

DEEP LEARNING OF STRUCTURAL BRAIN MRI FOR DISEASE CLASSIFICATION & PROGNOSTICATION OF ALZHEIMER DISEASE & MILD COGNITIVE IMPAIRMENT



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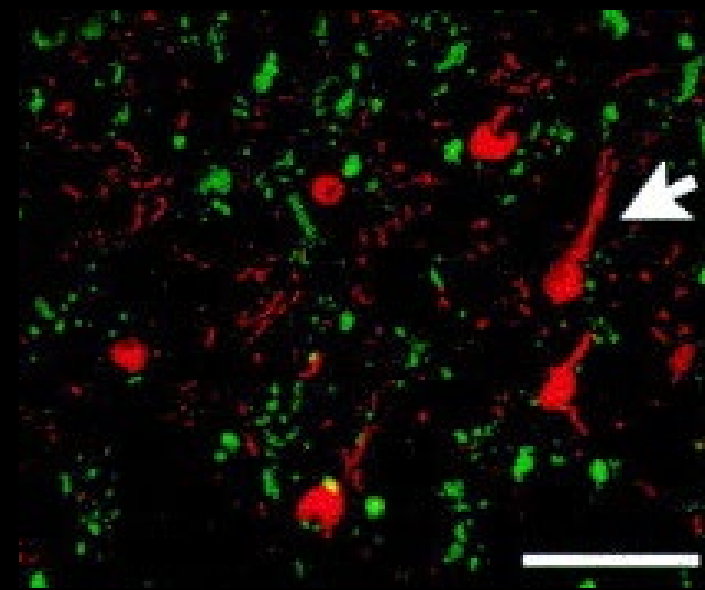


OBJECTIVES

- Briefly review **machine learning brain MRI** applications in AD/MCI
- Describe OSU AI lab experience in predicting **MCI prognosis**

ALZHEIMER DISEASE & MILD COGNITIVE IMPAIRMENT

- Alzheimer disease
 - Majority of dementia cases
 - Multifactorial causes
 - Clinical criteria for possible/probable AD
 - Neuropathology standard
- Mild cognitive impairment (MCI)
 - Up to 25% among elderly subjects
 - Heterogeneous intermediate stage
 - Prodromal stage with increased risk for dementia
 - Mixed prognosis (~10% to 15% progress to dementia each year)



Adapted from Sun et al., *J Neurosci Methods* 111: 17-27 (2001)



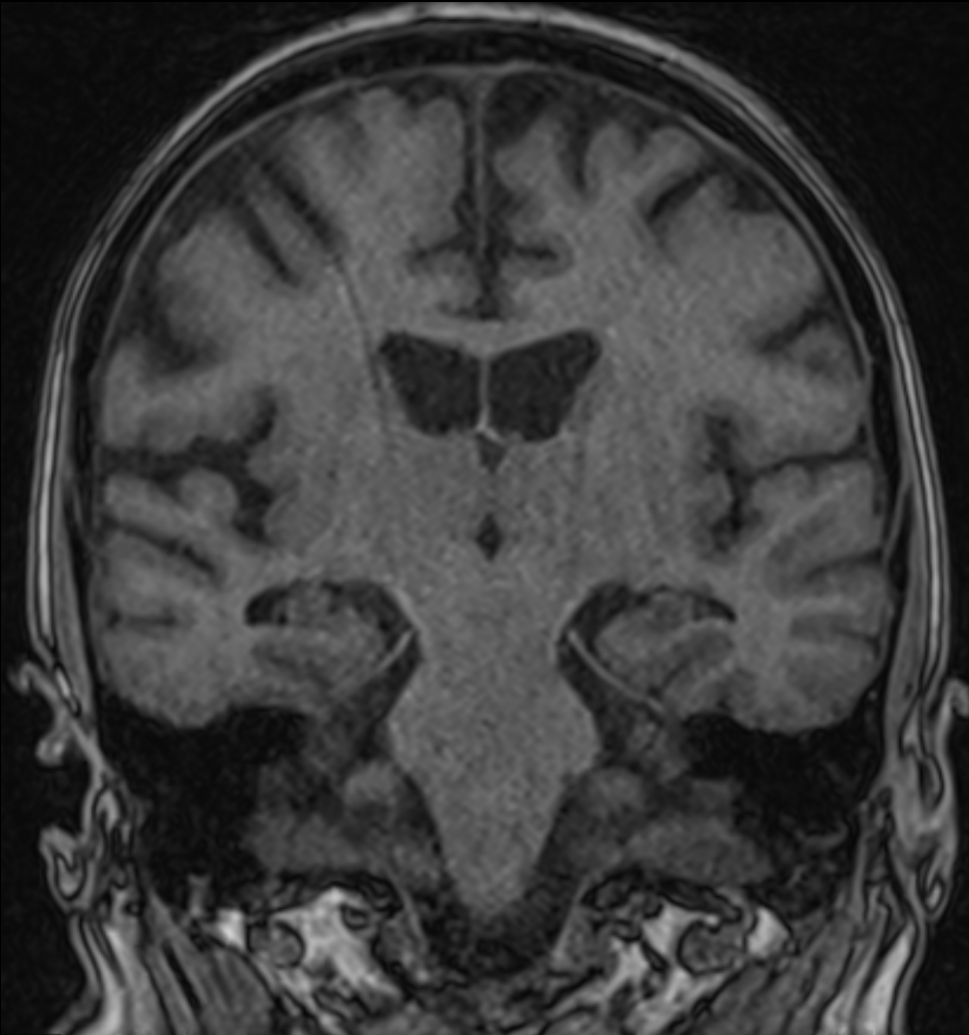
ROLE OF STRUCTURAL BRAIN MRI

- Brain MRI in workup of dementia
 - Qualitative assessment
 - Atrophy
 - Vascular insults
 - Quantitative morphometric analysis
 - Automated segmentation
 - Comparison to normative databases

Alzheimer Disease

Sex: Female

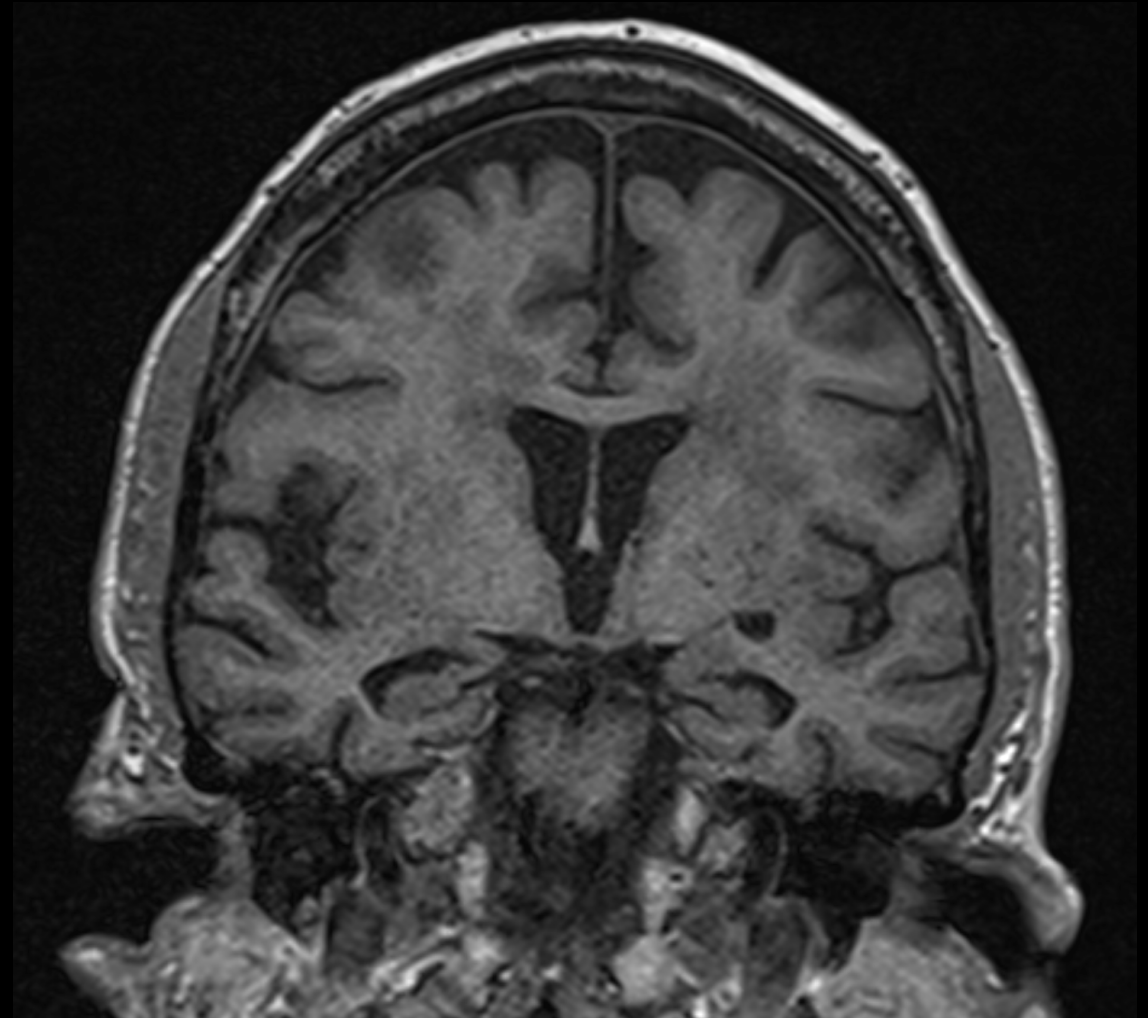
Age range: 50-54 years



Mild Cognitive Impairment (likely vascular etiology)

