**Supplementary Materials**

**Summary of Analyses and Supplementary Analyses**

**Summary of fMRI Analytic Procedures**

*Pre-processing*

Pre-processing (realignment and unwarping, spatial normalization into standardized MNI space, smoothing using an 8mm FWHM isotropic Gaussian kernel) and statistical analysis of fMRI data was conducted using Statistical Parametric Mapping (SPM8, Wellcome Department of Neurology, London). Motion correction was done by realigning and unwarping fMRI images to the initial image of each task run and then screened for motion artifacts using the Artifact Detection Tools (ART, www.nitrc.org/projects/artifact\_detect/). The motion parameters (three translation and three rotational) estimated during the realignment pre-processing stage were used to identify any problematic fMRI volumes in each participant’s entire scan and exclude participants with more than 25% volume outliers (none of our study participants were excluded). A volume frame was defined as an outlier (artifact) if the head displacement in x, y or z direction was greater than .5mm from the previous frame, or if the global mean intensity in the volume was greater than 3 standard deviations from the mean image intensity for the entire scan. For normalization to stereotactic MNI space, the T1-weighted SPGR images were normalized to standard space using the FMRIB nonlinear registration tool and the fMRI EPI data were coregistered to the T1 data using FMRIB linear registration tool17,18. The normalization warps from these procedures were stored for use in functional to standard space transformations. Global signal was estimated using a mask in the ventricles and white matter, and was removed from the motion corrected fMRI time series. All fMRI data were smoothed using an 8-mm Gaussian kernel and was high pass filtered using a cutoff period of 128 seconds.

*Functional connectivity*

A generalized psychophysiological interactions (gPPI) model identifies how task-specific changes in the BOLD signal across difference regions in the brain interact over time. This model generates a regressor of each task condition’s onset times, in this case for each emotion, and individually convolves this with the hemodynamic response function to form a psychological interaction term. This term is then multiplied by the estimated neural activity of the seed region (the physiological regressor), derived from the deconvolved BOLD signal of this seed, and other relevant covariates i.e. motion regressors. This differs from a standard PPI where the psychological regressor is created by producing the product of the condition onset times and a weighting/contrast vector before it is multiplied with the physiological term. The gPPI approach therefor generates a more accurate model of the interaction between multiple conditions and neural activity across the entire experimental space. This model allows us to explore the correlation between the BOLD response in various voxels or ROIs through the brain and neural activity in the seed region during any of multiple task conditions, providing a measure of task-related connectivity.

**Threat related activations for CPTSD, PTSD & TC groups in our hypothesized ROIs**

Using the repeated measures ANOVA design, we performed voxel-wise evaluation of activations for each of the participant groups to evaluate threat related activation effects of our task in our selected regions of interests. In the table below we report ROIs which demonstrated significant activation within each group.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Group** | **Region** | **Side** | **Coordinates** | |  | **Cluster** | **Z value** | **P (FWE)** |
|  |  |  | **x** | **Y** | **Z** | **Size** |  |  |
| **CPTSD** |  |  |  |  |  |  |  |  |
|  | *Supraliminal* |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
|  | Amygdala | R | 34 | 2 | -24 | 69 | 3.07 | 0.022 |
|  |  |  |  |  |  |  |  |  |
|  | Insula | R | 42 | 16 | -14 | 324 | 3.68 | 0.022 |
|  |  |  |  |  |  |  |  |  |
|  | DLPFC | R | 50 | 24 | 12 | 424 | 3.34 | 0.014 |
|  |  |  |  |  |  |  |  |  |
|  | *Subliminal* |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
|  | Insula | R | 34 | 32 | 8 | 661 | 3.47 | 0.03 |
|  |  |  |  |  |  |  |  |  |
|  | DLPFC | L | -36 | 28 | 26 | 212 | 2.93 | 0.041 |
|  |  | R | 38 | 34 | 14 | 217 | 3.65 | 0.005 |
|  |  |  |  |  |  |  |  |  |
| **PTSD** |  |  |  |  |  |  |  |  |
|  | *Supraliminal* |  | non-significant |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
|  | *Subliminal* |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
|  | sgACC |  | 4 | 24 | -4 | 256 | 3.1 | 0.016 |
|  |  |  |  |  |  |  |  |  |
|  | DLPFC | R | 44 | 22 | 14 | 318 | 3.51 | 0.008 |
|  |  |  |  |  |  |  |  |  |
| **TC** | *Supraliminal* |  |  |  |  |  |  |  |
|  | dACC |  | -6 | 26 | 32 | 86 | 2.76 | 0.041 |
|  |  |  |  |  |  |  |  |  |
|  | Insula | L | -38 | 2 | 18 | 67 | 3.79 | 0.011 |
|  |  | R | 42 | 22 | -10 | 383 | 3.6 | 0.02 |
|  |  |  |  |  |  |  |  |  |
|  | DLPFC | L | -40 | 12 | 26 | 492 | 4.97 | 0 |
|  |  | R | 46 | 22 | 12 | 478 | 4.22 | 0.001 |
|  |  |  |  |  |  |  |  |  |
|  | *Subliminal* |  | non-significant |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |

**Group comparisons of neural activations for Neutral Processing:**

In our main analysis we used contrasts of each individual emotion relative to the neutral emotion. However, considering that there is some evidence that suggests that neutral faces may not be suitable baseline comparisons (1), here we evaluate how the differences between the Complex PTSD and PTSD patient groups during processing of neutral stimuli may be driving the effects observed in our main analyses. We performed voxel-wise analyses group comparisons for Neutral vs. Rest (implicit baseline) contrast in the bilateral insula and right amygdala ROIs. There were no significant differences between the two groups for processing of Neutral faces. We also evaluated if there was significant activation within these ROIs for each group separately. Both groups exhibited significantly reduced insula activation during Neutral processing relative to the implicit baseline but neither of the groups had significantly increased or decreased activation in the right amygdala for Neutral vs. Rest contrast.

We also extracted mean BOLD estimates for each of the Threat emotions vs. Rest contrast using the bilateral insula and right amygdala ROI clusters found significant in the main analysis, and tested if differences between the Complex PTSD and PTSD groups remain significant. We found that the two groups were not significant for the threat emotions relative to the implicit baseline.

Together these results suggest that the difference between the two groups were most pronounced for comparison of brain activations during threat relative to neutral emotions and were not driven by differences in only neutral processing between these groups.

References

1. Filkowski MM, Haas BW. Rethinking the use of neutral faces as a baseline in fMRI neuroimaging studies of Axis-I psychiatric disorders. *J Neuroimag* 2017; 27: 281-291