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Brain Structural Connectome Accurately Classifies Alzheimer's Disease Related Dementia

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INTRODUCTION

There is an urgent, unmet need for clinically useful biomarkers of Alzheimer's disease related dementia (ADRD) based on non-invasive and affordable measures. This studies have focused on brain MRI-derived markers. We tested utility of brain's structural connectome in classification of Alzheimer's disease related dementia.

METHODS

Participants : We used data from 211 elderly people who visited the dementia clinic at Ilsan Hospital from 2009 to 2013. Diagnosis was made by physicians based on history taking, neuropsychological evaluations and MMSE. Participants included 110 with diagnosis of Alzheimer's disease, 64 with mild cognitive impairment and 37 subjective mild cognitive impairment. MRI acquisition and analysis : Firstly, we estimated morphometrics measures using Freesurfer image analysis pipeline from T1 and FLAIR images. Morphometric measures (N=948 per subject) include volumes of the hippocampal subdivisions, and thickness, surface area, and volume of cortical/subcortical regions. Secondly, we estimated structural connectome using the diffusion MRI analysis pipeline, Mrtrix 3. The connectome measures (N= 33,698 per subject) include counts of streamlines, a surrogate measure of structural connectivity, and mean length of streamlines given any two brain regions based on multiple atlases. Classification : We built several machine learning models using the large-scale brain MRI-derived phenotypes to predict diagnosis of AD and MCI, respectively. Logistic regression (L1 regularization) and support vector machine (SVM) was used.

RESULTS

In prediction of Alzheimer's disease(AD) vs. subjective mild cognitive impairment(SMI), models based on both morphometric and connectomic estimates showed good classification accuracy (SVM accuracy = 0.98±0.011; LR accuracy=0.97±0.009; ten-fold cross validation). In prediction of MCI (mild cognitive impairment), models also showed good classification accuracy (SVM accuracy=0.93±0.05; LR accuracy=0.86±0.042; Figure 1). We also compared morphometry- and connectome-based models and testing model performance as a function of numbers of features. In prediction of AD, classification accuracy of the connectome-based model is similar to that of the combined model, significantly outperforming that of morphometry-based model (Figure 2). Likewise, in prediction of MCI, classification accuracy of the connectome-based model is similar to

that of the combined model, significantly outperforming that of morphometry-based model.

CONCLUSIONS

In this study, we showed that large-scale MRI-derived brain phenotypes, including the whole brain morphometric and connectomic estimates, can be used to reliably classify Alzheimer's disease related dementia. This shows potential clinical utility of the machine learning models using large-scale MRI-derived brain phenotypes in prediction of risk for ADRD.

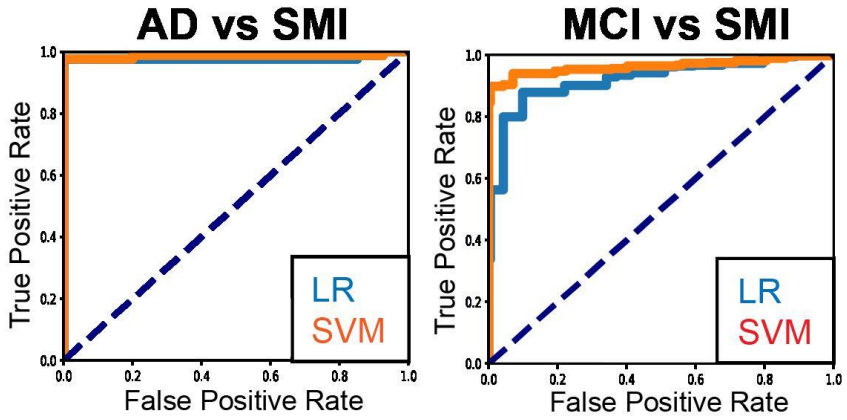

Figure 1. Classification accuracy of Logistic regression and support vector machine.

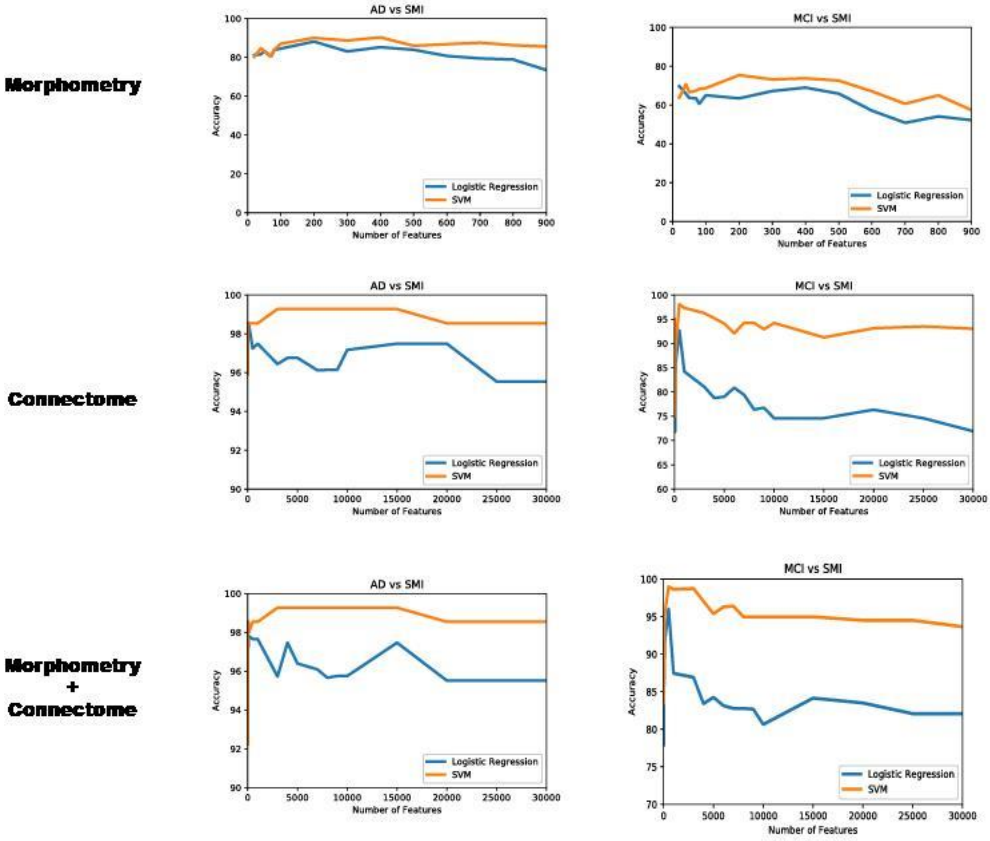

Figure 2. Classification accuracy of the mophometry-based model, connectome-based model and the combined model.