Sex: Female

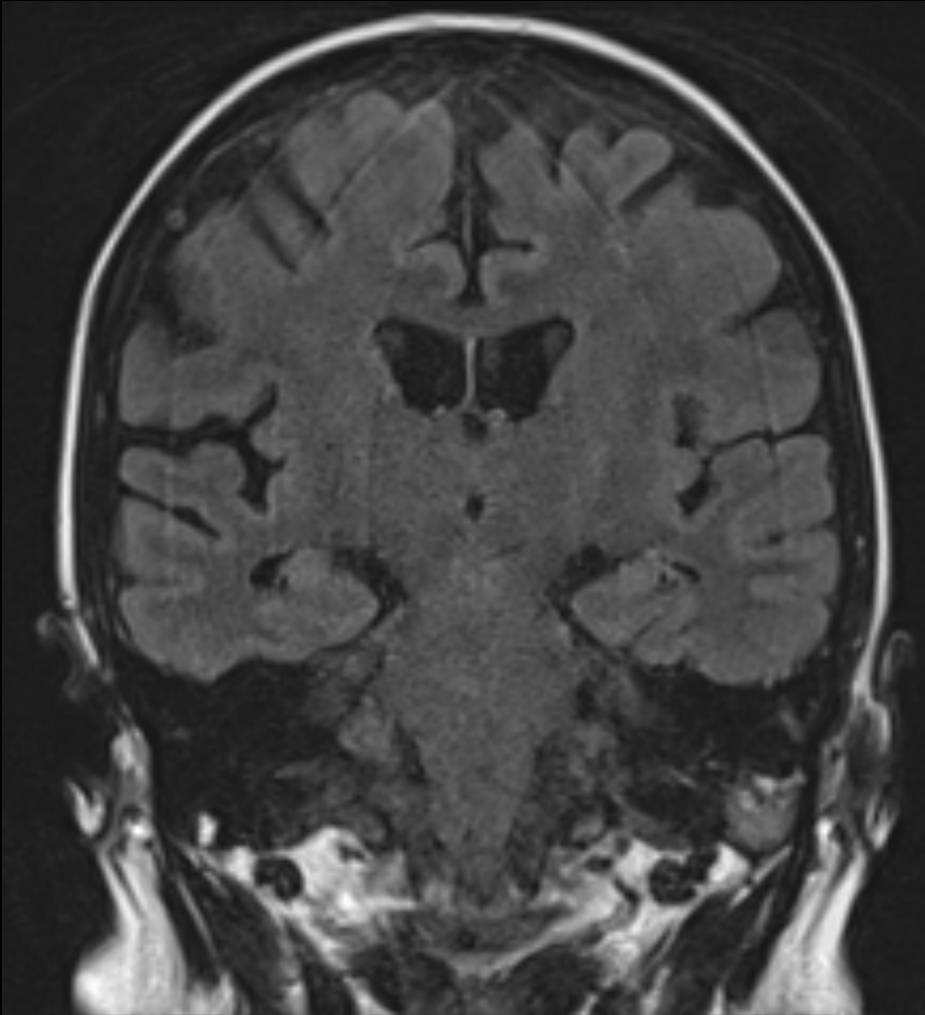
Age range: 80-84 years



Alzheimer Disease

Sex: Female

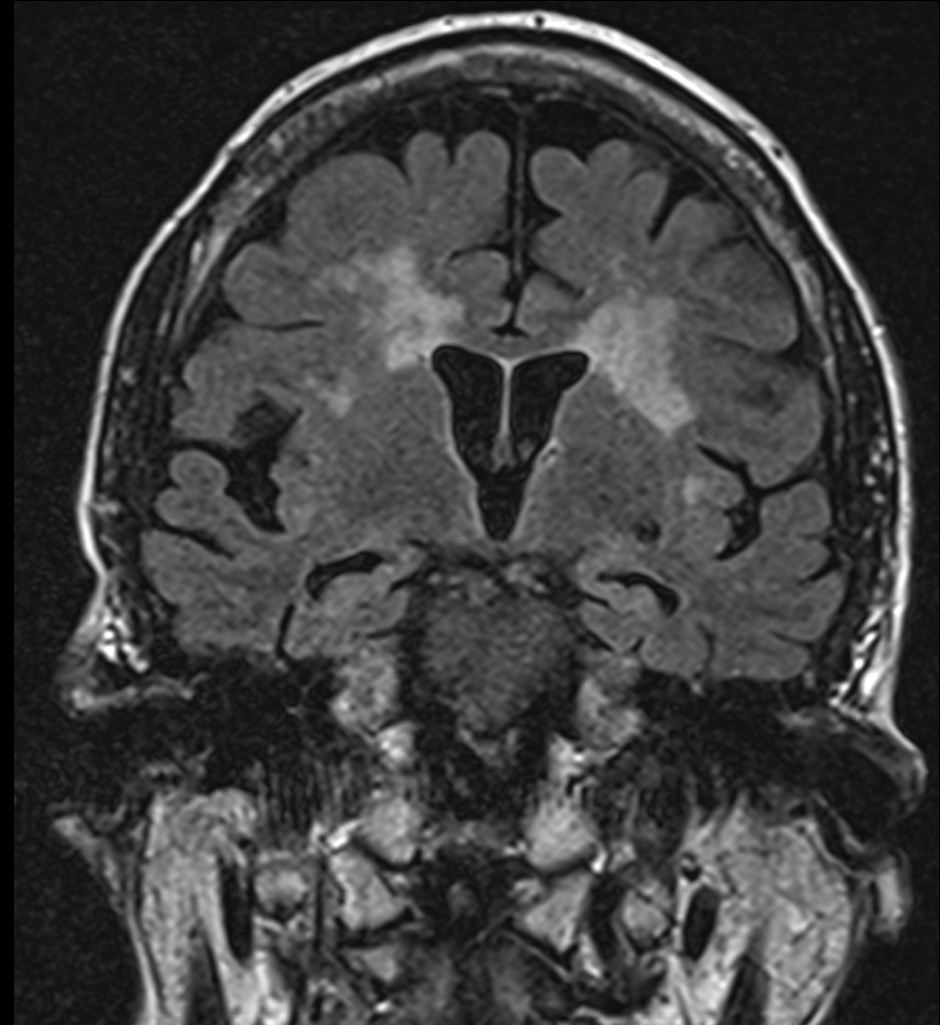
Age range: 50-54 years



Mild Cognitive Impairment (likely vascular etiology)

Sex: Female

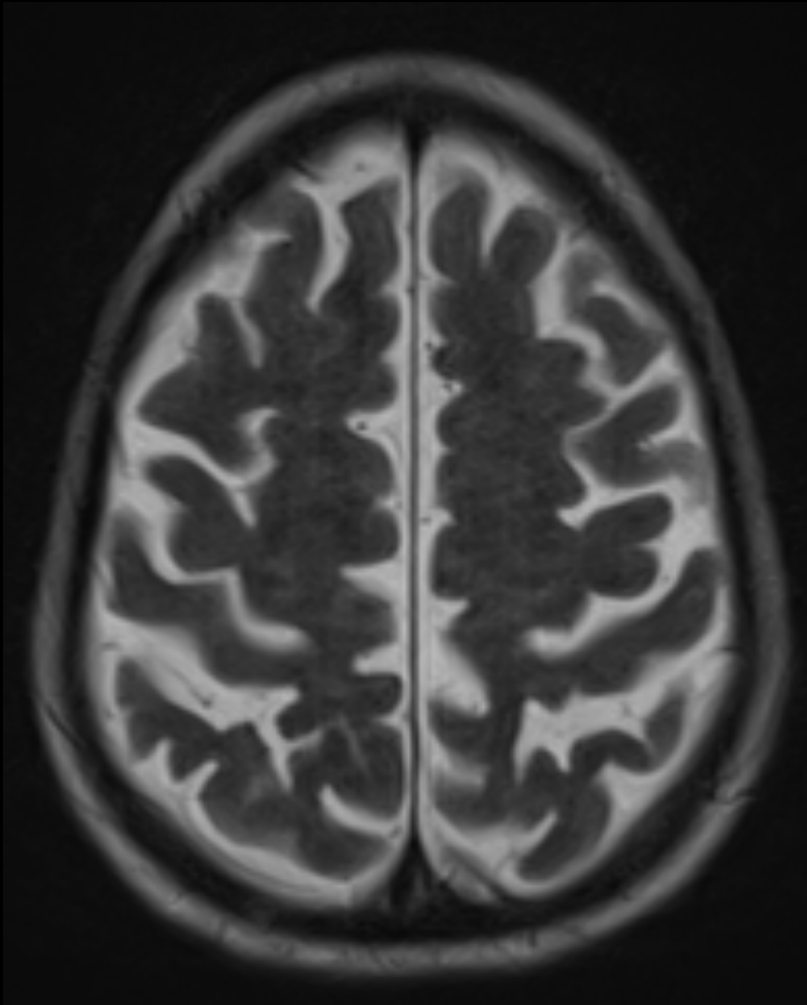
Age range: 80-84 years



Alzheimer Disease

Sex: Female

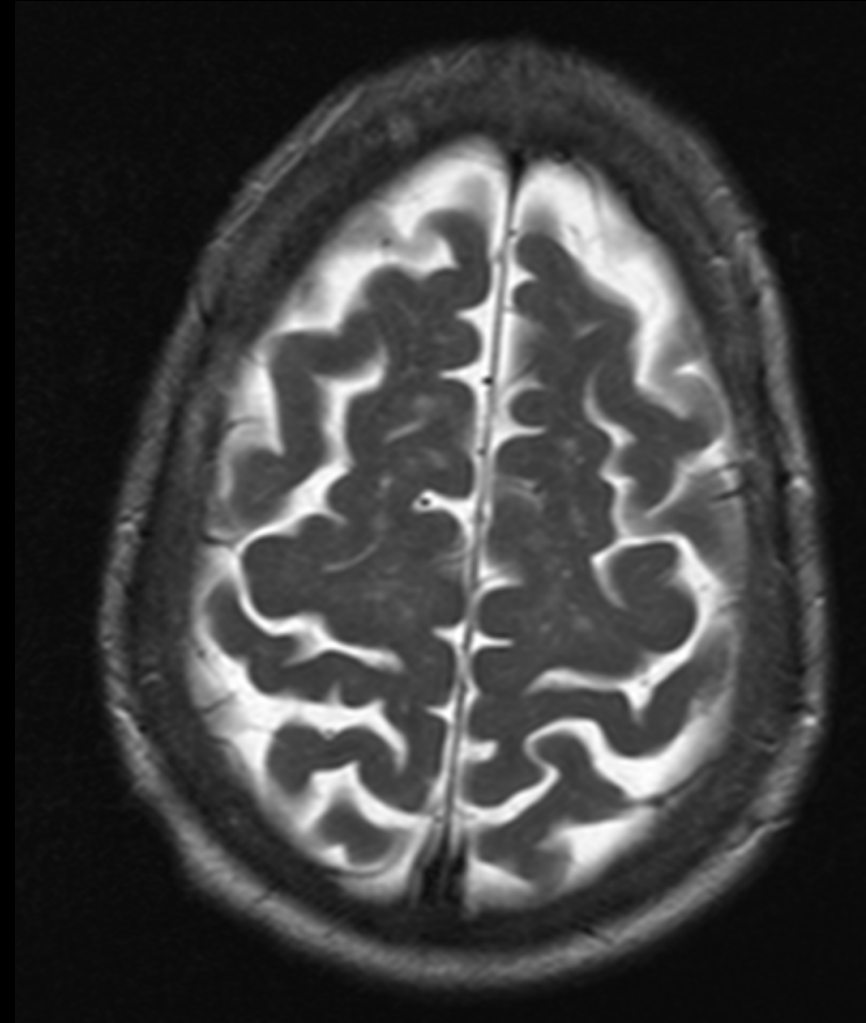
Age range: 50-54 years



Mild Cognitive Impairment (likely vascular etiology)

