Multimodal Investigations in Cognitively Normal Elderly with Different Types of Apolipoprotein E (apoE) Genotype Polymorphism: Brain Volume, Diffusion Anisotropy, and Cerebral Blood Flow MRI Study

M-J. Kim[1], G-H. Jahng[1], S-M. Kim[1], C-W. Ryu[1], S-Y. Lee[2], H-Y. Lee[3], and W-C. Shin[3]

[1]Department of Radiology, Kyung Hee University Hospital-Gangdong, Kyung Hee University, Seoul, Seoul, Korea, Republic of, [2]Department of Biomedical Medical Engineering, Kyung Hee University, [3]Department of Neurology, Kyung Hee University Hospital-Gangdong, Kyung Hee University, Seoul, Seoul, Korea, Republic of

Introduction: The apolipoprotein E (apoE) epsilon 4 allele increases a risk of Alzheimer's disease (AD) [1]. All apoE isoforms inhibit amyloid beta protein aggregation, but apoE4 is less effectively than apoE2 or 3. Numerous studies reported that there was relationship between apoE4 allele load and regionally specific brain cortical atrophy in AD [2-3]. However, there was no study in investigating a multimodal approach in non-demented elderly subjects. Therefore, the objective of this study was to prospectively evaluate brain cortical atrophy using the 3D T1-weighted image (3D T1WI), micro-regional structure changes using diffusion tensor (DT)-MRI, and cerebral perfusion change using arterial spin labeling (ASL)-MRI in cognitively normal (CN) elderly across the apoE genotypes with the voxel-based analysis [3].

Methods and Materials: All subjects were tested K-MMSE (Korean version of mini-mental state examination) (mean score: 27.8) and CDR (Korean version of expanded clinical dementia rating scale), then, the genomic DNA was isolated from blood and the apoE allele was determined. Thirty-seven CN subjects were divided into demented carriers and non-demented carriers of the epsilon 4 allele including E2/E3, E3/E3 and E3/E4. There were no statistically significant differences between the groups for both age and gender ($P>0.05$). All subjects underwent volumetric 3D T1WI with the voxel size of 1 x 1x 1mm, DT-MRI with 32 directions and b-values of 0, 800 sec/mm^2 with the voxel size of 2 x 2 x 2 mm, and pulsed ASL-MRI on a 3 Tesla MRI System (Philips Healthcare, Achieva). Brain volumes from 3DT1WI, fractional anisotropy (FA)/trace from DT-MRI, and cerebral blood flow (CBF) from ASL-MRI were compared among the genotypes by analysis of variance (ANOVA) tests in SPM5. Significant differences were accepted at a threshold of none $p<0.001$ with the extent threshold was 10 voxels.

Results: 3DT1WI: On the apoE4 carriers, gray matter volumes were mainly reduced in the right cingulate gyrus (BA31) and left anterior cingulate on the limbic lobe, the right superior (BA39) and fusiform (BA37) and the left transverse (BA41) temporal gyrus, in the inferior (BA40) and left precuneus (BA7) on the parietal lobe, and in the bilateral frontal lobe (BA6,8, 9).

FA: On the apoE4 carriers, FA values were mainly reduced in the left posterior cingulate gyrus (BA31) on the limbic lobe, in the right medial (BA10) and the left medial (BA31) on the frontal lobe, the left inferior (BA37) temporal gyrus, in the right inferior (BA40) and left precuneus (BA7,23, 31) on the parietal lobe, and the claustrum on the sub-lobar.

Trace: On the apoE4 carriers, trace values were mainly increased the in right posterior cingulate gyrus (BA23,30) on the limbic lobe, in the right inferior (BA9) and medial (BA32) and middle (BA6) and precentral (BA6) and the left middle (BA6) and precentral (BA4,6,43) on the frontal lobe, in the right superior (BA41) and left superior (BA13) temporal gyrus, the left lingual (BA18) on the occipital lobe.

CBF: There were no significant differences for CBF among the apoE4 genotypes.

Fig.1. Results of 3DT1 volume (a) and FA (b) in the condition of (E2/E3 + E3/E3) >E3/E4 with ANOVA tests

a. 3DT1 volume b. FA

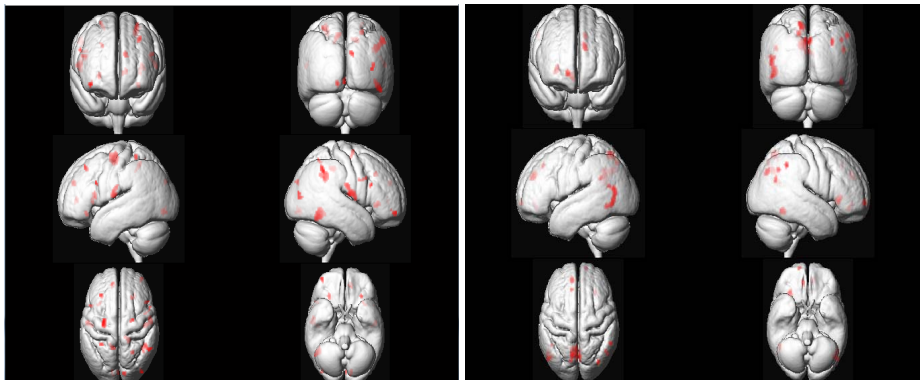
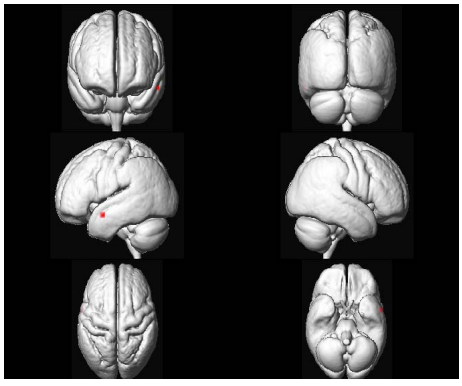


Fig.2. Results of 3DT1 volume in the condition of (E2/E3 + E3/E3) <E3/E4 with the ANOVA test



Discussions and Conclusions: Especially, in the carriers, there were significantly brain atrophy, FA and trace reduction compared with the non-carriers. However, CBF reduction was not shown in this study. The changes of gray matter volume or diffusion alternation may be more sensitive than those of CBF changes. These findings can be applied to clinical studies and research in Alzheimer's disease.

References: 1.van Duijn, C.M., et al., Nat Genet, 1994. **7**(1): p. 74-8. 2.Filippini, N., et al., Neuroimage, 2009. **44**(3): p. 724-8. 3.Ashburner, J. and K.J. Friston, Neuroimage, 2000. **11**(6 Pt 1): p. 805-21.