Machine learning based multi-modal prediction of future decline toward Alzheimer's disease: An empirical study

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CORNELL TECH

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MOTIVATION

- Alzheimer's disease (AD) is a neurodegenerative condition that progresses over decades.
- Early detection of individuals at high risk of future progression toward AD is likely to be of critical for successful clinical treatments.
- We present a large-scale study to characterize how predictable an individual subjects' future AD trajectory is, several years in advance, based on rich multi-modal data, and using modern deep learning methods.
- We quantify the contribution of different data types in prediction, which yields novel insights into the utility of different biomarkers.

MATERIALS AND METHODS

DATASET AND PREPROCESSING

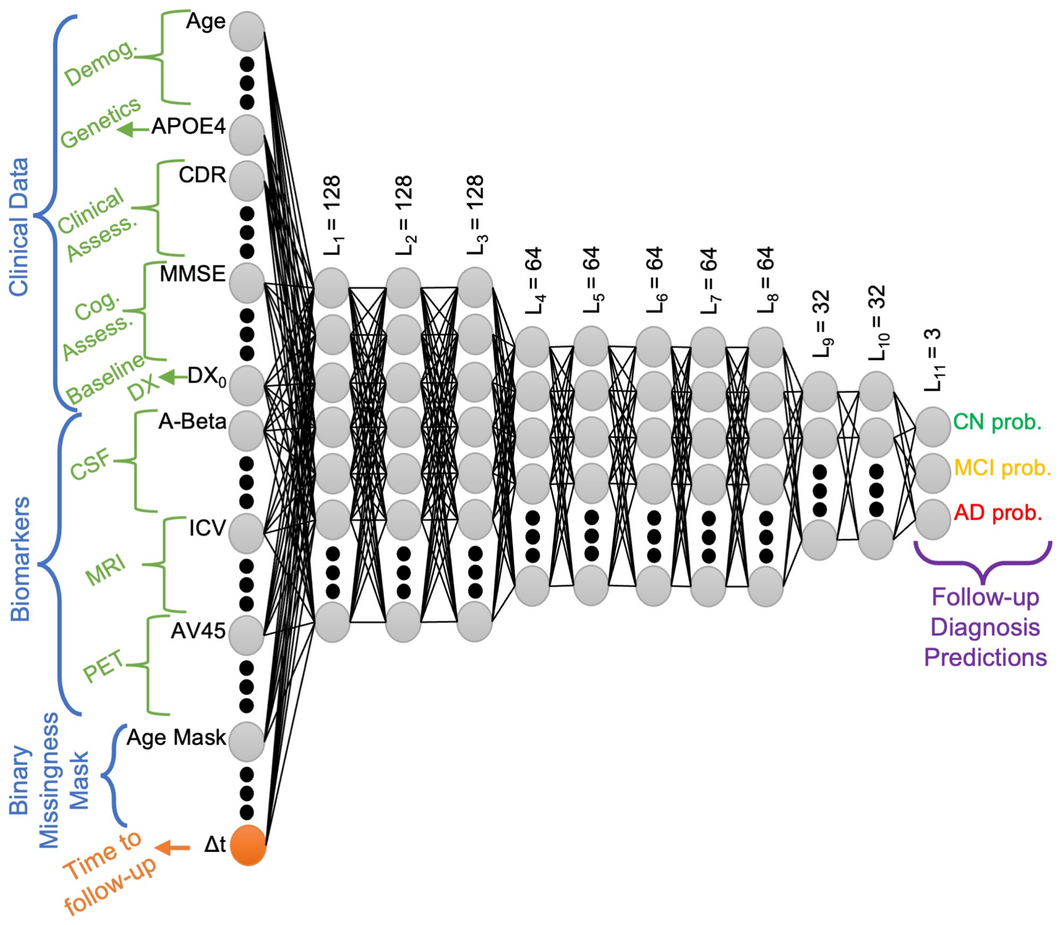
Table 1. Summary statistics of the participants at baseline in ADNI[1] database.

	CN baseline (n = 615)	**MCI baseline** (n = 789)
Female/Male	335 / 280	324 / 465
Age *(yr)*	73.19 ± 6.18	73.46 ± 7.39
Education *(yr)*	16.51 ± 2.57	15.93 ± 2.81
APOE4 *(0/1/2)*	430 / 169 / 14	371 / 313 / 98
Clinical Dementia Rating	0.04 ± 0.13	1.55 ± 0.89
Mini Mental State Examination	29.11 ± 1.11	27.52 ± 1.82

Table 2. The number of available subjects in each diagnostic group for annual follow-up visits.

