

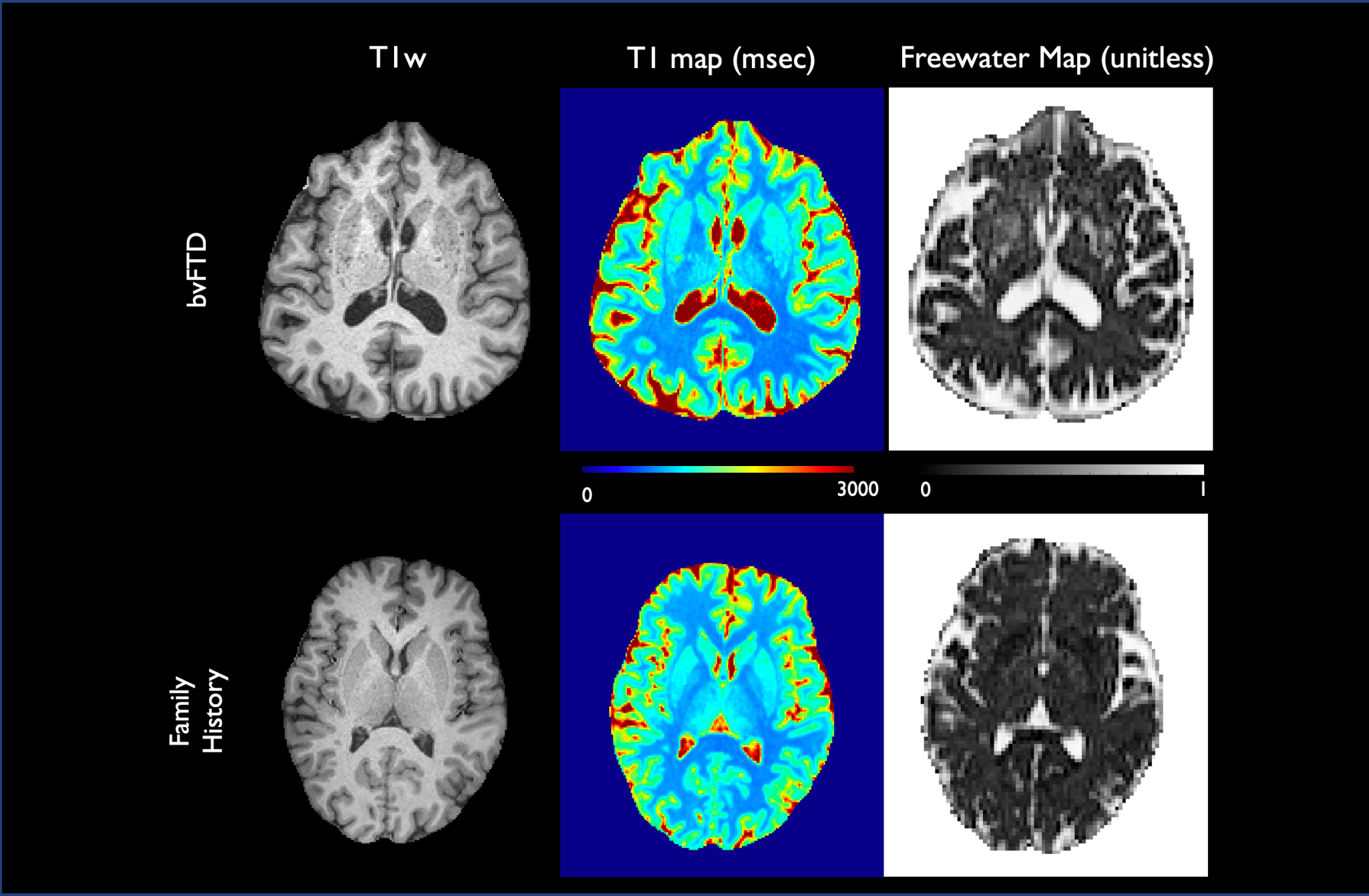
Both Freewater Diffusion and qT1 are increased in areas where FTLD-syndrome pathology is expected



