 49. Lanius RA, Bluhm RL, Coupland NJ, Hegadoren KM, Rowe B, Théberge J, *et al.* (2010): Default mode network connectivity as a predictor of post-traumatic stress disorder symptom severity in acutely traumatized subjects. *Acta Psychiatr Scand* 121:33–40.
 50. Maron-Katz A, Zhang Y, Narayan M, Wu W, Toll RT, Naparstek S, *et al.* (2020): Individual patterns of abnormality in resting-state functional connectivity reveal two data-driven PTSD subgroups. *Am J Psychiatry* 177:244–253.
 51. Hayes JP, Hayes SM, Mikedis AM (2012): Quantitative meta-analysis of neural activity in posttraumatic stress disorder. *Biol Mood Anxiety Disord* 2:9.
 52. Ross DA, Arbuckle MR, Travis MJ, Dwyer JB, van Schalkwyk GI, Ressler KJ (2017): An integrated neuroscience perspective on formulation and treatment planning for posttraumatic stress disorder: An educational review. *JAMA Psychiatry* 74:407–415.
 53. Seligowski AV, Harnett NG, Merker JB, Ressler KJ (2020): Nervous and endocrine system dysfunction in posttraumatic stress disorder: An overview and consideration of sex as a biological variable. *Biol Psychiatry Cogn Neurosci Neuroimaging* 5:381–391.
 54. Rabellino D, Tursich M, Frewen PA, Daniels JK, Densmore M, Théberge J, Lanius RA (2015): Intrinsic Connectivity Networks in post-traumatic stress disorder during sub- and supraliminal processing of threat-related stimuli. *Acta Psychiatr Scand* 132:365–378.
 55. Dunkley BT, Sedge PA, Doesburg SM, Grodecki RJ, Jetly R, Shek PN, *et al.* (2015): Theta, mental flexibility, and post-traumatic stress disorder: Connecting in the parietal cortex. *PLoS One* 10:e0123541.
 56. Klimesch W (2012): α -band oscillations, attention, and controlled access to stored information. *Trends Cogn Sci* 16:606–617.
 57. Hidalgo-Lopez E, Zeidman P, Harris T, Razi A, Pletzer B (2021): Spectral dynamic causal modelling in healthy women reveals brain connectivity changes along the menstrual cycle. *Commun Biol* 4:954.