**Methods and Materials**

*Meta-analytic approach*

Recreation of effect size maps from brain maps involved the transformation to Montreal Neurological Institute (MNI) stereotaxic space (in case that they were not already reported in this space) and the voxel-wise conversion of t-values (or p- or z-values) into effect sizes. Location of the maximum and minimum hyper/hypoactivation peaks in the recreated maps was manually checked to identify potential artifacts (e.g., image flip) during the conversion. For the recreation of effect size maps from peak information, effect-sizes were calculated following standard methods in those voxels containing a peak reported in the results table of the original studies, and for the remaining voxels, an effect-size was estimated depending on the distance to close peaks using an anisotropic unnormalized Gaussian kernel. This kernel assigns higher effect-sizes to those voxels more correlated with the peak, whereas small effect-sizes are assigned to those that, even if still neighboring, show only a small correlation at the population level. Both hyperactivation and hypoactivation are represented on the same map to correctly analyze those regions with higher between-study heterogeneity, i.e., where some studies report hyperactivation and other hypoactivation. Note also that if hyperactivation and hypoactivation were plotted on separate maps, some brain regions might falsely appear as hyperactivating and hypoactivating at the same time in the same study – which is logically impossible.

*Directionality Analysis*

The direction of changes in a difference map of group contrasts can be difficult to establish without additional information. Positive values in the difference map can reflect hyperactivation in the patients contrasts with regards to the controls contrasts or failure to deactivate in the controls contrasts with regards to the patients contrasts. Analogously, negative values in the difference map can also reflect hypoactivation in the controls contrasts with regards to the patients contrasts or a failure of activation in patients contrasts with regards to the controls contrasts. Therefore, further analyses were needed in order to correctly establish the directionality of the results. We meta-analyzed the within-group contrasts for those studies where group or subject maps were available (**Table 2**). Each activation location in the difference map was cross-checked in the within-group contrasts to determine whether it corresponded to an hyperactivation in the PTSD group or to a failure to deactivate in the TEHC group. Analogous analyses were performed for the reverse contrast.

*Additional meta-analysis*

One of the studies (YN) had limited signal coverage of superior frontal regions. The inclusion of a dataset that used a mask smaller than the meta-analytic template may have two opposite effects: improving the estimation of effect sizes within its mask, but biasing p-values. To improve the estimations of the effect size but at the same time ensure that results were not biased, we conducted the analyses twice, including and excluding the dataset. Overall, the meta-analyses produced similar results when including or excluding the study. Primary results included in the original manuscript correspond to the inclusion of this study. **Tables S2-4**, and **Figures S5-7** provides results corresponding to the omission of this study.

**Supplementary Tables**

**Table S1. Full-text articles excluded and reason**

|  |  |
| --- | --- |
| Full-text articles excluded with reason | Exclusion Reason |
| Thomaes, K., Dorrepaal, E., Draijer, N., de Ruiter, M. B., Elzinga, B. M., Sjoerds, Z., van Balkom, A. J., Smit, J. H., Veltman, D. J. (2013). Increased anterior cingulate cortex and hippocampus activation in Complex PTSD during encoding of negative words. Soc Cogn Affect Neurosci. 8(2): 190-200. doi: 10.1093/scan/nsr084. | No differential Conditioning |
| Tuescher, O., Protopopescu, X., Pan, H., Cloitre, M., Butler, T., Goldstein, M., Root, J. C., Engelien, A., Furman, D., Silverman, M., Yang, Y., Gorman, J., LeDoux, J., Silbersweig, D., Stern, E. (2011). Differential activity of subgenual cingulate and brainstem in panic disorder and PTSD. J Anxiety Disord. 25(2): 251-257. doi: 10.1016/j.janxdis.2010.09.010. | No differential Conditioning |
| Mahabir, M., Tucholka, A., Shin, L. M., Etienne, P., Brunet, A. (2015). Emotional face processing in post-traumatic stress disorder after reconsolidation impairment using propranolol: A pilot fMRI study. J Anxiety Disord. 36: 127-133. doi: 10.1016/j.janxdis.2015.10.004. | No differential Conditioning |
| Brunetti, M., Sepede, G., Ferretti, A., Mingoia, G., Romani, G. L., Babiloni, C. (2015). Response inhibition failure to visual stimuli paired with a "single-type" stressor in PTSD patients: an fMRI pilot study. Brain Res Bull, 114: 20-30. doi: 10.1016/j.brainresbull.2015.03.001. | No CS+ vs CS- cue comparison |
| Steiger, F., Nees, F., Wicking, M., Lang, S., Flor, H. (2015). Behavioral and central correlates of contextual fear learning and contextual modulation of cued fear in posttraumatic stress disorder. Int J Psychophysiol, 98(3 Pt 2): 584-593. doi: 10.1016/j.ijpsycho.2015.06.009. | No CS+ vs CS- cue comparison |
| Rougemont-Bücking, A., Linnman, C., Zeffiro, T. A., Zeidan, M. A., Lebron-Milad, K., Rodriguez-Romaguera, J., Rauch, S. L., Pitman, R. K., Milad, M. R. (2011). Altered processing of contextual information during fear extinction in PTSD: an fMRI study. CNS Neurosci Ther. 17(4): 227-236. doi: 10.1111/j.1755-5949.2010.00152.x. | No CS+ vs CS- cue comparison |
| Shvil, E., Sullivan, G. M., Schafer, S., Markowitz, J. C., Campeas, M., Wager, T. D., Milad, M. R., Neria, Y. (2014). Sex differences in extinction recall in posttraumatic stress disorder: a pilot fMRI study. Neurobiol Learn Mem. 113: 101-108. doi: 10.1016/j.nlm.2014.02.003. | Sample overlap (YN unpublish) |
| Sripada, R. K., Garfinkel, S. N., Liberzon, I. (2013). Avoidant symptoms in PTSD predict fear circuit activation during multimodal fear extinction. Front Hum Neurosci. 7: 672. doi: 10.3389/fnhum.2013.00672. | Sample overlap (Garfinkel 2014) |
| Helpman, L., Marin, M. F., Papini, S., Zhu, X., Sullivan, G. M., Schneier, F., Neria, M., Shvil, E., Malaga Aragon, M. J., Markowitz, J. C., Lindquist, M. A., Wager, T., Milad, M., & Neria, Y. (2016). Neural changes in extinction recall following prolonged exposure treatment for PTSD: A longitudinal fMRI study. NeuroImage. Clinical, 12, 715–723. | Sample overlap (YN unpublished) |
| Marin, M. F., Song, H., VanElzakker, M. B., Staples-Bradley, L. K., Linnman, C., Pace-Schott, E. F., Lasko, N. B., Shin, L. M., & Milad, M. R. (2016). Association of Resting Metabolism in the Fear Neural Network With Extinction Recall Activations and Clinical Measures in Trauma-Exposed Individuals. The American journal of psychiatry, 176 (9), 930–938. | No whole brain analysis |

