



Left-Predominant Hippocampal Atrophy Associated With LATE-NC

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Introduction

Limbic-predominant age-related TDP-43 encephalopathy (LATE) causes an amnesic syndrome that closely mimics Alzheimer’s disease and commonly co-occurs with it. No validated in vivo biomarkers exist for TDP-43 pathology yet, and diagnosis is confirmed postmortem. MRI-based surrogate markers may help identify limbic TDP-43 involvement during life. Prior autopsy and MRI studies suggest that a higher middle-inferior temporal gyrus (MITG)-to-hippocampus volume ratio may distinguish TDP-43 pathology from AD. We evaluated MRI volumetric measures in our autopsy-confirmed cohort with mixed dementias and LATE neuropathologic change (LATE-NC).

Methodology

We included 27 participants with autopsy-confirmed neuropathology and antemortem MRI from the University of British Columbia. MRI scans were acquired from clinical scanners between 2004 and 2022. The cohort encompassed Alzheimer’s disease and/or Lewy body disease, with and without LATE-NC. Twelve individuals with LATE-NC (LATE+) were age- and sex-matched to 15 individuals without LATE-NC (LATE-). We quantified MRI-based hippocampal volumes (left, right, and mean) and MITG volumes using Statistical Parametric Mapping (SPM12), and calculated MITG-to-hippocampus volume ratios (Table 1). Three clinicians visually rated medial temporal atrophy (MTA) bilaterally and we analyzed mean left, right, and average MTA scores. We used a general linear model to compare volumetric and visual measures between groups, and examined relationships between visual MTA ratings and volumetric MRI measures using Spearman correlations (Table 2).

Results

Participants were predominantly right-handed (>80%) and 41% female, with mean age of onset 67.6 ± 7.3 years and mean age of death 77.0 ± 6.6 years. Visual MTA scores did not differ significantly between LATE+ and LATE- participants. Volumetric analysis demonstrated significantly reduced left hippocampal volume in LATE+ participants compared with LATE- participants ($p = 0.04$), while right and mean hippocampal volumes were not significantly different. MITG volumes and MITG-to-hippocampus volume ratios showed no significant group differences. Visual MTA scores correlated inversely with MITG volume ($p = -0.42$, $p = 0.03$) but not significantly with hippocampal volume ($p = -0.24$, $p = 0.24$).

Conclusion

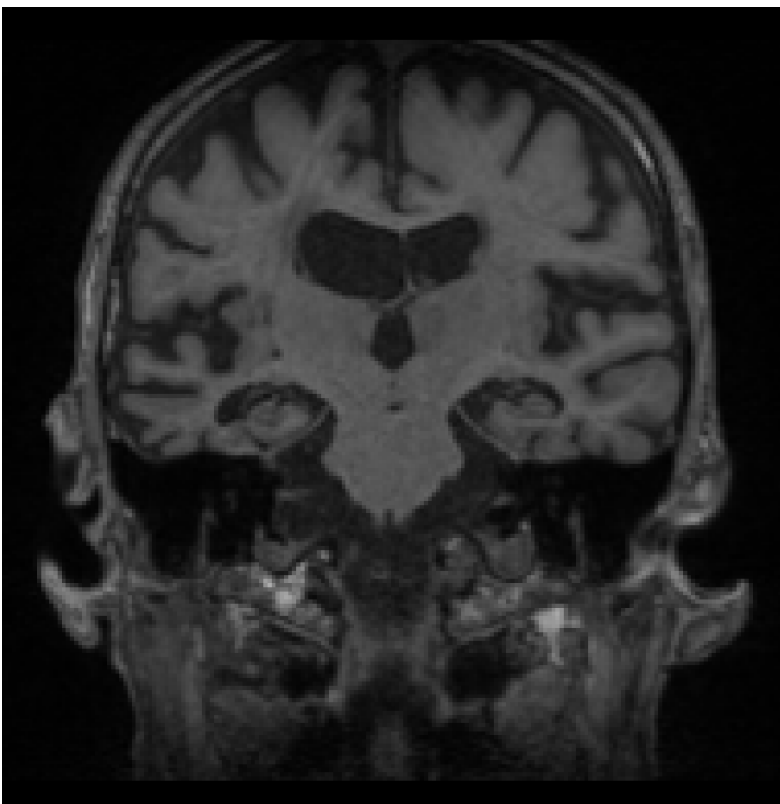
LATE-NC was associated with significant left-predominant hippocampal atrophy detectable by volumetric MRI but not consistently by visual MTA ratings. Future longitudinal studies are needed to compare visual and SPM-based measures, characterize progression of asymmetry, and relate imaging findings to LATE stages to validate asymmetric hippocampal atrophy as a sensitive in vivo marker for LATE-NC.