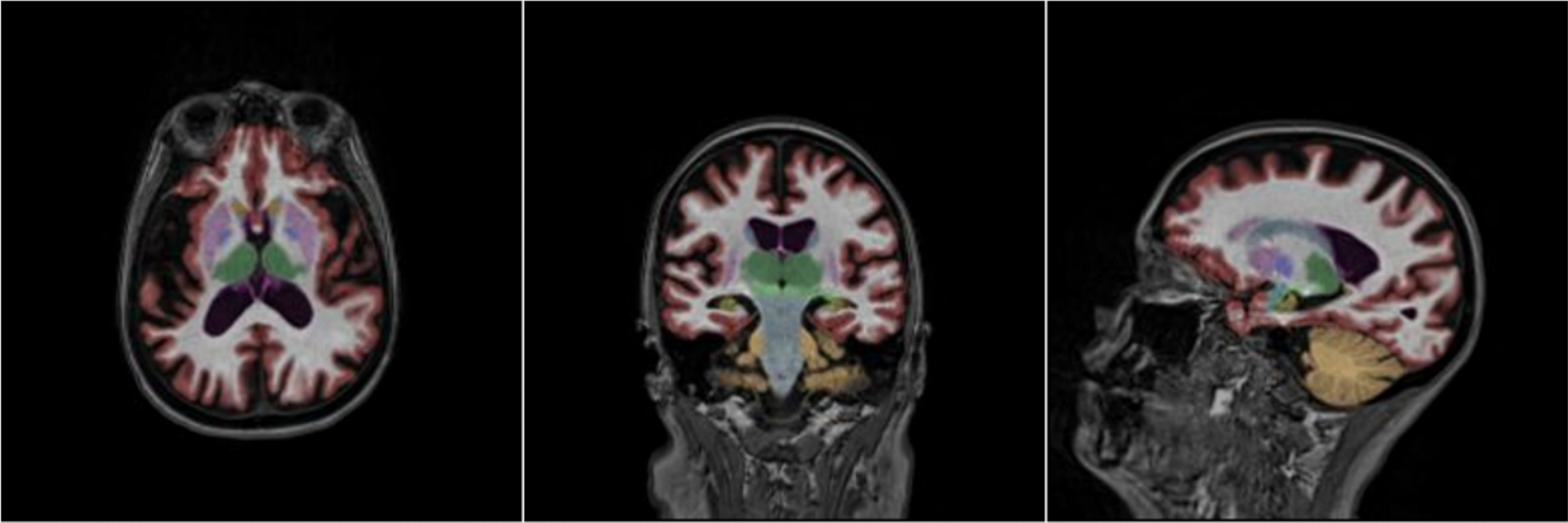
Sex: Female

Age range: 80-84 years

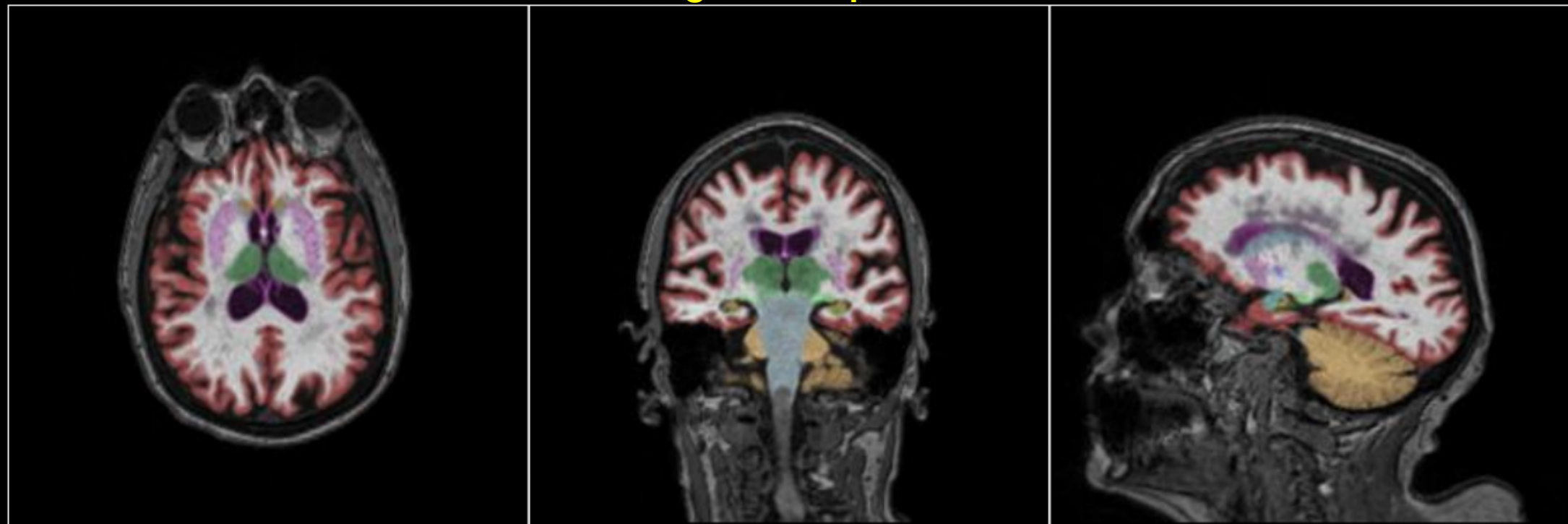


MORPHOMETRY RESULTS

Alzheimer Disease

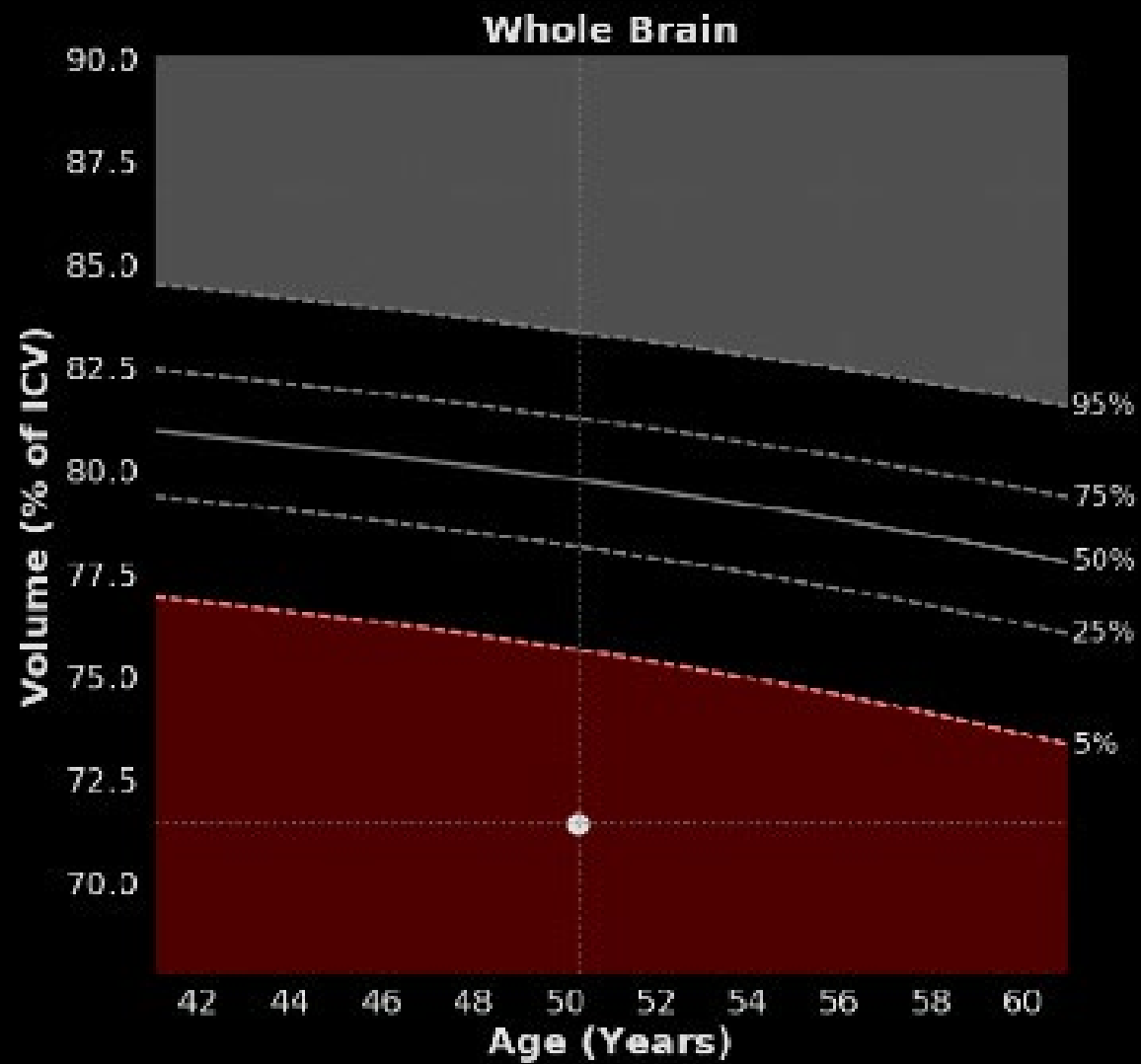


Brain Structure	Volume (cm³)	% of ICV (5%-95% Reference Percentile)	Reference Percentile
Ventricles	46.50	3.65 (0.78 - 3.01)	99
Cerebellum	92.82	7.28 (7.78 - 10.01)	1
Whole Brain	911.29	71.46 (75.67 - 83.37)	1
Hippocampi	5.04	0.39 (0.46 - 0.60)	1
Frontal Lobes	135.38	10.62 (11.82 - 14.36)	1
Temporal Lobes	104.40	8.19 (8.45 - 10.25)	2
Brainstem	15.36	1.20 (1.36 - 1.74)	1
Parietal Lobes	89.44	7.01 (6.94 - 8.78)	6
Cerebral WM Hypointensities*	0.35	0.03 (0.00 - 0.12)	67

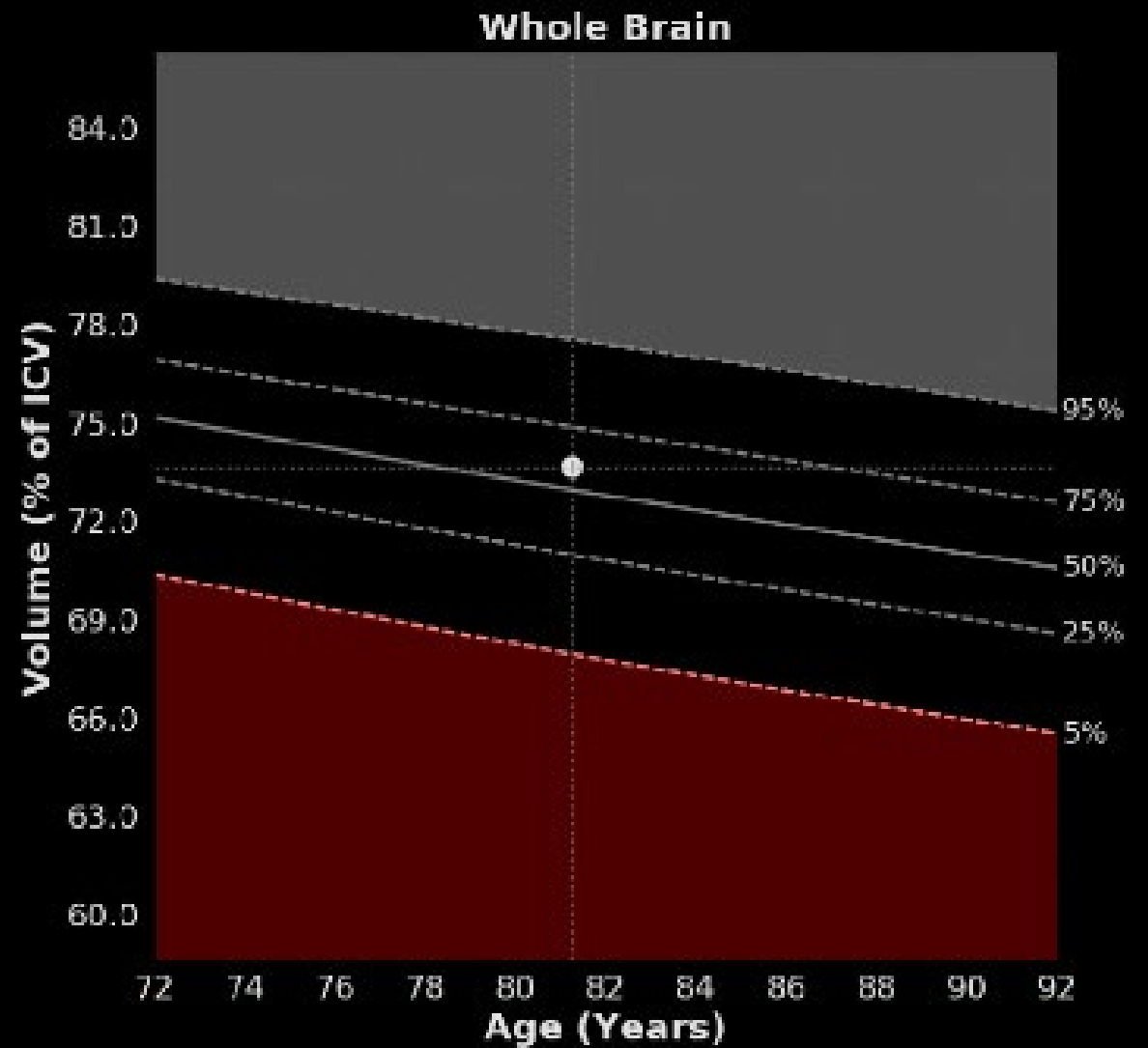
MORPHOMETRY RESULTS**Mild Cognitive Impairment**

Brain Structure	Volume (cm ³)	% of ICV (5%-95% Reference Percentile)	Reference Percentile
Ventricles	40.08	3.09 (2.21 - 5.95)	35
Cerebellum	117.79	9.09 (7.24 - 9.54)	83
Whole Brain	955.08	73.66 (67.96 - 77.57)	60
Hippocampi	4.35	0.34 (0.35 - 0.50)	3
Frontal Lobes	127.24	9.81 (9.70 - 12.17)	7
Temporal Lobes	94.05	7.25 (6.97 - 8.97)	11
Brainstem	20.40	1.57 (1.34 - 1.75)	64
Parietal Lobes	87.17	6.72 (5.89 - 7.63)	43
Cerebral WM Hypointensities*	8.61	0.66 (0.02 - 0.49)	97

