Neuropsychiatric symptoms in demented subjects with biomarker-based diagnosis

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Background

Behavioral and psychological symptoms of dementia (BPSD) are a common feature in patients with cognitive impairment, often stressful and uneasy to treat. Previous published evidence suggests a link between BPSD patterns and specific cerebrospinal fluid (CSF) biomarkers profiles, mainly elevated tau and p-tau in both preclinical and symptomatic Alzheimer's disease (AD) (1). However, in this regard, results are not yet conclusive, particularly in non-AD dementias. Objective: to study the impact of BPSD: i) in different forms of cognitive impairment (MCI, AD, FTD, LBD and VD); ii) in biological clusters based on ATN classification in AD group (2); iii) to search for potential correlations between BPSD and biomarkers levels.

Methods

A total of 71 patients with cognitive impairment due to neurodegenerative or small vessel disease underwent a complete dementia diagnostic workup, including neuropsychological assessment, 3T MR imaging and, in 61 out of 71 subjects, lumbar puncture with CSF biomarkers assay. The impact of BPSD was assessed using the Neuropsychiatric Inventory (NPI) and the items were clustered according to Aalten et al (3).

Results

Patient's age ranged 54-86 years (74.5±7.0 yrs) and 56.3% (N=40) were females; MMSE= 18.8±6.4 (4.9-24.4) and education= 7.4±3.7 years. Considering all diagnostic groups (i), higher scores were found for hallucinations in LBD (p<0.01) and for apathy in LBD and FTD (p<0.05). When primary dementias were concerned (AD, LBD and FTD), psychotic and mood clusters showed higher scores in LBD (p<0.05)(Figure 1, panel a and b), while higher scores of the apathic cluster were found in FTD (p<0.05) (Figure 1. panel c). In AD patients(ii), confirmed by β_{1-42}/p-tau ratio, we detected only 4 ATN groups: A+T-N- (N=1), A-T-N+ (N=1), A-T+N+ (N=13), and A+T+N+ (N=17), and no significant difference was found in NPI scores. Finally, among primary dementias (iii), a negative correlation was found between total NPI score and tau levels (p<0.05) (Figure 2).

