Exploring Resting-State fMRI-Based Biomarkers for Alzheimer's Disease Detection Using a Functional Data Analysis Approach

Ido JI [1]

[1]The department of Bio AI Convergence, Chungnam National University

Research Background

AD and RS-fMRI

- AD
  Alzheimer's disease (AD) is an incurable brain disorder that slowly destroys memory and thinking skills with brain atrophy.
- RS-fMRI
  Resting-state fMRI (rs-fMRI) enables the identification of disrupted functional connectivity patterns and neural network alterations, which can serve as potential biomarkers for early diagnosis and disease progression monitoring.
- BOLD signal
  The BOLD (Blood-oxygen-level-dependent) signal of fMRI is an indirect measure of neural activity in the brain.

Research Objective

Functional data analysis (FDA)

- FDA
  Functional data analysis (FDA) is a statistical approach for analyzing and modeling data that are observed as continuous functions or curves, often collected over time or space.
- Time-Series Data
  BOLD signal can be regarded as a time series data, so the signal can be treated as a continuous function using FDA. However, this approach have been understudied in AD research.

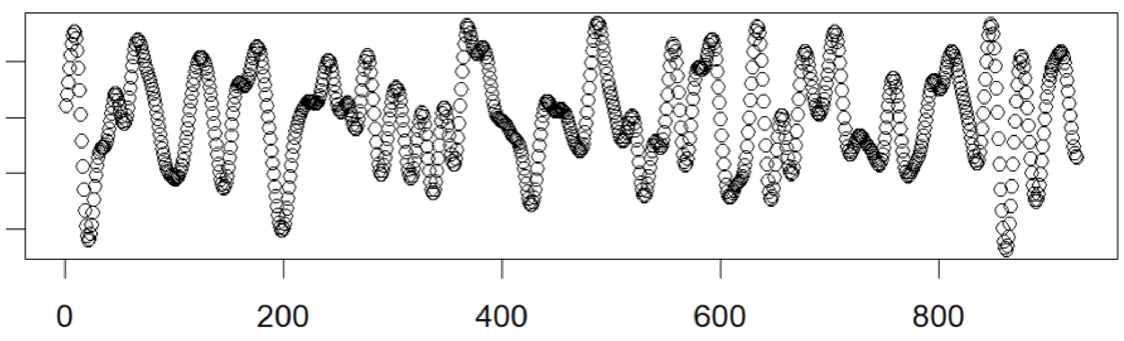


Figure 1. A BOLD signal observed discretely

objectives

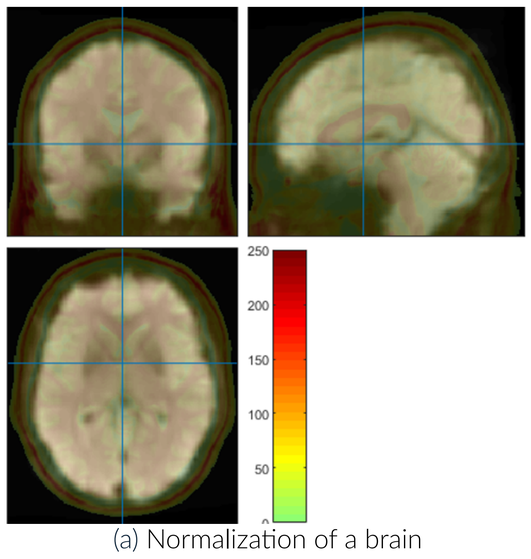
- Objective 1:
  To identify the brain regions of interest (ROIs) that significantly impact Alzheimer's disease (AD) detection
- Objective 2:
  To demonstrate that FDA approach leads to improved classification performance when compared to the traditional functional connectivity method

Data acquisition

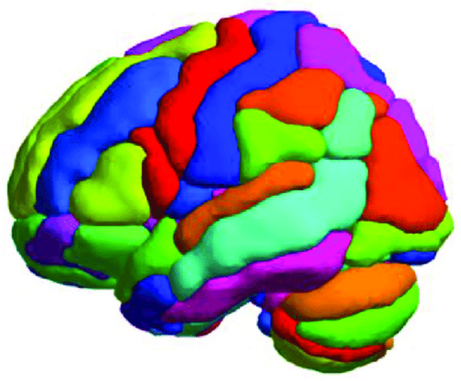
- The rs-fMRI data was acquired from ADNI(Alzheimer's Disease Neuroimaging Initiative).
- The subjects were 24 AD and 221 CN.
- For the preprocessing, MATLAB, DPABI, and SPM12 were used.