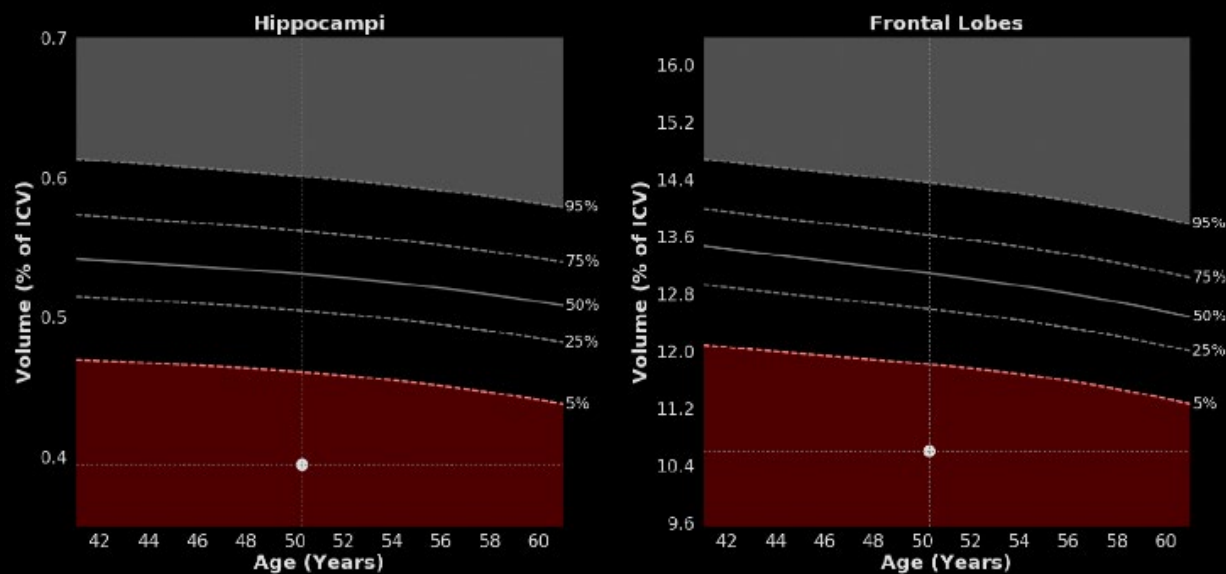
Alzheimer Disease



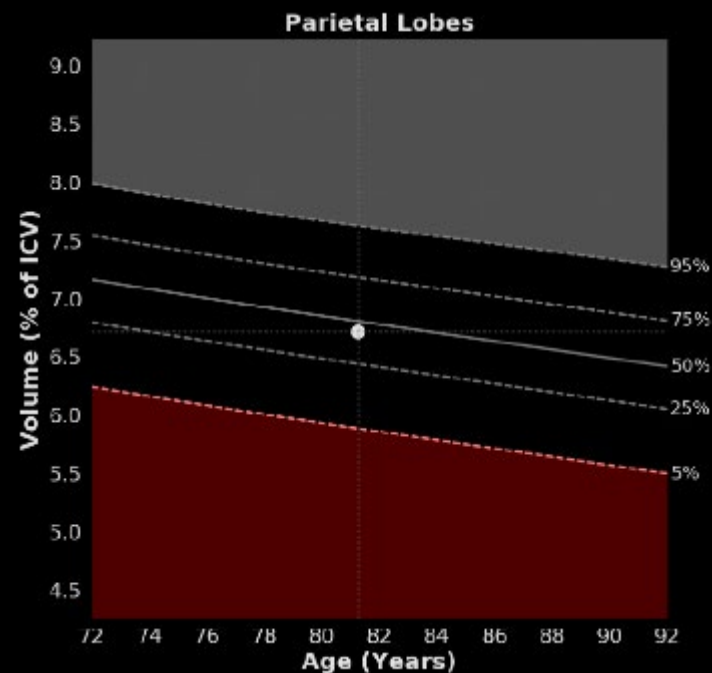
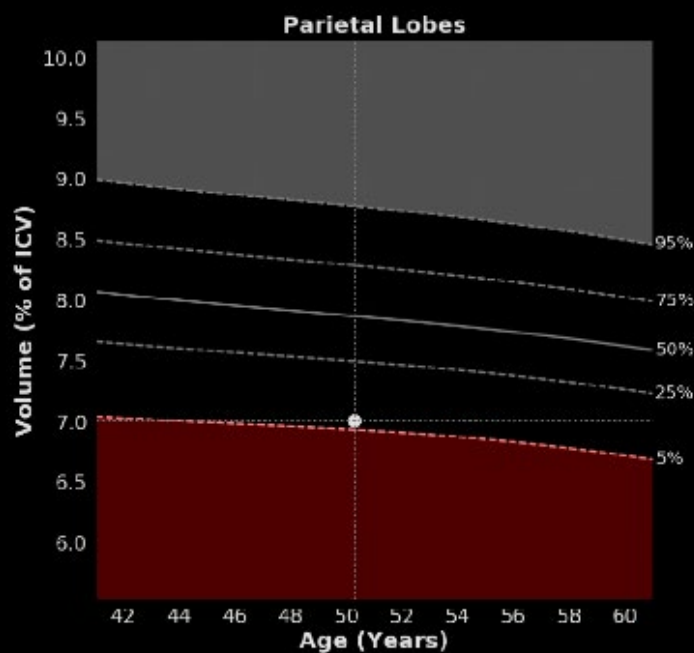
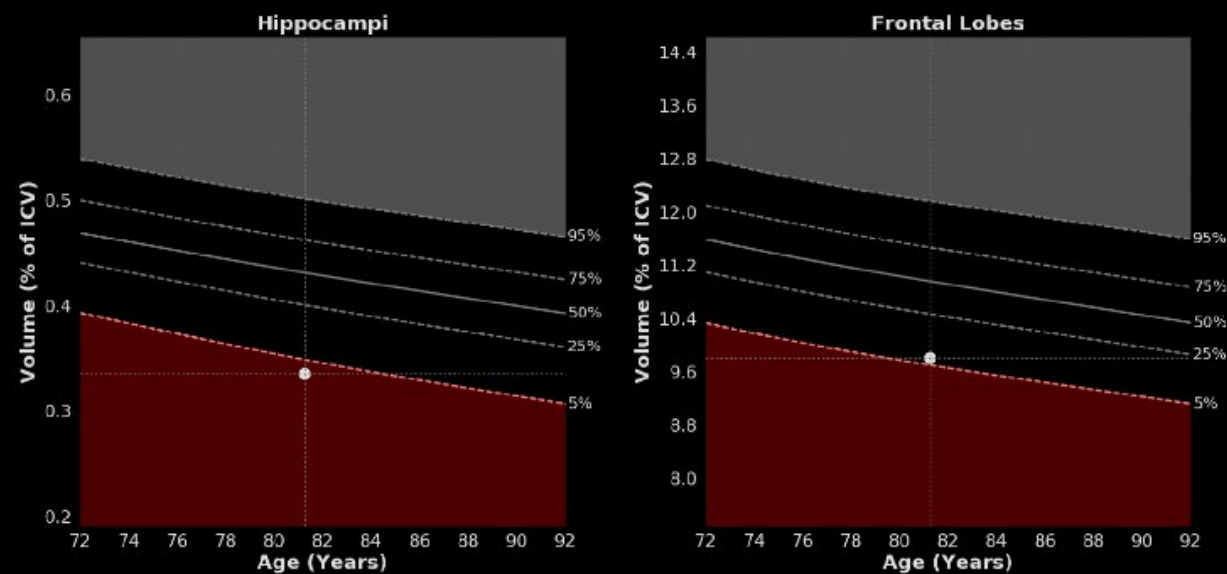
Mild Cognitive Impairment



Alzheimer Disease

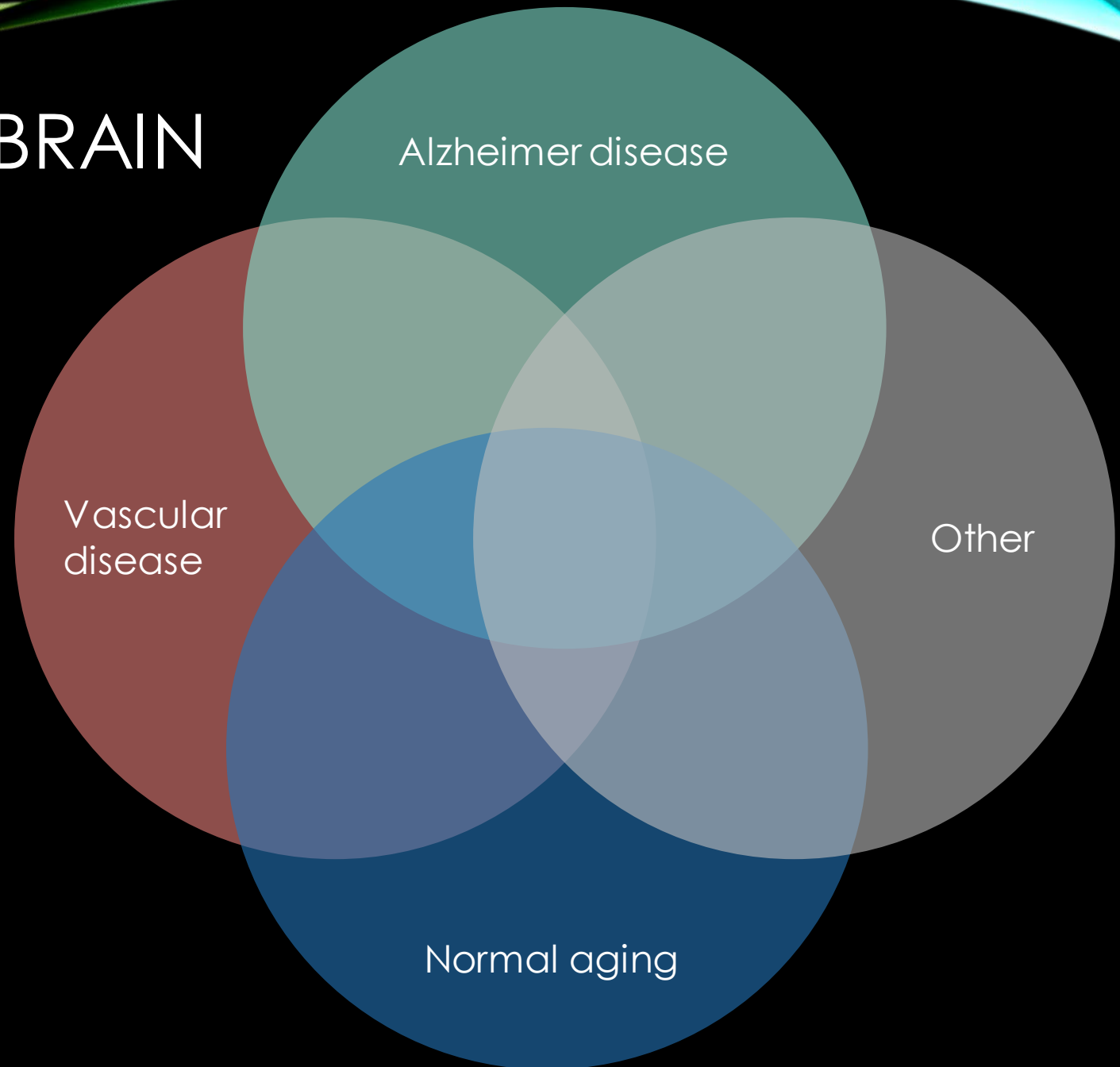


Mild Cognitive Impairment



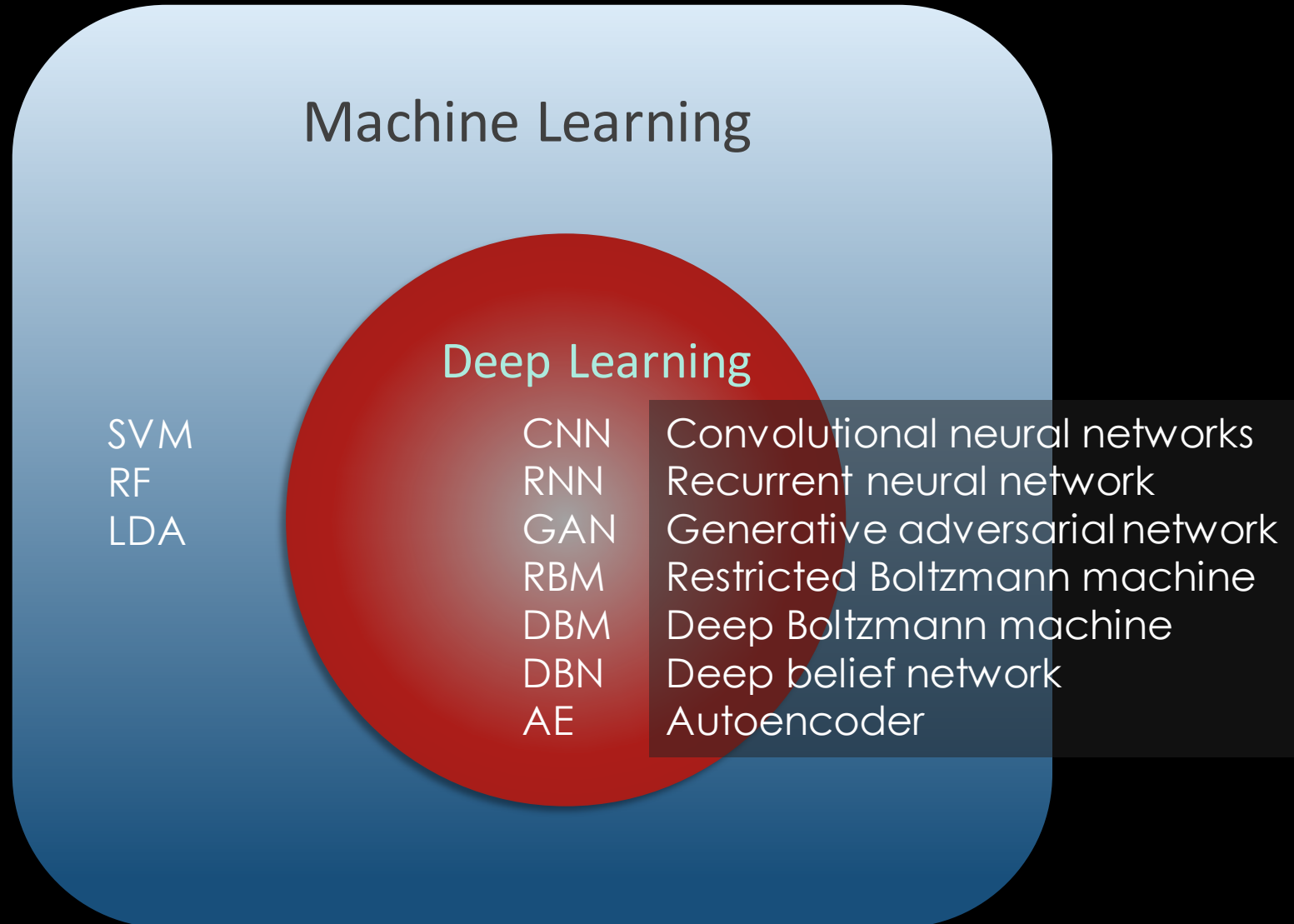
CHALLENGES TO INTERPRETATION OF BRAIN IMAGING

