A comprehensive deep learning model for the tracking of Alzheimer's Disease

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INTRODUCTION

Despite a clear clinical need, there are no generalizable tools to distinguish between Alzheimer's Disease (AD) and Mild Cognitive Impairment (MCI), or to identify patients who will progress from MCI to AD. Significant work has been done to develop deep learning networks for this purpose. However, models employing ^{18}F-FDG PET images and longitudinal data are underdeveloped yet may offer distinct advantages over other models.[1,2,3]

The goal of this work was to develop a comprehensive convolutional neural network (CNN) to diagnose AD and MCI and to predict disease progression using ^{18}F-FDG PET images.

DATASET

787 FDG PET scans and corresponding clinical data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database were compiled. Each scan was classified as normal control (NC), stable MCI (sMCI), progressing MCI (pMCI), or Alzheimer's Disease (AD).

- ❑ A scan was classified as sMCI if that patient was never diagnosed with AD within the length of the study.
- ❑ A scan was classified as pMCI if that patient was diagnosed with MCI at the time of the scan, but would later convert to AD.

The pMCI patients were further classified using longitudinal information. Time to conversion (TTC) for each pMCI scan was calculated as the difference between the date of the current scan and the future date of diagnosis of AD. The pMCI group was thus refined by whether or not a patient would convert to AD within three years.

	AD	pMCI		sMCI	NC
		(TTC≤3yr)	(TTC>3yr)		
Number of scans	170	190	104	125	198
Mean Age	77.2	75.4		74.9	77.7
Mean MMSE	20.9	27.0		28.0	29.1

Table 1: Description of the dataset obtained from ADNI and used in this study.

DATA PRE-PROCESSING

The data were obtained from the ADNI database with the minimum amount of pre-processing offered. Each FDG PET scan was then pre-processed using Statistical Parametric Mapping (SPM12). Brain extraction, rigid registration to a custom FDG template,[4] spatial normalization to the Montreal Neurological Institute (MNI) space, and global mean intensity normalization were performed on each image.

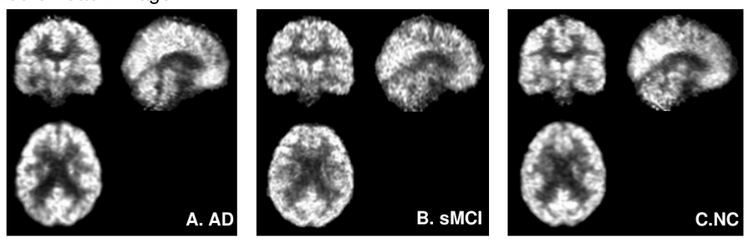

Figure 1: Example preprocessed FDG PET scans from (A) a patient diagnosed with AD, (B) a patient diagnosed with MCI, and (C) a normal control patient.

METHODS

The 3D-CNN used here was adapted from previous work by Spasov et al.[5] The model architecture, shown in Figure 2, employs 3D separable and grouped convolutional layers along with several fully connected layers, keeping the number of parameters relatively low to limit overfitting. Model inputs included 3D-FDG PET images and clinical data (age, gender, and MMSE cognitive test score).

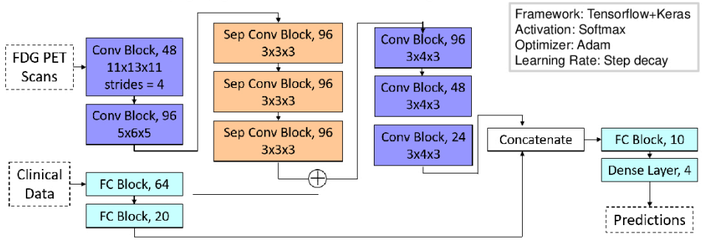

Figure 2: Model architecture of the 3D-CNN used in this work.

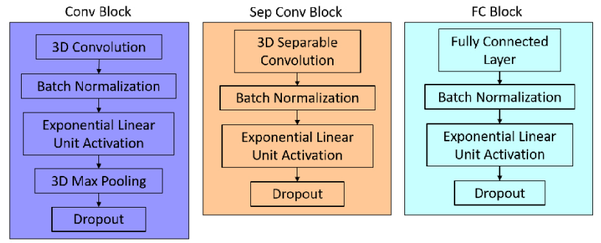

Figure 3: Description of each of the blocks used in the model architecture. Figure adapted from Spasov et al.[5]

The pMCI patients with TTC > 3 years were combined with the sMCI group to create a 4-class deep learning model to classify AD, pMCI (≤3yr), sMCI, and NC. Training was optimized for accuracy holding 15% of the scans for validation and testing. The model was trained until loss convergence of validation and training sets. An example learning curve is provided in Figure 4.

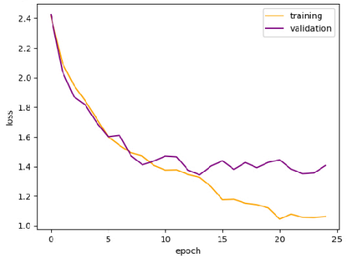

Figure 4: Example learning curves for the training and validation sets. A small amount of overfitting can be observed after the 15th epoch.

RESULTS

Performance was assessed using ROC analysis. The model achieved an area under the curve (AUC) of 0.873, 0.808, 0.788, and 0.729 for the AD, pMCI, sMCI, and NC classes, respectively. The ROC curve is shown in Figure 5. The normalized confusion matrix (Figure 6) provides a visual representation of how frequently each class was predicted for each of the classes.

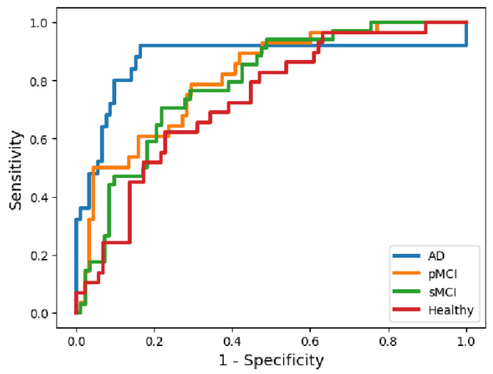

Figure 5: ROC curve for the 4-class model.

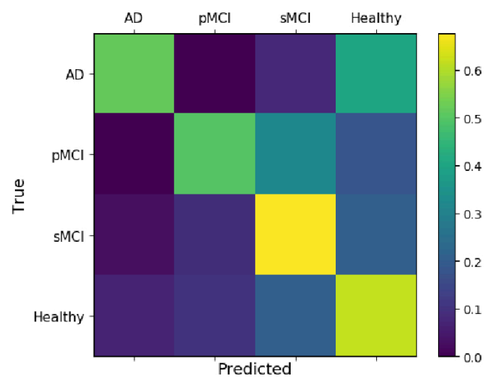

Figure 6: Confusion matrix showing the relative 4-class model performance, normalized by the total number of scans.

CONCLUSIONS

We have developed a functional model which can both distinguish various stages of the Alzheimer's Disease spectrum as well as predict the conversion of MCI to AD within three years.

The model achieved an AUC greater than 0.72 for each of the four classes: AD, pMCI, sMCI, and NC.

NEXT STEPS

We plan to continue to improve the performance of the model by adding capacity to the network and increasing the size of the dataset.

One limitation of the longitudinal information is the large uncertainty on the TTC value due to inconsistencies in scan acquisition. Future study will thus explore the sensitivity of the TTC classification of the pMCI patients, and the ability of the model to distinguish multiple classes of pMCI scans with varying ranges of TTC values.

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*Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu).

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