

**P056** mGluR5 inhibition reverses the inhibitory effect of tumour necrosis factor- $\alpha$  on long-term potentiation  
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Pro-inflammatory cytokines are known to be elevated in several neuropathological diseases that are associated with learning and memory. We have previously demonstrated in our laboratories that the inhibition of long-term potentiation (LTP) in the dentate gyrus of the rat hippocampus, by tumour necrosis factor (TNF- $\alpha$ ), represents a biphasic response, an early phase dependent on p38 mitogen activated protein kinase (MAPK) activation and a later phase possible dependent on protein synthesis. We have investigated the effect of the specific mGluR5 antagonist, MPEP, on the inhibitory effect of TNF- $\alpha$  on LTP in the rat dentate gyrus *in vitro*. Recordings of field excitatory postsynaptic potentials (EPSPs) were made from the medial perforant path using standard methods. Perfusion of TNF- $\alpha$  20 min prior to tetanic stimulation inhibited LTP. Perfusion of MPEP for 40 min prior to application of TNF- $\alpha$  reversed the inhibitory effect of TNF- $\alpha$  on LTP. These results show a new role for mGluRs in TNF- $\alpha$  inhibition of LTP. A connection between the activation of mGluRs and the activation of the p38 MAPK remains to be resolved. These studies will provide valuable tools to forward our understanding of the mechanisms of action of TNF- $\alpha$  on synaptic plasticity.