Conclusions

BPSD prevalence from this biologically-defined cohort is consistent with data from previous studies on clinically-diagnosed subjects. No significant impact of amyloidosis was observed on BPSD severity in AD patients; conversely, a negative correlation was found between tau levels and NPI total score. This new finding might reflect the larger range of disease severity observed in our group than in those of the previous studies. High NPI scores associated to low tau levels suggest a limited contribution of neurodegeneration in the genesis of BPSD. Nevertheless, further studies considering the confounding effect of disease severity are needed.
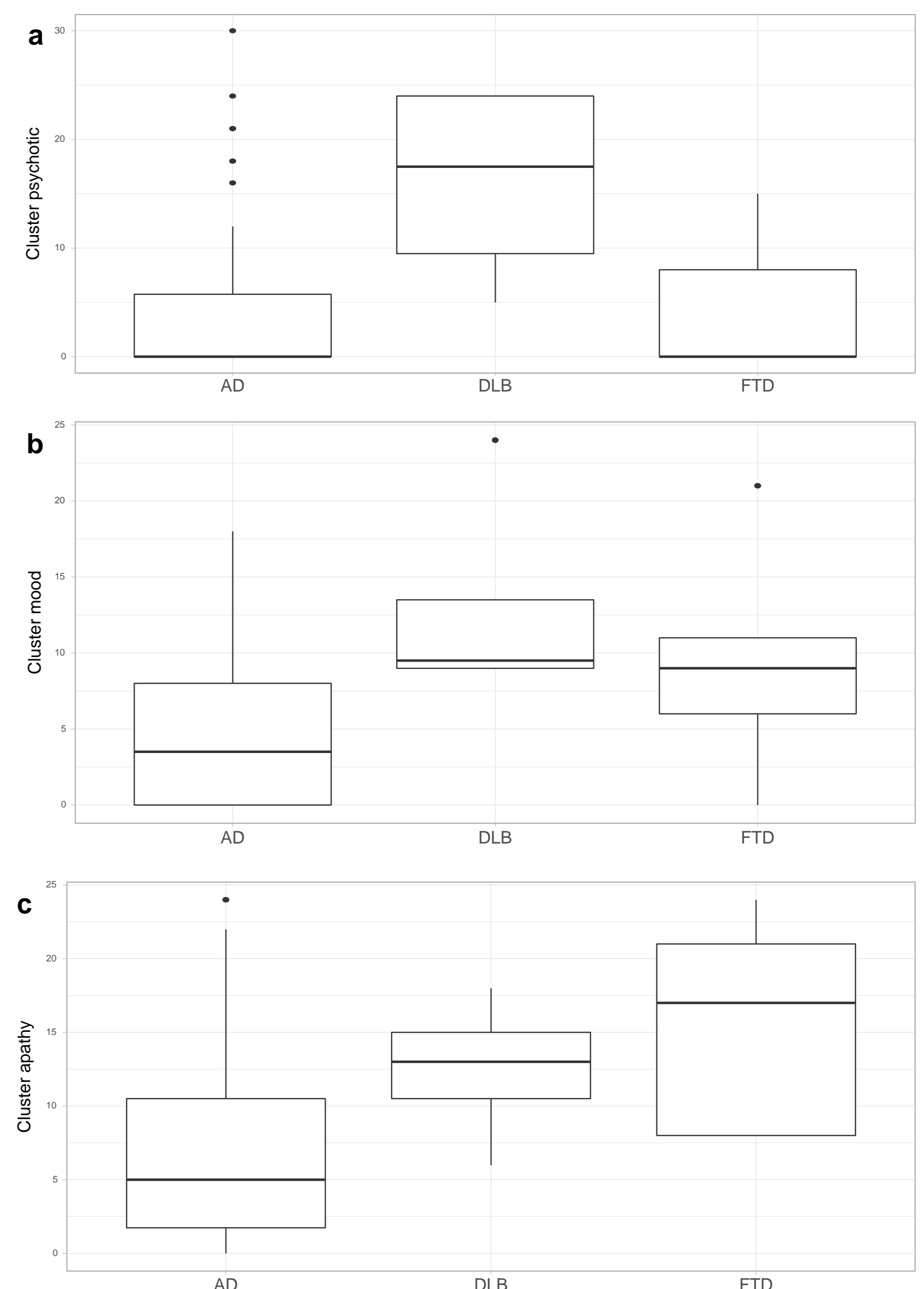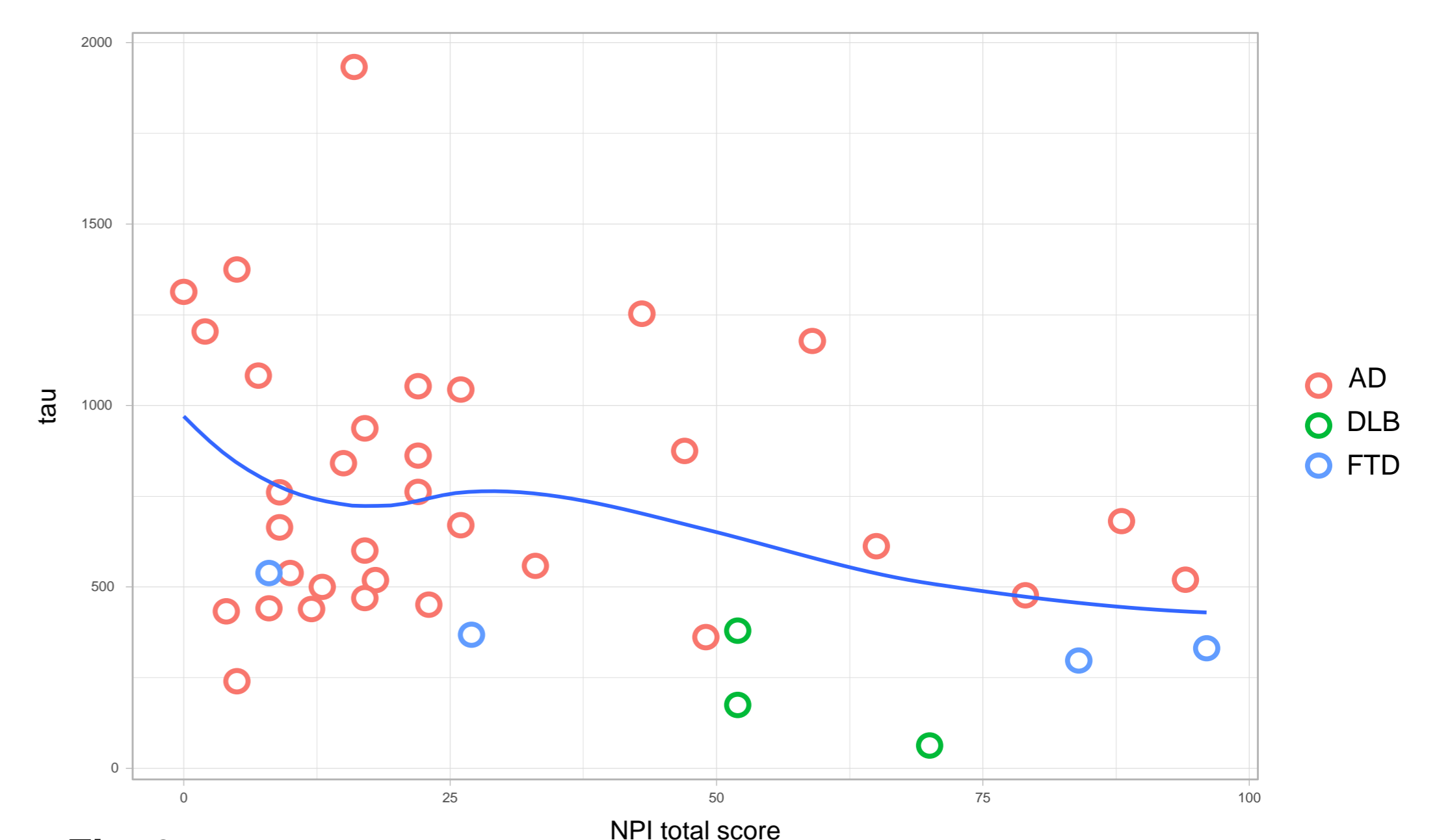

Fig. 1

Fig. 2

Reference

1. Babulal GM, Ghoshal N, Head D, et al. Mood Changes in Cognitively Normal Older Adults are Linked to Alzheimer Disease Biomarker Levels. Am J Geriatr Psychiatry. 2016 Nov;24(11):1095-1104.
2. Jack CR Jr, Bennett DA, Blennow K, et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. Alzheimers Dement. 2018 Apr;14(4):535-562.
3. Aalten P, Verhey FR, Boziki M, et al. Neuropsychiatric syndromes in dementia. Results from the European Alzheimer Disease Consortium: part I. Dement Geriatr Cogn Disord. 2007;24(6):457-63. Epub 2007 Nov 7. Review