Free-water Diffusion and Quantitative T1 mapping in FTLD - A Pilot Study

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BACKGROUND

- Neuroinflammation has been proposed as a common feature of neurodegenerative diseases (NDs)¹
- Differences in inflammatory profiles have been observed between NDs suggesting disease specific inflammatory profiles²
- In frontotemporal lobar degeneration (FTLD), neuroinflammation and proteinopathy are expected in frontal and temporal regions, depending on subtype
- Free-water diffusion (FWD) and T1 maps are non-specific biomarkers of neuroinflammation, where increased tissue water caused by cytokine release is expected to increase both FWD and T1 values^{3,4,5}
- AIM:** investigate T1 mapping and FWD as candidate biomarkers for neuroinflammation in FTLD syndromes

METHODS

- Subjects:** qT1 and FWD maps were generated in an ongoing project of 10 gene-negative healthy controls with a family history of FTLD (4M, 6F, mean age 46±13) and 19 FTLD patients (8 corticobasal syndrome (CBS, 4M 4F, mean age 68±5), 2 semantic variant primary progressive aphasia (svPPA, 2F, mean age 83±9), 2 nonfluent variant primary progressive aphasia (nvPPA, 1M1F, mean age 741±3), 4 progressive supranuclear palsy (PSP, 3F, 1M mean age 80±4), and 3 behavioural variant frontotemporal dementia (bvFTD) (3M, mean age 68±8).
- MRI:** T1-weighted MPRAGE, diffusion-weighted EPI (two shells) for free-water mapping, and MP2RAGE for qT1 mapping were acquired on a Siemens MAGNETOM Prisma 3T scanner, using a 20ch head coil. Scanning parameters are in Table 1.
- Image Processing:** Skull stripping and binary mask creation were done using ICMapp3r on T1-weighted MPRAGE scans. MP2RAGE T1 maps were corrected for B1+ using a separately acquired B1+ map. Diffusion data preprocessing included 1) Synb0 to generate a undistorted b0 image, 2) FSL's topup for phase-encoding distortion correction and 3) FSL's eddy for eddy current, motion and susceptibility distortion correction. Free-water maps were calculated according to the model proposed by Pasternak et al., (2009) using the eddy processed diffusion data in MATLAB. FWD and T1 maps were co-registered using FSL flirt.
- Statistical Analysis:** A w-score approach was used to assess significant differences in qT1 and FWD between FTLD subgroups and healthy controls in disease-relevant ROIs. Pearson's correlations were conducted to assess the relationship between qT1 and FWD-derived w-scores and GFAP, NfL and MoCA as markers of neuroinflammation, neurodegeneration and cognition respectively.

Acquisition	Voxel Size (mm3)	Scan Time	Other Parameters
MPRAGE	1mm ³ isotropic	5:09	TE = 2.3ms, TR = 2300ms, α = 9°, TI = 900ms
MP2RAGE	1mm ³ isotropic	14:08 (2 × 7:04)	TE= 2.3ms, TR = 4500ms, TI1/TI2=850/2600ms, α1/ α2 = 5°/6°
Diffusion	2mm ³ isotropic	12:20	TE= 8 ms, TR= 5600 ms, α= 90°, Number of diffusion directions= 126, Phase-encoding direction= P >> A, SMS= 3, b-value = 2000 s/mm ₂

Table 1. Scanning parameters for MPRAGE (T1w), MP2RAGE (qT1 mapping) and Diffusion (for freewater mapping) acquisitions.

RESULTS

FWD maps show good contrast between tissue and CSF, whereas T1 maps show good contrast between grey matter, white matter and CSF. Significant increases in qT1 and FWD (w-score > 2.33, α < 0.05) were observed in areas where pathology is expected in each FTLD subtype. No significant associations were observed between qT1 or FWD and cognition (MoCA) or biomarkers for neuroaxonal injury (NfL) or neuroinflammation/astrogliosis (GFAP).

