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## INTRODUCTION

Distinguishing Alzheimer's disease (AD) from frontotemporal dementia (FTD) is challenging due to overlapping clinical features. Advances in blood-based biomarkers now provide opportunities for the biological differentiation of these neurodegenerative disorders. Our study aimed to investigate clinical, neuropsychological, behavioural, genetic, and plasma biomarker features that distinguish AD from FTD in a large Brazilian cohort.

## METHODS



### Participants (Table 1):

- 245 cognitively healthy controls (CN)
- 58 AD patients
- 45 FTD patients

Recruited from two Brazilian centers: USP-SP/UFMG.



### Assessments:

Demographics, clinical evaluation, neuropsychiatric symptoms, neuropsychological testing, genetical and blood-based biomarkers analyses.



### Statistical analyses:

Non-parametric tests.

### PLASMA BIOMARKERS (SUBSAMPLE)

- Subsample with available plasma: 58 participants  
- AD = 25 | FTD = 22 | CN = 11
- Measured on Lumipulse®G600II platform
- Biomarkers  
- p-tau217 - NfL - Aβ42/40 ratio  
- p-tau181 - Aβ42 - GFAP



## RESULTS

FTD cases included: bvFTD (68.9%), svPPA (17.8%), nvPPA(6.7%), PPA-non-specified (4.4%), and PSP(2.2%). Initial symptoms differed significantly between groups ( $p<0.001$ ), with memory complaints predominating in AD and behavioural/language symptoms in FTD (Bar Chart 1). At evaluation, AD exhibited greater memory impairment ( $p<0.001$ ), while FTD had higher language ( $p=0.004$ ) and behavioural ( $p<0.001$ ) deficits (Bar Chart 2).

## RESULTS (cont.)

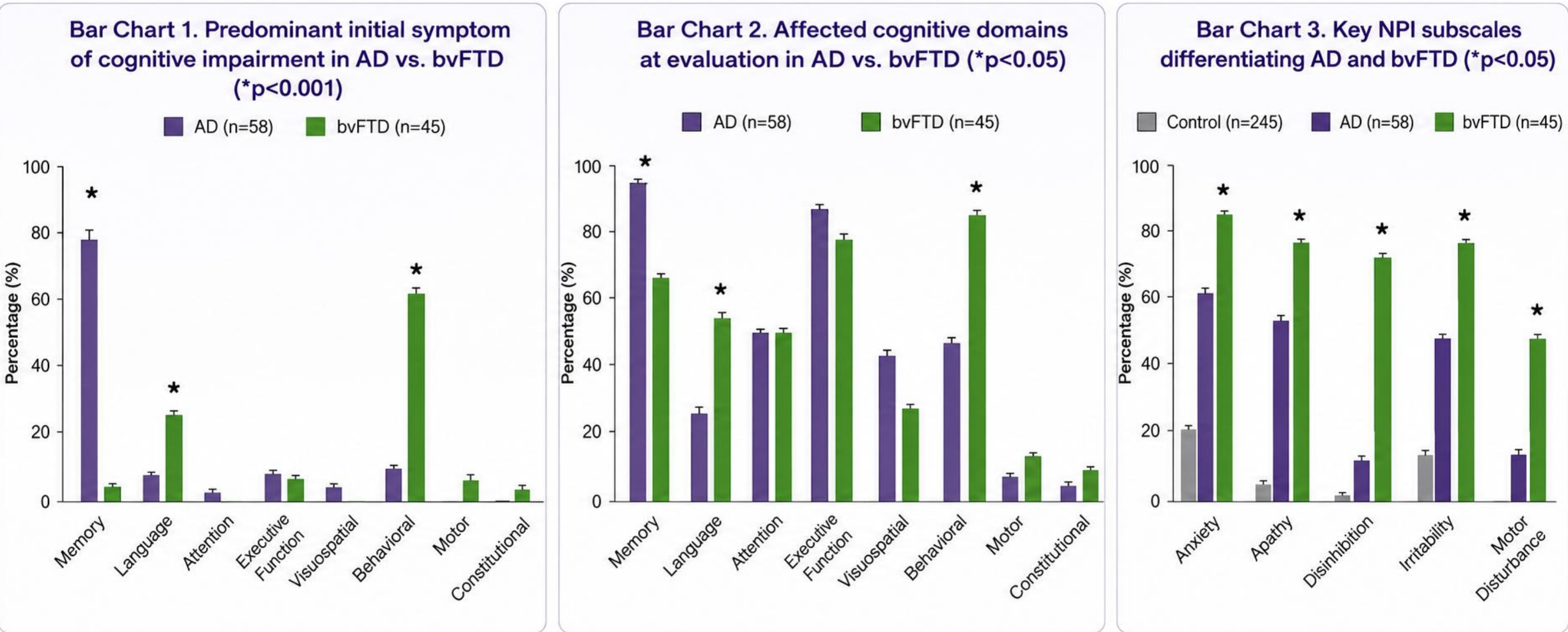
Total NPI scores were higher in FTD than AD ( $p<0.001$ ), driven by disinhibition ( $p<0.001$ ), motor disturbance ( $p<0.001$ ), apathy ( $p=0.013$ ), irritability ( $p=0.004$ ), and anxiety ( $p=0.007$ ) (Bar Chart 3). AD performed worse than FTD on delayed visuospatial recall (Benson Figure Delayed,  $p<0.001$ ). Two familial FTD cases carried the *TARDBP* I383V pathogenic mutation.

