METABOLOMIC SIGNATURES AND MACHINE LEARNING MODELS FOR DISTINGUISHING ALZHEIMER'S DISEASE AND DEMENTIA WITH LEWY BODIES

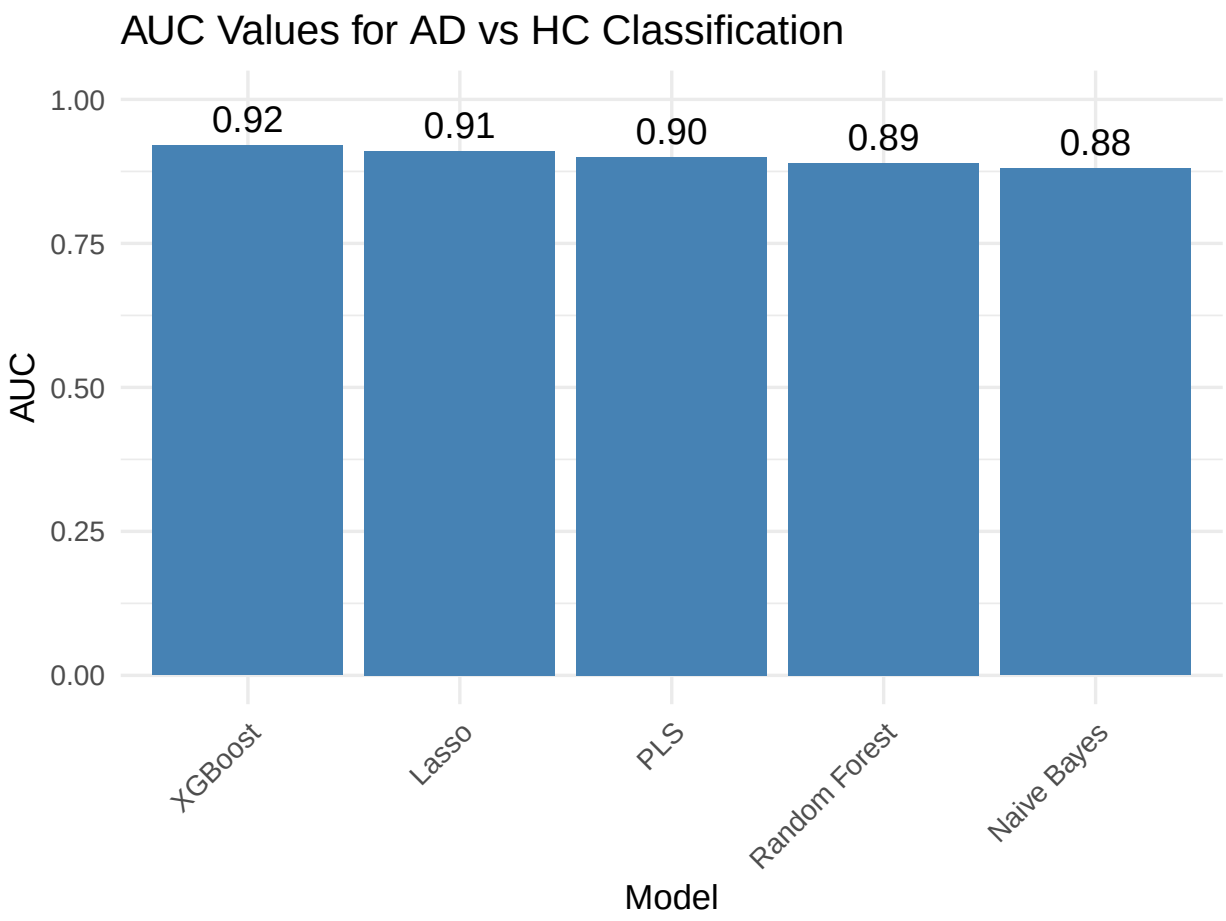
Objectives

Alzheimer's Disease (AD) and Dementia with Lewy Bodies (DLB) are difficult to distinguish clinically due to overlapping symptoms, resulting in delayed or incorrect diagnoses. This study uses metabolomic profiles from serum samples and machine learning models to identify key biomarkers that distinguish these conditions.

Methods

1. Data analysis pipeline:
    - Quality control
    - Management of missing data
    - Exclusion of biomarkers with >20% missing values
    - Imputation of values below LOD using LOD/2
2. Exploratory Data Analysis:
    - Principal Component Analysis (PCA)
    - ANOVA to examine influence of batch, age, gender, and group
3. Statistical Analysis:
    - T-tests
    - Fold changes
    - Area Under the Curve (AUC) analysis
4. Machine Learning Models:
    - Lasso
    - Random Forest
    - Naive Bayes
    - Partial Least Squares (PLS)
    - XGBoost
5. Model Evaluation:
    - Repeated cross-validation
    - ROC curves
    - Variable importance assessment
    - APOE genotype influence investigation

Results



- Significant biomarkers identified for:
  - AD vs HC
  - AD vs DLB
  - DLB vs HC
- Adjustments made for age and gender
- Machine learning models achieved AUC values ~0.9 for AD vs HC
- APOE genotype enhanced model accuracy

Conclusions

1. Distinct metabolomic signatures observed between AD, DLB, and HC
2. Machine learning models demonstrated high classification accuracy
3. Ongoing work:
   - Extending to ~2000 urine samples from DELCODE cohort
   - Developing non-invasive and cost-effective approach for early AD detection and monitoring

Future Directions

- Validate findings in larger, diverse cohorts
- Investigate longitudinal changes in metabolomic profiles
- Integrate metabolomics with other -omics data for comprehensive disease understanding
- Develop clinical decision support tools based on metabolomic signatures