

# Applying 3DPCANet and Functional Magnetic Resonance Imaging to Aided Diagnosis of Alzheimer's Disease

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## Research Article

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# 1 Applying 3DPCANet and Functional Magnetic Resonance 2 Imaging to Aided Diagnosis of Alzheimer's Disease

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## 8 Abstract

9 Alzheimer's disease (AD) is a progressive neurodegenerative disease, which changes the  
10 structure of brain regions by some hidden causes. In this paper for assisting doctors to make  
11 correct judgments, an improved 3DPCANet method is proposed to classify AD by combining  
12 the mean (mALFF) of the whole brain. The main idea includes that firstly, the functional  
13 magnetic resonance imaging (fMRI) data is pre-processed, and mALFF is calculated to get  
14 the corresponding matrix. Then the features of mALFF images are extracted via the improved  
15 3DPCANet network. Finally, AD patients with different stages are classified using support  
16 vector machine (SVM). Experiments results based on public data from the Alzheimer's  
17 disease neuroimaging initiative (ADNI) show that the proposed approach has better  
18 performance compared with state-of-the-art methods. The accuracies of AD vs. significant  
19 memory concern (SMC), SMC vs. late mild cognitive impairment (LMCI), and normal  
20 control (NC) vs. SMC reach respectively 92.42%, 91.80%, and 89.50%, which testifies the  
21 feasibility and effectiveness of the proposed method.

22 **Keywords:** Alzheimer's disease; functional magnetic resonance imaging; 3DPCANet;  
23 support vector machine; mean amplitude of low-frequency fluctuation

24

## 25 0 Introduction

26 Alzheimer's disease (Alzheimer's disease, AD) is one of the most common neurological  
27 diseases of the brain, which seriously endangers the life and health of patients. By the end of  
28 2019, more than 10 million AD patients occurred in China which had the largest number of  
29 people with AD in the world [1]. AD firstly attacks the hippocampus where study and  
30 memory are processed [2]. In the early stage of this disease, the symptoms are forgetfulness  
31 and confusion. With the aggravation of the disease, visual space of the patient decreases, and  
32 patients cannot distinguish or deal with things alone. Patients' memories loss is serious,  
33 which leads to heavy burden for both patients and society. Therefore, the early diagnosis and  
34 timely treatment of AD is of great significance. In recent years, with the rapid development  
35 of computer and neuroimaging, it has become a mainstream trend to use computers and  
36 medical imaging to diagnose and analyse AD. Jiang [3] et al. VGGnet is used to extract  
37 normal control (NC) and early mild cognitive impairment (EMCI) sMRI image the deep

38 embedded features of the image, and Lasso is used to select the extracted features. Finally,  
39 SVM is used to classify the selected features. At present, the technical difficulties mainly  
40 include the extraction of effective features in medical imaging, as well as the design and  
41 construction of classification models with good robustness and simple structure.

42 Functional magnetic resonance imaging (fMRI) [4-5] is a non-invasive method which  
43 measures blood oxygen level dependent (BOLD) signal in the brain region at a certain  
44 moment and are widely used in AD research [6-9]. Zhou [10] et al. analyzed the locations of  
45 the lesion area, and used kernel principal component analysis (KPCA) to extract features.  
46 Finally, Adaboost is used to classify AD. Based on the automatic anatomical marker  
47 template, Li [11] et al. divided brain fMRI of each AD subject into 116 brain regions, and  
48 constructed a full brain function connection matrix by extracting the time series of each brain  
49 region. Then KPCA is used for feature extraction, and adaboost algorithm is used to classify.  
50 Using traditional machine learning methods like KPCA nonlinear image features can be  
51 extracted, but deep features are lacking. Therefore, in this paper, the traditional 3DPCANet  
52 network is improved. Max-pooling layer and activation function layer are added behind the  
53 convolutional layer for increasing the depth of network. So, the deep and nonlinear image  
54 features are extracted, and the classification accuracy of AD patients is increased.