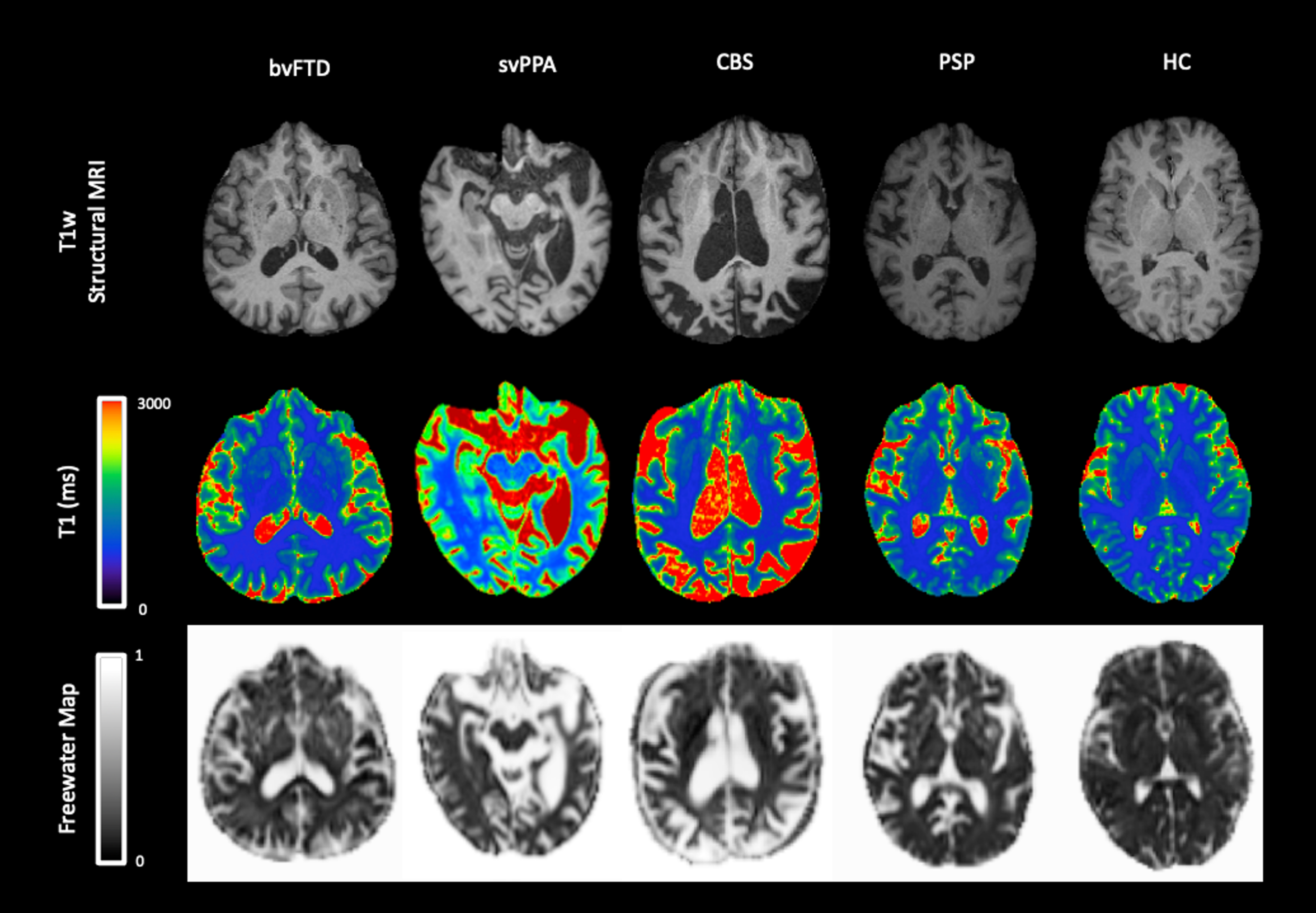


Figure 1. Example T1 and freewater maps from patients in each of the 5 included groups (left to right: behavioural variant frontotemporal dementia, semantic variant primary progressive aphasia, corticobasal syndrome, progressive nuclear palsy and clinically normal with family history of FTLD).

