**Multimodal Deep Learning Algorithm as a Tool for Dementia Clinical Trial Screening**

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## ABSTRACT

Dementia is a complex disease due to various etiologies. However, new multimodal deep learning algorithms were developed to improve the diagnosis of dementia into different categories of normal cognition (NC), mild cognitive impairment (MCI), Alzheimer's disease (AD), and non-AD dementias (nADD). One of the core difficulties in implementing Dementia clinical trials, especially the AD trials lies in the diagnostic ambiguity of Alzheimer's, where symptomatic overlap with other cognitive disorders often leads to misdiagnosis. There are usually high screen failure rates in dementia clinical trials which is a burden for the sponsor due to the manual verification of the screening that hinders the process. I am exploring an application of a multimodal deep learning algorithm as a tool for the clinical trial patients' disease screening verification to reduce the cost of the clinical study while improving the quality, accessibility, and speed. The accuracy assessment of the deep learning algorithm will be presented by comparing its results to a neurologist's evaluation. The results will be described using the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) in a real-world clinical trial setting. I will try to explore the optimal set of input variables used for the algorithm to balance the accuracy, cost, and time of the medical exams.


## 1. INTRODUCTION

### 1.1 Literature Review

Dementia, as defined by the International Statistical Classification of Diseases and Related Health Problems (ICD), is "a syndrome due to disease of the brain, usually of a chronic or progressive nature, in which there is disturbance of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity,

language, and judgment" (World Health Organization, 2019). Dementia is not a specific pathology but rather a syndrome which can be caused by approximately 55 diseases (Geldmacher & Whitehouse, 1996). The most common illnesses that lead to neurodegeneration and dementia are Alzheimer's disease (62%), vascular dementia (17%), mixed dementia (10%), dementia with Lewy bodies (4%), frontotemporal dementia (2%), parkinson's dementia (2%) and other (3%) (Vermeiren et al., 2020). Alzheimer's disease (AD), characterized by the accumulation of amyloid-beta plaques and aggregation of tau protein tangles in the brain which leads to death of neurons(Scheltens et al., 2021), is the most common cause of dementia which affects 44 million people with an average age of 65 worldwide (Dumurgier 2020; Scheltens et al., 2021; Hendrie, 1998). The number of AD patients is expected to triple by 2050. Thus, it is a serious public health concern that has puzzled the most experienced researchers worldwide. AD was such a critical issue that President Obama signed into law a plan named National Alzheimer's Project Act (NAPA) to effectively prevent and treat this disease by 2025 (Obama Administration Presents National Plan to Fight Alzheimer's Disease, 2012).

The development of effective treatments depends on high quality clinical trials, particularly the accurate selection of patients for enrollment with correct disease diagnosis. The current diagnosis of dementia related to Alzheimer's disease mainly follows the National Institute on Aging and Alzheimer's Association NINCDS-ADRDA criteria. These criteria are mainly based on single modal of neuropsychological tests like the Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog), the Mini-Mental State Examination (MMSE), and the Clinical Dementia Rating scale (CDR) (Balsis et al., 2015);

Alzheimer's disease is often misdiagnosed with other dementias. For example, the differential diagnosis between Alzheimer's disease and vascular dementia remains challenging

due to overlaps of symptoms and risk factors (Kalaria, 2002). Moreover, dementia can be a mixed type, combining Alzheimer's disease, vascular dementia, and other dementia disorders (Jellinger, 2007).

A new group of biomarkers have been researched in understanding AD progression, leading to improvements of diagnostic accuracy of AD (Budelier & Bateman, 2019; Hurtado et al., 2018; Bai et al., 2021; Chang et al., 2021; Zetterberg & Blennow, 2021; Aerqin et al., 2022; Badhwar et al., 2019; Tan et al., 2021; Xie et al., 2021). Biomarkers for amyloid-beta and tau proteins in cerebrospinal fluid (CSF); and brain imaging techniques such as magnetic resonance imaging (MRI) and positron emission tomography (PET) (Walhovd et al., 2010) were developed.

AI based computational models in dementia research have been transformative, enabling the application of multimodal deep-learning algorithms to improve patients' disease screening accuracy (Wong-Lin et al., 2020). These algorithms combine diverse data types, such as neuroimaging, body fluid biomarkers, genetic and proteomic data to detect early-stage dementia (Senanarong, 2021; Karako et al., 2023). Supervised machine learning models have been particularly effective in biomarker discovery and neuroimaging studies (Skolariki & Exarchos, 2020).

## 1.2 Gap

The challenge of diagnosing Alzheimer's disease accurately sets a significant barrier in the development of effective treatments. The variety of biomarkers required for AD diagnosis highlights the disease's complex and nonhomogeneous nature. These include advanced imaging methods like MRI and PET scans, detailed neuropsychological evaluations, and cerebrospinal fluid (CSF) analysis. There is no single test that can definitively diagnose AD. This diagnostic

challenge leads to misdiagnosis, impacting the enrollment of suitable candidates in clinical studies. Participants with similar symptoms but different underlying conditions can introduce variability and in study results, preventing medical researchers from discovering the true efficacy and safety of potential treatments. Therefore, there's an urgent need for better diagnostic tools that can accurately identify AD. Improved diagnostic methods will improve the clinical trial quality and efficiency by lowering testing costs and refining participant selection.

### 1.3 Research Question or Project Goal

The objective of this project is to investigate and validate a multimodal prediction model of explainable artificial intelligence (XAI) for the precise classification of possible dementia patients into four distinct categories: normal cognition (NC), mild cognitive impairment (MCI), Alzheimer's disease (AD), and non-Alzheimer's dementias (nADD). I will investigate multiple models to create the optimal mix of multimodal input data to find the equilibrium among diagnostic precision and cost-effectiveness of model input. By validating the model from the real world clinical trial data, this study will test the effectiveness of this model in accurately diagnosing dementia participants automatically with the economic benefit of reducing screen failure rates and associated expenses in dementia-related clinical trials. The model's performance will be assessed by comparing model diagnosis and expert evaluations conducted by trained physicians based on the  accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) within a real world clinical trial setting.

## 2. METHOD

## 2.1 Justification for chosen method

The primary methodology of this research is the multimodal classification prediction model described by (El–Sappagh et al., 2021). This model is based on the explainable artificial intelligence (XAI) principles. XAI principles accompany each diagnostic decision with a comprehensible rationale, thereby fostering trust and transparency in clinical settings of AI model use.

Previous generations of AI models rely on a single data source of neuroimaging or CSF concentration. Matching the multifaceted nature of AD, this study model includes a diverse list of clinical assessments and biomarkers.

SHapley Additive exPlanations (SHAP) framework was used in the modeling for the random forest classifier's decisions. The framework provides both global and instance-based explanations of the decision assisting the model user to understand the reason behind the diagnosis.

The model accuracy and reliability were evaluated using F1-scores in cross-validation settings. The explanations generated from the algorithm were checked with medical literature for consistency.

In this study, I am extending the application of El-Sappagh et al.'s model to the realm of clinical trial patient selection. By adapting this model to use in the clinical trial application, my goal is to reduce the high screen failure rates endemic to dementia trials. I hypothesize that the model's multimodal, explainable, and accurate nature will translate into more efficient and cost-effective patient screening processes, ultimately accelerating the development of AD therapeutics.

