
RESEARCH ARTICLE

Multimodal Deep Learning for Alzheimer’s Disease Diagnosis: Integrating Neuroimaging and Genetic Data

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| ABSTRACT

Conventional diagnosis of Alzheimer’s disease (AD) has usually relied upon data from individual modalities, which inherently restricts how data can be comprehended for understanding the disease process. To this end, in the current study, we present a novel multimodal deep learning framework that integrates clinical assessments, genomic information and imaging characteristics to enhance diagnosis and disease staging. This study uses Contrastive Stack Denoising Autoencoder and 3D CNNs to represent genetic data (e.g. single nucleotide polymorphisms, or SNPs), clinical test scores, and MRI scans. In addition to the correct categorization of people into three groups, AD, MCI, and CN. Compared with existing interpretability methods, this method selects the most prominent features by clustering them and performing perturbation analysis. Using data from the Alzheimer’s Disease Neuroimaging Initiative (ADNI), we show through experiments that our proposed deep learning framework outperforms traditional machine learning methods, including support vector machines, random forests, and k-nearest neighbors, for these imaging features. The multimodal model outperforms the single-modality models across all metrics, including accuracy, precision, recall, and F1 scores. This by itself validates the therapeutic relevance of the model, as it highlights classic AD proteins that are present in the disease, including the hippocampus, amygdala, and the Rey Auditory Verbal Learning Test (RAVLT), which are all widely known to be impacted in AD as per conventional medical knowledge of the disease.

| KEYWORDS

Deep Learning, Alzheimer’s Disease, Alzheimer’s Disease Neuroimaging Initiative (ADNI), Genetic Data, cognitively normal (CN).

| ARTICLE INFORMATION

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1. Introduction

Deep learning has demonstrated remarkable potential as a clinical decision support tool for a range of diseases, including diabetic retinopathy, cancer, and Alzheimer’s disease (AD), especially in the field of medical imaging (Syed Nazmul Hasan, 2025). Deep learning outperforms traditional shallow learning models in several tasks mainly because it often gives up the critical need for human effort in properly designing the feature space in which the model is to be trained; but rather allows for automatically extracting the most predictive features directly from raw data (Siddiqa et al., 2024). This has been shown to single-modality data types, including medical images, electronic health records (EHRs) and genetic markers such as SNPs (Saimon et al., 2023). Artificial intelligence, especially deep learning capabilities, is well-equipped to handle such cases of incomplete data and is thus best suited for complicated medical cases (Gulshan et al., 2016; Weng et al., 2017). Here we present a novel deep learning-based approach for predicting the stages of Alzheimer’s disease employing a tri-modal dataset (Nirupam Das 2025). AD is currently the sixth leading cause of death and the most common neurodegenerative condition in the United States. The global economic burden of the disease is expected to surpass \$2 trillion by 2030, highlighting the critical need for early and accurate diagnosis (Mohammad Abdul et al., 2024). Despite these advances in clinical research, fewer than 50 percent of patients receive an accurate diagnosis based on clinical symptoms alone. To gain further insight into the disease, ongoing research continues to exploit data from Alzheimer’s initiatives applying data mining methods (Schulam et al., 2015).

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AD biomarkers can vary from clinical scores such as mini-mental state examination (MMSE) and symptoms that can be observed in a clinical setting, such as memory loss, to neuroimaging-based and genetic and protein-based biomarkers (Miah et al., 2025). However, most of the previous studies are based on single-modality data, which hinders a synergistic view of disease progression (Miah, 2025). Previous research has successfully combined different imaging modalities²⁴ with some studies, including fMRI, PET, imaging genetics, and structural MRI, but rarely comes with integration of wider data types (Zhou & Troyanskaya, 2015).

As a solution to this problem, we improve AD stage prediction using deep learning on a truly multimodal dataset, including imaging, EHR, and SNP genomic data to classify patients from cognitively normal (CN) to mild cognitive impairment (MCI) and AD (Cui et al., 2019; Lee et al., 2019). Our method combines these data sources utilizing classification layers like decision trees, random forest, SVM, and k-nearest neighbors, and exhibits the robustness of our proposed technique on the ADNI37 dataset comprising 808 SNPs with 503 MRIs and the clinical data from 2004 patients (Shen et al., 2014). Deep learning achieves impressive results on a variety of clinical data; however, one big difficulty is that model predictions are often not interpretable. To remedy this, we propose a new perturbation and clustering-based approach to extract the most prominent features influencing model decisions (Mia Md Tofayel Gonee et al., 2021).