Table 1. LATE+ vs LATE– Comparisons

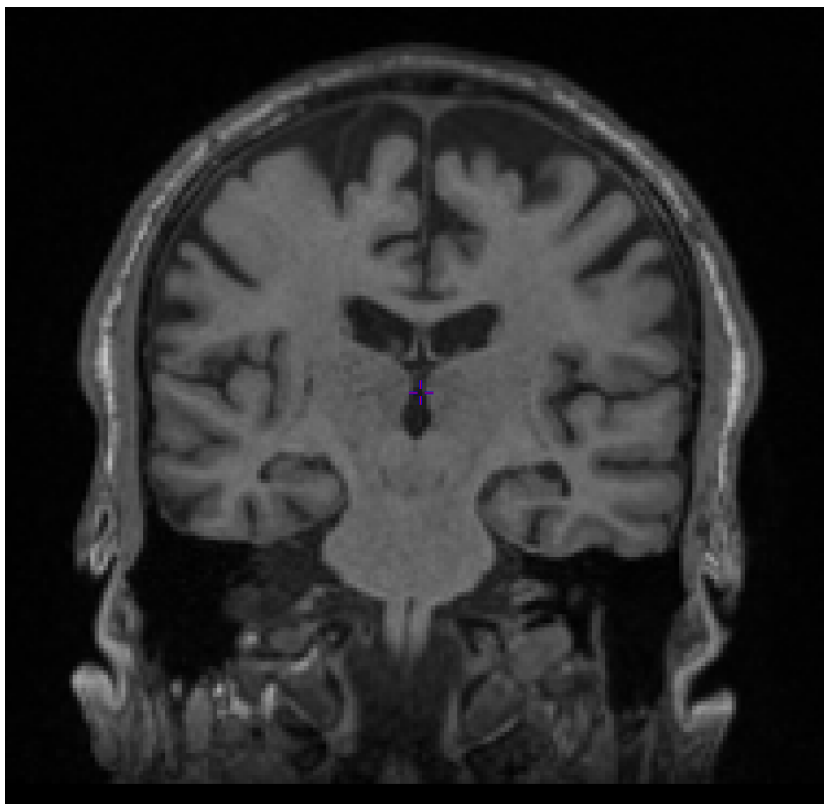
Variable	Result	p-value
Visual MTA Score	No difference	NS 0.7
Left Hippocampal Volume	↓ in LATE+	0.04
Right Hippocampal Volume	No difference	NS 0.27
Mean Hippocampal Volume	No difference	NS 0.10
MITG Volume	No difference	NS 0.84
MITG/Hippocampus Ratio	No difference	NS 0.34