55 Convolutional Neural Networks (CNN) is a feedforward neural network which is one of  
56 classic deep learning algorithms, and is mainly used for image feature extraction and  
57 classification. More and more researchers combine CNN with medical imaging to assist  
58 doctors for diagnosing diseases [12-15]. Rachna [16] et al. proposed a CNN model based on  
59 the transfer learning, in which the ImageNet dataset was used to pre-train VGG-16, and  
60 patients with the AD, NC, and MCI were then classified. Zhang [17] et al. designed a CNN  
61 using positron emission computed tomography (PET) and magnetic resonance imaging  
62 (MRI) as input. The obtained features were fused with those obtained by the mini-mental  
63 state examination (MMSE) and the clinical dementia rating (CDR). Then the fused features  
64 were inputted into CNN to realize the classification of AD, NC and MCI. Most of the  
65 research content of the above papers is to classify AD, NC and MCI, which does not  
66 accurately diagnose the stage of the patient with AD. Significant memory concern (SMC)  
67 stage exists between NC and MCI, and MCI patients are divided into EMCI and late mild  
68 cognitive impairment (Late MCI, LMCI). Compared with EMCI, patients with LMCI showed  
69 significant declines in cognition, memory, and self-care. Due to the small changes in the  
70 brain structure of AD patients on adjacent development stages, it is difficult to extract  
71 effective classification features. While the model proposed in this paper may be used to  
72 classify more detailed subgroups of AD patients, and to better assist medical personnel to  
73 diagnose the disease.

74 PCANet is a simple CNN, proposed by Chan [18] et al, by which the deep features of the  
75 sample data are learned based on the traditional principal component analysis (PCA). Li [19]  
76 developed 3D-PCANet deep network for MRI feature extraction, and realizes the automatic  
77 classification of MRI by combining the obtained data information with the support vector  
78 machine (SVM) classifier. Although 3DPCANet can extract the deep features of the image,  
79 the phenomenon of feature redundancy will happen which gravely affects the image  
80 classification. For solving this problem, the traditional 3DPCANet is improved in this paper.  
81 The max-pooling layer is added behind each layer of convolutional layer. Therefore, the  
82 redundant features are reduced. In addition, the activation function layer (rectified linear unit,  
83 ReLU) is added for learning nonlinear features. Because the overall depth of the proposed

84 model is deepened, deeper features of the images can be extracted. Although CNN combining  
 85 with medical images has shown excellent performance in AD-assisted diagnosis, most of  
 86 CNNs can only process two-dimensional images and cannot deal with high-dimensional data,  
 87 especially four-dimensional fMRI data. Therefore, in this paper four-dimensional fMRI data  
 88 is firstly changed into three-dimensional data. Then 3DPCANet model improved by adding  
 89 max-pooling layer is used to extract features of fMRI data. Finally, SVM is used for  
 90 classification. The experimental results verified the effectiveness of the proposed method.  
 91 Contributions of this paper are as follows.

92 (1) The fMRI scan image is four dimensional, features cannot be directly extracted. In  
 93 the experiment, fMRI images are converted to mean amplitude of low-frequency (mALFF)  
 94 3D image for feature extraction;

95 (2) Replace the manual function extraction with CNN. As a result, human error can be  
 96 reduced and more desirable classification characteristics can be extracted.

97 (3) We can improve the 3DPCANet network and reduce the redundancy of functions by  
 98 adding a maximum pooling layer after each layer of the line layer.

99 (4) Classify AD patients at different stages in order for medical personnel to accurately  
 100 diagnose them.

## 101 1 Materials and Methods

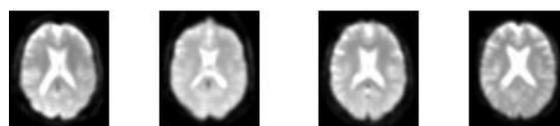
### 102 1.1 Experimental data preprocessing

103 The fMRI data used in this experiment came from Alzheimer's Disease Neuroimaging  
 104 Initiative (ADNI). The experimental data contained fMRI image data of 202 subjects,  
 105 including 34 AD patients, 57 EMCI patients, 35 LMCI patients, 50 NC control groups, and  
 106 26 SMC patients. The basic information for each subject in the experimental data is shown in  
 107 Table 1.

108 Table 1: Statistical analysis of subjects' information.

fMRI	Number of people	Male/Female	Age
AD	34	18/16	57~88
EMCI	57	34/23	57~90
LMCI	35	14/21	58~88
NC	50	28/22	66~91
SMC	26	14/12	65~83

109 The pre-processing of fMRI data is implemented based on data processing & analysis for  
 110 brain imaging (DPABI) [20] software package. The fMRI image processing includes  
 111 eliminating the first 10 time points, time horizon correction, head movement correction,  
 112 spatial normalization, nonlinear drift and other processing. The fMRI pre-processed sample  
 113 data is shown in Figure 1.



