Identifying Alzheimer patients based on the analysis of graphs constructed from resting state fMRI data

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Diagnosing Alzheimer's Disease (AD), especially in the early stage, is costly and burdensome for the patients, since it comprises a battery of psychological tests and an extraction of disease specific biomarkers from the cerebrospinal fluid. A cheaper and more convenient procedure would be a diagnosis based on images obtained through fMRI. Based on previous polymodal studies demonstrating disrupted inter- and intra-cortical connectivity in AD [1], we argue that the functional connectivity of the whole cortex might be a good predictor for the cause of the disease. In resting state fMRI, previous attempts to analyze graph properties of whole brain networks contradict each other [2]. In our opinion there are two general critical points in the methodology of these studies that are likely to contribute to the variability of the results. First, we criticize that the activities of the brain areas (graph nodes) that are used to calculate the functional connectivities (weights of the graph edges) are composed of functionally inhomogeneous signals, as individual brains are often mapped onto a standard atlas brain of known functional coherent areas [2,3]. The second problem consists in converting the resulting weighted graphs into simple graphs, by setting weights above an arbitrary threshold $w_{\min}$ to 1, and those below it to 0 [2] . The drawback here is that there is no validation for an optimal threshold, and information that might be relevant in AD may be lost. In this work we address the first problem by applying an activity-driven, region-growing clustering algorithm derived from image processing [4]. In order to guarantee functionally homogeneous clusters, the threshold for inclusion of a voxel in a region is regulated by a heterogeneity criterion [3]. Applying this algorithm, we end up with undirected weighted graphs with varying numbers of nodes for three sets of data: healthy elderly controls, mild cognitive impairment and Alzheimer's disease. Targeting the second problem, we analyze the dependence of graph theoretic measures (shortest path length, in- and out-degree distribution, clustering coefficient, modularity and minimal spanning tree [5]) on $w_{\min}$. Finally, we investigate the distribution of these measures for each data set to determine candidates for a predictive measure.

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