This paper makes the following contributions: shows that deep learning using multimodal data had significantly better performance than unimodal models in AD stage prediction, presents an interpretable mechanism to discover important features, and proposes novel deep learning architectures that consistently outperform the shallow ones on various datasets (Mia Md Tofayel Gonee et al., 2022).

2. Data description

In this study, we used data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) to further study the progression of both early-stage Alzheimer's disease (AD) and mild cognitive impairment (MCI) (Mia Md Tofayel Gonee et al., 2020). The ADNI database contains a wealth of clinical, imaging, and genetic data for over 2,220 participants across four phases of research. Note that we use only the second half of these cohorts (ADNI2 only), and since ADNI3, a full expanded set for the current analysis is available, but their availability is projected to ADNI1 and ADNI-GO only, as ADNI3 is underway and expected to be completed in 2022 (Md Habibullah Faisal, 2022). Cross-sectional MRI and PET/MRI images were acquired on the imaging dataset. Clinical or electronic health record (EHR) data includes clinical test results, medication information, imaging-derived scores, demographic data, and biochemical test results (Md Ekrim et al., 2024). Genetic information comes from whole-genome sequencing of 819 individuals from the ADNI cohort. Of the 2004 subjects included in the analyses, 226 subjects had all 3 data types (imaging + EHR + SNP), 588 had SNP + EHR, 284 had imaging + EHR, and the rest of the participants had EHR data only. It is also crucial to understand that the raw imaging and associated genetic datasets are still slowly but surely becoming available, and are not yet fully released (for analysis) (Manik et al., 2025).

3. Study design for novel DL and multi-modality data analysis

This study assessed the utility of imaging, genetic (SNP) and EHR data to predict and classify the stage of Alzheimer's disease (AD) in this study (Mahmud, Orthi, et al., 2025). The results show that the deep learning models outperform classic or shallow learning models, including decision trees, random forests, one-vs-one support vector machines (SVM), and k-nearest neighbors (KNN) (Kaur et al., 2023). This study also combined each of the three modalities in a multimodal approach to characterize AD stage more comprehensively (Mahmud, Barikdar, et al., 2025). Hence, we propose the following three data-fusion strategies: using hand-crafted features combined with conventional classifiers, by direct concatenation of features from multiple modalities, and lastly via shallow models with feature-level fusion (Khair et al., 2024). In intermediate-feature-level fusion, a deep network is used to map initial components to intermediate features, which are then fed into a terminal classification layer (Khair et al., 2025). Vote-based decision-level fusion from independent single-modality model predictions. In this study, we assess four different combinations of two data modalities (Kamal et al., 2025):

Imaging + SNP + EHR

Imaging + EHR

SNP + EHR

SNP + Imaging

For each of these combinations, we perform two separate system-classification tasks: The three categories are as follows: (1) Alzheimer's disease (AD), (2) moderate cognitive impairment (MCI), and (3) CN (cognitively healthy). A deeper dive: Difference Between AD and CN to ensure robust performance evaluation over each configuration of the model, internal cross-validation and evaluation on a separate external set was performed for each model (Yeasmin et al., 2025).

4. Goal-oriented multi-modality data analysis and other novel DL

The proposed research involves multi-modality data from the literature, along with its potentialities of utilizing advanced deep learning (DL) based methods for achieving a goal-oriented analysis of such information (Tiwari et al., 2024). Performance on the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset is shown for both cross-validation internally and test externally

(Tiwari et al., 2025). Evaluation metrics of each deep learning model, such as average accuracy, precision, recall and F1 scores, along with baseline shallow (shallow) models, are used for comparisons. F1 scores for individual data modalities emphasize the benefit of using various data sources in combination, as well as the better performance of deep learning models, compared to single-modality models (Tasnim et al., 2025).