**Table S2. Results of meta-analysis for the CS+ > CS- contrast during conditioning including all studies: regional differences in activation at p<0.005, z>1 and cluster size >10 voxels.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | MNI Coordinates | | | |  | |  | |  | |  | | |  |  | |  | |  |  |
| Region | Laterality | x | y | z | SDM-Z | | P | | Voxels | | I2 | | JK | Egger test P | | | Funnel Plot Description | | | Q P |  |
| **PTSD>TEHC** |  |  |  |  |  | |  | |  | |  | |  |  | | |  | | |  |  |
| Orbitofrontal Cortex | R | 10 | 50 | -2 | 2.704 | | 0.000032 | | 146 | | 0.00% | | 5/6 | 0.54 | | | No bias | | 0.520252 | |  |
| Superior Temporal Pole | L | -46 | 6 | -18 | 2.423 | | 0.000139 | | 57 | |  | | 6/6 |  | | |  | |  | |  |
| Amygdala | L | -20 | -6 | -16 | 2.869 | | 0.000014 | | 51 | | 0.00% | | 6/6 | 0.97 | | | No bias | | 0.463977 | |  |
| Hippocampus | L | -38 | -30 | -12 | 2.318 | | 0.000233 | | 38 | | 3.24% | | 5/6 | 0.55 | | | No bias | | 0.395747 | |  |
| Insula | R | 38 | -18 | 0 | 2.284 | | 0.000273 | | 39 | | 2.55% | | 4/6 | 0.22 | | | Very slightly biased | | 0.400115 | |  |
| Cerebellum |  | 0 | -50 | -32 | 2.391 | | 0.000162 | | 34 | |  | | 5/6 |  | | |  | |  | |  |
| Postcentral Gyrus | R | 54 | -4 | 20 | 2.377 | | 0.000177 | | 32 | |  | | 5/6 |  | | |  | |  | |  |
| Superior Temporal Gyrus | L | -52 | -8 | -8 | 2.323 | | 0.000229 | | 29 | |  | | 5/6 |  | | |  | |  | |  |
| Superior Temporal Pole | R | 48 | 4 | -18 | 2.107 | | 0.000624 | | 27 | |  | | 5/6 |  | | |  | |  | |  |
| Hippocampus | R | 22 | -12 | -14 | 2.374 | | 0.000178 | | 23 | | 0.00% | | 4/6 | 0.99 | | | No bias | | 0.655143 | |  |
| Ventromedial Prefrontal Cortex | R | 10 | 64 | 20 | 2.03 | | 0.000876 | | 17 | | 0.00% | | 3/6 | 0.71 | | | No bias | | 0.835369 | |  |
| Superior Temporal Pole | R | 38 | 2 | -14 | 1.811 | | 0.002249 | | 15 | |  | | 2/6 |  | | |  | |  | |  |
| Subgenual Anterior Cingulate Cortex | L | -2 | 4 | -8 | 2.038 | | 0.000845 | | 14 | | 0.00% | | 3/6 | 0.68 | | | No bias | | 0.937847 | |  |
|  |  |  |  |  |  | |  | |  | |  | |  |  | | |  | |  | |  |
|  |  |  |  |  |  | |  | |  | |  | |  |  | | |  | |  | |  |
| **TEHC>PTSD** |  |  |  |  |  | |  | |  | |  | |  |  | | |  | |  | |  |
| Superior Occipital Cortex | L | -18 | -86 | 22 | -3.408 | | 0.000018 | | 83 | |  | | 6/6 |  | | |  | |  | |  |
| Middle Frontal Cortex | R | 44 | 52 | 4 | -3.125 | | 0.000084 | | 61 | |  | | 6/6 |  | | |  | |  | |  |
| Middle Temporal Gyrus | L | -60 | -34 | -16 | -3.087 | | 0.000102 | | 41 | |  | | 5/6 |  | | |  | |  | |  |
| Middle Occipital Cortex | R | 40 | -68 | 16 | -2.705 | | 0.000710 | | 22 | |  | | 3/6 |  | | |  | |  | |  |
| Thalamus | L | -8 | -6 | 8 | -2.783 | | 0.000489 | | 21 | | 13.20% | | 3/6 | 0.12 | | | No bias | | 0.330225 | |  |
| Superior Occipital Cortex | L | -26 | -68 | 24 | -2.66 | | 0.000868 | | 20 | |  | | 2/6 |  | | |  | |  | |  |
| Middle Occipital Cortex | L | -34 | -78 | 8 | -3.118 | | 0.000088 | | 19 | |  | | 4/6 |  | | |  | |  | |  |
| Inferior Temporal Gyrus | L | -56 | -24 | -24 | -3.141 | | 0.000077 | | 16 | |  | | 4/6 |  | | |  | |  | |  |
| Precentral Gyrus | R | 50 | 2 | 32 | -2.635 | | 0.000972 | | 10 | |  | | 2/6 |  | | |  | |  | |  |
|  |  |  |  |  |  | |  | |  | |  | |  |  | | |  | |  | |  |
|  |  |  |  |  |  | |  | |  | |  | |  |  | | |  | |  | |  |

