FuseMe: Classification of sMRI images by fusion of Deep CNNs in 2D+ε projections

Conference Paper · June 2017

DOI: 10.1145/3095713.3095749

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FuseMe: Classification of sMRI images by fusion of Deep CNNs in 2D+ε projections.

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ABSTRACT

The methods of Content-Based visual information indexing and retrieval penetrate into Healthcare and become popular in Computer-Aided Diagnosis. Multimedia in medical images means different imaging modalities, but also multiple views of the same physiological object, such as human brain. In this paper we propose[1] a multi-projection fusion approach with CNNs for diagnostics of Alzheimer Disease. Instead of working with the whole brain volume, it fuses CNNs from each brain projection sagittal, coronal, and axial ingesting a 2D+ε limited volume we have previously proposed. Three binary classification tasks are considered separating Alzheimer Disease (AD) patients from Mild Cognitive Impairment (MCI) and Normal control Subject (NC). Two fusion methods on FC-layer and on the single-projection CNN output show better performances, up to 91% and show competitive results with the SOA using heavier algorithmic chains.

KEYWORDS

Deep learning, structural MRI, Convolutionnel Neural Network (CNN), Alzheimer's disease (AD), Fusion multiple source.

CBMI, June 19-21, 2017, Florence, Italy

ACM ISBN 978-1-4503-5333-5/17/06…$15.00
http://dx.doi.org/10.1145/3095713.3095749

1 INTRODUCTION

The methods of Content-Based visual information indexing and classification penetrate into Healthcare and become popular in Computer-Aided Diagnosis with the use of medical images of different modalities [1] [2]. Structural MRI is one of them. It is widely used as one of cues for diagnostics of Alzheimer disease (AD) [3]. AD is the most prevalent neurodegenerative brain disease in the elderly subjects, its prevalence is estimated to be around 5% after 65 years old and a staggering 30% for the more than 85 years old in developed countries [4], from now to 2050 it is estimated that 0.64 Billion people in the world will be diagnosed with AD. It has become a major social and economic issue and its effects are devastating not only for the diseased but also for their families. Today, the diagnostics of AD is invasive, one of the main tests is rachisynthesis, which is painful and dangerous for a patient. Hence a strong effort of research community is allocated today to the increase of efficiency of non-invasive methods, such as MRI classification to give an answer for each subject whether he is suffering from the disease or not. The classification of MRI images has followed the same methodological "history" of classical Content-Based Image Indexing and Retrieval. Leaving behind costly volumetric methods [5], the research community started using feature-based method deploying classical SIFT and SURF descriptors [6]. More interesting and better adapted to MRI digitized signal features were proposed in our previous works [2]. All these approaches were embedded in the classification frameworks on the basis of kernel (single or multiple)-based methods with Support Vector Machines (SVM) and other conventional classifiers [7]. Since recently, due to the increased computational power of general-purpose computers with GPU, the winning classification model represent Deep Neural Networks, and specifically Convolutional Neural Networks (CNN) in what concerns image classification.

Indeed they outperform any other classifiers in variety of image classification tasks. In this paper we continue our research on design and use of CNNs in the classification problems in medical image domain. We have to solve a set of binary classification problems to separate NC subjects from AD, NC from MCI and MCI from AD. Namely we are interested today, how we can fuse information from different projections of the brain in sMRI using a CNN architecture. We first identify the most discriminative projection from sMRI data. Then we propose a fusion frameworks with CNNs and benchmark and analyze their performances with similar approaches. The paper is organized as following. In Section 2 related work is presented, in Section 3 we briefly introduce our previous approach "2D+ε" for a single-projection classification and develop fusion schemes. Experiments and results are presented in Section 4 and section 5 concludes the paper.

2 RELATED WORK

In spite of its success in the classification problems tasks, CNNs are in their infancy to be used for decision making in brain medical image classification. Still their use is massively researched today completed with domain knowledge of AD phenomena in the brain. Here we will briefly discuss some of them.

