Classifying Alzheimer's MRI scans using 2D and 3D convolutional neural networks

Bouke Regnerus and Raoul Fasel[1]

***Abstract*— Dementia and other cognitive diseases are a big problem in the current society. One of the most common forms of dementia is Alzheimer's Disease. A lesser form of dementia called Mild Cognitive Impairment often transistions into full Alzheimer's. It is hard for humans to correctly diagnose early forms of Alzheimer's and especially hard to differentiate between them. In this paper the possibilities of classifying human MRI scans using convolutional networks are explored. The classification is on three classes Mild Cognitive impairment, Alzheimer's Disease and clinically normal. Finally a working model is presented using 3D convolutional layers that has good performance on the three classes**

I. INTRODUCTION

Alzheimers Disease is the most common form of dementia. It is associated with brain degeneration that causes problems such as memory impairment and disorientation. The cause of this degeneration is currently not fully understood. However it is clear that Alzheimer's disease does not strike quickly but is a degrading process that is very slow and can take multiple decades to develop into a form that can even hinder daily activities. This means that humans diagnosed with a Mild Cognitive Impairment could actually have an early stage of Alzheimer's Disease, according to A.J Mitchell et al. [1] this likelihood is significant with an annual conversion rate of 5-10%. In 2015 more than five million Americans were victim of this disease.[2]

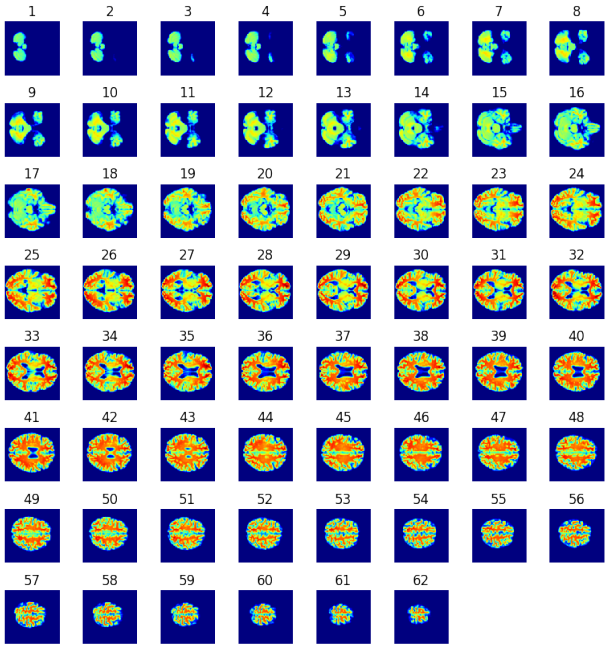
This paper describes the process of improving the performance of a neural network that classifies sliced MRI-scans. The main focus of this of this research is the usage of multiple channels in the network. In other words, the network will be able to use all slices at once instead of only one. The improvement should come from features that are shared between multiple slices

A. The challenge

The data set consists of MRI scans from 321 subjects (112 of whom are cognitively normal at at least one time point, 129 mild cognitive impairment, 150 Alzheimer's disease) each with multiple scans on different dates. The scans contain sets of images. These sets represent the 3D brain into 62 2D axial slices. The images are already preprocessed and split into train, validation, and test sets.

[1]B. Regnerus and R. Fasel are with Faculty of Electrical Engineering, Mathematics and Computer Science, University of Twente, 7500 AE Enschede, The Netherlands.

Furthermore demographic data is included: clinical diagnosis, age and sex. The dataset was acquired from the Alzheimers Disease Neuroimaging Initiative(ADNI)[17] The challenge that this data set offers is to build an accurate classifier that can classify individual brain images into one of three classes: Clinically Normal (CN), Mild Cognitive Impairment (MCI), or Alzheimer's Disease (AD). The slices in the scan sets can be used in different ways to train the classifier. For example selecting only a few slices and using them as input. Another way would be combining multiple slices and use that as an input. The best method for selecting these slices has to be found in order to optimise the classifier. Figure 1 is an example of a scan set, containing the 62 different MRI slices for one subject.



:

Fig. 1: Slices of a brain scan from the ADNI data set, a female of aged 71 classified with Mild Cognitive Impairment (MCI) Visualisation source code can be found on Github[20].

.

B. Research Questions

What are the performance differences between 2D- and 3D-convolutions on a three dimensional dataset consisting of layered images?

