

A Machine Learning Approach to Sensory-based Cognitive Risk Prediction in the Older Population of Southern Italy

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Across a 636-participant 8-year cohort and a deep-phenotyping case-control extension, hearing and vision were the most robust sensory predictors of cognition; central auditory processing (CAPD) and plasma p-tau217 emerged as the strongest correlates of MCI.

INTRODUCTION

Background

Sensory decline is common in ageing and linked to higher risk of cognitive impairment, but it is unclear how individual or combined sensory domains predict cognitive status.

Aim

To predict sensory-based cognitive risk in older adults from Southern Italy using machine learning, across two complementary analyses: a population cohort with longitudinal cognition, and a deep-phenotyping case-control extension.

Zephyr ≥ 60 y deep-phenotyping sub-cohort

↓
n = 786

Multi-modal panel • audiology • OCT-A • MRI MPRAGE-3D • plasma AD proteins • chemosensory • 10-y exposome

↓
complete

~ 212 • disabling peripheral HL (ARHL / PTA > 45 dB), otological disease, or major cerebral malignancy

CAPD-assessable pool • central processing isolated

↓
n = 274

~ 74 • incomplete biomarker / imaging panel or withdrawn consent

Nested case-control • 1:1 matched on age, sex, education
100 MCI cases • 100 cognitively-healthy controls

Extension cohort — MENTOR nested case-control sampling (final n = 200).

METHODS

Primary — GreatAge cohort

636 adults ≥65, cognitively healthy at baseline, followed 8 years (outcome: MMSE). Baseline sensory battery: vision (retinal vessel density), hearing (PTA + central SSI-ICM), smell (Sniffin' Sticks), taste. Multivariable regression + a random-forest-guided weighted linear ensemble.

Extension — MENTOR (deep phenotyping)

Nested case-control in the ZEPHYR ≥60 y sub-cohort: 100 MCI vs 100 controls (1:1). Central auditory processing disorder (CAPD; Gates + SSI) plus OCT-A retina, MRI MPRAGE-3D, plasma AD proteins and a 10-y exposome; multi-modal soft-probability XGBoost classifier.

RESULTS

Two complementary analyses converge on the same sensory signal.

Primary — GreatAge • baseline predictors of 8-y MMSE

Predictor	Effect	p
Vision — retinal vessel density	↑ higher MMSE	<0.05
Hearing — PTA / SSI-ICM	↑ higher MMSE	<0.05
Olfaction / taste	no association	n.s.
Older age / lower education	↓ greater decline	<0.01

Extension — MENTOR • adjusted association with MCI

Term	aOR	95% CI	p
CAPD (central auditory)	8.17	3.43–19.47	<0.001
Plasma p-tau217 (per SD)	3.36	1.97–5.73	<0.001
PM _{2.5} (per +5 µg/m³)	2.05	1.28–3.28	0.003
NO ₂ (per +10 µg/m³)	1.74	1.12–2.71	0.014
Education (per year)	0.73	0.66–0.82	<0.001

CONCLUSIONS

A • CAPD + MCI (OvR AUC 0.95)

B • CAPD without MCI (OvR AUC 0.93)

C • Clean reference (OvR AUC 0.97)

D • MCI without CAPD (OvR AUC 0.90)

Extension (MENTOR): multi-modal XGBoost — per-group importance and one-vs-rest AUC (macro-AUC 0.93; MCI-detection AUC 0.96).

Take-home

Across a population cohort and a deep-phenotyping extension, hearing and vision were the most robust sensory predictors of cognition.

In deep phenotyping, central auditory processing (CAPD, aOR ≈ 8) and plasma p-tau217 were the strongest correlates of MCI, with air pollution adding independent risk; the multi-modal classifier reached macro-AUC 0.93.

Combining simple sensory screening with targeted deep phenotyping may enable early identification of cognitive risk and timely prevention.

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AAIC>26