

# Cortical Volume Predictors of TauC2, Neurofilament Light , and GFAP Levels in Cognitively Unimpaired Individuals

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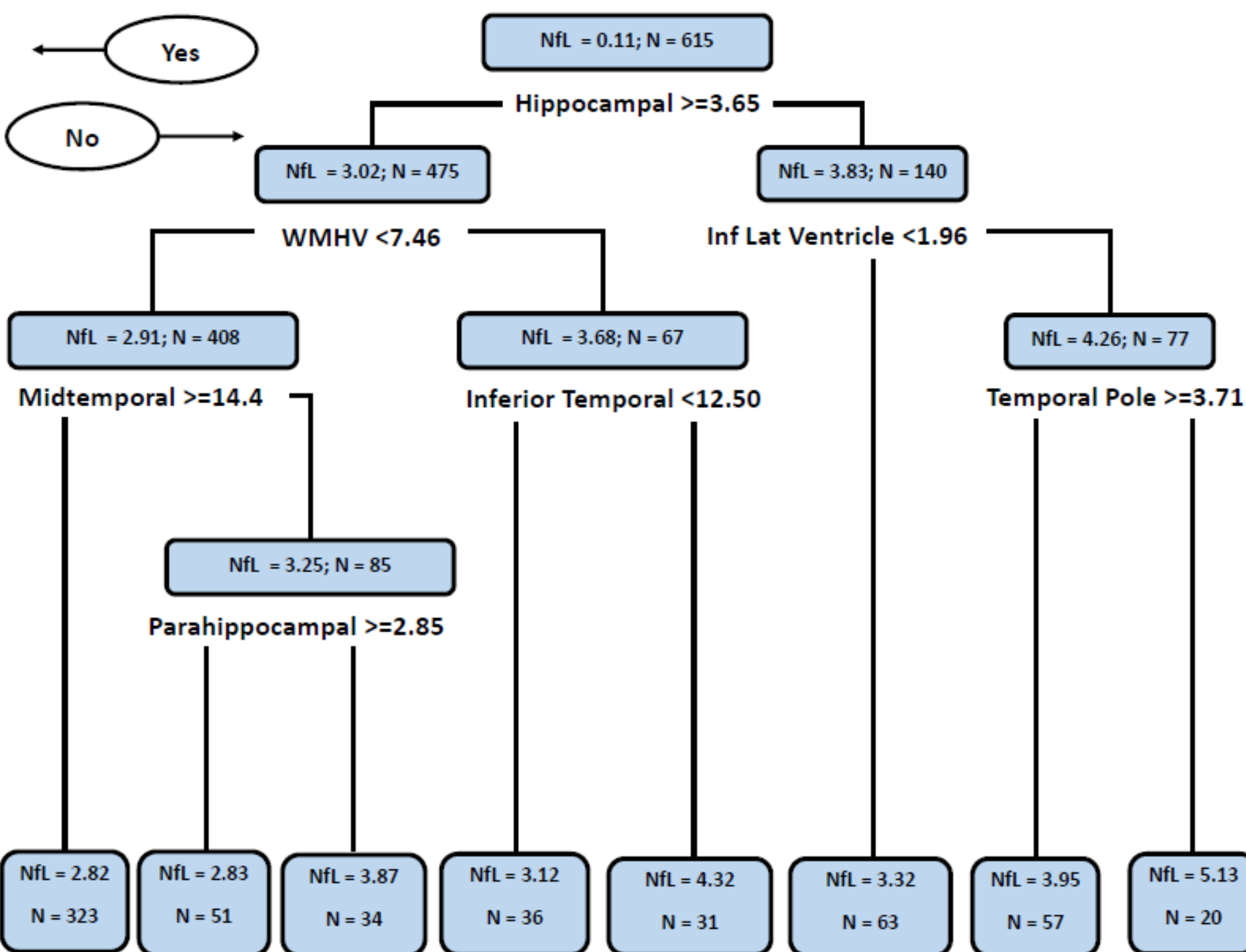
## Background

- TauC2 is a novel combinatory measure of phosphorylated Tau-181 (pTau181) and apolipoprotein (APOE) E4 in plasma. Prior studies have shown there to be a correlation between TauC2 levels and brain atrophy.
- Neurofilament-light (NfL) is a non-specific biomarker of neurodegeneration also correlated with Alzheimer’s disease-related brain atrophy.
- We aim to identify cortical volumetric measures that predict TauC2 levels and NfL levels in cognitively unimpaired individuals.

