

Supplementary Data:

Supplementary Table 1: Biomarker status of participants clinically suspected of having Alzheimer's disease dementia or amnesic MCI due to Alzheimer's disease below and above the age of 75

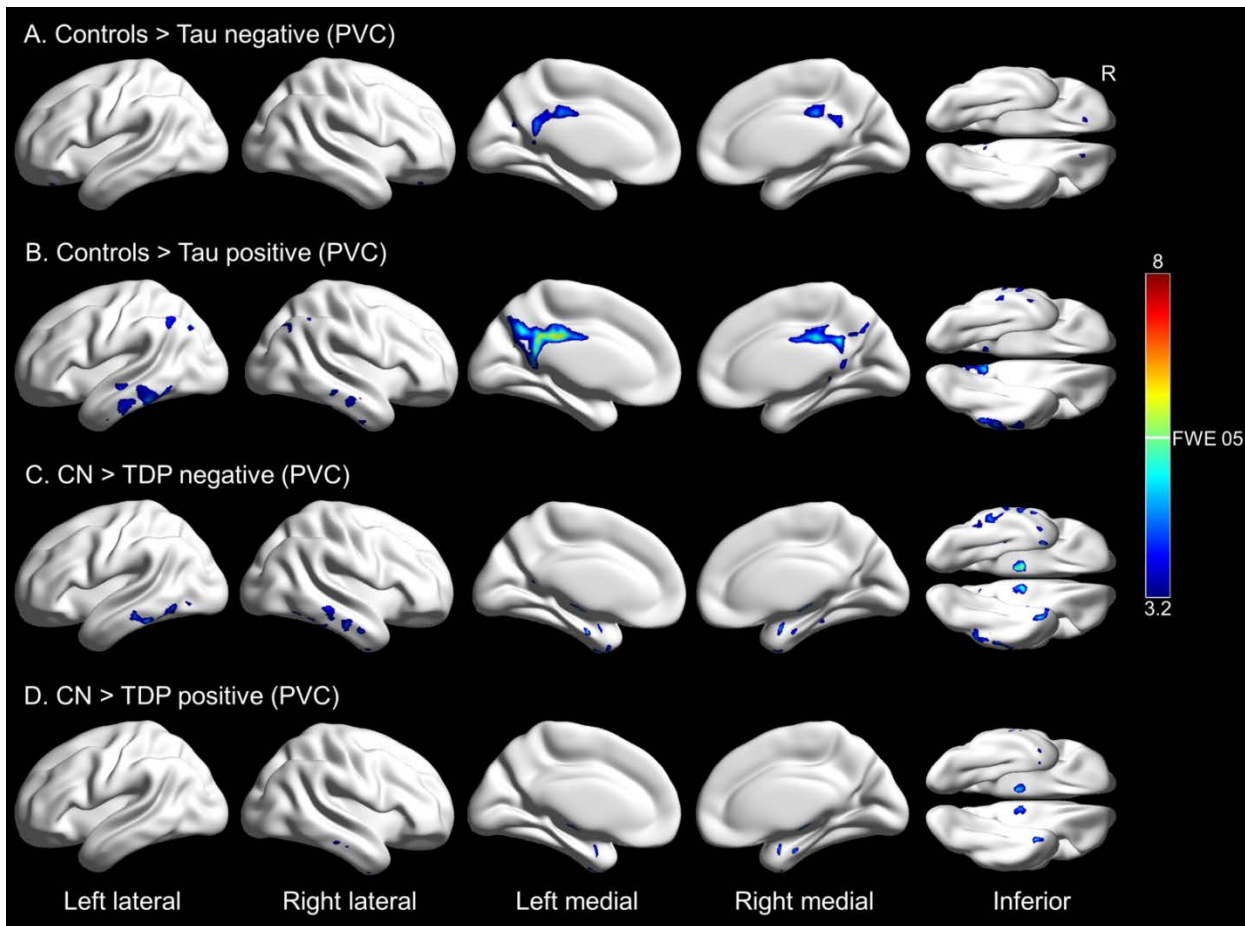
| | Tau-positive | Tau-negative | % T-negative |
|----------|---------------------|---------------------|---------------------|
| < 75 y/o | 50 | 1 | 1.96% |
| ≥ 75 y/o | 21 | 9 | 30% |

Of the 81 participants who were clinically suspected of having Alzheimer's disease and who had flortaucipir PET results available, ten fell below the cut-point used in the present study. Only one of these was below the age of 75. This participant had corticobasal syndrome thought to be due to Alzheimer's disease, with elevated tau-PET signal in keeping with this diagnosis albeit not involving the meta-ROI regions. The remaining 9 were 75 years-old or older, confirming our suspicion that tau-negative dementia masquerading as Alzheimer's disease dementia or amnesic MCI is primarily a phenomenon of those ≥ 75 years-old. The 9 tau-negative and 15/21 tau-positive cases were included in our study as they had FDG-PET imaging available.

