BEHAVIORAL DEFICITS CORRELATE WITH INTRACELLULAR AB PATHOLOGY IN A NEW
WILDTYPE APP MOUSE MODEL

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Introduction: Mice overexpressing wildtype human APP where one of the first transgenic AD-models, generated to study Ab sequestration. However they hardly developed AD-pathology and had no behavioral deficits. Since intracellular Aß species, suspected to be pivotal for the loss of synapses and neurons, moved in the focus of research, wildtype APP mice are again of interest, in particular because they represent sporadic AD.

Aim: Our goal was to characterize a new mouse model overexpressing the human APP695 isoform under control of the neuron specific Thy-1 promoter. This study concentrates on age-dependent alterations like memory deficits, intracellular amyloid load and inflammation.

Methods: wt hAPP695 Tg mice, 6, 9 and 12 months of age, were investigated in terms of behavior in the Morris Water Maze.

Aß_{1-40}, Aß_{1-42} and APP-levels were determined by Western blot and ELISA in one brain hemisphere. The other hemisphere was systematically screened for intracellular amyloid load and inflammatory responses by immunohistochemistry.

Results: In accordance with past results, the new APPwt mice exhibit behavioural deficits as learning and memory impairments in the MWM. Biochemically, increased amounts of Aß_{1-40} and Aß_{1-42} were detected throughout the brain, especially in the cortex and the hippocampus.

Interestingly, histological analyses point to high levels of intracellular hAPP expression, - but no plaques - in cortex, hippocampus and thalamus. Furthermore, no inflammatory responses were observed.

Conclusions: These human APPwt mice could be a useful tool for efficacy studies investigating AD drug candidates and reflect a unique model to investigate effects on a single target - soluble intracellular Aß.