Assisted Diagnosis of Alzheimer's Disease Based on Deep Learning and Multimodal Feature Fusion

Problem: Early detection of AD

Objective:

- classification AD versus NC and AD versus MCI using sMRI
- Classification LMCI versus EMCI using fMRI images

Methods:

- lightweight network ShuffleNet (sMRI)
- PCANet (fMRI)

Dataset: multi modal MRI images from ADNI

Preprocessing:

- VBM-DARTEL method is used to preprocess sMRI using SPM8 software
- Software DPABI is used to preprocess fMRI

Result:

- AD versus NC (AUC: 86.9)
- AD versus MCI (AUC: 91.9)
- MCI versus NC (AUC:67.3)
- the difference between LMCI and EMCI is very slight (AUC: 58.0)

Limitations

- the classification effect of MCI versus NC is poor hand, because MCI is the early stage of the AD patient, the brain gray matter structure has not changed significantly, and the network is difficult to locate the disease characteristics.
- the model is not fully trained. Similarly, because the difference between LMCI and EMCI is very slight, the result of LMCI versus EMCI is worst.

Conclusions

- **3DShuffleNet** is used to build an **sMRI**-assisted diagnosis model, and **PCANet** is used to build an **fMRI** assisted diagnosis model.
- compared with single modality, better classification results on multiple modalities are obtained

Summary

Ehsan Hosseini-Asl and Adrien Payan [6] used 3D convolutional neuralnetworks and autoencoders to capture AD biomarkers. Zhenbing Liu used a multiscale residual neural network to collect multiscale information on a series of image slices and to classify AD, mild cognitive impairment (MCI), and NC. Ciprian D. Billones [8] improved the VGG-16 network for constructing classification model of AD, MCI, and NC. Junchao Xiao [9] used stacked automatic encoders and functional connection matrices to classify migraine patients and normal people. Meszl´enyi Regina [10] proposed a dynamic time normalization distance matrix, Pearson correlation coefficient matrix, warping path distance matrix, and convolutional neural network to realize AD-assisted diagnosis. VBM-DARTEL [13] method is used to preprocess sMRI images including segmentation, generating specific templates generation, flow fields generation, and normalization. above preprocessing steps are all implemented using SPM8 software. Medical image processing software DPABI is used to preprocess fMRI images including the data removal of the first 10 time points, slice timing, realignment, normalization, smoothing, detrending, filtering, and extracting time series to calculate function link matrix. sMRI features extracted by the **3DShuffleNet** network are fused with the fMRI features extracted by the **PCANet**. Compared with single modality, better classification results on multiple modalities are obtained

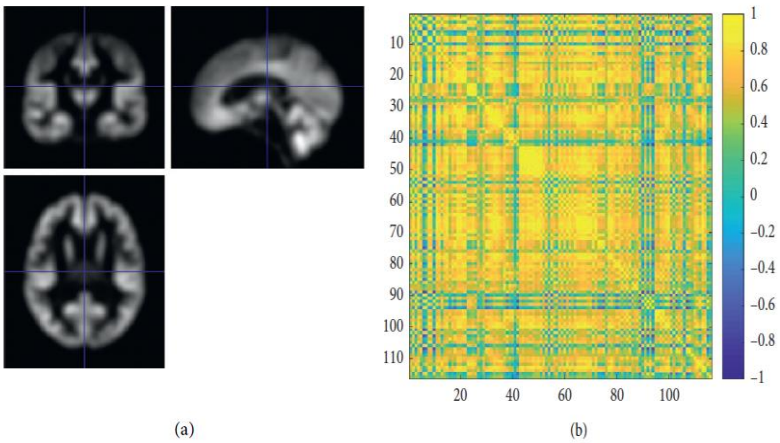

Figure 1: Preprocessing results of (a) sMRI data and (b) fMRI data.