## 2.2 Data Collection

The model has been validated using the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, which includes a wide spectrum of AD-related cases. I employed the same ADNI database for building my model, in which the models are trained and validated with 992 subjects.

The models were also tested with a real-world clinical trial study. This data was collected as a part of a real world clinical trial in Alzheimer's disease. Trial data contains 439 subjects who enrolled the study based on AD diagnosis. Inclusion criteria included male and female subjects aged 60 to 85; NINCDS-ADRDA criteria (McKhann et al., 2011); CDR Standard Global score of 1 to 2; MMSE score ≥14 and ≤24; amyloid-beta (Aβ) PET scan; evidence of progressive cognitive decline in last year, etc. During study, different modalities were collected such as medical history, FDG-PET, MRI, lab tests, neuropsychological assessments, genetics.

Among the most discriminant and informative 28 features for the modeling, common features were selected with my study dataset: ADAS-Cog 11, MMSE, CDR sum of boxes (CDRSB), gender, and ethnicity. Other available common features were utilized which include Apolipoprotein E (APOE) ε4 genotype, MRI volumes of whole brain, hippocampus, ventricles, and intracranial region.

As a result, the model integrates selected 10 features and 992 subjects from ADNI dataset: 183 cognitively normal, 372 stable mild cognitive impairment (MCI), 240 progressive MCI, and 197 AD; and 439 subjects diagnosed as AD from the real world clinical trial data.

## 2.3 Prediction Models

Random forest, a machine learning algorithm that generates a single result by aggregating the output of several decision trees, is used as the diagnostic algorithm in this research, due to its robust and accurate characteristics among machine learning models. Four experiments are conducted to fully utilize the features and maximize the number of participants: i) using 6 features without model optimization, ii) using 6 features with model optimization, iii) using 10 features without model optimization, and iv) using 10 features with model optimization. The 6-feature experiments build the random forest model using APOE ε4 genotype (APOE4), CDR Sum of Boxes (CDRSB), 11-item version of ADAS-Cog (ADAS11), MMSE, gender (PTGENDER), ethnicity (PTETHCAT), while the 10-feature experiments add four more features, which are Ventricles, Hippocampus, Whole Brain, intracranial volume (ICV).

The models are trained and validated using the ADNI datasets with five-fold cross-validation and then used to diagnose participants in the second dataset. The evaluation metric used in this research is accuracy, which is the percentage of correctly classified instances out of the total instances.

## 3. RESULTS

### 3.1 Findings

The analysis shows that across the two datasets, the distribution of features varies greatly, except for the APOE4 allele, which remains consistent (Figure 1). Table 1 details the performance metrics of four distinct experiments conducted: i) a random forest detection model utilizing six features without any model optimization, ii) the same random forest model using six features but with grid search optimization, iii) a random forest model utilizing ten features without optimization, and iv) the ten-feature random forest model enhanced with grid search

optimization. The findings reveal that applying grid search optimization marginally increases the detection accuracy by 0.1%. Moreover, incorporating additional MRI-derived features boosts the accuracy further by 0.9%. The specific results of these detection efforts are depicted in Figures 2 to 5. Based on confusion matrices (Fig. 2-5), PPV = TP / (TP + FP) and NPV TN / (TN + FN) were calculated: i) for 6-feature model without optimization PPV=64.9% and NPV=90.5%; ii) for 6-feature model with optimization PPV=66.1% and NPV=90.8%; iii) for 10-feature model without optimization PPV=65.1% and NPV=91.9%; iv) for 10-feature model with optimization PPV=65% and NPV=91.3%.

The 6-feature model without optimization diagnosed only 4.9% of AD patients. All others (95.1%) were misdiagnosed. Despite the minor enhancement from optimization, the prediction accuracy of the 6-feature model displayed considerable difference compared to the same model but without optimization. Optimized model prediction of misdiagnosed patients decreased to 51.7% (Tables 2 and 3). Conversely, the 10-feature model, regardless of optimization status, consistently predicted misdiagnosis in all cases (Tables 4 and 5).

In the second part of the experiment, two more features were added: amyloid-beta 42/40 ratio in plasma and CDR Global score. However, due to a lack of data of amyloid-beta (Aβ) 42/40 ratio for a significant number of subjects for these two features, experiments from the first part were run one more time but with decreased number of subjects so that importance of added new features (Tab. 6) could be compared.

Distributions for those 6 models (Fig. 6 – Fig. 11) have also been compared, which are slightly different as shown in Figure 1, that most likely is caused by the fact that clinical trial data doesn’t contain CN and MCI.

Some examples of natural-language explanations are provided to understand random forest (RF) model decisions which are shown in Tables 7 and 8 .

3.2 Quantitative or qualitative

This research employs a quantitative approach. It is based on computational evaluation of numerical data sourced from the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset and clinical studies. The data collection methodology typifies a quantitative strategy, focusing on distinct discriminant features like the Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog 11), Mini-Mental State Examination (MMSE), and Clinical Dementia Rating Sum of Boxes (CDRSB) scores, in addition to genetic markers and neuroimaging data. These quantifiable features were utilized for statistical analysis and interpretation.

The development of the random forest detection model further exemplifies this quantitative approach. It relies on the manipulation of numerical variables for predicting outcomes, employing the calculation of probabilities and the construction of decision trees based on the input data.

Moreover, the assessment of the model's efficiency through accuracy metrics reinforces the quantitative essence of the research. These metrics provide numerical evaluations of the model’s diagnostic precision.

The implementation of grid search optimization, aimed at refining model performance, constitutes a quantitative technique. It involves a methodical exploration within a predefined set of parameters to identify the most effective combination for maximizing accuracy.

Additionally, the statistical analysis conducted to compare feature distributions across the ADNI dataset and the clinical study data, utilizing statistical tests to ascertain significance levels,

is a cornerstone of quantitative research. This approach ensures the derivation of objective, measurable insights, affirming the utility of the multimodal deep learning algorithm for enhancing dementia screening within clinical trial settings.

