STRUCTURAL AND FUNCTIONAL BIOMARKERS OF CONVERSION TO ALZHEIMER'S DISEASE

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Background:
Only a small proportion (6.8-8.1%, [1]) of patients with Mild Cognitive Impairment (MCI) go on to develop Alzheimer's disease (AD). A key goal of this research is to develop a neuroimaging-based biomarker to distinguish MCI patients who go on to develop AD (MCI converters or MCIc), from those who do not (MCI stable or MCIs).

Methods:
Resting state 3T fMRI scans for MCI subjects were obtained from the ADNI database ([2], MCIc n=23, MCIs n=82) and the RADC database ([3], MCIc n=20, MCIs n=11). These MCIc subjects were further divided into MCIc <1yr, MCIc 1-2yr and MCIc >2yr depending on when the last scan was taken prior to AD diagnosis (Figure 1). A standard pipeline (Figure 2) was used to preprocess the scans, and parcellate the brain into 14 regions (Shirer et al, [4]). We calculated various measures of functional connectivity among these regions, including those based on zero-lag partial correlations (PC), lagged correlations (AR), and a graph-based metric of connectivity degree [5]. Structural MRI (sMRI) features, including surface area and thickness, were extracted with FreeSurfer to complement these functional features.

Based on these features, we trained an SVM classifier to predict whether an MCI subject will convert to AD or not. Recursive feature Elimination (RFE) was used to attain optimum accuracy, quantified with the area under the ROC curve (AUC), with the minimal number of features [6].

Results:
Among the functional connectivity metrics, zero-lag (partial) correlations (PC) significantly outperformed lagged correlations (AR) in terms of classification accuracy (Figure 3). sMRI features invariably improved the classification accuracies. A combination of sMRI, PC and degree metrics resulted in the maximum AUC for both the ADNI and RADC data (Figure 4).

Conclusions:
SVM-RFE combining structural and functional connectivity features provided significantly higher than chance classification accuracy. Our results can pave the way for predicting the development of AD in MCI subjects before the onset of severe dementia symptoms.
References: [1] PMID: 19236314, [2] PMID: 20042704, [3] PMID: 2314667, [4] PMID: 21616982, [5] PMID: 28333946, [6] PMID: 18672070