Supplementary Table 2: Details of excluded participants and biomarker status

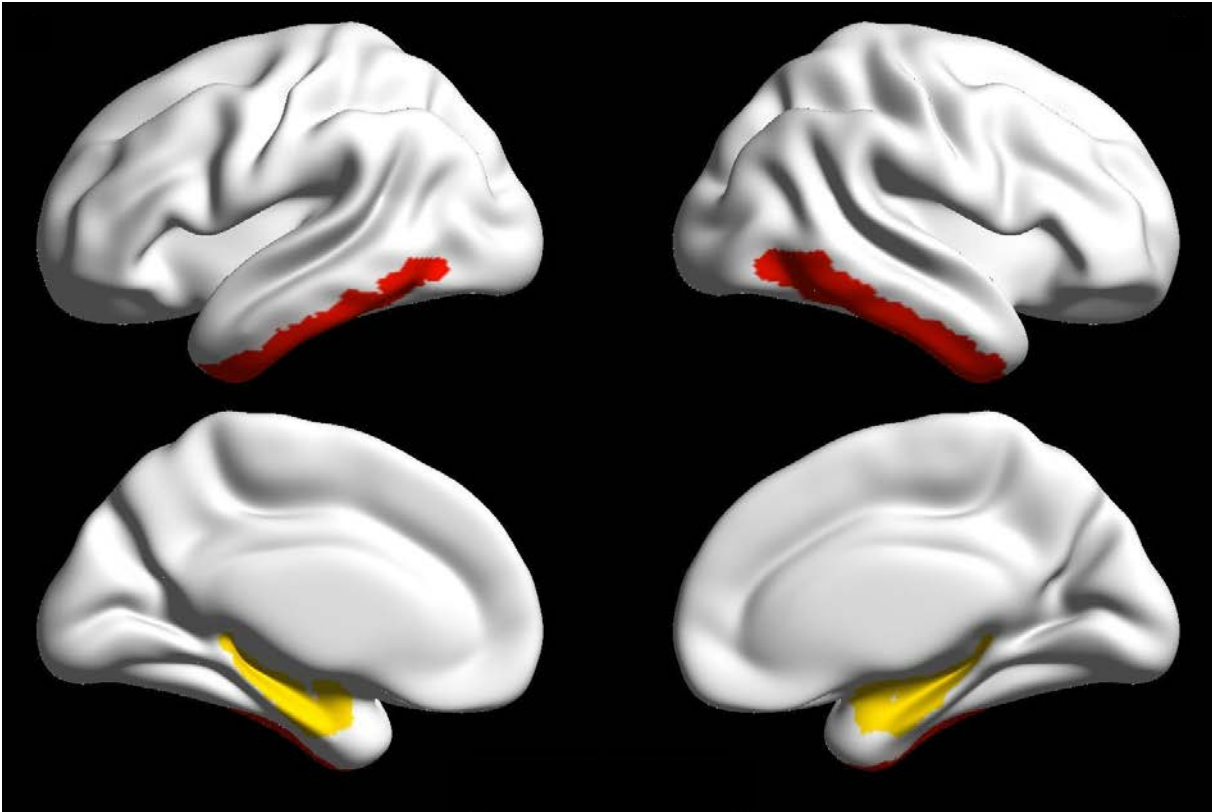
| Reason for Exclusion (N) | Amyloid / Tau-PET classification (A/T) |
|--|---|
| Lewy-body disease spectrum | |
| Probable Lewy body dementia (9) | (4 A-/T-, 5 A+/T+) |
| MCI with REM-sleep behavioral disorder (2) | (1 A-/T-, 1 A+/T-) |
| Non-amnestic dementia/MCI syndrome | |
| Semantic dementia (1) | (A+/T+) |
| Logopenic progressive aphasia (2) | (2 A+/T+) |
| Progressive supranuclear palsy (1) | (A+/T-) |
| Unclassifiable non-amnestic dementia (1) | (A-/T-) |
| Alternative, non-degenerative diagnosis accounting for cognitive symptoms | |
| Primary psychiatric disorder (3) | (2 A+/T-, 1 A-/T+) |
| Sedative medication use (2) | (2 A-/T-) |
| Normal pressure hydrocephalus (1) | (A-/T-) |
| Large hemispheric stroke (1) | (A+/T+) |

Supplementary Figure 1: Three-dimensional brain renderings showing results of FDG-PET analysis in after partial volume correction (PVC)



Results are shown at $p(\text{unc})=0.001$ with the height cut-off for family-wise correction (FWE) correction shown in the color bar. **A.** Compared to controls, tau-negative participants had hypometabolism in the posterior and middle cingulate **B.** Compared to controls, tau-positive participants similarly had hypometabolism in the posterior and middle cingulate, but also had precuneus and inferior temporal involvement. **C.** Compared to controls, pure Alzheimer's disease had patchy inferior temporal hypometabolism. **D.** Compared to controls, hippocampal sclerosis was associated with a few foci of hypometabolism in the anterior medial temporal lobe. Renders created using Brain Net Viewer (Xia *et al.*, 2013) (<https://www.nitrc.org/projects/bnv/>)

Supplementary Figure 2: Three-dimensional brain renderings showing results medial and inferior temporal ROIs



Medial temporal ROI was created by combining the amygdala and hippocampus parcellation from the AAL atlas (shown in yellow), while the inferior temporal ROI consisted of the inferior temporal parcellation from AAL (shown in red). Renders created using Brain Net Viewer (Xia *et al.*, 2013) (<https://www.nitrc.org/projects/bnv/>)

Supplemental Figure 3: Results of thickness based inferior/medial temporal analyses