114

115

Figure 1: Sample images after fMRI pre-treatment

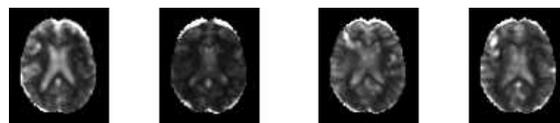
116 fMRI data is 4-dimensional data. At present, few CNNs exist for feature extraction of high-  
117 dimensional data, and most models are suitable for two-dimensional or three-dimensional  
118 images. In this paper, the fMRI data is converted into mALFF [21] image which is a form of  
119 3D image and is convenient to feature extraction using CNN. The ALFF image value is the  
120 square root of the power spectrum of the BOLD signal in the low frequency band  
121 (0.01Hz~0.08Hz). Low-frequency signal energy can be used to express the activity of  
122 neurons in different brain regions. The activity of cerebral cortex neurons can be reflected by  
123 the signal energy with frequency from 0.010 Hz to 0.027 Hz, and the activity of basal ganglia  
124 can be reflected by that with frequency from 0.027 Hz to 0.073 Hz. These areas will be  
125 influenced by AD. So ALFF is selected for image transformation. The ALFF calculation  
126 process is as follows:

127 (1) The time series of each voxel after removing the linear drift are first passed through a  
128 0.01HZ -0.08HZ band pass filter.

129 (2) The filtering result is subjected to fast fourier transform, and the power spectrum is  
130 obtained.

131 (3) The average value of the square root of power spectrum within 0.01-0.08Hz is calculated,  
132 which is ALFF.

133 Mean amplitude of low frequency fluctuations (mALFF) is obtained by dividing the average  
134 amplitude of low frequency fluctuations (ALFF) of all voxels in the whole brain. Because the  
135 brain structure of AD patients has changed, it is believed that the activity of neurons in each  
136 brain area will also change compared with the normal control group. The pre-processed fMRI  
137 data is further calculated mALFF. And the image after mALFF transformation is shown in  
138 Figure 2.



139

140

Figure 2: mALFF sample image

## 141 1.2 Improvement of 3DPCANet model

142 PCANet is a deep learning network in which uses PCA is used to learn channel convolution  
143 kernels, and to made binary hashes and statistics of blocks histograms for indexing and  
144 pooling. Li [19] et al. developed the PCANet model as a three-dimensional form for auxiliary  
145 AD diagnosis. On this basis, in this paper the max-pooling layer is added to improve the  
146 network behind the convolutional layer of the 3DPCANet model. The improved 3DPCANet  
147 convolutional neural network structure is shown in Figure 3.