Deep Learning in Alzheimer's disease: Diagnostic Classification and Prognostic Prediction Using Neuroimaging Data

Problem: Early detection of AD

Objective:

- Early detection of AD and
- Prediction of AD progression

Methods:

- Well-known pattern analysis methods, such as linear discriminant analysis (LDA), linear program boosting method (LPBM), logistic regression (LR), support vector machine (SVM), and support vector machine recursive feature elimination (SVM-RFE)
- Deep learning is used together with traditional machine learning methods, i.e., SVM as a classifier, it is referred to as a "hybrid method"

Dataset: multi modal MRI and PET images from ADNI

Result:

-The performance in AD/CN classification and/or prediction of MCI to AD conversion yielded better results in PET data compared to MRI

Limitations

- One weakness of deep learning is that it is difficult to modify potential bias in the network when the complexity is too great to guarantee transparency and reproducibility.

Future direction

- Progress will be made in deep learning by overcoming these issues while presenting problem-specific solutions.
- Form of learning that adapts to changes in data as it makes its own decision based on the environment, may also demonstrate applicability in the field of medicine.

Methods ,Results

TABLE 2 | Summary of 16 previous studies to systematically be reviewed.

References	Modality	Data processing/training	Classifier	AD:NC acc.	SEN	SPE	cMCI:ncMCI acc.	SEN	SPE	AD	cMCI	ncMCI	NC	Total
Suk and Shen (2013)	MRI, PET, CSF	SAE	SVM	**95.9**			**75.8**			51	43	56	52	202
Liu et al. (2014)	MRI, PET	SAE + NN	Softmax	**87.76**	88.57	87.22	76.92 (MCI:NC)	74.29	78.13	65	67	102	77	311
Suk et al. (2014)	MRI, PET	DBM	SVM	**95.35**	94.65	95.22	**75.92** 86.75 (MCI:NC)	48.04 95.37	95.23 65.87	93	76	128	101	398
Li et al. (2014)	MRI, PET	3D CNN	Logistic regression	**92.87**			76.21 (MCI:NC)			198	167	236	229	830
Li et al. (2015)	MRI, PET, CSF	RBM + drop out	SVM	**91.4**			**57.4** 76.21 (MCI:NC)			51	43	56	52	202
Suk et al. (2015)	MRI, PET, CSF	SAE + sparse learning	SVM	**98.8**			**83.3** 90.7 (MCI:NC)			51	43	56	52	202
Liu et al. (2015)	MRI, PET	SAE with zero-masking	Softmax	**91.4**	92.32	90.42	82.1 (MCI:NC)	60.0	92.32	77	67	102	85	331
Cheng et al. (2017)	MRI	3D CNN	Softmax	**87.15**	86.36	85.93				199			229	428
Cheng and Liu (2017)	MRI, PET	3D CNN + 2D CNN	Softmax	**89.64**	87.10	92.00				93			100	193
Aderghal et al. (2017)	MRI	2D CNN	Softmax	**91.41**	93.75	89.06	65.62 (MCI:NC)	66.25	65.0	188	399 (MCI)		228	815
Korolev et al. (2017)	MRI	3D CNN	Softmax	**80**	87 (AUC)		61 (MCI:NC) 56 (MCI:NC)	65 (AUC) 58 (AUC)		50	43 (MCI)	77 (eMCI)	61	111
Vu et al. (2017)	MRI, PET	SAE + 3D CNN	Softmax	**91.14**						145			172	317
Liu et al. (2018a)	PET	RNN	Softmax	**91.2**	91.4	91.0	78.9 (MCI:NC)	78.01	80.0	93	146 (MCI)		100	339
Liu et al. (2018b)	MRI	Landmark detection + 3D CNN	Softmax	**91.09**	88.05	93.50	**76.9**	42.11	82.43	159	38	239	200	636
Lu et al. (2018)	MRI, PET	DNN + NN	Softmax	**84.6**	80.2	91.8	**82.93**	79.69	83.84	238	217	409	360	1224
Choi and Jin (2018)	PET	3D CNN	Softmax	**96**	93.5	97.8	**84.2**	81.0	87.0	139	79	92	182	492

SEN = TP/(TP + FN), SPE = TN/(TN + FP). TP, true positive; TN, true negative; FP, false positive; FN, false negative. All data on this table were from ADNI.

