

Innovating Brain Health: An Italian Experience with a Community-Based Service

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OBJECTIVES

- To characterize the clinical, neuropsychological, neurophysiological, neuroimaging, genetic, and fluid biomarker profiles of individuals accessing the Brain Health Service (BHS) of San Raffaele Hospital in Milan.
- To identify early markers of neurodegenerative vulnerability and assess the clinical value of BHS multimodal assessments.

MATERIALS AND METHOD

- 52 participants accessed the BHS for positive family history of dementia, perceived cognitive changes, and/or interest in proactive cognitive health evaluation from February 2024-to-April 2025.
- They underwent comprehensive clinical/neurological and neuropsychological evaluations, brain MRI, electroencephalography (EEG), optical coherence tomography (OCT), and APOE genotyping.
- These participants agreed to undergo blood-sampling for plasma AD-biomarker-analysis as part of the ongoing research project.
- Participants were classified as A+ (n=22) or A- (n=30) based on plasma p-tau217 (cutoff=0.1325 pg/mL), and clinically stratified into cognitively normal (CN=15; CN+=6; CN-=9), subjective cognitive decline (SCD=18; SCD+=3; SCD-=15), and mild cognitive impairment (MCI=19; MCI+=13; MCI-=6).
- Clinical assessments included medical history and lifestyle/vascular risk factors. Neuropsychological evaluations covered memory, language, attention, executive function, and visuo-spatial abilities.
- Gray matter (GM) atrophy and white matter (WM) lesion load were assessed on MRI using standardized semiquantitative rating scales.
- We analyzed EEG features, including spectral metrics, and OCT data, including the average retinal layer thickness of both eyes.
- Groups were compared using ranked ANCOVAs, Kruskal-Wallis tests or chi-square tests. A support Vector Classifier (SVC) was applied to the Multicomponent dataset and to the Neuropsychological dataset only for the classification of A+ and A-.

Table 1. Features of the clinical sample

	CN	SCD	MCI	P (CN vs SCD)	P (SCD vs MCI)	P (CN vs MCI)
N	15	18	19			
Age (years)	55.1 ± 11.6	57.2 ± 9.7	65.1± 11.4	1.000	0.107	0.022
Sex (male/female)	6/12	10/8	11/8	0.180	0.886	0.134
Education (years)	16.1 ± 3.2	15.3 ± 4.1	14.1 ± 5.1	0.507	0.389	0.136
ApoE*	0\12\1\1\4\0	0\10\0\2\5\1	0\11\3\1\4\0	0.403	0.564	0.725
Plasma pTau-217	0.1 ± 0.1	0.1 ± 0	0.36 ± 0.48	0.195	0.031	0.111
MMSE	29 ± 1	29.4 ± 0.7	27.63 ± 2.39	0.930	0.063	0.582
FAB	17.6 ± 0.8	17.4 ± 1.1	15.68 ± 2.24	1.000	0.014	0.013
BDI II - Total score	6.4 ± 8.3	9.2 ± 8.9	8.9 ± 8.1	0.269	1.000	0.680

ApoE: 0=£2£2; 1= £3£3; 2= £4£4; 3= £2£3; 4= £3£4; 5= £2£4.

RESULTS

A+ cases were older than A-, reported higher alcohol consumption, and engaged in less physical activity, while sex, education and APOE genotype were similar. A+ participants showed poorer cognitive performance in tests assessing verbal learning, comprehension fluency, visuo-spatial abilities, attention and executive functions. MCI+ performed worse than MCI- on timed tests, while CN+ showed reduced semantic fluency compared to SCD-. Compared to A-, A+ showed reduced GM volume in the left medial temporal lobe, left fusiform gyrus, right precuneus and right anterior temporal gyrus (**Figure 1**), along with increased WM burden in periventricular and deep regions. Compared to A-, in A+ EEG analysis revealed a shift in power spectral density toward lower frequencies (delta-band, 1–4 Hz) in temporal and frontal regions, and OCT revealed increased global retinal nerve fiber layer thickness. The SVC analysis revealed the best features able to classify A+ and A- participants (**Figure 2**).

