Using the generalized additive model regression algorithm to predict depression levels in individuals with Alzheimer's and mild cognitive impairment.

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Introduction

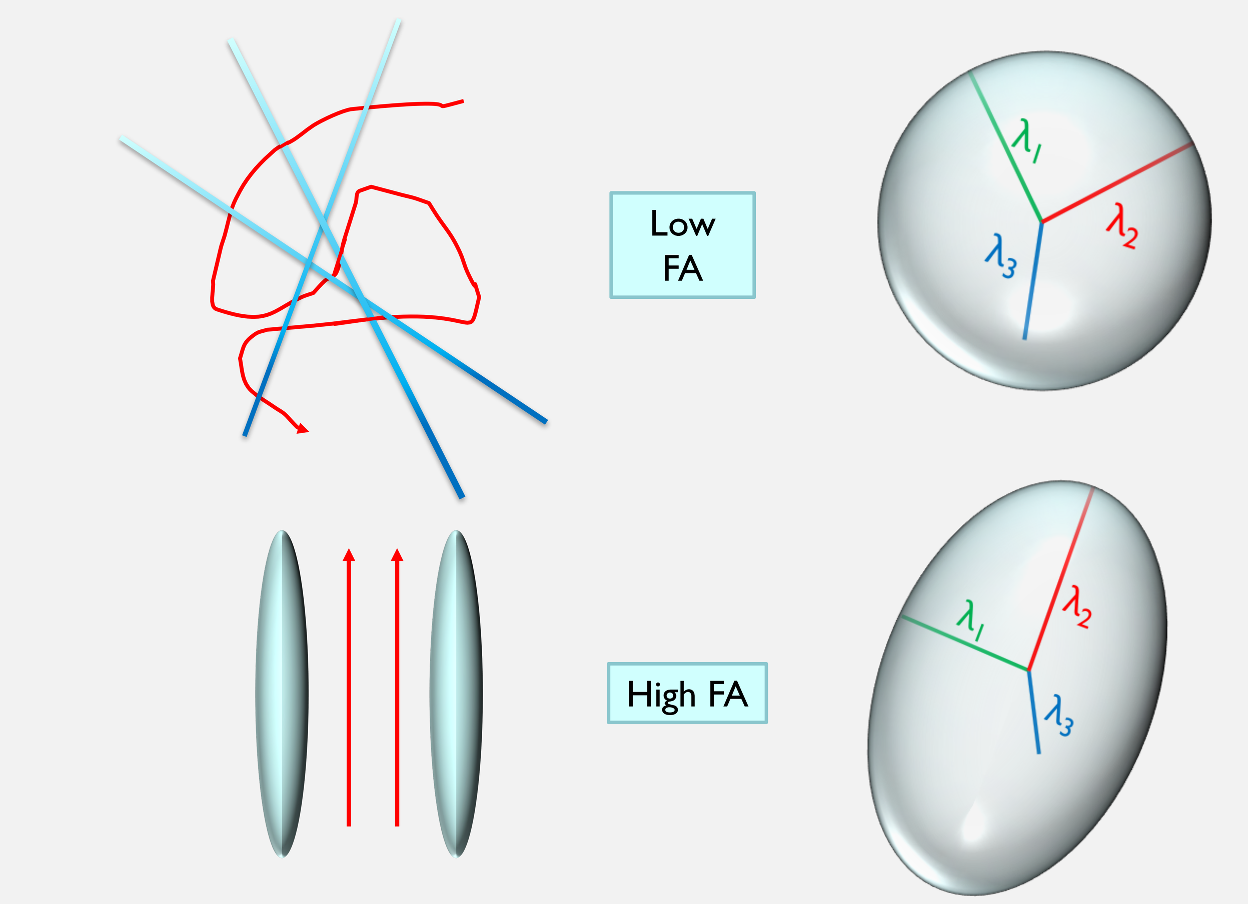
We attempted to use the generalized additive model to predict depression levels from microstructural integrity in individuals with healthy subjects and individuals with Alzheimer's Disease (AD)—a neurodegenerative disease marked primarily by decline in episodic memory—and mild cognitive impairment (MCI). Our two main goals were to:

(1) Understand the relationship between depression levels and white matter microstructural integrity in the brain.

(2) Predict depression levels based on microstructural integrity of white matter.