*Abbreviations*: MNI: Montreal Neurological Institute; SDM: Signed Differential Mapping; P: p-value; I2: Percentage of variance attributable to study heterogeneity; JK, Jackknife Sensitivity Test; Q P, Cochran’s Q p-value.

Note: Cluster p-values refer to the GRF probability of finding clusters with that size per the thresholds derived from the permutation test; when the maps were thresholded using threshold usual for GRF, many of the n.s. p-values became statistically significant.

**Table S3. Results of meta-analysis for the CS+ > CS- contrast during extinction learning including all studies: regional differences in activation at p<0.005, z>1 and cluster size >10 voxels.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | MNI Coordinates | | |  |  |  |  |  |  |  |  |
| Region | Laterality | x | y | z | SDM-Z | P | Voxels | I2 | JK | Egger test P | Funnel Plot Description | Q P |
| **PTSD>TEHC** | |  |  |  |  |  |  |  |  |  |  |  |
| Superior Temporal Cortex | R | 56 | -14 | 4 | 2.52 | 0.000144 | 226 | 0.00% | 5/5 | 0.16 | No bias | 0.445267 |
| Parahippocampal Gyrus | R | 28 | 4 | -30 | 2.83 | 0.000021 | 155 | 0.00% | 5/5 | 0.97 | No bias | 0.476693 |
| Insula | L | -44 | 6 | 4 | 2.466 | 0.000194 | 109 | 0.00% | 5/5 | 0.06 | No bias | 0.713681 |
| Cerebellum | R | 24 | -30 | -28 | 2.383 | 0.000315 | 60 |  | 3/5 |  |  |  |
| Cerebellum | R | 32 | -52 | -26 | 2 | 0.002178 | 46 |  | 3/5 |  |  |  |
| Superior Temporal Pole | R | 52 | 10 | -12 | 2.216 | 0.000737 | 16 | 0.00% | 3/5 | 0.00 | No bias | 0.457621 |
| Middle Occipital Cortex | L | -28 | -98 | 2 | 1.967 | 0.002598 | 15 |  | 4/5 |  |  |  |
| Middle Temporal Cortex | L | -56 | 0 | -24 | 2.312 | 0.000449 | 11 | 0.00% | 3/5 | 0.54 | No bias | 0.510883 |
| Occipital Cortex | R | 28 | -68 | 6 | 2.098 | 0.001322 | 10 |  | 2/5 |  |  |  |
| Cerebellum | R | 16 | -64 | -14 | 2.005 | 0.002125 | 10 |  | 1/5 |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| **TEHC>PTSD** | |  |  |  |  |  |  |  |  |  |  |  |
| Posterior Cingulate Cortex | L | -8 | -40 | 8 | -2.198 | 0.000092 | 172 | 0.00% | 5/5 | 0.43 | No bias | 0.606488 |
| Ventromedial Prefrontal Cortex | L | -10 | 60 | 14 | -2.366 | 0.000027 | 63 | 0.00% | 5/5 | 0.56 | No bias | 0.54704 |
| Thalamus | R | 4 | -22 | 20 | -2.266 | 0.000057 | 63 | 0.00% | 4/5 | 0.07 | No bias | 0.50328 |
| Orbital Frontal Cortex | R | 28 | 24 | -20 | -1.89 | 0.000620 | 36 | 0.00% | 5/5 | 0.44 | No bias | 0.446427 |
| Inferior Temporal Cortex | R | 50 | -30 | -18 | -1.941 | 0.000471 | 28 |  | 4/5 |  |  |  |
| Inferior Parietal Cortex | R | 46 | -74 | 36 | -1.901 | 0.000582 | 23 |  | 3/5 |  |  |  |
| Parietal cortex | R | 34 | -42 | 42 | -2.008 | 0.000319 | 18 |  | 3/5 |  |  |  |
| Hippocampus | L | -30 | -10 | -16 | -1.943 | 0.000464 | 17 | 0.00% | 3/5 | 0.2 | No bias | 0.747455 |
| Inferior Temporal Cortex | L | -46 | -42 | -12 | -2.025 | 0.000284 | 11 |  | 3/5 |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |

