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
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
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Intuitive visualization for convolutional neural networks detecting brain diseases in MRI scans

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Introduction

- Although deep learning approaches achieve high diagnostic accuracy to automatically detect neurodegenerative diseases -such as Alzheimer's disease- based on MRI and PET, they are currently not part of clinically applied diagnostic systems.
- The main reason for this lack of clinical use is the shortcoming in proper methods for model comprehensibility and interpretability for clinical users.

Aim of the study:

- Development of a convolutional neural network (CNN) model to achieve competitive diagnostic accuracy for detecting Alzheimer's disease in patients with dementia and mild cognitive impairment (MCI).
- Intuitive visualization to aid model comprehensibility and clinical utility using class activation mapping approaches to highlight contributing brain regions.

Methods

- MRI data from the *Alzheimer's Disease Neuroimaging Initiative* (ADNI) (Tab.1) were used for model training by applying a six-fold cross-validation scheme.
- Only patients with positive amyloid- β biomarker and controls with negative finding were included to improve the diagnostic confidence of the training sample.
- Twelve coronal slices covering the hippocampus area were selected, corrected for effects of age and gender using linear regression, and fed into the CNN model as separate channels (Fig.1).
- MRI data from the *DZNE – Longitudinal Cognitive Impairment and Dementia Study* (DELCODE) (Tab.1) were used as independent validation set.

Table 1 Sample characteristics.

	Male/Female	Age	Years of education	MMSE
ADNI (N=294)				
HC (n=126)	65/61(48.4%)	72.7 \pm 6.4	16.8 \pm 2.5	29.1 \pm 1.2
MCI (n=93)	50/43(46.2%)	72.3 \pm 7.4	16.4 \pm 2.8	27.1 \pm 1.9
AD (n=75)	40/35(46.7%)	75.0 \pm 8.5	15.6 \pm 2.8	22.9 \pm 2.1
Independent validation set				
DELCODE (N=332)				
HC (n=182)	75/107(58.8%)	69.0 \pm 5.3	14.8 \pm 2.7	29.4 \pm 0.9
MCI (n=89)	54/35(39.3%)	72.3 \pm 5.1	14.0 \pm 3.0	28.0 \pm 1.7
AD (n=61)	27/34(55.7%)	74.0 \pm 6.4	13.3 \pm 3.3	23.5 \pm 3.3

Abbreviations: AD – Alzheimer's dementia, MCI – mild cognitive impairment, HC – healthy controls, MMSE – mini mental status examination.

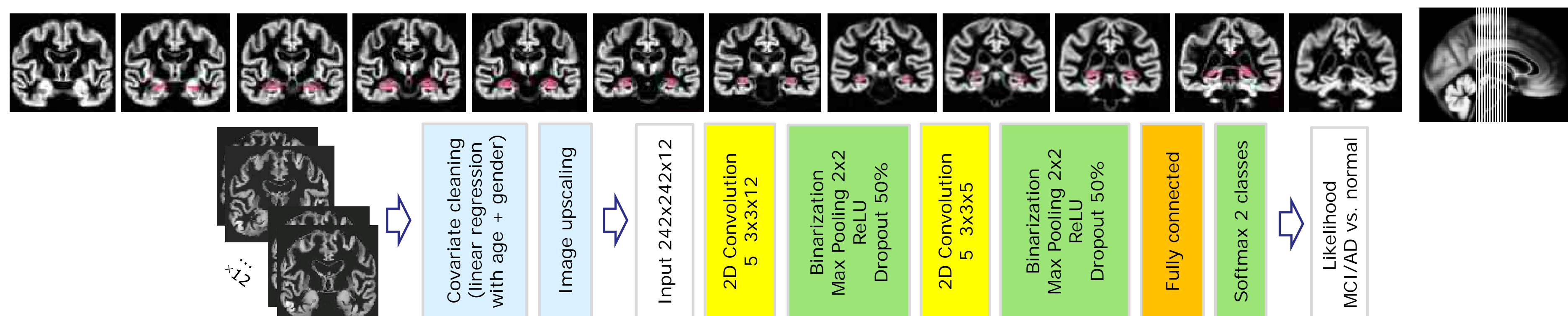


Figure 1 Input data (top) and deep learning model layout (bottom). Twelve coronal slices covering the hippocampus enter the model as separate input channels.