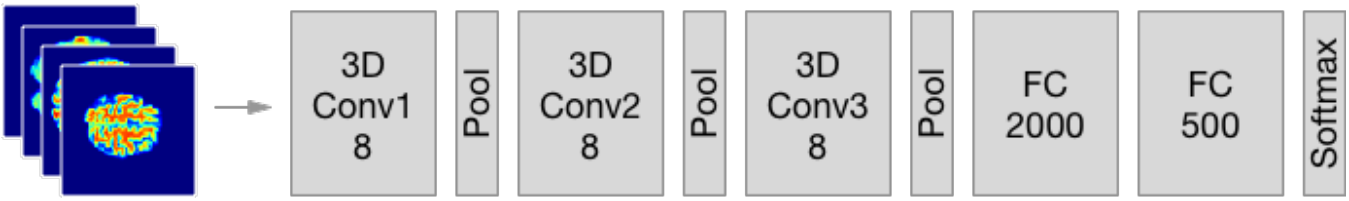


Fig. 2: The 3D convolutional network has 3 convolution layers, 3 max-pooling, and 2 fully connected layers, followed by a softmax output layer. All 3D convolution kernels are 3 x 3 x 3 with stride 1 in all three dimensions. Number of filters are denoted in each box. The 3D pooling layers are denoted as pool. All pooling kernels are 2 x 2 x 2. The output units of the fully connected layers are denoted in each box.

This question is answered with the support of the following questions:

- What are the differences between 2D and 3D convolution and -pooling layers?
- Is it possible to generate focus points using saliency maps?

II. Related Work

Traditional methods of classifying MRI scans are mostly done manually by humans using visual assessment. Ph Scheltens et al. [3] investigated this method in 1992 and they concluded that visual assessment is certainly possible and could even be used to assist in the diagnosis of a possible Alzheimer's disease. According to their research the method correctly classified 86% of the test subjects and 61% in the control group. This method looked at the atrophy of certain brain parts. The atrophy patterns could be learned by the neural network. Shi et al. [4] concluded that a deep network that combines the data from multiple layers of the brain scan instead of only using one slice and using data from different scanning techniques would improve the performance of the network.

Sarraf et al. [5] provide a working neural network that can classify MRI scan slices on Alzheimers disease with an accuracy of 98,84%. The network used was based on the LeNet5 network and was tested by using the ADNI database. It is important to note that this approach classifies 2d images in contrast to the goal of this paper which tries to improve the results by finding the relations between the different layers or images of a MRI scan. Furthermore, the provided network could distinguish between disease and no disease.

Ehsan Hosseini-Asl et al [14] provide a deep neural network that uses 3D convolution layers. The 3D layers are used in order to get more information out of the brain scans. They also include a comparison with other networks. It is important to note that their network can distinguish between three different classes while retaining a high accuracy. A network that makes use of 3D convolutions is apparently the best approach.

III. Learning Features with 3D Convolutional Neural Networks

We hypothesise that 3D convolutional neural networks are well suited for the classification of the ADNI Alzheimer's MRI scans data set since it consists of multiple layers (MRI slices) per subject. The layers are highly correlated and features could span over multiple layers. 3D convolutions and -pooling operations are performed spatially over multiple layers instead of just spatially. 3D convolutions are also used for operations on multiple frames of a video to encode spatio-temporal information. [4]

In figure 3 the difference between 2D convolutions, 2D convolutions on multiple channels and 3D convolutions applied on an image are illustrated. Both the 2D convolutions and 2D convolutions on multiple channels, for example RGB images, result in a 2D output layer. Therefore 2D convolutions lose a dimension of information after every convolution. Only the 3D convolutions preserve the 3rd layer of information of the input data, resulting in an output that consists of multiple layers. This phenomena is the same for 2D and 3D pooling. [15]

IV. Generate focus maps using saliency maps

The visualisation of image classification models is an important process in understanding deep neural networks in general. According to Simonyan et. al. [18] such saliency maps can be used for weakly supervised object localisation. For the classification of MRI images to detect Alzheimer's disease such a object localisation could eventually be a useful tool for doctors to study the visual markers caused by Alzheimer's disease that are used in the visual assessment of MRI scans. The concept for generating salience maps is pretty straight forward. Gradients are computed for each output category with respect to the input image. This should inform us about the value of the output category with respect to changes in the input image. Positive values in the gradients will increase the output value and vice-versa. Therefore visualising the gradients, which are the same shape as the input image, it should provide a visualisation of attention points. [18] Using neural network salience maps have been successfully applied in multiple fields as a useful tool for obtaining visual attention points. [19] We tried generating the salience maps using a Keras function where we obtained the weights from the model. However we were unable to obtain any relevant salience maps, this is due to the fact that research in salience maps is mostly done with 2d convolutions while we are using a 3D convolutional model. Therefore it is impossible at this point to say if salience maps could provide useful insight in detecting visual markers for Alzheimer's disease.

