Regulation of glutamate receptor trafficking by leptin

Jenni Harvey
Centre for Neuroscience, University of Dundee

It is well established that leptin is a circulating hormone that enters the brain and regulates food intake and body weight via its hypothalamic actions. However, it is also known that leptin receptors are widely expressed in the CNS and evidence is accumulating that leptin modulates many neuronal functions. In particular recent studies have indicated that leptin plays an important role in the regulation of hippocampal synaptic plasticity. Indeed leptin-insensitive rodents display impairments in hippocampal synaptic plasticity and defects in spatial memory tasks. We have also shown that leptin facilitates the induction of hippocampal long-term potentiation (LTP) via enhancing NMDA receptor function and that leptin has the ability to evoke a novel form of NMDA receptor-dependent long-term depression (LTD). In addition leptin promotes rapid alterations in hippocampal dendritic morphology and synaptic density, which are likely to contribute to the effects of this hormone on excitatory synaptic strength. Recent studies have demonstrated that trafficking of AMPA receptors is pivotal for activity-dependent hippocampal synaptic plasticity. However little is known about how AMPA receptor trafficking processes are regulated by hormonal systems. Here we present evidence that leptin rapidly alters the trafficking of AMPA receptors to and away from hippocampal CA1 synapses. The impact of these leptin-driven changes on hippocampal excitatory synaptic function will also be discussed.