Multi-Modal MRI Assessment of Hippocampal and Amygdalar Cortical Myelination Using T1/T2 and Synthetic Myelin Content Mapping in Adults with Early-Adulthood Trauma Exposure

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Introduction

- Neuroimaging research has investigated the relationship between post-traumatic stress disorder (PTSD) and gray matter changes, particularly within structures such as the hippocampus and amygdala[1]. These regions are key mediators of memory and fear, with the hippocampus regulating emotional memory contextualization and the amygdala moderating fear conditioning and emotional processing[1,2].
- Research focusing on myelin white matter correlation to PTSD are limited[3]. Previous work from our group identified increased myelination in the R hippocampus among veterans diagnosed with PTSD[4].

- MRI T1w/T2w ratio as a noninvasive proxy for myelin content to evaluate myelin alterations, via oligodendrocyte remodeling, resulting from trauma exposure[4].
- SyntheticMR (SyMRI) is a single-scan advanced imaging method that can generate multiple contrasts and create quantitative tissue segmentations, including myelin content maps[5,6] **(Figure 1,2).** Recent studies have demonstrated that SyMRI-derived myelin measures correlate with conventional myelin imaging methods, while offering faster acquisition and improved clinical feasibility[6].

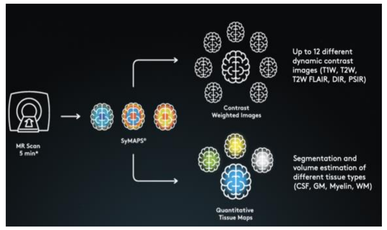


Figure 1: SyMRI imaging tool methodology[5]

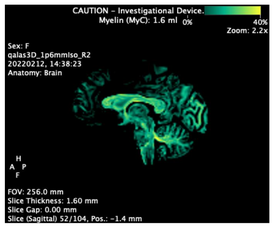


Figure 2: Myelin Contrast map

This study aims to measure multiple MRI biomarkers for grey matter myelination and validate hippocampal and amygdalar myelin ratios with T1w/T2w and synthetic Myelin Content (MyC) maps from SyMRI in adults with and without early adulthood TE.

Methods

- Participants with trauma exposure (TE) (mean age=30.1±3yrs; 29F/5M) were categorized using the Clinician Administered PTSD Scale (CAPS)
- Control group (mean age=29.1±3yrs; 10F/4M)

Level of TE	CAPS score	Sample Size
Low(Group 1)	0-10	N=14
Moderate (Group 2)	11-22	N=12
High (Group 3)	>23	N=7
Control	n/a	N=12

- Subjects completed 3T MRI scans: SyMRI Qalas (1.6mm^3 iso), T1 MPRage (0.8mm^3 iso), T2 SPC (0.8mm^3 iso)
- Myelin Concentration (MyC) maps were calculated from SyMRI **(Figure 2)**
- Structural T1/T2 images were calculated using T1 MPRAGE and T2 SPC scans
- All synthetic images and structural T1/T2 images were first linearly, then nonlinearly, registered to standard MNI 1mm^3 space using FMRIB Software Library (FSL)
- A priori regions of interest (ROIs, namely the left and right hippocampus and amygdala, were defined using well-validated Freesurfer (FS) per-subject volumetric parcellations
- Mean ROI intensities extracted from MyC and Structural T1/T2 using FS ROI masks
- Data was compared between TE vs without TE groups, among TE groups, and between MyC and standard T1/T2 ROIs

Results

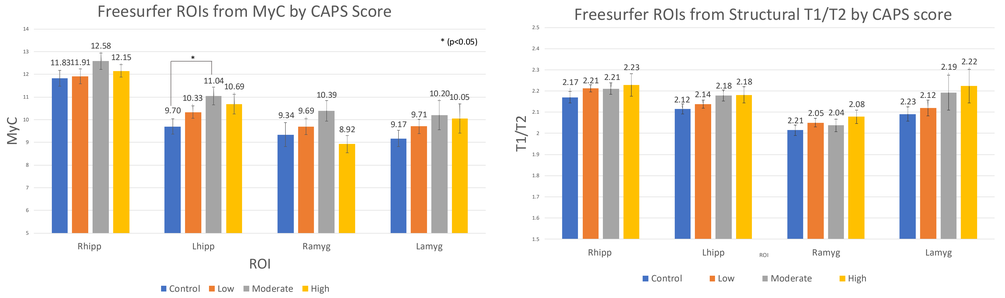


Figure 3: Freesurfer ROI myelin ratios from MyC and Structural T1/T2 by trauma severity

- One-way ANOVA revealed significant group differences in left hippocampal myelin water content (Lhipp_MyC: F=2.779, p=0.053). No other measures showed statistically significant group differences (all other p>0.2).
- For the significant ANOVA result (Lhipp_MyC), post-hoc t-tests revealed significant difference between Control and Moderate groups (p=0.042), with the Moderate group showing increased left hippocampal myelin water content compared to Controls. No other pairwise comparisons between groups reached statistical significance for any of the measures analyzed (all p>0.05).
- Given the a priori hypothesis that PTSD leads to hypermyelination in these ROIs, one-tailed t-tests were applied. Consistent with this hypothesis, one-sided linear regression demonstrated a significant positive association between left hippocampal T1/T2 ratio and CAPS scores (p = 0.044) and a trend for the left amygdala T1/T2 ratio and CAPS (p = 0.063).

