Salience Network Disruption in US Army Soldiers with PTSD

SUPPLEMENTAL INFORMATION

Image Processing

The Human Connectome Project (HCP) Pipelines (github.com/Washington-University/Pipelines) were adapted to process the imaging data (1). Briefly, the adapted minimal preprocessing included FreeSurfer automatic segmentation and parcellation of high-resolution structural scans, deletion of the first 5 volumes, slice timing correction, motion correction, intensity normalization, brain masking, and registration of *f*MRI images to structural MRI and standard template, while minimizing smoothing from interpolation. Then, the cortical gray matter ribbon voxels and each subcortical parcel were projected to a standard Connectivity Informatics Technology Initiative (CIFTI) 2mm grayordinate space. ICA-FIX was run to identify and remove artifacts (2,3), followed by mean grayordinate time series regression (MGTR; which is comparable to global signal regression in volume data). The latter two processing steps (FIX+MGTR) have been found to significantly reduce motion-correlated artifacts (4). In addition, there were no differences ($P > .1$) in head motion during *f*MRI session between the study groups at rest (mean ±*SEM*; PTSD = 0.09 ±0.009; CC = 0.07 ±0.003; HC = 0.09 ±0.013) and during symptoms provocation (mean ±*SEM*; PTSD = 0.10 ±0.008; CC = 0.09 ±0.009; HC = 0.10 ±0.012).

Details of global brain connectivity with global signal regression (GBCr) methods were previously described (5-16). Briefly, time series were demeaned and normalized, followed by generating dense connectomes correlating each vertex/voxel with all other vertices/voxels in the CIFTI grayordinates, and then transformed to Fisher *z* values. For each vertex/voxel, GBCr is calculated as the standardized (*z* scored) average across those Fisher *z* values with parcel-constrained smoothing (sigma = 4.2 mm), which generates a

map for each *f*MRI session where each vertex/voxel value represents the functional connectivity strength of that grayordinate with the rest of the brain. In graph theory terms, GBCr (also known as functional connectivity strength; FCS [17)]) is considered a weighted measure of nodal strength of a voxel in the whole brain network – determining brain hubs and examining the coherence between a local region and the rest of the brain (18).

Similar to previous studies (5-11,13,17), we have used GBCr, instead of GBC without global signal regression (GBCnr), because the study hypotheses were based on previous GBCr findings (5-7), which provided the rationale for the current report and will facilitate the interpretation of the study findings. In addition, previous work underscored the need for MGTR to adequately minimize spurious artifacts (4).

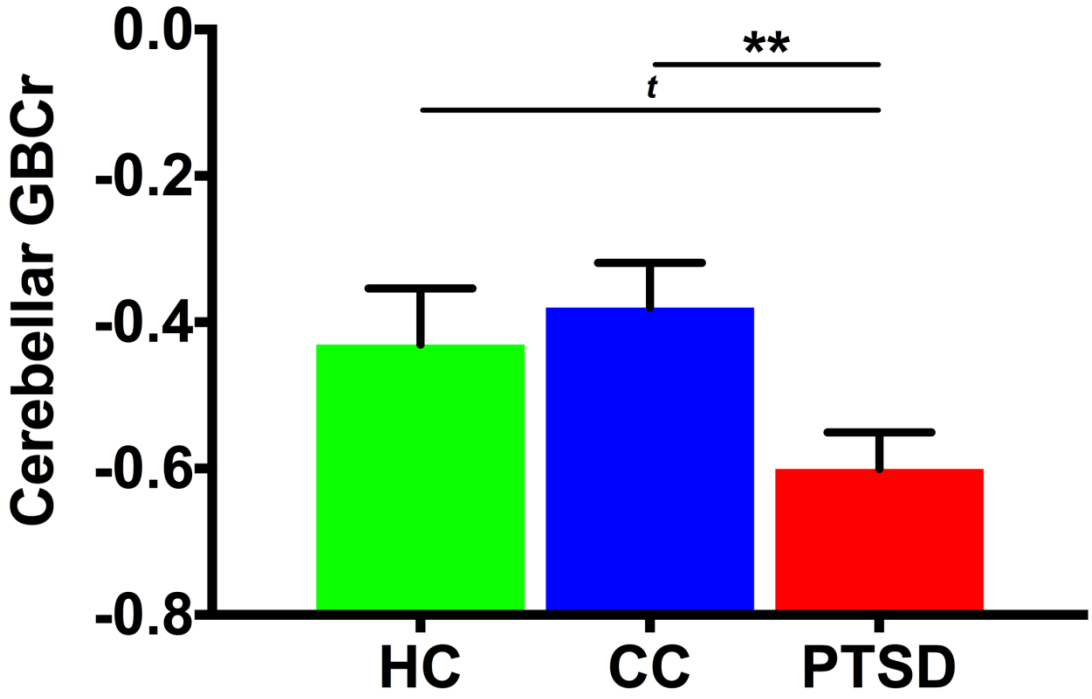

Figure S1. Overall Cerebellar Global Connectivity in US Army Soldiers with Posttraumatic Stress Disorder (PTSD). There was a significant main group effect with increased overall (i.e., at rest and during trauma recollection) global brain connectivity with global signal regression (GBCr) in PTSD compared to combat controls (CC), with a trend level significance, compared to healthy control (HC). ** $P \leq .01$; $^{t}P \leq .1$.

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