5. 3D convolutional neural network (DL) is superior to shallow models on imaging MRI data.

Experimental results show that 3D convolutional neural networks (a type of deep learning model) outperformed traditional shallow learning models for MRI imaging data (Sobuz et al., 2025). An MRI sample from a patient includes 9,108 3D voxels organized over five selected brain regions selected represented by a 3D matrix of dimension $22 \times 23 \times 18$. Fig. 1 shows deep and shallow data integration models. Fig. 2 shows combination deep models at the intermediate feature level for multi-modality characteristics (Siddiqa et al., 2025).

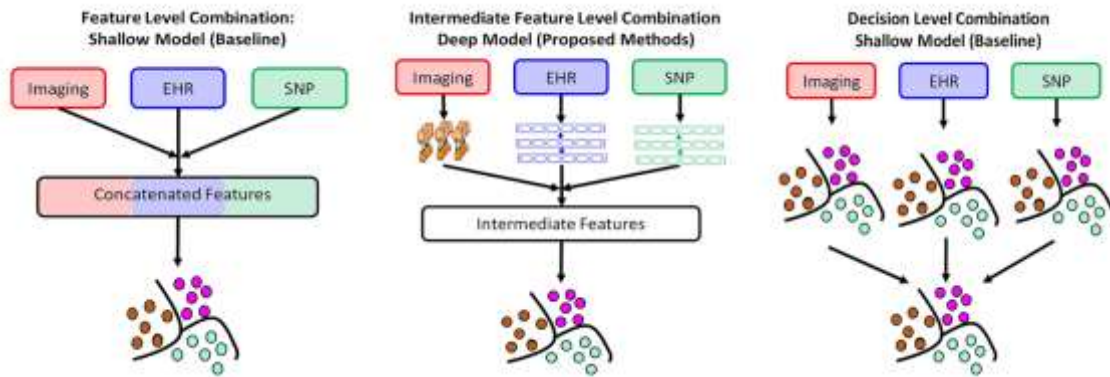


Fig. 1. Deep and shallow data integration models (Venugopalan et al., 2021).