Figure 1. VRS-MRI, Gray matter atrophy: A+ > A-

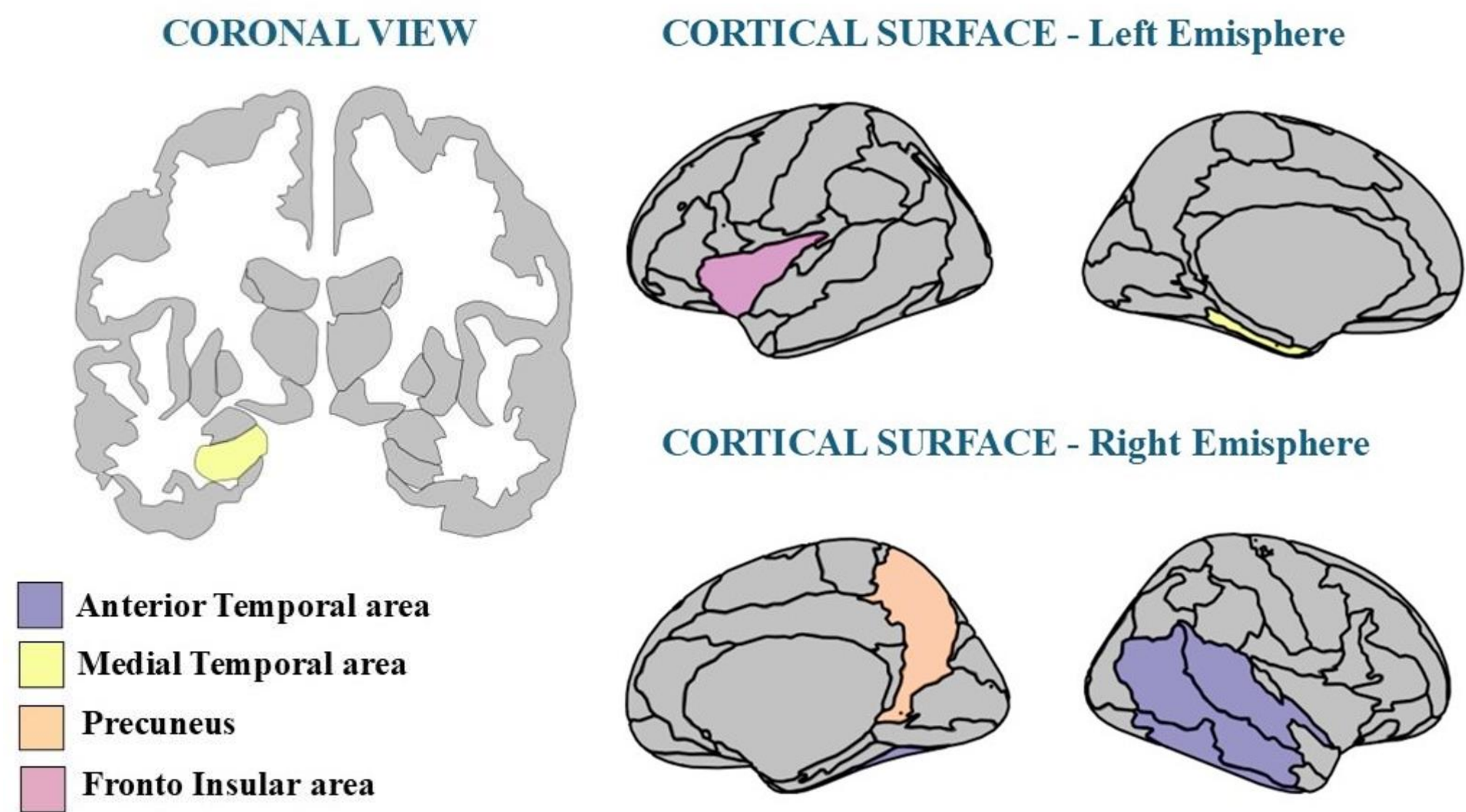
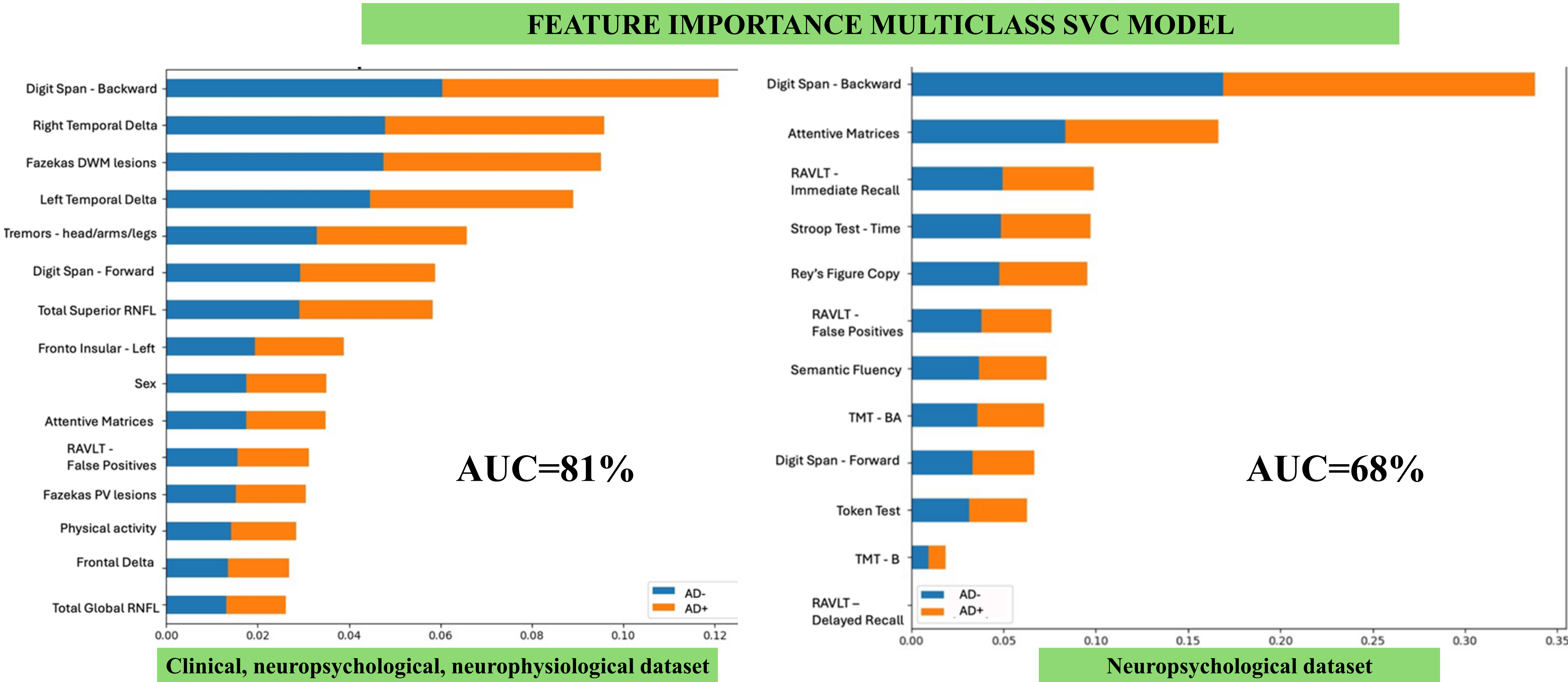


Figure 2. SHAP values indicating key measures differentiating AD+\AD- via SVC models



CONCLUSIONS

- Our findings support the feasibility and clinical relevance of plasma biomarkers, offered within a research framework, for the early detection of AD in individuals accessing a BHS.
- Early biomarker identification enables timely lifestyle interventions that may delay symptoms onset and/or autonomy loss.
- The BHS model provides a promising framework to detect at-risk individuals and guide preventive strategies.