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Multi-resolution Statistical Analysis of Brain Connectivity Graphs in Preclinical Alzheimer's Disease

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Abstract

There is significant interest, both from basic and applied research perspectives, in understanding how structural/functional connectivity changes can explain behavioral symptoms and predict decline in neurodegenerative diseases such as Alzheimer's disease (AD). The first step in most such analyses is to encode the connectivity information as a graph; then, one may perform statistical inference on various 'global' graph theoretic summary measures (e.g., modularity, graph diameter) and/or at the level of individual edges (or connections). For AD in particular, clear differences in connectivity at the dementia stage of the disease (relative to healthy controls) have been identified. Despite such findings, AD-related connectivity changes in preclinical disease remain poorly characterized. Such preclinical datasets are typically smaller and group differences are weaker. In this paper, we propose a new multi-resolution method for performing statistical analysis of connectivity networks/graphs derived from neuroimaging data. At the high level, the method occupies the middle ground between the two contrasts — that is, to analyze global graph summary measures (global) or connectivity strengths or correlations for individual edges similar to voxel based analysis (local). Instead, our strategy derives a Wavelet representation at each primitive (connection edge) which captures the graph context at multiple resolutions. We provide extensive empirical evidence of how this framework offers improved statistical power by analyzing two distinct AD datasets. Here, connectivity is derived from diffusion tensor magnetic resonance images by running a tractography routine. We first present results showing significant connectivity differences between AD patients and controls that were not evident using standard approaches. Later, we show results on populations that are *not* diagnosed with AD but have a positive family history risk of AD where our algorithm helps in identifying potentially subtle differences between patient groups. We also give an easy to deploy open source implementation of the algorithm for use within studies of connectivity in AD and other neurodegenerative disorders.

Keywords: Brain connectivity, Non-Euclidean wavelets, Multi-resolution analysis, Graph wavelets, Diffusion tensor imaging (DTI), Family history, Alzheimer's disease (AD)

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1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative condition characterized by severe loss of cognitive function and ability to carry out activities of daily living (McKhann et al., 2011).

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