In [8] the authors have taken a two-stage approach on the whole MRI brain scans, firstly they used a sparse auto-encoder to learn filters for convolution operations, and secondly they built a 3D CNN whose first layer uses these learned filters. The auto-encoder was made with 150 hidden units, and was trained on a set of 3D patches of size 5x5x5, extracted from the MRI scans. The 3D CNN architecture was made up of a convolutional layers followed by a max-pooling, a fully-connected layer of 800 units and the output units. In a 3-class classification problem (AD, NC, MCI) they achieved the accuracy of 89, 47% which was 4% higher than on a 2D projections. In case of pairwise binary classification problems they have achieved better accuracies AD vs. NC: 95.39%, AD vs. MCI: 86.84%, NC vs. MCI: 92.11%, in the case of 3D convolutional networks on the ADNI dataset that consists of 755 patients in each one of the three classes (AD, MCI, and HC), for a total of 2,265 scans. The main distinction from our work is that we focus on a specific part of the brain while they considered the whole brain, we use more than one convolutional layer and we did not pre-train features.

Another study using 3-D CNN [9] confirms that the usage of CNN is a good choice for classifying MRI scans as belonging to NC/MCI/AD individuals. The 3-D CNN was used on the whole brain and initialized with convolutional auto-encoders, training was done on the CA Dementia database and the resulting CNN was tested on 210 scans of the ADNI database. Comparisons with other techniques using various image modalities confirm that both the choice of using sMRI and CNN is relevant.

The studies [7], [1] [10] are focusing on prognosis, the problem here is to classify stable MCI (sMCI) vs. progressive MCI (pMCI), also called MCI converters (cMCI) i.e. MCI subjects that will be diagnosed with AD in a relatively short period of time. In [1] an accuracy of 65% for sMCI vs. pMCI was obtained, 70% in [7], 74% in [10] and 83% accuracy for sMCI vs. cMCI in [11].

Multiple modalities have been used in [5], MRI, PET scans and CSF biomarkers were fused to classify subject state disease, 93 regions-of-interest were extracted from MRI and PET scans. A total of 189 features were used by adding 3 bio-markers from the CSF, and principal component analysis (PCA) was applied.

In a recent paper [12], the authors use MRI image segmentation into three tissue types of Gray Matter (GM), White Matter (WM), and Cerebrospinal Fluid (CSF). They then parcel them into 93 region of interest (ROIs). Only the GM densities spatially normalized considered in this work which is widely used in the field for AD classification problem, the architecture named DeepESRNet was made up by two convolutional layers and a max-pooling layer, then two fully-connected layers. The proposed method achieve for AD vs. NC 91.02%, 92.72%, and 89.94%, and for MCI vs. NC 73.02%, 77.60%, 68.22%, Accuracy, Sensitivity, Specificity respectively.

In the above cited studies various brain regions were used: the whole brain, the hippocampal region or the cingulate posterior cortex together with the hippocampus, etc. In our work we focus on the hippocampal region as it is the strongest biomarker of Alzheimer disease and has not been sufficiently studied yet.

3 RELATED FUSION OF DEEP CNNs FOR CLASSIFICATION OF MRI SCANS IN 2D+ε FRAMEWORK

In this section we formulate our classification problem, briefly expose single-projection solution that we have previously proposed and introduce our fusion approach.

3.1 Problem formulation

In diagnostics of AD at a given time, the approach usually consists in solving three binary classification problems: AD vs. NC, NC vs. MCI, and AD vs. MCI.

We perform this classification tasks using only a Hippocampal ROI, as it is a biomarker of Alzheimer Disease.

In our previous work [14] we proposed a "2D+ε approach" for classification of subjects on sMRI brain scans in three pairwise classification problems: AD vs. NC, AD vs. MCI and NC vs. MCI. We briefly introduce it in the next sub-section.

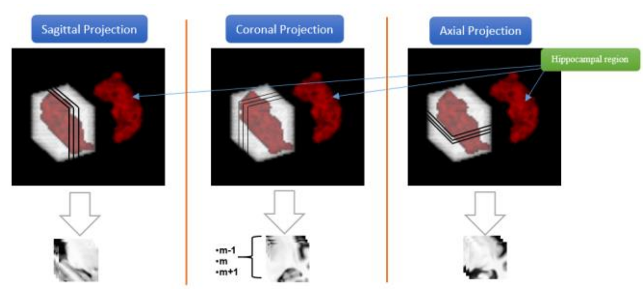

Figure 1: The three slices of each projection selected from the hippocampal region.

3.2 2D+ε Approach for classification on a single projection.

