Association of plasma Aβ42/Aβ40 with episodic memory performance and brain atrophy in individuals at risk of Alzheimer's disease

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BACKGROUND

Blood-based biomarkers that can accurately detect **subtle alterations of preclinical Alzheimer's disease** (AD) are urgently required to identify suitable candidates for early-stage clinical trials.

OBJECTIVE

To assess the ability of **plasma Aβ42/Aβ40 ratio**, as determined by a high-sensitivity antibody-free mass spectrometry-based assay, to detect early alterations in **episodic memory performance** and **brain atrophy** in individuals with subjective cognitive decline (SCD).

METHODS

Aβ40 and Aβ42 plasma levels were measured with **ABtest-MS** (Araclon Biotech) in 200 individuals with SCD from the FACEHBI cohort. Participants underwent the Spanish version of FNAME (**S-FNAME**) and the derived composite face-name, **SFN-N**, to evaluate episodic memory performance. Brain atrophy was assessed using MRI measures of **ventricular and hippocampal volume** normalized by total intracranial volume. Participants were classified as plasma Aβ42/Aβ40(+) or Aβ42/Aβ40(-) by applying a cutoff of 0.241 corresponding to the maximum Youden index, derived from ROC curve analyses to detect early Aβ-PET positivity. Group differences were examined using the Mann-Whitney test.

Table 1. Characteristics of the study population. *Data are median values (IQR) or number of cases (%). Differences between groups were tested using Mann-Whitney and Chi-square tests, as appropriate.*

	All	Aβ42/Aβ40 (-)	Aβ42/Aβ40 (+)	*P* value
Participants	200	137 (69%)	63 (31%)	
Age, years	67.0 (60.0-70.0)	64.0 (60.0-69.0)	69.0 (66.0-73.0)	**<.0001**
Female	126 (63%)	97 (71%)	29 (46%)	**<.0001**
***APOE* ε4 carrier**	52 (26%)	26 (19%)	26 (41%)	**.002**
S-FNAME, score	30.5 (20.0-43.0)	34.0 (22.0-48.0)	28.0 (18.5-35.0)	**.023**
SFN-N, score	-0.14 (-0.73-0.46)	-0.04 (-0.61-0.66)	-0.47 (-1.05-0.19)	**<.0001**
Ventricular vol., mm^3	25554 (20105-33600)	24167 (18619-31936)	28781 (23365-36100)	**.022**
Hippocampal vol., mm^3	3606 (3399-3821)	3621 (3454-3833)	3568 (3284-3758)	.097

RESULTS

Association of plasma Aβ42/Aβ40 with episodic memory performance

Subjects classified as plasma Aβ42/Aβ40(+) performed significantly worse on S-FNAME and SFN-N composite, than those Aβ42/Aβ40(-) (P=.023 and P<.001, respectively). A significant positive correlation was found between plasma Aβ42/Aβ40 and the SFN-N composite score (rho=0.193, P<.006).

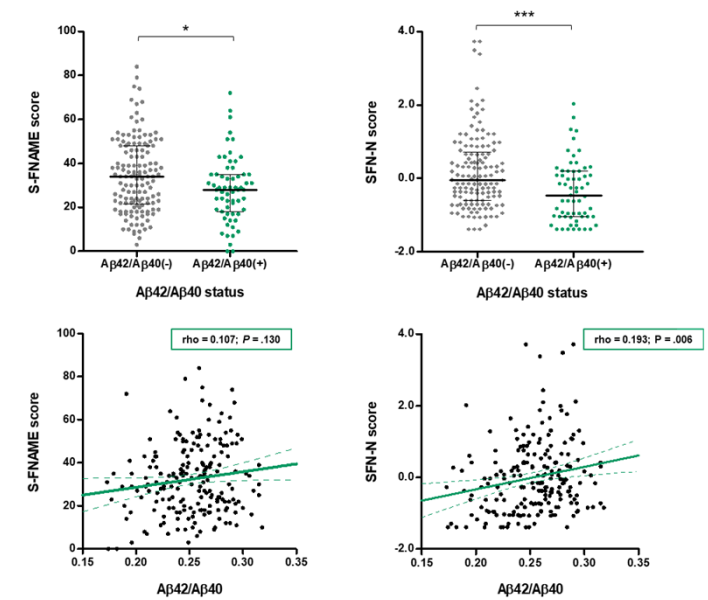

Figure 1. Association of plasma Aβ42/Aβ40 with episodic memory performance.
** P < .05, *** P < .0001, Mann-Whitney test.*

Association of plasma Aβ42/Aβ40 with brain atrophy

Plasma Aβ42/Aβ40 was also associated with brain atrophy, as evidenced by increased ventricular volume and reduced hippocampal volume in Aβ42/Aβ40(+) individuals (P=.022 and P=.097, respectively).

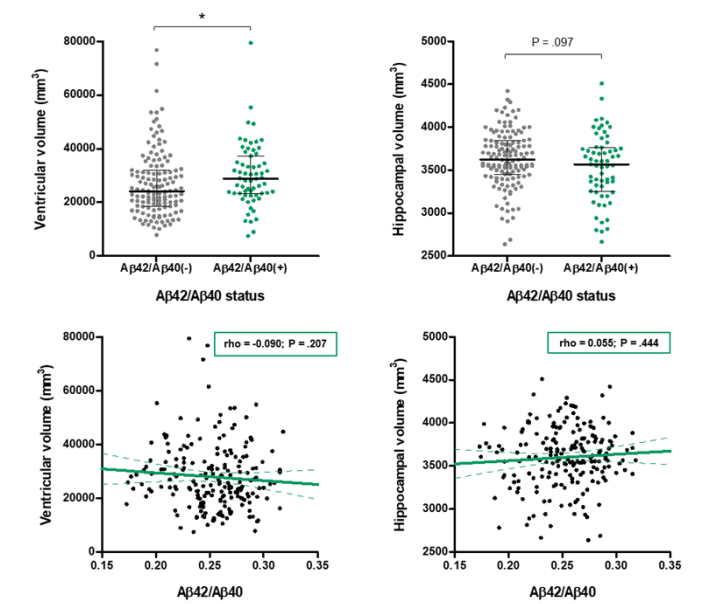

Figure 2. Association of plasma Aβ42/Aβ40 with brain atrophy.
** P < .05, Mann-Whitney test.*

CONCLUSION

Individuals with low plasma Aβ42/Aβ40 values performed worse on the S-FNAME and presented increased brain atrophy to some extent, suggesting that **plasma Aβ42/Aβ40**, as determined by this **MS-based assay, could detect the first subtle alterations in AD**.