*Abbreviations*: MNI: Montreal Neurological Institute; SDM: Signed Differential Mapping; P: p-value; I2: Percentage of variance attributable to study heterogeneity; JK, Jackknife Sensitivity Test; Q P, Cochran’s Q p-value.

Note: Cluster p-values refer to the GRF probability of finding clusters with that size per the thresholds derived from the permutation test; when the maps were thresholded using threshold usual for GRF, many of the n.s. p-values became statistically significant.

**Table S4. Results of meta-analysis for the CS+ > CS- contrast during extinction recall including all studies: regional differences in activation at p<0.005, z>1 and cluster size >10 voxels.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | MNI Coordinates | | |  |  |  |  |  |  |  |  |
| Region | Laterality | x | y | z | SDM-Z | P | Voxels | I2 | JK | Egger test P | Funnel Plot Description | Q P |
| **PTSD>TEHC** | |  |  |  |  |  |  |  |  |  |  |  |
| Cerebellum | R | 14 | -40 | -14 | 2.593 | 0.000261 | 172 |  | 3/4 |  |  |  |
| Orbital Frontal Cortex | R | 12 | 30 | -16 | 2.396 | 0.000557 | 110 | 0.00% | 2/4 | 0.64 | No bias | 0.419875 |
| Anterior Cingulate Cortex | L | -6 | 22 | 22 | 2.348 | 0.000668 | 33 | 1.43% | 1/4 | 0.71 | Slightly biased | 0.384967 |
| Pons | L | -10 | -10 | -14 | 2.163 | 0.001313 | 28 |  | 2/4 |  |  |  |
| Amygdala | R | 24 | 2 | -22 | 2.296 | 0.000816 | 26 | 0.94% | 2/4 | 0.75 | No bias | 0.387252 |
| Cerebellum | R | 12 | -66 | -30 | 1.988 | 0.002767 | 15 |  | 2/4 |  |  |  |
| Cerebellum | R | 36 | -60 | -34 | 2.017 | 0.002444 | 13 |  | 2/4 |  |  |  |
| Anterior Cingulate Cortex | R | 4 | 42 | 24 | 1.969 | 0.003002 | 10 | 0.00% | 1/4 | 0.52 | Moderately biased | 0.39643 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| **TEHC>PTSD** | |  |  |  |  |  |  |  |  |  |  |  |
| Thalamus | L | -16 | -24 | 4 | -1.792 | 0.004119 | 88 | 0.00% | 3/4 | 0.35 | No bias | 0.558475 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |

*Abbreviations*: MNI: Montreal Neurological Institute; SDM: Signed Differential Mapping; P: p-value; I2: Percentage of variance attributable to study heterogeneity; JK, Jackknife Sensitivity Test; Q P, Cochran’s Q p-value.

Note: Cluster p-values refer to the GRF probability of finding clusters with that size per the thresholds derived from the permutation test; when the maps were thresholded using threshold usual for GRF, many of the n.s. p-values became statistically significant.