3.3 Graph(s), Tables, and/or Figures, etc.

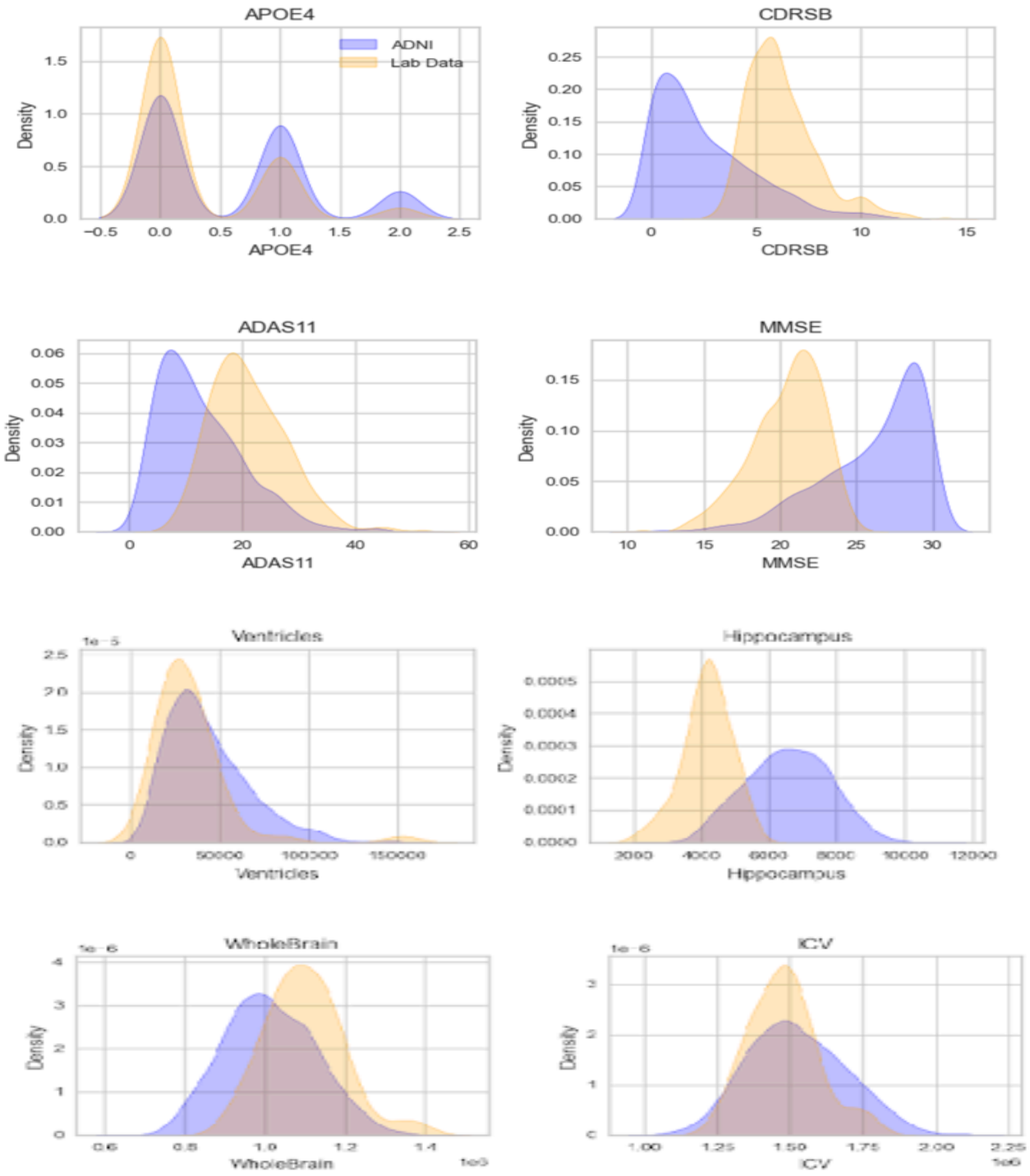


Figure 1. Distributions of the same feature in two datasets.

| Number of features | Model optimization | Accuracy |
|---|---|---|
| 6 | No | 82.5% (2.5%) |
| 6 | Yes | 82.6% (2.8%) |
| 10 | No | 83.3% (2.7%) |
| 10 | Yes | 83.4% (2.9%) |

Table 1. Detection accuracy of different experiments.

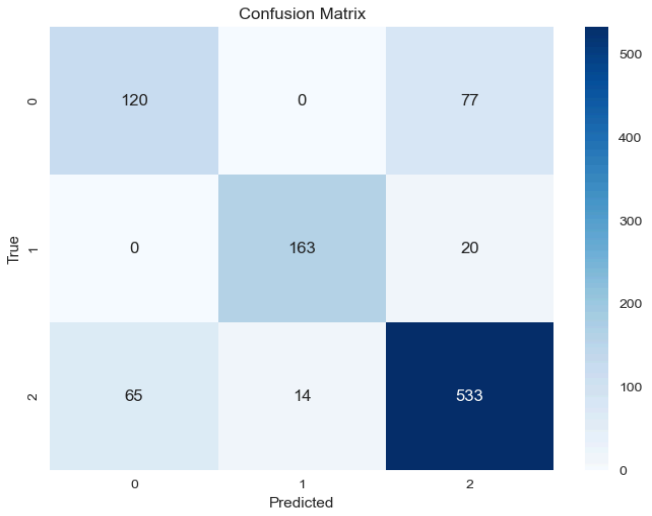


Figure 2. Confusion matrix of the detection results by random forests with 6 features and no optimization.

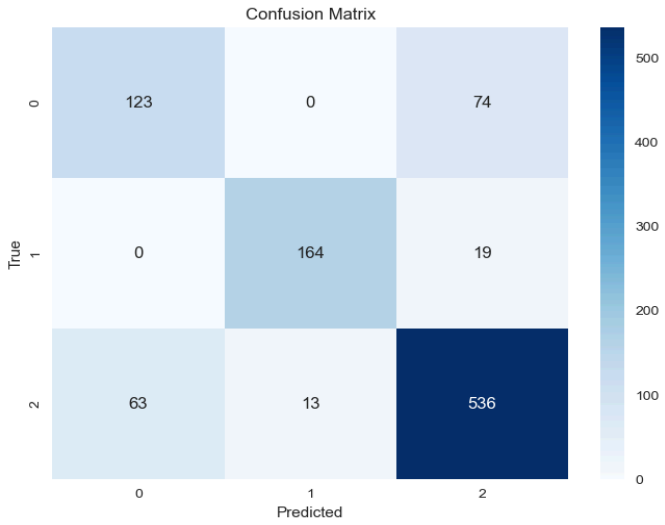


Figure 3. Confusion matrix of the detection results by random forests with 6 features and optimization.

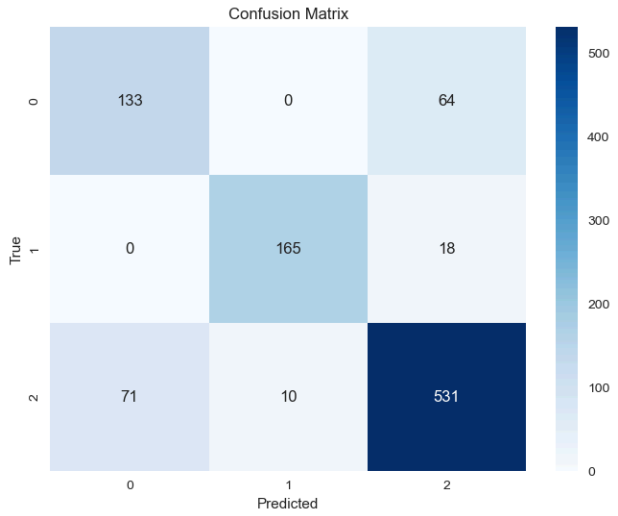


Figure 4. Confusion matrix of the detection results by random forests with 10 features and no optimization.

