FUNCTIONAL AND STRUCTURAL CHANGES TO THE CA1 NETWORK IN B-AMYLOID PATHOLOGY

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Introduction: Although much is known of the molecular pathogenesis of Alzheimer's disease (AD), much less is understood about how β-amyloid (Aβ) pathology affects cognition. An increased prevalence of seizures and abnormal EEG in AD, and a dissociation between neuropathological markers and cognitive function, all argue for a functional disturbance in the cortical network.

Aims: We have asked if we can identify functional and structural changes in the specific components of the hippocampal network in Aβ pathology, focussing GABAergic inhibition.

Methods: We have used a combination of electrophysiology and histology in APP/PS1 transgenic mice. These experiments will be complemented with behavioural testing and Ca$^{2+}$ imaging.

Results: We have compared the number of interneurons in different layers of hippocampal CA1 by staining for GAD67 and found a significant reduction in stratum radiatum interneurons in APP/PS1 mice (p< 0.05). We compared pyramidal cell somatically-recorded IPSPs in APP/PS1 and wild-type mice. We found no differences in miniature and spontaneous inhibitory events. However when stimulating with a paired-pulse protocol, significant differences in short term plasticity were seen at long interstimulus intervals (800ms, PPR(WT)=1.3±0.1, PPR(APP/PS1)=0.6±0.1, p< 0.001).

Conclusions: These results are in line with a selective change to specific sub-components of the CA1 network in Aβ pathology. Such a change could contribute to the computational deficits both in Aβ-overexpressing mice and in AD.