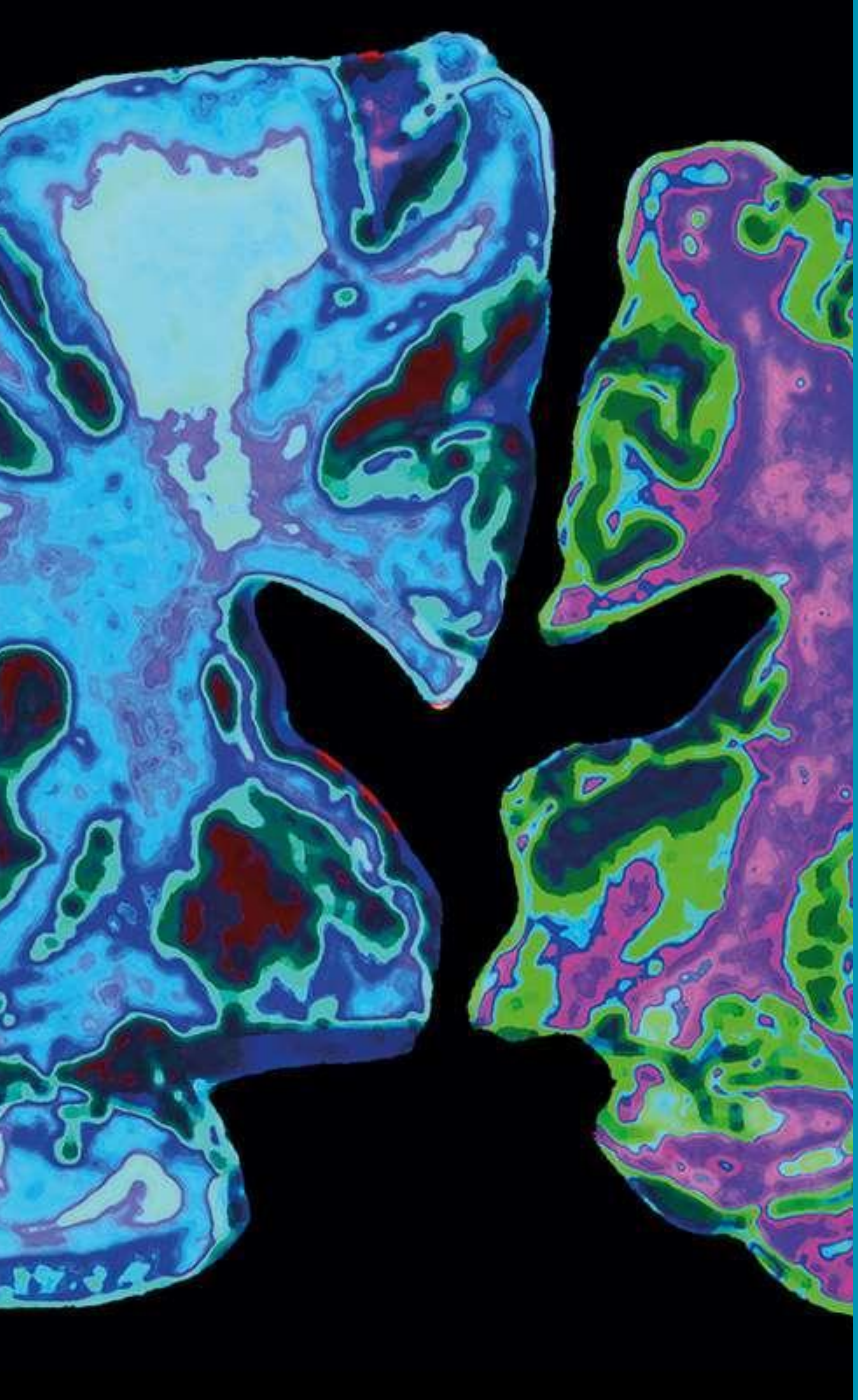


SAMSI UG WORKSHOP
NC STATE UNIVERSITY

Characterizing and Classifying Alzheimer’s Diagnosis

Frederick Donahey, Khoa Huynh, Linda Pan, Xin Tan, Lynn Zhu

Overview

1. Background
2. Objectives
3. Exploratory Data Analysis
4. Classification Methods and Results
5. Characterization of PET Scans
6. Conclusions

Background
Alzheimer’s disease - Neurodegenerative disease

Prevalence [1]

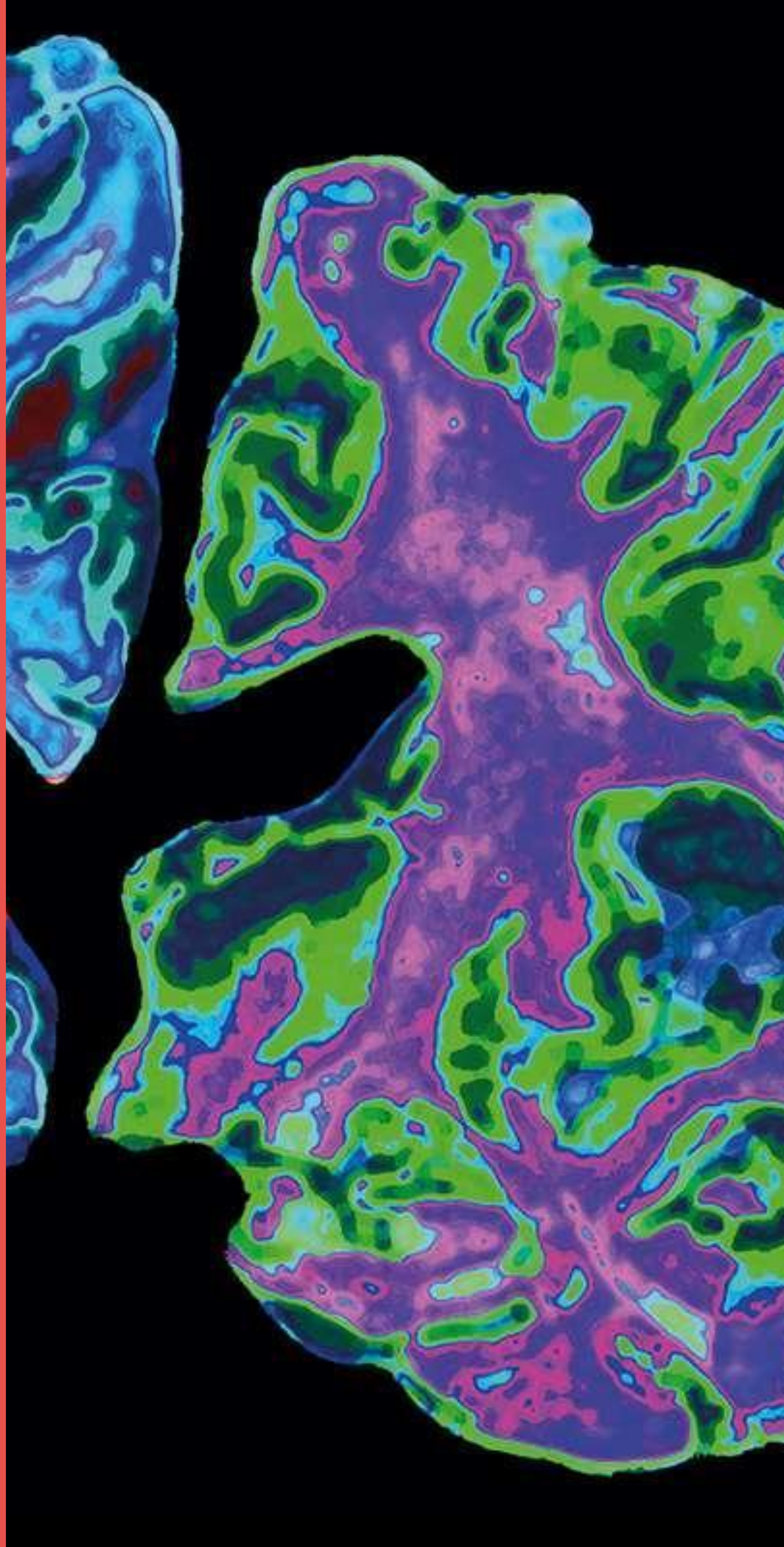
- 6th leading cause of death in the US
- Affects more than 5.8 millions Americans.

Pathology

- Extracellular beta amyloid plaque + intracellular neurofibrillary tangles
- Neuronal damage and brain region death

Treatment

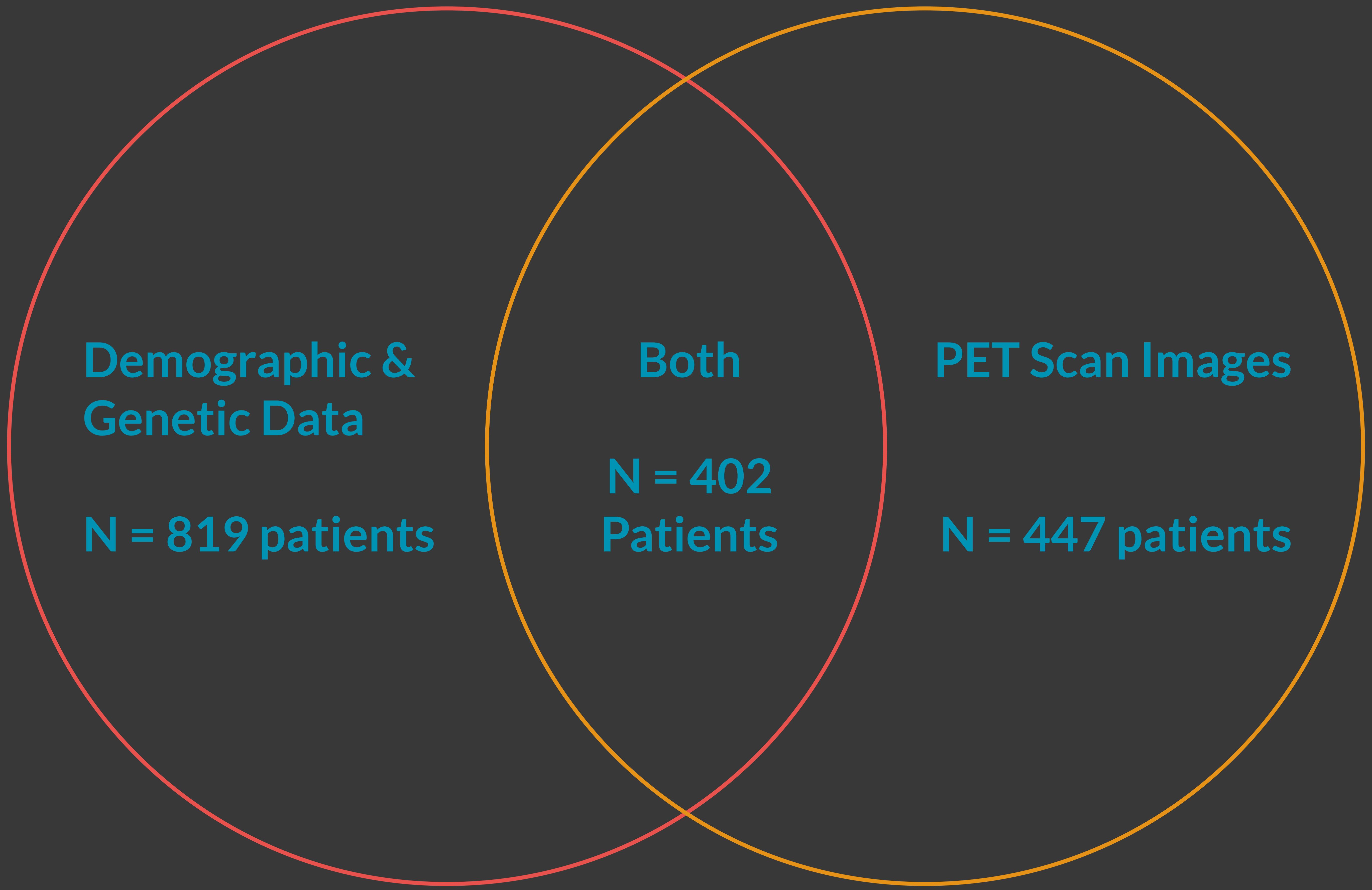
- Currently there is no cure for the disease and no way to reverse its progress