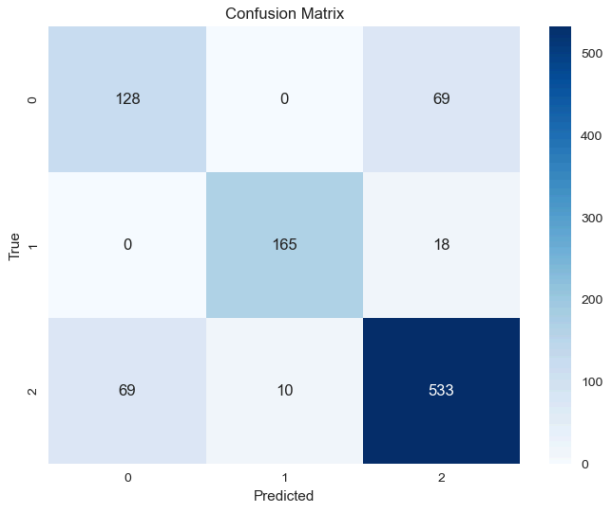


Figure 5. Confusion matrix of the detection results by random forests with 10 features and optimization.

| AD<br>n predicted (%) | MCI<br>n predicted (%) |
|---|---|
| **10 (4.9%)** | **203 (95.1%)** |

Table 2. Prediction results by random forests with 6 features and no optimization.

| AD<br>n predicted (%) | MCI<br>n predicted (%) |
|---|---|
| **98 (48.3%)** | **115 (51.7%)** |

Table 3. Prediction results by random forests with 6 features and optimization.

| AD<br>n predicted (%) | MCI<br>n predicted (%) |
|---|---|
| **0** | **47 (100%)** |

Table 4. Prediction results by random forests with 10 features and no optimization.

| AD<br>n predicted (%) | MCI<br>n predicted (%) |
|---|---|
| **0** | **47 (100%)** |

Table 5. Prediction results by random forests with 10 features and optimization.

| n features | n participants in training dataset | n participants in testing dataset | CN | MCI | AD | Optimization | Accuracy | n predicted AD | n predicted MCI |
|---|---|---|---|---|---|---|---|---|---|
| 6 | 1640 | 446 | 462 | 894 | 284 | - | 0.79 | 309 | 137 |
| 6 | 1640 | 446 | 462 | 894 | 284 | + | 0.8 | 0 | 446 |
| 10 | 1640 | 50 | 462 | 894 | 284 | - | 0.8 | 0 | 50 |
| 10 | 1640 | 50 | 462 | 894 | 284 | + | 0.8 | 0 | 50 |
| 7 | 1640 | 446 | 462 | 894 | 284 | - | 0.83 | 421 | 25 |
| 7 | 1640 | 446 | 462 | 894 | 284 | + | 0.83 | 44 | 402 |
| 8 | 283 | 356 | 88 | 187 | 8 | - | 0.88 | 0 | 356 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 8 | 283 | 356 | 88 | 187 | 8 | + | 0.89 | 0 | 356 |
| 11 | 1640 | 50 | 462 | 894 | 284 | - | 0.82 | 49 | 1 |
| 11 | 1640 | 50 | 462 | 894 | 284 | + | 0.82 | 0 | 50 |
| 12 | 283 | 26 | 88 | 187 | 8 | - | 0.89 | 0 | 26 |
| 12 | 283 | 26 | 88 | 187 | 8 | + | 0.89 | 0 | 26 |

Table 6. Summary of 12 experiments due to adding Aβ 42/40 ratio and CDR Global. 6 features: APOE ε4 genotype (APOE4), CDR Sum of Boxes (CDRSB), 11-item version of ADAS-Cog (ADAS11), MMSE, gender (PTGENDER), ethnicity (PTETHCAT). 7 features: 6 features + CDR Global. 8 features: 7 features + Aβ 42/40 ratio. 10 features: 6 features + 4 MRI features. 11 features: 7 features + 4 MRI features. 12 features: 8 features + 4 MRI features.

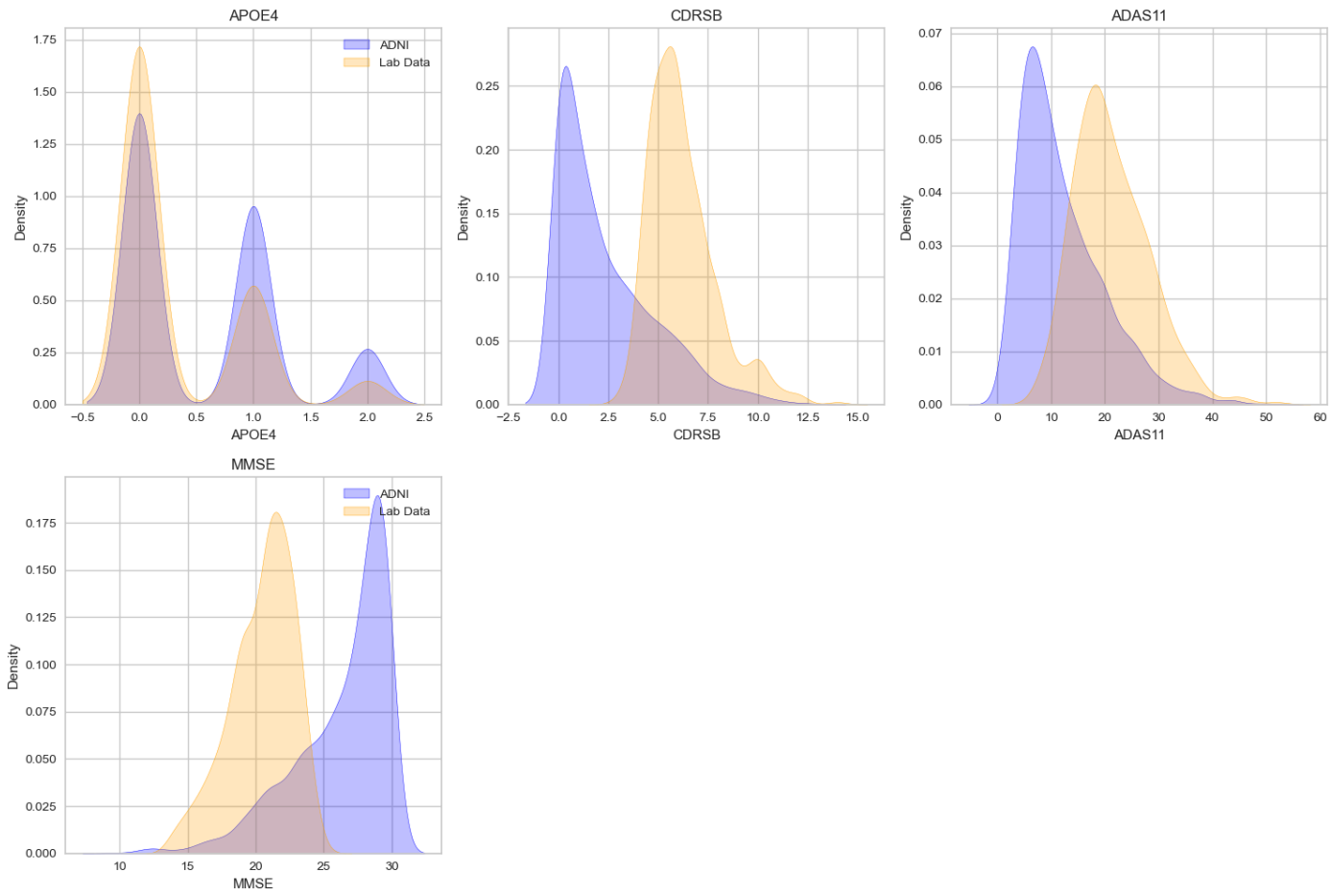


Fig. 6. Distributions of the same features in training (ADNI) and testing (Lab Data) for 6-feature model.