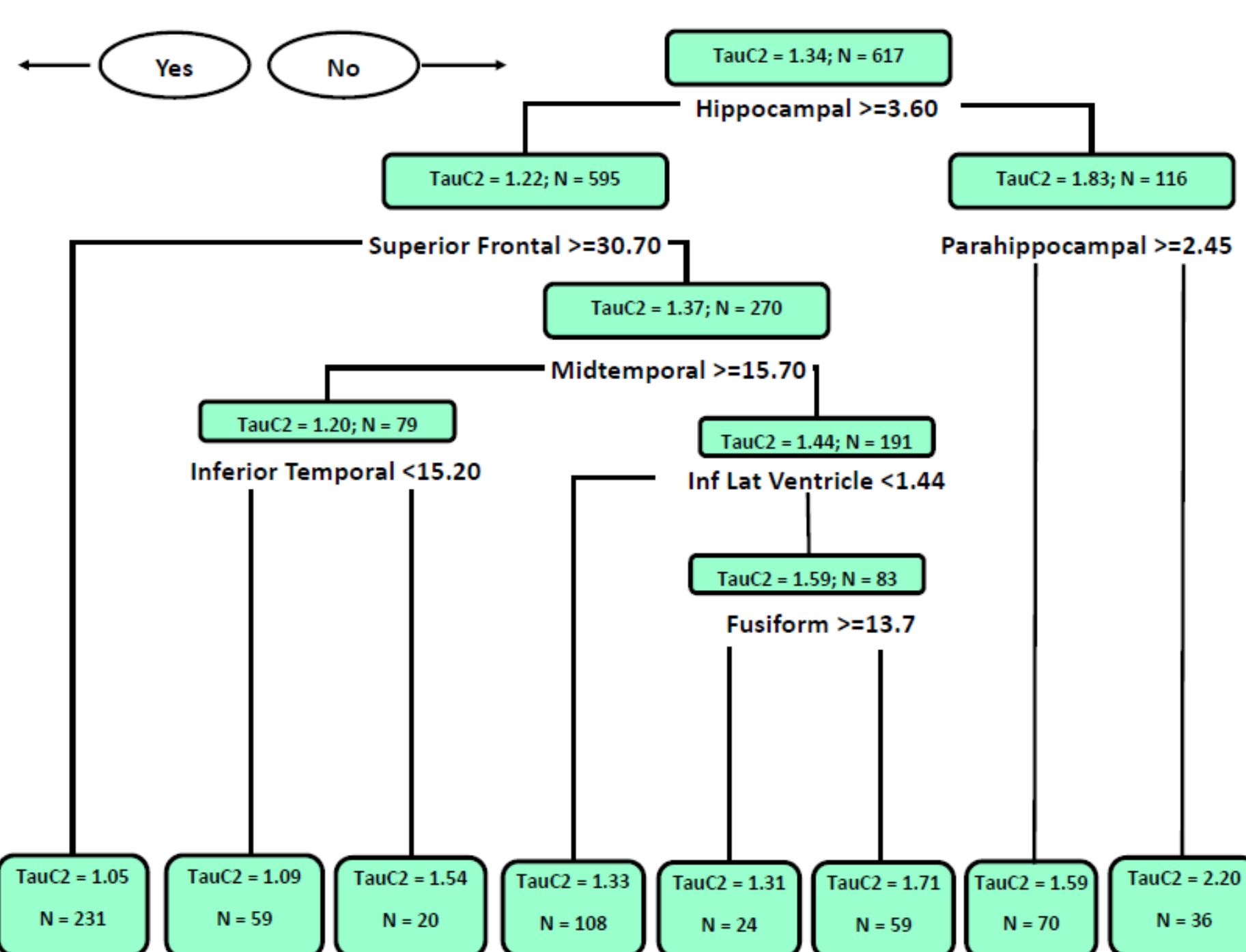
## Methods

- Data from 618 cognitively unimpaired (CU) individuals in the A4 clinical trial and LEARN cohorts were analyzed. The A4 clinical trial enrolled amyloid-positive, CU, older adult subjects, while the LEARN cohort consisted of amyloid-negative subjects.
- Cortical volume measures were derived using NeuroQuant. Plasma TauC2 and NfL samples were analyzed on the Roche Elecsys platform.
- Cortical volume measures from 19 different regions were entered into regression tree models using either TauC2 or NfL as dependent variables.

