Deep transfer learning for DTI- and MRI- based early diagnosis of cognitive decline and dementia

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Keywords: MRI, DTI, transfer learning, dementia, deep learning.

Abstract. Diffusion Tensor Imaging (DTI) and Magnetic Resonance Imaging (MRI) techniques have gained significant popularity in the diagnosis of neurodegenerative disorders. Combining brain scans with deep learning is receiving increasing attention in medical diagnostic applications. However, deep networks can learn powerful features and perform well only when a large amount of DTI or MRI image data are available. The paper attempts to reduce the dependence on massive training data by exploiting transfer learning of deep networks pretrained on ImageNet data for the diagnosis of dementia. Transfer learning can significantly reduce the length of the training, validation and testing process on a new dataset, and is based on the use of pretrained models which have demonstrated better performance than models trained from scratch in several applications. In this context, the paper investigates the potential of transfer learning, which is based on modifications of the AlexNet and VGG16 convolutional neural networks (CNNs), when MRI or DTI data are used for the classification of Mild Cognitive Impairment (MCI), AD and normal patient. Experiments based on data from the ADNI database demonstrate the high performance of the transfer learning methods in the detection of early degenerative changes in the brain. The highest accuracy of 99.75% in the diagnosis of AD was achieved with transfer learning of VGG models using DTI scans. The prediction of early cognitive decline with an accuracy of 93% was reached by VGG models processing MRI data.

1 Scientific Background

Mild cognitive impairment (MCI) belongs to the group of neurocognitive disorders characterized by minor problems with cognitive function, including memory, language, visual and spatial perception. Around 15% of the 65-year-olds with MCI develop dementia within a year, whilst around 30% of them develop it within 5 years. The most common course of dementia is Alzheimer's disease (AD). Neuroimaging technology is one of the key diagnostic approaches for the detection of early dementia. In this context, Magnetic Resonance Imaging (MRI) scans give detailed characteristics of the anatomical properties of the brain and cover around 50% of imaging data used for the diagnosis of brain diseases [1]. Also, Diffusion Tensor Imaging (DTI) provides the complex anatomy of the fibre tracts on the microstructural level and creates a brain-wide mapping of neuronal connections between the anatomical regions [2]. Both methods are widely used in the diagnosis of MCI and AD. Previous research has pointed

out that in the early phases of the disease white matter (WM) tract damage is happening earlier than gray matter (GM) destruction and progression of WM atrophy exceed the grey matter degeneration in patients with dementia [3, 4]. It was highlighted that there is a significant correlation between WM changes and regional GM atrophy in patients with AD and this affects the cognitive test performance [5]. At the same time, the correlation between GM atrophy and the damage of most WM tracts was not found in patients with the amnestic forms of MCI. In this vein, the study presented in this paper uses both imaging techniques for the early diagnosis of dementia.

In the last decade, a significant number of studies used machine learning methods for medical diagnosis [6, 7]. The highest popularity among traditional machine learning has been gained by approaches that use support vector machines (SVM), support vector regression (SVR), and random forest (RF) classifiers [6]. Advances in deep neural networks have opened a wide diagnostic opportunity in the classification and processing of medical imaging data offering additional benefits [7]. In particular, Convolutional Neural Networks (CNNs) have demonstrated great potential in medical image analysis [8]. A CNN consists of an input layer, hidden layers, and an output layer. Hidden layers of this network are divided into convolution, pooling, activation, and classification layers. Convolutional layers are used for feature engineering, pooling layers reduce the dimensions of the feature maps, activation layers normalize the feature maps by removing the negative values, and output layers produce the classification result. Additional layers that can be used in the CNN architecture are dropout and fully connected. The dropout layer reduces the model overfitting by eliminating the results with a probability of 0.5 and below. The fully connected layers compute a score of each class collected from convolutional layers.

Transfer learning, which forms the core of this paper, became noticeable in medical diagnostics only in recent years. Its popularity is growing as it is a fast and highly effective approach [9]. Transfer learning of pretrained networks is usually done by replacing the last three layers of the architecture. This allows adjusting the existing network to the newly inputted image classes.

