AI for mental health

Machine learning for predictive prognostic trajectories in dementia

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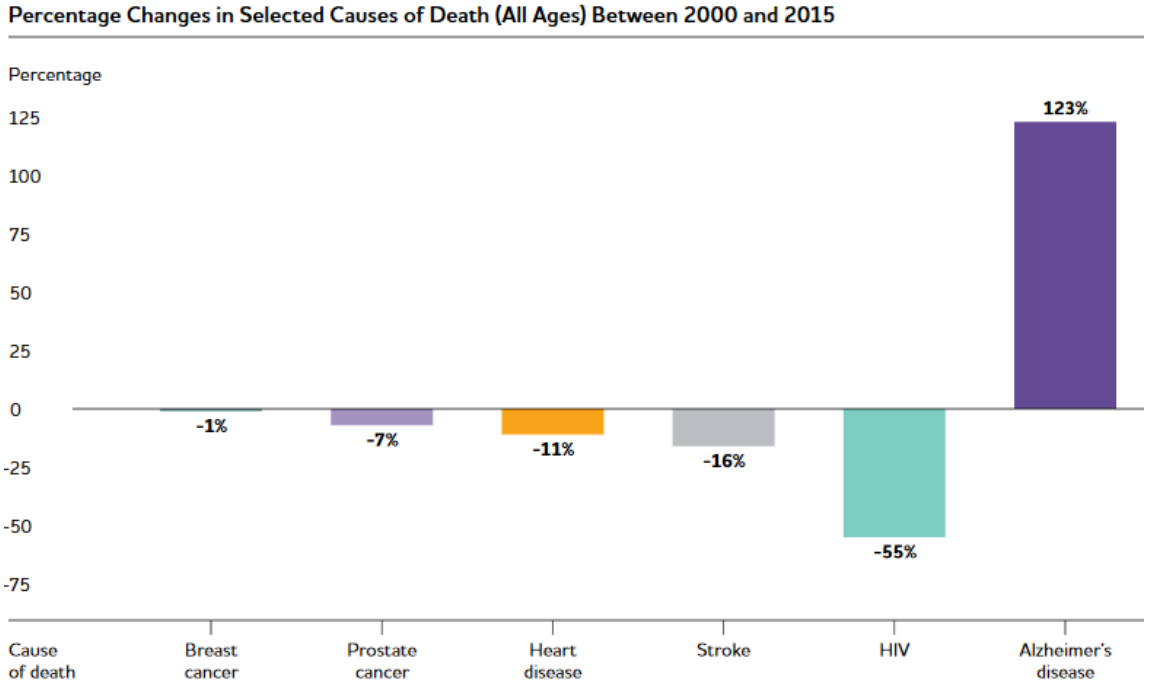
Alzheimer's Disease Health Economics

Every **65** seconds someone in the United States develops Alzheimer's disease.

1 in 3 seniors dies with Alzheimer's or another dementia.

$341,840 is the estimated lifetime cost of care for an individual living with dementia.

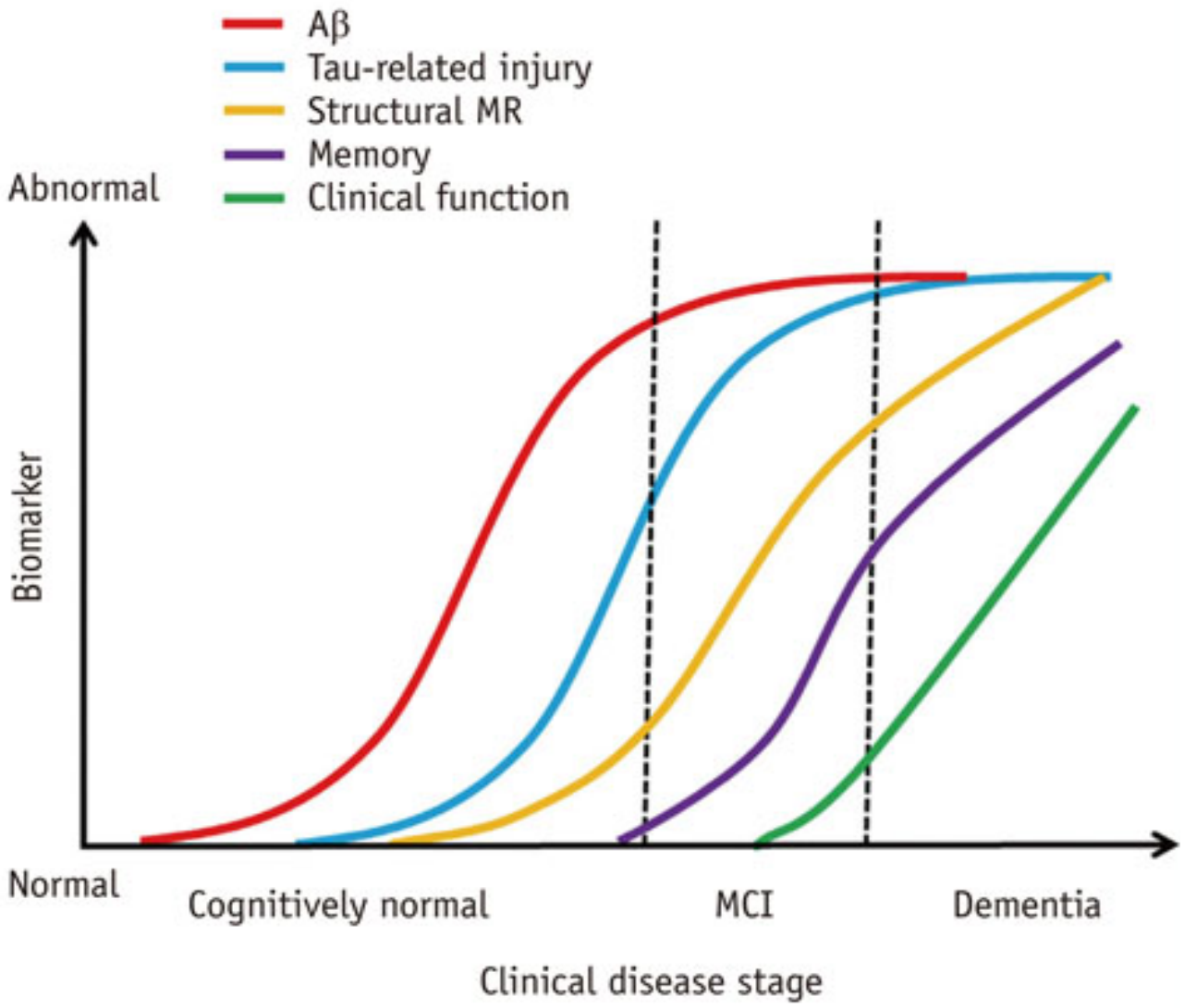
18.4 billion hours of care, valued at over $232 billion, are provided by family and other unpaid caregivers.



$7.9 trillion is the potential cost savings for the current U.S. population from early diagnosis of Alzheimer's.

Alzheimer's Association. 2018 Alzheimer's Disease Facts and Figures. Alzheimers Dement 2018;14(3):367-429.

Alzheimer's Disease Progression



Challenges of AI for Mental Health:

Patient heterogeneity

Sparse data

Costly, high invasive measures of neurocognitive health

Need for innovative healthcare solutions

Transparent and interoperable engines for:

