across racial and ethnic groups and between MCI and dementia.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: dementia - Alzheimer's disease
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Keyword 3: mild cognitive impairment
Correspondence: Grace J. Goodwin, University of Nevada-Las Vegas, goodwg1@unlv.nevada.edu

4 Resting State Functional Connectivity Impairments Implicate CNS Mechanisms Underlying Chronic Pain and Depression in Gulf War Veterans' Illness

Gabriell C Champion[1,2], Aliyah M Auerbach[3], Nayana Ambardekar[3], Thomas Novak[1,3], Anna Woodbury[1,3], Sheila A Rauch[1,3], Keith McGregor[4,5], Albert Y Leung[6,7], Kaundinya S Gopinath[1]
[1]Emory University, Atlanta, GA, USA. [2]Georgia State University, Atlanta, GA, USA. [3]Atlanta VA Health Care System, Decatur, GA, USA. [4]University of Alabama, Birmingham, AL, USA. [5]Birmingham VA Health Care System, Birmingham, AL, USA. [6]University of California San Diego, San Diego, CA, USA. [7]Veteterans Medical Research Foundation, San Diego, CA, USA

Objective: Around 200,000 veterans (up to 32% of those deployed) of the 1991 Gulf War (GW) suffer from GW veterans' illness (GWVI). GWVI is a poorly understood chronic medical condition, characterized by symptoms indicative of brain function deficits in multiple domains. Among the symptoms of brain impairment GWVI-related chronic headaches and body muscle and joint pain conditions (GWVI-HAP) are the most debilitating, affecting around 64% of the GWVI veterans. Further, depression carries a very high co-morbid rate (>50%) in patients with chronic pain, including GWVI-HAP. In this preliminary study, we examined the integrity of brain function networks in a group of GWI-HAP veterans, with resting state fMRI (rsfMRI).
Participants and Methods: Data from the first twenty-two GWVI-HAP veterans from two ongoing parallel clinical trials was examined. Of these 14 subjects (GWVI-HAP-DM) had mild depression (Hamilton Rating Scale for Depression (HSRD ≤ 13); and 8 subjects (GWVI-HAP-DS) had moderate to severe depression (HSRD > 14). Written informed consent was obtained from all participants in the protocol approved by the local Institutional Review Board. RsfMRI data was acquired on a Siemens 3T Prisma-Fit MRI scanner using a 10-minute whole-brain high resolution simultaneous multi-slice (SMS) gradient echo echo-planar imaging (EPI) sequence: TR/TE/FA = 2.2 sec/ 27 msec/80°, and analyzed with well-established image processing pipelines. Functional connectivity (FC) to different regions implicated in depression and chronic pain was assessed with seed-based correlation analysis. Between group differences in FC were obtained with 2-sample t-tests.
Results: GWVI-HAP-DS group exhibited significantly ($p < 0.05$) reduced FC compared to GWVI-HAP-DM between frontal lobe (medial (mPFC), and dorsolateral (dlPFC) prefrontal cortex) and the striatum. This indicates that malfunction of fronto-striatal circuits could be a source of the increased chronic pain and depression seen in veterans with GWVI- HAP-DS. Dysregulation of fronto-striatal networks has been implicated in major depressive disorder as well as many chronic pain conditions. In addition, FC between mPFC, and salience network (SN; anterior insula and dorsal anterior cingulate) and limbic (subgenual and ventral anterior cingulate) regions were also reduced in GWVI-HAP-DS. Similarly, mPFC and SN also exhibited reduced FC to pain processing regions (posterior insula, centromedian thalamus and cerebellum). These FC impairments could reflect greater deficits in regulation of and salience attribution to emotions and nociception in the GWVI-HAP-DS group. Finally, GWVI-HAP-DS also exhibited reduced FC between nodes of the default mode network. DMN impairments also have been observed in many depressive and chronic pain conditions.
Conclusions: The results of this preliminary analysis implicate impairments in cognitive control of emotion and nociception as a mechanism underlying the enhanced chronic pain and depression observed in GWVI-HAP veterans, especially those with moderate to severe depression. A fuller picture of deficits in FC in brain function networks is expected to emerge as more GWI-HAP subjects of both groups along with age matched healthy controls are examined in this ongoing project. Better understanding of impairments in these networks

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in GWI-HAP will benefit the rehabilitation of veterans with GWI-HAP.