P-tau217 showed the highest accuracy to distinguish AD from FTD (AUC=0.834). P-tau181 and Aβ42/40 also demonstrated excellent discrimination (AUC=0.828 and 0.824). NfL levels were higher in FTD than AD and controls (AUC=0.889 for AD; AUC=0.942 for FTD vs. CN) (Figure 2).

**Table 1:** Demographic characteristics of the Control, AD and FTD groups.

|                   | Controls (n=245)             | AD (n=58)                    | FTD (n=45)                    | p value |
|-------------------|------------------------------|------------------------------|-------------------------------|---------|
| Sex male n(%)     | 75 (31%) <sup>a</sup>        | 25 (43.1%) <sup>a,b</sup>    | 27 (61.4%) <sup>b</sup>       | <0.001  |
| Age (years)       | 58.5[48.0;68.8] <sup>a</sup> | 70.0[62.8;75.5] <sup>b</sup> | 66.0[60.3;70.8] <sup>b</sup>  | <0.001  |
| Education (years) | 15.0[11.0;17.0] <sup>a</sup> | 11.0[4.0;16.0] <sup>b</sup>  | 12.5[5.0;16.0] <sup>a,b</sup> | <0.001  |
| Age of onset      | -                            | 65.0[55.0;70.3]              | 62.0[53.0;66.0]               | <0.001  |
| MMSE              | 29[28.0;30.0] <sup>a</sup>   | 20 [17.0;24.5] <sup>b</sup>  | 23[18.0;27.0] <sup>b</sup>    | <0.001  |
| CDR sum of boxes  | 0[0.0;0.0] <sup>a</sup>      | 5.0[4.0;7.9] <sup>b</sup>    | 7.0[4.8;9.4] <sup>b</sup>     | <0.001  |

Values are medians and interquartile ranges (Q1;Q3). <sup>abc</sup> Different superscript letters indicate statistical differences between groups. ( $p < 0.05$ ; Kruskal-Wallis test).