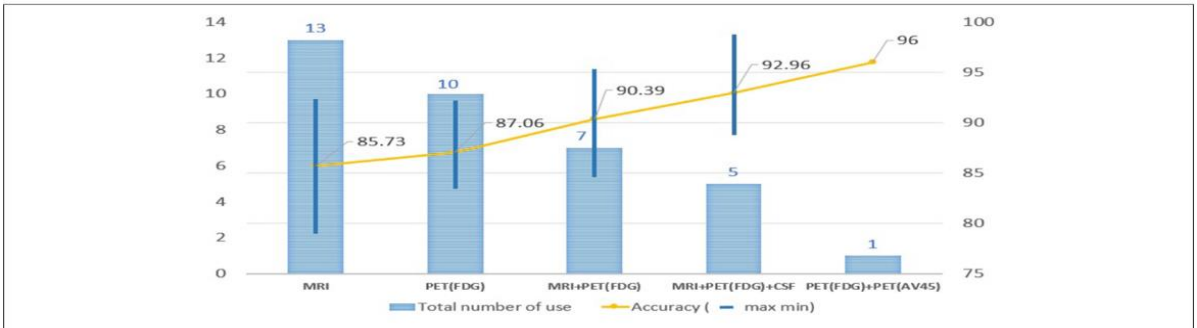

FIGURE 6 | Changes in accuracy by types of image resource. MRI scans were used in 13 studies, FDG-PET scans in 10, both MRI and FDG-PET scans in 12, and both amyloid PET and FDG-PET scans in 1. The performance in AD/CN classification yielded better results in PET data compared to MRI. Two or more multimodal neuroimaging data types produced higher accuracies than a single neuroimaging technique.

- The performance in AD/CN classification and/or prediction of MCI to AD conversion yielded **better results in PET data** compared to MRI.

Summary

Alzheimer's disease (AD), the most common form of dementia, is a major challenge for healthcare in the twenty-first century. An estimated 5.5million people aged 65 and older are living with AD, and AD is the sixth-leading cause of death in the United States. The global cost of managing AD, including medical, social welfare, and salary loss to the patients' families, was $277 billion in 2018 in the United States, heavily impacting the overall economy and stressing the U.S. health care system (Alzheimer's Association, 2018). AD is an irreversible, rogressive brain disorder marked by a decline in cognitive functioning with no validated disease modifying treatment (De strooper and Karran, 2016). Great deal of effort has been made to develop strategies for **early detection,** especially **at pre-symptomatic stages** in order to slow or prevent disease progression. One weakness of deep learning is that it is difficult to modify potential bias in the network when the complexity is too great to guarantee transparency and reproducibility. Progress will be made in deep learning by overcoming these issues while presenting problem-specific solutions. form of learning that adapts to changes in data as it makes its own decision based on the environment, may also demonstrate applicability in the field of medicine.Machine learning generally require **four steps:** feature xtraction, feature selection, dimensionality reduction, and feature-based classification algorithm selection. Well-known **pattern analysis methods,** such as linear discriminant analysis (LDA), linear program boosting method (LPBM), logistic regression (LR), support vector machine (SVM), and support vector machinerecursive feature elimination (SVM-RFE), have been used and hold promise **for early detection of AD and the prediction of AD progression** When deep learning is used together with traditional machine learning methods, i.e., SVM as a classifier, it is referred to as a **"hybrid method". Multimodal neuroimaging data** have been used to identify structural and molecular/functional biomarkers for AD. deep learning approaches have been applied to AD diagnostic classification using original neuroimaging data without any feature selection procedures. If the data is imbalanced, the chance of misdiagnosis increases and sensitivity decreases. Multimodal neuroimaging data such as **MRI and PET** have commonly been used in deep learning: **MRI** for *brain structural atrophy*, amyloid **PET** *for brain amyloid-b accumulation*, and **FDG-PET** *for brain glucose metabolism.* The performance in AD/CN classification and/or prediction of MCI to AD conversion yielded **better results in PET data** compared to MRI.

References	Modality	Methods	Dataset	Objective
Yu Wang et al (2021) https://doi.org/10.1155/2021/6626728	sMRI, fMRI	**ShuffleNet, PCANet**	ADNI	making correct diagnoses of AD disease
fnagi.2019. https://doi.org/10.3389/fnagi.2019.00220	MRI, PET, CSF	LPBM LDA LR SVM SVM-RFE 3DCNN 2DCNN SAE DBM	ADNI	- Early detection of AD - Prediction of AD progression