



Increased grey matter T1w/T2w ratio observed in FTD patients



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Introduction

- Frontotemporal dementia (FTD) presents with heterogeneous, progressive deficits in behavior, language, and cognition.¹
- FTD is associated with structural changes in the brain,² including grey matter (GM) volume loss on MRI.
- However, GM volume loss lacks specificity to detect subtle microstructural alterations observed in early-stage FTD, such as demyelination, inflammation, and iron accumulation. The ratio of T1-weighted and T2-weighted images on MRI (T1w/T2w) has been proposed as an in vivo proxy for overall microstructural integrity.³

Hypothesis

We hypothesized that FTD patients would exhibit altered T1w/T2w in subcortical and cortical GM compared to healthy controls.

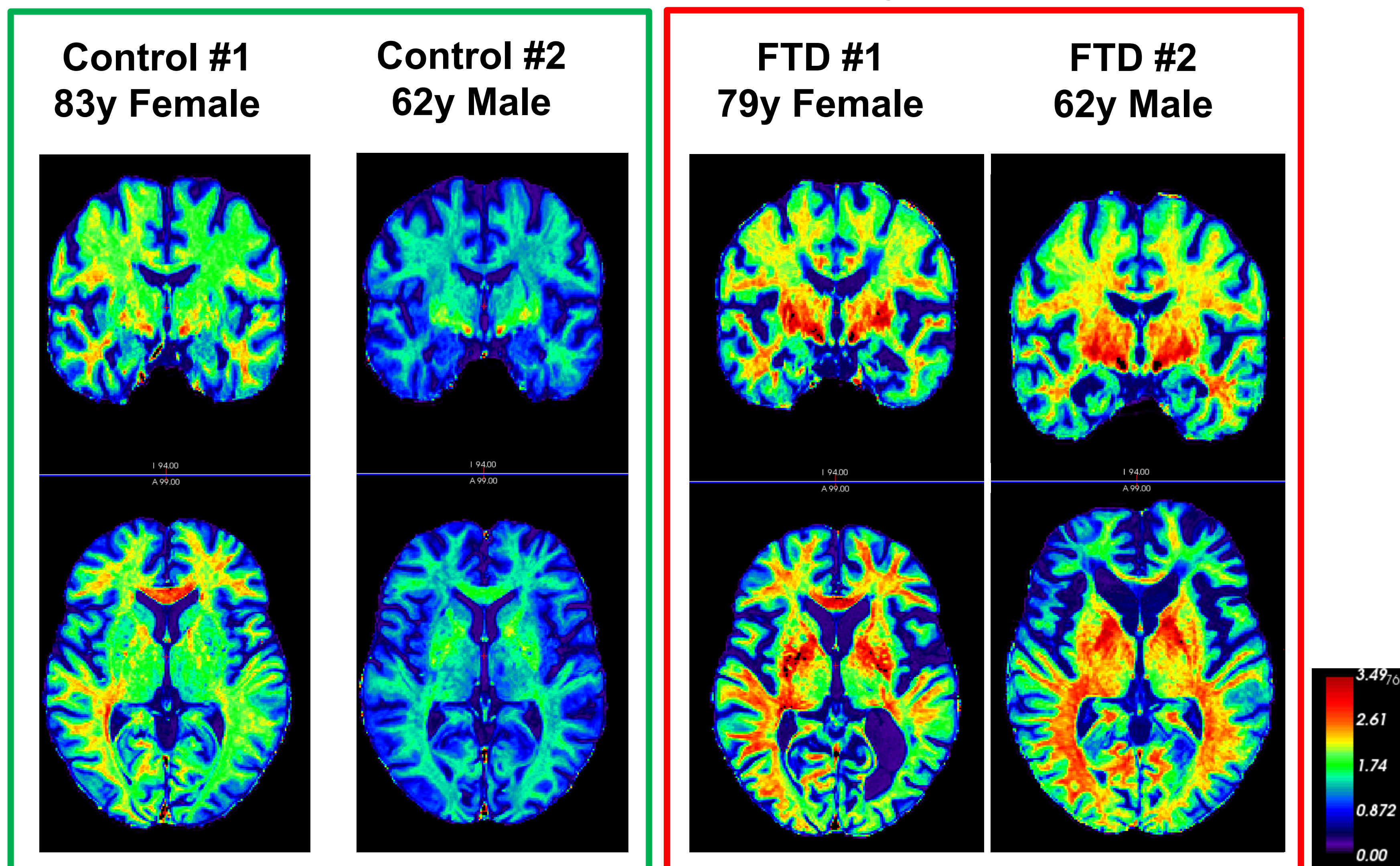
Methods

- All participants consented to be a part of the Canadian Consortium on Neurodegeneration in Aging (CCNA) COMPASS-ND Study.⁴ The participants underwent neuroimaging, neurological, cognitive and neuropsychological assessments.
- For this study, we only selected participants who were diagnosed with FTD (N=38) or who were recruited as cognitively normal controls (N=118).
- Mean age $\pm$ SD at baseline: FTD (67y $\pm$ 12), Controls (65y $\pm$ 11).
- Sex: FTD (55% F), Controls (60% F).
- Specific FTD types included behavioral variant FTD (n=16), Agrammatic Nonfluent Primary Progressive Aphasia (PPA) (n=10), Semantic PPA (n=3), Logopenic variant PPA (n=3), Corticobasal syndrome (CBS) nonfluent PPA (n=1), Unspecified PPA (n=1), and Progressive Supranuclear Palsy (PSP) (n=4).
- T1w and T2w MRI scans were acquired using 3T scanners according to the Canadian Dementia Imaging Protocol.⁵
- T1w and T2w images were spatially coregistered, followed by intensity standardization. Average T1w/T2w ratios were calculated within GM regions of interest defined by the Harvard-Oxford Atlases.
- This was a cross-sectional analysis using baseline images.
- General linear models were used to conduct group comparisons. The models were adjusted for age, sex, symptomatic status, and volumes of GM, white matter (WM), and WM hyperintensities.

Results

- T1w/T2w was significantly higher in the FTD patient group compared to controls in the following subcortical structures: the thalamus, putamen, and pallidum.
- Group differences in the caudate and hippocampus were nonsignificant.
- T1w/T2w was higher in cortical GM in the FTD patient group compared to controls, particularly in the temporal, parietal, and occipital lobes.
- Additionally, T1w/T2w was higher in WM in the FTD patient group across all lobes (frontal, temporal, parietal, and occipital).

Example cases from each group



Conclusions

- Microstructural integrity within GM may be altered in FTD patients compared to controls. In the context of FTD, a feasible explanation is iron accumulation and neuroinflammatory activity, processes that shorten T2 relaxation and elevate the T1w/T2w ratio.
- Future studies involving in vivo iron imaging (e.g., T2*-weighted MRI or quantitative susceptibility mapping) are warranted to better understand GM alterations in FTD.

References

[1] Johnen et al., Front Neurol 2019, PMID: 31231305

[3] Glasser et al., J Neurosci 2011, PMID: 21832190

[5] Duchesne et al., J Magn Reson Imaging, PMID: 30635988

[2] Cash et al., Neurobiol Aging 2018, PMID: 29172163

[4] Chertkow et al., Can J Neurol Sci 2019, PMID: 31309917

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