**Table S5. Results of meta-analysis for the CS+ > CS- contrast during conditioning excluding YN dataset: regional differences in activation at p<0.005, z>1 and cluster size >10 voxels.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | MNI Coordinates | | |  |  |  |  |  |  |  |  |
| Region | Laterality | x | y | z | SDM-Z | P | Voxels | I2 | JK | Egger test P | Funnel Plot Description | Q P |
| **PTSD>TEHC** |  |  |  |  |  |  |  |  |  |  |  |  |
| Orbitofrontal Cortex | R | 10 | 50 | -2 | 2.86 | 0.000016 | 213 | 0.00% | 4/5 | 0.16 | No bias | 0.217762 |
| Precentral Gyrus | L | -20 | -28 | 60 | 2.78 | 0.000024 | 151 |  | 5/5 |  |  |  |
| Lingual Gyrus | L | -2 | -64 | 8 | 2.444 | 0.000147 | 76 |  | 4/5 |  |  |  |
| Postcentral Gyrus | R | 8 | -32 | 58 | 2.179 | 0.000529 | 72 |  | 3/5 |  |  |  |
| Ventromedial Prefrontal Cortex | L | -4 | 54 | 22 | 2.467 | 0.000131 | 51 | 0.00% | 4/5 | 0.83 | No bias | 0.707166 |
| Superior Motor Area | R | 10 | -22 | 52 | 2.481 | 0.000122 | 48 |  | 4/5 |  |  |  |
| Middle Frontal Cortex | L | -26 | 38 | 32 | 2.302 | 0.000302 | 40 |  | 3/5 |  |  |  |
| Superior Parietal Cortex | R | 24 | -52 | 60 | 2.659 | 0.000048 | 35 |  | 4/5 |  |  |  |
| Postcentral Gyrus | R | 24 | -28 | 56 | 2.486 | 0.000119 | 34 |  | 5/5 |  |  |  |
| Ventromedial Prefrontal Cortex | R | 12 | 60 | 16 | 2.35 | 0.000240 | 34 | 0.00% | 4/5 | 0.82 | No bias | 0.745157 |
| Postcentral Gyrus | R | 48 | -10 | 32 | 2.274 | 0.000344 | 27 |  | 4/5 |  |  |  |
| Inferior Parietal Cortex | R | 54 | -14 | 24 | 2.549 | 0.000086 | 25 |  | 4/5 |  |  |  |
| Inferior Parietal Cortex | R | 54 | -4 | 20 | 2.185 | 0.000513 | 27 |  | 2/5 |  |  |  |
| Dorsolateral Frontal Cortex | R | 22 | 30 | 60 | 2.202 | 0.000477 | 25 | 0.00% | 3/5 | 0.22 | No bias | 0.520195 |
| Dorsomedial Frontal Cortex | R | 10 | 46 | 52 | 2.073 | 0.000845 | 26 | 0.00% | 2/5 | 0.98 | No bias | 0.413747 |
| Precentral Gyrus | R | 56 | -4 | 40 | 2.152 | 0.000594 | 25 |  | 3/5 |  |  |  |
| Dorsolateral Frontal Cortex | L | -22 | 16 | 56 | 2.39 | 0.000194 | 24 |  | 4/5 |  |  |  |
| Superior Temporal Cortex | R | 44 | -18 | 0 | 2.141 | 0.000622 | 25 |  | 2/5 |  |  |  |
| Superior Temporal Cortex | L | -52 | -6 | -6 | 2.12 | 0.000685 | 22 |  | 3/5 |  |  |  |
| Postcentral Gyrus | L | -60 | -14 | 22 | 2.341 | 0.000250 | 20 |  | 3/5 |  |  |  |
| Ventromedial Prefrontal Cortex | L | -8 | 54 | -8 | 2.236 | 0.000407 | 20 | 0.00% | 2/5 | 0.98 | No bias | 0.464923 |
| Superior Temporal Pole | L | -46 | 6 | -20 | 2.111 | 0.000708 | 18 |  | 3/5 |  |  |  |
| Putamen | R | 34 | 2 | 0 | 1.948 | 0.001468 | 16 |  | 3/5 |  |  |  |
| Superior Frontal Cortex | R | 24 | 36 | 42 | 2.123 | 0.000676 | 15 |  | 3/5 |  |  |  |
| Superior Frontal Cortex | R | 30 | 28 | 52 | 2.235 | 0.000411 | 15 |  | 3/5 |  |  |  |
| Middle Frontal Cortex | L | -28 | 34 | 48 | 1.967 | 0.001355 | 14 |  | 2/5 |  |  |  |
| Postcentral Gyrus | L | -34 | -32 | 56 | 1.961 | 0.001390 | 14 |  | 2/5 |  |  |  |
| Fusiform Gyrus | L | -30 | -34 | -16 | 2.288 | 0.000323 | 13 | 0.00% | 3/5 | 0.94 | No bias | 0.580375 |