early precision diagnosis

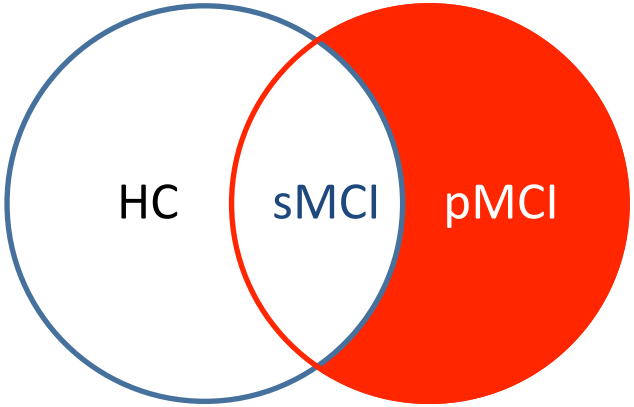
precise patient stratification

personalised interventions

from low-cost and non-invasive data

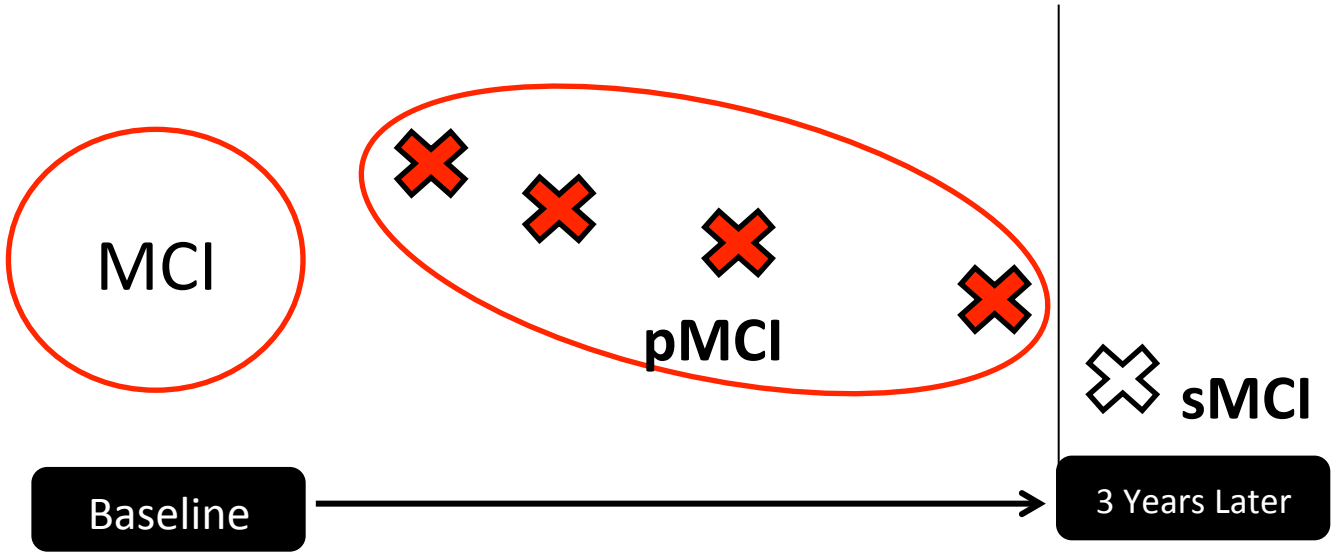
Task: patient stratification

Data: Alzheimer's Disease Neuroimaging initiative: ADNI

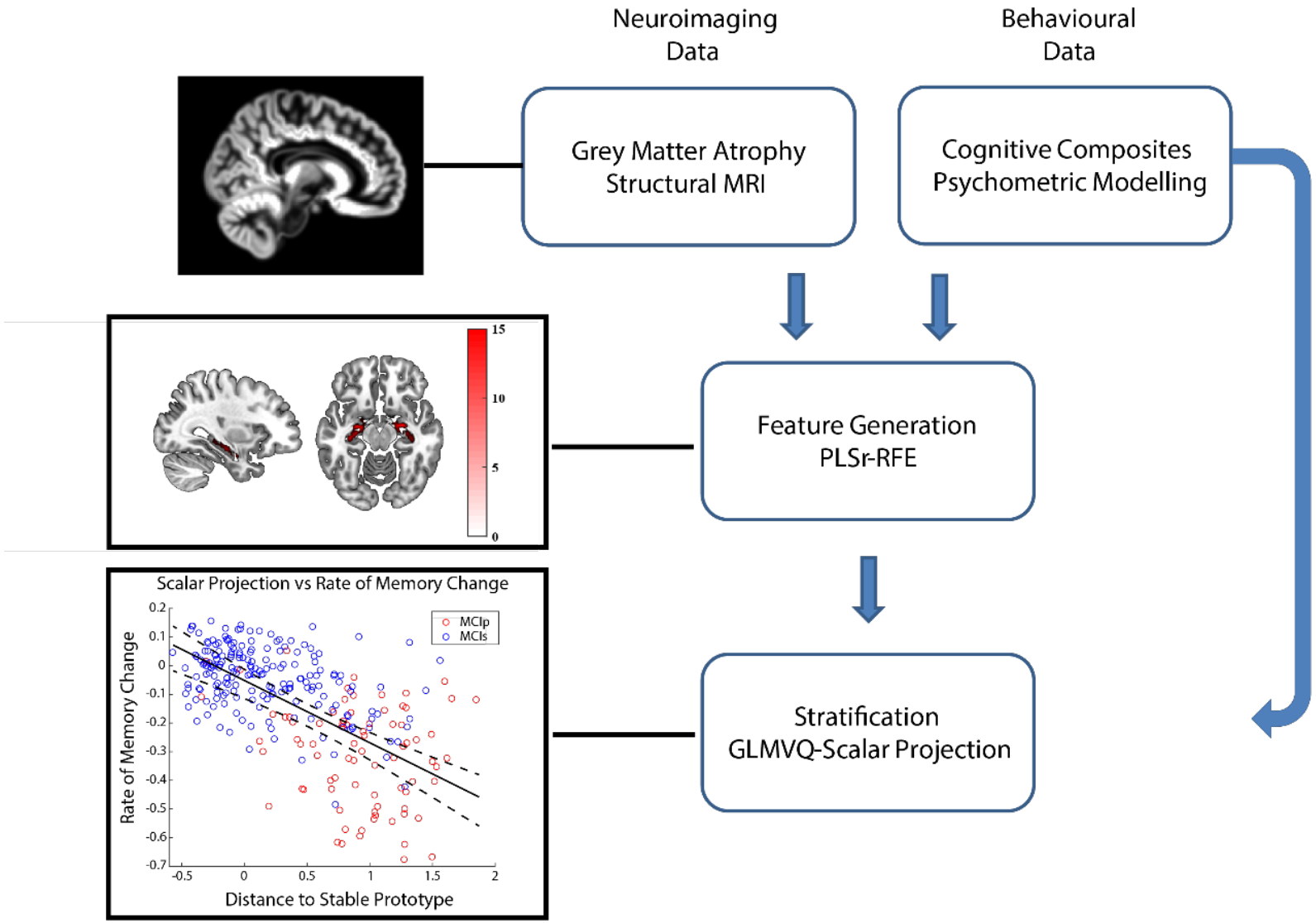


HC: healthy controls
sMCI: stable MCI
pMCI: progressive MCI

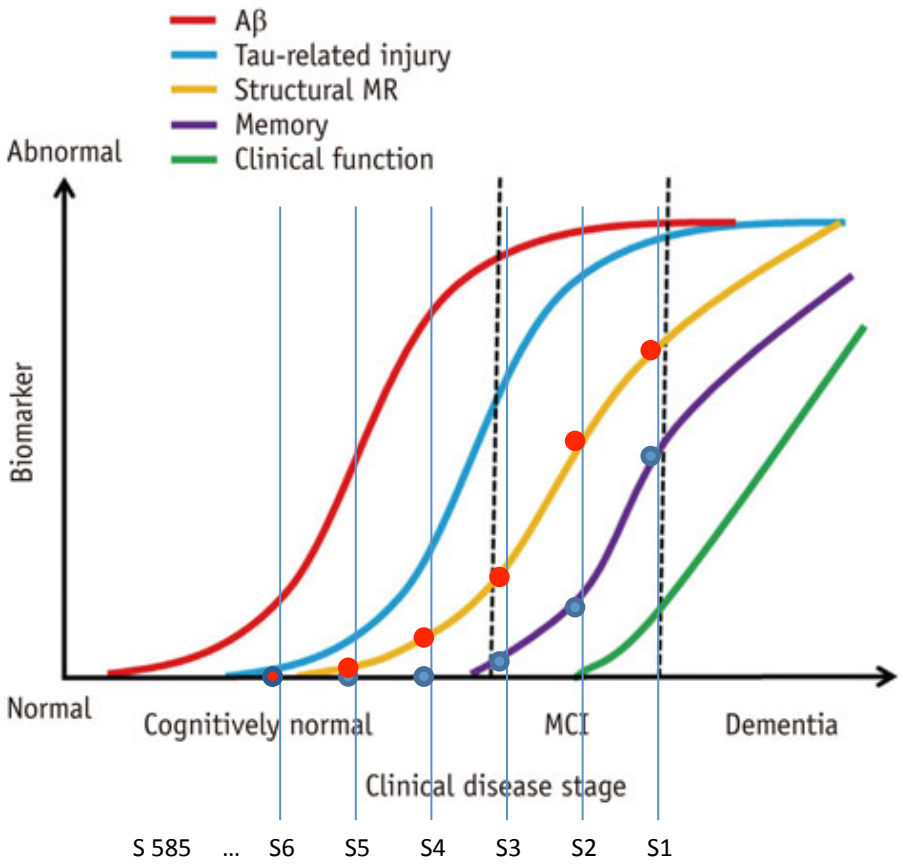
Risk of Mis-classification



Predictive Prognostic Machines on multimodal data



Biological Model: prediction of memory from Grey Matter