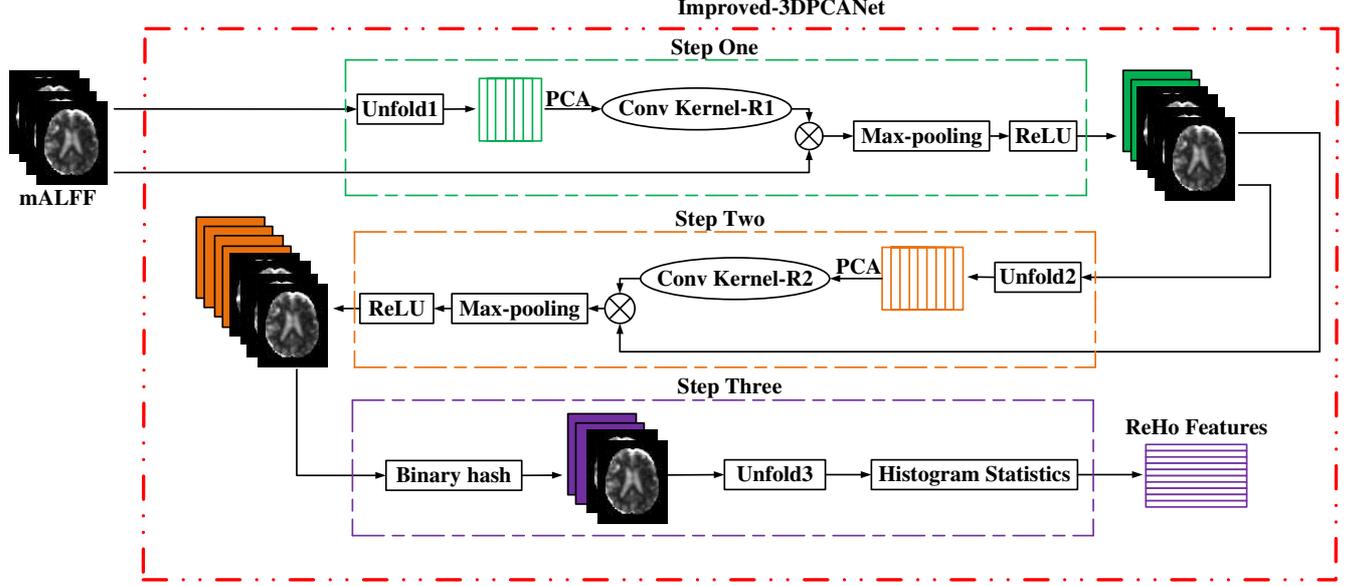


Figure 3: The framework of improved 3DPCANet.

148  
149

150  $N$  training image  $\{\Gamma_j\}_{j=1}^N$  of size  $L \times W \times H$  as the 3DPCANet input, 3DPCANet extracted  
151 features process as follows.

152 (1) Input Layer

153 Voxel blocks with size  $k_1 \times k_2 \times k_3$  around each voxel on the  $j$ -th training image is divided.  
154 The total number of blocks intercepted in each image is  $\beta_1$ . i.e.,  $\mathbf{x}_{j,1}, \mathbf{x}_{j,2}, \dots, \mathbf{x}_{j,i}, \dots, \mathbf{x}_{j,\beta_1}$ , where  
155 each  $\mathbf{x}_{j,i}$  represents the column vector of the  $i$ -th block in the  $j$ -th training image. These  
156 blocks are taken out and reshaped into a column vector, and standardization processing is  
157 performed. As shown in the following formula.

$$158 \quad \overline{\mathbf{X}}_j = [\overline{\mathbf{x}}_{j,1}, \overline{\mathbf{x}}_{j,2}, \dots, \overline{\mathbf{x}}_{j,i}, \dots, \overline{\mathbf{x}}_{j,\beta_1}] \quad (1)$$

159 Perform the above processing on all  $N$  training images, and arrange the processed  $N$   
160 training images sequentially into a new matrix  $X$  to obtain the following matrix.

$$161 \quad X = [\overline{\mathbf{X}}_1, \overline{\mathbf{X}}_2, \dots, \overline{\mathbf{X}}_j, \dots, \overline{\mathbf{X}}_N] \quad (2)$$

162 (2) Middle Layer

163  $T_1, T_2$  is filtering parameters of PCA in the two stages.

164 First stage PCA: For the matrix  $X$  is used PCA, PCA minimizes the reconstruction error  
165 on a group of standard orthogonal filters described as.

$$166 \quad \min_{V \in \mathbb{R}^{T_1}} \|X - VV^T X\|_F^2 \quad \text{s.t. } V^T V = I_{T_1} \quad (3)$$

167 where  $I_{T_1}$  is the identity matrix with size  $T_1 \times T_1$ . The solution  $V$  of this formula is the  
168 eigenvector of  $XX^T$ . The expression of the PCA filter is as shown in equation (4).

$$169 \quad \mathbf{w}_l^1 = \text{mat}(q_l(XX^T)) \in \mathbb{R}^{k_1 k_2 k_3}, l = 1, 2, \dots, T_1 \quad (4)$$

170 where  $\text{mat}$  is a function which maps the vector to the matrix  $\mathbf{w} \in \mathbb{R}^{k_1 k_2 k_3}$ .  $q_l(XX^T)$  represents  
171 the  $l$ -th feature vector of  $XX^T$ , and  $\mathbf{w}_l^1 \in \mathbb{R}^{k_1 k_2 k_3}$  is the  $l$ -th filter generated in the first step.

