Multimodal deep learning for Alzheimer's disease dementia assessment

Problem: make a differential diagnosis of Alzheimer's disease, differentiating between normal cognitive aging, MCI, AD, and other dementia etiologies.

Objective: strategy provides evidence that automated methods driven by deep learning may approach clinical standards of accurate diagnosis even amidst heterogeneous datasets, development and validation of a deep learning framework capable of accurately classifying subjects with **NC, MCI, AD, and nADD** in multiple cohorts of participants with different etiologies of dementia and varying levels of cognitive function.

Methodology:

Phase 1:

1- Using an automated thresholding technique to (Scan axes were reconfigured to match the standard orientation of MNI- 152 space).
2- The volume-of-interest was skull-stripped to isolate brain pixels. A preliminary linear registration of the skull-stripped brain to a standard MNI-152.

Phase 2:

Was designed to fine-tune the quality of linear registration and parcellate the brain into discrete regions.

Harmonization of non-imaging data: We specifically examined information related to demographics, past medical history, neuropsychological test results, and functional assessments.

Overview of the prediction framework:

(i) separation of NC from MCI and DE (COGNC task),

(ii) separation of MCI from NC and DE (COGMCI task

(iii) separation of DE from NC and MCI (COGDE task).

Following the sequential completion of the COG and ADD tasks, we were able to successfully separate AD participants from NC, MCI, and nADD subjects.

MRI-only model: We used post-processed volumetric MRIs as inputs and **trained a CNN model** to (transfer information between the COG and ADD tasks).

Non-imaging model:

We developed a range of traditional machine learning classifiers using all available non-imaging variables shared between the NACC and the OASIS datasets.

Fusion model:

The combination of data sources was accomplished by concatenating the DEMO and the ALZ scores derived from the MRI-only model to lists of clinical variables. As with our non-imaging model, the development and validation of fusion models were limited to NACC and OASIS only given the limited availability of non imaging data in other cohorts.

We trained all models on the NACC dataset using cross validation.

Interpret models with SHAP

Explain Image Classification by SHAP Deep Explainer

- **Train a CNN model on CIFAR10 dataset**
- **Compute SHAP values**
- **Visual the prediction result and SHAP values**

DataSet: Data from ADNI, AIBL, NACC, NIFD, OASIS and PPMI can be downloaded from publicly available resources. Data from FHS and LBDSU are available.

Imaging Type is :Structural

Field Stength:1.5 or 3 tesla.

Seq or imaging parameter :Whole brain.

Source of data:https://static-content.springer.com/esm/art%3A10.1038%2Fs41467-022-31037-5/MediaObjects/41467_2022_31037_MOESM4_ESM.zip

Result:

Evaluate Model: Since the ***gen_score*** method has already saved the raw predictions in csv, the evaluation pipeline just needs to look for those information from the corresponding experimental folders under ***tb_log***. Mean, std or **95%** confidence intervals are estimated using multiple independent experiments, for instance, from five-fold cross validation

where the COG_score is the continuous regression score from the model

the ADD_score is the probability of being ADD

the COG_pred is the predicted label (NC=0, MCI=1, DE=2)

the ADD_pred is the predicted label (ADD=1, nADD=0)

the COG is the true label (NC=0, MCI=1, DE=2)

the ADD is the true label (ADD=1, nADD=0)

Variable	COGnc task AUC	COGnc task AP	COGde task AUC	COGde task AP	ADD task AUC	ADD task AP
trailA	0.783	0.79	0.817	0.587	0.82	0.877
trailB	0.816	0.839	0.853	0.564	0.832	0.869
boston	0.791	0.762	0.825	0.59	0.569	0.867
digitB	0.726	0.719	0.783	0.458	0.833	0.891
digitBL	0.704	0.69	0.735	0.413	0.522	0.884
digitF	0.66	0.649	0.684	0.383	0.828	0.881
digitFL	0.632	0.624	0.654	0.329	0.54	0.865
animal	0.839	0.824	0.878	0.702	0.501	0.869
gds	0.647	0.633	0.6	0.275	0.608	0.895
lm_imm	0.872	0.86	0.907	0.722	0.638	0.913
lm_del	0.895	0.866	0.916	0.706	0.713	0.93
mmse	0.881	0.848	0.931	0.814	0.616	0.896
npiq_DEL	0.548	0.543	0.56	0.339	0.522	0.871
npiq_HALL	0.526	0.533	0.544	0.294	0.55	0.878
npiq_AGIT	0.597	0.574	0.628	0.357	0.501	0.86
npiq_DEPD	0.588	0.57	0.6	0.301	0.523	0.872
npiq_ANX	0.606	0.562	0.642	0.348	0.539	0.877
npiq_ELAT	0.513	0.527	0.516	0.246	0.506	0.866
npiq_APA	0.623	0.59	0.67	0.417	0.58	0.887
npiq_DISN	0.556	0.55	0.569	0.299	0.566	0.882
npiq_IRR	0.603	0.578	0.607	0.321	0.52	0.87
npiq_MOT	0.559	0.551	0.589	0.338	0.528	0.873
npiq_NITE	0.567	0.554	0.577	0.307	0.552	0.878
npiq_APP	0.575	0.561	0.595	0.32	0.541	0.875
faq_BILLS	0.794	0.742	0.828	0.79	0.811	0.859
faq_TAXES	0.807	0.762	0.836	0.801	0.522	0.872
faq_SHOPPING	0.733	0.676	0.88	0.752	0.536	0.875
faq_GAMES	0.706	0.673	0.841	0.689	0.871	0.879
faq_STOVE	0.632	0.602	0.73	0.55	0.53	0.876
faq_MEALPREP	0.709	0.677	0.853	0.71	0.821	0.886
faq_EVENTS	0.75	0.687	0.867	0.723	0.54	0.874
faq_PAYATTN	0.736	0.674	0.846	0.684	0.518	0.872
faq_REMDATES	0.82	0.756	0.828	0.778	0.827	0.871
faq_TRAVEL	0.781	0.716	0.908	0.766	0.501	0.864