Frist of all, the Hippocampal ROI was selected from the 3D volume of a single projection (e.g. sagittal) of the brain. To do this we followed a usual scheme in alignment and selection of ROIs in MRI scans. The Montreal Neurological Institute template (MNI) has been used, which represents an average of 152 individual brains. Each individual scan from our dataset was aligned on this template standard space using affine registration. Then the voxel intensity normalization was performed in order for similar structures to have similar intensities. We use a brain atlas called AAL [15] Automated anatomical Labeling to select the hippocampal region. The MNI template corresponds to the brain atlas AAL. By selecting voxels labelled as Hippocampal region in AAL and computing their bounding boxes, we get a sub-volume of the whole 3D projection, which encircles Hippocampus.

Then the median slice inside this volume was chosen and its two closest neighbors were considered. Hence from a 3D volume we moved to three 2D images, and called this “2D+ε approach”.

Thus extracted data represent images of low dimension 28x28 pixels taking into account the initial resolution of sMRI scans (121x145x121 voxels). Hence for the classification with a CNN network with usual convolution and pooling layers, we had to limit ourselves by a rather shallow architecture: 2 convolutional (Conv) and 1 fully connected (FC) layer (see Fig. 2).

Thus, from an implementation perspective, the input layer of the network constituted of 28x28x3 units receives data from three 28x28 central slices of the hippocampal region.

Taking into account a small amount of training data usual for medical image databases (see section 4), we proposed a specific data augmentation strategy; it consisted in flips, volume translations and blurring [14].

It is interesting to visualize the features to analyze and understand training process; In Fig. 3 the two left images (a) result from processing of AD subject. In (b) in same figure a NC example is given. One can distinguish quite different structures in these outputs of the first Conv. Layer and the 2nd max pooling layer.

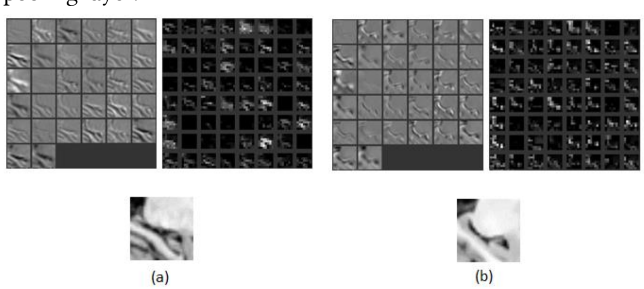

Figure 3: Features example patch of AD (a), NC (b) subjects and there features of conv1 and pool2 layers.

Using this 2D+ε approach for each projection we need to increase classification scores and a good way to do this is to fuse information from different projections.

3.3 Intermediate and Late fusion of the single-projections Networks.

Unlike our first approach as we have seen earlier, in this part we will build a multi-source architecture by the fusion of the three projections networks (sagittal, coronal, and axial), of the same architecture.

We consider two fusion methods: Intermediate Fusion which consists of a concatenation at the FC layer of three networks, and Late Fusion by algebraic and majority vote operators on the output scores of the three independent networks, each for one projection.

3.3.1 Intermediate Fusion

As noted above, fusion can be applied in different ways in the three networks, the only constraint is that the three input images have to be taken from the same subject and from the appropriate projection to feed correctly the networks.

Our architecture consists of three networks of sagittal, coronal, and axial projection independently which are combined in the intermediate fusion approach. Here we are talking about concatenation of fully connected layers.

To achieve the fusion, each network for a single projection is implemented using the same architecture 2D+ε approach that was made up of two convolutional layers, two pooling layers, followed by the ReLU activation function, and a fully-connected layer [14]. Then we make a concatenation layer that combines the three fully-connected layers. Afterwards we have a FC layer to merge the three combined layers to get two output scores in each binary classification task. An overview of the full architecture is given in Fig. 2.

3.3.2 Late Fusion

The main idea in this solution, is to make an aggregation operation on the outputs of the last layer of the networks which is a fully connected layer, as shown in Fig. 4.a the outputs are a real number scores. The other proposed operation Fig. 4.b that is we take the majority vote applied on the three networks decision probabilities results.

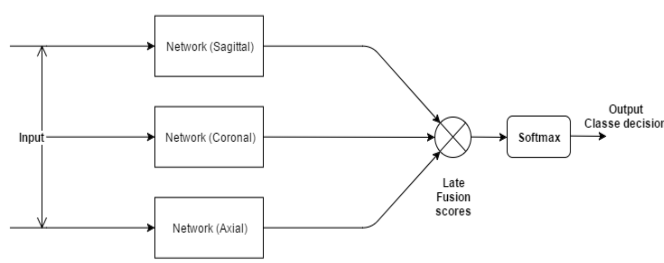

Figure 4.a) late fusion algebraic operations on scores.

