DOI: 10.1002/alz.057398

BIOMARKERS

POSTER PRESENTATION

Alzheimer's & Dementia®
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Free water in T2 FLAIR white matter hyperintensity lesions

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Abstract

Background: White matter (WM) free water (FW) is likely associated with cerebral small vessel disease (CSVD). FW is the fraction of unconstrained water within an image voxel, which can be estimated from diffusion-weighted images. T2-weighted Fluid-Attenuated Inversion Recovery (FLAIR) white matter hyperintensity (WMH) is a widely used index to assess the damages caused by CSVD. It is critical to characterize how FW content is altered in WMH lesions. In this work, we proposed a data processing framework to assess FW distributions in WMH and normal-appearing WM as well as in different WM fiber tracts.

Method: Single-shell diffusion-weighted image (SS-DWI) and T2 FLAIR image data of 133 cognitively normal (CN) adults (Table 1) were obtained from the ADNI dataset (http://adni.loni.usc.edu). FW maps were generated from SS-DWI images using the DIPY software package (https://dipy.org/). WMH lesions were identified with the lesion segmentation toolbox implemented in SPM. We co-registered FW and WMH maps of individual subjects in the MNI space. Then we derived group WM fiber tracts using the tract-based spatial statistics (TBSS). Finally, we examined the localization of WMH and FW in the major WM tracts.

Result: Figure 1 shows the FW map, FLAIR image, and WMH lesion from a representative subject. Figure 2 shows group average and individual FW distributions in WMH and normal-appearing WM. Two sample T-Test found that FW content in WMH is significantly higher than that in normal-appearing WM (mean FW and standard deviation FW in WMH are 0.430 and 0.112, mean FW and standard deviation FW in normal-appearing WM are 0.203 and 0.06, $P < 1\times10^{-30}$). TBSS based analysis showed that: 1) WMH lesions are mainly located in the corona radiata, posterior thalamic radiation, tapetum, superior fronto-occipital fasciculus, superior longitudinal fasciculus, corpus callosum, and sagittal stratum; 2) Compared with mean FW in normal-appearing WM, elevated FW content is mainly at the fornix, tapetum, cingulum hippocampus, superior fronto-occipital fasciculus, corpus callosum, sagittal stratum, and posterior thalamic radiation.

Conclusion: We developed an image processing pipeline to estimate FW changes in WMH lesions and normal-appearing WM. Free water content is elevated in WMH lesions, which is likely driven by CSVD.

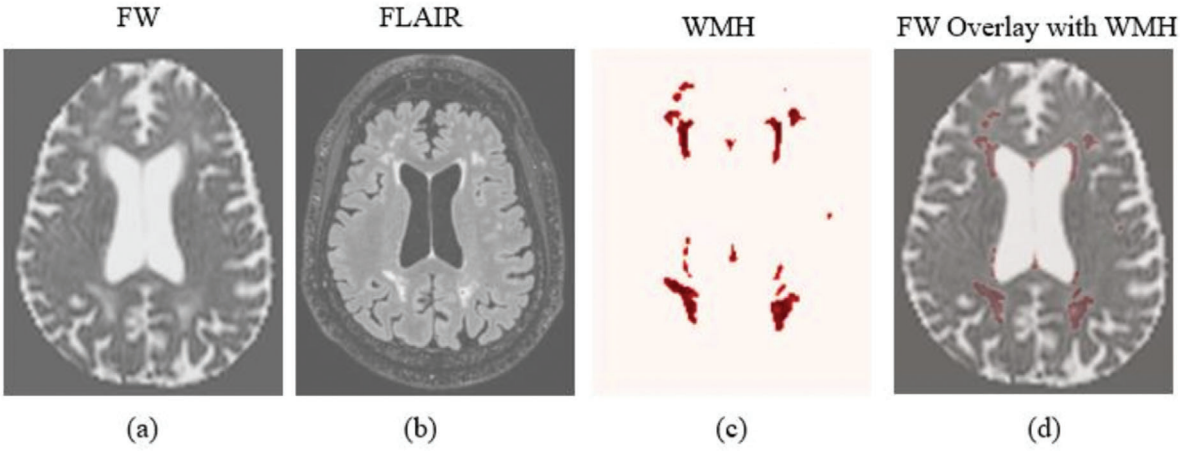

Figure 1. Representative images from an individual subject. (a) Free water (FW) map, (b) T2-weighted FLAIR image, (c) White matter hyperintensity (WMH) segmentation from the FLAIR image, and (d) Overlay of WMH on the FW map.