Table 2. Correlations With Visual MTA Score

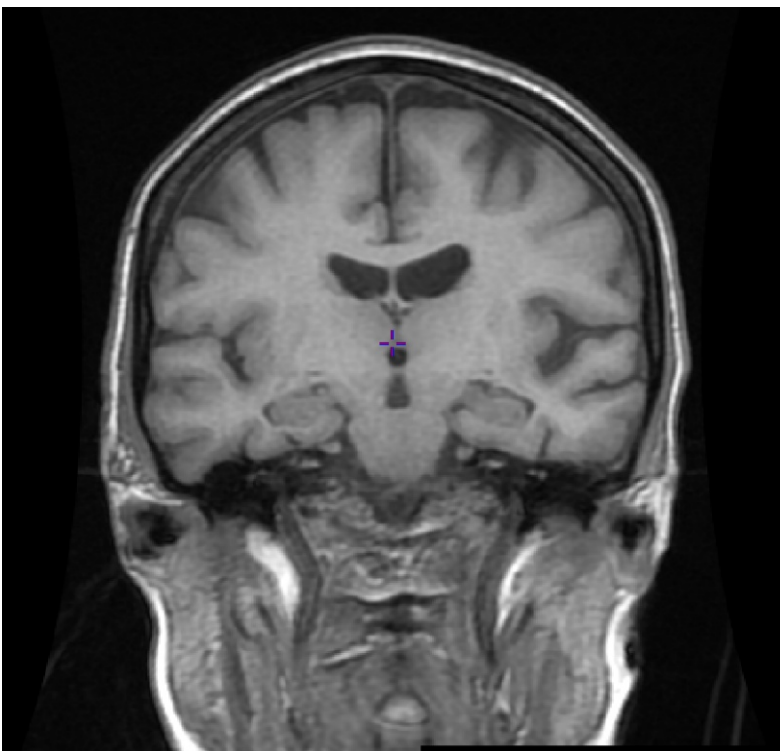
MRI Measure	Spearman ρ	p-value
Mean MITG Volume	–0.42	0.03
Left MITG Volume	–0.49	0.009
Mean Hippocampal Volume	–0.24	0.24
Left Hippocampal Volume	–0.34	0.07



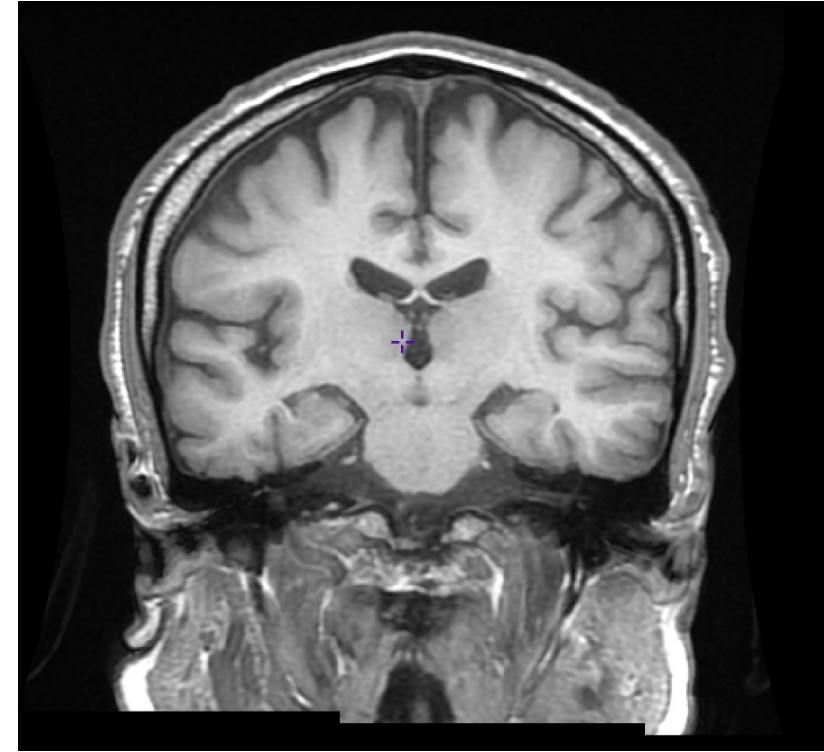
Subj with AD, TDP43, LBD
MTA 3(L), 3(R)



Subj with AD, TDP43, LBD
MTA 2(L), 3(R)



Subj with AD, Arteriolosclerosis
MTA 1(L), 1(R)



Subj with AD, LBD
MTA 2(L), 3(R)