172 The PCA filter is convolved with the  $j$ -th training image  $\Gamma_j$  in the original image, which  
 173 is expressed by the formula (5).

$$174 \quad \Gamma_{j,l}^1 = \Gamma_j * \mathbf{w}_l^1 \quad (5)$$

175 where the symbol ‘\*’ represents convolution, and the filter  $\mathbf{b}$  is used to convolve all  $N$   
 176 training images and to generate  $N * T_1$  images. Then the max-pooling layer and processing on  
 177 non-linear activation function ReLU are performed on the image  $\Gamma_{j,l}^1$  generated by formula  
 178 (5), which is expressed by the following equation.

$$179 \quad \Pi_{j,l}^1 = \text{ReLU}(\Gamma_{j,l}^1 \times \mathbf{P}^1) \quad (6)$$

180 where the symbol ‘ $\times$ ’ represents the max-pooling operation.  $\mathbf{P}^1$  denotes the max-pooling  
 181 layer in the first step, and  $\Pi_{j,l}^1$  represents the image after the maximum pooling layer is  
 182 processed.

183 Second stage PCA calculate: The  $j$ -th image in the  $N$  training images by the first step  
 184 generates  $T_1$  images, among which  $l$ -th image performed operations similar equations (1) and  
 185 (2) to get matrix  $Y$ .

$$186 \quad Y = [\overline{Y}_{1,1}, \overline{Y}_{1,2}, \dots, \overline{Y}_{j,1}, \overline{Y}_{j,2}, \dots, \overline{Y}_{j,l}, \dots, \overline{Y}_{N,1}, \overline{Y}_{N,2}, \dots, \overline{Y}_{N,T_1}] \quad (7)$$

187 The filter  $\mathbf{w}_h^2$  is obtained by the first stage PCA on the matrix  $Y$ . The image  $\Pi_{j,l}^1$   
 188 generated by formula (6) in the first step is convolved by the obtained PCA filter, which is  
 189 described by formula (8).

$$190 \quad \Pi_{j,l,h}^2 = \Pi_{j,l}^1 * \mathbf{w}_h^2 \quad (8)$$

191 Among  $N * T_1$  images generated in the first step, each image is used to generate  $T_2$  images  
 192 by formula (8). The maximum pooling layer and non-linear activation function ReLU  
 193 processing is performed on the image  $\Pi_{j,l,h}^2$  after convolution, as shown in the following  
 194 formula.

$$195 \quad \Omega_{j,l,h}^2 = \text{ReLU}(\Pi_{j,l,h}^2 \times \mathbf{P}^2) \quad (9)$$

196 Where  $\mathbf{P}^2$  denotes the max-pooling layer in the second step, and the image  $\Omega_{j,l,h}^2$  is  
 197 generated by max-pooling operation.

198 (3) Output Layer

199 The heaviside function  $H(\otimes)$  is used to binarize all  $N * T_1 * T_2$  images, and weighted  
 200 processing to get  $\mathbf{O}_{j,l}$ .

$$201 \quad \mathbf{O}_{j,l} = \sum_{h=1}^{T_2} 2^{d-1} \{H(\Omega_{j,l,h}^2)\} \quad (10)$$

202 Finally,  $\beta$  blocks with size  $k_7 \times k_8 \times k_9$  from  $\mathbf{O}_{j,l}$  each image is divided. The histogram of  
 203 each block is made statistics and vectorize the above results.

$$204 \quad \mathbf{F}_j = [\text{Bhist}(\mathbf{O}_{j,1}), \text{Bhist}(\mathbf{O}_{j,2}), \dots, \text{Bhist}(\mathbf{O}_{j,i}), \dots, \text{Bhist}(\mathbf{O}_{j,T_1})] \quad (11)$$

205 where  $\text{Bhist}(\mathbf{O}_{j,l})$  is a function of block division, histogram statistics and concatenation of  
 206 image  $\mathbf{O}_{j,l}$ .  $\mathbf{F}_j$  represents the final eigenvector of the  $j$ -th training images  $\Gamma_j$  using  
 207 3DPCANet

208  
209

## 210 **2 Results and Discussion**

211 In order to verify the robustness and effectiveness of the proposed model proposed in this  
212 paper, a series of experiments for patients with different stages of AD and NC control group  
213 were designed.