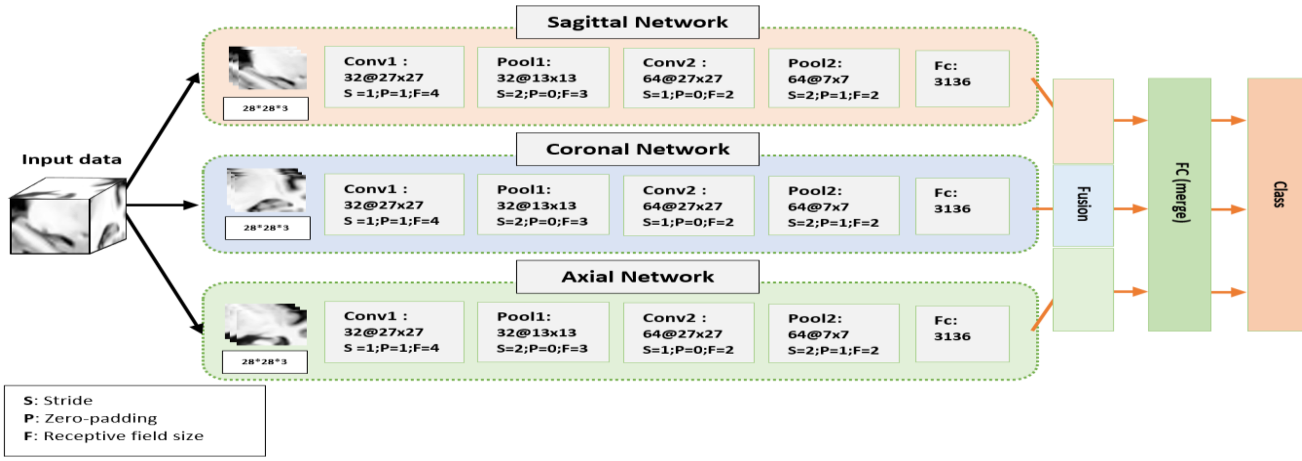

Figure 2: Architecture Fusion intermediate.

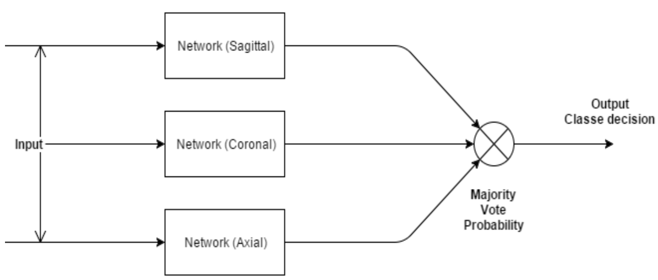

Figure 4.b) late fusion Majority Vote on probability single projection decision.

4 EXPERIMENTS AND RESULTS

In this section we describe the dataset used in our experiments and report the results of the proposed methods.

4.1 Material

We selected the screening MRI image from the ADNI database, this dataset includes 815 subjects split as 188 (AD, Alzheimer's diseases), 228 (NC, Normal Control) and 399 (MCI, Mild Cognitive Impairment). All the MR images are acquired using 1.5T MRI and collected from different acquisition sites (T1-weights MRI contrast).

Table 1: Demographic description of the ADNI screening 1.5T Images studied population (reduction subject details)

	#Subject	Age[range] /μ (σ)	Gender (M/F)	MMSE[range] /μ (σ)
AD	188	[55 91]/75.4(±7.52)	99/89	[18 27]/23.3(±2.03)
NC	188	[60 90]/76.2/(±5.18)	98/90	[25 30]/29.1(±1.03)
NC	228	[60 90]/76(±5.02)	118/110	[25 30]/29.1(±1.0)
MCI	188	[57 89]/74.9(±7.04)	124/64	[23 30]/27(±1.75)
MCI	228	[56 89]/74.9(±7.16)	148/80	[23 30]/26.9(±1.74)

In our experiments we have taken the same dataset that was used in our previous work [14] by reducing the number of original subjects as described in Table 1 (188 for AD vs. NC; 228 for MCI vs. NC; and 188 for AD vs. MCI a) in each binary classification networks. Also the same pre-processing alignment and normalization tasks [14] was performed on the data, and finally the extraction of the hippocampal region (ROI) was obtained by using a sequences of steps as in [14], to get the patches used to feed our networks.

