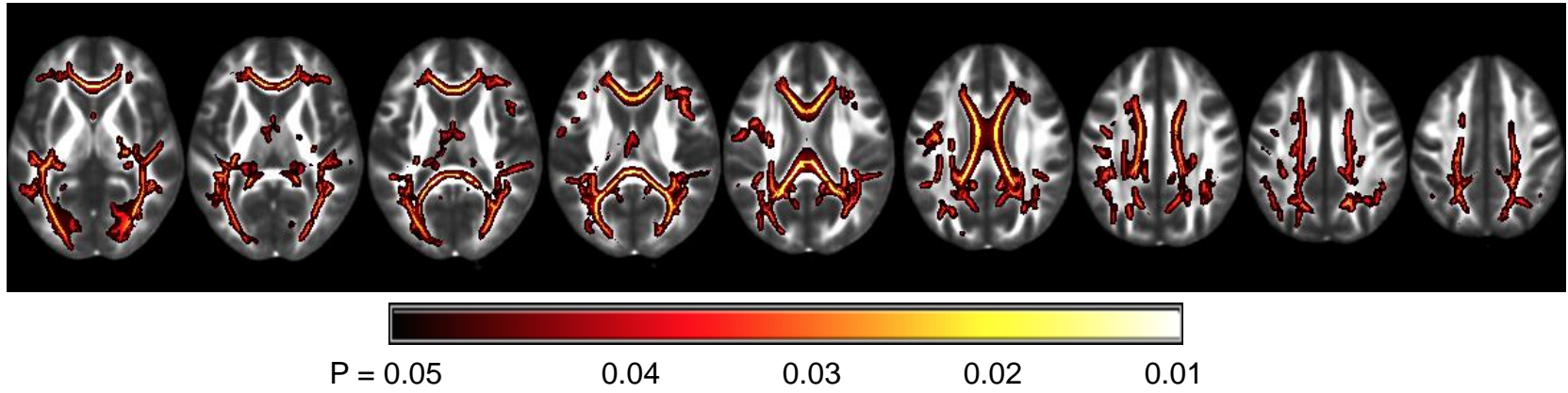
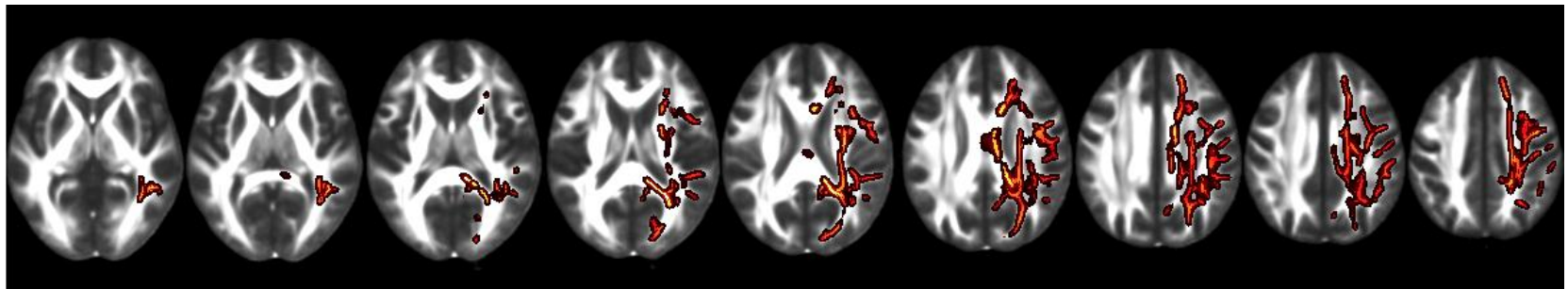


Supplemental Figure 1 – Metrics of brain volume for MS and HC (healthy control) cohorts. A. When segmenting tissue volumes, PwMS had reduced grey and white matter volume, counterbalanced by significantly greater cerebrospinal fluid (CSF) volume. When combining tissue metrics for total brain volume, PwMS also had significantly reduced total brain volume. B. Visualization of white and grey matter in people with MS. * $P < 0.05$; ** $P < 0.01$.