FIGURE 1

TABLE 1

Table 1
Subject Demographics.

Variable	Total Mean (SD)	Male Mean (SD)	Female Mean (SD)
	N = 133	N = 56	N = 77
Age	73.8 (8.7)	76.0 (8.6)	72.2 (8.5)
MMSE Score	28.9 (1.3)	28.8 (1.3)	29.0 (1.2)
ADAS-COG Score	9.2 (2.8)	9.7 (2.4)	8.8 (3.0)
Global CDR	0.04 (0.13)	0.06 (0.16)	0.03 (0.12)

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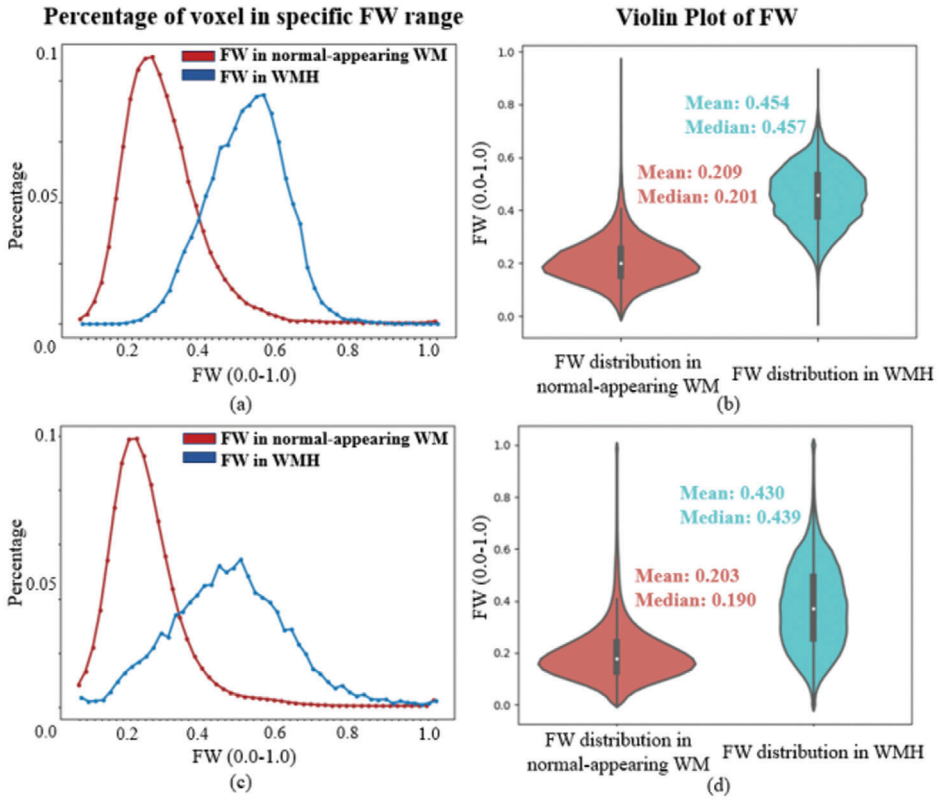

Figure 2. Free water (FW) distributions in white matter hyperintensity (WMH) and normal-appearing WM. (a) and (b) are FW distributions from an individual subject. (c) and (d) are the group average FW distributions. The range of FW (0.0-1.0) in (a) and (c) was divided into 50 bins, the percentage of voxels in a specific FW bin was calculated as N/M, where N is the number of voxels in a FW bin in WM, M is the total number of voxels in WM.

FIGURE 2