Deletion of murine Tau gene increases Tau aggregation in a human mutant Tau transgenic mouse model

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Neurofibrillary tangles (NFT) and amyloid plaques are the neuropathological hallmarks of Alzheimer Disease (AD). NFTs are composed of abnormally phosphorylated and aggregated tau proteins that form Paired Helical Filament-tau (PHF-tau). We have previously reported a tau transgenic mouse model (Tg30tau) overexpressing human 4R1N double mutant tau (P301S and G272V) and that develops AD-like NFTs in an age-dependent manner. Since murine tau might interfere with the toxic effects of human mutant tau, we set out to analyze the phenotype of our Tg30tau model in the absence of endogenous murine tau with the aim to reproduce more faithfully a model of human tauopathy. By crossing the Tg30tau line with tau Knock Out (TauKO) mice, we have obtained a new mouse line called Tg30xTauKO that expresses only exogenous human double mutant 4R1N tau. Whereas Tg30xTauKO mice express less tau proteins compared to Tg30tau, they exhibit decreased survival, more pronounced motor deficits, augmented Sarkosyl insoluble tau and increased number of Gallyas positive NFTs in the absence of neuronal loss in hippocampus. Taken together, exclusion of murine tau caused accelerated tau aggregation and a more severe phenotype during aging of this mutant tau transgenic model.