Microtubule associated protein tau (*MAPT*) H1 subhaplotypes and their associations with clinical features in Parkinson`s disease

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Aim: To assess associations of microtubule associated protein tau (*MAPT*) H1 subhaplotypes with clinical features in patients with Parkinson`s disease (PD). Methods: We included 856 Caucasian patients with PD in this study. All patients were seen at the Mayo Clinic Florida and had no known mutation causing PD. We retrospectively analyzed charts. The following clinical and demographic information was collected: age at PD onset, sex, disease duration, rate of disease progression, survival after PD onset, levodopa use, levodopa response, bradykinesia, rigidity, postural instability, resting tremor, postural tremor, dementia, dystonia, dyskinesia, autonomic dysfunction (gastrointestinal and urogenital), impulse control disorder, (pseudo-)hallucinations, depression, orthostatic hypotension, REM sleep behavior disorder (RBD), restless legs syndrome (RLS), and PD subtype (akinetic-rigid, tremor-dominant, gait difficulty, or mixed). Genetic analyses: Five *MAPT* variants tagging H1 subhaplotypes (rs1467967, rs242557, rs3785883, rs2471738, rs7521) were genotyped using TaqMan SNP genotyping assays (QuantStudio 7 Flex Real-Time PCR system, Applied Biosystems). Genotype call rates were 100% for each variant. Associations were calculated for all *MAPT* H1 subhaplotypes seen in 1% of patients. Results: Significant associations (P 0.0021) were observed between the H1b subhaplotype and a higher risk of orthostatic hypotension (OR=1.72); H1j and a lower risk of resting tremor (OR=0.14) and a higher risk of RBD (OR=3.21); H1r and a lower risk of bradykinesia (OR=0.14); H1v and a higher risk of RLS (OR=5.49). Additionally, suggestive associations (P 0.01) were noted for H1b (dyskinesia), H1f (dystonia and hallucinations), and H1v (depression). Conclusion: Several *MAPT* H1 subhaplotypes (H1b, H1j, H1r, and H1v) were significantly associated with specific clinical features seen in PD (orthostatic hypotension, resting tremor, RBD, bradykinesia, and RLS).