# Microglia-mediated neuroimmune suppression in PTSD is associated with anhedonia


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## BACKGROUND

- PTSD is associated with immune dysfunction, as noted by individuals with PTSD experiencing higher rates of systemic illness[1,2]
- Lipopolysaccharide (LPS) is a potent immune activator, we previously demonstrated robust increases in 18-kDa translocator protein (TSPO) a marker of microglia[3] following LPS administration
- Individuals with PTSD have lower levels of microglia at baseline, visualized by TSPO receptor PET imaging[4]
- **Aim:** To investigate the microglial response following an acute immune challenge, lipopolysaccharide (LPS), in humans using [$^{11}$C]PBR28 PET imaging.
- **Hypothesis:** Individuals with PTSD will have lower TSPO response as compared to those without PTSD.

## MATERIALS & METHODS

- [$^{11}$C]PBR28 positron emission tomography (PET) scans to measure 18-kDa translocator protein (TSPO) availability, a marker of microglia levels quantified by volume of distribution ($V_T$) estimated regionally, for key regions in the prefrontal-limbic circuit as identified in previous studies[4]

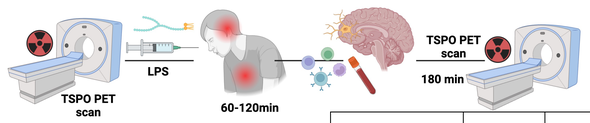



**Figure 1.** Schematic timeline of the scan protocol and challenge

**Table 1.** Demographics table for control and PTSD groups (N=15 each)

Mixed model linear regression and multifactor ANOVA were used to determine significance of data

| | HC (N=15) Mean (SD) or N (%) | PTSD (N=15) Mean (SD) or N (%) | Test of difference | P value |
|---|---|---|---|---|
| Age | 30.1 (8.3) | 32.2 (10.4) | 0.92 | 0.18 |
| Sex (%male) | 11 (73.3%) | 9 (60.0%) | 0.6 | 0.44 |
| Race/ethnicity (white, black) | 7 (46.7%), 3 (20.0%) | 7 (46.7%), 5 (33.4%) | 2.79 | 0.43 |
| Substance use (nictotine, alcohol, marijuana) | 7 (46.7%), 6 (40%) 3 (20.0%) | 7 (46.7%), 6 (40%), 5 (33.4%) | 0.32 | 0.61 |
| Age of index trauma | -- | 20.4 (7.0) | | |
| Years since index trauma | -- | 10.9 (7.3) | | |
| CAPS-5 total * N=12 | 0.6 (1.5) | 32 (11) | 10.95 | <.001 |
| PCL-5 (on scan day)* | 0.4 (0.9) | 43.7 (13.3) | 12.56 | <.001 |
| HAM-D total | 0.5 (1.2) | 13.5 (9.2) | 5.69 | <.001 |
| HAM-A total | 0.5 (1.1) | 10.1 (8.1) | 4.34 | <.001 |
| rs6971 binding status (HAB) | 8 (53.3%) | 14 (93.3%) | 6.14 | 0.013 |
| Injection dose (MBq) | 524.15 | 546.4 | 0.715 | 0.245 |
| LPS Dose (ng/kg) | 1.0 (0.01) | 1.0 (0.02) | 0.49 | 0.31 |

## RESULTS

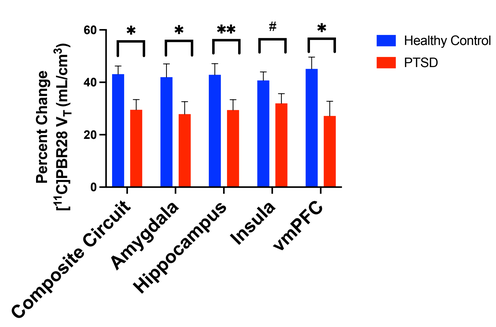



**Fig 2.** Individuals with PTSD had less robust microglia response to LPS than controls in the prefrontal limbic circuit. * indicates p <0.05, ** indicates p <0.01, # denotes p <0.06 (trending).

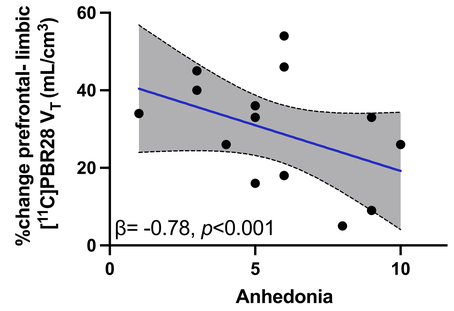
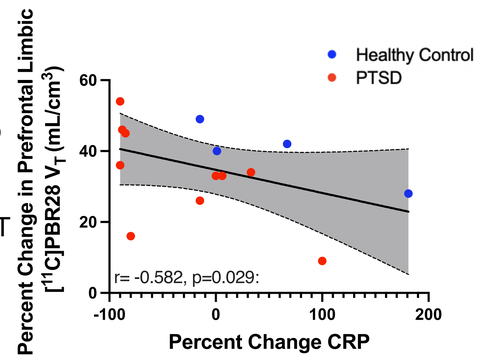
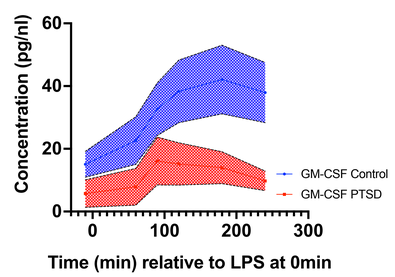



**Fig 3.** Individuals with more severe anhedonia, taken from CAPS scoring, symptoms of PTSD had less robust increase in TSPO following LPS.

**Fig 4.** Percent change in peripheral CRP values for the PTSD group, N=10 (red), and controls (blue), N=4, as compared to s change in [11C]PBR28 VT TSPO values. Greater CRP change was significantly associated with a smaller [11C]PBR28 VT TSPO change across all data in both groups (r= -0.58, p=0.02)



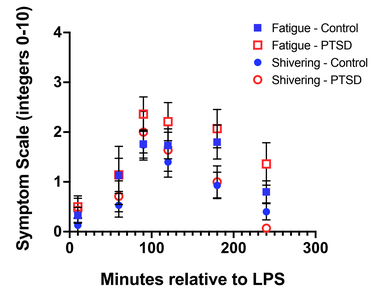




**Fig 4.** Although individuals with PTSD had lower overall microglia density and reduced microglia function, they largely did not have differences in peripheral cytokines, with the exception of GM-CSF (p = 0.007). There were no group differences between sickness symptoms.

## CONCLUSION

- Consistent with our prior work[4], TSPO availability was significantly lower in individuals with PTSD compared to HC in pre-frontal limbic circuit at baseline
- PTSD individuals demonstrated less robust TSPO response after LPS indicating reduced microglial function as compared to controls
- GM-CSF reduction indicated suppressed ability to mobilize immune system in PTSD
- No group difference in peripheral sickness symptoms
- These findings indicate a need to better understand the microglial changes in PTSD, and point to similar peripheral physiology despite central immune difference

## REFERENCES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