Figure 1

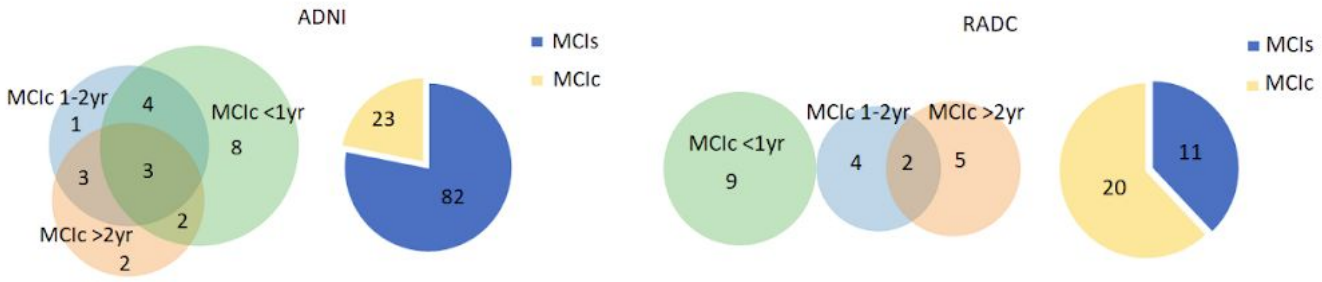


Figure 2

Figure 3

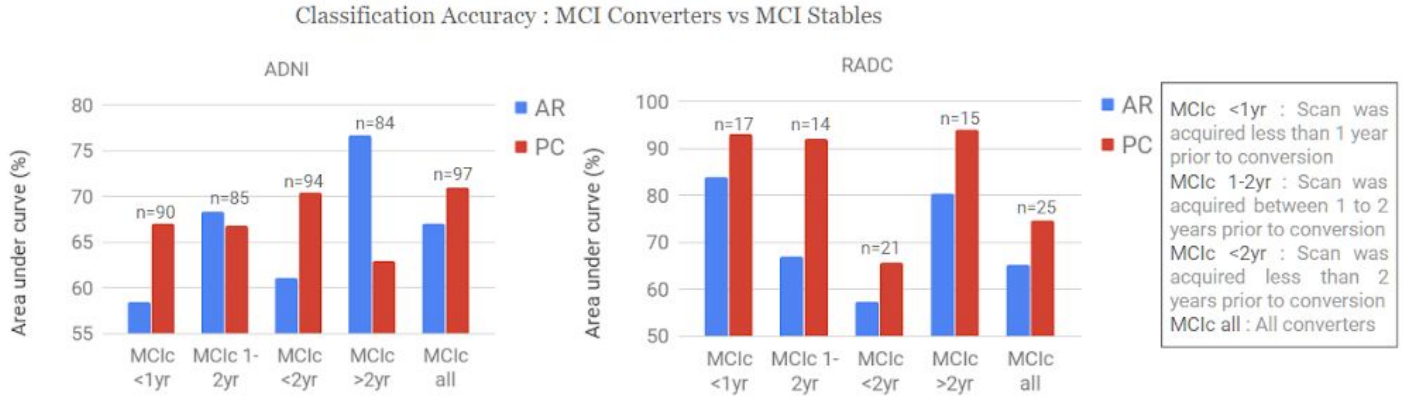
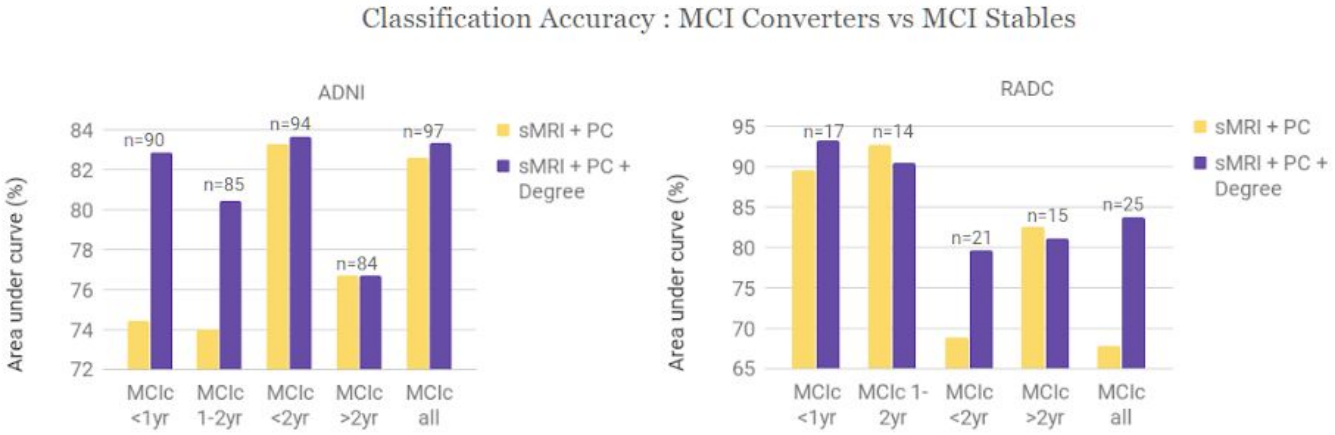


Figure 4


Classification Accuracy : MCI Converters vs MCI Stables
ADNI
Area under curve (%)
84
82
80
78
76
74
72
n=90
n=85
n=94
n=84
n=97
MCIc <1yr
MCIc 1-2yr
MCIc <2yr
MCIc >2yr
MCIc all
sMRI + PC
sMRI + PC + Degree
RADC
Area under curve (%)
95
90
85
80
75
70
65
n=17
n=14
n=21
n=15
n=25
MCIc <1yr
MCIc 1-2yr
MCIc <2yr
MCIc >2yr
MCIc all
sMRI + PC
sMRI + PC + Degree