differences in fractional anisotropy (FA) between groups. **Results:** The neuropsychological assessment did not show an influence of ApoE4 on measures of memory or attention. Structural analyses with VBM and DTI did not reveal any significant differences in gray matter and white matter volume or in FA between groups. In contrast to the neuropsychological and structural findings, there was an effect of APOE-ε4 on functional activation patterns during episodic memory associative encoding. Compared to the homozygote APOE-ε3 group, APOE-ε4 carriers showed reduced task-induced activation in dorsolateral prefrontal cortex bilaterally and in the left parietal cortex. **Conclusions:** These results suggest that the APOE-ε4 genotype affects neuronal function in young adults but not micro- and macrostructure, as detectable with VBM and TBSS. These findings are relevant to the question of potential preclinical disease-driving factors, providing a rationale for further studies assessing functional neuronal aberration as a possible independent risk factor for the development of subsequent neurodegeneration at older age.

O4-03-06 THE ROLE OF APOE GENOTYPE IN EARLY MILD COGNITIVE IMPAIRMENT (E-MCI): PRELIMINARY RESULTS FROM ADNI-2

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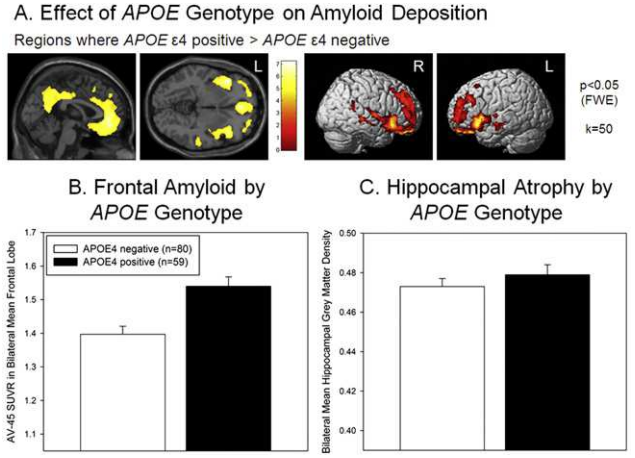
Background: Apolipoprotein E (APOE) genotype is the most significant genetic variant associated with late-onset Alzheimer's disease (AD) susceptibility and pathological features [1]. However, the role of APOE in very early prodromal stages of AD is not well understood. The new ADNI category of early amnestic mild cognitive impairment (E-MCI) provides an opportunity to evaluate the role of APOE-ε4 genotype on psychometric performance, amyloid deposition and neurodegeneration in patients with very mild clinical impairments. **Methods:** Baseline pre-processed AV-45 PET scans [2], 3T MRI scans [3], APOE genotype [4] and other quantitative phenotypes were downloaded from the ADNI website. Only participants categorized as E-MCI (n = 139) at baseline from ADNI-GO/2 were included. MRI scans were processed using VBM, as previously described [5]. AV-45 scans were co-registered to the concurrent MRI and normalized to MNI space using parameters generated from MRI segmentation. Differences between APOE-ε4 allele positive and negative participants in AV-45 standardized uptake on a voxel-wise basis were assessed using a two-sample t-test using SPM8. Region of interest (ROI) data was extracted from MRI and AV-45 scans using MarsBaR. Neuropsychological performance, cognitive complaints, and ROI data were compared between ε4 positive and negative participants using independent-samples t-tests (SPSS 19.0). **Results:** Approximately 42% of the E-MCI participants (n = 139) were APOE-ε4 positive (n = 59; 2 ε2ε4, 48 ε3ε4, 9 ε4ε4; Table 1). The ε4 positive E-MCI group showed lower performance on memory and global cognitive measures, but a trend toward fewer cognitive complaints, than APOE-ε4 negative participants (n = 80; 9 ε2ε3, 71 ε3ε3). On AV-45 PET, ε4 was associated with increased amyloid deposition, particularly in frontal and medial parietal lobar regions (Figure 1A; $P<0.05$ FWE, k=50). Similarly, ROI analyses indicated greater amyloid deposition in the frontal lobes of ε4 positive E-MCI participants (Figure 1B; $P<0.001$). By contrast, the presence of ε4 was not associated with greater hippocampal atrophy in this initial sample of E-MCI participants (Figure 1C). **Conclusions:** In E-MCI, APOE-ε4 genotypes are associated with greater amyloid deposition and cognitive changes, but not hippocampal neurodegeneration. References: [1] Corder (1993); [2] Jagust (2010); [3] Jack (2010); [4] Saykin (2010); [5] Risacher (2009).

Table 1
Demographics and neuropsychological test performance (Mean (SE))

	ε4 negative	ε4 positive	*P*-value
n	80	59	
Age (years)	71.97 (0.86)	70.81 (1.00)	ns
Gender (M, F)	39, 41	37, 22	ns
Education (years)	15.96 (0.30)	15.73 (0.35)	ns
Handedness (R, L)	71, 9	55, 4	ns
CDR-SB[a]	1.11 (0.08)	1.38 (0.09)	0.022
ADAS-Cog Total[a, b]	10.95 (0.53)	13.79 (0.61)	0.0007
RAVLT Total[a]	41.76 (1.03)	37.54 (1.20)	0.009
RAVLT Delayed Recall[a]	6.97 (0.42)	5.23 (0.49)	0.008
Trail-Making B-A[a, c]	53.90 (4.86)	69.38 (5.65)	0.042
ECog Patient Total	20.41 (1.08)	17.88 (1.25)	ns
ECog Informant Total	16.03 (1.11)	14.80 (1.29)	ns
ECog-Mem Patient Total	5.95 (0.23)	5.83 (0.27)	ns
ECog-Mem Informant Total	4.94 (0.28)	4.78 (0.33)	ns
ECog-Lang Patient Total	5.23 (0.30)	4.46 (0.35)	ns
ECog-Lang Informant Total	3.36 (0.33)	3.27 (0.38)	ns
ECog-VS Patient Total	2.58 (0.27)	1.85 (0.32)	ns
ECog-VS Informant Total	1.95 (0.24)	1.39 (0.28)	ns
ECog-Exec Patient Total	6.66 (0.48)	5.75 (0.55)	ns
ECog-Exec Informant Total	5.78 (0.50)	5.36 (0.58)	ns

[a]Adjusted for age, gender, education, and handedness
[b]Missing data for 1 ε4 negative participant
[c]Missing data for 3 participants (2 ε4 negative, 1 ε4 positive)



ORAL SESSIONS: O4-04 THE CLINICAL SPECTRUM OF DEMENTIA 2

O4-04-01 DIFFERENTIATING CLINICOPATHOLOGIC AND GENETIC ASPECTS OF HIPPOCAMPAL SCLEROSIS IN ALZHEIMER'S DISEASE FROM LIMBIC PREDOMINANT ALZHEIMER'S DISEASE AND "PURE" HIPPOCAMPAL SCLEROSIS

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Background: Hippocampal sclerosis (HpScl) is defined by the disproportionate neuronal loss compared to neurofibrillary tangle (NFT) accumulation in the hippocampus. "Pure" HpScl is uncommon, but is