Learning-Based Estimation of Functional Correlation Tensors in White Matter for Early Diagnosis of Mild Cognitive Impairment

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Abstract. It has been recently demonstrated that the local BOLD signals in resting-state fMRI (rs-fMRI) can be captured for the white matter (WM) by functional correlation tensors (FCTs). FCTs provide similar orientation information as diffusion tensors (DTs), and also functional information concerning brain dynamics. However, FCTs are susceptible to noise due to the low signal-to-noise ratio nature of WM BOLD signals. Here we introduce a robust FCT estimation method to facilitate individualized diagnosis. *First*, we develop a noise-tolerating patch-based approach to measure spatiotemporal correlations of local BOLD signals. *Second*, it is also enhanced by DTs predicted from the input rs-fMRI using a learning-based regression model. We evaluate our trained regressor using the high-resolution HCP dataset. The regressor is then applied to estimate the robust FCTs for subjects in the ADNI2 dataset. We demonstrate for the first time the disease diagnostic value of robust FCTs.

1 Introduction

Resting-state functional magnetic resonance imaging (rs-fMRI) has been widely applied as the non-invasive imaging technique for studying the human brain functional organization architecture. It was originally designed to detect the variations and covariations of the blood-oxygenation-level-dependent (BOLD) signals mostly related to the spontaneous neural activities [1]. The majority of rs-fMRI studies focus on the gray matter (GM), while the rs-fMRI signals in white matter (WM) pathways are treated as noise and artifacts. However, recent studies indicate that WM may also contain meaningful BOLD signals, which carry potentially valuable information complementary to GM-based rs-fMRI studies. Nevertheless, utilizing WM BOLD signals for basic and clinical neuroscience studies is challenging, as WM has blood vasculature that is much less denser, and also the BOLD signal in WM is significantly weaker than in GM [2].

Despite the challenges, attempts have been made to investigate WM fMRI. Early task-based fMRI studies have revealed consistent, reliable task activations in several corpus callosal WM areas linking activated GM structures [3, 4]. Recently, Ding *et al.*

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[5] found WM functional anisotropic patterns using local functional connectivity (FC) using rs-fMRI, which grossly resemble the anisotropic diffusivity reflected by diffusion tensor imaging (DTI) in several major WM structures. They employed functional correlation tensor (FCT) to capture such anisotropy, allowing functional WM tractography based on rs-fMRI data of a small group of healthy subjects. However, it is challenging when applied to other large cohorts, owing to the limited signal-to-noise ratio (SNR) of the WM BOLD signals. Moreover, the FCT estimation method proposed in [5] does not leverage any prior knowledge of DT data that can help overcome the SNR issue. Thus, a robust and reliable FCT estimation technique is important for greater utility of WM anisotropy in neuroscience studies and also as biomarkers for disease diagnosis.

In this paper, we propose a robust FCT estimation technique to address the aforementioned issues. *First*, we develop a novel patch-based correlation measurement strategy to suppress noise. *Second*, we propose to leverage the underlying WM fiber orientation information as prior knowledge when calculating the FCT. This is based on the finding that the dominant direction of the local WM FC anisotropic pattern, extracted from rs-fMRI, is roughly consistent with that of the diffusion tensors (DTs) from DTI [5] in major WM fiber structures. Thus, we can improve FCT estimation by increasing weighting along the dominant directions of DTs. Ideally, the DTs can be obtained from DTI [6]. In the case where DTI is not available, we employ a learning based method to predict the DTs from the rs-fMRI data. This is achieved by using random forest regression with cascaded learning strategy [7] to learn the FC-to-DT mapping [8, 9] with a training dataset containing both rs-fMRI and DTI. Thus, for a testing rs-fMRI, the learned mapping can be applied to predict DTs. Also note that to consider between-tissue difference, the tissue probability features of GM/WM/cerebrospinal fluid (CSF) from T1-weighted MRI are also used to guide the FC-to-DT mapping process.

2 Materials and Methods

Two datasets are employed in this paper: (1) The Human Connectome Project (HCP) [10] dataset and (2) the Alzheimer's Disease Neuroimaging Initiative Phase-II (ADNI2) dataset [11]. The HCP dataset contains high spatial and temporal resolution rs-fMRI, multi-shell diffusion MRI data, and T1-weighted MRI for each subject. It is hence suitable for training the regression model. The ADNI2 dataset focuses on capturing the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD) with both rs-fMRI and T1 MRI. It contains data for early MCI patients, which are used for validation of the improved FCTs in enhancing AD diagnosis.

2.1 Data Preprocessing

HCP Dataset: We randomly select 96 subjects from the dataset, which are all scanned with a customized Siemens Skyra 3T scanner with the same imaging