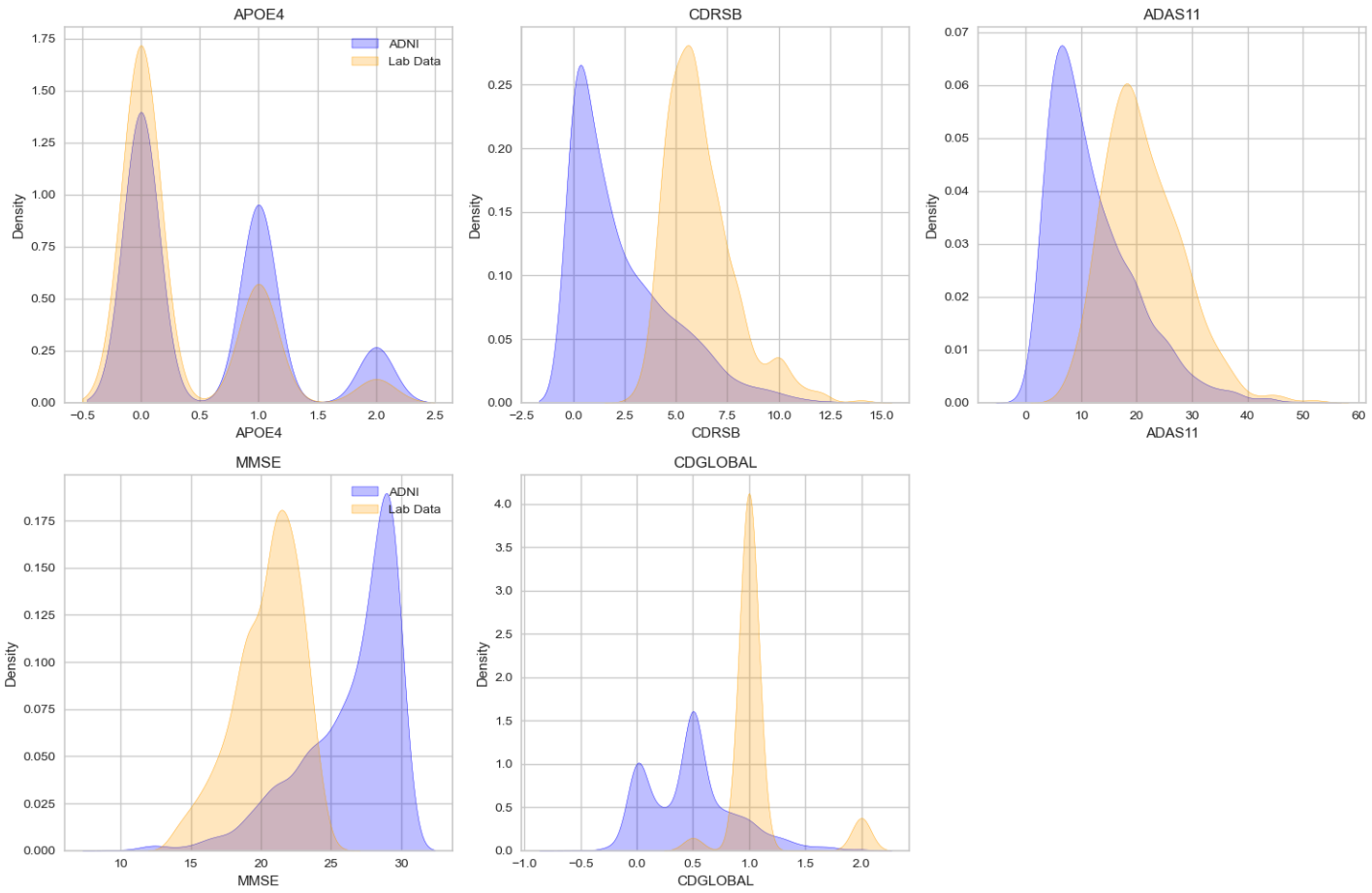


Fig. 7. Distributions of the same features in training (ADNI) and testing (Lab Data) for 7-feature model.