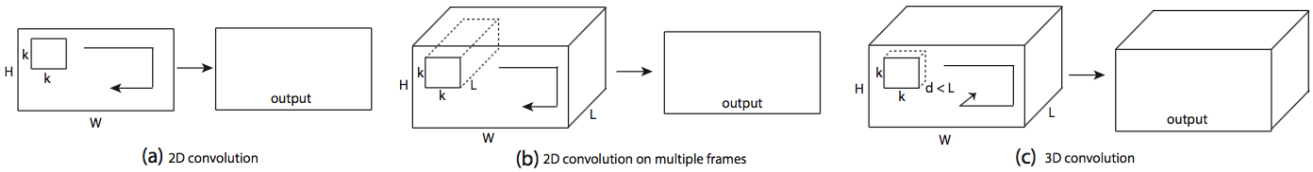


Fig. 3: Convolution type. [15]

TABLE I: Performance comparison*

Approach	Modalities	AD/MCI/NC	AD+MCI/NC	AD/NC	AD/MCI	MCI/NC
Suk et al. [6]	PET+MRI+CSF	n/a	n/a	95.9	n/a	85.0
Suk et al. [7]	PET+MRI	n/a	n/a	95.4	n/a	85.7
Zhu et al. [8]	PET+MRI+CSF	n/a	n/a	95.9	n/a	82.0
Zu et al. [9]	PET+MRI	n/a	n/a	96.0	n/a	80.3
Liu et al. [10]	PET+MRI	53.8	n/a	91.4	n/a	82.1
Liu et al. [11]	MRI	n/a	n/a	93.8	n/a	89.1
Li et al. [12]	PET+MRI+CSF	n/a	n/a	91.4	70.1	77.4
Sarraf et al. [13]	fMRI	n/a	n/a	96.8	n/a	n/a
Hosseini-Asl et al. [14]	MRI	89.1	90.3	97.6	95	90.8
Our solution	MRI	81	n/a	n/a	n/a	n/a

* This table was adapted from the performance comparison table given by Hosseini-als et al. [14]

V. Model

In this section we try to identify a good architecture for a 3D convolutional model. Since 3D convolutional neural networks can be very time consuming experiments where first done with a smaller data set to find a good architecture. The final architecture was then verified with the full-size data set. The experiments including the final architecture are developed using Keras[21], a neural network library for Python, and Jupyter Notebook[22], a tool that allows for quick experimentation.

As described in [16] experiments were done on 2D convolutional neural networks they yielded the best results with deeper networks and a kernel size of 3 x 3. D. tran et al.[15] did further research in 3D convolutional neural networks where the third dimension of the kernel was varied. It was concluded that 3D convolutional neural networks with 3 x 3 x 3 kernels performs best among the experimented networks. Furthermore the same research established pooling kernels of 2 x 2 x 2.

Both papers suggested the use of deep networks to get the best results, we therefore experimented with the batch size and depth of the network. There is a trade-off between quality of the network and the speed at witch the network can be trained. Because of time constraints and limited resources the resulting parameters were selected on speed above quality.

As previously mentioned related work on 3D convolutional networks for brain scans E. Hosseini-asl et al. [14] used a model which also uses convolutional kernels of 3 x 3 x 3 and pooling kernels of 2 x 2 x 2. The researchers used a network of three convolutional layers all of which have a batch size of 8, each followed by a pooling layer. After the convolution part there is a flatten layer followed by two fully connected layers which use the 'ReLu' activation function. Eventually a final fully connected layer with a 'Softmax' activation function is used in order to get to the three classes.

The convolutional neural network which was used for the final classification on the test dataset can be found in figure 2. The source code of the final model can be found on Github[20].

VI. Model Evaluation

Our model will be evaluated by comparing the performance of our model to models proposed by other papers. To be more specific the accuracy of our model will be compared with he accuracy of other models. The most relevant model is the model proposed by Hosseini-als et al[14] because their

research resembles ours, including 3D convolutions and three classes. furthermore their paper is the most recent

In order to easily compare the results the performance table gathered by Hosseini-als et al[14] was used and adapter. It can be seen in figure I. It is important to note that this table only compares accuracy. This paper also only compares accuracy because it is a metric that is easily retrievable.

