research should examine these relationships in larger samples.

Categories: Cognitive Intervention/Rehabilitation
Keyword 1: depression
Keyword 2: cognitive functioning
Keyword 3: post-traumatic stress disorder
Correspondence: Amber V. Keller Research Service, VA San Diego Healthcare System, San Diego, CA, USA SDSU/UC San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA, USA Amber.Keller@va.gov

3 Network Analysis of Neuropsychiatric Symptoms in Alzheimer's Disease

Grace J Goodwin, Stacey Moeller, Amy Nguyen, Samantha John
University of Nevada, Las Vegas, Las Vegas, NV, USA

Objective: Neuropsychiatric symptoms due to Alzheimer's disease (AD) and mild cognitive impairment (MCI) can decrease quality of life for patients and increase caregiver burden. Better characterization of neuropsychiatric symptoms is needed to identify effective treatment targets. The current investigation leveraged the National Alzheimer's Coordinating Center (NACC) Uniform Data Set (UDS) to examine the network structure of neuropsychiatric symptoms among symptomatic older adults with cognitive impairment.
Participants and Methods: The identified sample includes those from the NACC UDS (all versions) with complete data on the Neuropsychiatric Inventory Questionnaire (NPI-Q) at initial visit. The NPI-Q is an informant-based estimation of the presence and severity of neuropsychiatric symptoms (delusions, hallucinations, agitation or aggression, depression or dysphoria, anxiety, elation or euphoria, apathy or indifference, disinhibition, irritability or lability, motor disturbance, nighttime behaviors, appetite and eating problems). The following inclusionary criteria were applied for sample identification: age 50+; cognitive status of MCI or dementia; AD was the primary or contributing cause of observed impairment; and at least one symptom on the NPI-Q was endorsed. Participants were excluded if they endorsed "unknown" or "not available" on any NPI-Q items. The final sample (n = 12,507) consisted of older adults (M_{age}=73.94, SD_{age}=9.41; 46.2% male, 53.8% female) who predominantly identified as non-Hispanic white (NHW) (74.5% NHW, 10.9% non-Hispanic Black, 8.5% other, 5.8% Hispanic white, .3% Hispanic Black). The majority of the sample met criteria for dementia (77.6% dementia, 22.4% MCI) and AD was the presumed primary etiology in 93.9%.
The *eLasso* method was used to estimate the binary network, wherein nodes represent NPI-Q variables and edges represent their pairwise dependency after controlling for all other symptom variables in the network. In other words, the network represents the conditional probability of an observed binary variable (e.g., presence/absence of delusions) given all other measured variables (e.g., presence/absence of all other NPI-Q symptoms) (Finnemann et al., 2021; van Borkulo et al., 2014). Strength centrality and expected influence were calculated to determine relative importance of each symptom variable in the network. Network accuracy was examined with methods recommended by Epskamp et al. (2018), including edge-weight accuracy, centrality stability, and difference tests.
Results: Edge weights and node centrality (*CS*(cor=.7)=.75) were stable and interpretable. The network (*M*=.28) consisted of mostly positive edges and some negative edges. The strongest edges linked nodes within symptom domain (e.g., strong positive associations among externalizing symptoms). Disinhibition and agitation/aggression were the most central and influential symptoms in the network, respectively. Depression or dysphoria was the most frequently endorsed symptom, followed by anxiety, apathy or indifference, and irritability or lability.
Conclusions: Endorsed disinhibition and agitation yielded a higher probability of additional neuropsychiatric symptoms and influenced the activation, persistence, and remission of other neuropsychiatric symptoms within the network. Thus, interventions targeting these symptoms may lead to greater neuropsychiatric symptom improvement overall. Depression or dysphoria, while highly endorsed, was least influential in the network. This may suggest that depression and dysphoria are common, but not central neuropsychiatric features of AD pathology. Future work will compare neuropsychiatric symptom networks

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across racial and ethnic groups and between MCI and dementia.

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Keyword 1: dementia - Alzheimer's disease
Keyword 2: neuropsychiatry
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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