Time horizon *(yr)*	**CN baseline**		**MCI baseline**	
	CN	MCI	MCI	AD
1	427	14	674	110
2	527	32	431	218
3	181	41	317	261
4	230	49	202	286
5	123	54	127	292

PROPOSED MODEL

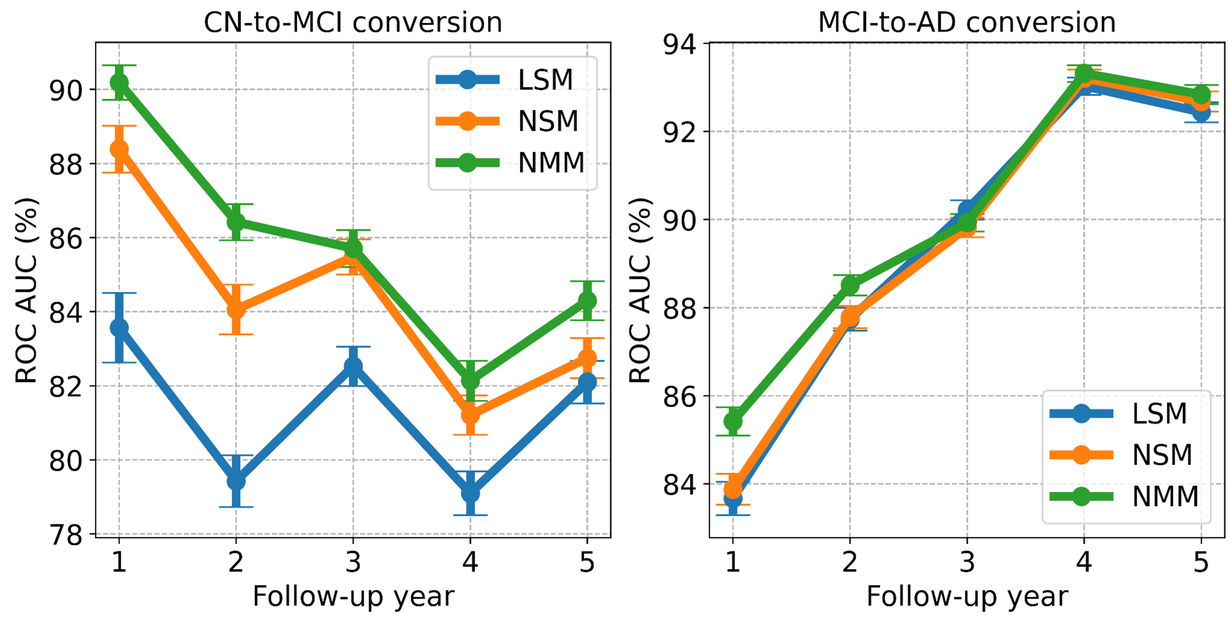


Feed-forward, fully-connected neural network architecture.

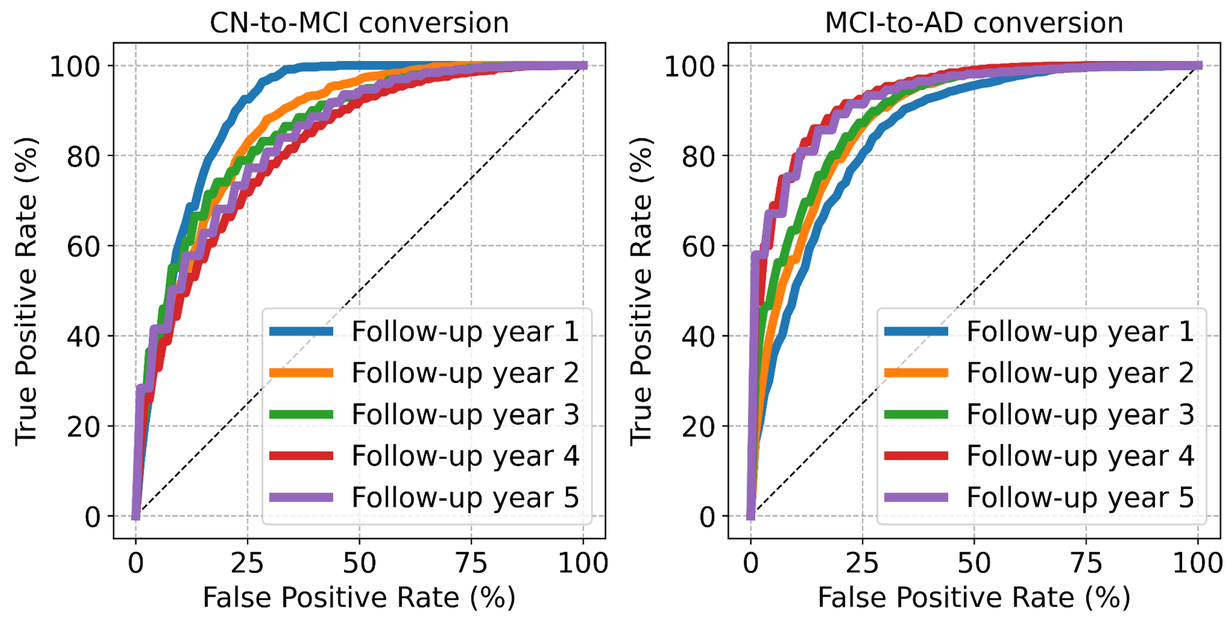
- Based on this architecture, three separate models are built: Linear Single-year Model (LSM), Nonlinear Single-year Model (NSM), and Nonlinear Multi-year Model (NMM).
- LSM neither has nonlinear ReLU activation between layers and nor the proposed time feature (Δt) neuron in input layer.
- NSM has ReLU activation between layers but does not have the Δt neuron in input layer.
- NMM has ReLU activation between layers and has the Δt neuron in input layer.
- A custom sample weighting scheme is used during training to overcome the imbalance in data.

