Association of the tau haplotype H2 with age at onset and functional alterations of glucose utilization in frontotemporal dementia.

OBJECTIVE: The microtubule-associated protein tau gene (MAPT) contains two extended haplotypes, H1 and H2, which have been linked with sporadic tauopathies. However, there is little evidence as to how these haplotypes may influence the clinical features of the disease. The aim of this study was to investigate the MAPT haplotypes in relation to risk for, and functional alterations of glucose metabolism in, patients with frontotemporal dementia (FTD).

METHOD: The authors investigated MAPT haplotypes in 142 individuals with FTD and 292 comparison subjects. Additionally, in a subset of 41 individuals with FTD and 16 comparison subjects, the authors undertook functional [18F]fluorodeoxyglucose positron emission tomography (PET) imaging.

RESULTS: MAPT haplotype distribution did not differ significantly between individuals with FTD and comparison subjects. However, the H2 haplotype was clinically associated with an earlier age at onset of FTD, which presented in a dose-dependent manner. Correspondingly, PET analysis revealed functional differences in glucose utilization patterns between MAPT haplotypes, with H2 carriers having a more pronounced hypometabolism in frontal brain areas than H1 carriers, which could not be accounted for by differences in duration of illness.
CONCLUSIONS: While the extended MAPT H1 and H2 haplotypes do not appear to confer risk for disease development, the H2 haplotype appears to modify age at onset and functionally shows a more severe decline of glucose utilization in frontal brain areas.