

POSTER PRESENTATION

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Investigating the effects of beta-amyloid on hippocampal signalling in Alzheimer's disease

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Alzheimer's disease (AD) is the leading form of dementia and is characterised clinically by cognitive decline and impairments to memory function. The protein amyloid- β ($A\beta$) is thought to be a key mediator of this neurodegeneration [1]. Mounting evidence suggests that soluble $A\beta_{1-42}$ oligomers ($oA\beta_{1-42}$) cause the impairments observed in early AD, which includes synapse loss and synaptic dysfunction. For example, $oA\beta_{1-42}$ inhibits hippocampal long-term potentiation (LTP) [2], an important synaptic plasticity thought to underlie memory formation in the brain [3]. We have recently found that postsynaptic infusion of $oA\beta$ into hippocampal neurons causes an increase in synaptic conductance attributed to changes in the excitatory glutamate receptor profile at the synapse. The relevance of this to synaptic dysregulation and consequence on hippocampal signalling is yet to be determined.

Here we take a computational approach to investigate how $oA\beta_{1-42}$ dysregulates signalling within the hippocampus. We first develop a biophysical model of synaptic potentiation in a CA1 neuron, based on a simple kinetic synapse model and Hodgkin-Huxley formalism [4], which successfully reproduces the conductance increase observed in single-cell patch clamp experiments following $oA\beta$ application. We then extend this to investigate how this affects signalling across a small network of CA1 neurons, analysing the importance of connectivity strength and number of affected neurons to the overall dynamics of the system. Recent studies have suggested that there are two distinct types of CA1 neurons with different electrophysiological properties [5]. Therefore we also consider the impact a heterogeneous population would have on signalling across the network.

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