Our Data

Demographic and Genetic Data:

- Age
- Sex
- MMSE Score
- APOE4
- Site
- Ethnicity
- Race
- Marriage Status



Data Source: ADNI (http://adni.loni.usc.edu/)

Diagnosis of Alzheimer's disease

Mental Status Test -
Mini-Mental State Examination (MMSE)

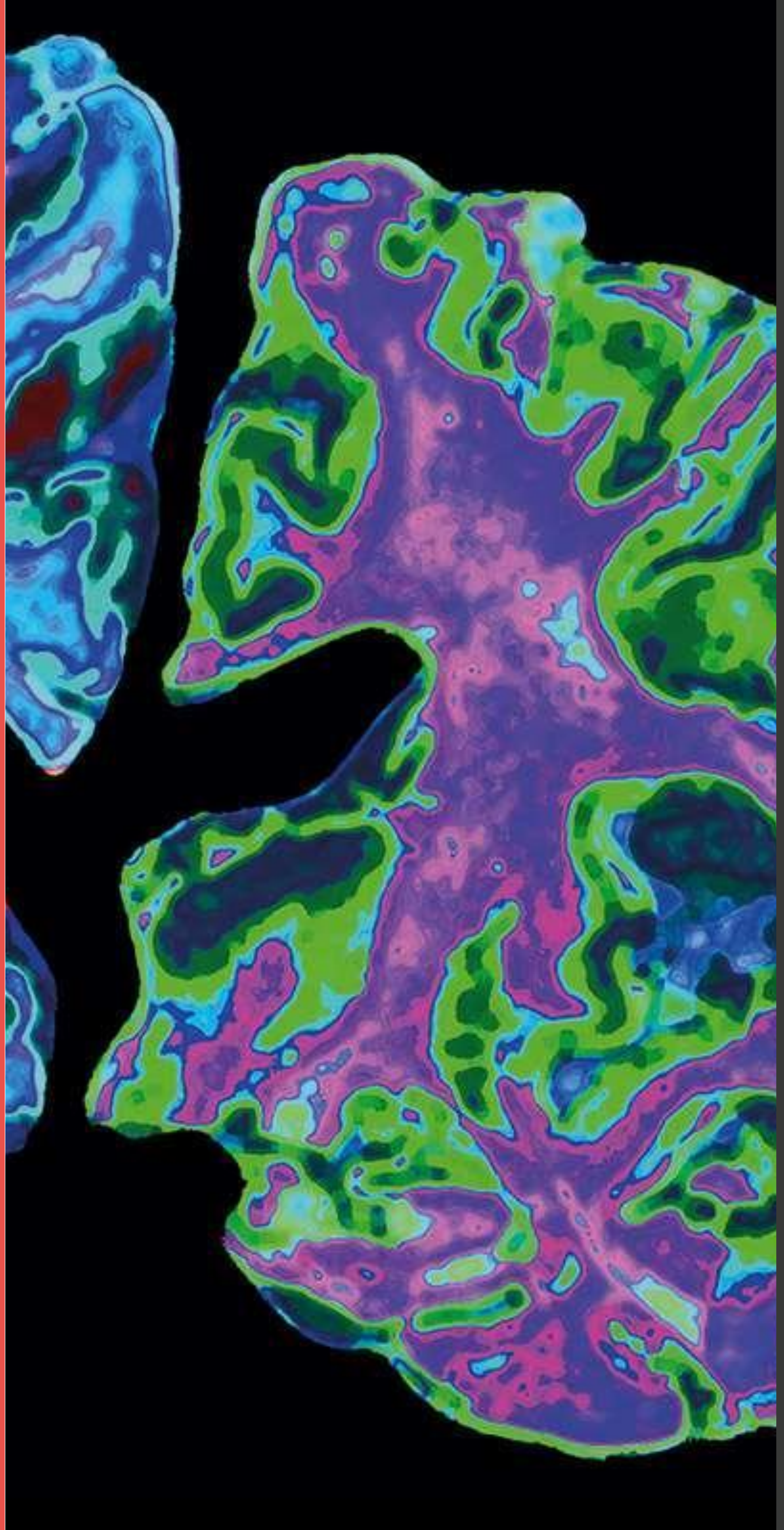
Maximum score of 30

- 20-24 = Mild dementia
- 13-20 = Moderate dementia
- <12 = Severe dementia

Alzheimer's patients decrease on average 2-4 points each year

Brain Imaging
- Positron Emission Tomography (PET) Scan

- Capture the image of the activity (metabolic level) of brain.
- Used to rule out other conditions such as brain tumor, Louis body dementia and Parkinson's disease with Louis body



Genetic Risk Factor: ApoE4

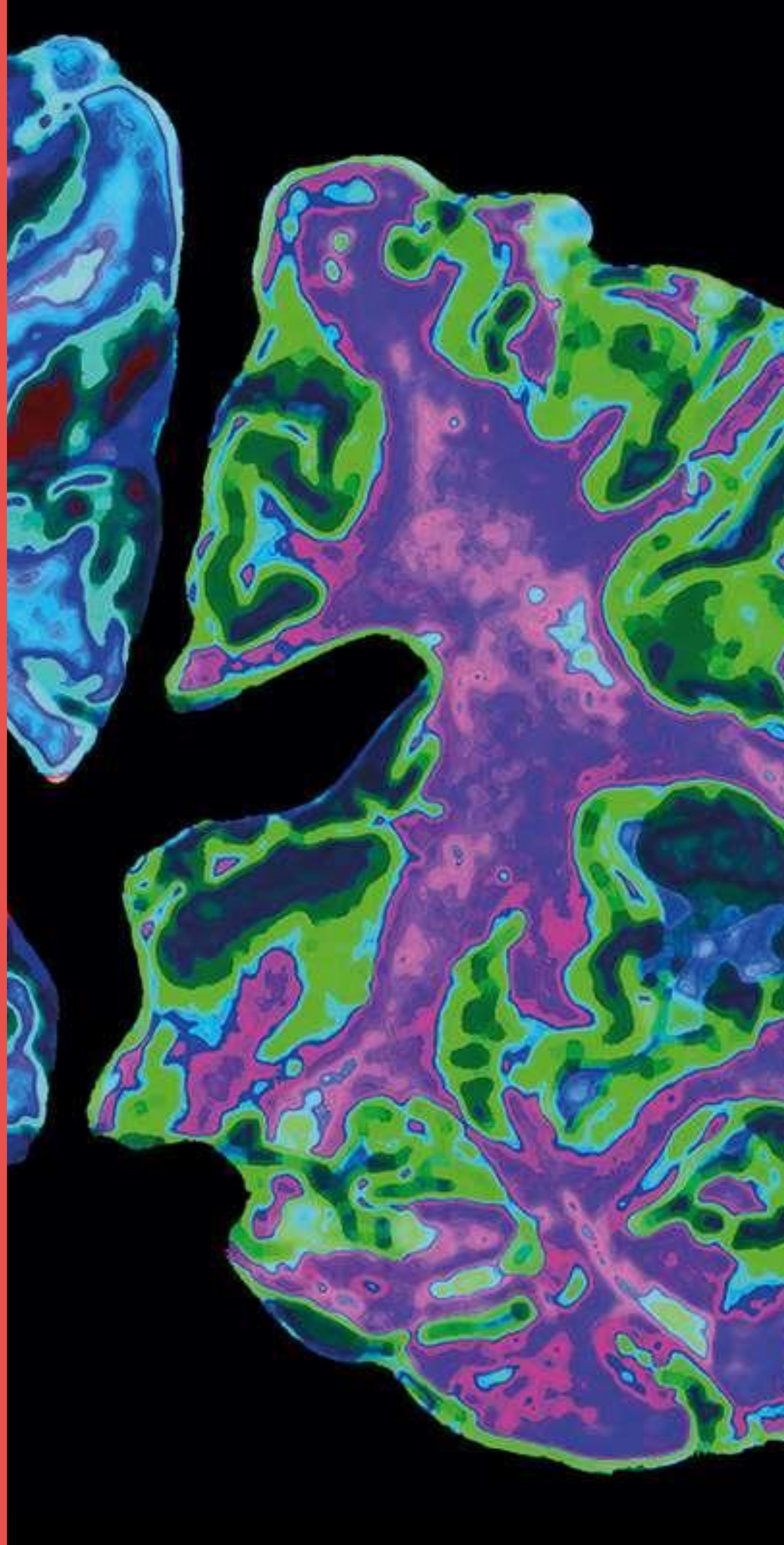
There exist three alleles for the ApoE gene:

- ApoE2
- ApoE3
- ApoE4

The presence of the ApoE4 allele increases the risk of developing Alzheimer's disease

[2]

Genotype	E2/E2	E2/E3	E2/E4	E3/E3	E3/E4	E4/E4
Disease Risk	40% less likely	40% less likely	2.6 times more likely	Average risk	3.2 times more likely	14.9 times more likely



Objectives and Methods

1. Characterize diagnoses

- Healthy
- Mild cognitive impairment (MCI)
- Alzheimer's disease (AD)

in PET scan images

Methods:

- PCA
- Tensor-on-scalar Regression

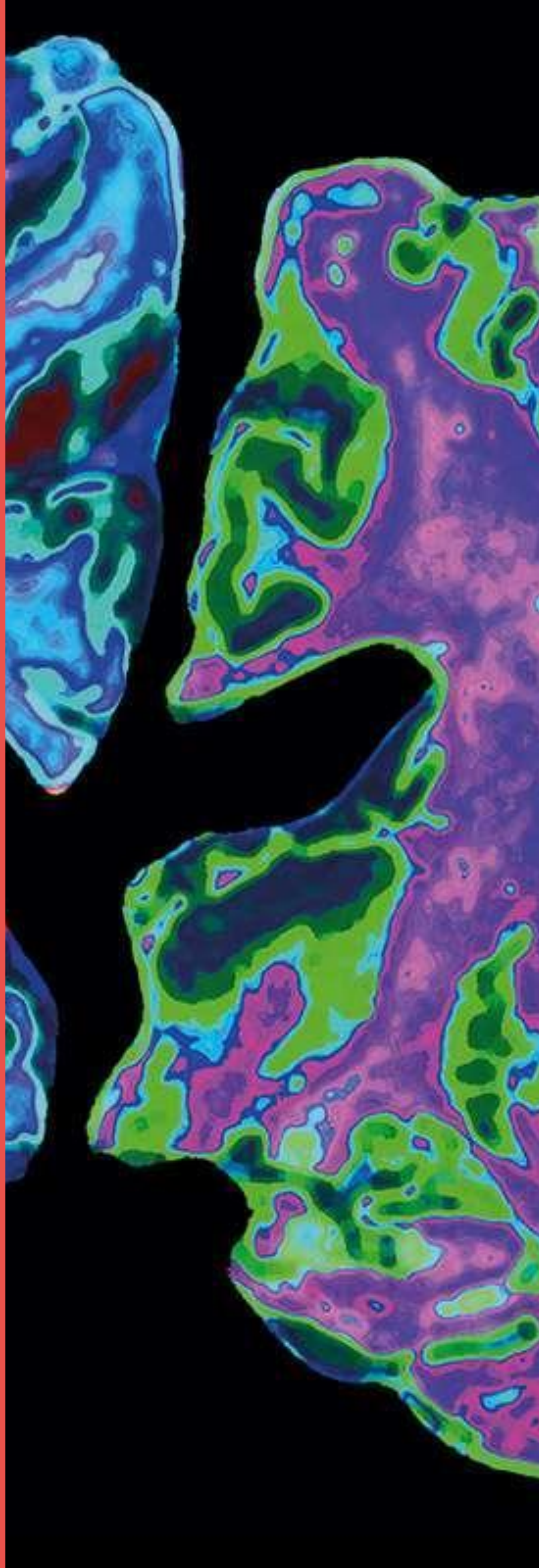
2. Classify patients

Patients into the **three diagnoses** based on:

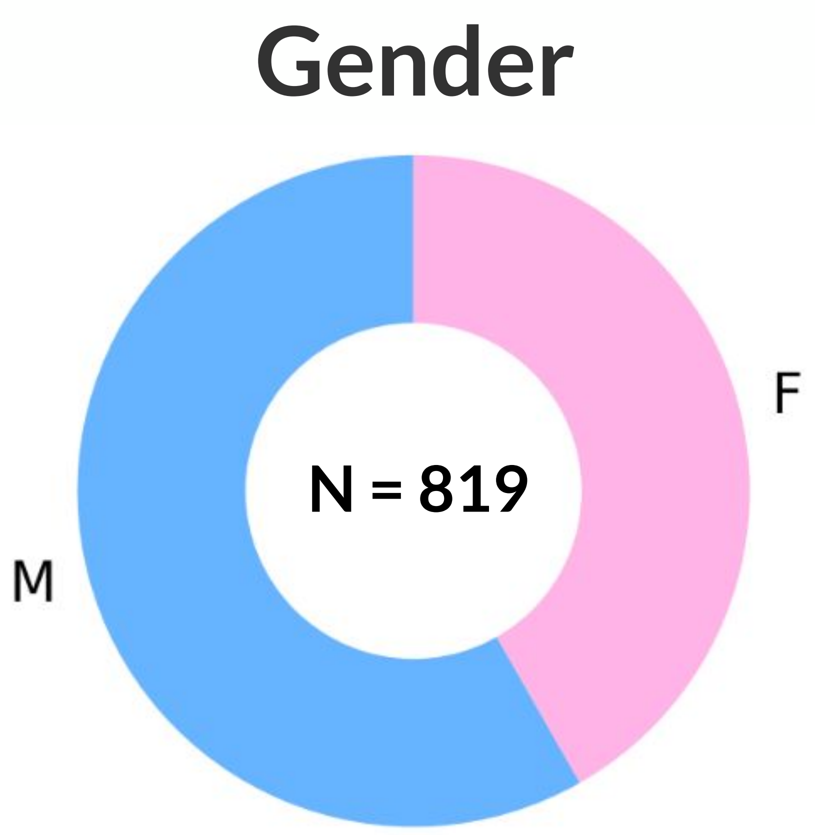
- demographic data
- genetic characteristics

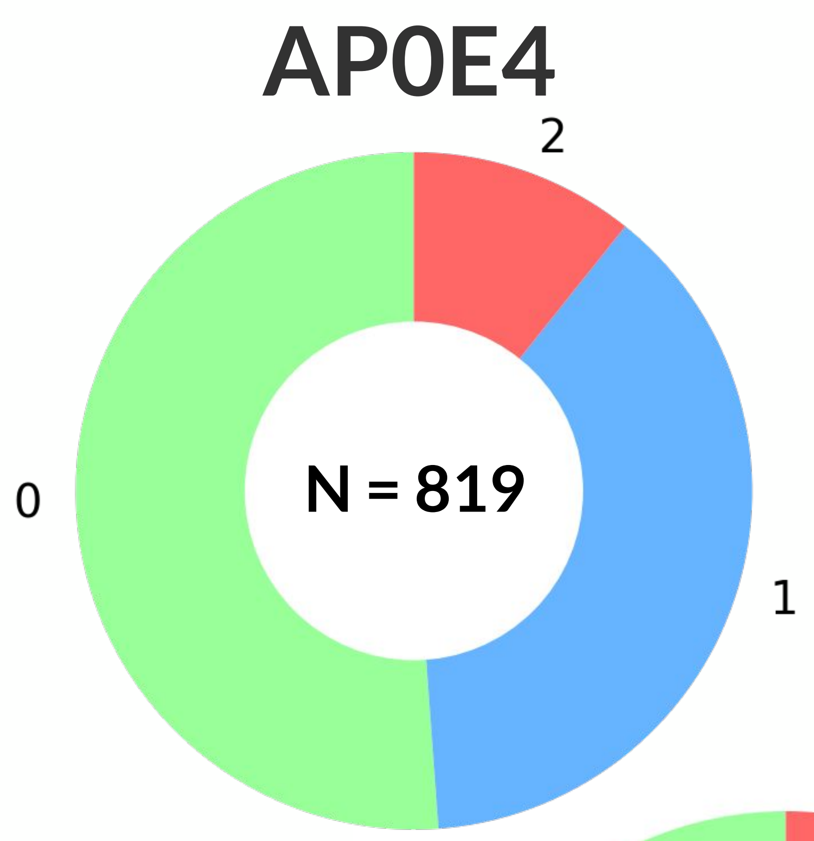
Methods:

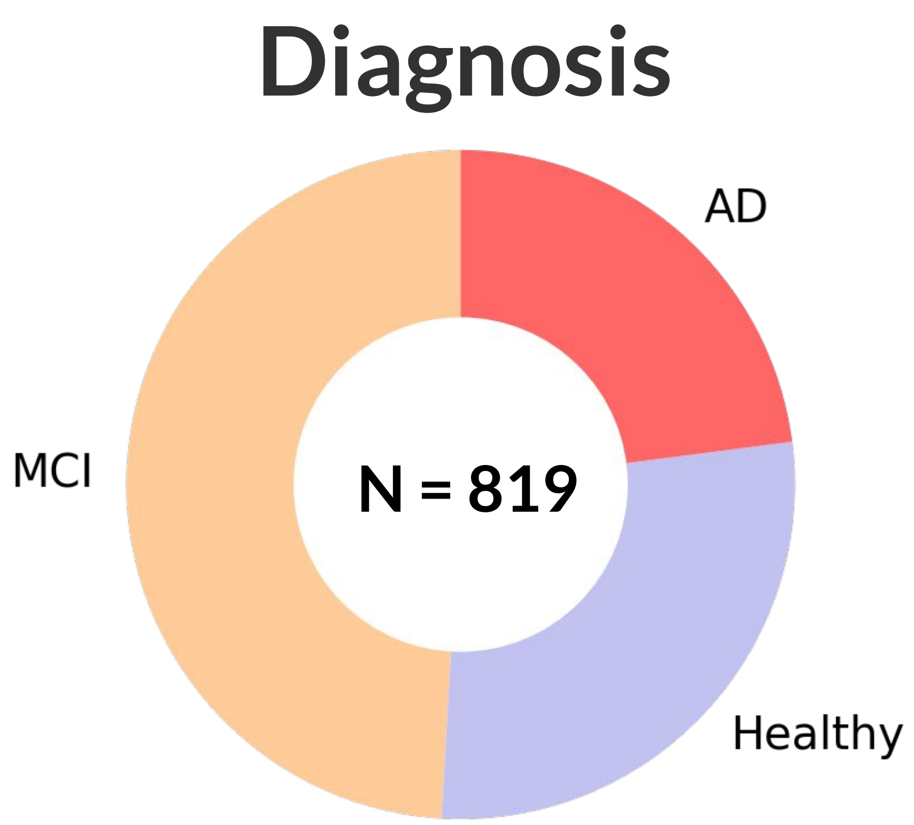
- Decision Tree (DT)
- Random Forest (RF)
- Neural Network (NN)
- Gradient Boosting Machine (GBM)