Background

- **Diffusion Tensor Imaging (DTI):** A method of measuring and imaging water diffusion in the brain used to answer specific research questions using "tensors" to represent water diffusion directionality in the brain.
- **Fractional Anisotropy (FA):** A measure of constraint in the directionality of water diffusion:



$$FA = \sqrt{\frac{1}{2}}\frac{\sqrt{(\lambda_1-\lambda_2)^2+(\lambda_2-\lambda_3)^2+(\lambda_3-\lambda_1)^2}}{\sqrt{{\lambda_1}^2+{\lambda_2}^2+{\lambda_3}^2}}$$

Background

- **Geriatric Depression Scale (GDS):** 15-item measure of depression. Scores over 4 are considered "depressed".
- **Generalized Additive Model (GAM):** Expansion of the generalized linear model built from the sum of non-parametric functions for corresponding variables.

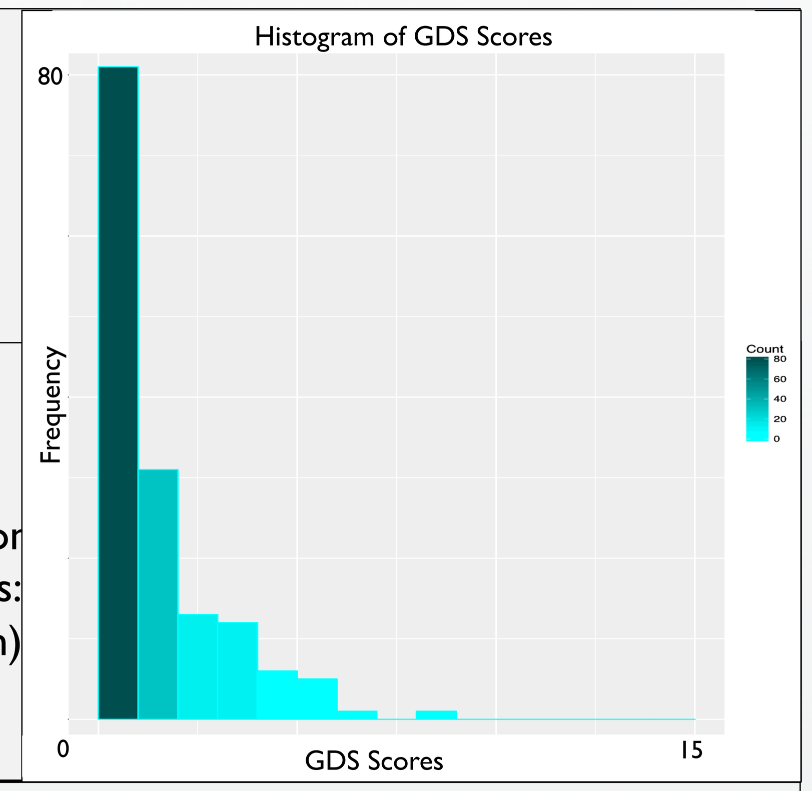
Construction of the GAM

$$\underbrace{y = \beta_0 + f_1(x_1) + \cdots + fn(xn)}\quad \text{prediction model}$$

$$\underbrace{\sum_{i=1}^{n}(y_i - f(x_i))^2}_{\text{minimizes squares}} + \underbrace{\lambda\int_a^b [f''(x_i)^2]dx}_{\text{measures smoothness of function}}\quad \text{smoothing spline}$$

