

Reduced Salience and Enhanced Central Executive Connectivity Following PTSD Treatment

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 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 \pm SEM; Pretreatment: PCT = $.10 \pm .018$; CPT = $.09 \pm .007$; CC = $.07 \pm .004$; Posttreatment: PCT = $.07 \pm .008$; CPT = $.07 \pm .005$; CC = $.06 \pm .003$) and during symptoms provocation (Pretreatment: PCT = $.09 \pm .006$; CPT = $.12 \pm .019$; CC = $.09 \pm .009$; Posttreatment: PCT = $.13 \pm .031$; CPT = $.10 \pm .007$; CC = $.10 \pm .012$).

Details of global brain connectivity with global signal regression (GBCr) methods were previously described (5-17). 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 fMRI 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 (18)) 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 (19).

Similar to previous studies (5-12,14,18,20), we have used GBCr, instead of GBC without global signal regression (GBCnr), because the study hypotheses were based on previous GBCr findings (6-8), which provided the rationale for the current report and will facilitate the interpretation of the study findings (see Ref (7) for additional justification). In addition, previous work underscored the need for MGTR to adequately minimize spurious artifacts (4).

Cerebellar Clusters

Using a GLM comparable to the salience and executive ROIs, we found significant effects of group ($F_{(2,55)} = 7.2, p = .002$), time ($F_{(1,55)} = 25.8, p < .001$), task ($F_{(1,55)} = 79.2, p < .001$), and task*time ($F_{(1,55)} = 47.3, p < .001$), task*group ($F_{(2,55)} = 9.1, p < .001$), and time*group interactions ($F_{(2,55)} = 25.8, p < .001$) on the cerebellar ROI. There were no time*group and no time*task*group interactions (all p values $> .1$). The post-hoc analyses results are shown in Fig. S2.

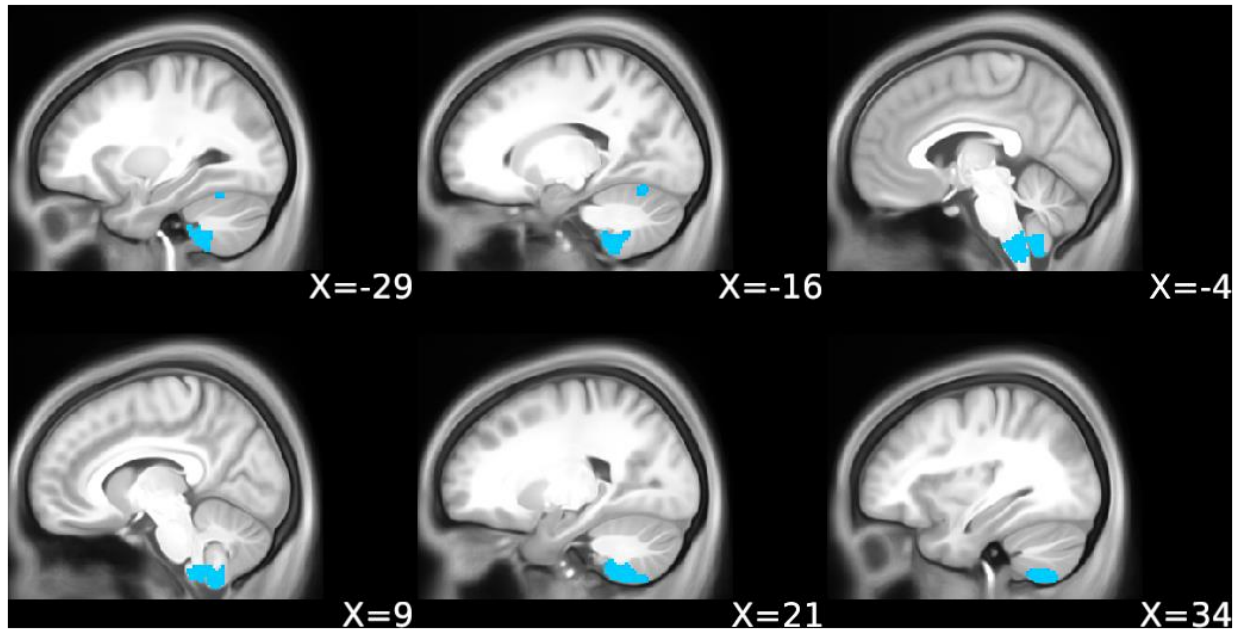


Figure S1. Cerebellar Global Connectivity Post-treatment. The blue clusters mark the vertices with reduced global brain connectivity with global signal regression (GBCr) in posttraumatic stress disorder (PTSD) compared to controls during symptom provocation ($p < .005$ and corrected $\alpha = .05$).

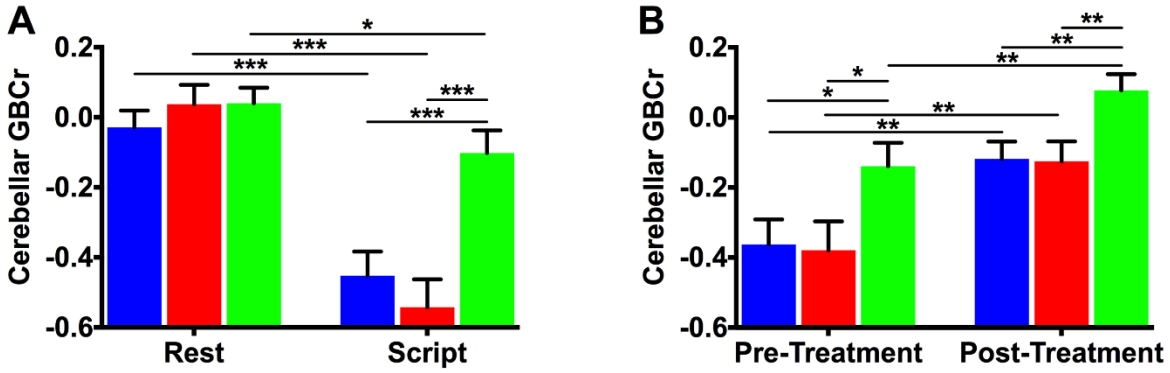


Figure S2. The Effects of Evidence-based Psychotherapy on Cerebellar Connectivity.

A. There was a significant group by task interaction effect on executive global brain connectivity with global signal regression (GBCr), with more pronounced reduction in GBCr during trauma recollection (i.e., script imagery) compared to during resting state in posttraumatic stress disorder (PTSD) patients treated with present-centered therapy (PCT; blue) or cognitive processing therapy (CPT; red), compared to combat control (CC; green). The lower GBCr values in PTSD compared to CC were significant only during trauma recollection, but not a rest. **B.** There was no time by group interaction, such as the increase in GBCr posttreatment was comparable regardless of group affiliation. * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$.

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