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BIOMARKERS

POSTER PRESENTATION

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BIOMARKERS (NON-NEUROIMAGING)

Plasma neurofilament light chain predicts Alzheimer's disease in patients with subjective cognitive decline and mild cognitive impairment: a longitudinal study

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Abstract

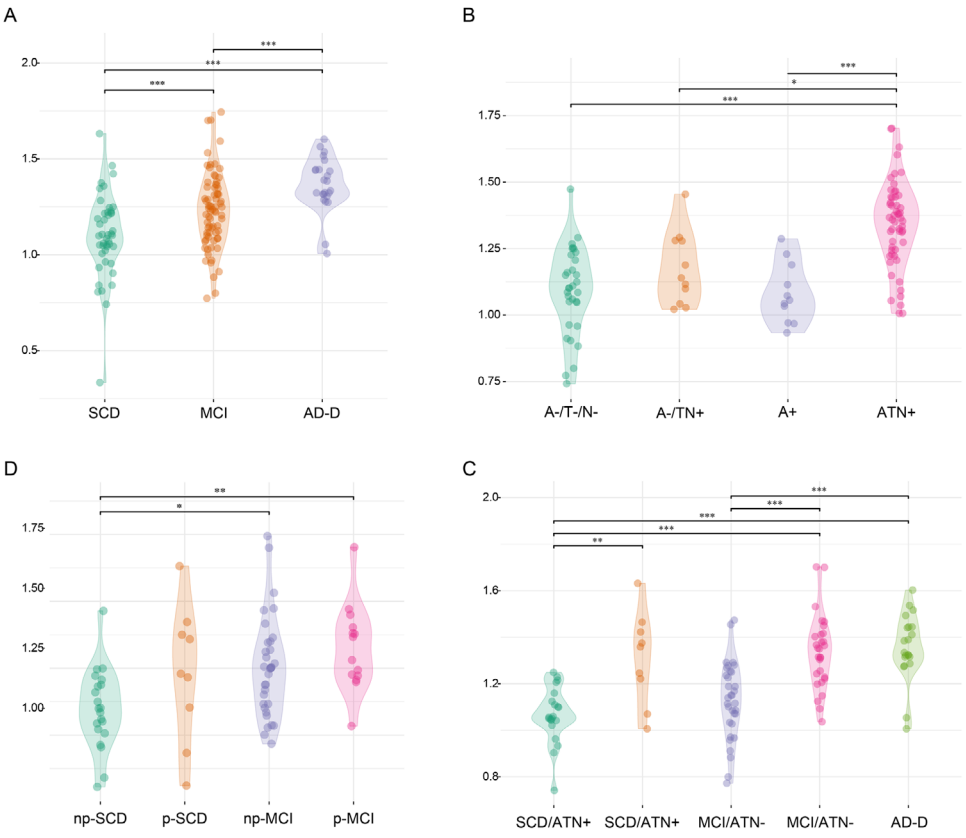
Background: Subjective cognitive decline (SCD) and mild cognitive impairment (MCI) represent a target population for early detection of Alzheimer's Disease (AD). Nevertheless, both MCI and SCD are common and heterogeneous conditions. We aim to evaluate the accuracy of plasma neurofilament light chain (NfL) in predicting AD and the progression of cognitive decline in patients with SCD and MCI.

Method: 140 patients (45 SCD, 73 MCI, and 22 AD dementia [AD-D]) underwent plasma NfL and CSF biomarker measurement at baseline. A subgroup of patients also underwent amyloid-PET and ^{18}F-FDG-PET brain scans. They were rated according to the A/T/N system and followed up for a mean time of 2.72±0.95 years. Forty-eight (19 SCD, 29 MCI) had plasma NfL measurement also after two years from baseline.

