Resting-State fMRI Multi-Spectral Connectivity Networks for Classification of Mild Cognitive Impairment Patients

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Introduction: Alzheimer's disease (AD) is one of the most prevalent dementia in older adults which is characterized by cognitive and intellectual deficits. It can be serious enough to interfere with daily life and has no effective treatment. With world-wide population aging, this disease has become a serious problem and a huge burden to the healthcare system, especially in developed countries. Mild cognitive impairment (MCI), often a prodromal phase of AD, is frequently considered to be a good target for early diagnosis and therapeutic interventions of AD. However, MCI is difficult to diagnose due to the subtlety of cognitive impairment, especially for individuals who show very mild or no significant cognitive impairment symptoms. It is hence crucial to develop algorithms that can identify subtle diagnostic biomarkers for early detection of MCI, in order to provide possible early treatment and thus delay the transition from MCI to AD. We propose in this abstract an effective network-based multivariate classification algorithm, using multi-spectral connectivity networks derived from resting-state fMRI time series, to accurately identify MCI patients from normal controls.

Materials: The study involved a cohort of 37 participants, 12 MCI patients and 25 socio-demographically matched healthy controls. Demographic and clinical information of the participants are summarized in Tab. 1. For each subject, resting-state functional images in blood oxygenation level dependent (BOLD) contrast were acquired axially parallel to the horizontal plane connecting the anterior and posterior commissures (AC-PC line) using a 3.0 Tesla GE scanner with TE = 32 ms, TR = 2000 ms, acquisition matrix = 64 x 64 and a rectangular FOV of 256 x 256 mm^2, resulting in a voxel dimension of 4 x 4 x 4 mm^3. A total of 34 slices were acquired using a SENSE inverse-spiral pulse sequence in the same plane as the T1-weighted images. All the subjects were told to keep their eyes open and stare at a fixation cross in the middle of the screen during scanning, which lasted for 5 minutes.

Tab. 1. Demographics and clinical information of the participants.

	MCI	Normal
No. of subjects	12 (6 males)	25 (9 males)
Age (mean ± SD)	75.0 ± 8.0	72.9 ± 7.9
Years of education (mean ± SD)	18.0 ± 4.1	15.8 ± 2.4
MMSE (mean ± SD)	28.5 ± 1.5*	29.3 ± 1.1

*One of the patients does not have a MMSE score.

Method: The key of our approach involves an efficient characterization of resting-state fMRI time series via the following approaches: (1) Gray matter-masking to elucidate BOLD signal changes in gray matter by factoring out the contribution of white matter and cerebrospinal fluid (CSF); (2) Multi-spectral characterization to quantify detailed BOLD signal changes by decomposing the mean time series of each region-of-interest (ROI) into smaller frequency sub-bands; and (3) Graph theoretic analysis to characterize topological properties and strengths of brain functional connectivity networks through neurobiologically meaningful and computationally efficient measures. An overview of the proposed MCI classification framework is summarized graphically in Fig. 1. The fMRI images of each subject are first masked with their respective GM masks, and are then further parcellated into 116 regions using the Automated Anatomical Labeling (AAL) template [1]. The mean time series of each region is band-pass filtered ($0.025 \le f \le 0.100$ Hz) before performing the detailed characterization of BOLD signal changes in a multi-spectral fashion. This frequency interval is decomposed into five equally divided, distinct frequency sub-bands, resulting in five functional connectivity networks to account for the topological properties and subtle temporal changes of resting-state brain activities. Functional connectivity that examines interregional correlations in neuronal variability [2] is measured using pair-wise Pearson correlation coefficients between a given pair of ROIs. The proposed method prevents local and subtle temporal changes of BOLD signal to be averaged out as in the convention method where the analysis is performed on the whole signal spectrum. For building a MCI classifier, the local clustering coefficient of each network between each ROI and the remaining ROIs is extracted to serve as a feature. Then, features obtained from all ROIs are ranked according to their Pearson correlation with respect to the clinical labels, and are further sieved to select the most discriminant feature subset using the SVM-RFE algorithm [3]. Finally, support vector machines (SVMs) are trained using the selected feature subset.

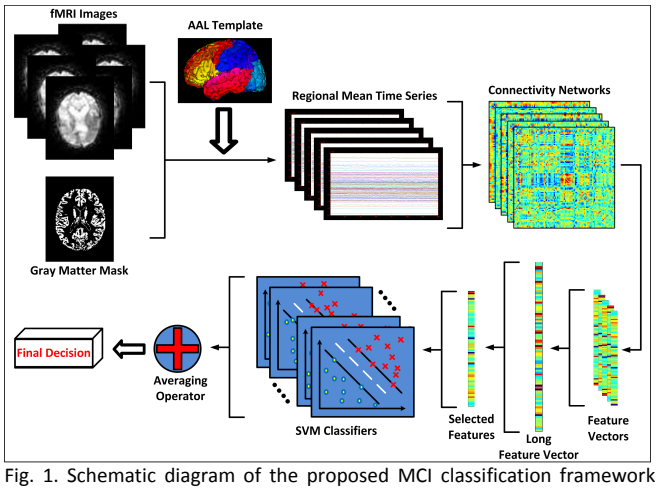

Fig. 1. Schematic diagram of the proposed MCI classification framework based on multi-spectral characterization of the resting-state fMRI time series.

Results: Classification accuracy was evaluated via leave-one-out cross-validation to ensure the generalization of performance. The classification accuracy by the proposed method is 86.5%, which is an increase of at least 18.9% from the conventional methods that using a single frequency band. Fig. 2 shows the receiver operating characteristic (ROC) curves of the proposed method over the conventional methods. Area under ROC curve (AUC) of our proposed method is 0.863, indicating good diagnostic power, especially in view of the relatively limited number of samples available in this study. Judging based on the selected features, parts of the prefrontal cortex, orbitofrontal cortex, temporal lobe, and parietal lobe provided the most discriminant information for classification, in line with results reported in previous studies [4, 5]. Furthermore, our findings demonstrated a relatively asymmetric brain atrophy pattern, i.e., the MCI group showing more left-hemisphere atrophy than the right-hemisphere.

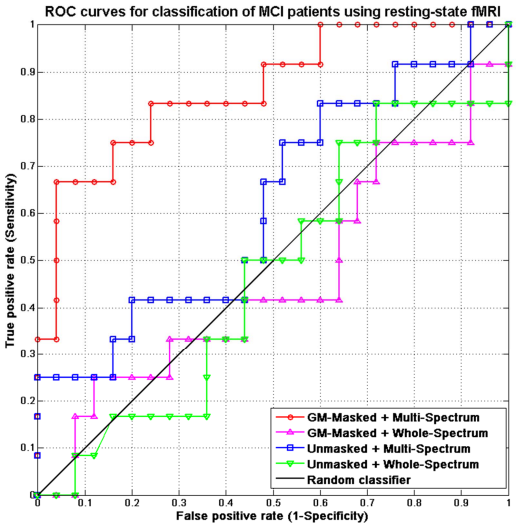

Fig. 2. ROC curves for classification of MCI patients using the resting-state fMRI.

Discussion: A novel high-dimensional pattern classification method, which is based on BOLD signal contrast, has been proposed to distinguish individuals with MCI from normal controls. The proposed technique employs a multi-spectral network characterization of the fMRI regional mean time series to effectively delineate the functional connectivity patterns at a whole brain level. Significant improvements and promising results indicate that the proposed framework can potentially serve as a complementary approach to clinical diagnosis of alteration in brain functions associated with cognitive impairment, especially at the early stages.

References:

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