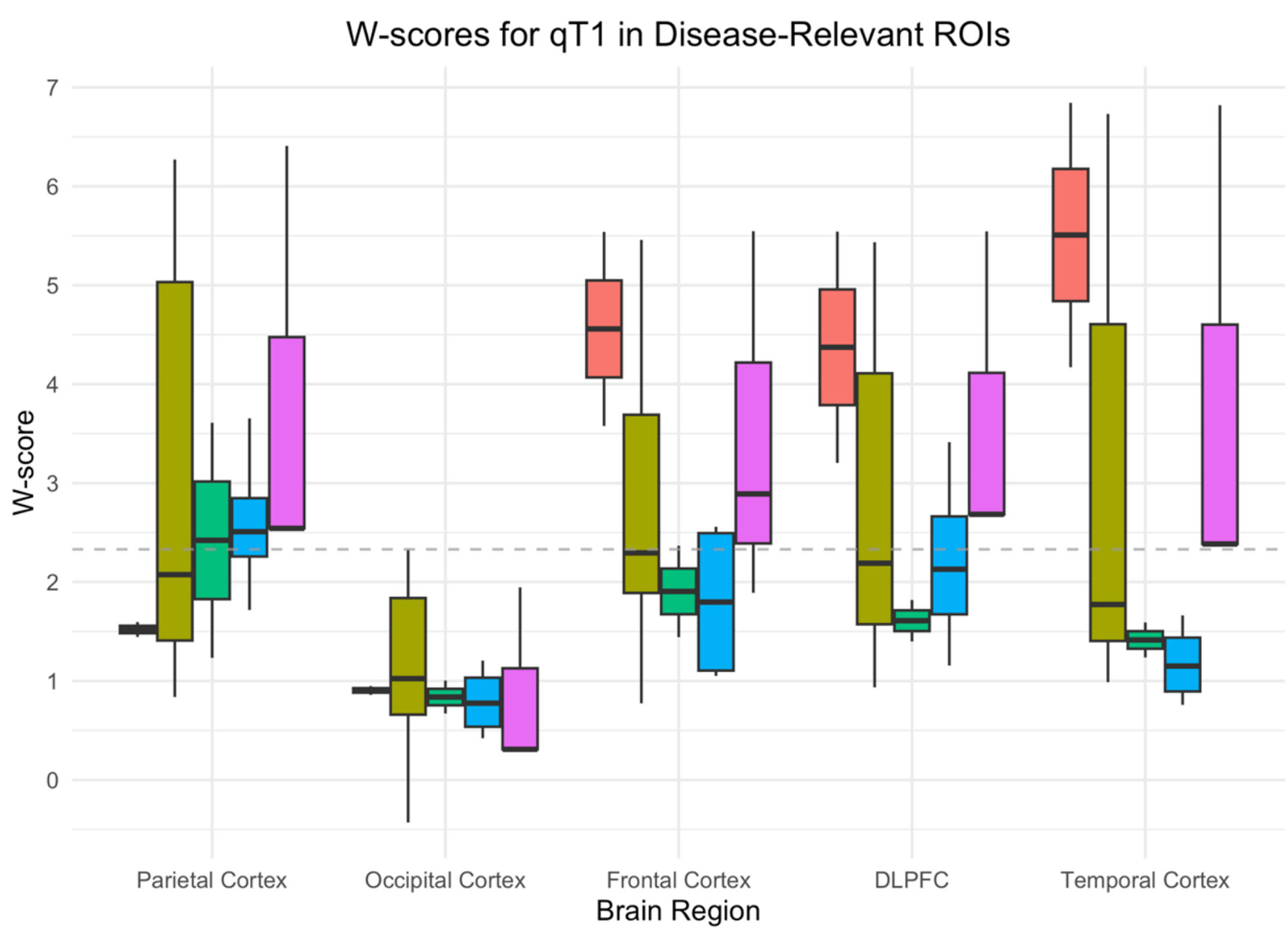


Figure 2. Boxplots of average qT1 w-scores in areas where pathology is expected (Frontal cortex, dorsolateral prefrontal cortex and temporal cortex) in comparison to areas where pathology is not expected (parietal cortex, occipital cortex) in our small sample of FTLD patients. In CBS, pathology is also expected in the parietal cortex, and the occipital cortex is used as the region where pathology is not expected. The horizontal dashed line corresponds to w-score = 2.33, the cutoff for significance (p < 0.01).