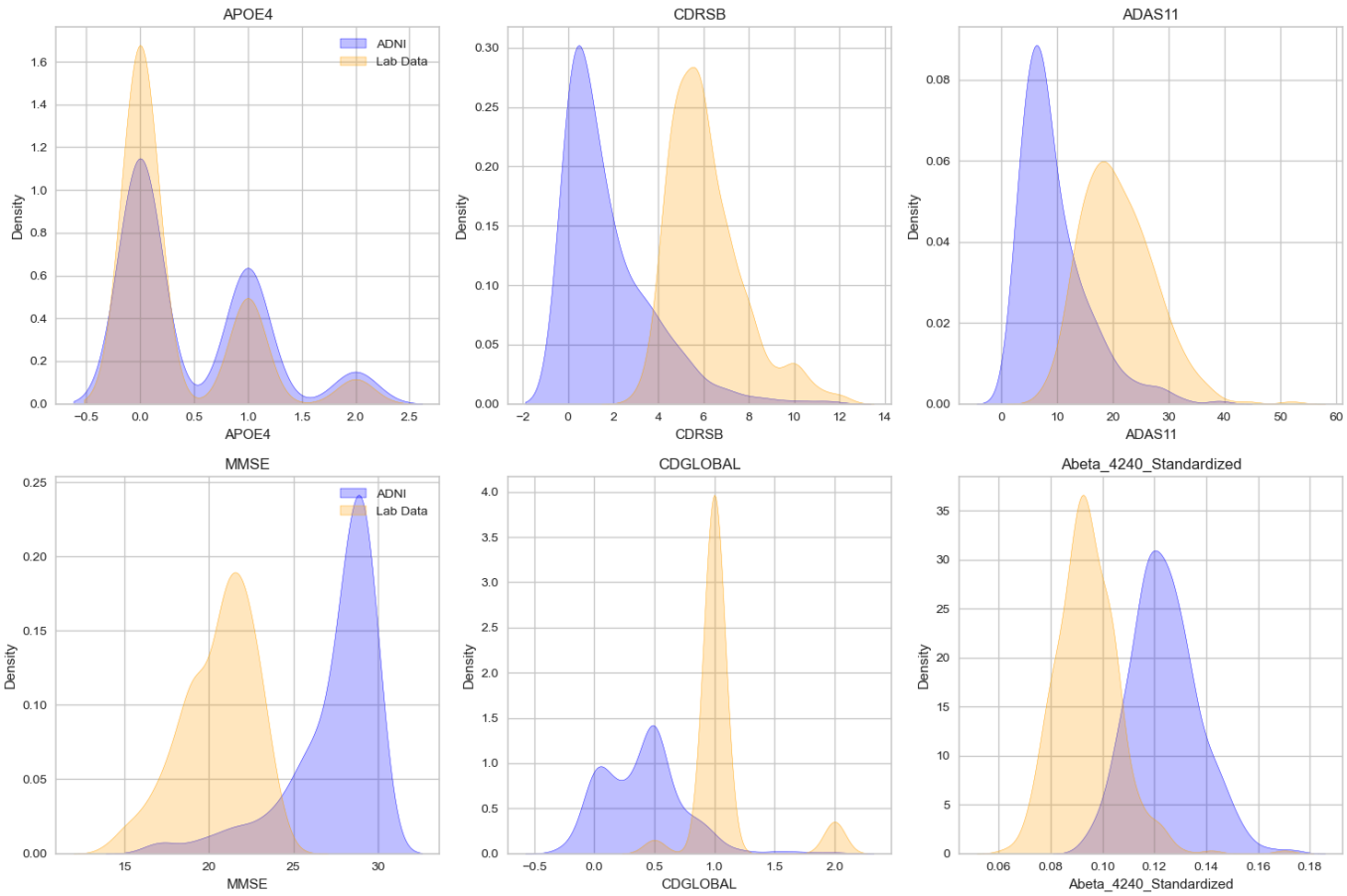


Fig. 8. Distributions of the same features in training (ADNI) and testing (Lab Data) for 8-feature model.

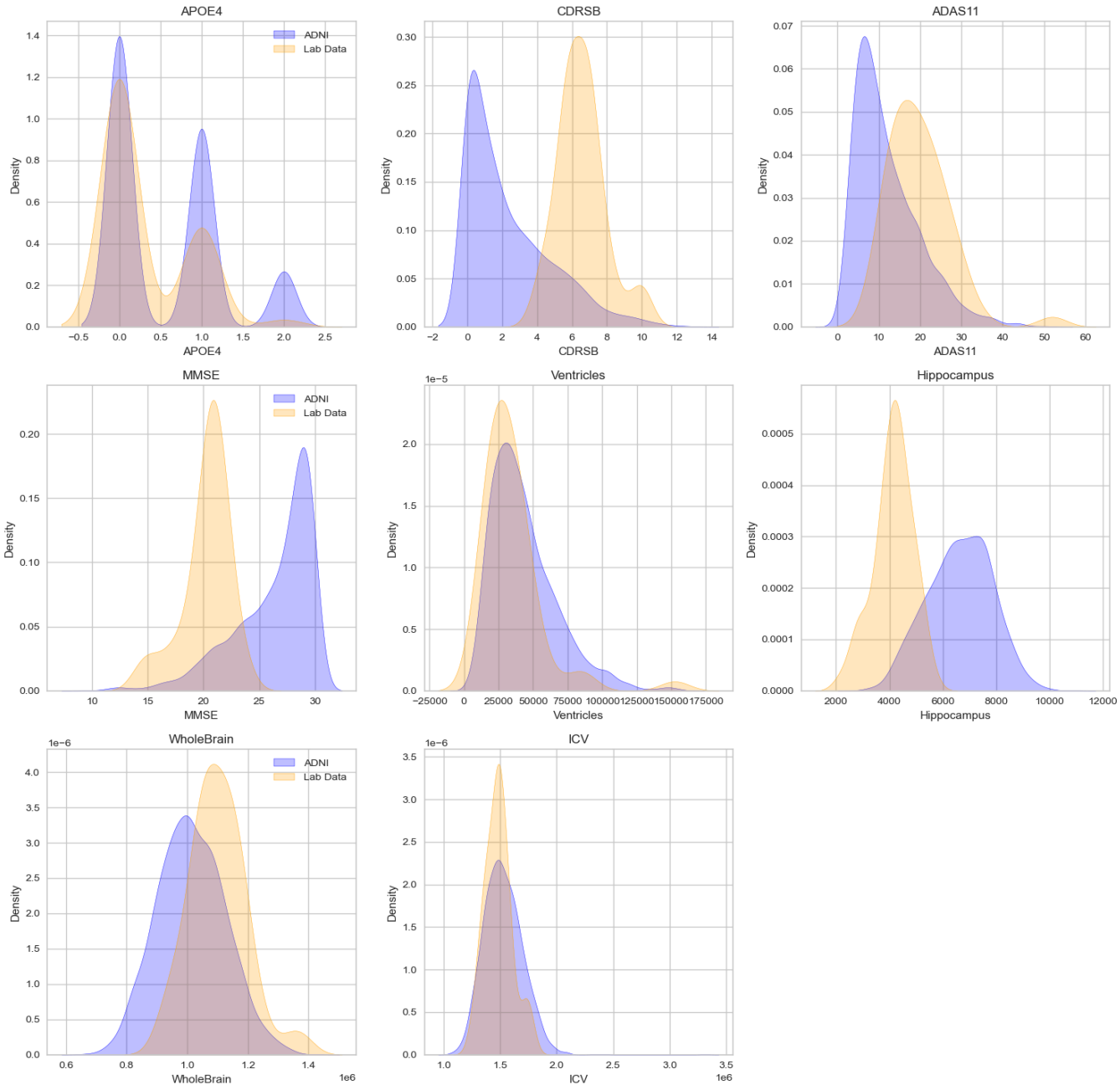


Fig. 9. Distributions of the same features in training (ADNI) and testing (Lab Data) for 10-feature model.

