

# Mechanisms underlying the tau protein-mediated effects of amyloid beta on synaptic plasticity

<https://www.neurodegenerationresearch.eu/survey/mechanisms-underlying-the-tau-protein-mediated-effects-of-amyloid-beta-on-synaptic-plasticity/>

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### Country

United Kingdom

## Title of project or programme

Mechanisms underlying the tau protein-mediated effects of amyloid beta on synaptic plasticity

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3

## Keywords

### Research Abstract

Amyloid beta (Abeta) and microtubule associated protein tau (MAPT or tau) are both implicated in memory impairment in mild cognitive impairment (MCI) and early Alzheimer's disease (AD), but whether and how they interact is unknown. We have recently shown (Shipton et al 2011 Journal of Neuroscience) that tau protein is required for Abeta-induced impairment of hippocampal long-term potentiation (LTP), a widely accepted cellular model of memory. Moreover, we showed that Abeta increases tau phosphorylation and that a highly-specific

inhibitor of the tau kinase, glycogen synthase kinase 3 (GSK3), blocks the increased tau phosphorylation induced by Abeta and prevents Abeta-induced impairment of LTP in wild-type mice. In this current proposal we investigate in detail the mechanisms whereby tau and Abeta interact to affect the electrophysiological properties of neurons in mice, which we then extend to human neurons in vitro. We will investigate in transgenic mice the interaction between Abeta and wild-type MAPT or disease-associated MAPT variants. We will extend the findings to human glutamatergic cortical projection neurons in culture by using zinc finger nuclease technology to generate MAPT<sup>-/-</sup> human neurons which we will then use to express the wild-type or mutant variants of tau protein to bring the work back from mouse to human neurons. Our work will have important implications for our understanding of how Abeta peptide and tau protein interact in the very earliest changes in synaptic dysfunction. Preventing the interaction between Ab and tau could prove to be a promising therapy for MCI and early AD.

**Further information available at:**

**Types:**

Investments < €500k

**Member States:**

United Kingdom

**Diseases:**

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**Years:**

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**Database Categories:**

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**Database Tags:**

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