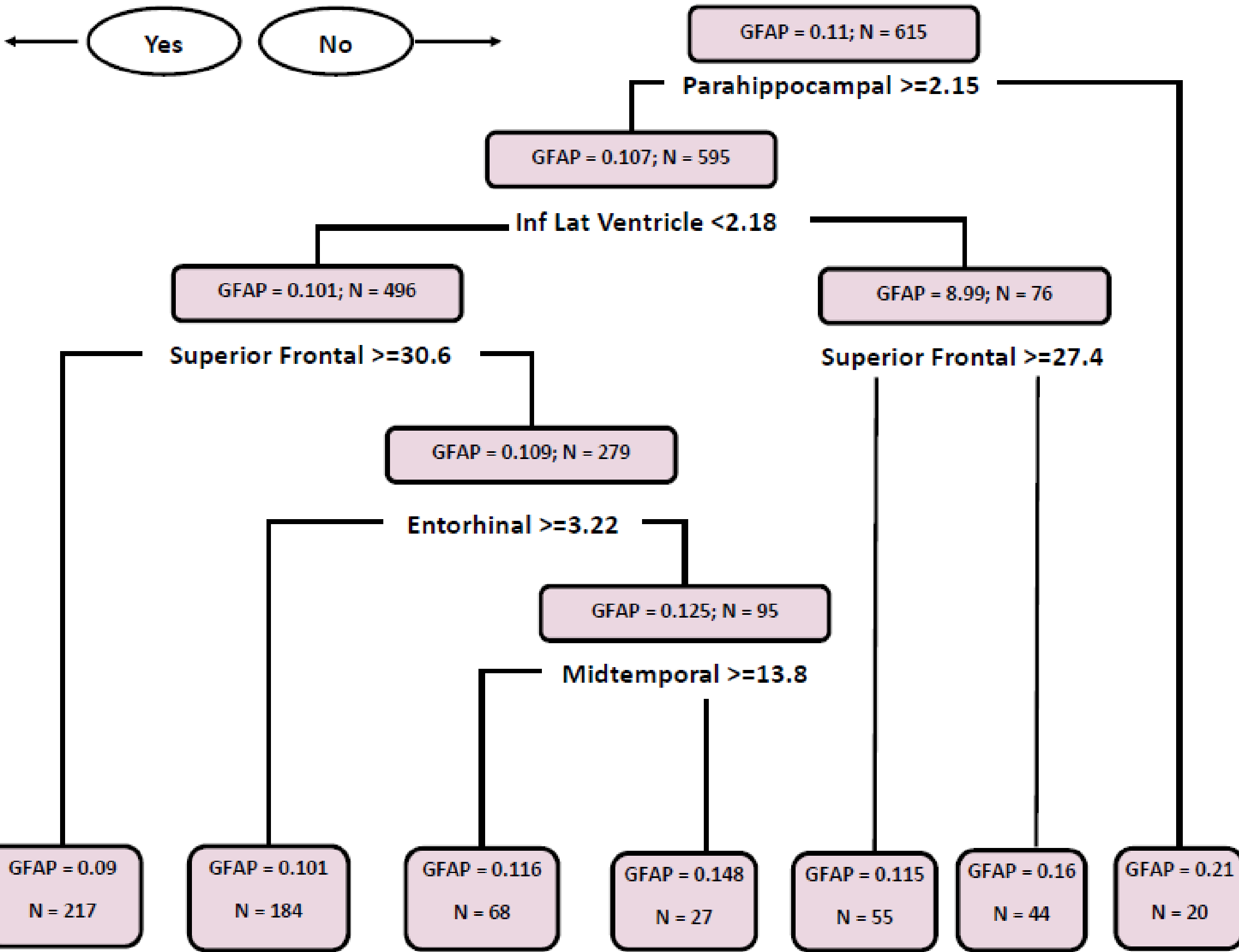
**NfL Regression Tree**



**TauC2 Regression Tree**



**GFAP Regression Tree**



## Results

- High TauC2 levels were associated with the lowest volumetric measures of the hippocampus and parahippocampal gyrus.
- Low TauC2 levels were associated with the highest volumetric measures of the hippocampus and superior frontal gyrus.
- High NfL levels were associated with the lowest volumetric measures of the hippocampus, inferior lateral ventricles, and temporal pole.
- Low NfL levels were associated with the highest volumetric measures of the hippocampus, white matter hyperintensity, and middle temporal lobe.

## Discussion

These findings show that cortical atrophy in several AD-related regions predicted both plasma Tau-c2 and NfL. For both markers, hippocampal volume was the best predictor. As hippocampal atrophy is a hallmark of Alzheimer’s disease (AD), this correlation might indicate a strengthened connection between AD and Tau-c2 or NfL. The findings from this study highlight the ability of established plasma markers of neurodegeneration to detect cortical atrophy in AD-related regions before individuals show significant cognitive decline. Understanding these biomarker predictors may be a useful step in advancing diagnostic tests and treating AD patients.