### 214 **2.1 Evaluation Criteria**

215 In the experiments, the data set is classified into two categories including positive and  
216 negative samples. The evaluation criteria used in these experiments are accuracy, sensitivity  
217 and specificity. The calculation equations are as follows:

$$\begin{aligned} \text{Accuracy} &= \frac{TP + TN}{TP + FN + FP + TN} \\ \text{Sensitivity} &= \frac{TP}{TP + FN} \\ \text{Specificity} &= \frac{TN}{FP + TN} \end{aligned} \quad (17)$$

219 TP and TN respectively represent the number of true-positive subjects and true-negative  
220 subjects. FP and FN respectively represent the number of false-positive subjects and false-  
221 negative subjects. The positive class label is 1, and the negative class label is 0. In order to  
222 comprehensively evaluate the proposed model, F1 score and the area under curve (AUC) are  
223 also used as evaluation indicators. The F1 value is calculated by precision and sensitivity, as  
224 shown in the formula (18).

$$\begin{aligned} \text{Precision} &= \frac{TP}{TP + FP} \\ \text{F1} &= \frac{2 * \text{Precision} * \text{Sensitivity}}{(\text{Precision} + \text{Sensitivity})} \end{aligned} \quad (18)$$

### 226 **2.2 Experimental results and analysis**

227 The experimental data included 34 AD patients, 57 EMCI patients, 35 LMCI patients, 26  
228 SMC patients and 50 normal control groups. In order to better test the effectiveness of  
229 mALFF images for AD classification and the robustness of the improved 3DPCANet model  
230 in this paper, a series of experiments were carefully designed and 5-fold cross-validation was  
231 used to reduce the contingency of experimental results.

232 The proposed method in this paper was compared with ones proposed in the literature [19]  
233 and the literature [22], [23], [24], [25], and the experimental results are shown in Table 2. In  
234 addition, AD patients at different stages also classified in this paper, and the experimental  
235 results were shown in Table 3.

Table 2: Comparison of experimental results.

Model	indicators	NC vs. AD	SMC vs. LMCI	NC vs. EMCI	LMCI vs. AD
Li [19]	ACC	83.95%	-	80.15%	82.53%
	AUC	88.42%	-	81.74%	81.24%
Dai [22]	ACC	78.95%	-	-	-
	SEN	81.25%	-	-	-
	SPE	77.27%	-	-	-
Ashkan [23]	ACC	80.00%	-	70.00%	83.33%
	SEN	80.00%	-	50.00%	80.00%
	F1	79.80%	-	66.70%	82.50%
Beheshti [24]	ACC	84.17%	-	70.38%	62.84%
	SEN	88.83%	-	78.17%	76.38%
	SPE	79.00%	-	60.22%	39.57%
Korolev [25]	AUC	86.00%	-	72.00%	64.00%
	ACC	87.20%	-	55.80%	59.98%
	AUC	78.91%	-	53.91%	61.92%
Ys [26]	ACC	87.30%	-	70.50%	-
	SEN	91.40%	-	75.2%	-
	SPE	79.30%	-	63.8%	-
3DPCANet +SVM+mALFF (our)	AUC	<b>89.10%</b>	-	78.00%	-
	ACC	87.78%	<b>91.80%</b>	81.82%	86.67%
	SEN	<b>96.00%</b>	91.43%	80.00%	<b>88.57%</b>
	SPE	77.50%	92.67%	84.00%	85.00%
	F1	<b>90.05%</b>	92.72%	82.62%	85.35%
Improved 3DPCANet+SVM +mALFF (our)	AUC	88.50%	88.09%	78.17%	<b>83.93%</b>
	ACC	<b>88.89%</b>	<b>91.80%</b>	<b>87.27%</b>	<b>89.33%</b>
	SEN	86.00%	<b>94.28%</b>	80.00%	85.71%
	SPE	<b>92.50%</b>	88.67%	<b>96.00%</b>	<b>92.50%</b>
	F1	89.57%	<b>92.92%</b>	<b>87.21%</b>	<b>88.08%</b>
	AUC	82.25%	<b>90.86%</b>	<b>89.83%</b>	83.57%

Table 3 Classification of patients with different stages of AD

indicators	NC vs. SMC	SMC vs. EMCI	SMC vs. AD	EMCI vs. LMCI	EMCI vs. AD
ACC	89.50%	88.43%	92.42%	84.21%	88.42%
SEN	94.00%	91.67%	88.00%	88.33%	90.00%
SPE	80.67%	81.33%	95.00%	77.14%	85.71%
F1	90.10%	91.65%	89.46%	87.44%	90.79%
AUC	89.53%	79.55%	86.83%	80.95%	85.48%

240 The conclusions can be drawn from the experimental results in Table 2. First, the  
241 3DPCANet+SVM+mALFF method proposed in this paper has an accuracy rate of 5.25%  
242 higher than that in the literature [19]. In addition, the accuracy and AUC area of MCI vs NC,  
243 MCI vs AD have been improved, because ALFF images can effectively reflect the activity of  
244 neurons in each brain area of the subject, and are a good feature expression method.  
245 Compared with the literature [19], fewer data sets were used in this paper and better  
246 classification results are obtained, which proved that mALFF images have the positive role in  
247 AD classification.

