Characterization of the Gray Matter-White Matter Distribution: An Automated Approach with Demonstration of Age-Related Decline

Background: Neuroimaging techniques offer valuable insights into the structural characteristics of the brain. A salient feature of the cerebrum is the distinct transition of voxel intensity at the gray matter-white matter interface (GWI). Leveraging this inherent difference in tissue composition – lower gray matter (GM) and higher white matter (WM) signal on T1-weighted (T1W) MRI--we introduce a novel metric and demonstrate its efficacy in capturing age-related effects.

Methods: 169 participants (98 female; mean age 55.6; SD 21.5; range 18-91 years) were studied between 2019 and 2023. Each participant underwent 3 Tesla MRI including field map and 3D T1W whole brain MRI (MP-RAGE, 1mm^3 isotropic voxels). We first performed whole-brain extraction and segmented the GWI region into orbitofrontal, frontal, occipital, temporal, parietal, and cingulate subregions within 5mm of the Freesurfer-defined cerebral GWI. Next, we quantified peak distance, computed as the difference in means of two fitted Gaussian distributions of T1-weighted voxel intensities, scaled by their common standard deviation. For each participant, whole-brain peak distance using all brain voxels was calculated. The mean peak distance was then computed for each subregion. We fit a linear model to the whole brain and each peak distance as a function of age, with biological sex included as a covariate.

Results: Greater whole-brain peak distance was associated with older age (estimate = -.07 ± 0.0083 per decade, p-value = 8.89e-15), indicating a decline in WM-GM distribution sharpness with advancing age . Among the six regions, the cingulate region exhibiting the sharpest decline with age (effect size = -0.12 per decade, p-value = <2e-16). Similarly, peak distance at the GWI declines with age in the orbitofrontal (effect size = -0.07 per decade, p-value = 2.93e-14), frontal (effect size = -0.07 per decade, p-value = 9.27e-15), parietal(effect size = -0.07 per decade, p-value =<2e-16), temporal (effect size = -0.05 per decade, p-value = <2e-16) and occipital(effect size = -0.04 per decade, p-value = 1.35e-13) regions.

Conclusion: GM-WM peak distance derived fromT1W MRI is sensitive to age-related changes across the whole brain and serves as a marker of cerebral GWI sharpness, with implications for understanding neurodevelopmental trajectories and identifying pathological deviations from expected aging processes.