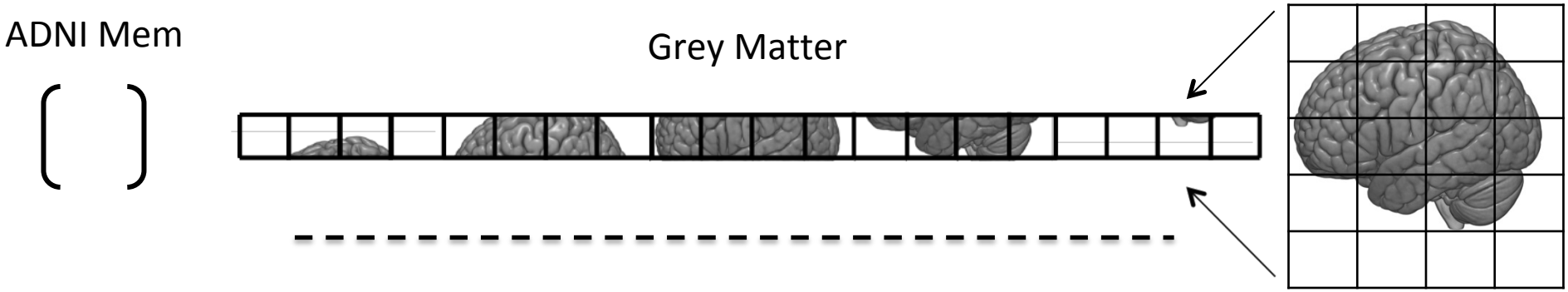


- Response Variable
  ADNI-Mem

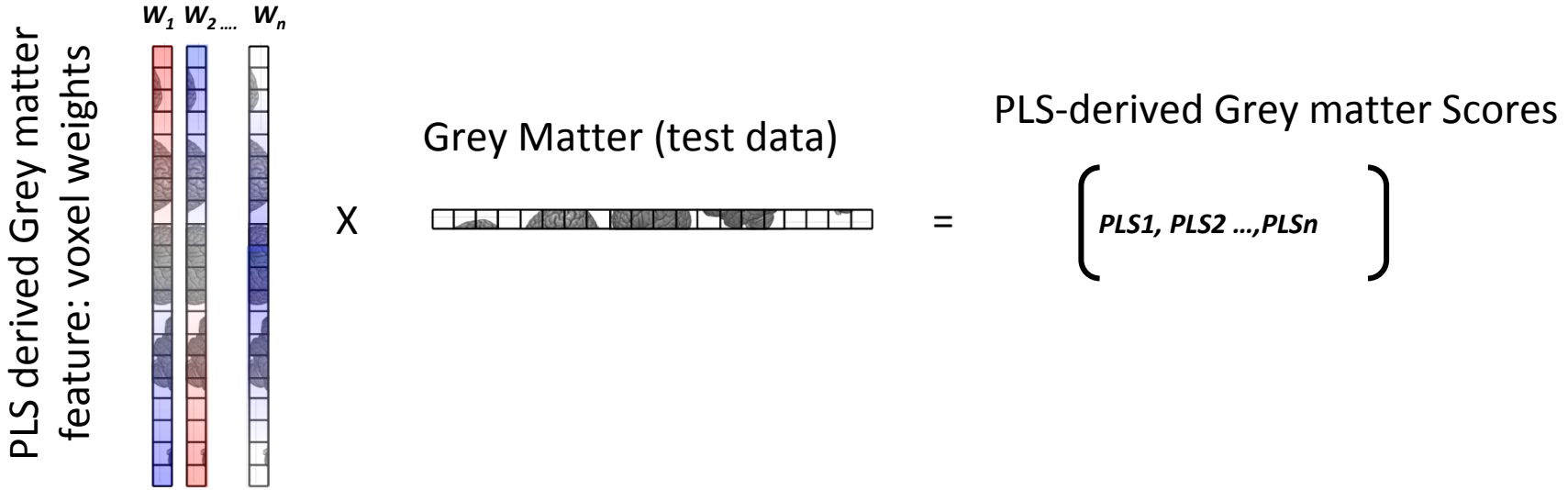
- Predictor Variable
  400,000 Measures
  (Grey Matter Voxels)
  per subject
  GM (Grey Matter)

Partial Least Squares Regression (PLSr)

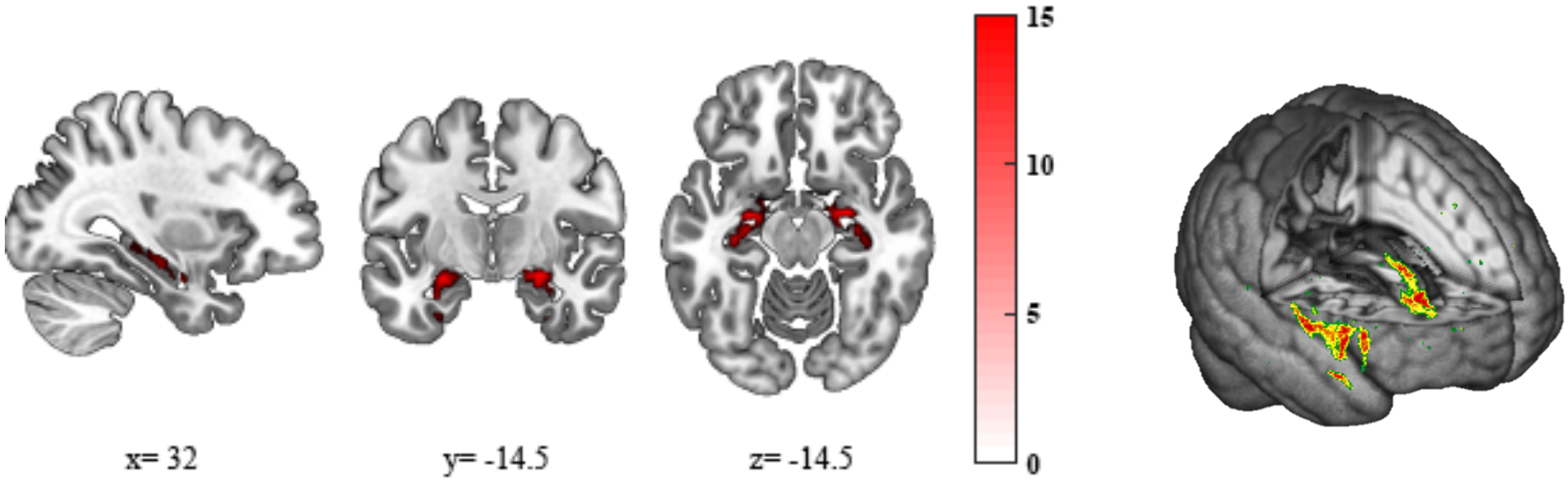
Grey Matter Features predictive of ADNI-Mem



PLS-derived Grey Matter Score



Within sample validation: sMCI vs. pMCI

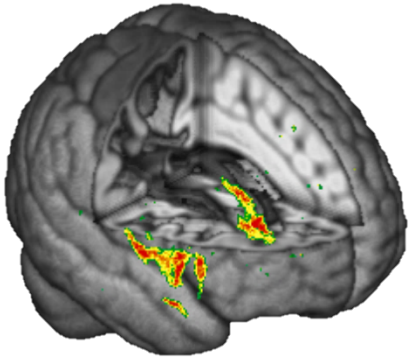


Mean test performance: [r^2(**472**) = 0.1756, *P* < **0.0001**])

PLS-derived Grey Matter Score predicts cognitive decline: variance in ADNI-Mem scores