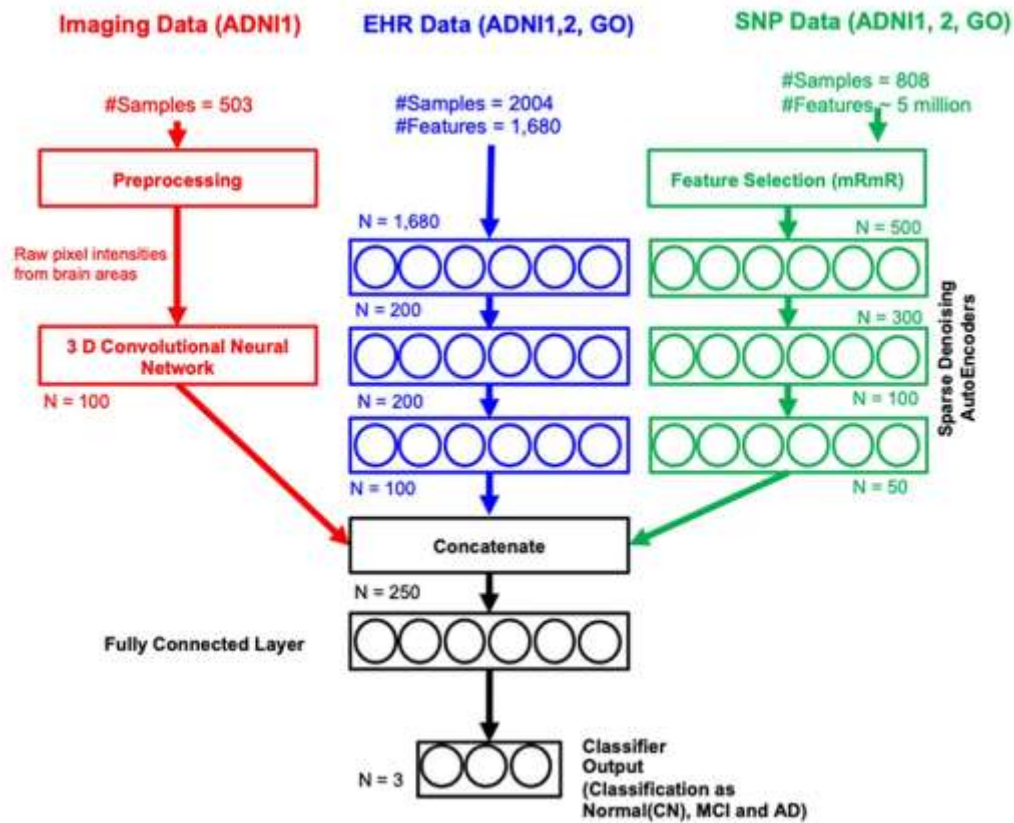


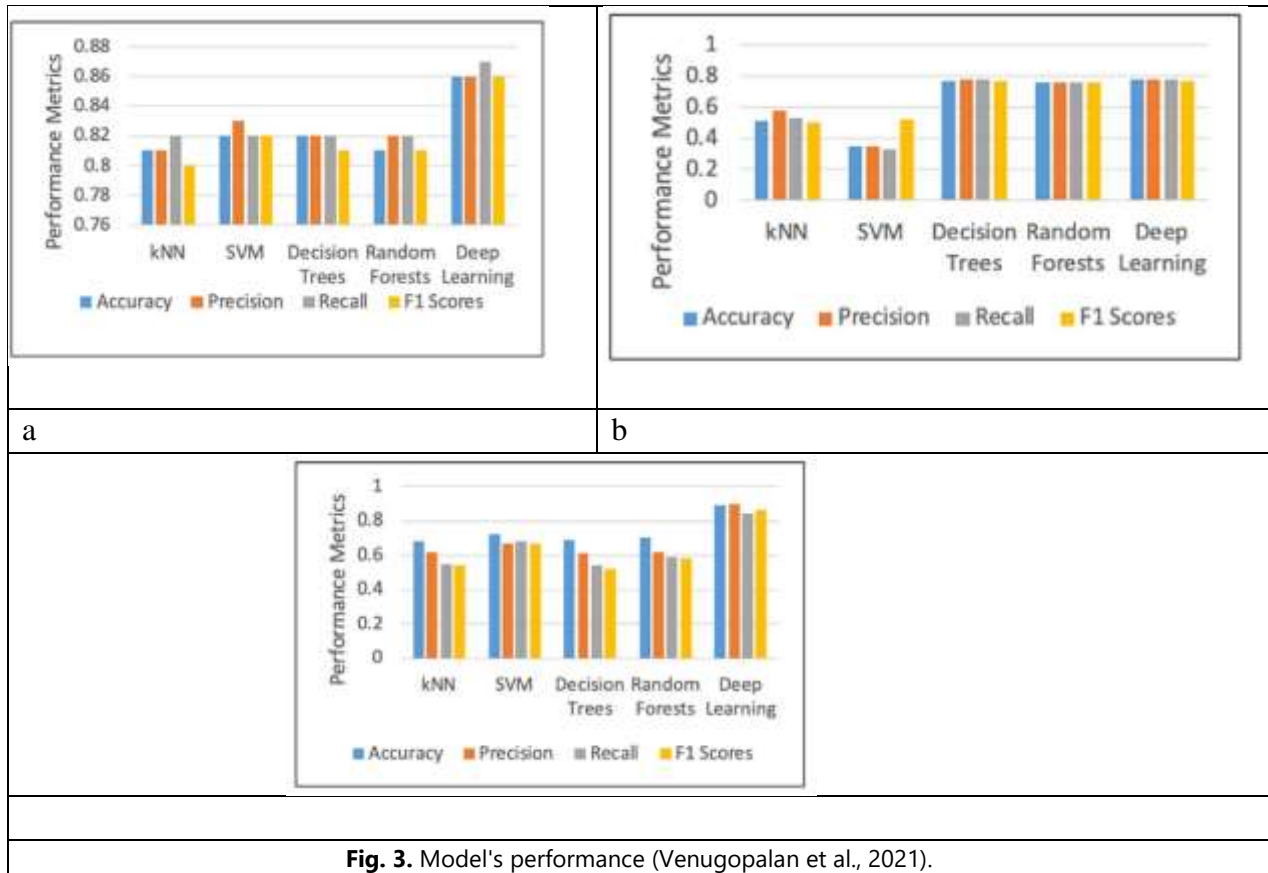
Fig. 2. Combination Deep Models at the Intermediate feature Level for Multi-modality Characteristics (Venugopalan et al., 2021).