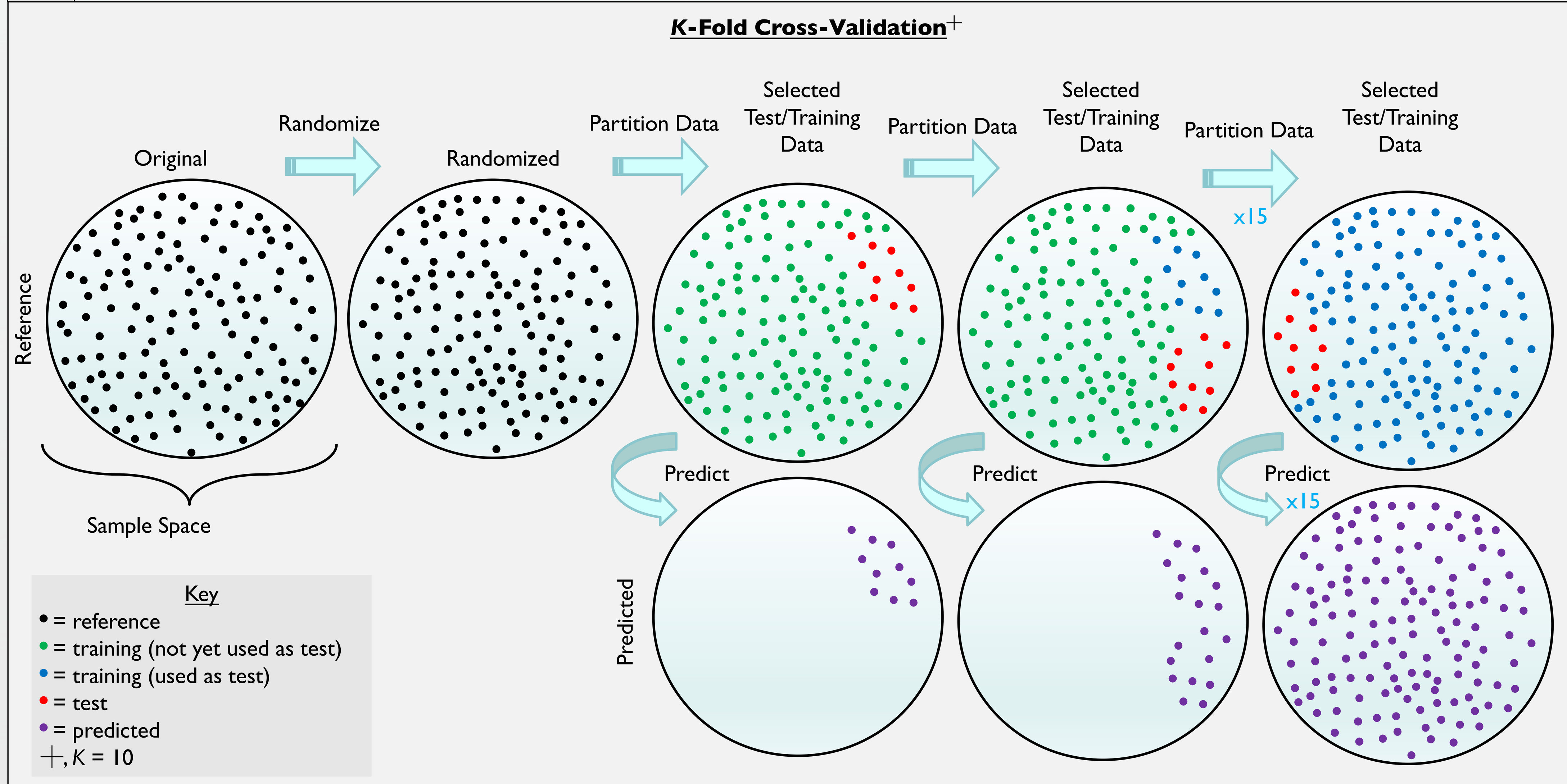
Methods

Subjects
- AD, MCI, or healthy controls (n=150)
  - Age: Mean = 73.30, S^2=50.89, Range=[55.0,0 90.30]
  - Gender: F_n=58, M_n=92
- From the Alzheimer's Disease Neuroimaging Initiative (ADNI)*
- Data: GDS scores and 56 FA means



Study 1: Linear Regression
- Tested simple model first for more simple interpretation of how variables are related.
- First, built linear model. Then, used backwards stepwise regression to omit non-significant terms (α=0.05) with the following models:
  - GDS predicted by demographic variables (age, sex, education)
  - GDS predicted by FA means.
  - GDS predicted by FA means and demographic variables

Study 2: GAM regression: model with moderate flexibility and interpretability
- Partitioned data between testing and training data. Used GAM to predict GDS scores from training data.



