Correlation Between APOE e4 Genotype and Hippocampal Atrophy on a Normal Control Cohort

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Introduction

The apolipoprotein E (APOE) e4 genotype is the most prevalent known genetic risk factor for Alzheimer's disease (AD), so APOE genotyping is considered critical in clinical trials of AD [1-3]. Here we examined the longitudinal effect of APOE e4 on hippocampal morphometry with normal control cohort.

Methods

1. All T1-weighted images were segmented with FSL/FIRST.
2. Hippocampal surfaces were reconstructed from the segmentations.
3. Conformal parameterizations of hippocampal surfaces were computed with holomorphic 1-form.
4. Point-to-point correspondences between hippocampal surfaces were computed by the inverse consistent fluid registration method, which was extended to work with general surfaces [4].
5. Surface deformations were measured by new multivariate statistics [5] consisting of radial distance and multivariate tensor-based morphometry (mTBM).
6. Permutation tests were used to perform group comparisons.

Experiments

This dataset includes two scans: patients did the second scans after two years of their first scans. We analyzed second scan dataset consisting of brain MRI scans from adults, aged 56 to 61, including 43 elderly healthy controls (CTL), 38 participants with mild cognitive impairment (MCI) and 27 AD patients. Subjects carrying no ApoE e4 allele (e3/e3) are called ApoE e4 noncarriers. Subjects carrying 1 ApoE e4 allele (e3/e4) are called heterozygous ApoE e4 carriers and subjects carrying 2 ApoE e4 alleles (e4/e4) are called homozygous carriers.

1. ApoE e4 carriers (e3/e4 and e4/e4) versus noncarriers (e3/e3) in the normal control cohort, as shown in Fig.1. Right side: p<0.5489. Left side: p < 0.0086.

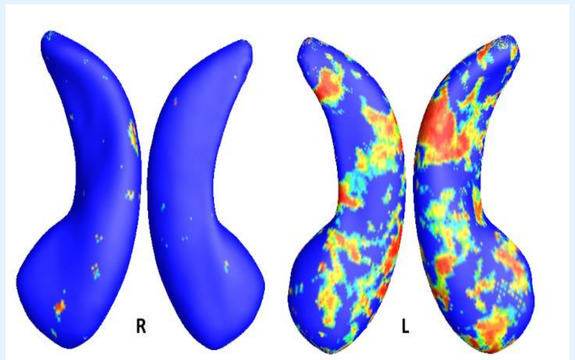

Figure 1. Illustration of local shape differences (p-values) between the ApoE e4 carriers (e3/e4 and e4/e4) and noncarriers (e3/e3) in the normal control cohort.

2. ApoE e4 heterozygous carriers (e3/e4) versus noncarriers (e3/e3) in the normal control cohort, as shown in Fig.2. Right side: p<0.4778. Left side: p < 0.0165.

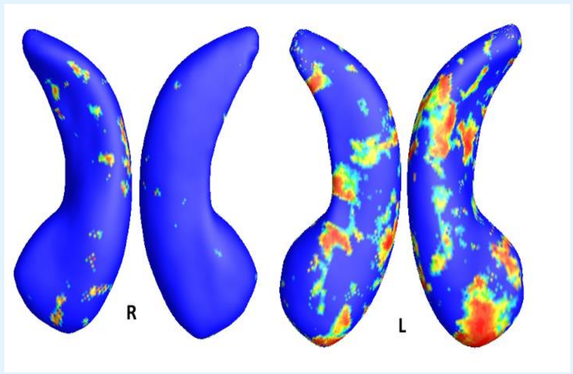

Figure 2. Illustration of local shape differences (p-values) between the ApoE e4 heterozygous carriers (e3/e4) and noncarriers (e3/e3) in the normal control cohort.

3. ApoE e4 homozygous carriers (e4/e4) versus noncarriers (e3/e3) in the normal control cohort, as shown in Fig.3. Right side: p<0.0916. Left side: p < 0.0192.

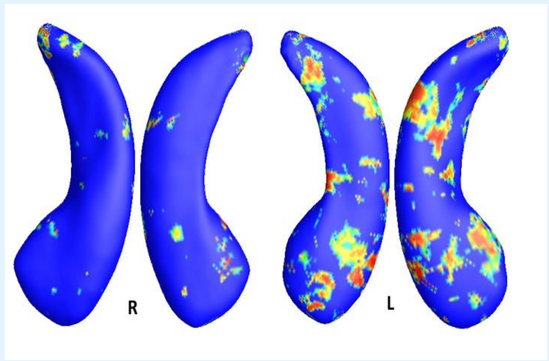

Figure 3. Illustration of local shape differences (p-values) between the ApoE e4 homozygous carriers (e4/e4) and noncarriers (e3/e3) in the normal control cohort.

4. ApoE e4 homozygous carriers (e4/e4) versus heterozygous carriers (e3/e4) in the normal control cohort, as shown in Fig.4. Right side: p<0.2018. Left side: p < 0.0768.

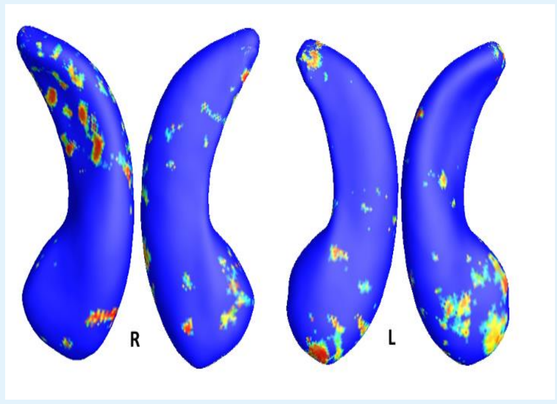

Figure 4. Illustration of local shape differences (p-values) between the ApoE e4 homozygous carriers (e4/e4) and heterozygous carriers (e3/e4) in the normal control cohort.

In our experiments, using Hotelling's T^2 test, firstly we found significant differences between the APOE e4 noncarriers (e3/e3) and carriers (e3/e4 and e4/e4) of the left part of hippocampus: p < 0.0086, but not in right part: p < 0.5489. Secondly, we found significant differences between the APOE e4 noncarriers (e3/e3) and the heterozygous APOE e4 carriers (e3/e4) of the left part of hippocampus: p < 0.0165, but not in right part: p < 0.4778. Thirdly, we also found significant differences between the APOE e4 noncarriers (e3/e3) and the homozygous APOE e4 carriers (e4/e4) of the left part of hippocampus: p < 0.0192, but not in right part: p < 0.0916.

Conclusion

We found significant hippocampal surfaces differences between ApoE e4 carriers and noncarriers, between ApoE e4 noncarriers and the heterozygous APOE e4 carriers, and between ApoE e4 noncarriers and the homozygous APOE e4 carriers.

References

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