In the deep learning models, the initial fully connected layer is made up of 100 nodes, structured as 5 groups of 20. This is followed by a second fully connected layer containing 20 nodes (Sadik et al., 2024). As shown in Fig. 3, convolutional neural network (CNN) models using imaging data significantly outperform traditional shallow learning approaches, achieving the highest average F1 scores and precision. Table 1 shows a summary of the model's accuracy and prediction. Fig. 3 also displays the Model's performance (Prabha et al., 2024).

Table 1. Summary of the model's accuracy and prediction.

<i>Metrics</i>	KNN	SVM	Decision Trees	RF	Deep Model
<i>Accuracy CN vs AD</i>	0.82 ±.04	.81 ±.06	.81 ±.07	.80 ±.09	.87 ±.03
<i>Precision CN</i>	0.80 ±.10	.81 ±.08	.84 ±.12	.80 ±.14	.91 ±.07
<i>Precision AD</i>	0.86 ±.12	.85 ±.12	.84 ±.11	.81 ±.12	.89±.08
<i>Recall CN</i>	0.84 ±.13	.86 ±.13	.78 ±.12	.85 ±.14	.88 ±.08
<i>Recall AD</i>	0.81 ±.2	.80 ±.11	.86 ±.08	.86 ±.10	.89 ±.2
<i>MeanF1</i>	0.80 ±.07	.82 ±.5	.78 ±.09	.81 ±.08	.89 ±.03

CN					
MeanF1	0.82 ±.06	.86 ±.2	.86 ±.04	.85 ±.06	.85 ±.09
AD					



Shallow and deep autoencoder models have similar behavior on EHR data, the study found (Prabha et al., 2024). The patients are stratified into three classes using EHR information with 2004 patients with 1680 normalized attributes per patient, AD, MCI, and CN (Noor et al., 2024). We represent each text file extract with a 722-dimensional feature vector, and the auto-encoder we built has three layers with a total of 200, 100, and 50 nodes (Nilima et al., 2024). To enable proper training, Adam is trained on the deep networks with a maximum count of epochs of 25, a number which states how many epochs Adam is trained on the full dataset. After hyperparameter optimization, the initial training and fine-tuning are regularized with coefficients of 0.03. Dropout was used on every layer (0.6 frequency). Results show autoencoders give better performance in comparison to other tree models and model families (Noor et al., 2024).

6. Results of multi-modality categorization.

The intermediate features generated by the single-modality deep models are concatenated and sent into a second classification layer for integration (Nilima et al., 2024). The three modalities in deep modes are imaging, EHR, and SNP analysis. Zeros can be employed to mask the lack of a specific modality. Alternative classification layers include support vector machines, decision trees, random forests, and KNN (Md Alamgir Miah, 2025). Indeed, the 0.78 ± 0.0 accuracy cannot be obtained by internal CV within SHALLOW models. The deepest models for HER+SNP combinations outperform the best single-modalities DL. The EHR and imaging combinations are better than DLs with deep models using a single modality (Manik et al., 2025). Based on the results, it turns out that random forests outperform all others on the external set, shallow models perform worse than DL ones in combination. By contrast, because very few participants have both data modalities, performance without out-of-sample data is poor (Khair et al., 2025).

7. Discussion for novel DL and multi-modality data analysis

The single-modalities deep models outperform the shallow models either because they merge with a more complex decision surface and learn the most suitable feature combination during the training process (Kaur et al., 2023). Deep models allow computation of complex decision boundaries on multiclass classification data due to the structural architecture of the model, thus, it can be useful in the prediction of problems like Multi-Cluster Inclusion (MCI), the clinical problem used as research subject in the field of Alzheimer's disease (Kamruzzaman et al., 2025). The multidimensionality of deep models, for example, allows them to learn correlations between data of various modalities and thus makes them much more robust to noisy data. But when the dataset is smaller, deep models couldn't do as good a job as there is less training data available for networks than there are actuators (Kamruzzaman et al., 2024). The combinations EHR + SNP, EHR + Imaging SNP, and EHR + Imaging performed best. To handle the small sample size, we can apply techniques like domain adaptation and transfer learning. For other types of data or new domains, pretrained network parameters can be fine-tuned using neural networks already trained with similar datasets. As for future research, our goal is to add an end-to-end training step and to combine auto-encoders with more integration approaches (Johora et al., 2024).

