Introduction

Previous research of the brain structural changes in Alzheimer’s disease (AD) attempted to find the biologically meaningful surrogates of AD from neuroimaging data to improve the AD diagnosis sensitivity and facilitate effective presymptomatic diagnosis and treatment of AD. As the major genetic risk factor for late onset AD, the apolipoprotein E (ApoE) e4 allele is associated with an increased risk of AD where the higher dose (the number of e4 alleles in a person’s ApoE genotype) the more chance to suffer from AD. In this study, we aim to characterize the morphometric changes of AD-related brain regions, e.g. hippocampus and lateral ventricle, with respect to the different ApoE e4 gene dose in cognitively normal elderly.

Methods

1. The hippocampus was segmented from T1 images by using FSL software package[1]. For ventricular segmentation, in this research, we used a novel pipeline[2]. Based on segmented binary volume masks, we extracted hippocampal and ventricular boundaries and constructed triangular surface meshes.

2. Later, the surfaces were further smoothed and a surface fluid registration algorithm was applied to non-linearly register the grid surfaces to a common template.

3. Finally, we extracted the morphometric features[3]. Then the Hotelling’s T2 test was performed on each vertex. We conducted the statistical test for both cross-sectional and longitudinal analysis.

Experiments

115 normal subjects from Arizona APOE cohort were included in this study, including 39 e4 non-carriers (e3/e3), 38 APOE e4 heterozygotes (e3/e4) and 38 APOE e4 homozygotes (e4/e4). We studied the cross sectional data on both baseline and 24-month follow up data. We also studied APOE e4 effects by studying the longitudinal atrophy rates.

In both longitudinal and cross sectional analysis, we observed the group differences in left hippocampus and lateral ventricle after correcting for multiple comparisons. APOE e4 homozygotes plays an important role in altering structural shape in those two regions. What’s more, revealed by the longitudinal studies, patterns of APOE e4 genes effect are quite different. We found that morphological variation of hippocampus appears in heterozygotes and homozygotes but failed to follow the similar trend in lateral ventricle.

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References