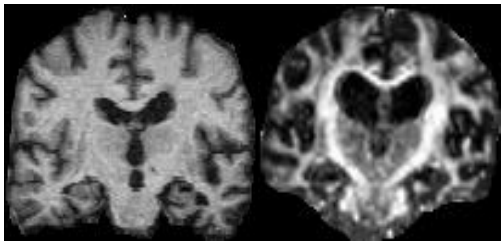
The paper explores the classification potential of popular CNN architectures, such as the AlexNet and the VGG16 networks, that have been trained on ImageNet data (www.image-net.org). Transfer learning enables quick adaptation of these computational models to new classes of medical imaging data from MRI or DTI with minimal image preprocessing. The aim is to understand how transfer learning with deep networks can be used to inform the design of DTI or MRI based diagnostic tools for binary and multiclass classification of early mild cognitive impairment (EMCI), Alzheimer's disease (AD) and Normal (healthy) Controls (NC). This approach could offer new opportunities for quick and efficient diagnostics of different medical conditions including neurodegenerative disorders.

2 Materials and Methods

Brain scans used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). The created datasets include T1-waited images of structural MRI and DTI data of fractional anisotropy of 150 subjects at the age between 55 and 65 for the Early Mild Cognitive Impairment (EMCI) and Normal Cognitively (NC), and at the age between 65 and 90 for Alzheimer's Disease (AD). Images were processed and classified in Matlab using commodity hardware (Windows10 Enterprise, Intel (R) Core (TM), i7-7700 CPU@ 3.60 GHz, 16 GB RAM).

Initially, we created MRI and DTI datasets of 2D images from the ADNI3 database. Images were taken from the same type of 3T scanners, Siemens Medical Solutions (see details available on ADNI: http://adni.loni.usc.edu/methods/mri-tool/mri-acquisition). For MCI and NC classes

we used patient data at the age between 55 and 65 to minimize the ageing effect on imaging data. After that, the MRI and DTI brain images were normalized using the histogram stretching technique and resized to 256×256 pixels with RGB colour channels as typically done for deep learning image processing and classification. Then, the brain of a single 2D image was segmented from the skull and other surrounding tissues using region growing and double thresholding methods (see Fig. 1). MRI and DTI sets of 1200 images obtained from 150 subjects were balanced across classes and used for binary and multiclass diagnostic problems.



(a) (b)

Figure 1: (a) Segmented brain from MRI slice (b) Segmented brain from DTI slice.

The classification tasks were processed using transfer learning of two CNN architectures, the AlexNet and the VGG16 [7, 8], where the last 3 layers were replaced by a fully connected layer, a Softmax layer and an output layer, which was configured for binary or multiclass (3 classes) classification depending on the type of the diagnostic tasks. When the cross-entropy loss function is used for training, the outputs of the Softmax layer can be interpreted as values of a probability distribution, which helps to produce the diagnostic outcome.

In general, AlexNet has been found to provide a short training time, while the VGG16 is known for its low error rate. AlexNet and VGG16 were originally configured and trained for 1000 classes using ImageNet data. AlexNet consists of 8 layers, has a size of 227MB and includes 61.0 million parameters. This network requires an input image size of 227×227×3 (227 wide, 227 high, 3 colour channels). The size of VGG16 is much bigger and equal to 515MB. This network has 16 layers and 138.0 million parameters it requires an input image size of 224×224×3.

The following settings were used for retraining/finetuning both models on DTI and MRI data: N = 5 is the number of epochs each dataset was trained, mini-batch size = 128, validation data frequency = 50, initial learning rate = 0.0001. The stochastic gradient descent with momentum (SGDM) was used as the network optimization method. All brain images were resized to the required input sizes of two trained networks and fed into the model. 80% of the images were used for training, 10% for validation, and 10% for testing. All the results below are presented for unseen MRI and DTI image data.

3 **Experiments and Results**

Experiments were conducted with the updated configurations of AlexNet and VGG16, as described above, using DTI and MRI data. Four classification problems were tested: three binary classification tasks (EMCI vs. NC, AD vs. NC, and AD vs. EMCI) composed of 400 images each, and one multiclass task (AD vs EMCI vs NC) using 600 images with a balanced number of AD, EMCI, and NC subjects.

Table 1: Average classification performance (over 5 runs) of the two models on unseen DTI and MRI test data.