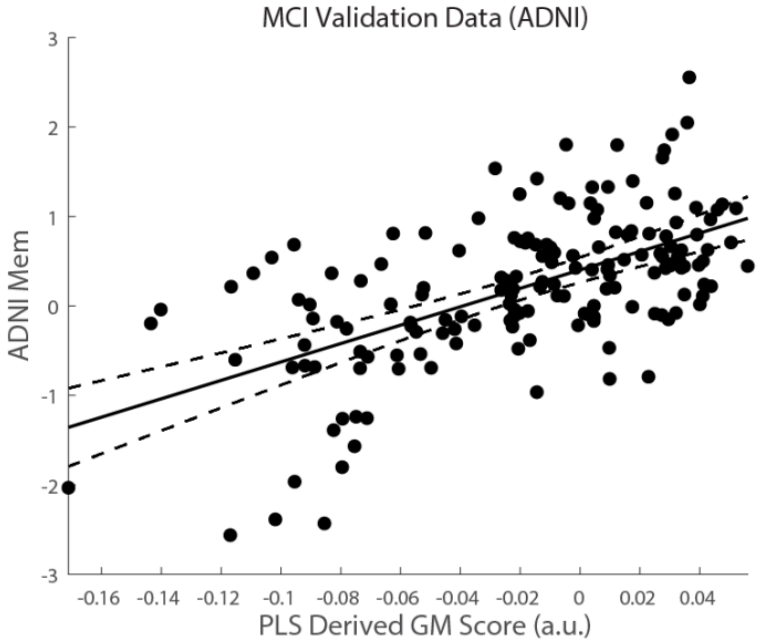
Out of sample validation

Voxel Weights Matrix

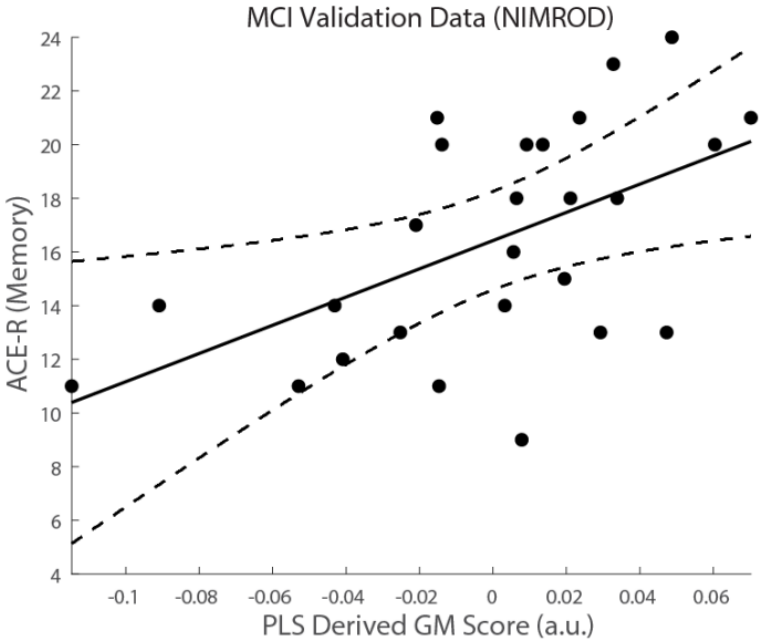


x

T1 Structural

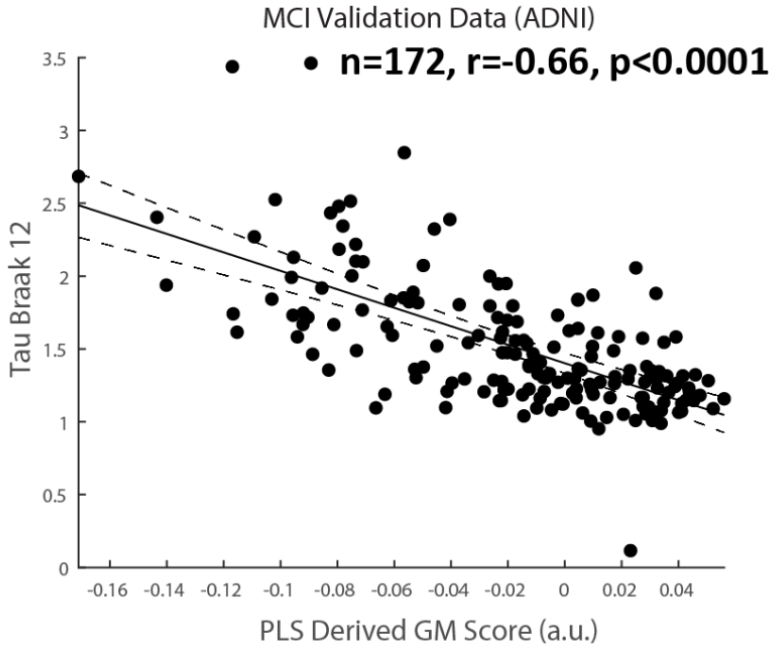


n=163, r=0.59, p<0.0001



n=26, r=0.55, p=0.004

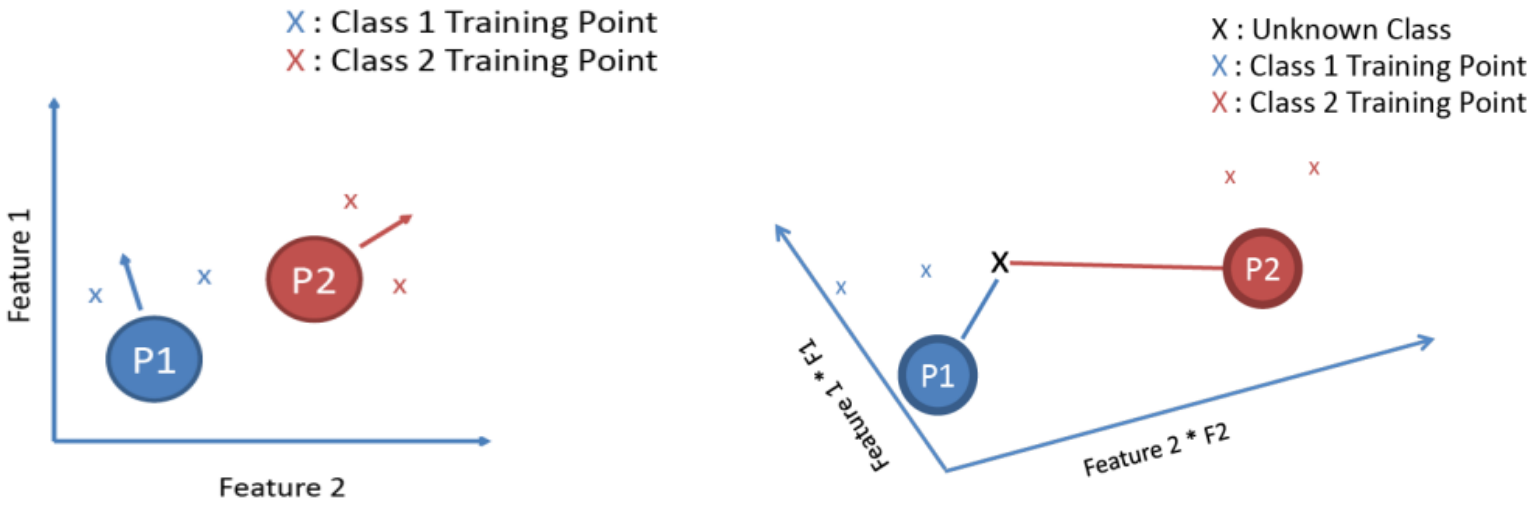
PLS-derived Grey Mater Score predicts Tau



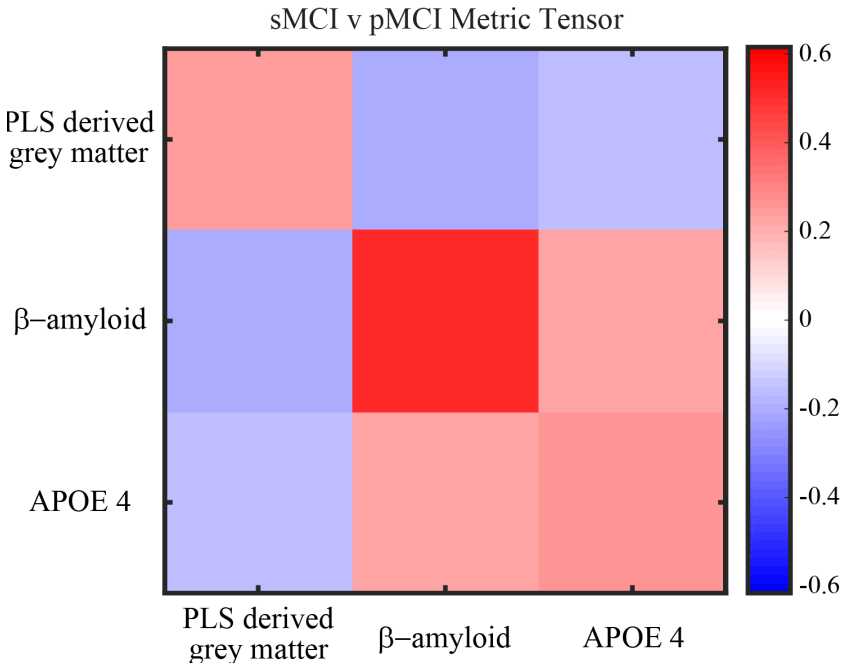
Braak Stage	Threshold	Tau Positive v Tau Negative				GM Score v Tau
		p	t	Cohen d	Pos/Neg	r^2
tau Braak 12	1.95	<.0001	10.7	2.13	27/419	0.37
tau Braak 34	1.89	<.0001	8.4	1.52	33/413	0.17
tau Braak 56	1.93	<.0001	5.9	1.32	21/425	0.08

