Neurofibrillary degeneration (NFD) results from the aggregation of abnormally phosphorylated Tau proteins into filaments. NFD severity is correlated to cognitive impairment and often considered as neuronal death.

Using our Thy-Tau22 transgenic Tau model where Tau pathology is mainly focused in the hippocampal formation, we analyzed the kinetics of Tau phosphorylation, NFD and neuronal death in parallel to electrophysiological and behavioural parameters. In Thy-Tau22 mice, from 3 to 9 months old, Tau phosphorylation and NFD are early events following by cognitive impairment as identified by Morris water maze, T- and Y mazes and LTD abnormalities. In the hippocampus, neuronal death is not observed before 12-15 months. However, other brain regions such as median septum display neuronal loss (i.e. loss of cholinergic markers).

It is possible to decrease this Tau pathology and prevent cognitive deficits in these mice by therapeutic approaches including voluntary physical exercise and immunotherapy.

Altogether, these data suggest that NFD is a transient state before neuronal death and that therapeutic interventions are possible at that stage.

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