| Superior Parietal Cortex | R | 16 | -54 | 54 | 2.397 | 0.000188 | 12 |  | 3/5 |  |  |  |
| Amygdala | L | -20 | -8 | -16 | 2.19 | 0.000501 | 12 | 12.00% | 2/5 | 0.63 | No bias | 0.333039 |
| Occipital cortex | R | 18 | -88 | 40 | 2.34 | 0.000252 | 11 |  | 3/5 |  |  |  |
| Postcentral Gyrus | R | 46 | -26 | 62 | 1.977 | 0.001291 | 12 |  | 1/5 |  |  |  |
| Orbitofrontal Cortex | L | -30 | 26 | -18 | 2.224 | 0.000431 | 10 | 18.70% | 2/5 | 0.50 | No bias | 0.295584 |
| Superior Temporal Cortex | R | 62 | -16 | -2 | 2.179 | 0.000529 | 10 |  | 1/5 |  |  |  |
| Inferior Parietal Cortex | R | 54 | -26 | 22 | 1.945 | 0.001494 | 10 |  | 2/5 |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| **TEHC>PTSD** |  |  |  |  |  |  |  |  |  |  |  |  |
| Occipital Cortex | R | 34 | -72 | 22 | -2.77 | 0.000077 | 71 |  | 4/5 |  |  |  |
| Nucleus Accumbens | R | 2 | 22 | -4 | -2.809 | 0.000059 | 62 | 0.00% | 3/5 | 0.05 | No bias | 0.53083 |
| Cerebellum | R | 26 | -74 | -22 | -2.8 | 0.000062 | 53 |  | 4/5 |  |  |  |
| Occipital Cortex | L | -18 | -86 | 22 | -3.068 | 0.000012 | 50 |  | 5/5 |  |  |  |
| Middle Temporal Cortex | L | -60 | -34 | -16 | -2.854 | 0.000045 | 49 |  | 4/5 |  |  |  |
| Superior Parietal Cortex | R | 18 | -70 | 62 | -3.181 | 0.000006 | 47 |  | 5/5 |  |  |  |
| Occipital Cortex | L | -34 | -78 | 8 | -2.643 | 0.000203 | 43 |  | 3/5 |  |  |  |
| Cerebellum | L | -28 | -74 | -24 | -2.512 | 0.000453 | 40 |  | 3/5 |  |  |  |
| Inferior Temporal Cortex | R | 62 | -40 | -16 | -2.541 | 0.000382 | 34 |  | 2/5 |  |  |  |
| Inferior Temporal Cortex | R | 44 | -78 | -8 | -2.761 | 0.000083 | 30 |  | 5/5 |  |  |  |
| Middle Frontal Cortex | R | 30 | 50 | 0 | -2.697 | 0.000135 | 30 |  | 5/5 |  |  |  |
| Middle Frontal Cortex | R | 46 | 50 | 4 | -2.914 | 0.000030 | 28 |  | 5/5 |  |  |  |
| Middle Temporal Cortex | L | -64 | -46 | 10 | -2.697 | 0.000135 | 28 |  | 2/5 |  |  |  |
| Occipital Cortex | L | -4 | -100 | -10 | -2.689 | 0.000145 | 25 |  | 3/5 |  |  |  |
| Dorsolateral Frontal Cortex | R | 50 | 22 | 26 | -2.43 | 0.000717 | 25 |  | 2/5 |  |  |  |
| Inferior Parietal Cortex | R | 38 | -66 | 44 | -2.385 | 0.000910 | 24 |  | 3/5 |  |  |  |
| Middle Occipital Cortex | R | 32 | -62 | 32 | -2.601 | 0.000266 | 22 |  | 3/5 |  |  |  |
| Occipital Cortex | R | 20 | -64 | 28 | -2.57 | 0.000326 | 21 |  | 3/5 |  |  |  |
| Inferior Temporal Cortex | L | -54 | -22 | -24 | -2.378 | 0.000939 | 20 |  | 2/5 |  |  |  |
| Middle Occipital Cortex | L | -16 | -98 | 10 | -2.555 | 0.000352 | 18 |  | 2/5 |  |  |  |
| Fusiform Gyrus | R | 32 | -70 | -12 | -2.365 | 0.001004 | 17 | 0.00% | 3/5 | 0.70 | No bias | 0.464923 |
| Lingual Gyrus | R | 16 | -88 | -8 | -2.328 | 0.001202 | 13 |  | 1/5 |  |  |  |
| Inferior Parietal Cortex | L | -48 | -66 | 46 | -2.589 | 0.000286 | 12 |  | 3/5 |  |  |  |
| Insula | R | 40 | 0 | 16 | -2.43 | 0.000720 | 12 | 0.00% | 2/3 | 0.58 | No bias | 0.366862 |
| Cerebellum | L | -36 | -58 | -26 | -2.528 | 0.000413 | 12 |  | 3/5 |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |