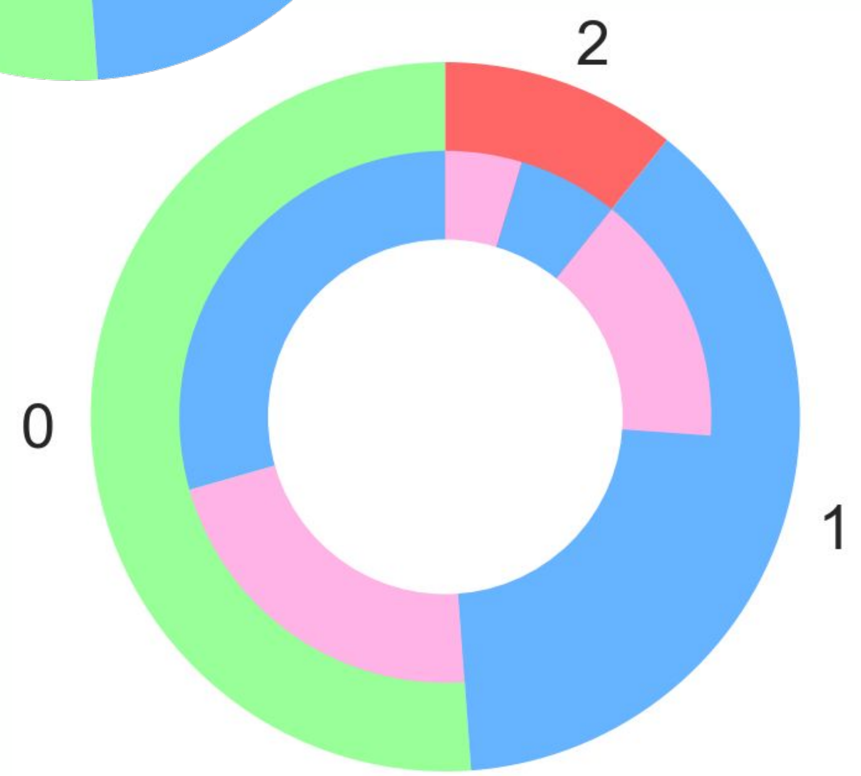


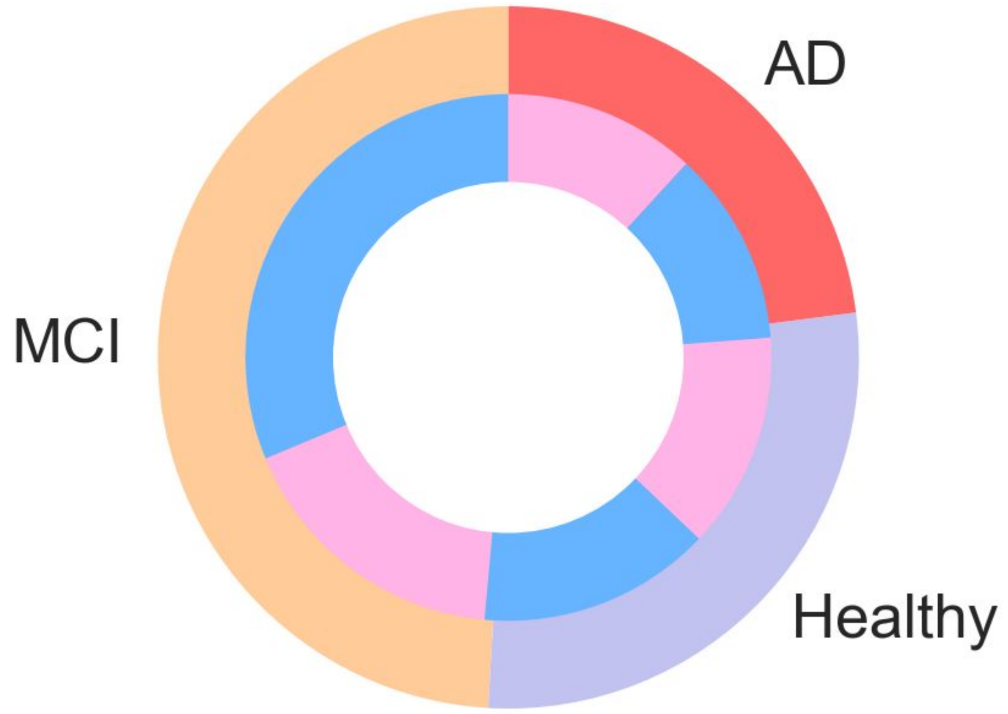
Exploratory Data Analysis

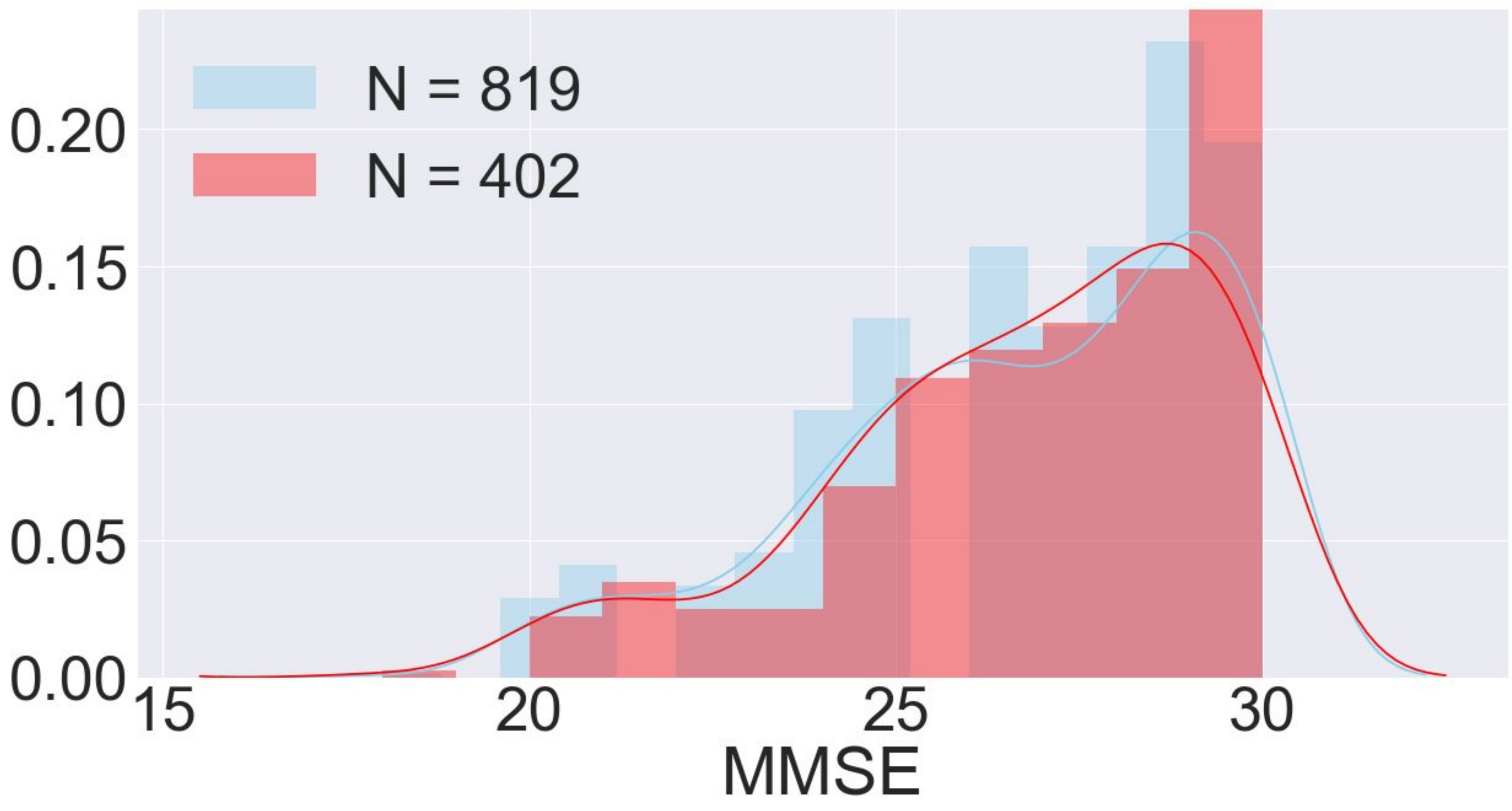


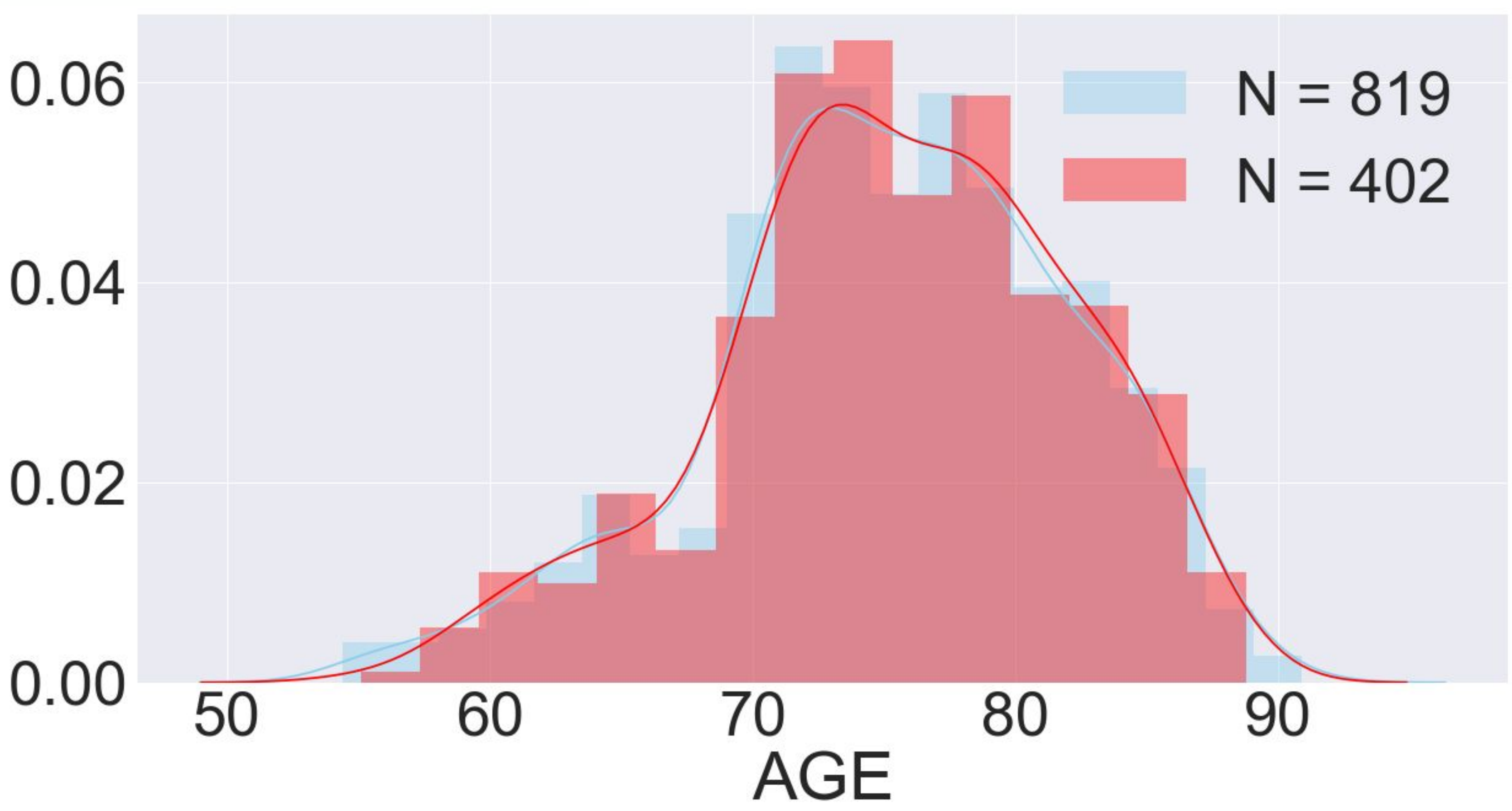


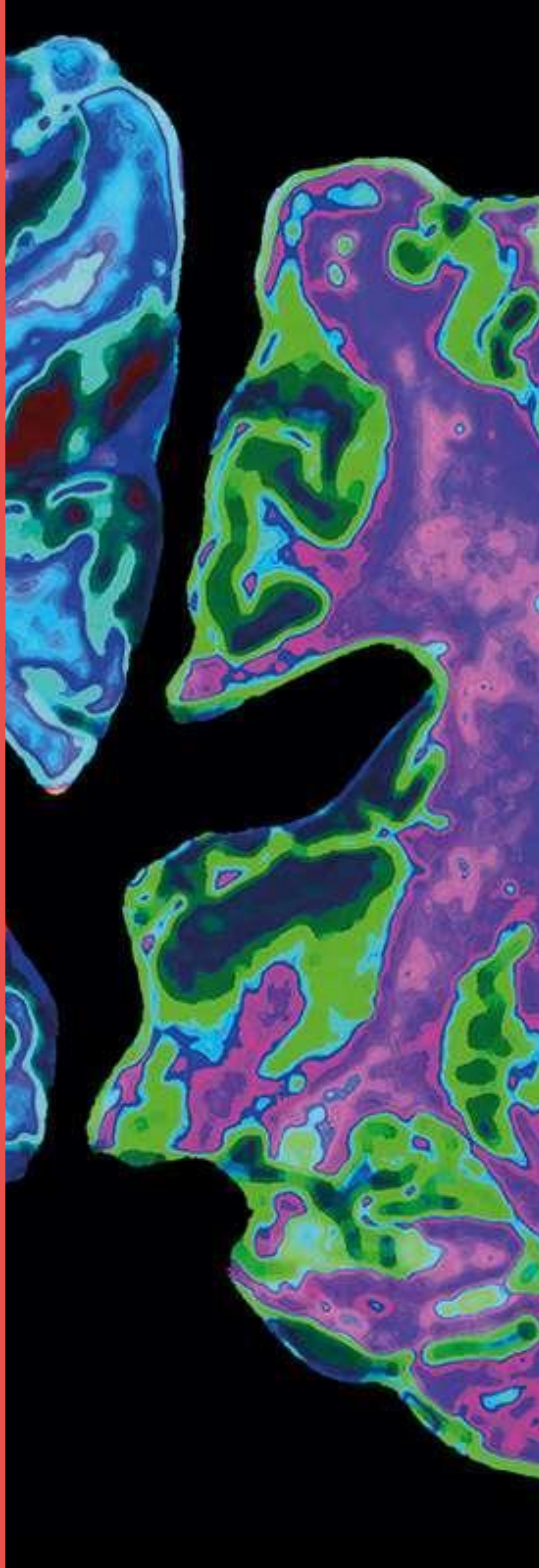






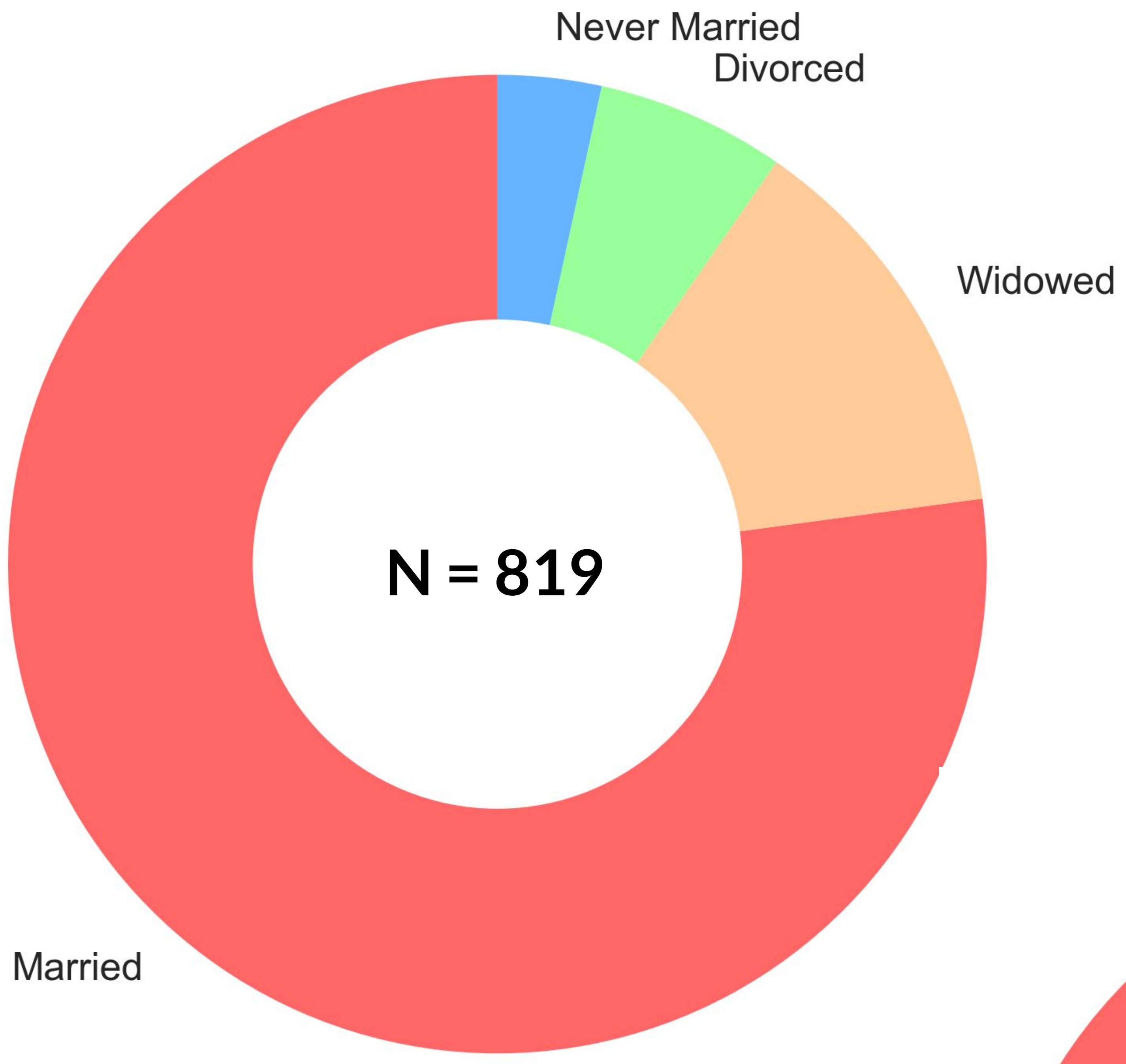




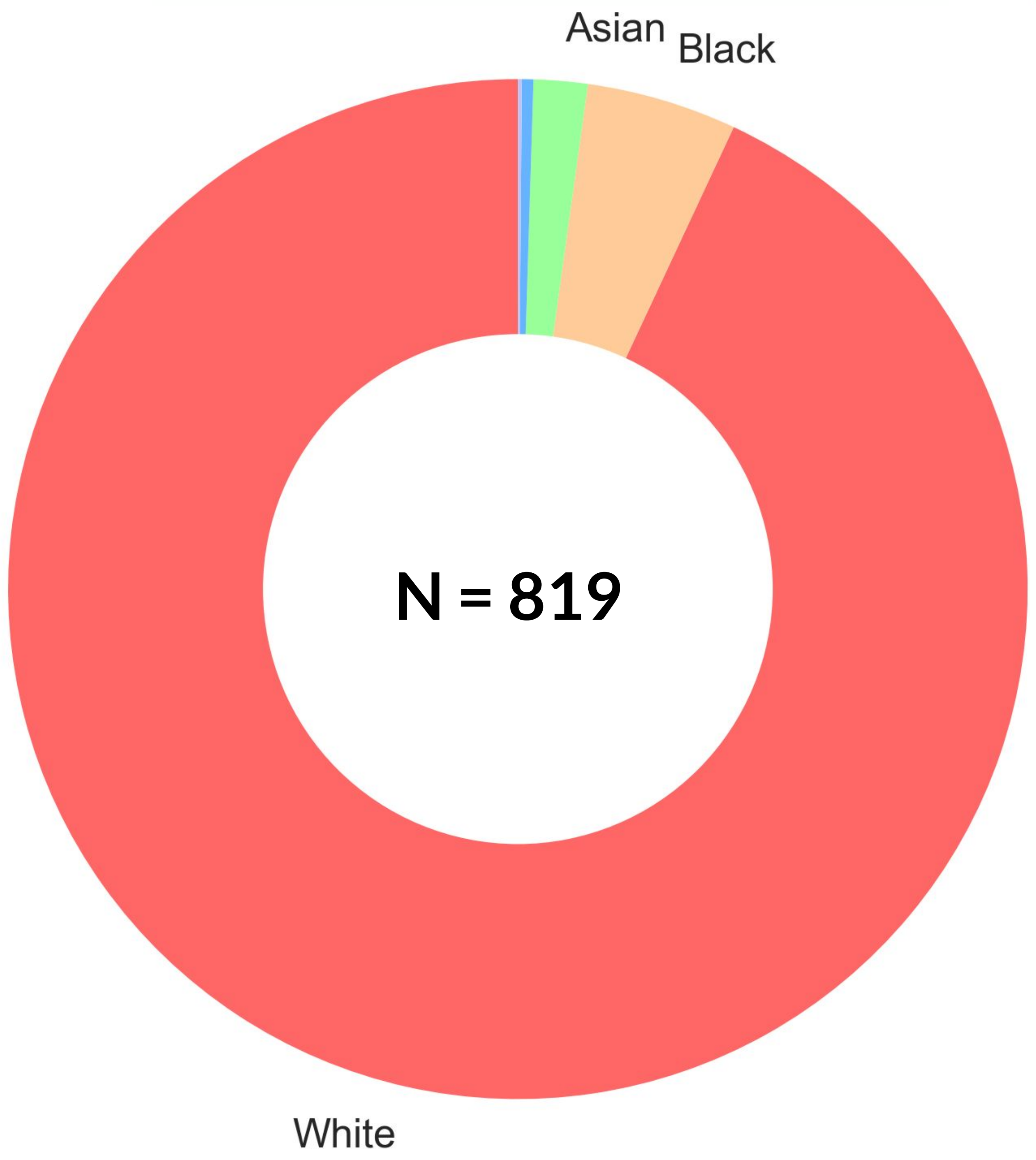


Exploratory Data Analysis

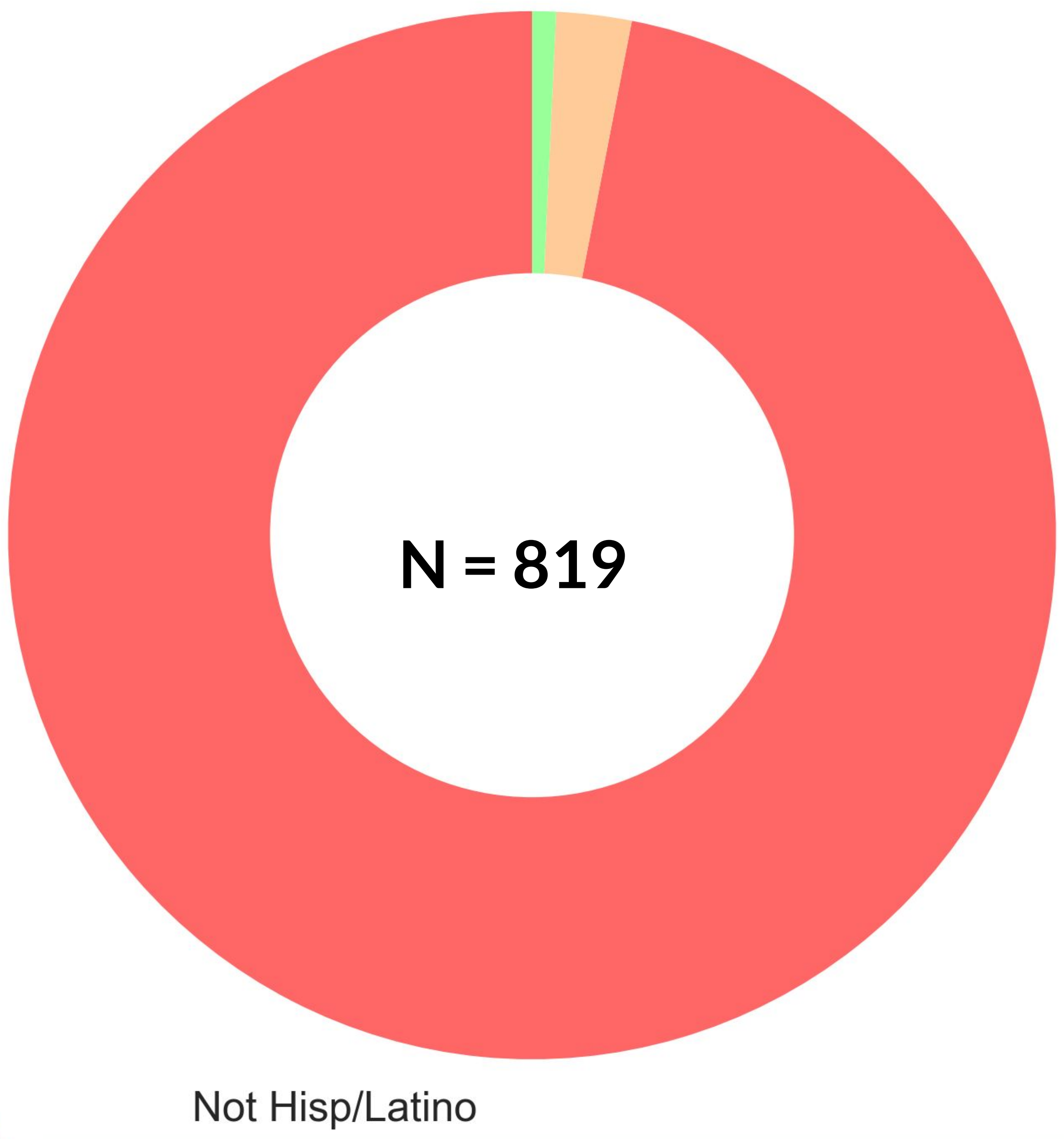
Married Status