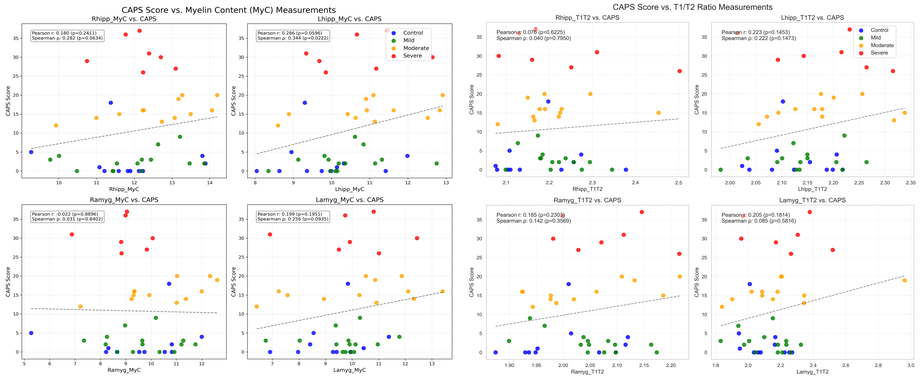


Figure 4: CAPS Correlations for all trauma severity groups using MyC (left) and T1/T2 (right)

- MyC measures of myelin water content were positively correlated with CAPS scores in the left hippocampus (Spearman ρ=0.344, p=0.02), and marginally in the right hippocampus (Spearman ρ=0.282, p=0.06) and left amygdala (Spearman ρ=0.256, p=0.09).
- T1/T2 measures of myelin were marginally correlated with CAPS scores in the left hippocampus (Spearman ρ=0.222, p=0.15)

Additional Correlation Analysis between T1/T2 ratio and myelin water content (MyC) measures:

- T1/T2 ratio and myelin water content were positively correlated in the right hippocampus (r=0.377, p=0.011), the left hippocampus (r=0.366, p=0.013), as well as the left amygdala (r=0.311, p=0.038), but not in the right amygdala (r=0.237, p=0.117).
- These findings indicate that T1/T2 ratio and myelin water content measures, though methodologically distinct, share moderate correlations in most regions examined, suggesting they may be capturing related aspects of myelin integrity.

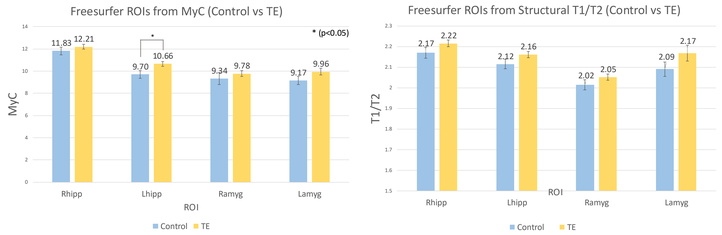


Figure 5: Controls vs Patients with TE for MyC and Structural T1/T2

- We found a significant difference between controls and patients (combined low, moderate, and high) in left hippocampus (Lhipp_MyC: t=-2.476, p=0.022, one-tailed p=0.011).
- The left hippocampus T1/T2 ratio (Lhipp_T1T2: t=-1.683, p=0.107, one-tailed p=0.054) approached significance with the one-tailed test (patient>control). The right hippocampus measures did not reach statistical significance (Rhipp_T1T2: t=-1.413, p=0.174, one-tailed p=0.087; Rhipp_MyC: t=-0.688, p=0.499, one-tailed p=0.250).
- No significant 2 group differences were seen in amygdala measures (Ramyg_T1T2: t=-1.259, p=0.223; Lamyg_T1T2: t=-1.501, p=0.143; Ramyg_MyC: t=-0.736, p=0.472; Lamyg_MyC: t=-1.522, p=0.140).

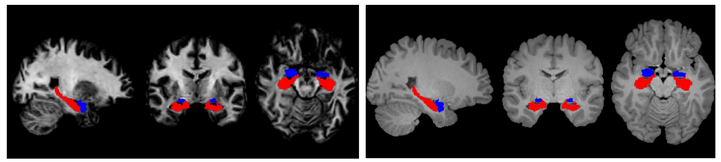


Figure 6: Hippocampus and Amygdala ROI masks overlayed on MyC (left) and T1w (right) images

Conclusions

Trauma exposure in early adulthood is associated with increased left hippocampal myelin content, as detected by SyMRI-derived Myelin Content maps. Myelin alterations showed a positive correlation with PTSD symptom severity, supporting myelin disruption as a potential neurobiological marker of trauma-related pathology. T1/T2 ratio imaging showed convergent trends with SyMRI findings.

Future Directions and Limitations

This study is limited by sample size and the categorical grouping of CAPS scores, which was addressed through correlation analyses. The cross-sectional design precludes causal inferences about trauma exposure and myelin changes. Future work will focus on increasing sample size, comparing image registration strategies (e.g., analysis in native T1 space versus standard MNI space), and incorporating synthetic T1w and T2w images from SyMRI to provide additional validation of trauma-related myelination changes.

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