- Brain imaging in dementia may show findings consistent with multiple coexisting processes
- Role for AI in identifying relevant patterns?



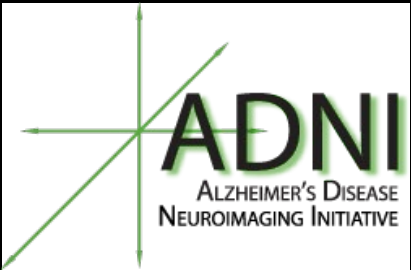
ARTIFICIAL INTELLIGENCE

- Machine Learning
 - Predictions or decisions without explicit programming
 - “learning through experience”
 - Finding generalizable predictive patterns
- Deep Learning
 - Hierarchical design
 - Each layer progressively extracts higher-level features from an input



PRIOR DEEP LEARNING STUDIES ON AD

All of these
studies use ADNI



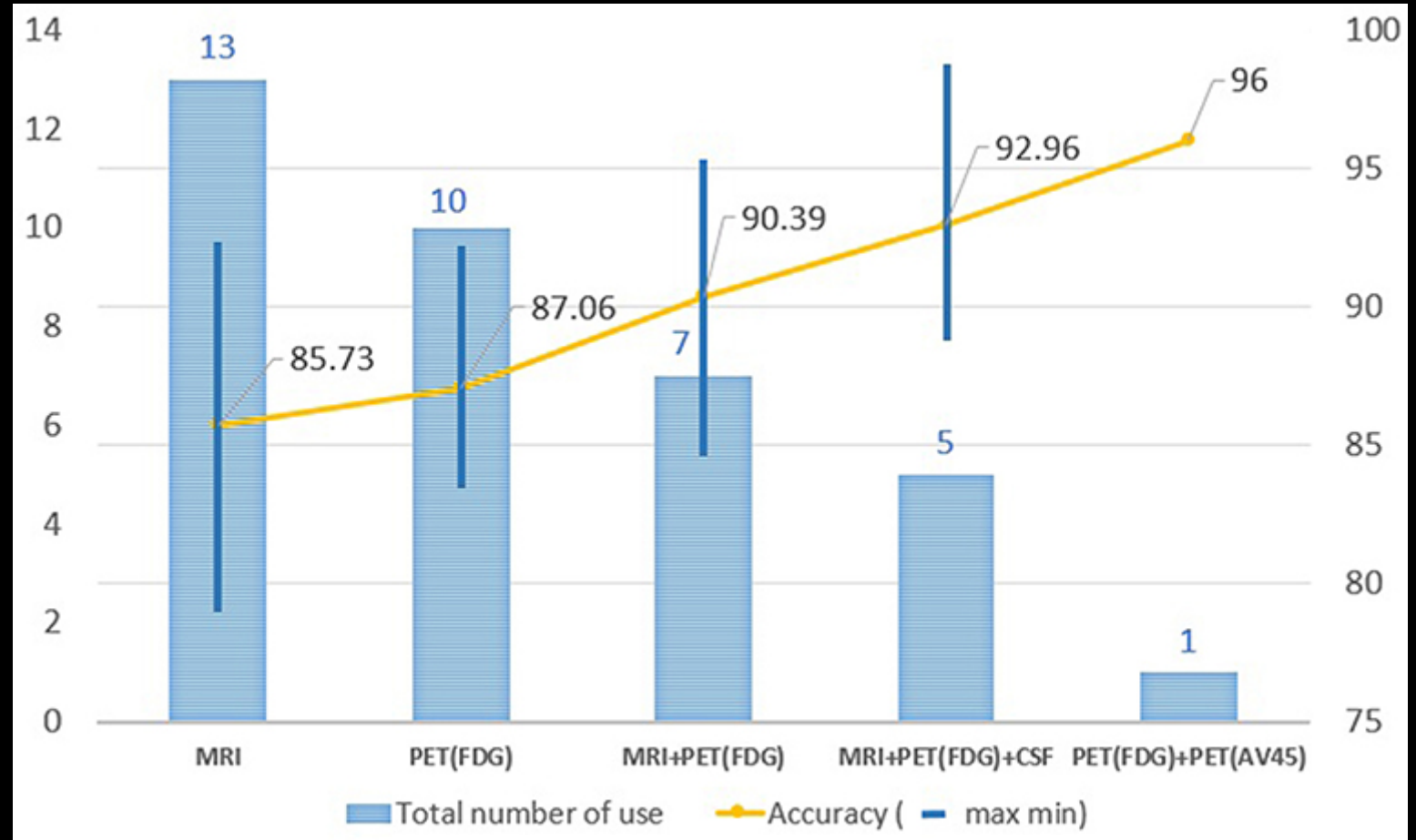
References	Modality	Data processing/training	Classifier	AD:NC acc.	SEN	SPE	cMCI:ncMCI acc.	SEN	SPE	AD	cMCI	ncMCI	NC	Total
Suk and Shen (2013)	MRI, PET, CSF	SAE	SVM	95.9			75.8			51	43	56	52	202
Liu et al. (2014)	MRI, PET	SAE + NN	Softmax	87.76	88.57	87.22	76.92 (MCI:NC)	74.29	78.13	65	67	102	77	311
Suk et al. (2014)	MRI, PET	DBM	SVM	95.35	94.65	95.22	75.92 86.75 (MCI:NC)	48.04 95.37	95.23 65.87	93	76	128	101	398
Li et al. (2014)	MRI, PET	3D CNN	Logistic regression	92.87			76.21 (MCI:NC)			198	167	236	229	830
Li et al. (2015)	MRI, PET, CSF	RBM + drop out	SVM	91.4			57.4 76.21 (MCI:NC)			51	43	56	52	202
Suk et al. (2015)	MRI, PET, CSF	SAE + sparse learning	SVM	98.8			83.3 90.7 (MCI:NC)			51	43	56	52	202
Liu et al. (2015)	MRI, PET	SAE with zero-masking	Softmax	91.4	92.32	90.42	82.1 (MCI:NC)	60.0	92.32	77	67	102	85	331
Cheng et al. (2017)	MRI	3D CNN	Softmax	87.15	86.36	85.93				199			229	428
Cheng and Liu (2017)	MRI, PET	3D CNN + 2D CNN	Softmax	89.64	87.10	92.00				93			100	193
Aderghal et al. (2017)	MRI	2D CNN	Softmax	91.41	93.75	89.06	65.62 (MCI:NC)	66.25	65.0	188	399 (MCI)		228	815
Korolev et al. (2017)	MRI	3D CNN	Softmax	80	87 (AUC)		61 (IMCI:NC) 56 (IMCI:NC)	65 (AUC) 58 (AUC)		50	43 (IMCI)	77 (eMCI)	61	111
Vu et al. (2017)	MRI, PET	SAE + 3D CNN	Softmax	91.14						145			172	317
Liu et al. (2018a)	PET	RNN	Softmax	91.2	91.4	91.0	78.9 (MCI:NC)	78.01	80.0	93	146 (MCI)		100	339
Liu et al. (2018b)	MRI	Landmark detection + 3D CNN	Softmax	91.09	88.05	93.50	76.9	42.11	82.43	159	38	239	200	636
Lu et al. (2018)	MRI, PET	DNN + NN	Softmax	84.6	80.2	91.8	82.93	79.69	83.84	238	217	409	360	1224
Choi and Jin (2018)	PET	3D CNN	Softmax	96	93.5	97.8	84.2	81.0	87.0	139	79	92	182	492

SEN = TP/(TP + FN), SPE = TN/(TN + FP). TP, true positive; TN, true negative; FP, false positive; FN, false negative. All data on this table were from ADNI.

Adapted from Jo et al., *Front Aging Neurosci* 11: 220 (2019)