VII. RESULTS

TABLE II: Performance results

	Precision	Recall	F1-score	Support
CN	98%	96%	97%	159
MCI	67%	79%	74%	157
AD	77%	67%	72%	153
avg / total	82%	81%	81%	469

The final model described in the previous chapter was evaluated using a test set of 469 brain scans. Table II show the performance metric of the model on the test set. The overall accuracy was 81%. As seen in the performance comparison in table I, the accuracy comes close to the performance of the 3D network proposed by Hosseini-Asl et al. [14]

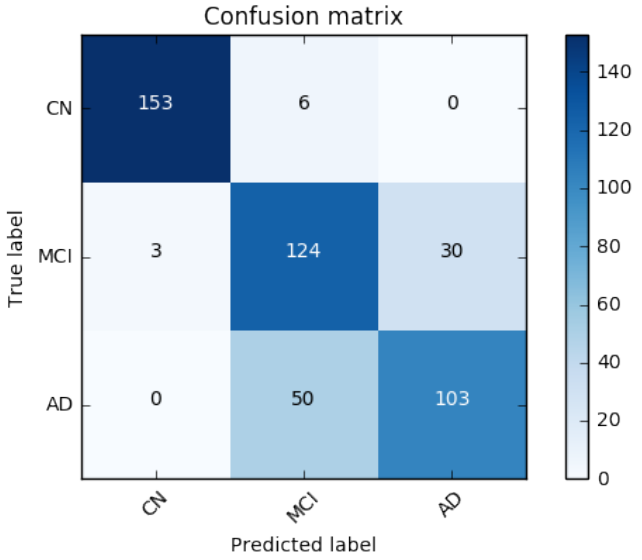


Fig. 4: Confusion matrix of the results

In the confusion matrix (figure 4), it can be seen that no patients that are clinically normal (CN) are classified with Alzheimer's disease (AD) and visa-versa. The confusion table also shows that there is a high degree of uncertainty between patients that have mild cognitive impairment (MCI) and are classified with Alzheimer's disease (AD) and patients that have Alzheimer's disease (AD) and are classified with mild cognitive impairment (MCI).

VIII. CONCLUSION AND DISCUSSION

According to the results and the research done on 3D convolutional networks it was observed that 3D convolutional networks preform well on classifying MRI brain scans. Even with time constraints and lack of resources a relatively high accuracy was reached. The accuracy was much higher than the model that used 2d convolutions provided by Liu et al. [10]. However it is still hard to say if a 3D convolutional network is always better further research is therefore needed to substantiate this hypothesis. Also because only the model accuracy was compared it could be that, when using different metrics, the overall model performance is different.

The confusion matrix (figure 4) shows that the highest uncertainty is between patients that have mild cognitive impairment (MCI) and are classified with Alzheimer's disease (AD) and patients that have Alzheimer's disease (AD) and are classified with mild cognitive impairment (MCI). This is to be expected because a mild cognitive impairment will often lead to an Alzheimer's diagnosis and there is no clear line differentiating them. [1] It is therefore hard to correctly classify a person correctly. This could result into wrongly labeled data and could also result into a distribution that is hard to separate for the model. One solution would be creating a scale that could be used to determine the severeness of cognitive impairments.

The results from the confusion matrix also indicate that the model would perform well when distinguishing clinically normal (CN) with Alzheimer's diagnosed (AD), when leaving out the MCI cases.

Research also showed that in theory it is possible to generate saliency maps for the neural network. However we did not manage to generate the correct saliency maps for this network and therefore it remains unknown if saliency maps could be a helpful tool for detecting visual markers that could help with the diagnosis of Alzheimer's disease.

Further research should be done to optimise this model even further. Most importantly without time and resource constraints because fine tuning deep neural networks requires multiple runs of the same model with different parameters.

Research could also be done in combining multiple specialised models. For example the combination of a model that can accurately distinguish between clinically normal (CN) and Alzheimer's disease (AD) together with a model that can accurately determine the severity of the Alzheimer's disease (AD).

REFERENCES

[1] A. J. Mitchell and M. Shiri-Feshki, Rate of progression of mild cognitive impairment to dementia - meta-analysis of 41 robust inception cohort studies, Acta Psychiatr. Scand., vol. 119, no. 4, pp. 252265, 2009.