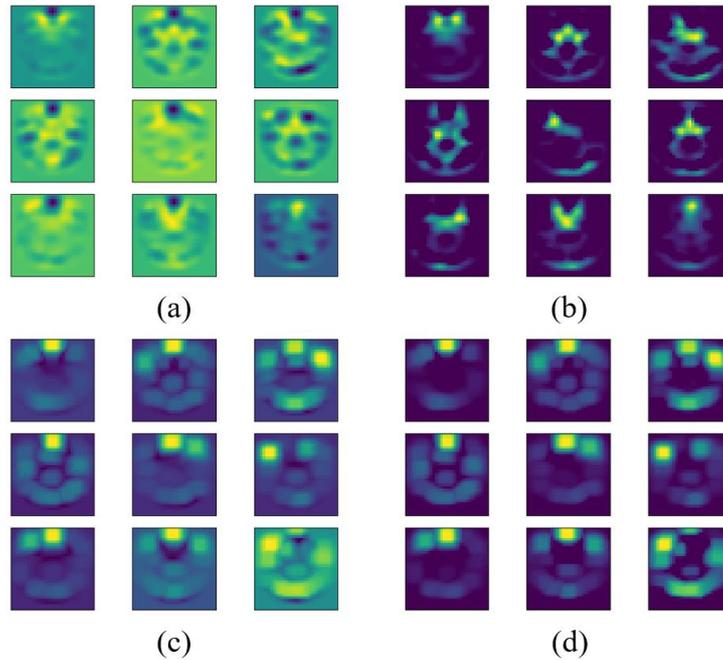


Fig.4 PCANet model outputted feature diagram

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249

250 Second, after the traditional 3DPCANet model is improved, the classification performance of  
 251 AD is significantly enhanced. For example, the accuracy, F1 value, specificity and other  
 252 evaluation indicators of NC and AD, NC and EMCI are improved, and the specificity of the  
 253 latter is increased by 12%, AUC is increased by 11.66%. Non-linear features of the image and  
 254 the texture features of the image cannot be extracted by 3DPCANet. Fig4(a) presents the output  
 255 feature map of the 3DPCANet convolutional layer. It can be seen from Figure (a) that the  
 256 brain texture, and the structure of each brain area are not clear. In this paper, the convolved  
 257 feature map passes in sequence through the ReLU layer, the max-pooling layer, and the  
 258 combination layer (max-pooling and ReLU layer). The feature maps are shown in (b), (c),  
 259 and (d) in Figure 4 respectively. In Figure 4 (b), the image sparsity increases after the feature  
 260 map passes through the ReLU layer, highlighting the image features because the ReLU  
 261 activation function changes the voxels with a voxel value less than 0 to 0, and the voxel with  
 262 a voxel value greater than 0 remains unchanged. After max-pooling, the feature  
 263 map is compared with Figure 4 (a), texture features and brain structure of the image are  
 264 revealed, because the max-pooling layer can learn the texture features of the image and  
 265 reduce the redundant features of the image. Therefore, in this paper, max-pooling  
 266 layers and the ReLU layers are inserted after each convolutional layer in 3DPCANet, and the  
 267 output feature map has a clear texture and large sparseness, thereby increasing the generalization  
 268 ability of the model.

269 Thirdly, only AD and NC were classified in the literature [22], while other stages of AD  
 270 including SMC, EMCI and LMCI were also classified in this paper, which can assist medical  
 271 personnel to diagnose patients in different stages of AD more accurately, and the results are  
 272 of more practical significance. Compared with literature [23], [24], [25] and [26], the method  
 273 proposed in this paper can more accurately diagnose patients at different stages of AD.

