Integrating MRI Multivariate Markers with Cognitive Neuropsychological Scores for an Optimal Decisional Space in Predicting Alzheimer's Disease

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Abstract: Regional brain atrophy is a typical structural symptom of Alzheimer's disease (AD). Magnetic resonance imaging (MRI) scans capture brain structure with high resolution and are often processed with automated segmentation and parcellation algorithm like FreeSurfer to generate regional measures, like cortical volume, cortical thickness and surface area, which are widely used as inputs in classification algorithms. For this study, FreeSurfer was used to obtain 34 cortical thickness measures and 35 surface area measures for each hemisphere and 51 regional volumes across the brain. This paper proposes to combine these subject specific MRI measures with scores of cognitive neuropsychological test, Mini-Mental State Examination (MMSE), as input to an optimal decisional space for the classification process. A novel sorting and selection method of variables is proposed to construct this decisional space. This space is one that uses the highest statistically ranked variables as its dimensions to delineate subjects with Alzheimer's disease (AD) from cognitively normal controls (CN). Specifically, 189 structural MRI scans with 60 AD patients and 129 CN were used for empirical evaluations. A feature extraction technique involving statistical testing and error analysis was implemented to determine the significant MRI variables that yielded the optimal classification performance between CN and AD patients using support vector machines (SVM). Moreover, this study aims to find out which combination of MRI measures with neuropsychological test coupled with different normalization techniques can best predict AD using the proposed multivariate feature selection and classification method. The study showed that subcortical volumetric measures of right hippocampus and left inferior lateral ventricle have the highest power in discriminating between AD and CN groups. The results show an average accuracy of 85.1% (sensitivity: 65.7%; specificity: 94.1%) using only the two aforementioned volumetric measures. When MMSE scores were included as the third dimension, the average accuracy improved to 92.3% (sensitivity: 82.8%; specificity: 96.7%). Results also indicate neuropsychological test score contains the most discriminative information among single measure models, and out of the three MRI measures, cortical volumes is a better predicator than other two; Normalization approaches does not enhance the performance much if any. Hierarchical model of neuropsychological test and cortical volumes without normalization yield the best classification accuracy for this study. The approach considered for selecting and then ranking MMSE together with other MRI measures could augment other classification methods reported in the literature and could yield broader impact in reevaluating the different variables as predictive measures of AD. Moreover, this decisional space, in longitudinal studies, could serve to gauge the progression of AD for every patient and inform on early intervention measures.

Keywords: Alzheimer's disease (AD); multi-dimensional classification; AD biomarkers; Support Vector Machines (SVM); Mini-Mental State Examination (MMSE); neuropsychological test; brain atrophy

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