4.2 Experiments

The experiences were performed using the public available Caffe framework [16], as described previously, and we use the 2D+ε network as the basis for our fusion network.

The parameters that were used in the training phase are:

- 60.000 iterations which gives about 1000 epochs,
- the Learning rate : 0.0001 ; Learning policy : fixed
- Momentum : 0.9
- Batch-size : 256

4.3 Results

In the *first* series of experiments we identify the most discriminative projection for our binary classification tasks.

In the Fig. 5.a) are shown three curves of accuracy and loss for single projection each. One can see that the sagittal projection ensures a little higher accuracies than coronal projection after stabilization. In Table 2 are given results for the three projections at the iteration #60.000 we selected after stabilization. Analyzing results of different projections, we state that the sagittal projection is the most discriminative. Indeed, in the most "clear" classification task from physiological point of view AD/NC, it performs the best in all three metrics. This is the case also for NC/MCI classification task. Nevertheless, in AD/MCI there is no consensus on metrics. Indeed AD/MCI is probably the most difficult classification task as it is difficult to trace the separation between Mild Cognitive Impairment (MCI) and already installed Alzheimer disease even for medical experts.

Table 2: Comparison of single-projection results.

	Sagittal			Coronal			Axial		
	AD vs. MCI	AD vs. NC	NC vs. MCI	AD vs. MCI	AD vs. NC	NC vs. MCI	AD vs. MCI	AD vs. NC	NC vs. MCI
Accuracy	62,50 %	**82,80 %**	**66,12 %**	**66,40 %**	80,15 %	57,56%	61,72%	79,69%	61,25 %
Specificity	60,00 %	**79,61 %**	**58,70 %**	57,89 %	78,53 %	**58,71 %**	**68,75%**	78,12%	55,00 %
Sensitivity	64,00 %	**85,89 %**	**73,75 %**	**75,10 %**	82,67%	56,35 %	54,63%	81,25%	67,50 %

Table 3: Results of Intermediate on FC layer.

	Fusion		
	AD vs. MCI	AD vs. NC	NC vs. MCI
Accuracy	63.28%	**85.94%**	65.61%
Specificity	60.94%	**84.38%**	**66.23%**
Sensitivity	65.62%	**87.50%**	65.12%

In the *second* series of experiments we explore if i) fusion of results from different projections in the same 2D+ε perspective improves the scores and ii) by which fusion method.

The results of our intermediate fusion scheme on FC layer are presented in Fig. 5.b) in comparison with the best performing sagittal projection. The corresponding figures are presented in the Table 3. The proposed fusion scheme with fusion of FC layers performs the best in all three metrics Accuracy, Specificity and Sensitivity compared to the most discriminative sagittal projection.

In order to benchmark this intermediate fusion scheme with a classical algebraic operators and other late fusion schemes, we performed three experiments with i) max, ii) mean and a majority vote. These outcomes are illustrated in Fig. 4 and results are presented in Table 4 below. The max and mean fusion were done on the results of scores before their binarization, and the majority vote after the binarization of scores. The AD/NC classification gives the best results with Majority vote. This simple fusion scheme clearly outperforms intermediate fusion on Fully Connected layers, the improvement is of 5.5% in average. With regard to the single sagittal projection it is of 8.6%. In NC/MCI classification, max and mean fusion give better results than FC fusion and single sagittal, but the difference is very small (0.25%).

To position our approach with regard to the literature, we compare it with the most recent work in [12]. Note that a strict comparison is not possible as we use ADNI screening dataset and the authors of [12] do use baseline dataset. Both of them contain a strong intersection, but the screening dataset is larger.

Nevertheless, the number of scans is similar. The difference is that we balance the number of subjects in all classification tasks. Particularly for AD/NC classification we use 188 scans for each class. In this paper the authors segment the brain into grey matter (GM), white mater (WM) and cerebrospinal fluid (CFS). Then they parcelate GM into 93 regions and use normalized densities of these regions as features as an input into a Deep ensemble sparse regression network. For the AD/NC classification problem we obtain the same figures in accuracy (91,41% vs. 91,02%), better results in sensitivity (93,75% vs. 92,72%) and we are nearly the same in specificity (89,06% vs. 89,94%).

Figure 5: a) AD vs. NC: comparison of the three single projections curves (Accuracy and Loss).

Table 4: Comparison of late fusion results.