8. Study the design of novel feature extraction to assist in DL model interpretation

Research design of new feature extraction for the understanding of DL models. DL has the challenge of model interpretation, which is often regarded as a hurdle for realistic biological applications (Islam et al., 2025). The weights of a deep model can influence the outcomes through a series of combinations over several layers, leading to a non-clinically meaningful 65 output. In this work, we propose a new way to interpret a model by masking a single feature independently and probing drop-out accuracy (Fig. 4). For feature extraction, it ranks the features that have the highest precision drop. Table 2 shows the extraction of features from deep models and the results of the internal and external tests (Imran et al., 2024).

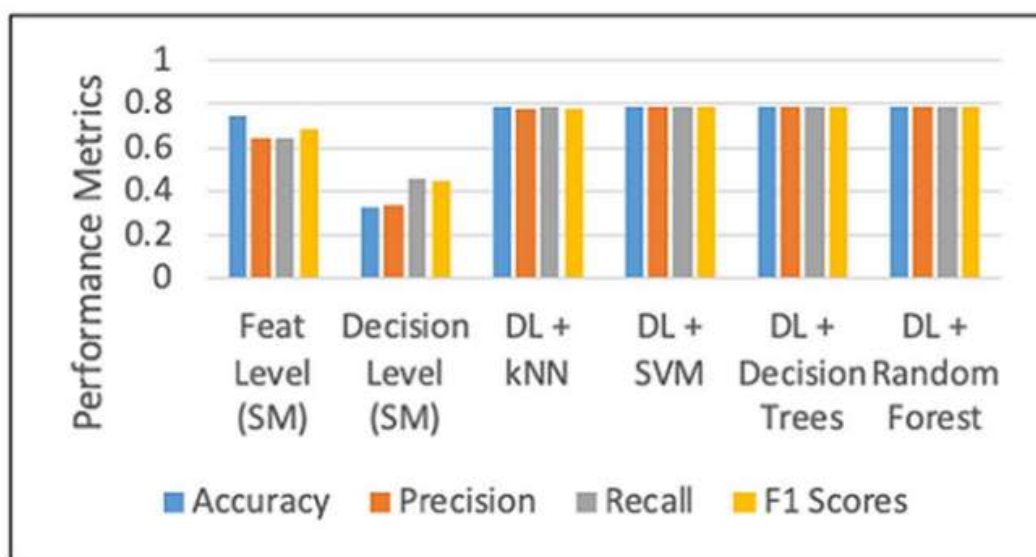


Fig. 4. The performance from internal cross-validation for predicting Alzheimer's stage while combining each data modality.

Table 2. The extraction of features from deep models and the results of the internal and external tests

Models	Test Performance
EHR (CN, MCI, AD)	Accuracy Performance 0.77 Precision Performance 0.77 Recall 0.78 F1 Scores: 0.77
Imaging	Accuracy Performance 0.85

Prediction (CN, AD)	Precision Performance 0.84 Recall 0.84 F1 Scores: 0.84
SNP Prediction (CN, MCI/AD)	Accuracy: 0.67 Precision: 0.67 Recall: 0.58 F1 Scores: 0.54
EHR + SNP + Imaging Prediction (CN, MCI, AD)	0.79 0.78 0.79 F1 Scores: 0.79
EHR + SNP Prediction (CN, MCI, AD)	0.79 0.79 0.80 F1 Scores: 0.79
EHR + Imaging Prediction (CN, MCI, AD)	0.78 0.77 0.78 F1 Scores: 0.78