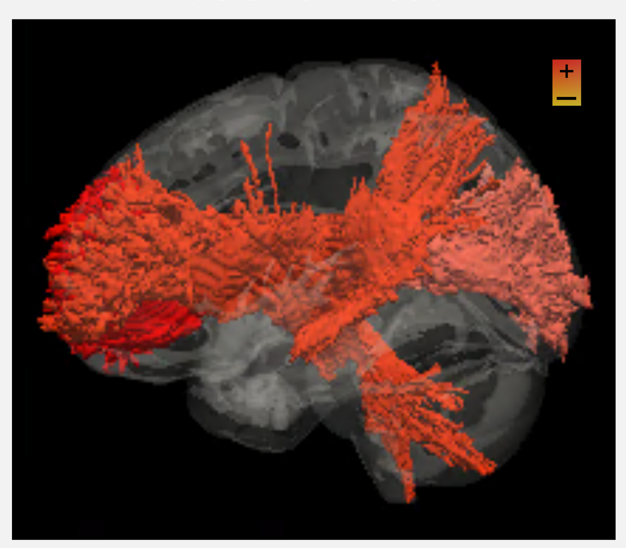
Methods

Assessing GAM:
1. **MSE**: measures the difference between the predicted and reference depression scores.
2. **Accuracy:** proportion of correctly predicted values
3. **Sensitivity:** proportion of positives that are true positives.
4. **Specificity:** proportion of negatives that are true negatives.
5. **Area Under the Receiver Operator Curve:** plots true positive rate (sensitivity) over false positive rate (1- sensitivity.).

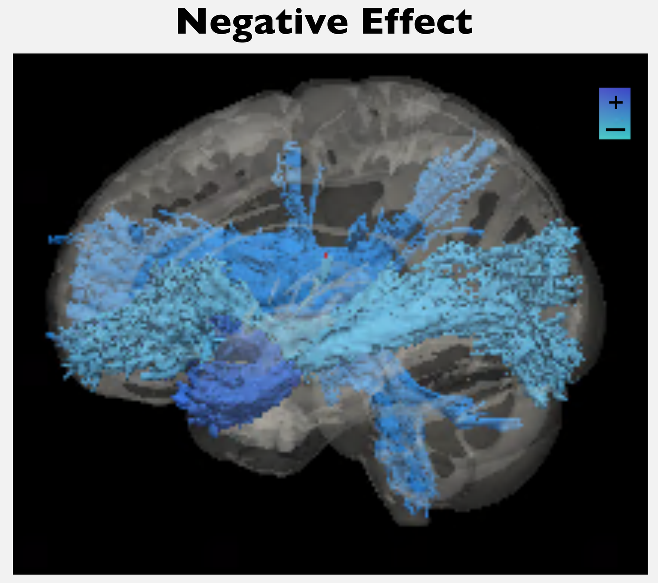
Results

Study 1
- No demographic variables were significant at α=0.05.
- Variance explained by model without demographic variables:
  - 24.15%
- Variance explained by model including demographic variables:
  - 00.41%
- No Significant variables after correcting for multiple comparisons with Bonferroni adjustment.

Positive Effect



Negative Effect



Results

Study 2

Continuous Outcome

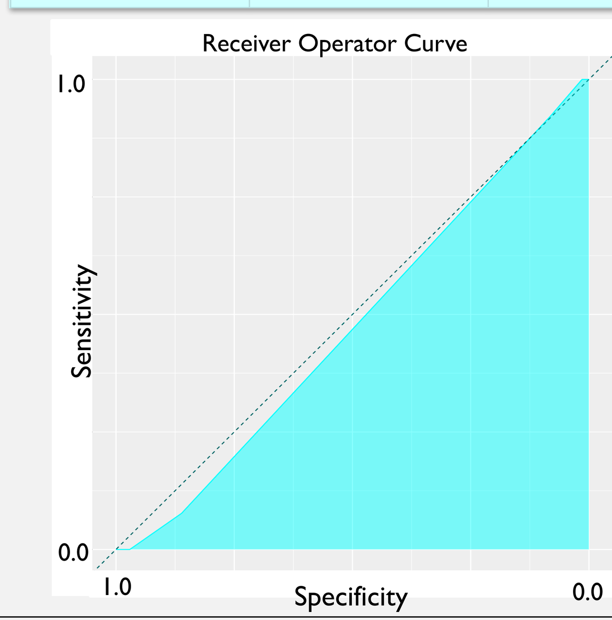
Points from Reference Value	Accuracy
0	0.21
1	0.46
2	0.71
3	0.81

Binary Outcome

Measure	Estimate
Accuracy	0.79
Sensitivity	0.86
Specificity	0.00
MSE	0.19
Area Under ROC	0.43

Confusion Matrix

Reference \ Predicted	0	1
0	118	13
1	19	0



Conclusion

Study 1
- None of the coefficients were significant after correction for multiple comparisons with Bonferroni adjustment for the models with and without demographic variables.

Study 2
- The GAM did a poor job at predicting depression, when modeled as both as a continuous and binary outcome.

Acknowledgements

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***ADNI | Alzheimer's Disease Neuroimaging Initiative." *ADNI*. Alzheimer's Disease Neuroimaging Initiative, n.d. Web. 16 May 2017.** *National Institutes of Health Grant U01 AG024904*