ApoE and age at onset in AD: a cortical pattern matching study

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Objective. ApoE ε4 is a risk factor for AD. Aim of this study was to identify patterns of cortical atrophy in ApoE ε4 carriers and non-carriers in early (EO, age at onset$\leq$65) and late-onset AD (LO, age at onset>65) using the cortical pattern matching (CPM) algorithms [1,2].

Methods. High resolution 3D MR images of 14 EO and 14 LO (age 62$\pm$5 and 78$\pm$6) similar for clinical severity (MMSE of 20$\pm$4 in both groups) and for ApoE ε4 genotypic frequencies (ε4-/ε4+: 7/7 in both groups), and of 30 age-matched controls, divided into young (YC, n=15) and elderly (EC, n=15) were processed. EO and LO were separated into ε4 carriers (EOε4+ and LOε4+) and non-carriers (EOε4- and LOε4-). CPM was used to identify regions where the cortical gray matter (GM) was different between AD and age-matched controls. 40 sulci were manually outlined and used to match anatomy across subjects by mean of elastic warping. Cortical GM was measured as the local proportion of GM at thousand of homologous cortical surface points in each subject [1]. P-maps were created comparing with a T-test EOε4+ *vs* YC, EOε4- *vs* YC, LOε4+ *vs* EC, and LOε4- *vs* EC. Maps of the average GM percentage reduction were created for each AD subgroup computing at each cortical point the ratio between the mean GM of the AD group and of the pertinent control group. Lobar volumes were computed for each subject by applying lobar masks to the anatomically matched images and pooling GM values over homologous cortical lobar locations.

Results. On the left, atrophy was located mainly in the temporal lobe in EOε4+ as compared to YC, and in the parietal and frontal lobes in EOε4- (*p*=.0001 for both comparisons, permutation test [2]). On the right patterns of atrophy were similar although with greater parieto-occipital involvement in non-carriers (*p*<.0002). LOε4+ showed significant atrophy in the temporal lobes bilaterally (*p*<.0003 for left and right hemispheres). LOε4- were affected mainly in the right temporal and frontal lobe (*p*=.0006) while the left temporal lobe was relatively spared (*p*=.0045).

In EO GM loss was of 25% or more in large neocortical areas. On the left side, EOε4+ and EOε4- loss was 19 *vs* 16% in the temporal, 20 *vs* 25% in the parietal, 13 *vs* 18% in the frontal lobe. On the right side loss was 25 *vs* 20% in the parieto-occipital lobe. GM loss in LO was milder (between 15-20%) and reached 25% in restricted areas of the temporal lobe. LOε4+ and LOε4- loss in the left and right temporal lobes was 15 *vs* 10% and 17 *vs* 13% respectively. LOε4- showed greater involvement than LOε4+ in the right frontal lobe (11 *vs* 7%).

Conclusions. This study suggests a region-specific effect of the ε4 allele in both EO and LO, showing greater involvement of the temporal lobes in ε4 carriers, of the right frontal lobe in LO non-carriers, and of the posterior areas (mainly on the right) in EO non-carriers.

References & Acknowledgements:

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