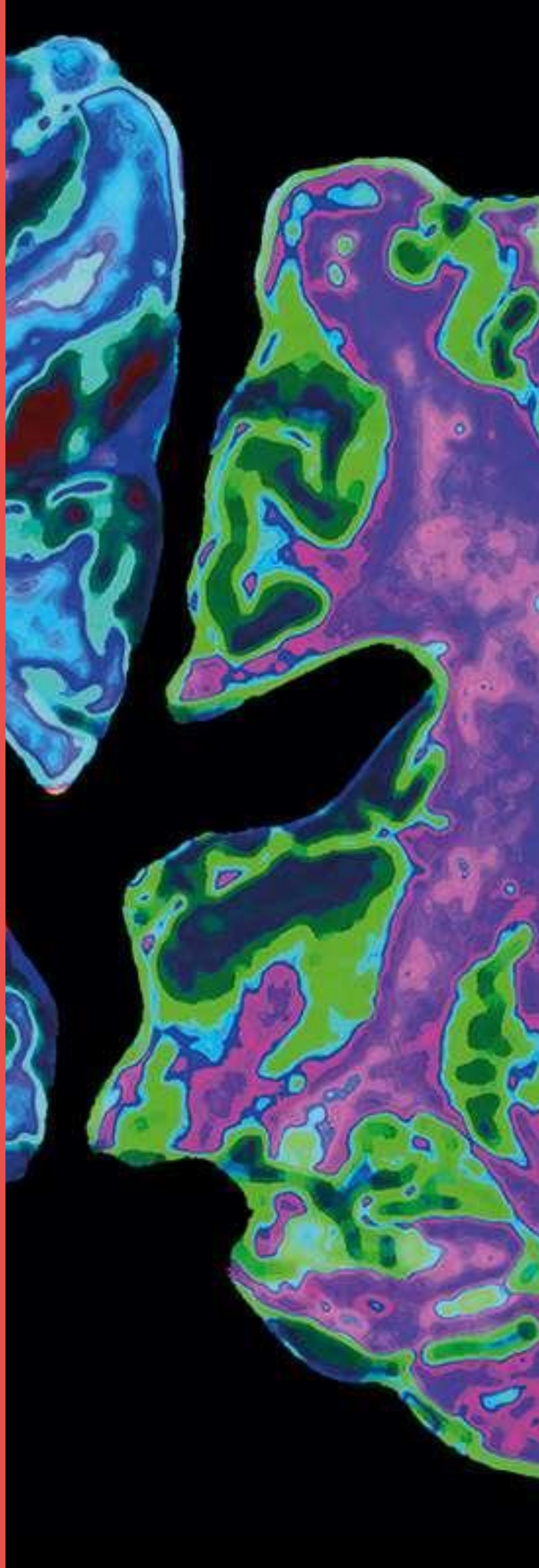


Race



Ethnicity



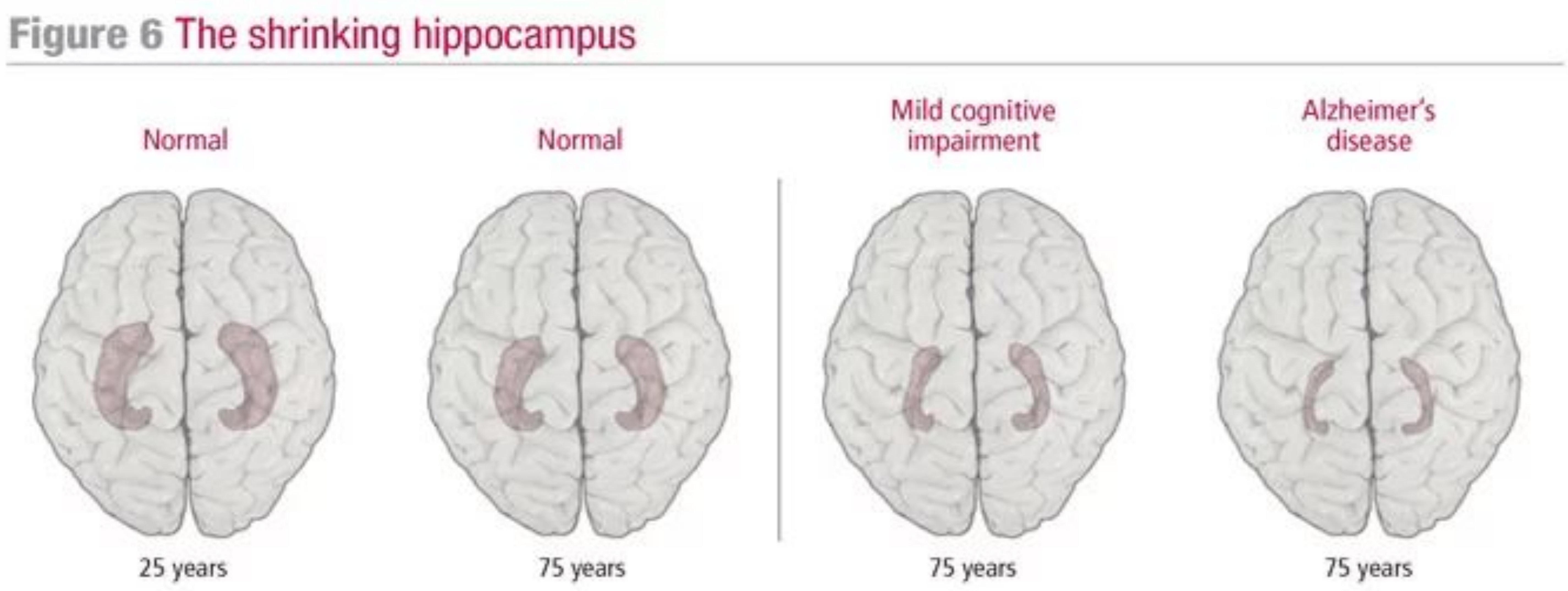


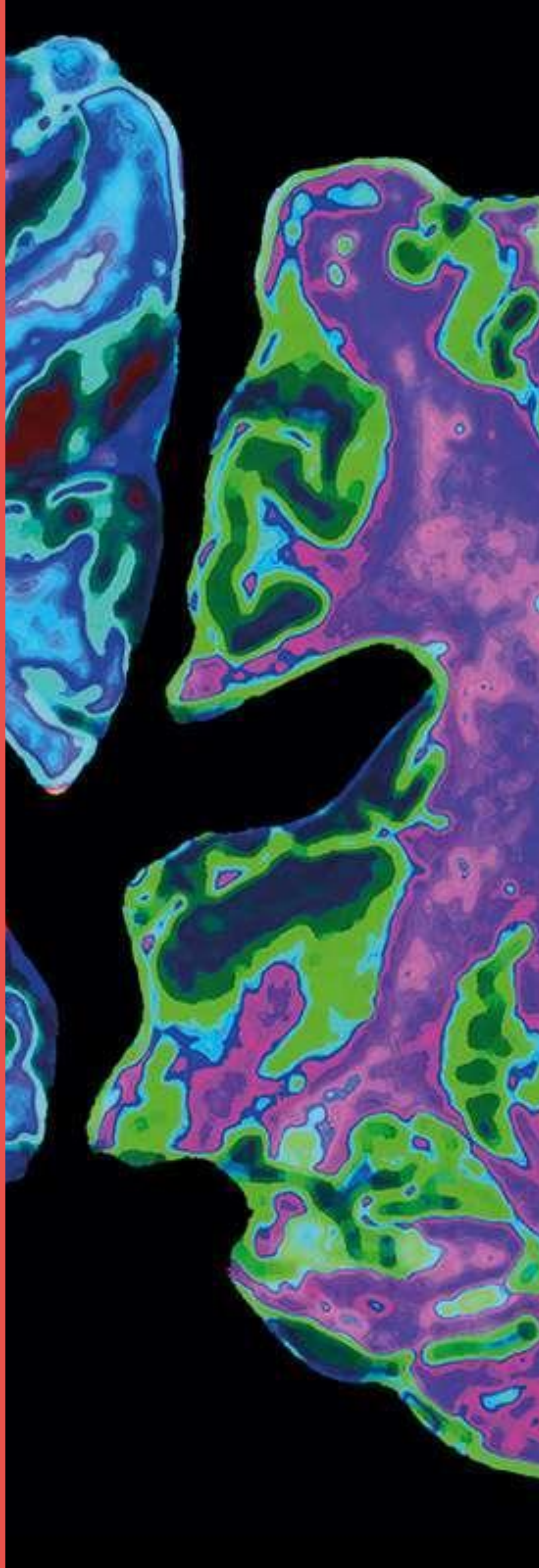
Exploratory Data Analysis

Healthy

MCI

AD





Classification Methods (Supervised)

Decision Tree

- Required little of work for data preparation
- Easy to interpret
- Base learner for RF and GBM

Neural Network

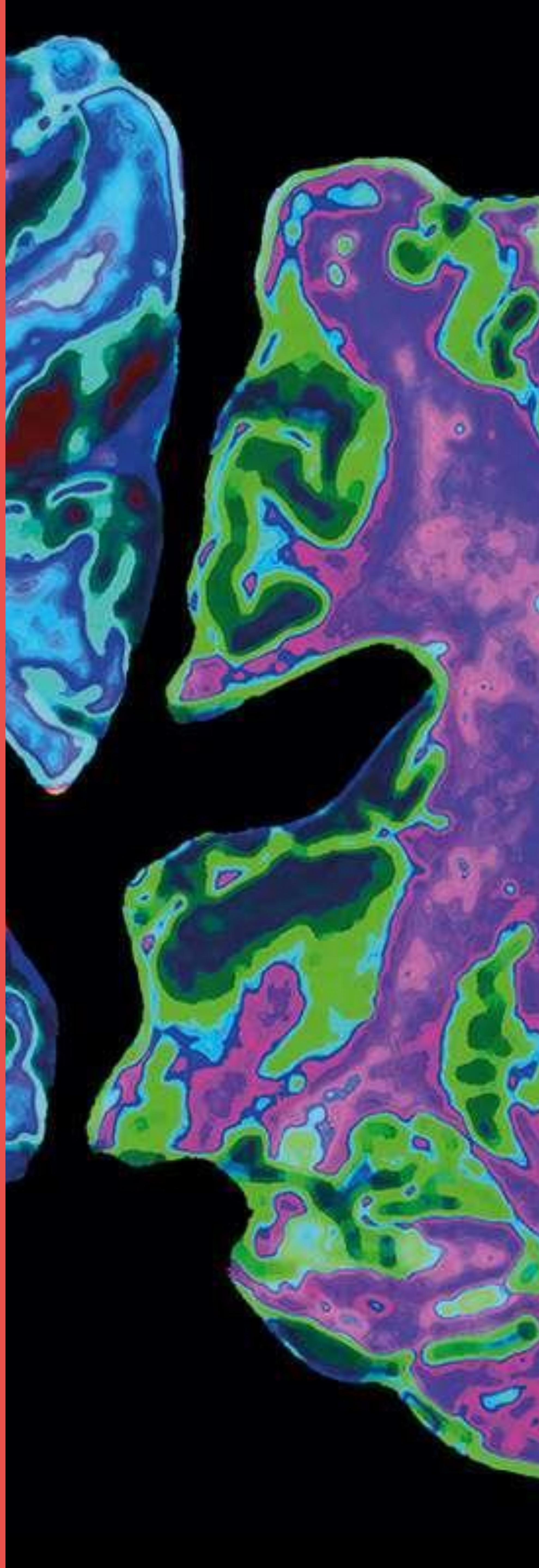
- Neural Network can used for classification problem
- Simulate the parameter and choose the best model base on MSE and accuracy

Random Forest

- Random Forest can used for classification problem
- Base learner as Decision Tree
- Low bias and high variance

Gradient Boosting Machine

- Gradient Boosting Machine can used for classification problem
- Base learner as Decision Tree
- High bias and low variance



