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Interpretable Identification of Mild Cognitive Impairment Progression Using Stereotactic Surface Projections

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Abstract.
Mild Cognitive Impairment (MCI) brings an increased risk of progressing to Alzheimer's disease (AD). Early identification of a risk of MCI progression could help patients get early treatment to slow progress of the disease. We used 3D Stereotactic Surface Projections (SSP) of Positron Emission Tomography (PET) brain images to train a classification model to identify MCI patients at risk of progressing to AD, which achieved 88.0% accuracy, 85.3% sensitivity, and 90.6% specificity. For model transparency purposes, we generated saliency map explanations from the trained model and evaluated these using radiologist feedback.

Keywords. Alzheimer's Disease, Mild Cognitive Impairment, Explainable AI

1. Introduction

Alzheimer's Disease (AD) is the most common type of Dementia, accounting for 60-80% of all cases worldwide [1]. AD is a progressive disease preceded by Mild Cognitive Impairment (MCI). The importance of studying MCI is evidenced by its increased risk of progression to AD, especially in older patients. In general, while healthy adult controls progress to AD at a maximum rate of 2% annually, MCI patients progress at a rate of 10%-25% [2]. For this reason, studying and identifying MCI progression is useful for early treatment of Dementia, especially with the introduction of a Food and Drug Administration (FDA) approved drug [3].

Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET), which measures glucose metabolism, is a recommended imaging strategy for visual diagnoses of MCI

[1] Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators can be found at: https://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf

progression [4]. 3D Stereotactic Surface Projections (SSP) of FDG PET summarize volumetric brain images to 2D images by projecting them to predefined surfaces and comparing them against healthy control groups [5]. Even though 3D SSP has been seen to improve visual diagnosis of dementia, its use for automated image classification has been limited. Since 3D SSP reduces slices in brain images into a few informative images, we hypothesize that it can achieve higher performance and better interpretability than using volumetric 3D brain images. To the best of the authors' knowledge, 3D SSP versions of FDG PET brain images have not been used for computer assisted identification of MCI progression.

A classification accuracy of 82.6% and a sensitivity of 84.8% was reported when classifying between stable and progressive MCIs using a random forest with Long Short-Term Memory [6] (and this was the best result when compared with logistic regression, Support Vector Machines, and Low-Density Separation). Even though automated methods to identify people with MCI at risk of progressing to AD show promise, their performance remains low. Also, while feature-attribution based surrogate model explanations have been used for automated AD diagnosis [7] and non-feature attribution explanations have been used for medical images [8], interpretability of MCI progression identification models using brain images is still a challenge due to the volumetric nature of the dataset. In addition, even though some works have quantified localization accuracy of explanations using expert annotation for computer assisted radiological diagnosis [9], effectiveness of the currently available MCI progression model explanations have not been verified by radiologists.

We trained a Convolutional Neural Network (CNN) model to identify MCI patients at risk of progressing to AD and deployed a post-hoc visualization based explanation, called Gradient weighted Class Activation Mapping (GradCAM). To address the issue of explanation complexity that arises due to the volumetric nature of brain images, we used SSP images for model development and diagnosis. Furthermore, a radiologist with specialist expertise in PET-CT evaluated the effectiveness of the explanations generated from the model.

2. Methods

Model Training and Explanation. Data used in the preparation of this article was obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database [2]. We extracted FDG PET images of MCI participants from the ADNI database. We then labelled those that remained as MCI during the study as *stable MCI*, and those that progressed to AD at a future time point as *progressive MCI*. To study progression of MCI, 30 stable and 30 progressive MCI participants who stayed relatively longer than other participants in the ADNI study were used in this analysis. On average, the 60 participants were imaged 4.56 times. In addition to these, FDG PET images of 13 healthy participants from ADNI were selected as the control group to compute 3D SSP.

In total, we generated 500 left and right lateral SSP images of the FDG PET images collected from the 60 MCI participants using a template from ADNI. We used 200 SSP

[2]The ADNI was launched in 2003, led by Principal Investigator Michael W. Weiner, MD (adni.loni.usc.edu). The primary goal of ADNI has been to test whether medical data can be used to measure progression of MCI and early AD. For up-to-date information, see www.adni-info.org

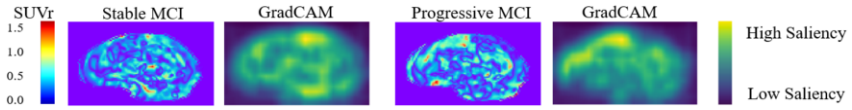

Figure 1. Sample SSP image inputs viewed against Standard Uptake Value ratios (SUVr) colorbar and their GradCAM explanations visualized using VIRIDIS colormap. The SUVr values are small because they have been subtracted from mean SUVr values of the healthy control groups.

images, which were generated from FDG PET images of 11 progressive and 11 stable MCI participants, as a training dataset and 300 SSP images from the remaining participants as a test dataset. Our CNN model contains six 2D convolutional layers followed by a fully connected layer of size 1024, and it was trained using Adam optimizer with a decaying learning rate starting with $1e^{-3}$. After training our model we used GradCAM with test images to visualize salient image regions (Figure 1).

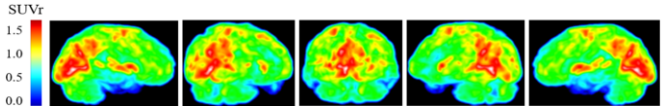

Figure 2. Frames from 5 time points of a sample sagittal video projection built using Mango software.

Radiologist User Evaluation. We used video versions of brain images for easier visualization and radiologist evaluation against saliency map explanations. We built an eight second sagittal video projection, for each of 32 FDG PET images that were selected from the test dataset, using Mango software[3] (frames at 5 time points from a sample video can be seen in Figure 2). First, a radiologist diagnosed the 32 videos of brain images and identified brain regions associated with their diagnosis, then viewed the corresponding GradCAM explanations generated from the trained CNN and answered a single-item questionnaire: '*GradCAM correctly highlights brain regions associated with my diagnosis result*' on a Likert scale (ratings are: 1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree.)

3. Results and Conclusion

We achieved 88.0% accuracy, 85.3% sensitivity and 90.6% specificity in classifying stable and progressive MCI images on the test dataset, which beats current state of the art [6]. The use of 3D SSP images as model inputs has helped achieve better performance and provides an easily interpretable explanation for better transparency since explanation is presented on a few images instead of interpreting all slices of a volumetric FDG PET brain image. We also involved a radiologist to evaluate our model's explanation effectiveness. On a 5 rating Likert scale, 16 images scored 4, while the remaining 3, 7, and 6 images scored 5, 3, and 2 ratings, respectively. We accredit the less than 3 scores of the 13 images to small average number of scans taken during the study which was at 3.5 while the overall average number of scans of the images in our study was at 4.56. This shows us that there is still room to improve explanation accuracy. In future work, we plan

[3] https://ric.uthscsa.edu/mango/

to perform a wider evaluation of different explanations and to refine our model for more accurate explanations towards increasing radiologists' trust.

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