

**P047** Peroxisome Proliferator Activated Receptor Agonists Modulate Synaptic Transmission and beta Amyloid (A $\beta$  1-40) Mediated Impairment of Long-Term Potentiation in the Rat CA1 *in vitro*.

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We have investigated the effects of PPAR $\alpha$  and  $\gamma$  agonists on synaptic transmission and beta amyloid (A $\beta$  [1-40])-mediated impairment of LTP. Field excitatory postsynaptic potentials (EPSPs) were recorded in area CA1 from adult rat hippocampal slices (350  $\mu$ M). LTP was induced by high frequency stimulation (HFS; 10 trains of 10 pulses at 200 Hz), and control LTP was recorded 60 min post-HFS. A $\beta$  [1-40] (200 nM), applied 60 min pre-HFS, significantly reduced LTP. The PPAR $\gamma$  agonist, troglitazone, perfused for 30 min, did not alter LTP compared to control. When slices were perfused with troglitazone for 30 min and A $\beta$  [1-40] for a further 60 min, the depression in LTP was significantly attenuated when compared with A $\beta$  [1-40] alone. The PPAR $\alpha$  agonists, clofibrate and WY-14,643 (20  $\mu$ M), both caused a significant increase in baseline synaptic transmission 60 min following application. However, neither agent significantly altered LTP. When slices were perfused with clofibrate for 30 min and A $\beta$  [1-40] for a further 60 min, the depression in LTP was significantly attenuated when compared with A $\beta$  [1-40] alone. This demonstrates that prior treatment with PPAR agonists reduces the A $\beta$ -mediated impairment of LTP.