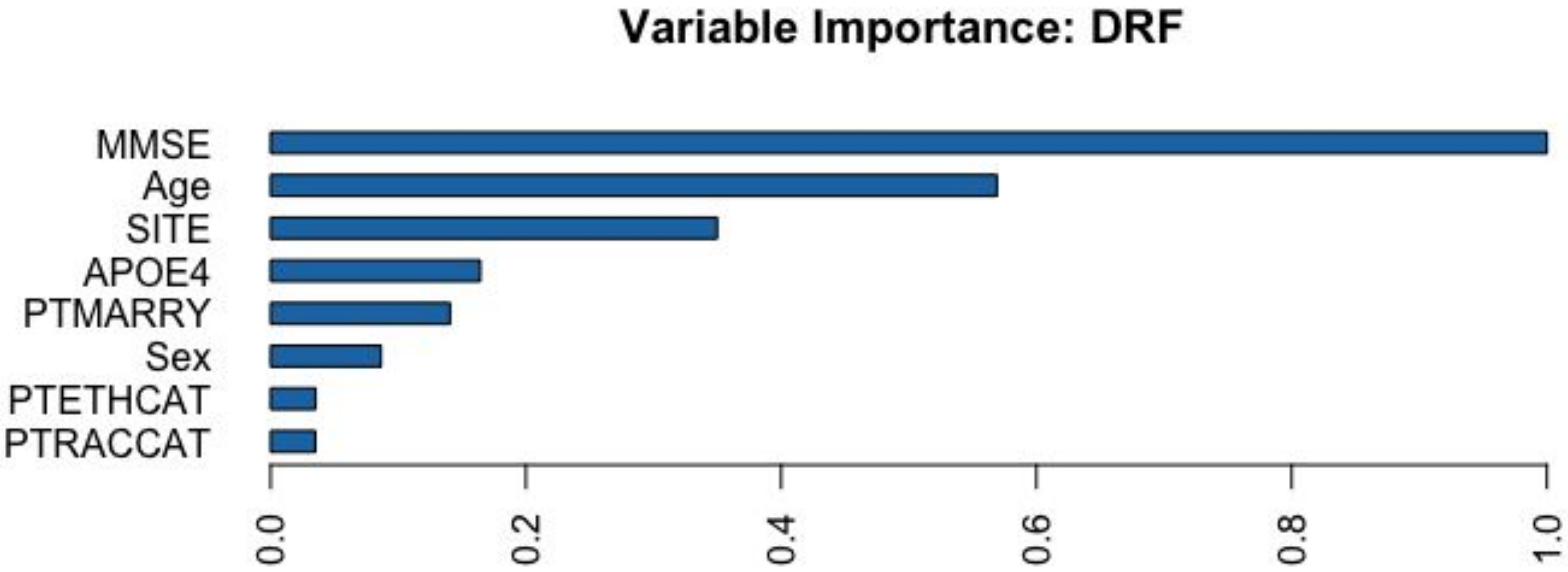
Neural Network Classification Result

Predicted

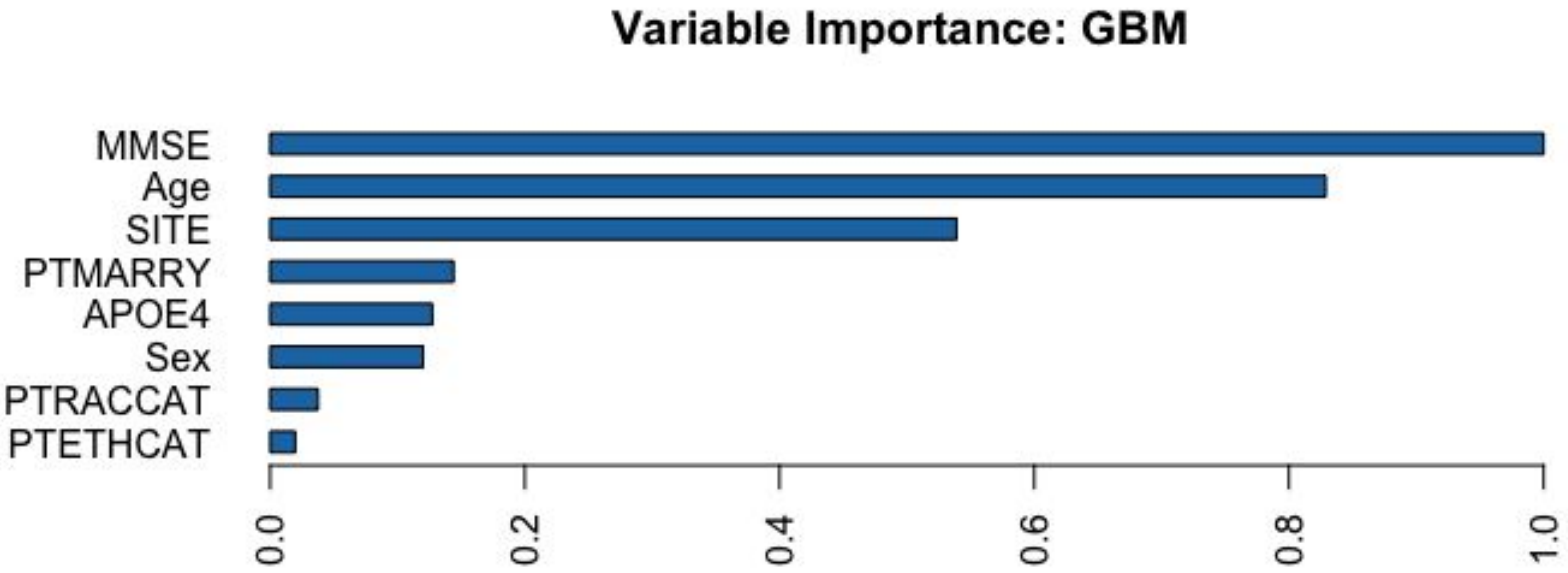
Actual

	AD	CN	LMCI	Error		Rate
AD	14	0	10	0.4167	=	10 / 24
CN	0	15	5	0.2500	=	5 / 20
LMCI	7	4	29	0.2750	=	11 / 40
Totals	21	19	44	0.3095	=	26 / 84

Variable Importance for Random Forest



Variable Importance for Gradient Boosting Machine



Classification Results: Accuracy

	AD	Healthy	MCI	Total
DT	**75%**	62.5%	73.2%	71.6%
NN	**75%**	85%	80%	79.8%
RF	41.7%	50%	80%	61.9%
GBM	70.8%	**90%**	**87.5%**	**83.3%**

Baseline: 33%

Characterizing PET Scans: Regularized Tensor-on-scalar Regression [3]

$$Y = \mathbf{X}\boldsymbol{\Gamma} + \varepsilon$$

Y ($n \times M$): vectorized images

$\mathbf{X}$ ($n \times p$): patient's data

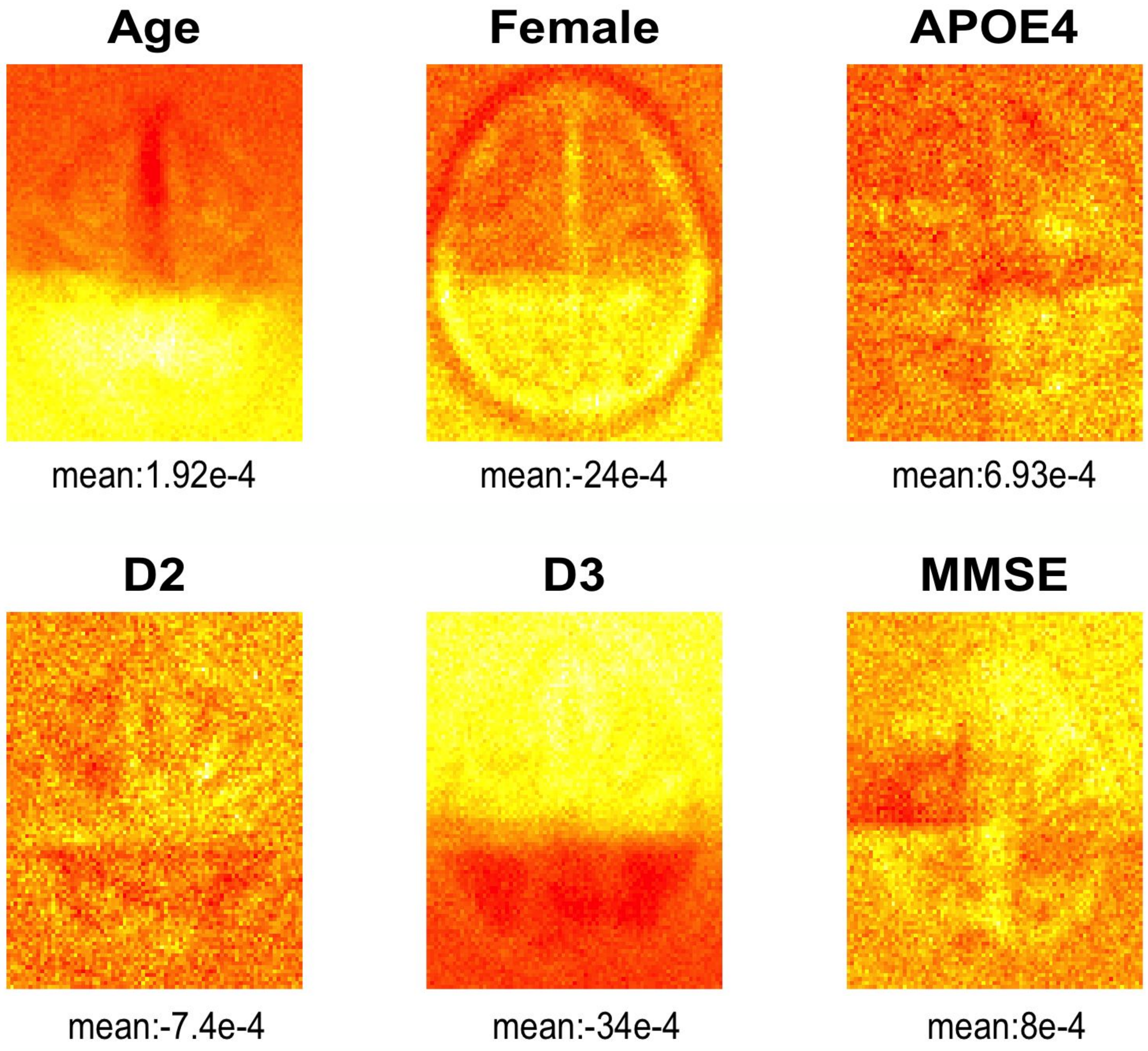
$\boldsymbol{\Gamma}$ ($p \times M$): coefficient to estimate

M: # picture voxels, e.g. $79 \times 95 = 7505$

n: # images/subjects, e.g. 402

p: # parameters in scalar data, e.g. 6

$$min \frac{1}{2} ||Y - X\Gamma||_F^2 + \lambda ||X\Gamma D||_{l_1}$$

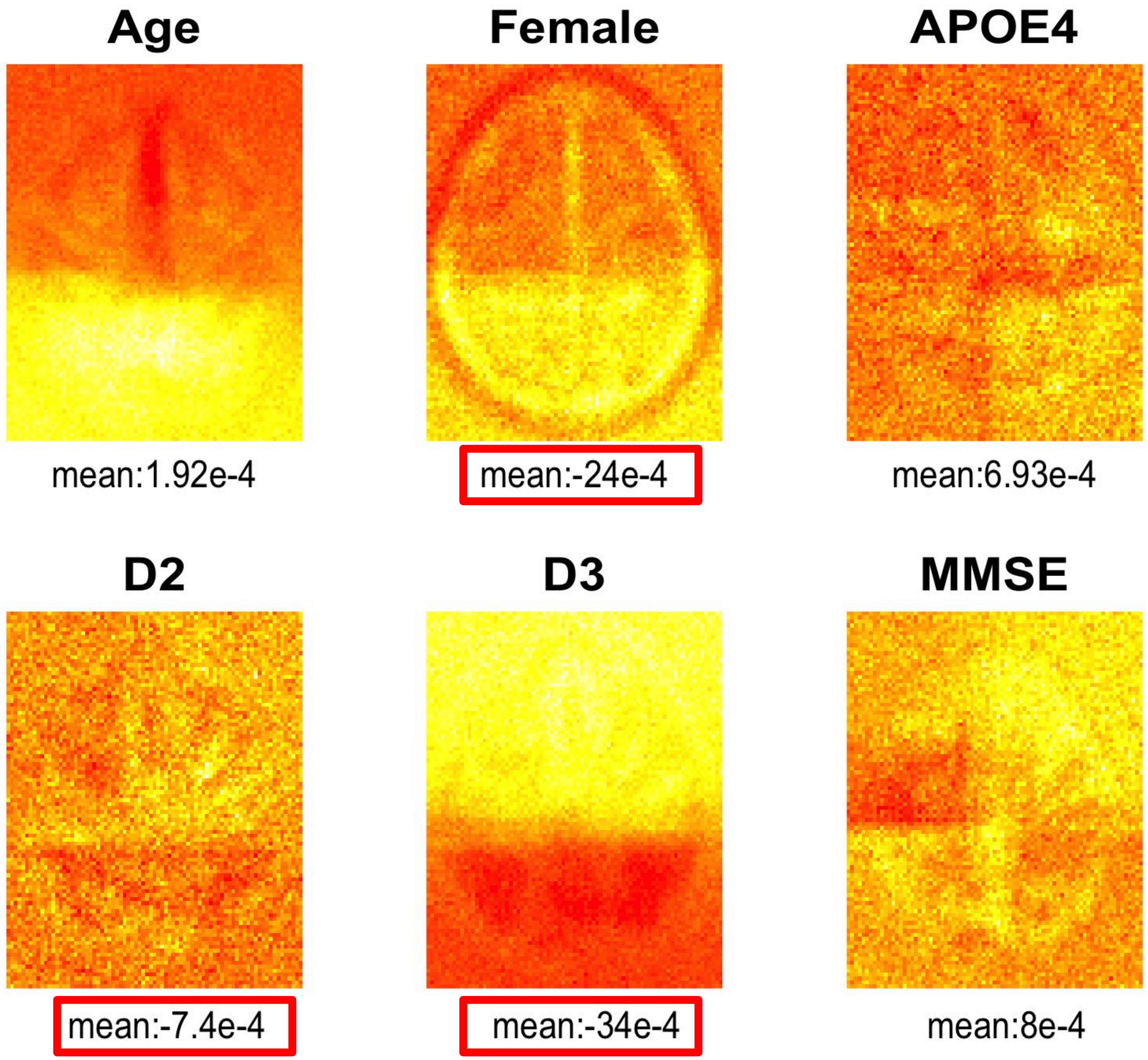


Characterizing PET Scans: Regularized Tensor-on-scalar Regression [3]

Diagnosis stage 2 and Diagnosis stage 3 results in a decrease of brain activity compared with Diagnosis stage 1.

