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The relation between APOE genotype and cerebral microbleeds in cognitively unimpaired middle- and old-aged individuals

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Positive associations between cerebral microbleeds (CMBs) and APOE-ε4 (apolipoprotein E) genotype have been reported in Alzheimer's disease, but show conflicting results. We investigated the effect of APOE genotype on CMBs in a cohort of cognitively unimpaired middle- and old-aged individuals enriched for APOE-ε4 genotype. Participants from ALFA (Alzheimer and Families) cohort were included and their magnetic resonance scans assessed (n = 564, 50% APOE-ε4 carriers). Quantitative magnetic resonance analyses included visual ratings, atrophy measures, and white matter hyperintensity (WMH) segmentations. The prevalence of CMBs was 17%, increased with age ($p < 0.05$), and followed an increasing trend paralleling APOE-ε4 dose. The number of CMBs was significantly higher in APOE-ε4 homozygotes compared to heterozygotes and non-carriers ($p < 0.05$). This association was driven by lobar CMBs ($p < 0.05$). CMBs co-localized with WMH ($p < 0.05$). No associations between CMBs and APOE-ε2, gray matter volumes, and cognitive performance were found. Our results suggest that cerebral vessels of APOE-ε4 homozygous are more fragile, especially in lobar locations. Co-occurrence of CMBs and WMH suggests that such changes localize in areas with increased vascular vulnerability.

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