AGE-DEPENDENT CHANGES IN SPINE DENSITY AND MORPHOLOGY IN A TRANSGENIC MOUSE MODEL OF ALZHEIMER'S DISEASE

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Introduction: Previous studies have shown that overexpression of APP or mutations thereof lead to Aβ production. These peptides are important for initiating the pathogenesis of Alzheimer's disease.

Aim: Our aim was to analyse the contribution of Aβ in possible changes in spine density and spine morphology at different ages of APP$_{SDL}$ transgenic mice.

Methods: To visualize dendritic spines and evaluate the spine number, Golgi staining was performed on coronal sections of APP$_{SDL}$ transgenic and control mice. To obtain spine morphology data mice were crossed with the Thy1-GFP M line, which expresses EGFP in few neurons. Analyses were performed on confocal laserscanning micrographs using a computer-assisted approach. The amount of Aβ in the brains of different age groups was determined by ELISA.

Results: We report a lower spine density in APP$_{SDL}$ mice vs controls observed in Golgi-stained brain slices as well as in slices from Thy1-GFP M mice by about 18-22% at all ages. Algorithm-based analyses revealed a slight decrease in mean spine lengths with age in hippocampal subregions of APP$_{SDL}$ transgenic mice. Spine volume strongly decreased with age with no consistent difference between APP$_{SDL}$ transgenic and control mice and a shift from mushroom to thin spines could be observed. Amyloid plaques developed at the age of 21 months.

Conclusions: Our data indicate that spine densities are reduced in hippocampal subregions of APP$_{SDL}$ transgenic mice and suggest the development of morphological changes of the remaining spines in a transgenic mouse model of AD.