FA: HC > PwMS

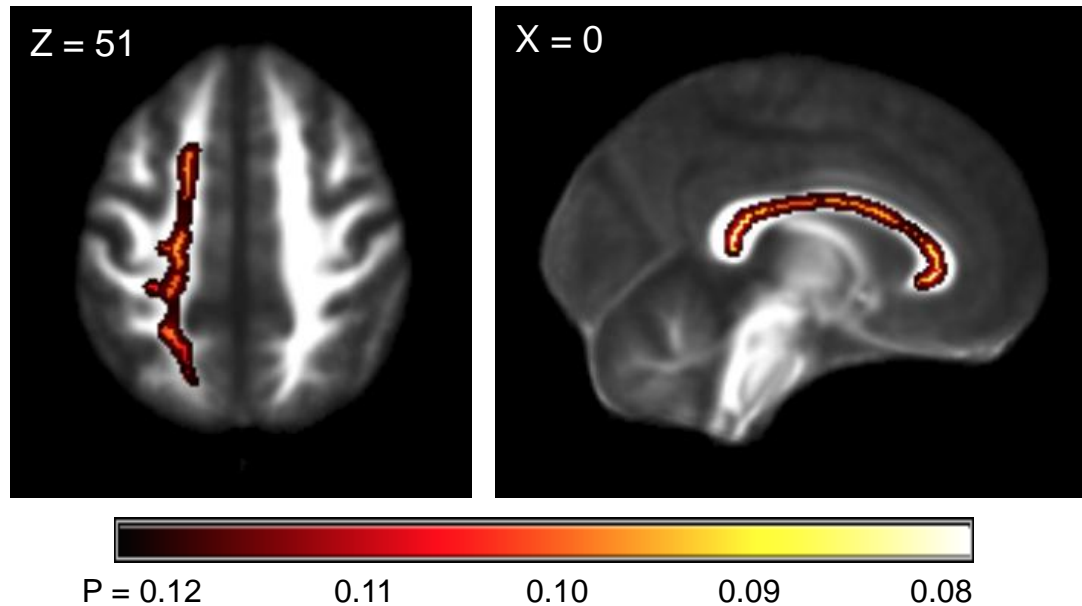


MD: PwMS > HC

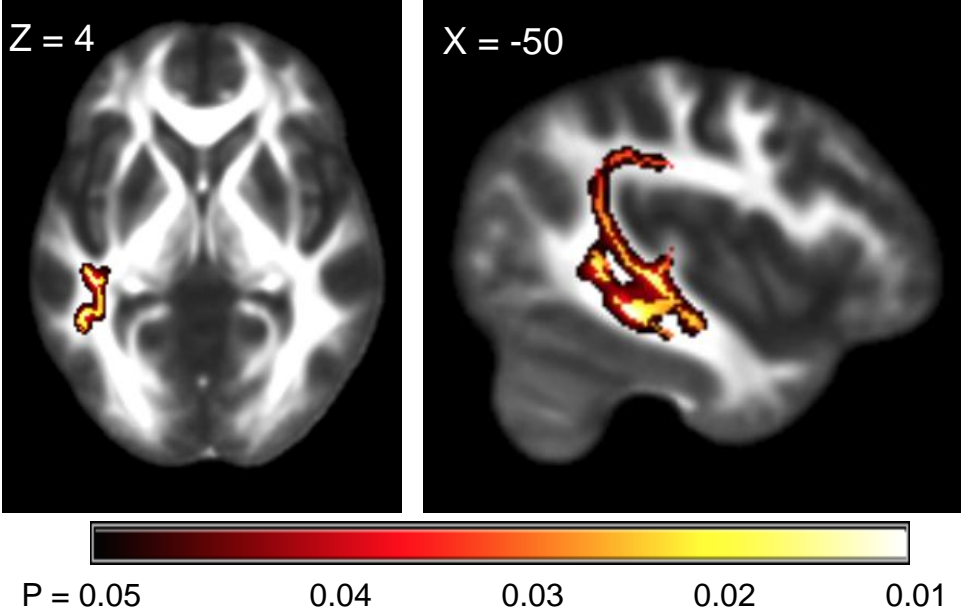


Supplemental Figure 2 – Comparisons of FA and MD in people with MS (PwMS) and healthy controls (HC).