Machine Learning Framework

Generalised Metric Learning Vector Quantisation: GMLVQ

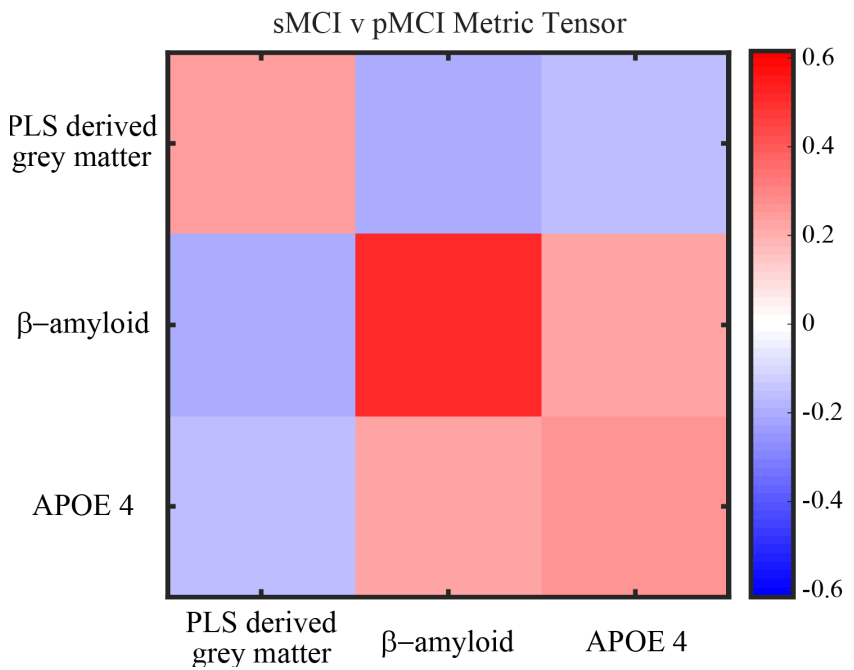


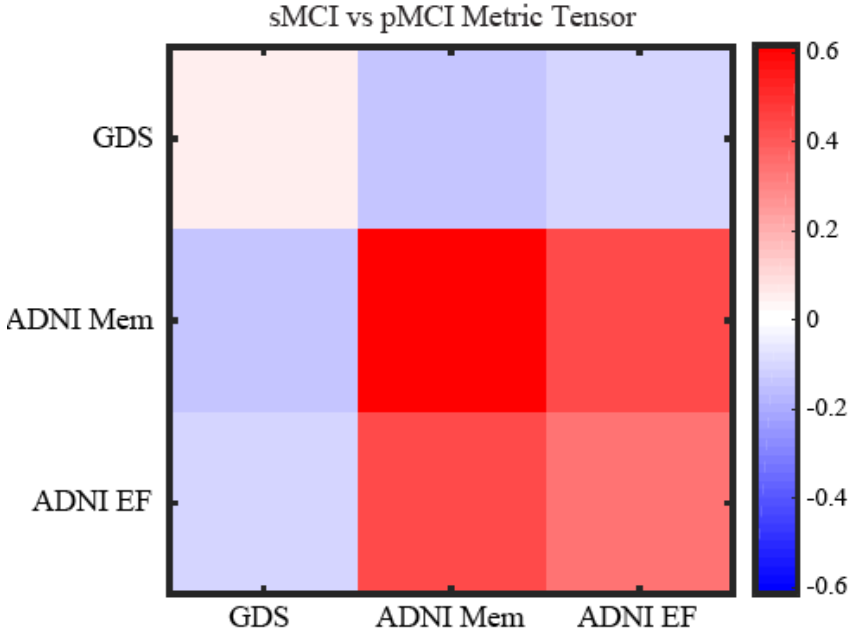
Biological model: sMCI vs. pMCI



Data Type	**Accuracy**	**1-MAE**	**sensitivity**	**specificity**
Biological	81.9	81.7	81.1	82.3

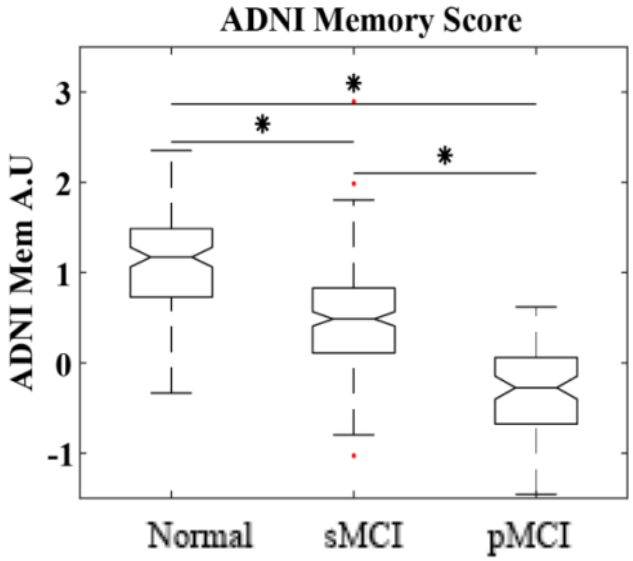
Biological vs. Cognitive model

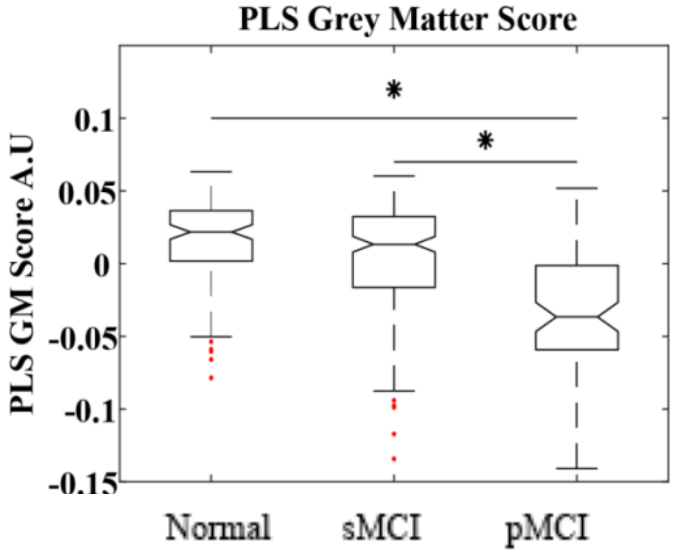




Data Type	**Accuracy**	**1-MAE**	**sensitivity**	**specificity**
Biological	81.9	81.7	81.1	82.3
Cognitive	81.4	82.4	84.9	79.8