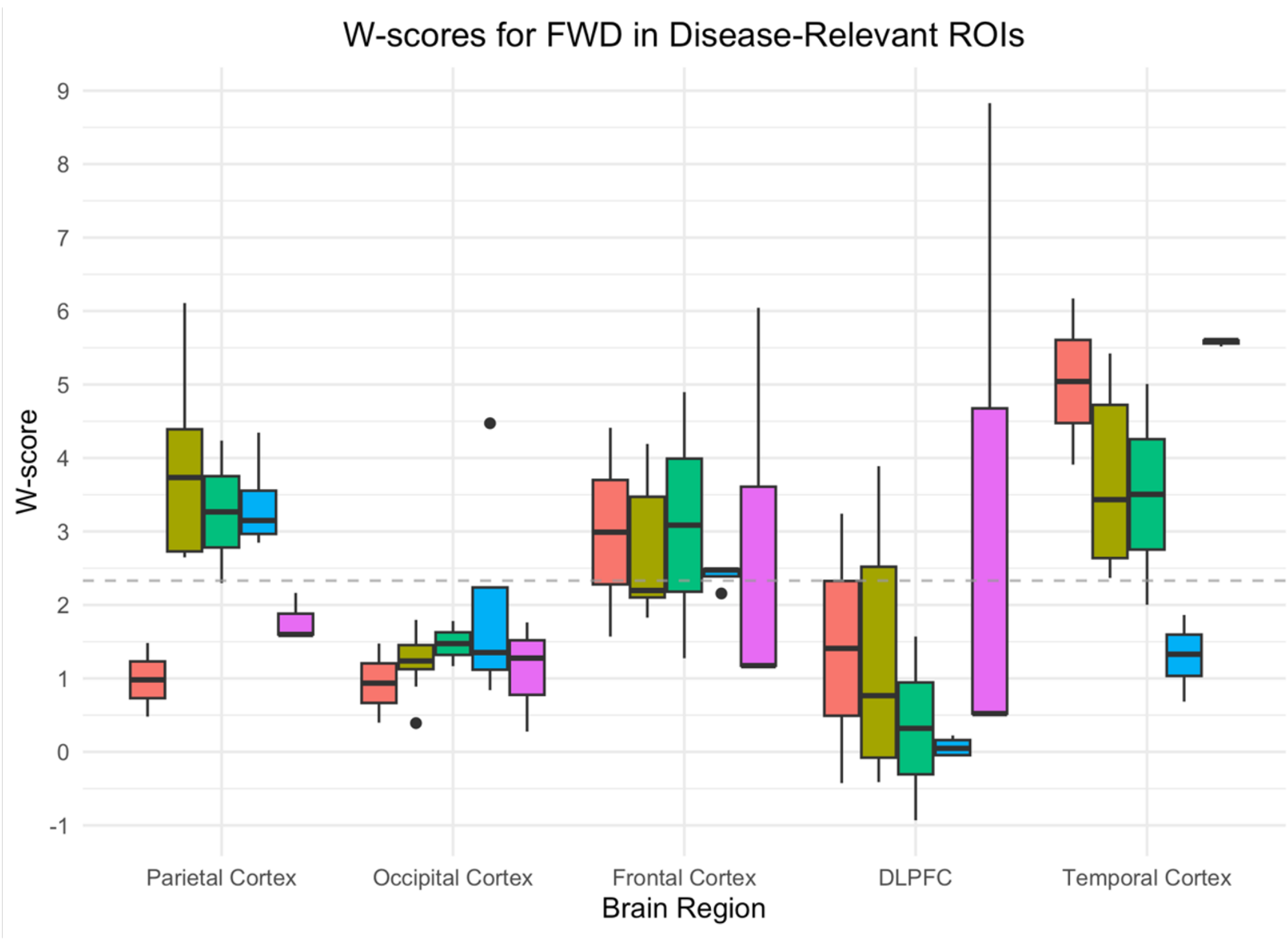


Figure 3. Boxplots of average FWD w-scores in areas where pathology is expected (Frontal cortex, dorsolateral prefrontal cortex and temporal cortex) in comparison to areas where pathology is not expected (parietal cortex, occipital cortex) in our small sample of FTLD patients. In CBS, pathology is also expected in the parietal cortex, and the occipital cortex is used as the region where pathology is not expected. The horizontal dashed line corresponds to w-score = 2.33, the cutoff for significance (p < 0.01).

CONCLUSION

- Our preliminary results in 29 subjects suggest that both FWD and qT1 are increased in areas where pathology is expected in FTLD syndromes.
- Further studies will expand sample size in both patients and controls, as well as examine the relationship between FWD, qT1 and biofluid based neuroinflammatory biomarkers. FWD and qT1 are potential candidate neuroimaging-based biomarkers for neuroinflammation in NDs.

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