9. Analysis and findings of new feature extraction to understandability of DL Models

The most common EHR components extracted included brain volumes, memory tests, and imaging summary scores (Table 1). Some of the indications of AD have been observed in terms of changes in brain volume and memory (Imran et al., 2024). Prototypical imaging signs captured, to date, as validated biospecimens in PET and MRI studies^{47,48,49} are volume and architecture of the hippocampus^{46,47} and dedicated areas in limbic and cortical regions⁴⁵. Last, for SNP features, chromosomes 10, 4, 19, 1 and 5 were selected. SNP + Imaging + EHR and SNP + EHR select other EHR elements (metabolic indicators, brain volume, and memory tests) associated with known risk factors for AD. Selected EHR+ Imaging features include brain sizes, clinical dementia scores, and metabolites. Image + SNP selections: For brain regions with more SNPs (than SNP traits) , Hippocampus/Amygdala. To visualize the correlations in the intermediate features, we also k-means cluster the intermediate features from SNP and EHR data (Methods) (Hossain et al., 2025). Now plotting the clusters for the inter and raw data in this case, and it can be seen that the inter features provide a more separation than the original features. RMSE has been determined as our final metrics to encompass the intermediate qualities which depict subtle correlations (Supplementary Fig. 5).

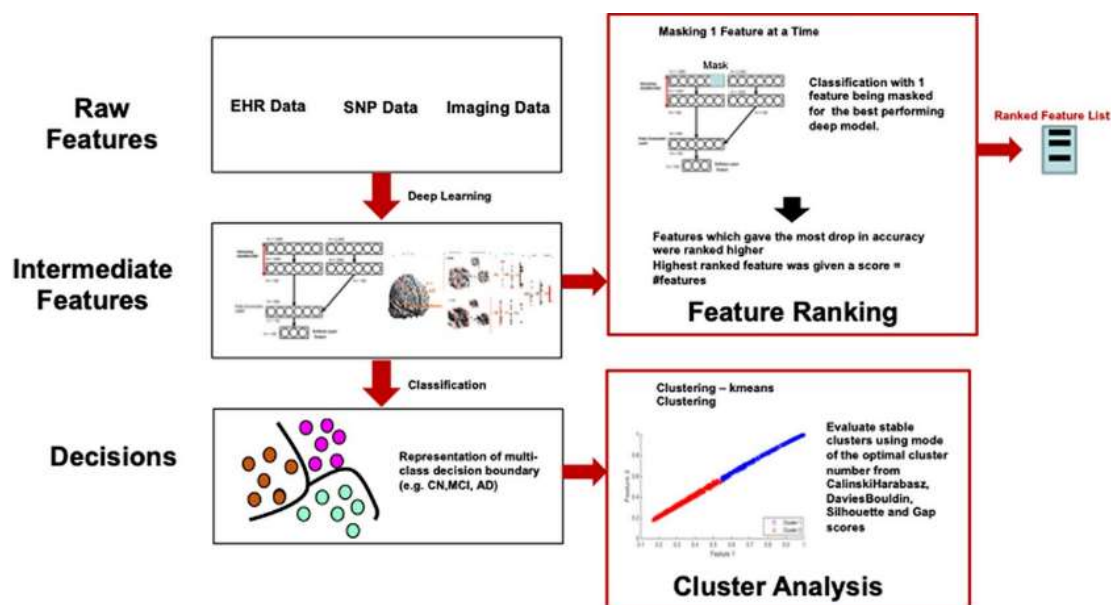


Fig. 5. Facilitating feature extraction for deep model interpretations.

10. Conclusions

AD patients are not only challenging to diagnose, but AD staging currently suffers from poor prognosis assessment accuracy. This paper showcases the abilities of deep learning in multi-modal data fusion, such as:

- ❖ New perturbation and clustering-based extractability techniques that make it possible to interpret model predictions based on AD stages.
- ❖ Demonstration of deep models outperforming shallow models for single-modality predictions of the AD stage.
- ❖ Development of a novel multi-modal data fusion framework that outperforms single-modality DL techniques.
- ❖ 3D convolutional network architecture to analyze MRI imaging data for AD
- ❖ While performance has improved, our study remains limited by small sample sizes. In the future, we plan to test our models on a larger and more diverse data set.

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