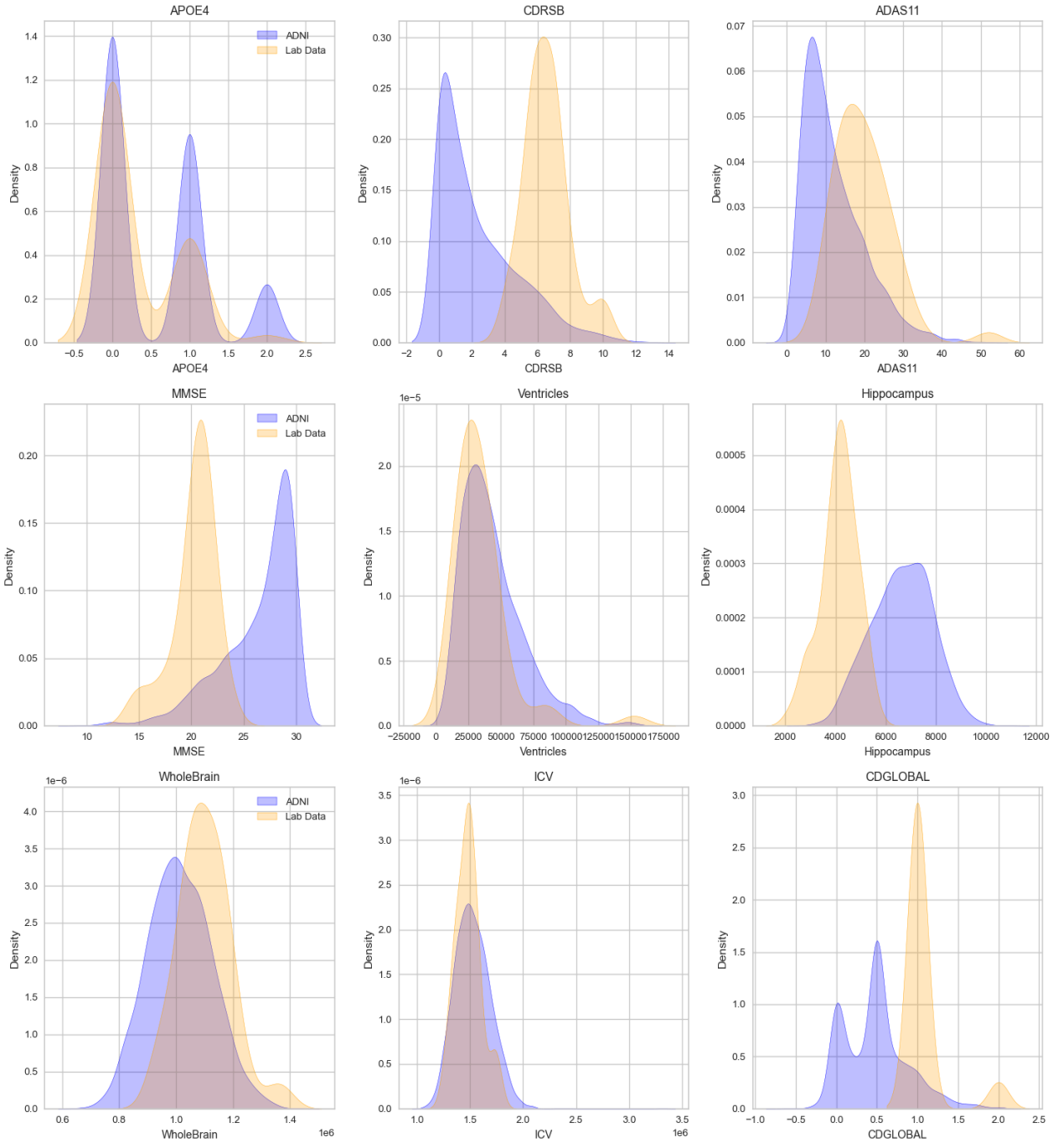


Fig. 10. Distributions of the same features in training (ADNI) and testing (Lab Data) for 11-feature model.

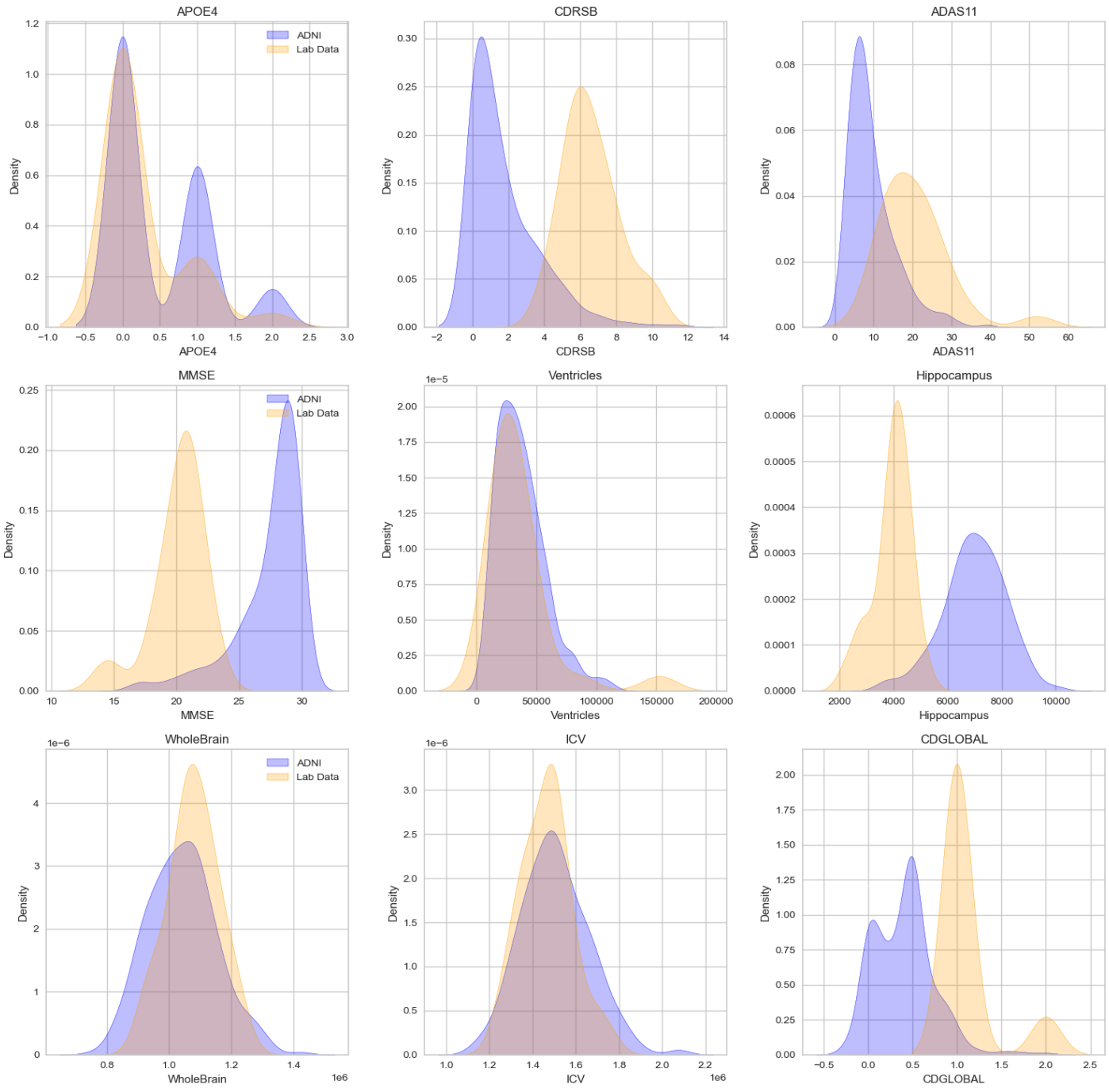


Fig. 11. Distributions of the same features in training (ADNI) and testing (Lab Data) for 12-feature model.

| |
|---|
| **Subject ID: 113-0013**. **Diagnosis:** MCI |
| |
| Explanations based on MRI, Medical History, Lab Tests, Symptoms, and Vital Signs modalities Ventricles<br>1. *Based on MRI dataset:*<br>MCI because Intracranial Volume is **HIGH**, Ventricles is **LOW**, and Hippocampus is **MEDIUM**.<br>2. *Based on Medical History dataset:*<br>MCI because APOE4 is **LOW**, Cardiovascular History is **HIGH.**<br>3. *Based on Lab Tests dataset:*<br>MCI because Monocytes is **HIGH**, Cholesterol is **LOW**.<br>4. *Based on Symptoms dataset:*<br>MCI because Depression is **NO**.<br>5. *Based on Vital Signs dataset:*<br>MCI because Height is **HIGH**, BMI, and Heart Rate are **LOW**, and Temperature is **MEDIUM**. |

**Table.** 7**. Explainer for case-study 1.**

| **Subject ID: 116-0010**. **Diagnosis:** AD |
|---|
| |
| Explanations based on Medical History, Cognitive Scores, Genetics, and Symptoms modalities<br>1. *Based on Medical History dataset:*<br>AD because Cardiovascular History is **NO**, APOE4 is **HIGH**, and Psychiatric History are **YES**.<br>2. *Based on Cognitive Scores dataset:*<br>AD because CDGLOBAL is **LOW**, and CDRSB is **MEDIUM**.<br>3. *Based on Genetics dataset:*<br>AD because ABETA is **POSITIVE** and TAU is **POSITIVE**.<br>4. *Based on Symptoms dataset:*<br>AD because Depression is **YES**. |

Table. 8. Explainer for case-study 2.