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Correspondence: Gabriell Champion, Emory University, gchampi@emory.edu

5 White Matter Tract Shape as a Predictor of PTSD Symptom Severity in Trauma-Exposed Black American Women

Olivia C Haller[1], Tricia Z King[1], Xin Ma[2], Negar Fani[3], Suprateek Kundu[2]
[1]Georgia State University, Department of Psychology, Atlanta, GA, USA. [2]Division of Biostatistics and Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, GA, USA. [3]Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, USA

Objective: Machine learning studies of PTSD show promise for identifying neurobiological signatures of this disorder, but studies to date have largely excluded Black American women, who experience disproportionately greater trauma and have relatively higher rates of PTSD. PTSD is characterized by four symptom clusters: trauma reexperiencing, trauma avoidance, hyperarousal, and anhedonia. A prior machine learning study reported successful PTSD symptom cluster severity prediction using functional MRI data but did not examine white matter predictors. White matter microstructural integrity has been related to PTSD presence and symptoms, and unexplored metrics such as estimates of tract shape may provide unique predictive utility. Therefore, this study examines the relationship between white matter tract shape and PTSD symptom cluster severity amongst trauma-exposed Black American women using multiple machine learning models.
Participants and Methods: Participants included 45 Black American women with PTSD (M_{age}=40.4(12.9)) and 89 trauma-exposed controls (M_{age}=39.8(11.6)). Shape and diffusion metrics for the cingulum, corpus callosum, fornix, inferior longitudinal fasciculus, superior longitudinal fasciculus, and uncinate fasciculus were calculated using deterministic tractography. Current symptom severity was calculated using the PTSD Symptom Scales. Input features included tract metrics, questionnaire responses, and age. The following regression models were generated: least absolute shrinkage and selection operator (LASSO), ridge, elastic net, and gaussian process (GPR). Additionally, two forms of latent-scale GPR, one without (lsGPR) and with (sp-lsGPR) node selection via spike and slab priors, were calculated. The performance of regression models was estimated using mean square error (MSE) and R^2.
Results: sp-lsGPR performed at or above other models across all symptom clusters. LASSO models were comparable to sp-lsGPR for avoidance and hyperarousal clusters. Ridge regression and GPR had the weakest performance across clusters. Scores for sp-lsGPR by cluster are as follows: reexperiencing M_{MSE}=0.70(0.17), M_{R2}=0.56(0.13); avoidance M_{MSE}=0.75(0.17), M_{R2}= 0.51(0.13); hyperarousal M_{MSE}=0.57(0.18), M_{R2}=0.66(0.12); anhedonia M_{MSE}=0.74(0.27), M_{R2}=0.57(0.13). The top three ranked posterior inclusion probabilities for white matter tracts across sp-lsGPR models include four sections of the cingulum, three sections of the corpus callosum, the right fornix, the left inferior longitudinal fasciculus, the first segment of the right superior longitudinal fasciculus, and the right uncincate fasciculus. The greatest posterior inclusion probability value for the sp-lsGPR models was the left frontal parahippocampal cingulum for the hyperarousal cluster.
Conclusions: Results support the combined predictive utility of white matter metrics for brain imaging regression models of PTSD. Results also support the use of sp-lsGPR models, which are designed to balance interpretable linear models and highly-flexible non-linear models. The sp-lsGPR model performance was similar across clusters but was relatively better for the hyperarousal cluster. This finding contrasts with prior machine learning work using functional data which was unable to predict hyperarousal scores above chance (M_{R2}=0.06). These diverging findings highlight the importance of examining both functional and structural data in PTSD populations. Differing findings may also be related to sample characteristics as the prior study was conducted in China. Black American

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