
Abstract:

Alzheimer's disease (AD) disrupts selectively and progressively (increasing with severity) functional connectivity of intrinsic brain networks (IBNs), most prominent in the default mode network. Given that IBNs' functional connectivity depends on structural connectivity, we hypothesize for our study selective and progressive changes of IBN based structural connectivity in AD. To achieve strong statistical evidence, we introduce a novel statistical method based on the edge frequency distributions of structural connectivity networks. Such non-Gaussian distributions are compared in a multiple testing scheme, combining a flexible nonparametric test statistic with permutation based strong control of the family wise error rate. We assessed 26 healthy elderly, 23 patients with AD-dementia, and 28 patients with mild cognitive impairment (MCI) by resting-state functional MRI, diffusion tensor imaging, and clinical-neuropsychological testing including annual follow-up assessment. After 3 years, 50% of the patients with MCI converted to AD. Tractography of diffusion tensor data identifies structural connectivity networks between regions of IBNs, which are detected by an independent
component analysis of resting state fMRI data. We find that IBNs' structural connectivity is selectively and progressively disrupted with primary changes in the default mode network. Correspondent results are found for IBNs' functional connectivity. In addition, structural connectivity across the nodes of all IBNs separated individual MCI patients converting to AD from non-converters. Conclusively, our study provides a new approach to analyze connectivity networks by their non-Gaussian edge frequency distributions and achieves strong statistical evidence by application of the family wise error rate. Data analysis provides selective and progressive disruptions of IBN's structural connectivity in AD and demonstrates the increased power of our method compared to recent studies.

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