Beta Amyloid mediated blockade of Long Term Potentiation in the CA1 region of mouse hippocampal slices is partially attenuated by Cannabidiol

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The major non-psychoactive plant derived constituent of marijuana, Cannabidiol (CBD), has become a therapeutic target in a number of disease processes including Alzheimer’s disease (AD). CBD has been shown to be an anti-inflammatory agent that can protect against the neurotoxic effects of beta amyloid peptide (Aβ) via antioxidant actions. The activity of GSK-3β can also be modulated by CBD (Esposito et al., 2006). This serine-threonine kinase is known to play a critical role in the expression of LTP (Peineau et al., 2007). Aβ, found in high concentration in AD brain is known to attenuate hippocampal LTP a cellular model of learning. The effects of acute or chronic CBD on synaptic plasticity including hippocampal long-term potentiation (LTP), however have not yet been investigated. In addition the potential neuro-protective effects of CBD against Aβ mediated attenuation of LTP has yet to be determined.

Here, we investigated the effect of acute application of 10µM CBD on the expression of LTP in the CA1 region of hippocampal slices from C57black 6 mice; Attenuation of LTP in the presence of Aβ in the form of Amyloid derived diffusible ligands (500 nM) was also determined. The potential neuroprotective effect of pre-treatment with CBD prior to application of Aβ was also investigated on LTP.

C57/Black6 mice (6-12 weeks) were used to prepare hippocampal slices (400µm). LTP was induced via high frequency stimulation (HFS) consisting of two trains of stimuli at 100Hz for 1s, with an inter-train interval of 30 seconds. Slices were pretreated with CBD or ADDLs alone for 30 minutes or with CBD for 30 minutes followed by a 30 minute application of ADDLs prior to induction of LTP.

Pretreatment with CBD alone had no effect on the expression of LTP measured at 60 minutes following high frequency stimulation (134.7±6.9%, n=5) compared to control LTP (150.9±6.3%, n=10). Application of Aβ for 30 minutes prior to HFS resulted in a significant depression in fEPSP amplitude and an inhibition of LTP compared to control (93.6±10.7%, n=4), P<0.001. Pretreatment with CBD for 30 minutes prior to ADDL application caused in a partial attenuation of Aβ –mediated inhibition of LTP (122.6±7.2%, n=6), P<0.05.

Future experiments will investigate the effect of chronic CBD treatment on LTP in aged wild type and APP/swePS1dE9 mice.

References:

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