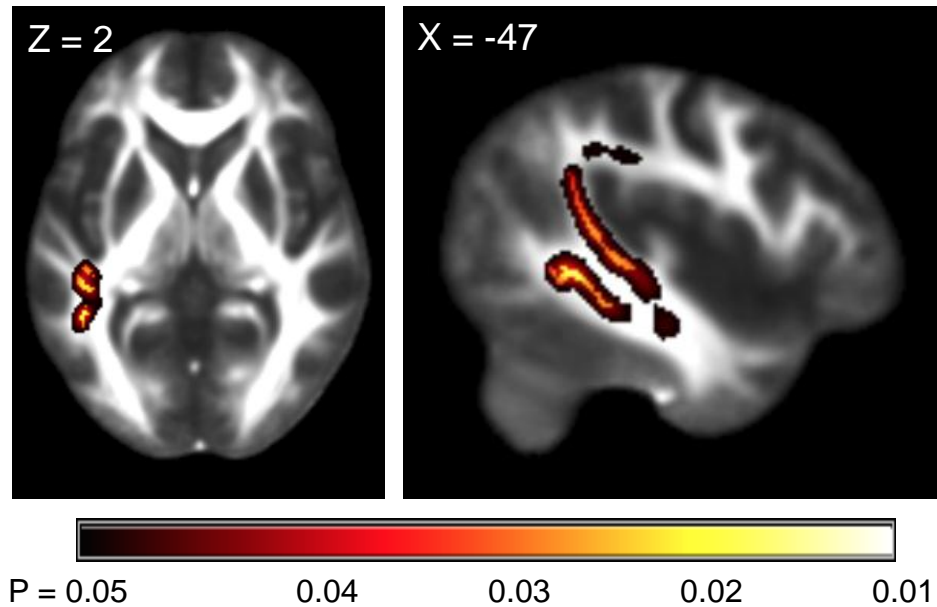
Top figure depicts TBSS whole-brain group comparisons of WM microstructural integrity (assessed via fractional anisotropy) showing the contrast of HC > PwMS. PwMS had a large network of impaired WM integrity (reflected by lower FA values), most notably within interhemispheric callosal fibers. Bottom figure depicts TBSS whole-brain group comparisons of WM microstructural integrity (assessed via mean diffusivity) showing the contrast of PwMS > HC. For both figures analysis is restricted to those white matter voxels that constitute the skeleton of the brain's connective architecture, whereby this skeleton can be matched across subjects. PwMS had a right-lateralized network of impaired WM integrity (reflected by higher MD values), most notably within corona radiata and superior longitudinal fasciculi. No significant results were found for the opposite contrasts. Results are multiple comparison-corrected and controlled for age, gender, brain volume, and EDSS.



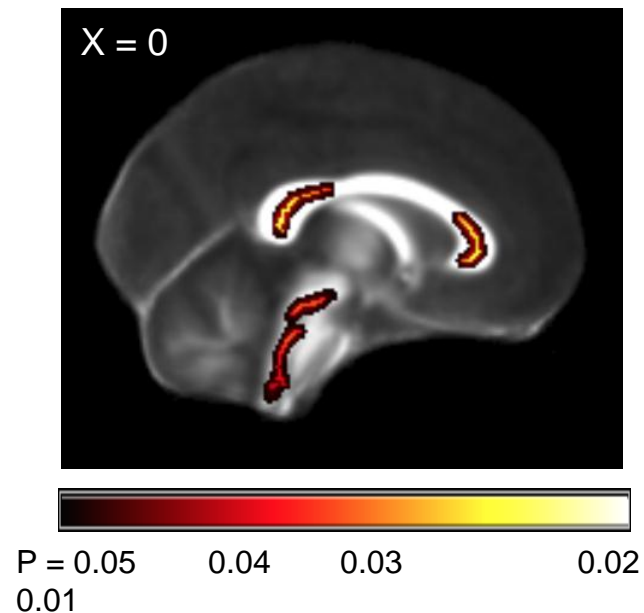
Supplemental Figure 3 – Brain map representing areas where FA is correlated to temporal improvement. When relaxing the statistical threshold, PwMS had significant associations between temporal improvement and fractional anisotropy (FA) localized to the corpus callosum and the left hemisphere's superior longitudinal fasciculus. Results are multiple comparison-corrected and controlled for age, gender, brain volume, and EDSS.



Supplemental Figure 4 – Brain map representing areas where MD is correlated to temporal improvement. PwMS had significant associations between temporal improvement and mean diffusivity (MD) localized to the left hemisphere’s arcuate fasciculus. Results are multiple comparison-corrected and controlled for age, gender, brain volume, and EDSS.



Supplemental Figure 5 – Brain map representing areas where MD is correlated to retention of improvement. PwMS had significant associations between retention improvement and mean diffusivity (MD) localized to the left hemisphere's arcuate fasciculus. Results are multiple comparison-corrected and controlled for age, gender, brain volume, and EDSS.



Supplemental Figure 6 – Brain map representing areas where FA is correlated to temporal performance. PwMS had significant associations between mean temporal performance and fractional anisotropy (FA) localized to the corpus callosum (genu and splenium) and within the brainstem for PwMS. Results are multiple comparison-corrected and controlled for age, gender, brain volume, and EDSS.