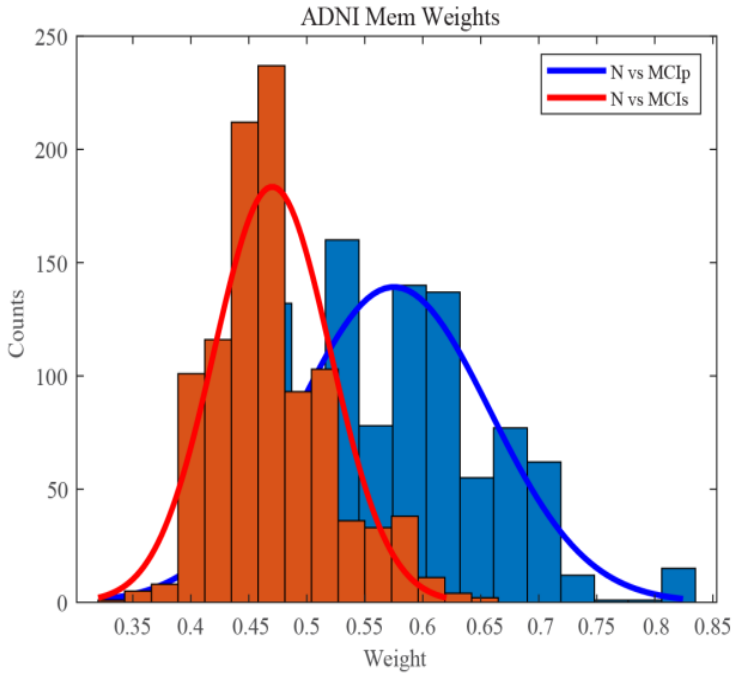
Healthy controls vs. sMCI; pMCI

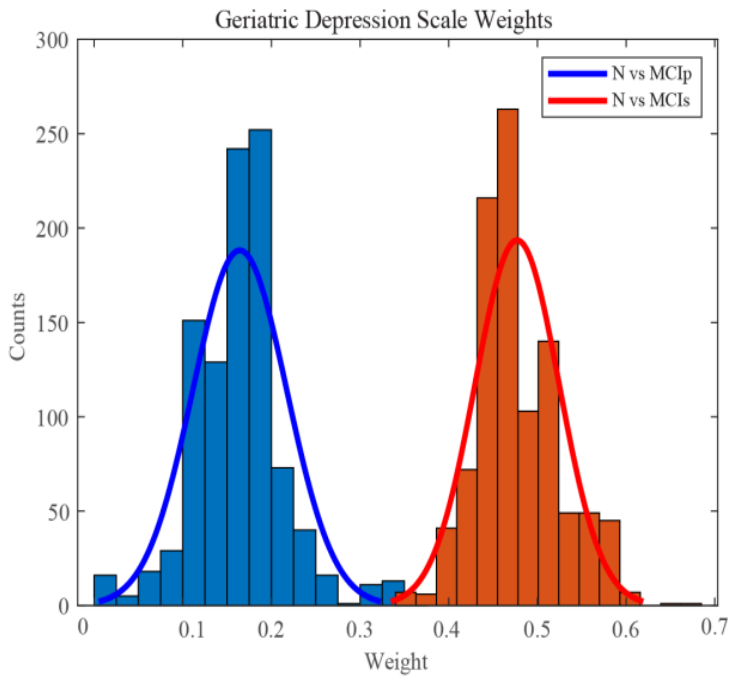




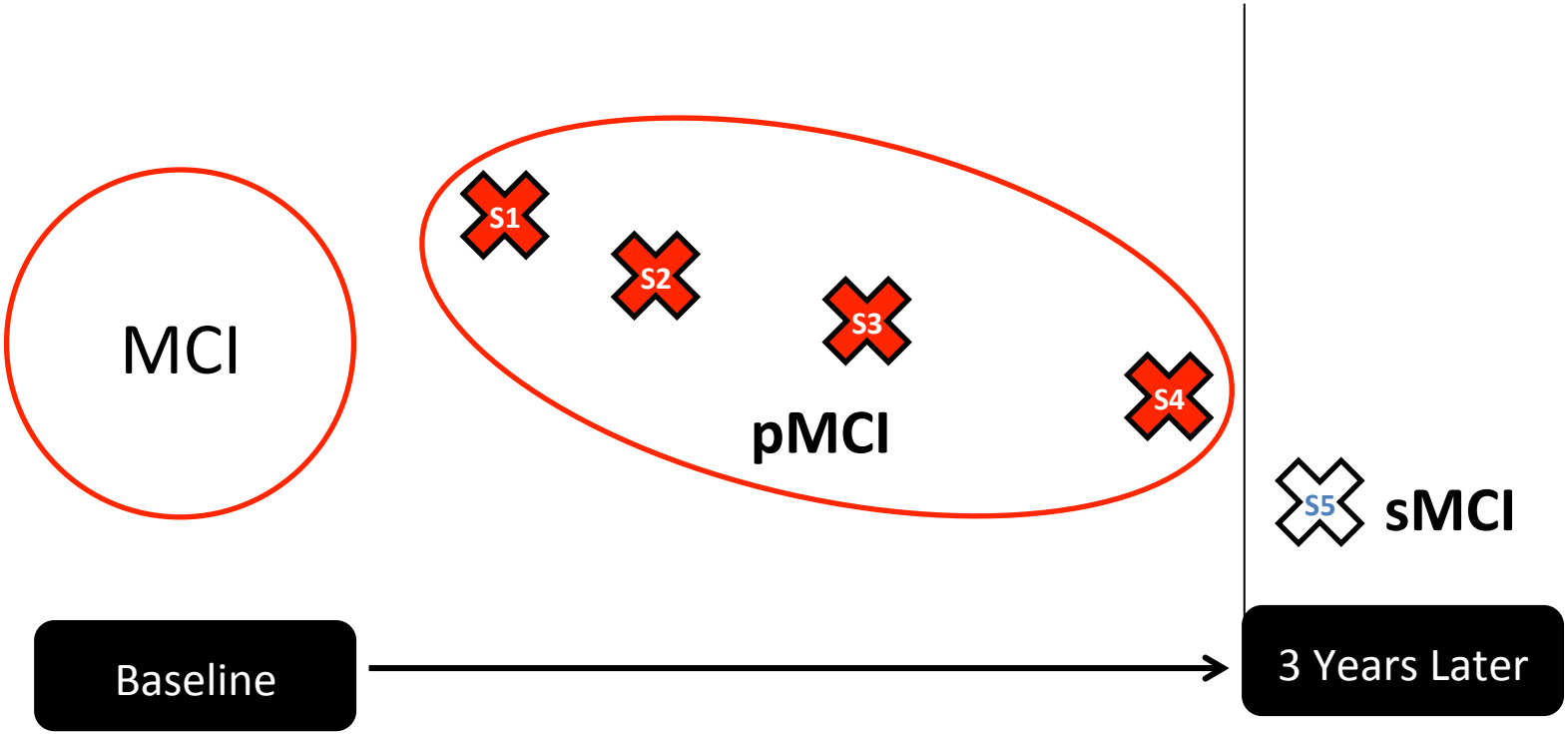
PLS-derived Grey Matter Score relates to pathology vs. symptomatology