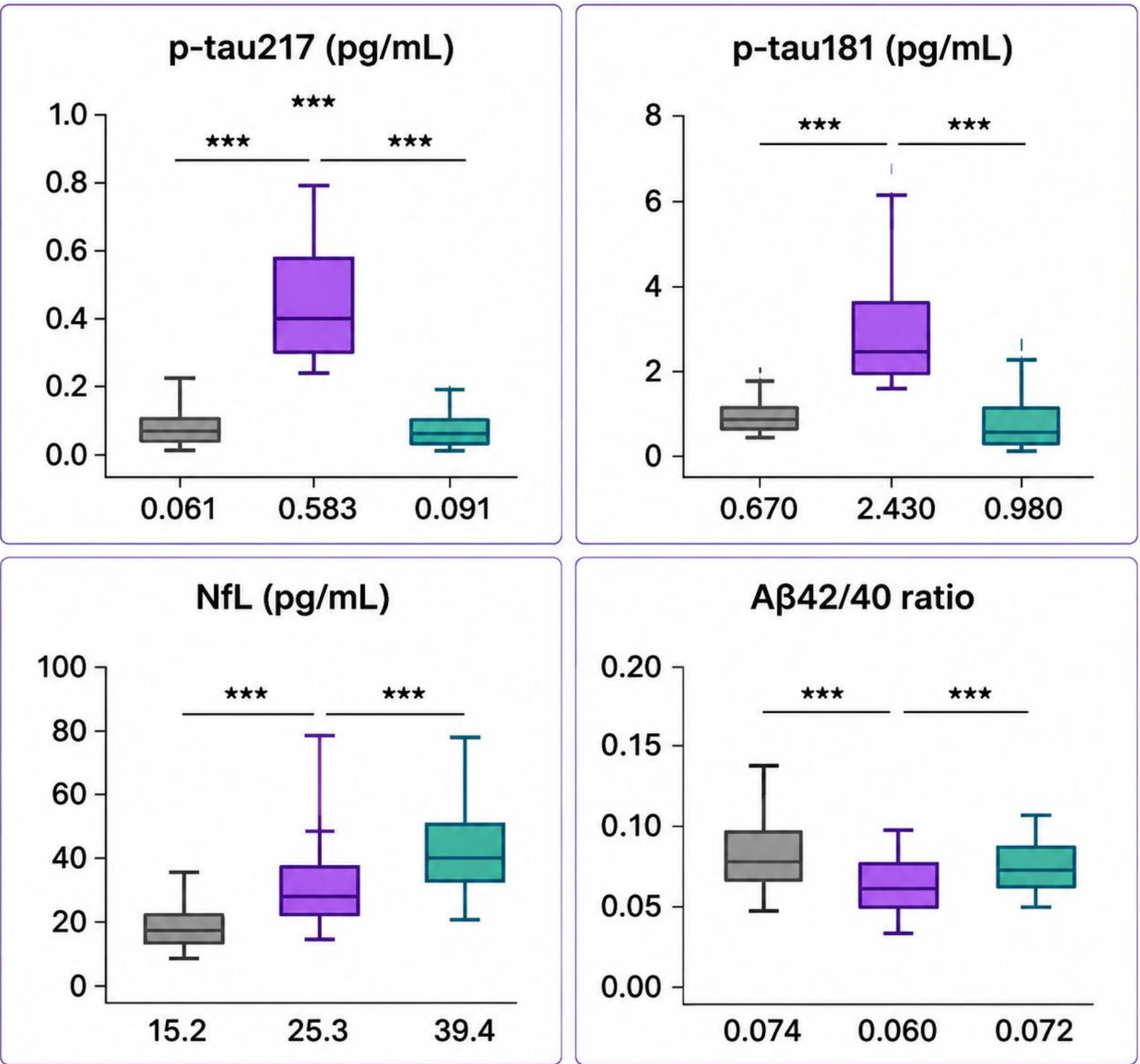
## CONCLUSIONS

In this Brazilian cohort, clinical features and plasma biomarkers provided complementary information for the differential diagnosis of AD and FTD. Memory impairment predominated in AD, whereas behavioural symptoms and higher NPI scores characterized FTD. Among blood-based biomarkers, p-tau217, p-tau181, and Aβ42/40 demonstrated the strongest performance for identifying AD pathology, while NfL was particularly informative for FTD. These findings support the implementation of blood-based biomarkers as accessible tools for differential dementia diagnosis in Latin America.

## BLOOD-BASED BIOMARKERS (SUBSAMPLE)

**Figure 1.** Plasma biomarker levels in CN, AD, and FTD.

■ CN (n=11) ■ AD (n=25) ■ FTD (n=22)



Boxes represent the interquartile range, center lines indicate medians, and whiskers indicate minimum-maximum values. \*\*\*p < 0.0001 (Kruskal-Wallis test, Mann-Whitney U test with Bonferroni correction)

**Figure 2.** ROC curves for AD vs. FTD