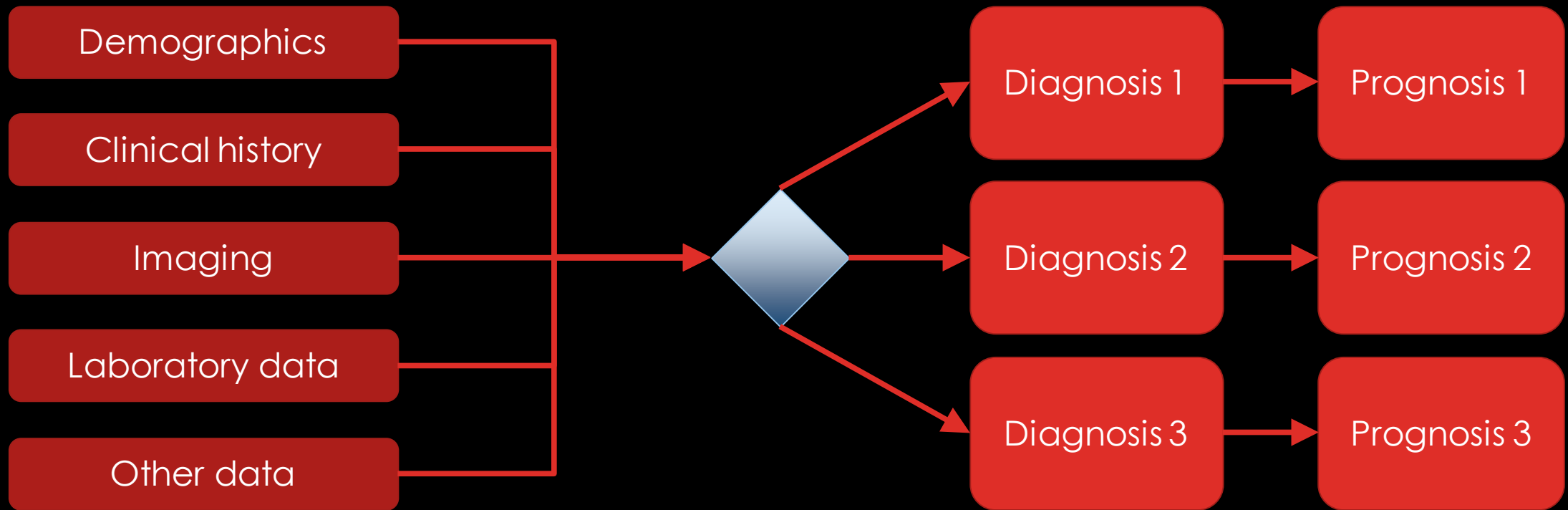
PRIOR DEEP LEARNING STUDIES ON AD

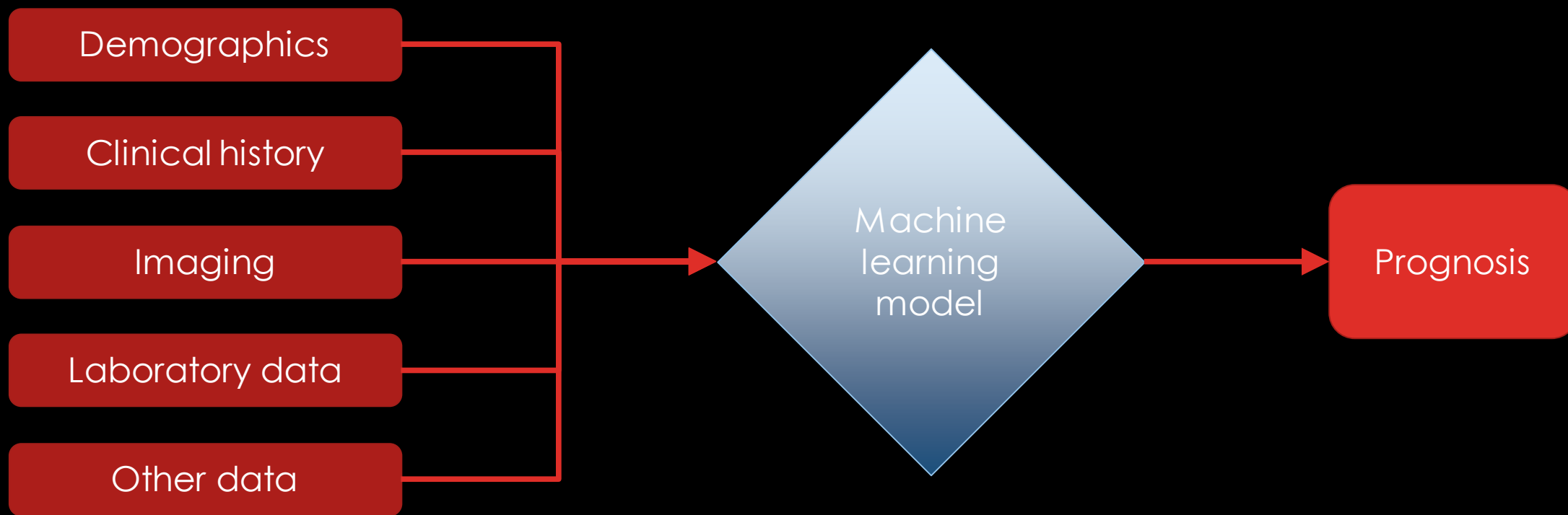
Disease classification (AD vs normal) generally performs better when multiple modalities are used



Adapted from Jo et al., *Front Aging Neurosci* 11:220(2019)

INFORMATION FLOW IN MEDICINE



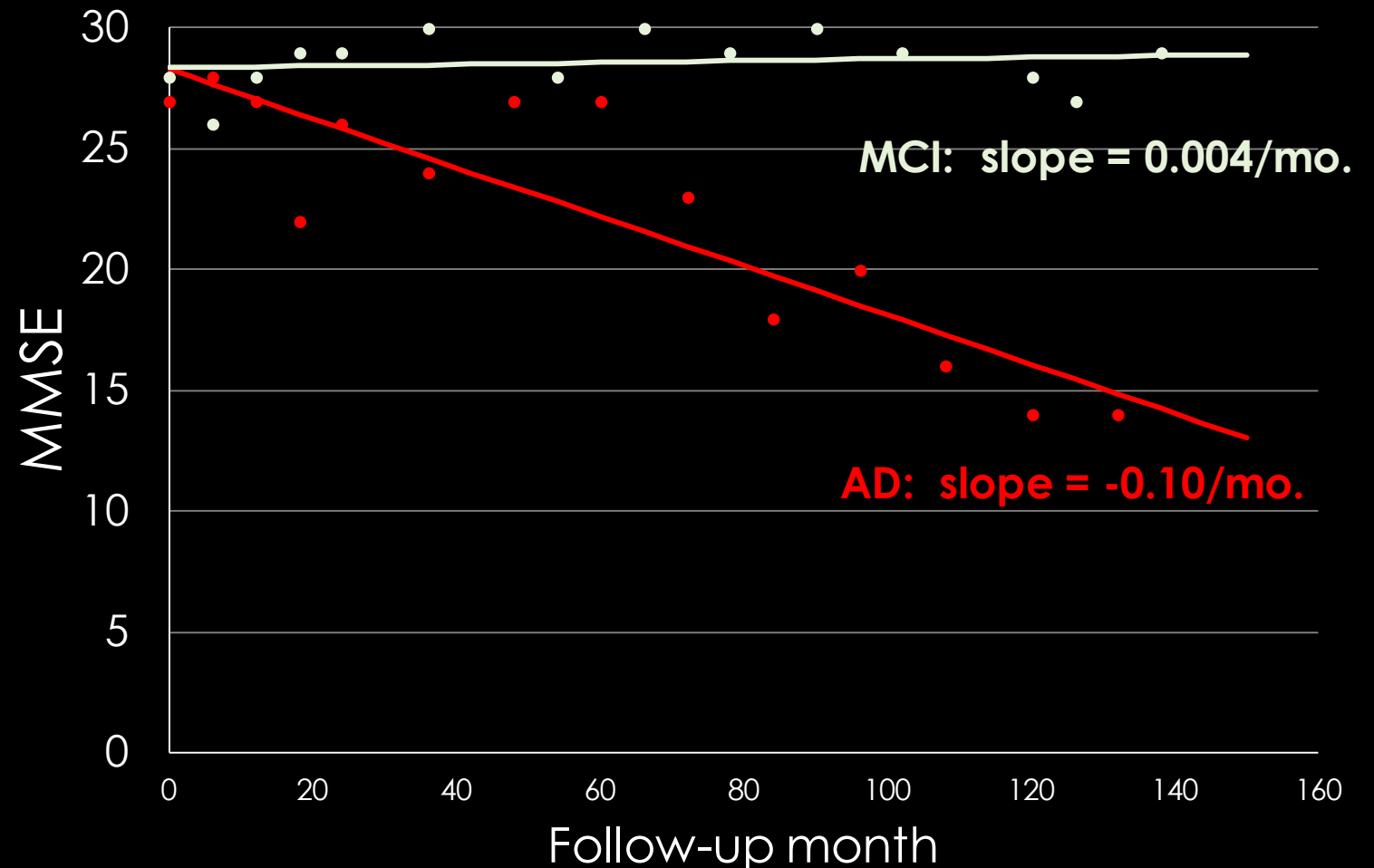




CAN **LONG-TERM COGNITIVE DECLINE**
RATES BE PREDICTED BY
BASELINE MRI IMAGING?

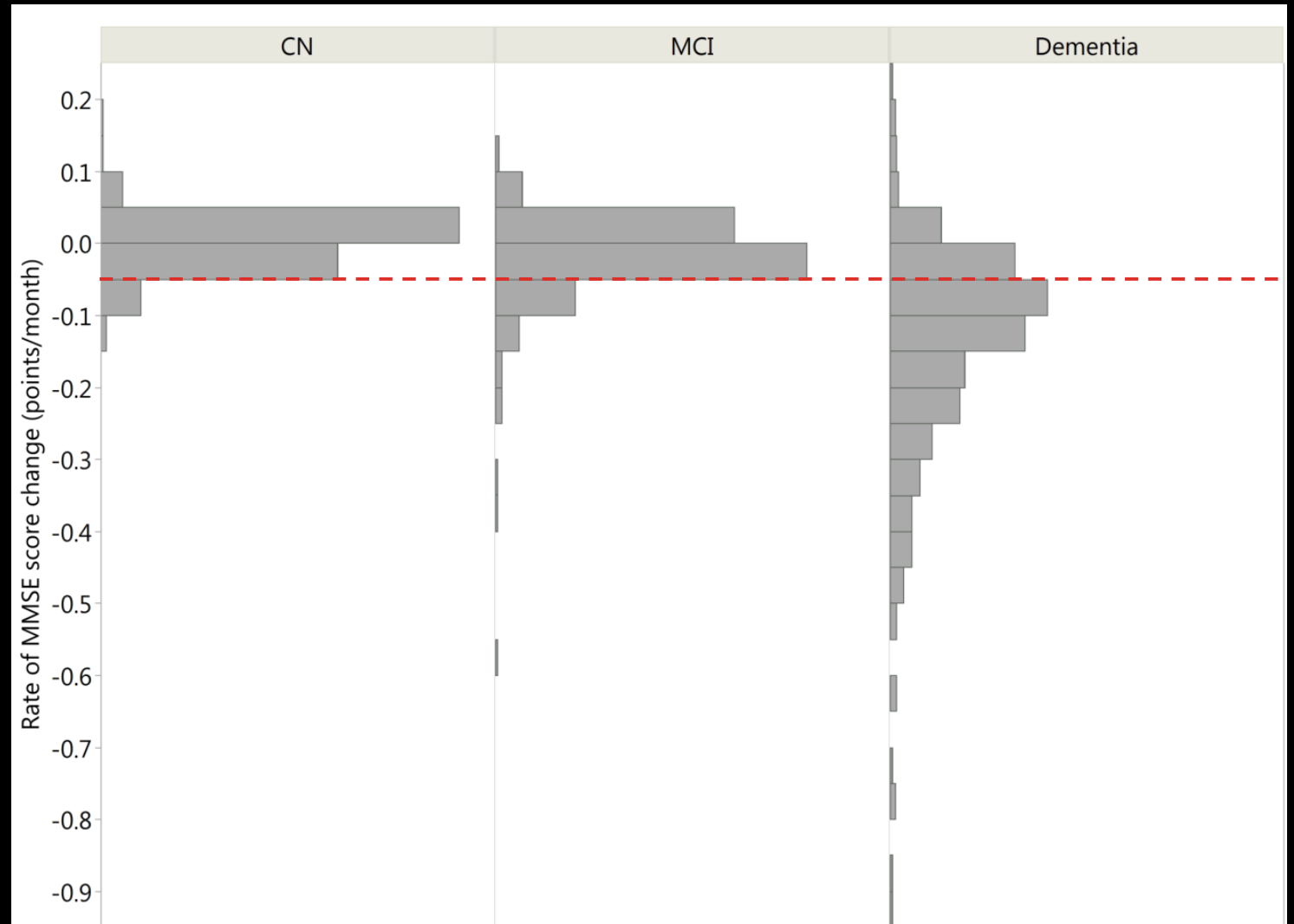
AN OBJECTIVE PROGNOSTIC METRIC TO CAPTURE RATE OF MENTAL DECLINE

- Extracted outcome metric from serial MMSE scores
- Slope of regression line as a metric for rate of decline
- For inclusion:
 - Minimum 4 data points
 - Minimum 2 years follow-up



RATES OF MMSE SCORE CHANGE BY *FINAL DIAGNOSIS*

- Threshold of MMSE rate change below -0.05/mo. (or -0.6/yr) to capture “fast decline”



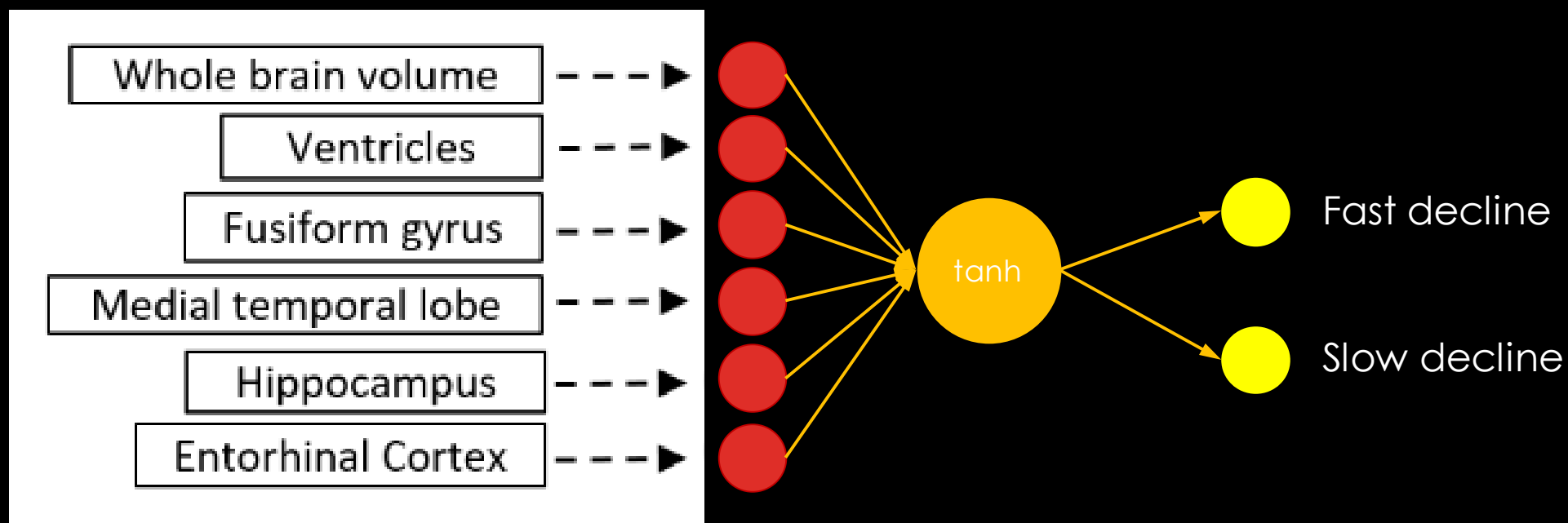
MENTAL STATUS DECLINE RATES AMONG BASELINE MCI PATIENTS

Final Diagnosis	Median Annual Rate of Change in MMSE	Slow or No Decline	Fast Decline
CN	0.031	58 (98%)	1 (2%)
MCI	-0.11	290 (82%)	62 (18%)
Dementia	-1.3	60 (21%)	227 (79%)