*Abbreviations*: MNI: Montreal Neurological Institute; SDM: Signed Differential Mapping; P: p-value; I2: Percentage of variance attributable to study heterogeneity; JK, Jackknife Sensitivity Test; Q P, Cochran’s Q p-value.

Note: Cluster p-values refer to the GRF probability of finding clusters with that size per the thresholds derived from the permutation test; when the maps were thresholded using threshold usual for GRF, many of the n.s. p-values became statistically significant.

**Table S6. Results of meta-analysis for the CS+ > CS- contrast during extinction learning excluding YN dataset: regional differences in activation at p<0.005, z>1 and cluster size >10 voxels.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | MNI Coordinates | | |  |  |  |  |  |  |  |  |
| Region | Laterality | x | y | z | SDM-Z | P | Voxels | I2 | JK | Egger test P | Funnel Plot Description | Q P |
| **PTSD>TEHC** | |  |  |  |  |  |  |  |  |  |  |  |
| Superior Temporal Pole | L | -50 | 4 | 0 | 1.999 | 0.000040 | 899 | 0.00% | 4/4 | 0.72 | No bias | 0.40933 |
| Amygdala | R | 26 | 2 | -28 | 2.436 | 0.000002 | 509 | 0.00% | 4/4 | 0.69 | No bias | 0.421266 |
| Superior Temporal Cortex | R | 56 | -12 | 0 | 1.698 | 0.000279 | 307 | 0.00% | 2/4 | 0.50 | No bias | 0.396352 |
| Middle Occipital Cortex | L | -22 | -102 | -2 | 1.515 | 0.000862 | 130 |  | 2/4 |  |  |  |
| Inferior Occipital Cortex | R | 36 | -92 | -4 | 1.48 | 0.001053 | 52 |  | 2/4 |  |  |  |
| Superior Temporal Pole | R | 50 | 6 | -8 | 1.458 | 0.001182 | 29 | 0.00% | 3/4 | 0.03 | No bias | 0.723963 |
| Middle Temporal Cortex | R | 48 | -10 | -18 | 1.534 | 0.000769 | 22 |  | 3/4 |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| **TEHC>PTSD** | |  |  |  |  |  |  |  |  |  |  |  |
| Ventromedial Prefrontal Cortex | R | 2 | 58 | 12 | -1.722 | 0.000133 | 121 | 0.95% | 3/4 | 0.96 | No bias | 0.387176 |
| Inferior Temporal Cortex | L | -46 | -34 | -18 | -1.753 | 0.000005 | 105 |  | 3/4 |  |  |  |
| Precentral Gyrus | L | -34 | -2 | 50 | -1.753 | 0.000005 | 106 |  | 3/4 |  |  |  |
| Inferior Temporal Cortex | L | -50 | -60 | -8 | -1.753 | 0.000005 | 81 |  | 3/4 |  |  |  |
| Inferior Occipital Cortex | R | 16 | -40 | -2 | -1.514 | 0.001296 | 66 |  | 2/4 |  |  |  |
| Precentral Gyrus | L | -12 | -12 | 68 | -1.74 | 0.000051 | 60 |  | 3/4 |  |  |  |
| Hippocampus | L | -34 | -20 | -14 | -1.754 | 0.000005 | 55 | 1.24% | 3/4 | 0.86 | No bias | 0.385819 |
| Precentral Gyrus | L | -26 | -12 | 64 | -1.562 | 0.000896 | 53 |  | 2/4 |  |  |  |
| Superior Parietal Cortex | L | -48 | -66 | 48 | -1.479 | 0.001655 | 52 |  | 2/4 |  |  |  |
| Mid Cingulate Cortex | R | 16 | -30 | 44 | -1.606 | 0.000622 | 46 | 4.74% | 3/4 | 0.47 | No bias | 0.369189 |
| Mid Cingulate Cortex | R | 10 | -28 | 28 | -1.754 | 0.000002 | 43 | 0.11% | 3/4 | 0.87 | No bias | 0.391117 |
| Ventromedial Prefrontal Cortex | L | -10 | 60 | 16 | -1.697 | 0.000221 | 40 | 0.00% | 3/4 | 0.66 | No bias | 0.408339 |
| Middle Frontal Cortex | L | -32 | 22 | 34 | -1.559 | 0.000918 | 42 |  | 3/4 |  |  |  |
| Precentral Gyrus | L | -38 | 4 | 38 | -1.535 | 0.001114 | 33 |  | 2/4 |  |  |  |
| Superior Occipital Cortex | L | -18 | -84 | 46 | -1.541 | 0.001057 | 33 |  | 2/4 |  |  |  |
| Inferior Temporal Cortex | R | 50 | -66 | -8 | -1.466 | 0.001813 | 30 |  | 3/4 |  |  |  |
| Anterior Cingulate Cortex | R | 6 | 38 | 0 | -1.573 | 0.000824 | 23 | 0.00% | 2/4 | 0.77 | No bias | 0.412847 |
| Parietal Cortex | L | -8 | -42 | 6 | -1.519 | 0.001245 | 21 |  | 2/4 |  |  |  |
| Caudate | L | -18 | 8 | 18 | -1.568 | 0.000858 | 19 | 0.00% | 3/4 | 0.51 | No bias | 0.45052 |
| Parietal Cortex | L | -2 | -58 | 62 | -1.414 | 0.002576 | 17 |  | 2/4 |  |  |  |
| Cerebellum | L | -32 | -36 | -30 | -1.496 | 0.001473 | 11 |  | 2/4 |  |  |  |
| Orbitofrontal Cortex | R | 30 | 30 | -14 | -1.577 | 0.000795 | 11 | 0.00% | 3/4 | 0.56 | No bias | 0.463163 |
| Putamen | R | 32 | 6 | -8 | -1.467 | 0.001800 | 11 | 0.00% | 2/4 | 0.67 | No bias | 0.555908 |
| Caudate | R | 16 | 30 | 0 | -1.727 | 0.000112 | 10 | 0.00% | 1/4 | 0.83 | No bias | 0.407604 |
| Cerebellum | L | -16 | -38 | -18 | -1.435 | 0.002237 | 11 |  | 3/4 |  |  |  |
| Corpus Callosum | R | 0 | -16 | 22 | -1.636 | 0.000463 | 10 |  | 2/4 |  |  |  |
| Superior Parietal Cortex | R | 22 | -82 | 48 | -1.501 | 0.001413 | 10 |  | 2/4 |  |  |  |
| Middle Occipital Cortex | L | -38 | -82 | 34 | -1.366 | 0.003459 | 10 |  | 0/4 |  |  |  |
| Superior Frontal Cortex | R | 20 | 32 | 36 | -1.335 | 0.004201 | 10 |  | 2/4 |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |

*Abbreviations*: MNI: Montreal Neurological Institute; SDM: Signed Differential Mapping; P: p-value; I2: Percentage of variance attributable to study heterogeneity; JK, Jackknife Sensitivity Test; Q P, Cochran’s Q p-value.

