

Neurocognitive Indices and Machine Learning to Predict Time to Alzheimer’s Conversion in MCI: A Systematic Review

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Machine learning frameworks trained on neuropsychological scores and digital cognitive metrics predict MCI-to-AD conversion with high accuracy (up to 91–95%), while explainable AI tools (SHAP/LIME) successfully translate these algorithms into transparent, actionable profiles for clinical practice.

INTRODUCTION	METHODS	RESULTS	REFERENCES																														
- Predicting the progression from Mild Cognitive Impairment (MCI) to Alzheimer's disease (AD) remains a major clinical challenge. - Current biomarkers (neuroimaging and CSF) provide high accuracy but are often costly, invasive, and not widely accessible. - Machine Learning (ML) models using low-cost, non-invasive neurocognitive and behavioral data offer a promising alternative for early prediction. - The integration of Explainable AI (XAI) improves transparency and supports clinical decision-making.	- Design: Systematic literature review following PRISMA 2020 guidelines. - Databases: PubMed, Scopus, and Web of Science. - Search: Terms related to MCI, subtle/subjective cognitive decline, ML methods, granular cognitive measures, and conversion outcomes. - Eligibility: Studies using supervised ML with process-based neurocognitive or behavioral measures to predict conversion; studies based only on global cognitive scores or standalone biomarkers were excluded.	<table><tr><th>APPROACH & CORE FEATURES</th><th>KEY STUDIES</th><th>AI / ML MODELS</th><th>PERFORMANCE METRICS</th><th>MAIN PROGNOSTIC FINDING</th></tr><tr><td>Traditional & Fine-Grained Scores - Delayed memory recall (RAVLT, Logical Memory) - Functional scales (FAQ, MMSE) </td><td>D'Amore et al., 2025; Formica et al., 2023; Russo et al., 2024 ;Zarei et al., 2025</td><td> Random Forest - Support Vector Machine (SVM) - Gradient Boosting </td><td>Accuracy: 83.8–91.0%AUC: 0.91</td><td>Delayed recall and functional measures are the strongest predictors of conversion.</td></tr><tr><td>Digital & Process-Level Biomarkers - Speech paralinguistics - Drawing micro-distortions (Cube Copying) </td><td>García-Gutiérrez et al., 2024; Shinozaki et al., 2025</td><td> Deep Learning (PatchCore) - Neural Networks </td><td>AUC: 0.85F1: 0.84</td><td>Speech dynamics and early constructional deficits detect conversion at preclinical/MCI stages.</td></tr><tr><td>Behavioral & Subjective Features - Neuropsychiatric symptoms (NPI-Q, GDS-15) - Subjective Cognitive Decline (SCD) </td><td>Dauphinot et al., 2024; Gómez-Ramírez et al., 2020; Mallo et al., 2020</td><td> Random Forest - Permutation-based Models </td><td>Accuracy: 88.0%Median conversion: 25 months</td><td>Depression, anxiety, stress, and subjective complaints accelerate conversion risk.</td></tr><tr><td>Longitudinal & Time-Series Modeling - Variable-length clinic visits tracking - Disease State Index (DSI) trajectories </td><td>Chu et al., 2025; Jia et al., 2025; Runtti et al., 2014</td><td> Residual Sharing GRU (RGRU-EDCF) - Supervised DSI models </td><td>Accuracy: 76.9–95.2%MAE: 1.27–2.12</td><td>Time-series models improve 3-year cognitive forecasting despite missing data.</td></tr><tr><td>Brain Aging Biomarkers - Biological brain age gap (BrainAge delta) - Neurobiological topological structures </td><td>Battista et al., 2020; Garcia Condado et al., 2025; Li et al., 2025</td><td> Brain Vision Graph Neural Network (BVGNN) </td><td>AUC: 0.885–0.945MAE: 2.39 years</td><td>Higher BrainAge predicts faster decline; each extra year increases risk by ~29%.</td></tr></table>	APPROACH & CORE FEATURES	KEY STUDIES	AI / ML MODELS	PERFORMANCE METRICS	MAIN PROGNOSTIC FINDING	Traditional & Fine-Grained Scores - Delayed memory recall (RAVLT, Logical Memory) - Functional scales (FAQ, MMSE)	D'Amore et al., 2025; Formica et al., 2023; Russo et al., 2024 ;Zarei et al., 2025	Random Forest - Support Vector Machine (SVM) - Gradient Boosting	Accuracy: 83.8–91.0% AUC: 0.91	Delayed recall and functional measures are the strongest predictors of conversion.	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Alzheimers Res Ther. 2024;16:26. - Runtti H, et al. J Alzheimers Dis. 2014;39(1):49–61. - Mallo SC, et al. Int Psychogeriatr. 2020;32(3):381–392. - Li Z, et al. JMIR Aging. 2025;8:e73004. - Jia N, et al. Biomed Signal Process Control. 2025;102:107253. - Gómez-Ramírez J, et al. Sci Rep. 2020;10(1):20630. - Garcia Condado J, et al. NeuroImage. 2025;321:121548. - Dauphinot V, et al. Alzheimers Res Ther. 2024;16(1):166. - Chu C, et al. Age Ageing. 2025;54(7):afaf198. - Battista P, et al. Neurosci Biobehav Rev. 2020;114:211–228.
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CONCLUSIONS		CONTACT																															
High predictive accuracy: ML models based on low-cost cognitive and behavioral measures predict MCI-to-AD conversion with up to 91–95% accuracy. Process-based metrics outperform global scores: Speech features, learning slopes, and reaction-time variability capture subtle cognitive decline more effectively than traditional assessments. Explainable AI enhances clinical applicability: SHAP and LIME provide transparent, patient-specific explanations that support clinical decision-making. Multimodal approaches improve prediction: Combining cognitive, behavioral, and BrainAge-related markers strengthens early detection and risk stratification.		Palak Mahant Dass NeuroADaS Lab Email: pmahant@uoc.edu LinkedIn: www.linkedin.com/in/palak-mahant-408574120 																															