MMSE decrease of ≥ 0.6 /yr

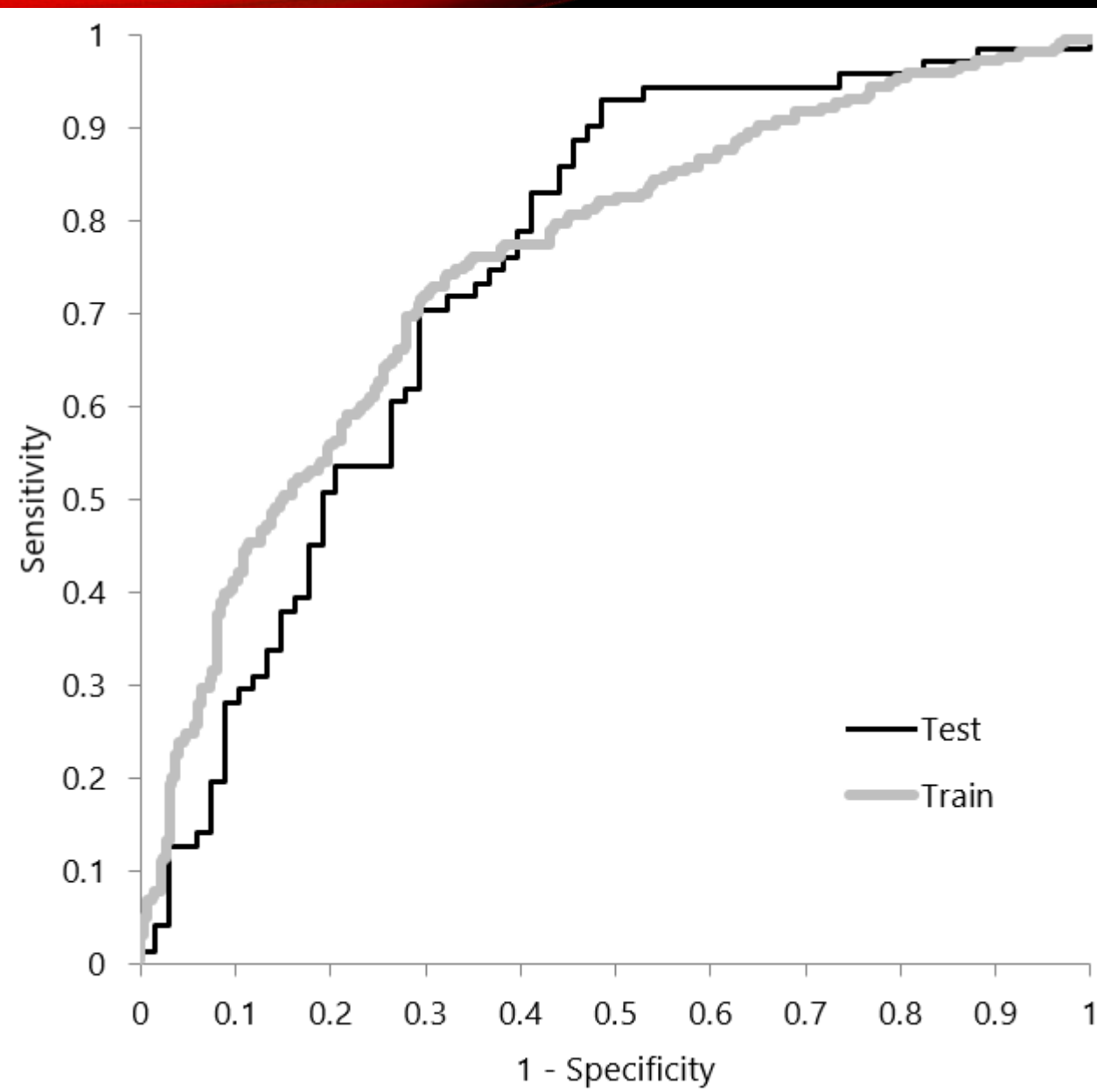
CAN REGIONAL BRAIN VOLUMES **AT BASELINE** PREDICT COGNITIVE DECLINE?

Simple machine learning model to predict fast vs slow decline



(Regional volumes computed using FreeSurfer & normalized to total intracranial volume)

MODEL PERFORMANCE ON PATIENTS WITH MCI AT BASELINE



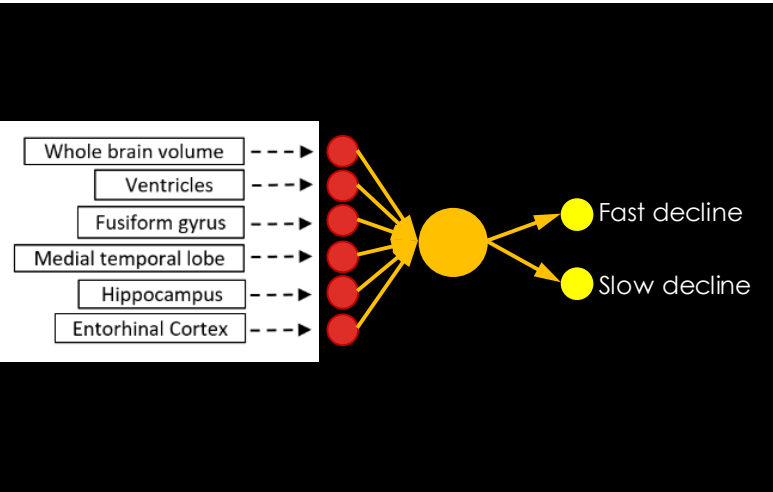
- 6 regional volumes on baseline MRI can predict fast vs slow cognitive decline

Accuracy: **$71 \pm 0.05\%$**

AUC: **0.75 ± 0.06**

MODEL DETAILS

$$P = \frac{1}{1 + e^{\left(B + A \times \tanh \frac{D + \sum_i C_i X_i}{2} \right)}}$$



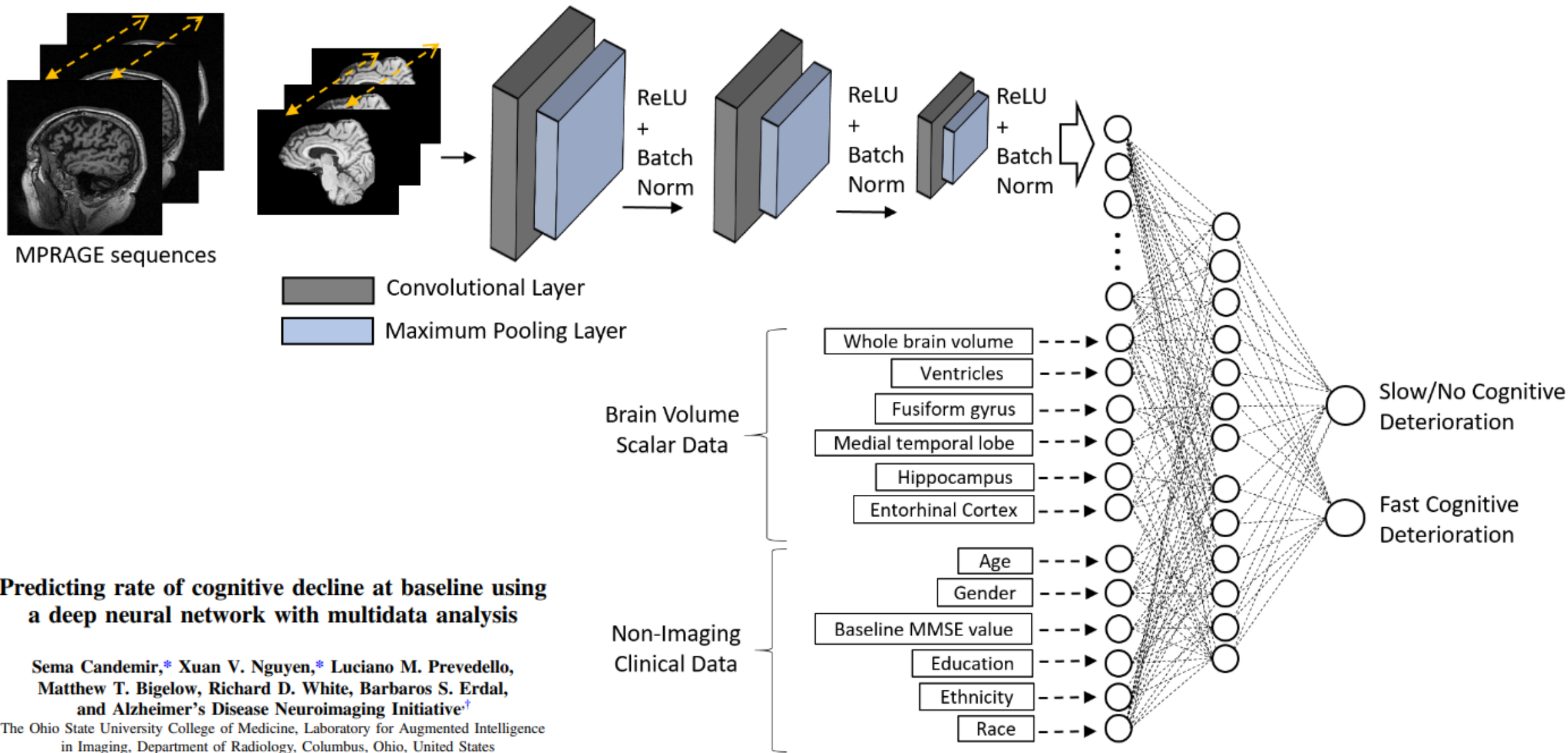
Predicting Mental Decline Rates in Mild Cognitive Impairment From Baseline MRI Volumetric Data

Xuan V. Nguyen, MD, PhD, Sema Candemir, PhD, Barbaros Selmur Erdal, PhD,
Richard D. White, MD, MS, and Luciano M. Prevedello, MD, MPH

		Model Parameter Estimates	Mean of Input Data (X_i)	SD of Input Data
A		-1.6		
B		0.8		
C ₁	Whole brain	-20	0.67	0.052
C ₂	Ventricles	-57	0.025	0.013
C ₃	Fusiform gyrus	-454	0.012	0.0016
C ₄	Medial temporal lobe	-584	0.013	0.0018
C ₅	Hippocampus	-877	0.0045	0.0008
C ₆	Entorhinal cortex	-1242	0.0023	0.0005
D		35		