Lower MMSE score correlates with a lower brain activity.

Higher age and non-zero APOE4 type correlates with a higher brain activity. Thus, collinearity issues still exist.



Conclusions

Important Features

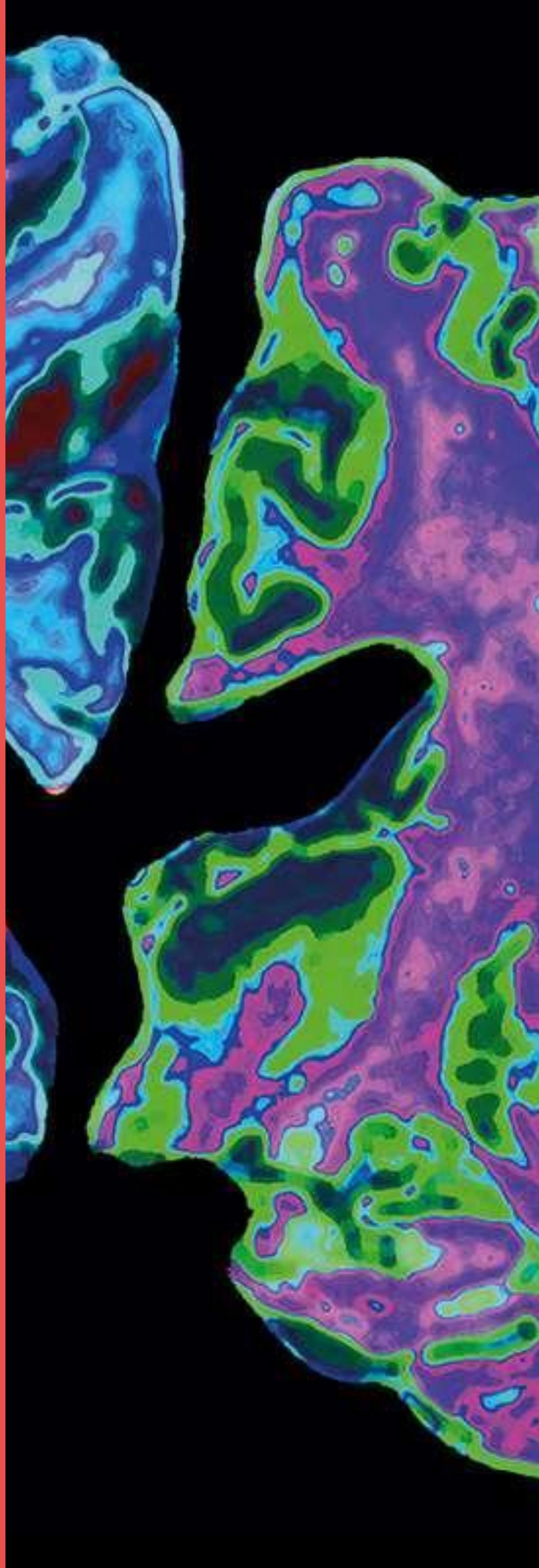
- Age
- MMSE
- Site

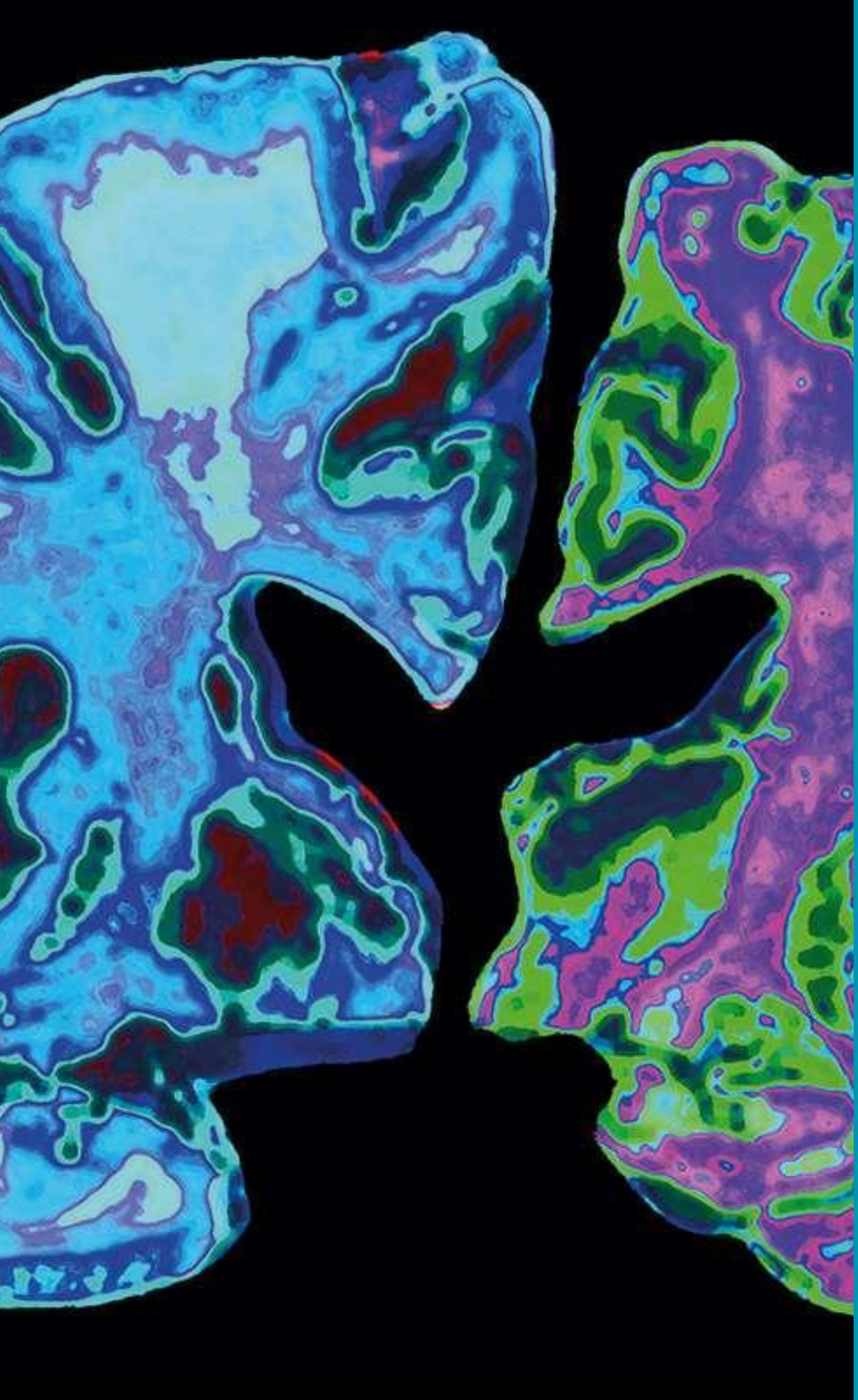
Classification

Significant accuracy above baseline can be achieved - could be used to help doctors make diagnoses

Future Works

- Improve the efficiency of tensor-on-scalar regression
- Compare the coefficient map with result of other algorithms





SAMSI
NC State University
Dr. Xinyi Li
Dr. Mansoor Haider
Thomas Gehrmann

THANK YOU!

Reference

[1] Alzheimer's and Dementia. (n.d.). Retrieved from https://www.alz.org/alzheimer_s_dementia

[2] Powles, R. (2016, August 18). Why Does ApoE4 Increase Alzheimer's Risk? Retrieved from http://longevityreporter.org/blog/2016/8/18/why-does-apoe4-increase-alzheimers-risk

[3] Total Variation Regularized Tensor-on-scalar Regression. (n.d.). Retrieved from https://arxiv.org/pdf/1703.05264.pdf

[4] Overview about h2o. Retrieved from http://docs.h2o.ai/h2o/latest-stable/h2o-docs/index.html

Gradient Boosting Machine with Parameter

```
Confusion Matrix: Row labels: Actual class; Column labels: Predicted class
       AD CN LMCI  Error       Rate
AD     17  1    6 0.2917 =  7 / 24
CN      1 18    1 0.1000 =  2 / 20
LMCI    2  3   35 0.1250 =  5 / 40
Totals 20 22   42 0.1667 = 14 / 84
```

```
Confusion Matrix: Row labels: Actual class; Column labels: Predicted class
       AD CN LMCI  Error       Rate
AD     15  0    9 0.3750 =  9 / 24
CN      0 16    4 0.2000 =  4 / 20
LMCI    4  4   32 0.2000 =  8 / 40
Totals 19 20   45 0.2500 = 21 / 84
```

```
Confusion Matrix: Row labels: Actual class; Column labels: Predicted class
       AD CN LMCI  Error       Rate
AD     12  0   10 0.4545 = 10 / 22
CN      0 12    3 0.2000 =  3 / 15
LMCI    6  3   36 0.2000 =  9 / 45
Totals 18 15   49 0.2683 = 22 / 82
```

Best Neural Network model base on simulate parameter

```
> nn1_confusion_best_model_mse
Confusion Matrix: Row labels: Actual class; Column labels: Predicted class
       AD CN LMCI  Error       Rate
AD     13  0   11 0.4583 = 11 / 24
CN      0 15    5 0.2500 =  5 / 20
LMCI    5  8   27 0.3250 = 13 / 40
Totals 18 23   43 0.3452 = 29 / 84
> nn1_confusion_best_model_accuracy
Confusion Matrix: Row labels: Actual class; Column labels: Predicted class
       AD CN LMCI  Error       Rate
AD     18  1    5 0.2500 =  6 / 24
CN      0 17    3 0.1500 =  3 / 20
LMCI    2  6   32 0.2000 =  8 / 40
Totals 20 24   40 0.2024 = 17 / 84
```

Random Forest Classification

Confusion Matrix: Row labels: Actual class; Column labels: Predicted class

	AD	CN	LMCI	Error	Rate
AD	10	1	13	0.5833	= 14 / 24
CN	1	10	9	0.5000	= 10 / 20
LMCI	4	4	32	0.2000	= 8 / 40
Totals	15	15	54	0.3810	= 32 / 84

Decision Tree Classification Result

Confusion Matrix and Statistics

	Reference		
Prediction	AD	CN	LMCI
AD	18	1	5
CN	0	10	6
LMCI	1	10	30

Overall Statistics

Accuracy : 0.716
95% CI : (0.605, 0.8107)
No Information Rate : 0.5062
P-Value [Acc > NIR] : 9.833e-05

Kappa : 0.5443

Mcnemar's Test P-Value : 0.1979

Statistics by Class:

	Class: AD	Class: CN	Class: LMCI
Sensitivity	0.9474	0.4762	0.7317
Specificity	0.9032	0.9000	0.7250
Pos Pred Value	0.7500	0.6250	0.7317
Neg Pred Value	0.9825	0.8308	0.7250
Prevalence	0.2346	0.2593	0.5062
Detection Rate	0.2222	0.1235	0.3704
Detection Prevalence	0.2963	0.1975	0.5062
Balanced Accuracy	0.9253	0.6881	0.7284

Principal Component Analysis