Results

- Area under the curve and diagnostic accuracy are given in Fig.2.
- Group mean CNN activation maps indicate hippocampal areas as most informative for the model (Fig.3 left).
- Individual subject's activation maps show more distributed cortical and subcortical regions to contribute to the model's decision (Fig.3 right).

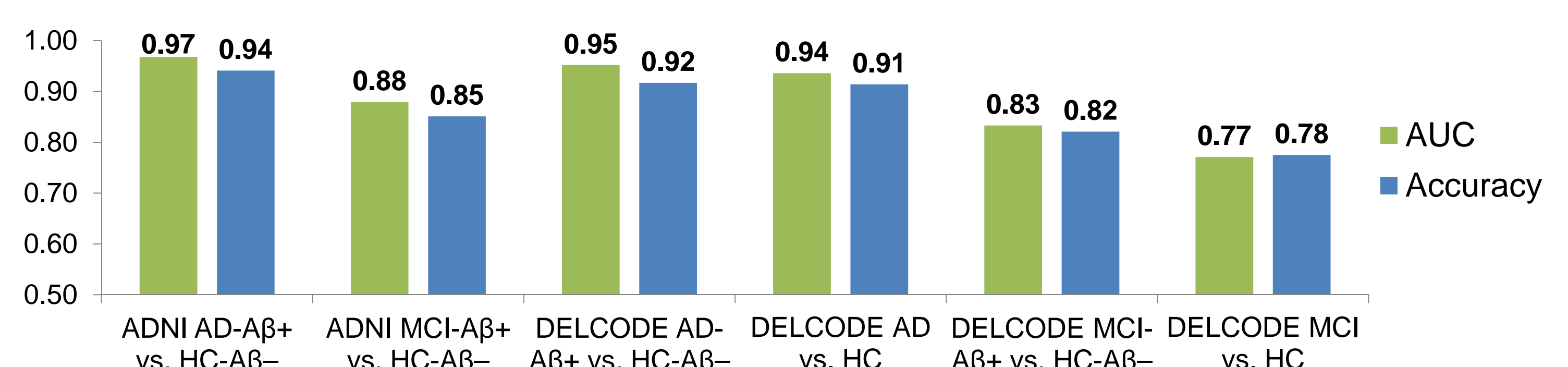


Figure 2 Area under the curve (AUC) and diagnostic accuracy.

Abbreviations: AD – Alzheimer's dementia, MCI – mild cognitive impairment, HC – healthy controls, Aβ+/- – amyloid- β biomarker positive/negative.

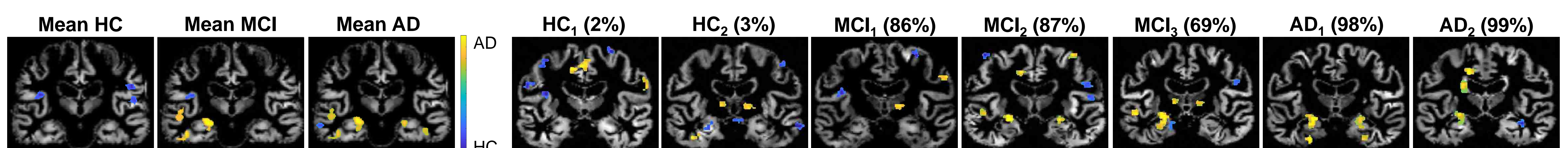


Figure 3 Group average (left) and individual subject's activation maps (right) as well as likelihood scores for Alzheimer's disease returned by the CNN model.

Discussion and conclusion

- Results applying 2D convolutional layers provide high diagnostic accuracy and promising results for the visualization of individual subject's CNN activity maps.
- Extension of the CNN toolbox for 3D convolutional layers recently became available in MATLAB R2019a and will provide activation maps with higher spatial information.

- Prospectively, we will focus on generating textual explanations from the input images [1] to enhance model interpretability and clinical utility.

Acknowledgement

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