ROLE OF GLUTAMATE RECEPTORS IN Aß-MEDIATED FACILITATION OF LONG-TERM DEPRESSION OF SYNAPTIC TRANSMISSION IN VIVO

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Introduction: Amyloid ß-protein (Aß) oligomers can potently disrupt synaptic plasticity including long-term potentiation (LTP) and long-term depression (LTD). Recently, we found that GluN2B subunit-containing NMDA receptor antagonists prevent Aß-mediated inhibition of hippocampal LTP in vivo (Hu et al. PNAS 2009). However, the mechanisms of the effects of Aß on LTD in vivo remain unclear.

Aims: Here we studied the effects of soluble synthetic Aß1-42 on LTD.

Methods: LTD was induced by low frequency stimulation (LFS), in the CA1 area of anaesthetized adult male Wistar rats.

Results: We found that:

(i) application of 900 pulses at 1Hz at high intensity induced a robust and large LTD, whereas application of 300 pulses at 1Hz induced relatively small LTD;

(ii) acute intracerebroventricular (i.c.v.) injection of soluble Aß42, at a dose which did not affect baseline synaptic transmission, markedly facilitated LTD induced by 300 pulses but not 900 pulses;

(iii) co-systemic injection of the selective GluN2B antagonist Ro 25-6981 (6mg/kg, i.p.) and the selective mGluR5 antagonist MTEP (8mg/kg, i.p.) completely prevented Aß-mediated facilitation of LTD, whereas administration of either Ro 25-6981 or MTEP alone appeared less effective.

Conclusions: These data support our previous finding that Aß can facilitate hippocampal LTD in vivo (Kim et al. J Neurosci 2001) and suggest that both GluN2B-containing NMDARs and mGluR5 are involved in this Aß-mediated disruption.

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