[2] Alzheimers Association, 2015 Alzheimers Disease Facts and Figures: Includes a Special Report on Disclosing a Diagnosis of Alzheimer's Disease. 2015.

[3] P. Scheltens, D. Leys, F. Barkhof, D. Huglo, H. C. Weinstein, P. Vermersch, M. Kuiper, M. Steinling, E. C. Wolters, and J. Valk, Atrophy of medial temporal lobes on MRI in probable Alzheimers disease and normal ageing: diagnostic value and neuropsychological correlates, J. Neurol. Neurosurg. Psychiatry, vol. 55, no. 10, pp. 967972, Oct. 1992.

[4] B. Shi, Y. Chen, P. Zhang, C. D. Smith, and J. Liu, Nonlinear feature transformation and deep fusion for Alzheimers Disease staging analysis, Pattern Recognit., vol. 63, pp. 487498, 2017.

[5] S. Sarraf, D. D. DeSouza, J. Anderson, G. Tofighi, and For The Alzheimers Disease, DeepAD: Alzheimers Disease Classification via Deep Convolutional Neural Networks using MRI and fMRI. 2016 [Online]. Available: http://dx.doi.org/10.1101/070441

[6] Heung-Il Suk and Dinggang Shen, Deep learning-based fea- ture representation for ad/mci classification, in Proceed- ings of the Medical Image Computing and Computer-Assisted InterventionMICCAI 2013, pp. 583590. Springer, 2013.

[7] Heung-Il Suk et al., Hierarchical feature representation and multimodal fusion with deep learning for AD/MCI diagnosis, NeuroImage, vol. 101, pp. 569582, 2014.

[8] xiaofeng Zhu et al., A novel matrix-similarity based loss function for joint regression and classification in AD diagno- sis, NeuroImage, vol. 100, pp. 91105, 2014.

[9] Chen Zu et al., Label-aligned multi-task feature learning for multimodal classification of Alzheimers disease and mild cog- nitive impairment, Brain Imaging and Behavior, pp. 112, 2015.

[10] Siqi Liu et al., Multimodal neuroimaging feature learning for multiclass diagnosis of alzheimers disease, Biomedical Engineering, IEEE Transactions on, vol. 62, no. 4, pp. 1132 1140, 2015.

[11] M. Liu et al., Inherent structure based multi-view learning with multitemplate feature representation for Alzheimers dis- ease diagnosis, IEEE Trans. Biomed. Eng., vol. PP, no. 99, pp. 11, 2015.

[12] Feng Li et al., A robust deep model for improved classification of AD/MCI patients, IEEE J. Biomed. Health Inform., vol. 19, no. 5, pp. 16101616, 2015.

[13] Saman Sarraf and Ghassem Tofighi, Classification of alzheimers disease using fmri data and deep learning convolu- tional neural networks, arxiv:1603.08631 [cs.CV], 2016.

[14] E. Hosseini-Asl, R. Keynton, and A. El-Baz, Alzheimers disease diagnostics by adaptation of 3D convolutional network, in 2016 IEEE International Conference on Image Processing (ICIP), 2016 [Online]. Available: http://dx.doi.org/10.1109/icip.2016.7532332

[15] D. Tran, L. Bourdev, R. Fergus, L. Torresani, and M. Paluri, Learning Spatiotemporal Features with 3D Convolutional Networks, in 2015 IEEE International Conference on Computer Vision (ICCV), 2015 [Online]. Available: http://dx.doi.org/10.1109/iccv.2015.510

[16] K. Simonyan, A. Zisserman. Very deep convolutional networks for large-scale image recognition. CoRR, abs/1409.1556 , 2014.

[17] The Alzheimers Disease Neuroimaging Initiative http://adni.loni.usc.edu/

[18] Deep Inside Convolutional Networks: Visualising Image Classification Models and Saliency Maps

[19] Learning-Based Prediction of Visual Attention for Video Signals

[20] "Raoulfasel/Alzheimers-Mri-Deep-Learning". github.com/RaoulFasel/alzheimers-mri-deep-learning N.p., 2017. Web. 3 Feb. 2017.

[21] "Keras Documentation". Keras.io. N.p., 2017. Web. 2 Feb. 2017.

[22] "Project Jupyter". Jupyter.org. N.p., 2017. Web. 2 Feb. 2017.