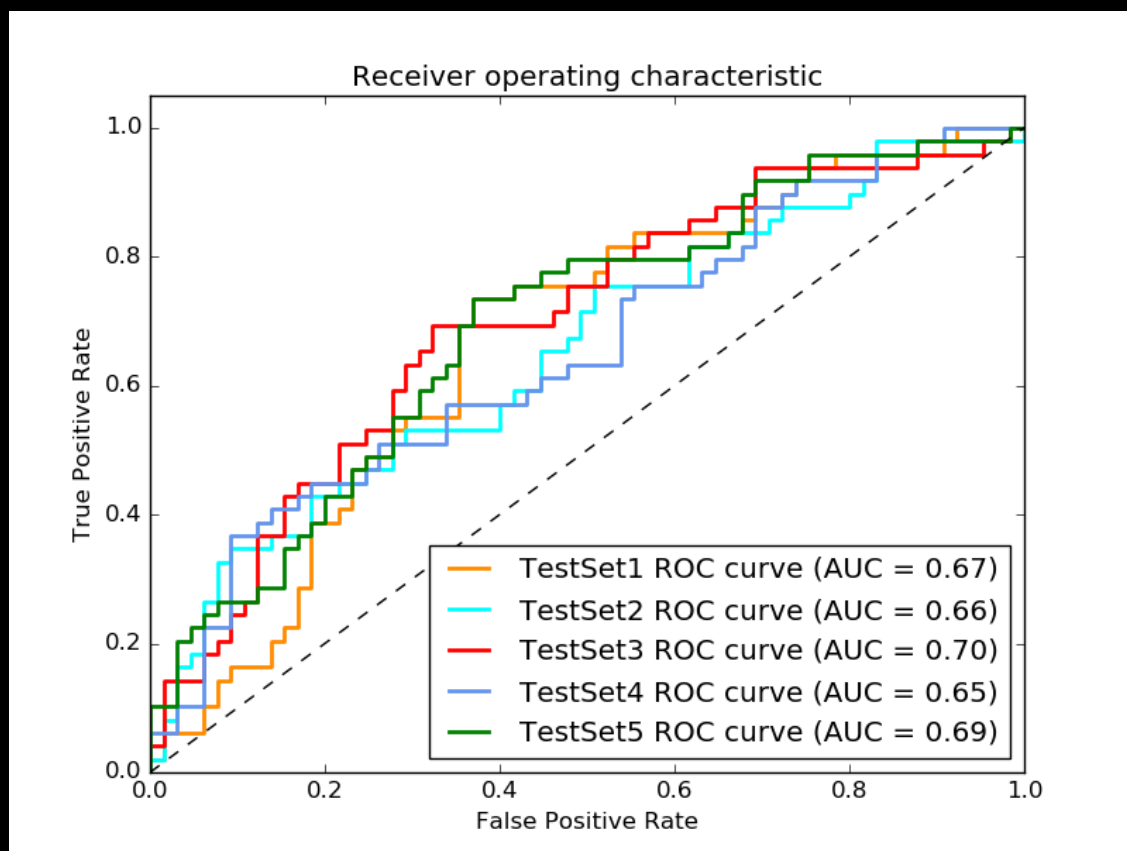
CAN WE IMPROVE PREDICTION WITH
DEEP LEARNING?



Sema Candemir,* Xuan V. Nguyen,* Luciano M. Prevedello,
 Matthew T. Bigelow, Richard D. White, Barbaros S. Erdal,
 and Alzheimer's Disease Neuroimaging Initiative[†]
 The Ohio State University College of Medicine, Laboratory for Augmented Intelligence
 in Imaging, Department of Radiology, Columbus, Ohio, United States

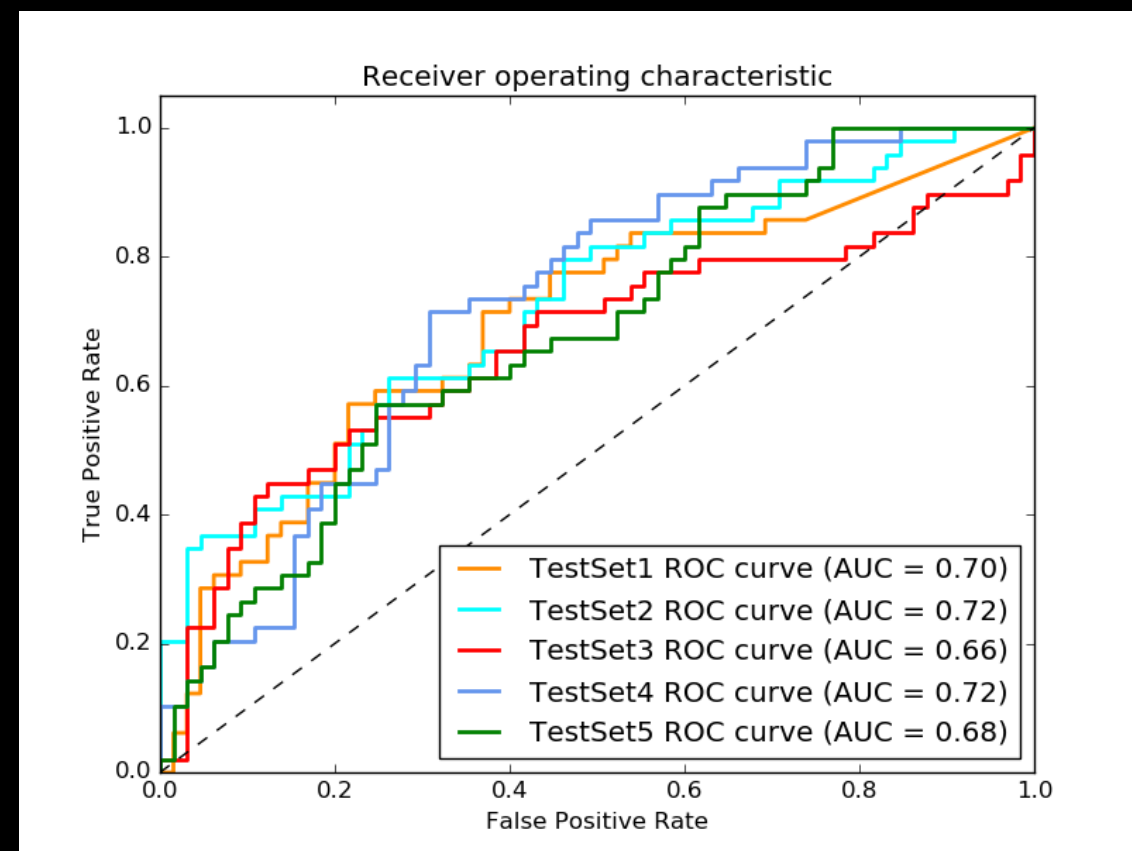
MODEL PERFORMANCE: FAST VS SLOW DECLINE

MRI deep learning only



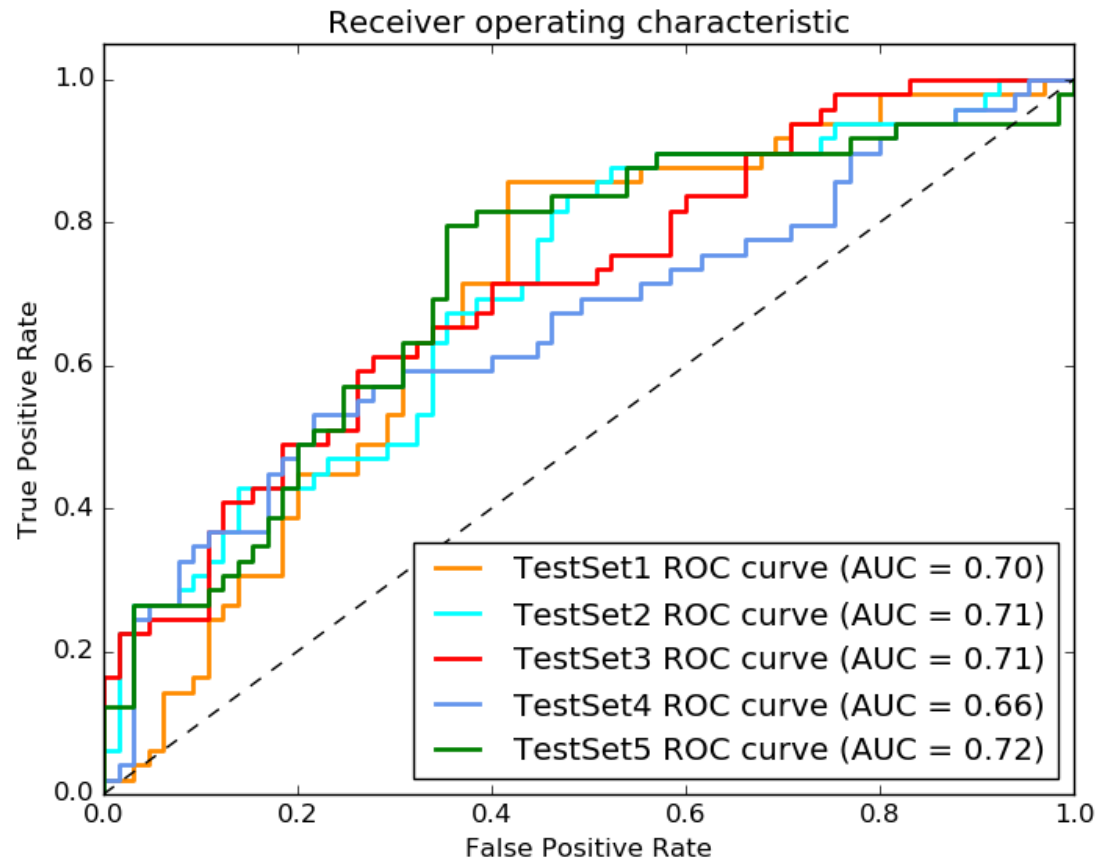
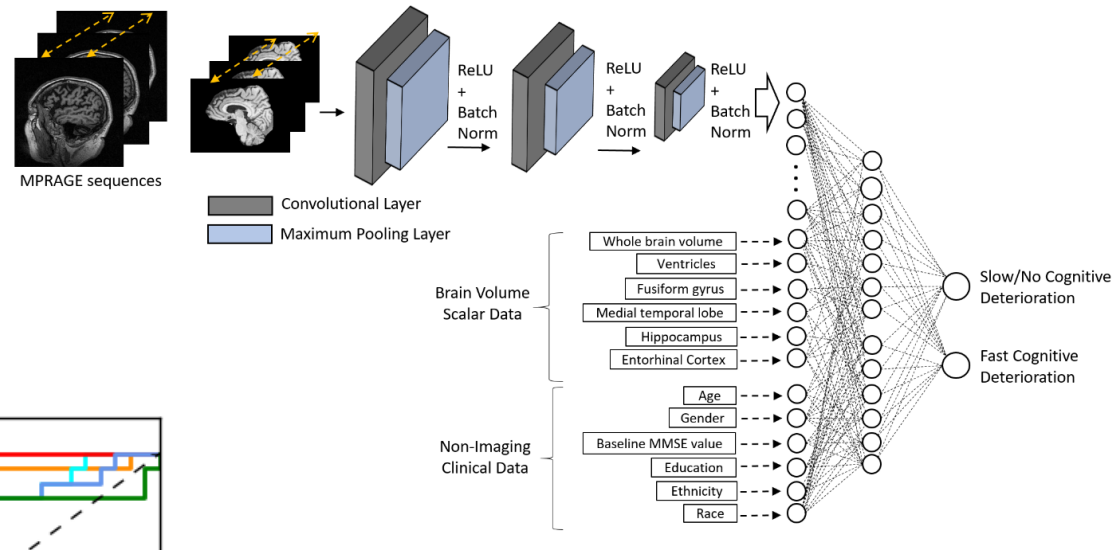
AUC 0.67

Scalar data only (brain volumes,
baseline MMSE, and
demographics)



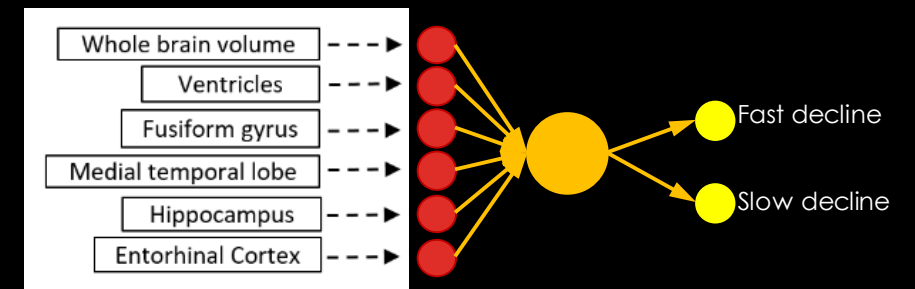
AUC 0.67

Hybrid (MRI deep learning, scalar brain volumes, baseline MMSE, and demographics)



AUC 0.70

For comparison, the simpler model had AUC of 0.75



CONCLUSIONS

- Multiple deep learning models exist for AD/MCI disease classification and prognosis
- Models using structural MRI perform better when more data (CSF, PET, demographics) are included
- Good prediction of long-term mental status decline using a simple machine learning model (perceptron) applied to only baseline MRI volumetric data

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 - (<http://aii.osu.edu>)
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- Engin Dikici, PhD