Model	Multiclass AD, EMCI, NC		Binary AD vs EMCI		Binary EMCI vs NC		Binary AD vs NC	
	DTI	MRI	DTI	MRI	DTI	MRI	DTI	MRI
VGG16								
Acc	0.8438	0.8950	0.7400	0.7813	0.9100	0.9300	0.9975	0.9350
Precision	0.8600	0.8900	0.7450	0.7950	0.9200	0.9200	1.0000	0.9200
Recall	0.8329	0.8990	0.7376	0.7737	0.9020	0.9388	0.9950	0.9485
F-score	0.8462	0.8945	0.7413	0.7842	0.9109	0.9293	0.9975	0.9340
AUC	0.9766	0.9800	0.8581	0.8787	0.9700	0.9800	0.9998	0.9756
AlexNet								
Acc	0.7088	0.7200	0.6900	0.7463	0.8500	0.8500	0.9900	0.8600
Precision	0.7000	0.7050	0.7200	0.7376	0.8700	0.8600	0.9900	0.8600
Recall	0.7125	0.7268	0.6792	0.7525	0.8365	0.8431	0.9900	0.8600
F-score	0.7062	0.7157	0.6990	0.7450	0.8529	0.8515	0.9900	0.8600
AUC	0.9052	0.8550	0.8900	0.8900	0.9000	0.9200	0.9957	0.9600

Table 1 summarises models' classification performance in testing, after applying the transfer learning process described in Section 2. Five independent runs were conducted in each case. The metrics shown include accuracy rate (Acc), the area under the curve which plots parametrically the true positive rate vs the false positive rate (AUC), and the F-score, which is commonly used for evaluating the performance of machine learning models. It is defined as the harmonic mean of the model's Precision and Recall (see Table 1).

The highest performance of 89.50 % (0.98 of AUC, 0.89 of F-score) in the multiclassification task is achieved with VGG16 on MRI data. The best results in the binary classification tasks are obtained by VGG16 nets using MRI data: AD vs EMCI (78% of accuracy, 0.88 of AUC, 0.78 of F-score); EMCI vs NC (93% of accuracy, 0.98 of AUC, 0.93 of F-score). These results compare well with previous research that only investigated DTI [9] or MRI data [10]. The AD vs NC task is diagnosed better by transfer learning with the VGG16 classifier when DTI data are used, although AlexNet-based transfer learning also performs well.

It is worth noticing that the time spent for training and testing the two transfer learning architectures differs significantly (commodity hardware was used for all experiments as described in Section 2). AlexNet required approximately 1.3 hours for multiclassification and 0.85 hours for binary classification, whilst the VGG16 took 15.7 hours and 9.7 hours respectively.

4 Discussion and Future Work

The experimental study demonstrated that deep transfer learning is a promising technique for the detection of cognitive decline when MRI data are used. At the same time, using DTI data gives an advantage in the early diagnosis of Alzheimer's disease with deep transfer learning.

The performance of the classifiers used in the research indicates the advantage of the VGG16-based models over the AlexNet ones, since the average error rate of AlexNet-based

models is 7.4% higher than the VGG16 models. The advantage of the VGG16, however, comes at a price since these models take 8 to 15 times longer to train and test than AlexNets.

From a medical perspective, the findings align with previous research that showed degeneration of the white matter of the brain is connected to and correlated with gray matter atrophy in cases of Alzheimer's disease. Axons of neurons can be affected earlier than the neurons themselves and can symbolize the early onset of the disease. DTI can detect these changes quicker than MRI and become the method of choice in the early diagnosis of Alzheimer's forms of dementia. The white matter in patients with MCI is affected significantly less. Thus, in the diagnosis of MCI and the transformation of some of its forms to AD, MRI technologies help computational models perform better compared to DTI. This can be explained by the fact that cognitive decline in the case of MCI might have different morphological grounds when the destructive process does not involve the white matter only. The nature of MCI is more complex and might have another, vascular reason, for amnestic and cognitive decline. Only 30% of MCI progress to AD.

This work can be extended in two directions. The first direction focuses on longitudinal studies inside image classes based on the evaluation and analysis of the changes of WM tracts during the progression of dementia using transfer learning of Convolutional Neural Networks A second line of the research is the use of additional biomarkers (features) that can potentially improve the diagnosis of MCI using Deep Learning methods.

Acknowledgements

Data collection and sharing for this project was funded by the Alzheimer's Disease Neuroimaging Initiative (ADNI) (National Institutes of Health Grant U01 AG024904) and DOD ADNI (Department of Defense award number W81XWH-12-2-0012).

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