## 4. DISCUSSION

### 4.1 Significance

Implementing a multimodal deep learning model in a practical clinical study environment represents a noteworthy advancement in diagnosing neurodegenerative diseases. This research has pinpointed critical features that are essential in accurately classifying Alzheimer's disease (AD) and monitoring its progression. The model's capacity to deliver high prediction accuracy

with a relatively small set of biomarkers highlights its effectiveness and potential for real-world application. The impact of these findings is multifaceted.

Firstly, the model's dependance on a concise yet effective set of features for AD diagnosis suggests that a more simplified diagnostic process is achievable without sacrificing accuracy. This aspect is particularly valuable in clinical environments where comprehensive testing may be cost-prohibitive or not universally accessible.

Secondly, the encouraging outcomes from the model's application lay the groundwork for its further improvement and adaptation. By incorporating more biomarkers and clinical data, the model's diagnostic precision, in terms of sensitivity and specificity, can be enhanced, leading to more accurate AD detection. Furthermore, the model's cost-efficiency and quick turnaround make a strong argument for its integration into regular clinical workflows, notably in early screening of AD across varied patient groups.

## 4.2 Interpretations

The observed inconsistency in feature distribution between the ADNI dataset and the Lab Data (Figure 1) is attributed to the distinct composition of subject groups within each dataset. The ADNI dataset encompasses three categories: cognitively normal (CN) individuals, those with mild cognitive impairment (MCI), and patients diagnosed with Alheimer's disease (AD), whereas the Lab Data exclusively comprises individuals diagnosed with AD by physicians. This variation naturally explains the shift in distribution, as higher scores in CDRSB and ADAS11 indicate more severe cognitive impairment, while higher MMSE scores are linked to better cognitive function.

The predictive outcomes from the model, which predominantly classified patients as having MCI rather than AD, warrant a nuanced interpretation. Two principal factors may account for this observation.

Firstly, the model's reliance on cognitive scores and genetics as the main predictive features, while MRI modalities did not emerge as significant for the AD class, could be instrumental in this pattern. Cognitive assessments alone, without the support of more definitive biomarkers, may not possess the specificity required to distinguish AD from other forms of dementia, such as vascular dementia. This is due to the symptomatic commonalities that AD shares with other cognitive disorders, which neuropsychological tests alone may not adequately differentiate.

Secondly, I labeled ADNI data in 3 groups: CN, MCI, and AD. However, further subcategorization should have been taken into account because MCI can be divided into 2 groups: MCI due to Alzheimer's disease and MCI due to other etiology. Consequently, the model probably treated all dementia as AD patients because MCI patients progress into AD only if it is due to AD. Nonetheless, MCI, due to etiology patients, will progress into dementia due to other etiology.

These insights highlight the intricate nature of AD diagnosis and the necessity for comprehensive diagnostic strategies. Moreover, they emphasize the importance of strict protocol adherence in clinical research to safeguard the validity and reliability of the outcomes.

The second part with 12 experiments (Tab. 6) underlines the importance of usage of concentrations of Aβ in blood and CDR global scores because accuracy is increased when utilizing both features. However, there is a notable limitation of a model that uses 8 features due to the low number of subjects. It is necessary to find data from a higher number of subjects to

build better predictions. Further, adding grid search optimization to 6-, 7-, and 11-feature models gives different prediction results compared with non-optimized same models although accuracy hasn't changed significantly. This finding leads to the conclusion that my diagnostic AI model doesn’t work correctly, and more work is needed to find out what causes such a major shift in predictions when using optimization.

Natural language-based explanations are necessary for understanding random forest (RF) model decisions. Moreover, these case-study explainers allow us to take a look at a broader picture of patients’ profiles. These explainers include biomarkers which RF model didn’t consider informative and discriminant, however, medical experts prefer individualized explanations for each specific patient according to his/her conditions that cover a wider range of biomarkers than the RF model, which has been found to be very important.

### 4.3 Connections

This research has underscored the value of cognitive assessments as dependable markers for forecasting (AD). The (MMSE), (CDRSB), and (ADAS-Cog 11) have proven to be vital in the AD diagnosis process. In contrast, data from magnetic resonance imaging (MRI) did not demonstrate remarkable predictive power for AD in my studies. Furthermore, the significance of the apolipoprotein E ε4 allele in AD diagnosis remains uncertain, suggesting the need for further studies to clarify its role and potential utility in identifying the disease.

# 5. CONCLUSION

## 5.1 Limitations

The investigation acknowledges a number of limitations. Primarily, the exclusive reliance on cognitive assessments and the APOE ε4 genetic marker falls short of providing an all-encompassing method for distinguishing Alzheimer's disease (AD) from other forms of dementia. In particular, the omission of cerebrospinal fluid (CSF) biomarkers, namely amyloid-beta (Aβ) and tau protein levels, stands out as a significant shortfall. The inclusion of these markers could markedly improve the accuracy of AD diagnostics.

The model didn’t encompass the fourth group of patients who were suspected patients with AD, however, their MCI or dementia turned out to have other etiology, like vascular dementia or Parkinsonism.

## 5.2 Implications

The outcomes of this study indicate that a more inclusive array of biomarkers is essential to refine diagnostic precision. Expanding the diagnostic framework to include a wider range of genetic markers, biochemical indicators, patient medical history, and neuroimaging data could furnish a more comprehensive understanding of the disease. Such an approach is likely to result in enhanced patient care and outcomes.

## 5.3 Future Research

My next step is to relabel patients in consideration to the fact that not all mild cognitive impairments are caused by AD. It is also necessary to look into each patient's profile throughout the whole timeline of diagnosis to exclude those who were misdiagnosed at the beginning of

ADNI research. Correct categorization of patients is a key to understanding disease progression and building AI models as a diagnostic tool.

Alzheimer's disease is a substantial economic burden as there are direct medical costs for individuals, families and organizations such as nursing homes. Alzheimer's disease's indirect consequences, such as loss of productivity, cause high societal costs (Meek, 1998). Despite numerous treatment approaches that have been investigated over the years, there is yet neither curative nor preventive treatment (Passeri et al., 2022). In addition, the escalating prevalence and financial strain underscore the urgent necessity for further research to understand the nature of AD and discover effective treatment.

Looking ahead, my future research efforts will be directed towards a deeper understanding of AD's main pathophysiological underpinnings, specifically the build-up of Aβ plaques and tau protein tangles. The goal is to determine a conversion factor for these proteins from blood plasma samples to CSF, thereby improving the predictive power of my model, and to incorporate patient medical history information to more accurately differentiate AD from vascular dementia. To ensure the accuracy and reliability of the model's predictions, it is necessary to consult an AD diagnostic expert for validation of my approach, thereby affirming the model's utility in diagnosing patients based on study data.

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