Healthy controls vs. sMCI; pMCI

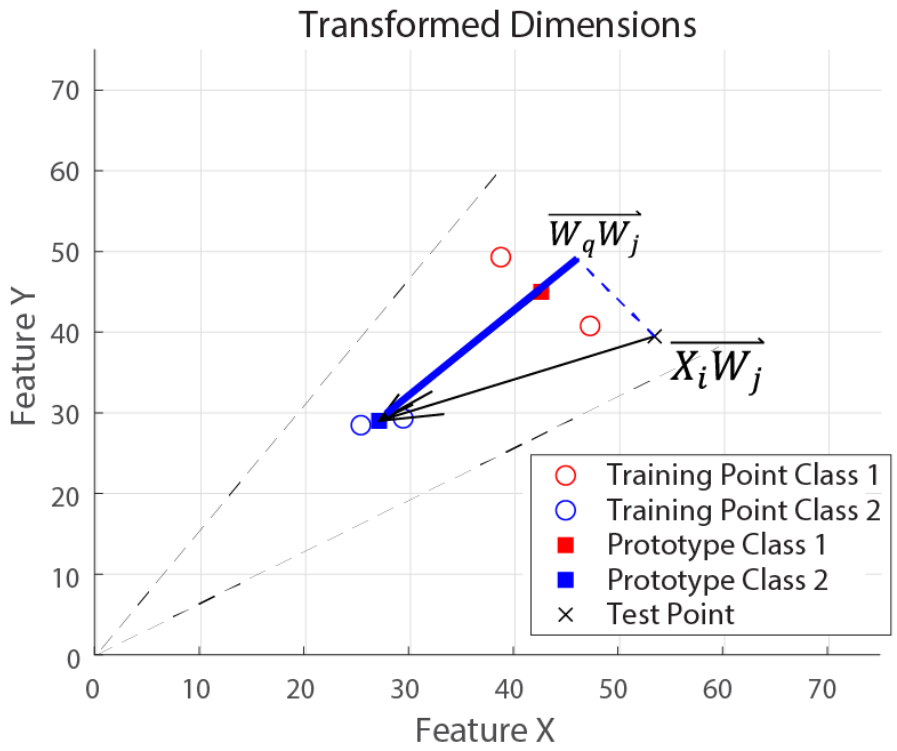




Binary vs. continuous predictions: risk of mis-classification

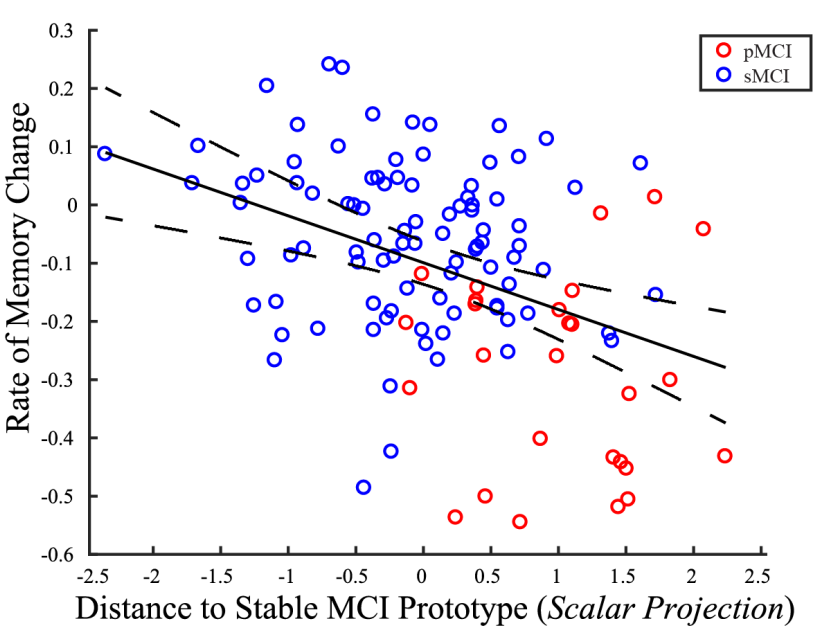


GLMVQ Scalar Projection: determine distance from stable MCI prototype



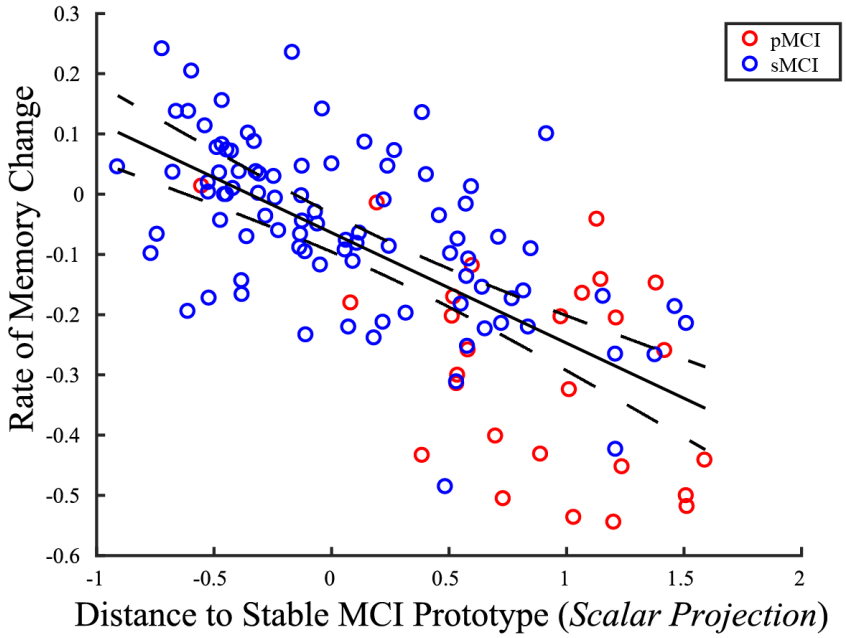
Projection score predicts rate of memory change

Cognitive model



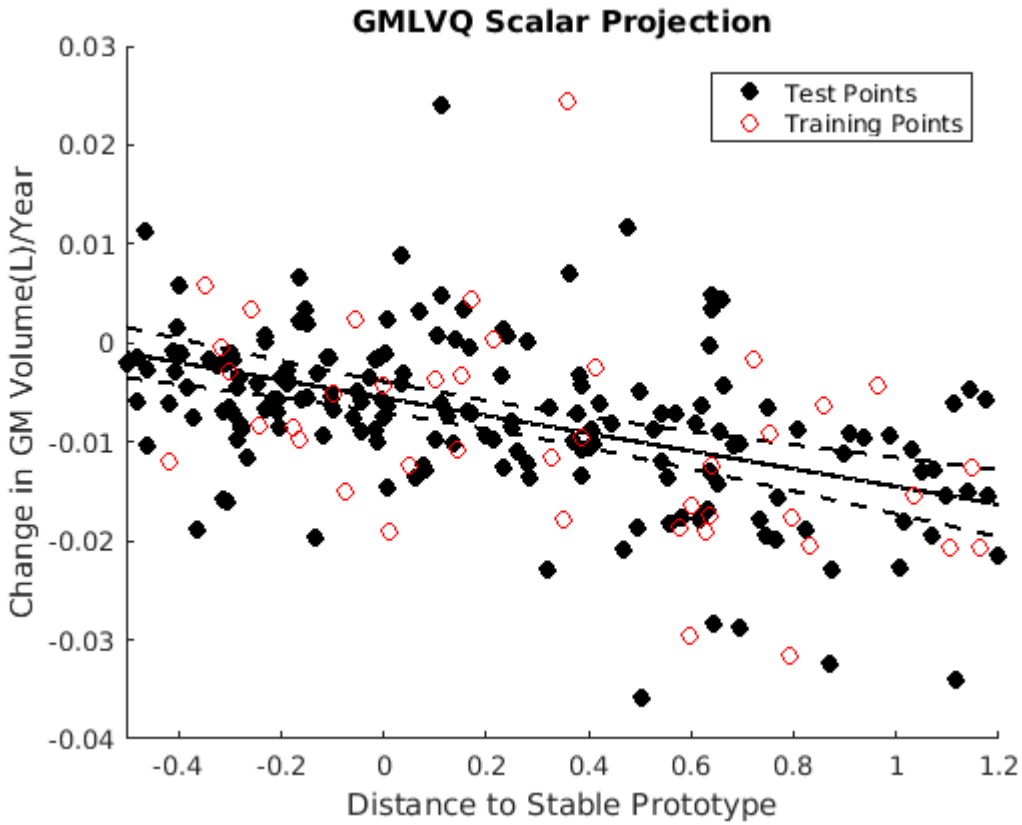
r= -0.41 [-0.5 -0.32]

Biological model



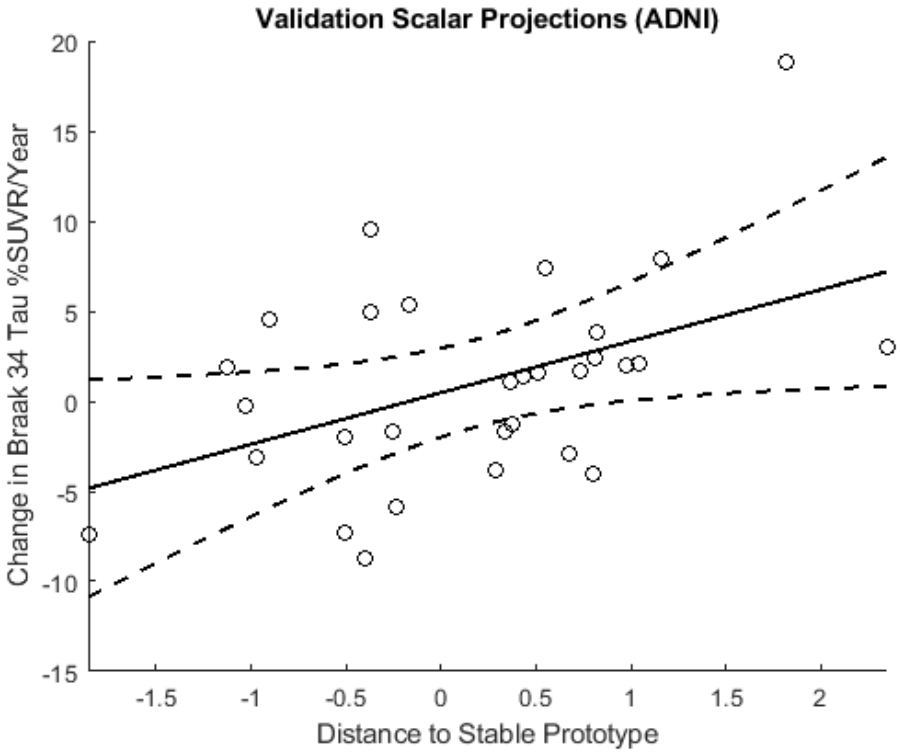
r= -0.55 [-0.62 -0.47]

Projection Score predicts rate of Grey matter volume change



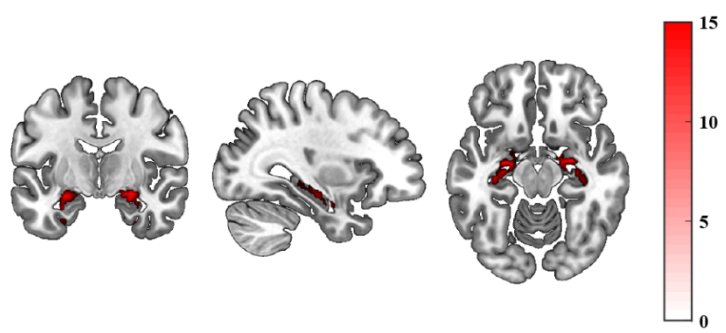
n=171, r=-0.41 , CI[-.53 -0.26] p<.0.0001