Note: Cluster p-values refer to the GRF probability of finding clusters with that size per the thresholds derived from the permutation test; when the maps were thresholded using threshold usual for GRF, many of the n.s. p-values became statistically significant.

**Table S7. Results of meta-analysis for the CS+ > CS- contrast during extinction recall excluding YN dataset: regional differences in activation at p<0.005, z>1 and cluster size >10 voxels.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | MNI Coordinates | | |  |  |  |  |  |  |  |  |
| Region | Laterality | x | y | z | SDM-Z | P | Voxels | I2 | JK | Egger test P | Funnel Plot Description | Q P |
| **PTSD>TEHC** | |  |  |  |  |  |  |  |  |  |  |  |
| Cerebellum | R | 12 | -44 | -20 | 2.158 | 0.000809 | 190 |  | 1/3 |  |  |  |
| Precentral Gyrus | R | 50 | -10 | 46 | 1.961 | 0.002913 | 55 |  | 1/3 |  |  |  |
| Parahippocampal Gyrus | R | 28 | -2 | -32 | 2.02 | 0.002223 | 45 | 0.00% | 1/3 | 0.74 | No bias | 0.368727 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| **TEHC>PTSD** | |  |  |  |  |  |  |  |  |  |  |  |
| Dorsolateral Frontal Cortex | R | 16 | 26 | 56 | -1.087 | 0.000020 | 655 |  | 2/3 |  |  |  |
| Thalamus | L | -8 | -32 | 8 | -1.086 | 0.000020 | 404 | 0.61% | 2/3 | 0.40 | No bias | 0.365624 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |

*Abbreviations*: MNI: Montreal Neurological Institute; SDM: Signed Differential Mapping; P: p-value; I2: Percentage of variance attributable to study heterogeneity; JK, Jackknife Sensitivity Test; Q P, Cochran’s Q p-value.

Note: Cluster p-values refer to the GRF probability of finding clusters with that size per the thresholds derived from the permutation test; when the maps were thresholded using threshold usual for GRF, many of the n.s. p-values became statistically significant.

**Supplementary Figure Legends**

Supplementary Figure 2. Brain regions with consistently significantly higher brain functional activation in PTSD (red), TEHC (green), and overlap (yellow) for the CS+ > CS- (top; positive) and CS- > CS+ (bottom; negative) contrast during conditioning determined by meta-analysis. Results are displayed at p<.005 (Cluster size > 10 voxels) on the MNI 152 T1 0.05mm template.

Supplementary Figure 3. Brain regions with consistently significantly higher brain functional activation in PTSD (red), TEHC (green), and overlap (yellow) for the CS+ > CS- (top; positive) and CS- > CS+ (bottom; negative) contrast during extinction learning determined by meta-analysis. Results are displayed at p<.005 (Cluster size > 10 voxels) on the MNI 152 T1 0.05mm template.

Supplementary Figure 4. Brain regions with consistently significantly higher brain functional activation in PTSD (red), TEHC (green), and overlap (yellow) for the CS+ > CS- (top; positive) and CS- > CS+ (bottom; negative) contrast during extinction recall determined by meta-analysis. Results are displayed at p<.005 (Cluster size > 10 voxels) on the MNI 152 T1 0.05mm template.

Supplementary Figure 5. Brain regions with consistently significantly higher brain functional activation in PTSD compared to TEHC (red) and TEHC compared to PTSD (green) for the CS+ > CS- contrast during conditioning excluding YN dataset determined by meta-analysis. Results are displayed at p<.005 (Cluster size > 10 voxels) on the MNI 152 T1 0.05mm template. Abbreviations: AMG, Amygdala; FG, dmPFC, dorsomedial PFC; Fusiform Gyrus; NAcc, Nucleus Accumbens; OFC, Orbitofrontal Cortex; PFC, Prefrontal Cortex; vmPFC, ventromedial PFC.

Supplementary Figure 6. Brain regions with consistently significantly higher brain functional activation in PTSD compared to TEHC (red) and TEHC compared to PTSD (green) for CS+ > CS- contrast during extinction learning excluding YN dataset determined by meta-analysis. Results are displayed at p<.005 (Cluster size > 10 voxels) on the MNI 152 T1 0.05mm template. Abbreviations: ACC, Anterior Cingulate Cortex; AMG, Amygdala; HIP, Hippocampus; MCC, Mid Cingulate Cortex; OFC, Orbitofrontal Cortex; PFC, Prefrontal Cortex; STG, Superior Temporal Gyrus; vmPFC, ventromedial PFC.

Supplementary Figure 7. Brain regions with consistently significantly higher brain functional activation in PTSD compared to TEHC (red) and TEHC compared to PTSD (green) for CS+ > CS- contrast during extinction recall excluding YN dataset determined by meta-analysis. Results are displayed at p<.005 (Cluster size > 10 voxels) on the MNI 152 T1 0.05mm template. Abbreviations: PHG, Parahippocampal gyrus; THA, Thalamus.