Supplementary Material

1.0 Supplementary Methods

1.1 Automated LC delineation. LC delineation was performed using a semi-automated procedure which has been previously described (Dahl et al. 2019). The TSE and MPRAGE scans were resampled to twice their native resolution, after which MPRAGE scans were pooled to create a whole-brain template. Resampled TSE scans were coregistered to whole-brain template-coregistered MPRAGE scans, and resulting scans were pooled to generate an TSE template. Following coregistration of the TSE template to the MPRAGE template and the MPRAGE template to MNI 0.5mm linear space, transformations from previous steps were used to warp resampled TSE scans and the TSE template to MNI 0.5mm linear space.

The ANTs routines and parameters used for LC delineation were the same as those described by Dahl et al. (2019) except for the following deviations. First, resampling of scans was performed with the ANTs ResampleImage routine. Second, template building was performed using the antsMultivariateTemplateConstruction.sh routine. Third, for construction of the initial (as opposed to the full) whole-brain template, we used a subset of 27 MPRAGE scans (16 from younger adults, 11 from older adults) all of which had `qoffset_x`, `qoffset_y`, and `qoffset_z` values within 1 standard deviation of the mean across all scans. This resulted in an initial template with high spatial alignment which was then used for alignment of all scans during construction of the whole-brain template. Finally, TSE scans and the TSE template were warped to MNI 0.5mm linear space, rather than whole-brain template space, for the purpose of comparing locations of hyperintensities on TSE scans and the TSE template with available LC maps (Dahl et al. 2019; Ye et al. 2021).

2.0 Supplementary Results

2.1 Comparison of manual and automatic calculation of LC intensity. To validate the automated LC delineation approach, we compared the peak LC intensities derived from this method with those derived from a manual LC anatomical tracing procedure that has been previously described (Clewett et al. 2018; Clewett et al. 2016; Shibata et al. 2006). For the manual approach, left and right LC ROIs were hand drawn by two blinded raters on each participant's native-resolution TSE T1-weighted image using FSLeyes image viewer. In the axial plane, raters first identified the slice where LC signal intensities were most apparent near the floor of the fourth ventricle. A 1x1mm ROI was then drawn on the voxel with peak intensity in each hemisphere. To measure reference intensity, a 10x10mm ROI was drawn on the dorsal pontine tegmentum, placed six voxels above and equidistant between the left and right LC ROIs in the axial plane. Intensity values were then extracted from the three ROIs and LC contrast ratios were calculated using the same LC contrast equation described in Section 2.6.3. Intraclass correlations coefficients between raters indicated high interrater reliability for LC peak intensities in the left (ICC = .94, $p < .001$, 95% CI [.899, .963]) and right hemispheres (ICC = .84, $p < .001$, 95% CI [.747, .903]). With high accordance established, peak intensities were averaged across raters for each hemisphere. Comparisons of the manually and automatically derived peak LC intensities revealed high correspondence for the left (ICC = .93, $p < .001$, 95% CI [.879, .955]) and right hemisphere (ICC = .90, $p < .001$, 95% CI [.837, .939]).

Supplementary References

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