Projection score predicts rate of Tau change



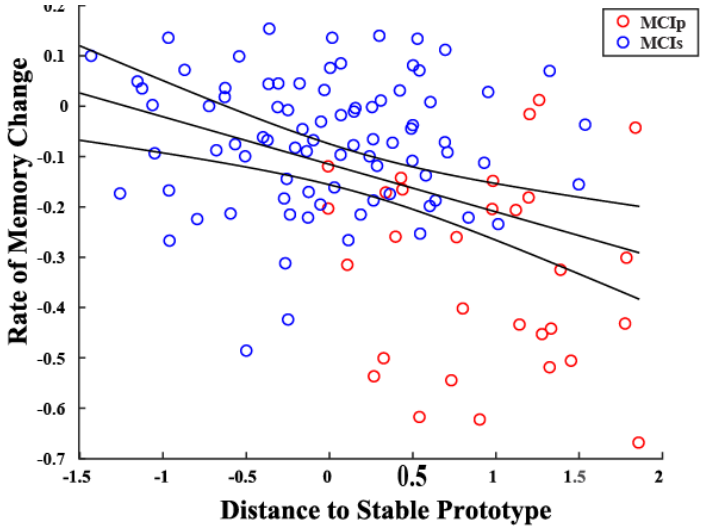
Braak 34 n=30, r=0.46 p=0.01

Scalar projection: out of sample validation



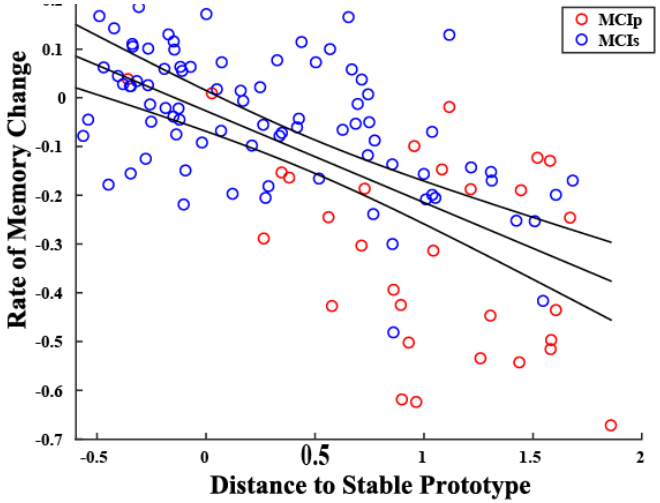
x 126 MCI 3 Years Clinical Follow-up

Cognitive model



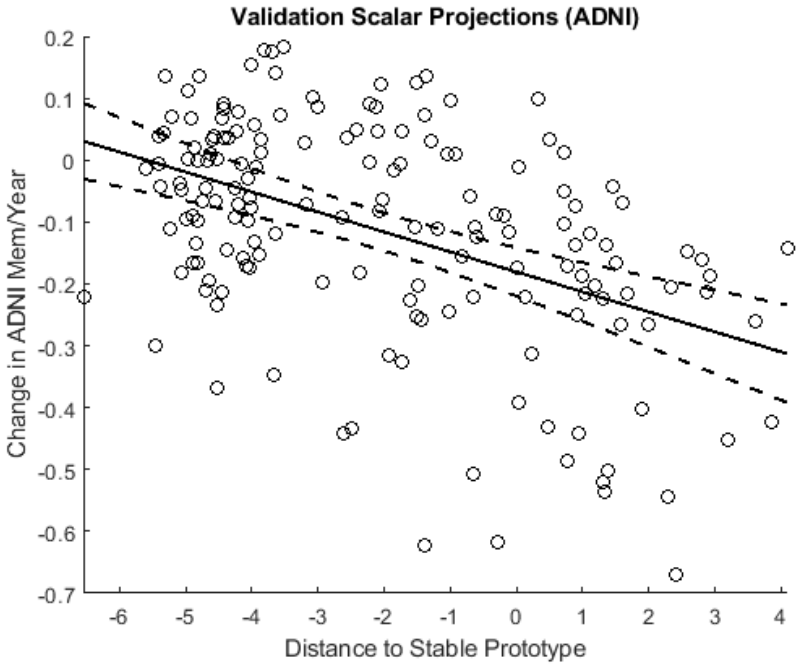
r(**116**) = -0.4, *P* < **0.0001**

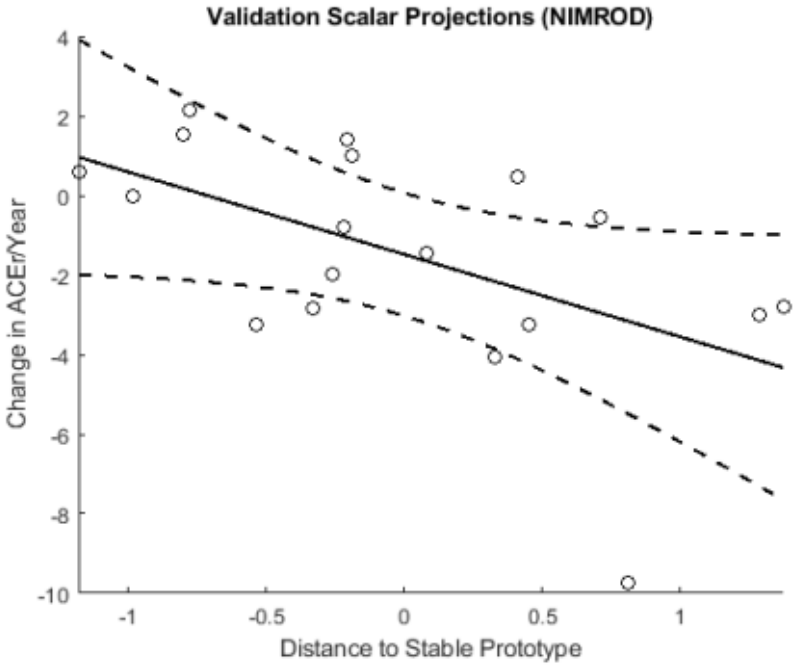
Biological model



r(**116**) = -0.65, *P* < **0.0001**

Interoperability across cohorts



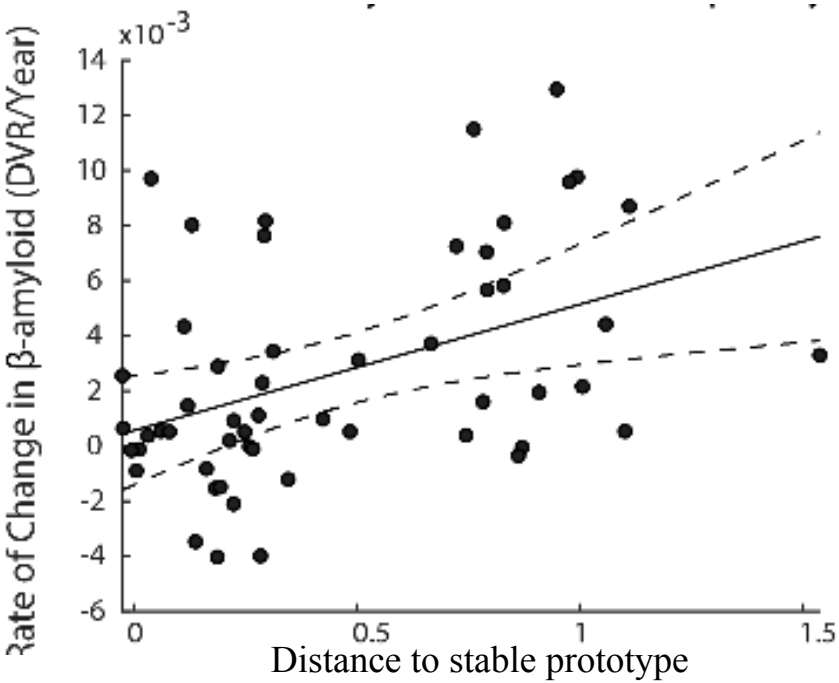


n=163, r=-0.47, p<.0.0001

n=18, r=-0.55, p=0.02

Scalar projection from model trained on ADNI predicts cognitive decline in a different cohort (NIMROD)

Predicting disease in asymptomatic individuals



n=54, r=-0.44, p=0.001

Scalar projection from model trained on ADNI predicts Beta-amyloid change in preclinical sample (BAC)

Transparent and interoperable engines for early diagnosis and prediction in dementia

- Linear metric learning classifies MCI patients into stable vs. progressive based on low-cost less invasive data (i.e. cognitive data)

- Transparent multivariate modelling returns interpretable biomarker-based features that inform precise prediction of cognitive decline

- Scalar projection model defines prognostic trajectories from baseline data, reduces risk of misclassification, and generalises predictions across cohorts and asymptomatic individuals.

Thank you





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Dementias Platform UK

The Leverhulme Trust

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