Measuring Brain Activity from Resting-State fMRI independent components in Alzheimer disease

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Background: Alzheimer disease (AD) is a progressive neurodegenerative condition characterized clinically by cognitive dysfunction and memory impairments, and characterized pathologically by the accumulation of amyloid plaques and neurofibrillary tangles. Resting-state (RS)-fMRI measures spontaneous low frequency fluctuations (<0.1 HZ) in the blood oxygen level dependent (BOLD) signal. Previous RS-fMRI studies have found decreased connectivity within the default mode network (DMN) in subjects with early stage AD and mild cognitive impairment (MCI). In this study we define a new biomarker of neuronal activity of the RS-fMRI signal. We hypothesized that this RS-fMRI measure of neuronal activity could be sensitive to the early stage of AD, as it should be proportional to neuronal metabolism and hence glucose consumption. Therefore the purpose of this study was to compare this novel RS-fMRI based biomarker between normal elderly subjects and people with AD in four specific brain regions.

Methods: RS-fMRI data (acquired with a single shot echo planar imaging (EPI) pulse sequence) and 3D T1-weighted anatomical images (gradient echo MP-RAGE sequence) were obtained from the Alzheimer disease neuroimaging initiative (ADNI) database for 15 normal elderly controls (NEC), and 15 subjects with AD. The brain was extracted from the RS-fMRI data and then co-registered to MNI-152 space. An independent component analysis (ICA) method was applied to each dataset (30 components). Each component was matched to a template to identify resting state networks followed by neuronality testing to identify non-artefactual components using a support vector machine classifier. We defined a measure of brain activity in a pixel based on the RS-fMRI temporal signal fluctuation using the summation of the square root of the standard deviation of the RS-fMRI signal integrated across all neuronal components. The brain activity image was registered to the structural T1-weighted image to measure brain activity from manually selected ROIs: Caudate Nucleus, Thalamus, Cerebellum and Posterior Cingulate (PC). Average brain activity was compared between groups using an unpaired t-test. Pooling all groups, we tested whether there was an association between the mini mental state examination (MMSE) cognitive score and brain activity in each ROI.

Results: There was a significant decrease in the brain activity for AD subjects compared to NEC subjects in the cerebellum (p<0.05), and in the thalamus (p<0.05). There was a significant correlation between MMSE score and brain activity in the thalamus (r=0.44, p< 0.05), cerebellum (r= 0.44, p< 0.05), and the PC (r=0.37, p< 0.05).

Conclusion: AD subjects showed a significant decrease in integrated RS-fMRI measured brain activity in the cerebellum and thalamus. The measurement of neuronal activity by RS-fMRI may provide complementary information to existing markers of neurodegeneration in evaluating disease progression and response to therapy.