RESULTS

IMPACT OF MULTI-YEAR TRAINING

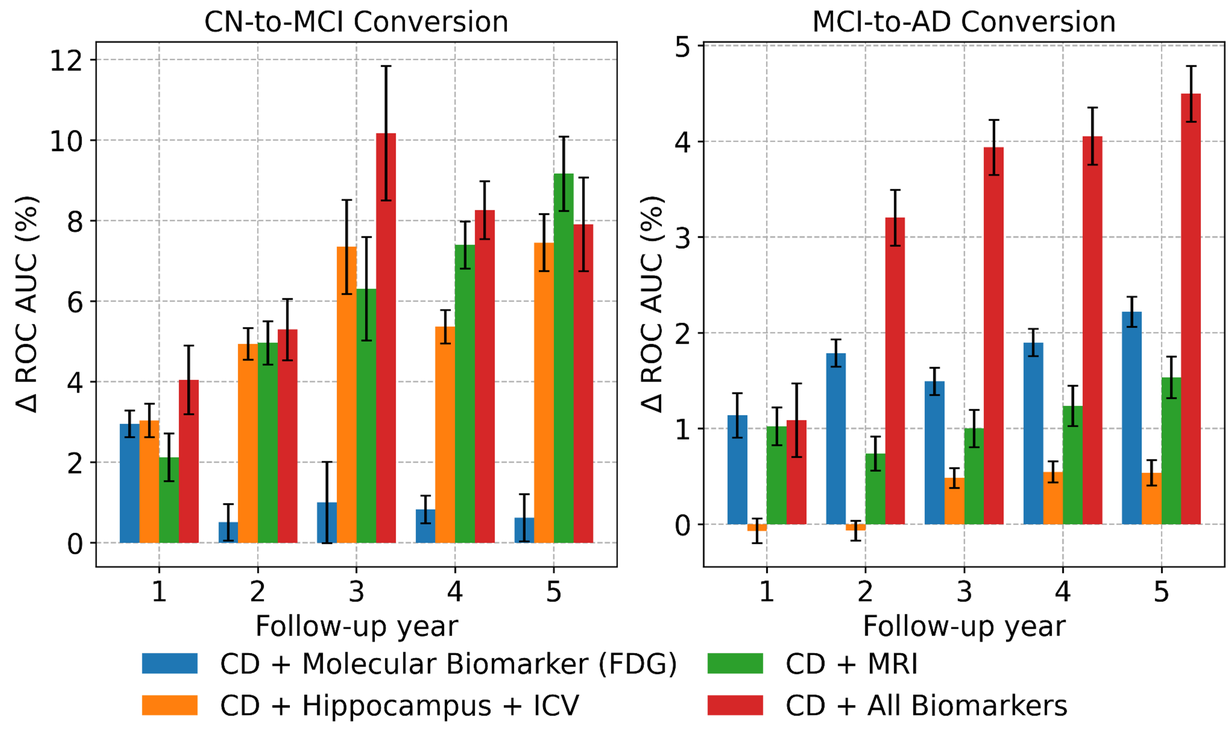


Prediction performance of different models. Average ROC AUC values and corresponding standard error bars.



ROC curves of NMM for each follow-up year. Average ROC curves obtained over 200 random initializations are displayed.

CONTRIBUTION OF DIFFERENT BIOMARKERS



Δ ROC AUC values obtained with various biomarker combinations versus follow-up years. CD: Clinical Data; FDG: Fluorine-18-Fluorodeoxyglucose PET. ICV: Intracranial Volume.

CONCLUSION

- Our proposed model (NMM) performs better for both CN and MCI individuals than the single-year models.
- Molecular biomarkers are only helpful in MCI, but not in CN.
- Structural magnetic resonance imaging (MRI) biomarkers (hippocampus volume, specifically) offer a significant performance boost for CN-to-MCI conversion but not MCI-to-AD conversion.
- In a future study, we will extend NMM to exploit structural data, such as whole-brain images, and longitudinal input features.

REFERENCE

[1] Mueller SG, Weiner MW, Thal LJ, Petersen RC, Jack CR, Jagust W, et al. Ways toward an early diagnosis in Alzheimer's disease: The Alzheimer's Disease Neuroimaging Initiative (ADNI). Alzheimer's & Dementia. 2005;1:55–66. doi:10.1016/j.jalz.2005.06.003