Disrupted cholinergic transmission in mice with Alzheimer's disease-like tauopathy (AD) but not in mice with frontotemporal lobar degeneration-like tauopathy (FTLD).

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An important enzyme associated with the brain cholinergic system is acetylcholinesterase (AChE, E.C.3.1.1.7). The AChE staining in cortex and hippocampus coincides with much of the cholinergic innervation originating from the basal forebrain. AChE activity in cortex and hippocampus was evaluated in two tauopathic mouse models: Line 1 (L1), with mild Alzheimer's disease-like tauopathy and Line 66 (L66) with severe frontotemporal lobar degeneration-like tauopathy (FTLD) relative to age-matched wild-type NMRI mice. Analysis was performed in 3 and 12.5-month-old mice to assess cortical and hippocampal cholinergic innervation originating from the basal forebrain. For AChE histochemistry, brain sections were stained with the method of Geneser-Jansen and Blackstad (1971). Computer image analysis system (NIS-Elements BR 4.30.00 Software) was used for quantitation of the intensity of staining (relative optical density – ROD) measured in the arbitrarily defined areas (75,000+/-500 mm^2) across the entire depth of cortical and hippocampal layers.
In cortex and hippocampus intensity of AChE staining was significantly lower in L1 in comparison with L66 and NMRI lines of both age groups. Additionally, in L1 mice a characteristic bilaminar pattern of laminar distribution of AChE-rich fibres in layers II and V was not clearly visible. AChE histochemical staining data suggest that there is an impairment of the basal forebrain cholinergic projection in L1 mice what corresponds with observed lower intensity of ChAT and p75 immunohistochemical staining in basal forebrain neurons of these mice. Tauopathy of AD-type seems to be associated with destruction and disorganization of the cholinergic projections extending to both cortex and hippocampus.