	Neuroradiologists	MR-only model
Accuracy	0.566±0.054 [0.516-0.616]	0.692±0.035 [0.649-0.735]
F-1	0.571±0.070 [0.506-0.636]	0.920±0.044 [0.865-0.975]
Sensitivity	0.589±0.122 [0.476-0.702]	0.464±0.090 [0.352-0.576]
Specificity	0.543±0.142 [0.412-0.674]	0.750±0.022 [0.723-0.777]
MCC	0.135±0.108 [0.035-0.235]	0.435±0.057 [0.364-0.506]

Limitations:

Increasing the accuracy.

Summary:

Shangran Qiu, Matthew I. Miller, Prajakta S. Joshi, they do implementation of a deep learning framework that accomplishes 2 diagnostic steps to identify persons with normal cognition (NC), mild cognitive impairment (MCI), Alzheimer's disease (AD) dementia, and dementia due to other etiologies (nADD). We demonstrated that the framework compares favorably with the diagnostic performance of neurologists and neuroradiologists. To interpret the model,We also created t three separate models: (i) MRI-only model, (ii) Non-imaging model, (iii) Fusion model, we conducted SHAP (SHapley Additive exPlanations) analysis on brain MRI and other features to reveal disease-specific patterns that correspond with expert-driven ratings and neuropathological findings.

Multiclass diagnosis of stages of Alzheimer's disease using linear discriminant analysis scoring for multimodal data

Problem: diagnosis of stages of Alzheimer's disease.

Objective: we propose a framework that can diagnose AD.

Methodology: In this study, we proposed an LDA-based scoring strategy approach for AD multiclass diagnosis in the presence of four modalities, i.e., MRI, FDG-PET, CSF, and genetic features. Using convolutional neural networks (CNNs), to extract and fuse multimodal data from neuroimages.

using three-way classification (AD versus MCI versus NC) and four-way classification (AD versus progressive MCI (pMCI) versus stable MCI (sMCI) versus NC) with multimodal data including those related to MRI, positron emission tomography (PET), CSF, and genes.

Methods	validation	NC vs. AD	sMCI vs. pMCI
hybrid CNN and RNN [30]	5-fold CV	89.1%	72.5%
Ensemble of deep CNN [19	4-fold CV	99.3%	–
3D-CNN and FSBi-LSTM [17]	10-fold CV	94.8%	65.4%
Multi-Modality 3D CNN [18]	Fixed dataset	90.1%	76.9%
3D densely connected CNN [31]	Fixed dataset	97.4%	78.8%
CNN and ensemble learning [32]	5-fold CV	84%	62%
This study	5-fold CV	93.4%	81.2%

DataSet: ADNI, The evaluation was conducted by five-fold cross-validation. 80% of the samples were used to train the LDA and classifiers, and the remaining 20% were used.

Result: Obtained accuracy of 66.7% and 57.3% in three-way and four-way classifications. LDA was trained with 80% samples with their labels during five-fold cross-validation, and the "n_components" parameter was set to 1 to retain the most discriminative component as score. The target age of age correction was set to 75, which is near the average age (73.3) of all subjects.

Limitations:

The requirement of too many modalities would limit the practical usage of this approach.

Accuracy 57.3%, need to increase.

Summary:

Weiming Lin, Qinquan Gao, Min Du, Weisheng Chen, Tong Tong, In this study, we proposed an LDA-based scoring strategy approach for AD multiclass diagnosis in the presence of four modalities, i.e., MRI, FDG-PET, CSF, and genetic features. The LDA was used to calculate a score representing the pathological information from each modality, and the scores from different modalities ensured that the classifier could easily discriminate between different groups. LASSO and PCA were used to exclude irrelevant and interferential components before LDA, and a binary ELM-based tree decision classifier was built for multiclass classification. The experimental results indicated that the LDA scoring significantly improved the multiclass diagnosis. Benefiting from the information obtained from multiple modalities and the scoring strategy, we achieved a promising performance with an accuracy of 66.7% and F1-score of 64.9% for three-way diagnosis, and an accuracy of 57.3% and F1-score of 55.7% for four-way diagnosis, which were significantly better than the original method. When compared to other studies, the proposed approach also showed a better performance. Although multimodal data help to improve the performance of AD diagnosis, the requirement of too many modalities would limit the practical usage of this approach. However, the

more efficient multimodal fusion approach in this study is still useful for further AD studies, such as AD longitudinal trajectory modeling.

Reference	Objective	Methods	DataSet
Computers in Biology and Medicine (2021) www.elsevier.com/locate/compbiomed	propose a framework that can diagnose AD.	hybrid CNN and RNN Ensemble of deep CNN 3D-CNN and FSBi-LSTM Multi-Modality 3D CNN 3D densely connected CNN CNN and ensemble learning	ADNI
Multimodal deep learning for Alzheimer's disease dementia assessment. Nat Commun 13, 3404 (2022). https://doi.org/10.1038/s41467-022-31037-5	differential diagnosis of Alzheimer's disease, differentiating between normal cognitive aging, NC, MCI, AD, and nADD, and other dementia etiologies.	CNN with other technics.	ADNI, AIBL, NACC, NIFD, OASIS ,PPMI, FHS and LBDSU.