Preprocessing pipeline

- Slice Timing Correction
- Head Motion Correction
- Nuisance Covariates Regression
- Filtering signals
- Normalization using EPI template
- Extracting BOLD signals from each ROI (Regions of interest)



(a) Normalization of a brain



(b) AAL template dividing brain regions into 116 ROIs

Figure 2. RS-fMRI preprocessing

Classification Modeling

- B-spline Basis expansion
  B-spline basis expansion is employed to analyze the BOLD signals obtained from resting-state fMRI data for each ROI.

$$f(t) \approx \sum_{j=1}^{J} c_j \phi_j(t)$$

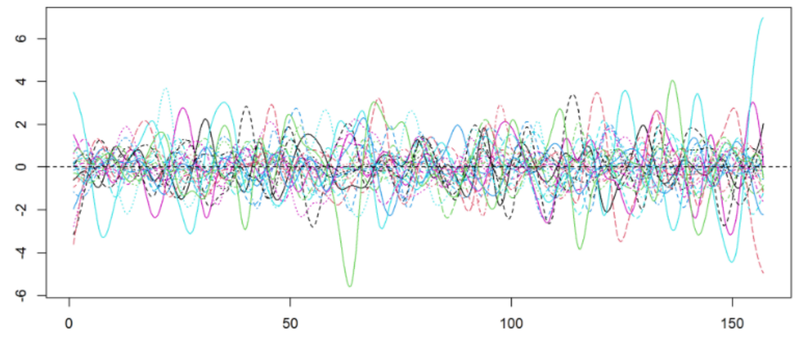


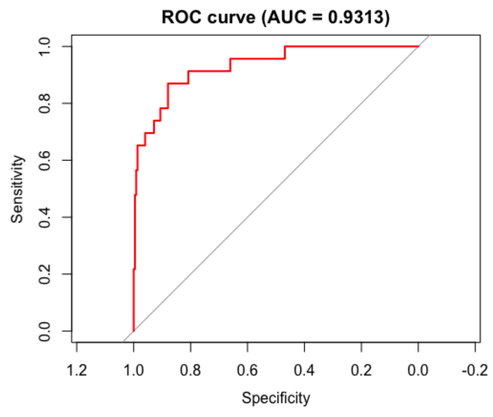
Figure 3. BOLD signals smoothed by B-spline basis expansion

- Functional PCA
  PC scores explaining more than 90% for each ROI variation were selected.
- Group lasso logistic regression
  The group lasso logistic approach was utilized for both ROI selection and classification tasks using those selected PC scores as features.

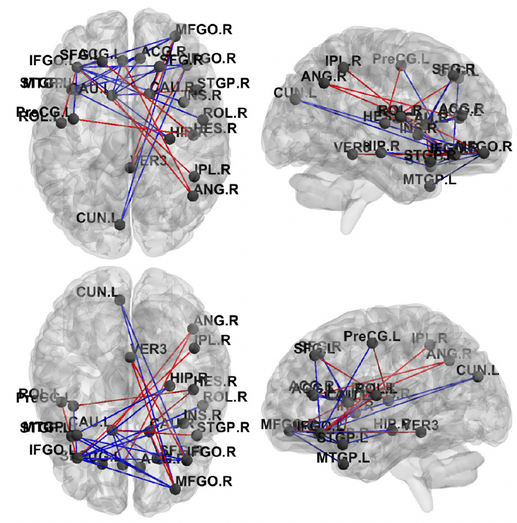
$$\hat{\boldsymbol{\beta}} = \arg\min_{\boldsymbol{\beta}} \left\{ -\frac{1}{N} \sum_{i=1}^{N} [y_i \log(p_i) + (1 - y_i) \log(1 - p_i)] + \lambda \sum_{g=1}^{G} w_g \|\boldsymbol{\beta}_g\|_2 \right\}$$

Results and discussion

- Model performance
  The classification model demonstrated strong performance, achieving an AUC of 0.9313, which indicates high accuracy in distinguishing between AD and CN.
- The functional connection
  The classification model's selected ROIs enable a more focused discussion on the specific brain regions associated with AD research, which are listed in the following table.



(a) The receiver operating characteristic (ROC) curve and its area under the curve (AUC)



(b) The functional connections of the shown pairs of ROIs were selected as important factors for the classification

Figure 4. The results of classification

ROI	Functions
right inferior occipital gyrus	odor and visual information processing
dorsolateral area of left superior frontal gyrus left middle frontal gyrus	cognition
orbital part of right middle frontal gyrus orbital part of right inferior frontal gyrus	processing and responding to external stimuli
left precentral gyrusleft rolandic operculum	auditory-motor integration
orbital part of left inferior frontal gyrus temporal pole of left superior temporal gyrus	stimuli processing from unexpected to expected

Table 1. The representative seleted ROIs and their functions

Conclusions

- Results
  The FDA approach proved effective in AD research, especially classification.
- Further Study on modeling
  Since there exists a wide array of FDA techniques and group regularization methods, further exploration and application should be needed in future.
- Patients groups Furthermore, exploring preclinical stages between AD and CN groups warrants further investigation.

ido.ji@o.cnu.ac.kr