	Max			Mean			Majority Vote		
	AD vs. MCI	AD vs. NC	NC vs. MCI	AD vs. MCI	AD vs. NC	NC vs. MCI	AD vs. MCI	AD vs. NC	NC vs. MCI
Accuracy	59,38 %	89,06 %	**66,25 %**	63,28 %	89,84 %	**66,25 %**	**69,53 %**	**91,41 %**	65,62 %
Specificity	57,81 %	85,94 %	**71,25 %**	64,06 %	85,94 %	68,75 %	67,19 %	**89,06 %**	66,25 %
Sensitivity	60,94 %	92,19 %	61,25 %	62,50 %	**93,75 %**	63,75 %	71,88 %	**93,75 %**	65,00 %

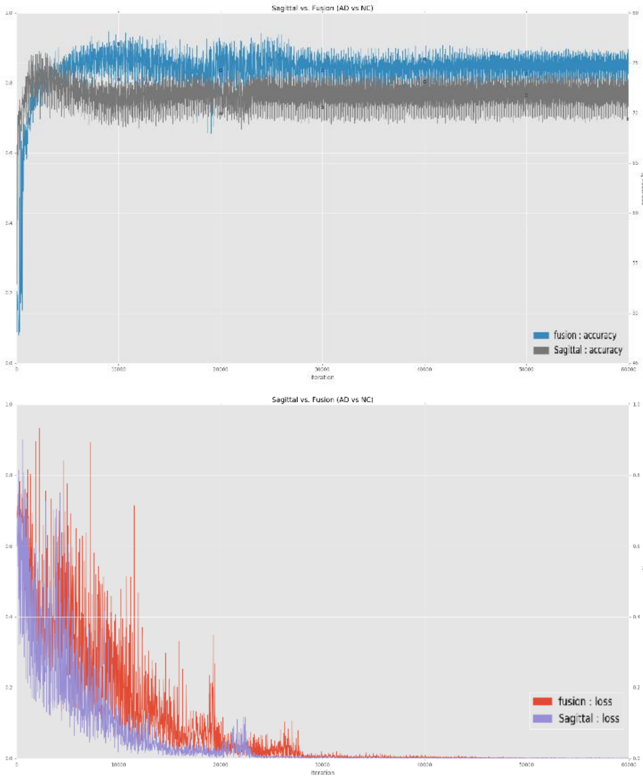

Figure 5: b) AD vs. NC: Comparison of Intermediate Fusion and Sagittal projection only (Accuracy and Loss).

The comparison of two other classification tasks is not possible as the authors of [12] are interested in the prediction of conversion of MCI into AD and are not considering AD/MCI and NC/MCI instantaneous classification results. Hence with much more simple method without preliminary fine segmentation we obtain the results which are very close to those in [12]. The experiments were run on Intel® Xeon® CPU E5-2680 v2 with 2.80GHz and with GPU acceleration in Caffe SW using Tesla K20Xm with 2496 CUDA cores. The times for train-validation task was about ~2h03m for intermediate fusion network and nearly ~41m30s for each single projection network.

5 CONCLUSION AND PERSPECTIVES.

In this paper we continued elaborating the 2D+ε approach in the task of classification of MRI in a study of three groups of subjects NC, AD and MCI.
In this classification, as well as in our previous works, we used the ROI in a brain, which is an Alzheimer biomarker that is Hippocampal region. We first studied the discriminative power of single projection data and stated that in accordance to the medical practice, the sagittal projection is more discriminative in terms of all metrics accuracy, specificity and sensitivity. To increase the classification power, we used two different fusion strategies. The first one – the intermediate fusion consists in a joint training of three Deep CNNs concatenating features in a FC layer. The second one consists in applying algebraic late fusion operators and a majority vote. The conclusion is indeed, that on the baseline classification problem, AD/NC, both fusion strategies achieve better performances. The winner is the majority vote, which results are comparable with the latest state-of-the-art methods which use much more complex approaches for input data preparation for Deep NNs.
In the follow-up of this research, we will use new transfer leaning schemes and add more imaging modalities.

ACKNOWLEDGMENTS

This work is being supported by French-Morocco Grant PHC AlClass 2016_2018. We thank Dr Pierrick Coupé for fruitful discussions.
Data used in the preparation of this article were obtained from the Alzheimer's disease Database Initiative (ADNI) database. A complete listing of ADNI investigators can be found at: www.loni.ucla.edu/ADNI/Collaboration/ADNI_Autorship_list.pdf database

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