Result: NfL levels were higher in AD-D than MCI and in MCI than SCD. In each group, patients with ATN profiles consistent with AD (A+/T+/N+ or A+/T+/N- [defined as ATN+]) had higher NfL levels (F[5,103] = 13.50, p<0.001, η^2 = 0.396) than patients classified as ATN- (including patients with normal AD biomarkers, isolate Aβ pathology [A+] and non-AD pathologic changes). NfL can distinguish ATN- and ATN+ patients with high accuracy (AUC = 0.82) and cut-off values of 19.45 pg/mL in SCD and 20.45 pg/mL in MCI provide the highest Youden's index. During the follow-up, nine (30%) SCD patients progressed to MCI (p-SCD) and 14 (29.79%) MCI patients developed AD-D (p-MCI). The previously defined cut-off values identified p-SCD with an 80.00% [95%C.I. = 65.69:94.31] accuracy. The rate of NfL change per year was higher in p-MCI (3.52±4.06 pg/mL) as compared to np-SCD (0.81±1.25 pg/mL) and np-MCI (-0.13±3.24 pg/mL) and np-MCI (-0.13±3.24 pg/mL) patients and in ATN+ (1.53±3.60 pg/mL) as compared to patients in the A+ group (-0.97±1.66 pg/mL). A rate of change

lower than 1.64 pg/mL can exclude progression to AD with a 92.86% (95%C.I. = 83.32:100) accuracy.

Conclusion: NfL concentration and change over time are increased in SCD and MCI patients with a biological demonstration of AD and can predict the progression of cognitive decline. Despite being considered a non-specific neurodegeneration biomarker, if applied to selected populations, NfL may be a reliable, non-invasive tool to detect the early stages of AD.



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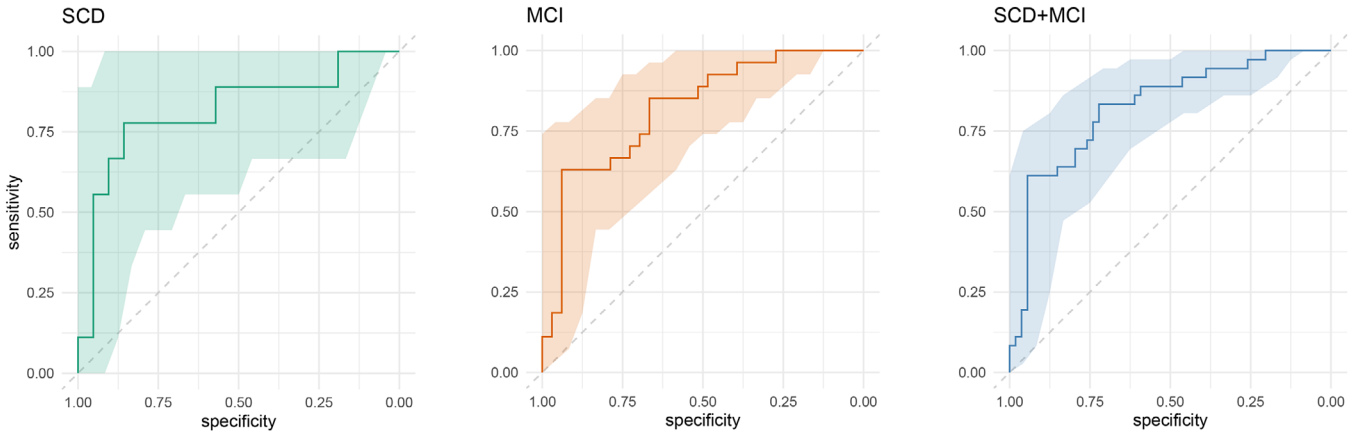

N	30
AUC	0.815
cut-off (pg/mL)	19.45
Accuracy	83.33 (69.99 : 96.67)
Sensitivity	55.56 (37.77 : 73.34)
Specificity	95.24 (87.62 : 100)
PPV	83.33 (70.00 : 96.67)
NPV	83.33 (70.00 : 96.67)

N	60
AUC	0.818
cut-off (pg/mL)	20.49
Accuracy	80.00 (69.88 : 90.12)
Sensitivity	62.96 (50.74 : 75.18)
Specificity	93.94 (87.90 : 99.98)
PPV	89.47 (81.71 : 97.24)
NPV	75.61 (64.74 : 86.48)

N	90
AUC	0.824
cut-off (pg/mL)	20.03
Accuracy	81.11 (73.02 : 89.20)
Sensitivity	61.11 (51.04 : 71.18)
Specificity	94.44 (89.71 : 99.18)
PPV	88.00 (81.29 : 94.71)
NPV	78.46 (69.97 : 86.95)