274 Fourth, the classification performance of SMC and LMCI, LMCI and AD also is improved,  
 275 which proves that the algorithm in this paper is also effective for the classification of SMC  
 276 and MCI patients with weak pathological differences. The main reason is that since the

277 maximum pooling layer is added behind the convolutional layer, redundant information in the  
278 feature map can be effectively reduced, over-fitting is prevented, and the activation function  
279 is increased. Therefore, the model can extract more nonlinear features, so that it is easy to  
280 distinguish the pathological differences of patients at different stages of development, and to  
281 get better classification performance.

282 As can be seen from the data in Table 3, because SMC and EMCI are the initial stage of AD,  
283 great differences on the brain structures between AD and SMC or EMCI exist. So, the  
284 classification results of SMC and AD, and EMCI and AD are better, with the accuracy of  
285 94.42% and 88.42% respectively. NC and SMC, SMC and EMCI are the adjacent  
286 development stages, so small differences on brain structure exist, and it is difficult to  
287 distinguish. The accuracy of experimental results is 89.50% and 88.43%, and the F1 value is  
288 90.10% and 91.65%, respectively. Both EMCI and LMCI belong to MCI stage, and it is  
289 difficult for medical personnel to distinguish patients in this stage. In this paper, the  
290 classification experiment of EMCI and LMCI also obtained good results, with F1 value of  
291 87.44%, AUC of 80.95% and accuracy of 84.21%. The experimental results prove that the  
292 improved 3DPCANet model is more suitable for AD classification.

### 293 3 Conclusions

294 In this paper, an assisted diagnosis method of Alzheimer's disease based on deep learning is  
295 proposed. Firstly, mALFF images are obtained after fMRI data is pre-processed. Then  
296 Transformation images are inputted to an improved deep learning network in which the max-  
297 pooling layer and activation function layer are added behind the traditional 3DPCANet  
298 convolutional layer. This improvement can reduce the redundant information in the feature  
299 map, increase network depth and prevent over-fitting. Finally, SVM is used for classification  
300 of AD patients with different stages. The experimental results in the data set of AD and NC  
301 control group at different stages show that compared with the traditional 3DPCANet model,  
302 the classification results are notably improved. The highest accuracy on SMC vs. LMCI  
303 reaches 91.80%, and that of LMCI vs. AD is 89.33%. It can be seen from the results that AD  
304 patients at different stages can be effectively classified using the proposed method in this  
305 paper. The research results can provide theoretical basis and guiding suggestions for the  
306 auxiliary diagnosis and treatment of AD.

### 307 Declarations

### 308 Ethics approval and consent to participate

309 In this paper, the dataset used is licensed by ADNI on September 24, 2019. ADNI gives the  
310 permission statement: Congratulations. Your request for access to the Alzheimer's Disease  
311 Neuroimaging Initiative (ADNI) Data has been approved. If you already had a LONI user  
312 account your permissions have been updated to provide you access to ADNI data. If you did  
313 not yet have an account, an account will be created for you and an e-mail with your account  
314 information will be sent to you shortly.

### 315 Consent for publication

316 All authors agree to be published

## 317 Availability of data and material

318 fMRI dataset used in this study comes from the Alzheimer's Disease Neuroimaging Initiative  
319 (ADNI). The fMRI dataset includes 34 AD patients, 57 EMCI patients, 35 LMCI patients, 26  
320 SMD patients, and 50 NC. Experimental data is obtained by sending an email to the ADNI  
321 and signing the related agreement. Since in this laboratory the classification of Alzheimer's  
322 disease is studied by the fusion of fMRI and sMRI image information, the subjects possessing  
323 fMRI images and sMRI images are selected in the ADNI dataset. The link on ADNI dataset  
324 is <http://adni.loni.usc.edu/>.

## 325 Competing interests

326 The authors declare that there is no conflict of interest regarding the publication of this  
327 manuscript.

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## 332 Author Contributions

333 Yu Wang is the corresponding author and the first author. Major contributions include fund,  
334 data set and experimental equipment acquisition, fusion algorithm ideas and program  
335 provider, supervision of experiments, and important modification of the paper.

336 Hongfei Jia, second author. Major contributions include experimental scheme and program  
337 design, model innovation, ALFF data preprocessing, and paper writer.

338 YifanDuan is the third author. Major contributions include REHO data preprocessing and  
339 paper modification.

340 Hongbing Xiao, the fourth author, Major contributions include fund acquisition and  
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