Plasma Biomarkers of Alzheimer's Disease in Individuals with Subjective Cognitive Decline: a single-center experience

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BACKGROUND

Blood-based biomarkers (BBMs) have gained the spotlight as less invasive diagnostic tools in Alzheimer's Disease (AD) diagnostic workup [1], opening to scenarios of identification of disease even at prodromal stages, as in Subjective Cognitive Decline (SCD).[2]

OBJECTIVE

To assess whether a panel of BBMs associated with AD - **plasma Aβ42/Aβ40 ratio** and phosphorylated tau (**p-tau181**) - could predict the **risk of conversion** from SCD to Mild Cognitive Impairment (MCI) or dementia.

To characterize the **clinical profile** of the **SCD** population, identifying features that may help forecast cognitive trajectories.

MATERIALS AND METHODS

50 SCD and 50 AD patients

Baseline plasma biomarker testing

Follow-up neuropsychological evaluation ≥18 months later.

Clinical risk factors assessment: insomnia, depression, comorbidities, migraine, and family history

RESULTS

- Six SCD participants (%) progressed to amnestic MCI and showed higher p-tau181 levels (Table 1).
- A multivariate regression analysis showed that **insomnia** significantly **predicted conversion** (p=0.042) (Table 2).
- **BBMs** did not independently predict conversion but were **linked to greater MMSE decline**.(Figures 1&2)

VARIABLE	SCD
Sex (M:F)	21:29
Age	70 (63–73)
Scolarity (years)	13 (8–15)
Plasma Aβ42/Aβ40 ratio	0.096 (0.088–0.105)
Plasma p-tau	1.295 (0.872–1.688)
Altered BBMs (Y:N)	17:37
CSF Aβ42 pg/mL	844.4 (531.50–881.25)
CSF Aβ42/Aβ40 ratio	0.082 (0.070–0.095)
CSF t-tau pg/mL	385.0 (213.0–481.0)
CSF p-tau pg/mL	29.4 (22.0–61.2)

Table 1 – Demographic characteristics and biomarker values of the SCD population.
Legend: SCD: Subjective Cognitive Decline; M: male; F: female; Aβ: amyloid beta; p-tau: phosphorylated tau; BBMs: blood-based biomarkers; Y: yes; N: no; t-tau: total tau

VARIABLE	OR (Odds Ratio)	CI 95% OR	P-value
Age	1.03	(-0.170-0.219)	0.804
Sex	1.82	(-2.499-3.695)	0.705
Plasma p-tau181	182.49	(-0.375-10.801)	0.068
Insomnia	85.429	(0.158-8.737)	**0.042***

Table 2 – Results from the multivariate regression analysis

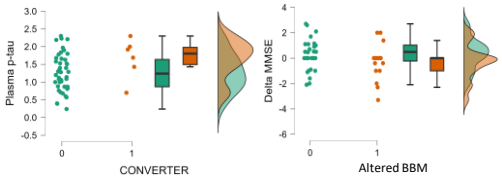

Figure 1 – Levels of plasma p-tau in *converters* and *non-converters*
Figure 2- MMSE decrease in individulas with BBM positivity

DISCUSSION AND CONCLUSIONS

SCD is a heterogeneous, potentially prodromal stage in the AD continuum. While BBMs did not independently predict phenoconversion, **biomarker-positive individuals** showed **greater MMSE decline**. In our real-world cohort **insomnia** emerged as a **significant predictor of progression to amnestic MCI**.

The use of a real-world cohort improves the applicability of findings to routine care, despite limitations such as small sample size and short follow-up. Overall, the study supports further exploration of BBMs in SCD and underscores the importance of longitudinal, real-world research to guide early intervention in preclinical AD.

REFERENCES
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