Recognition memory enables us to make judgments about whether or not we have encountered a particular stimulus before. Recognition memories are readily acquired during a single encounter and are essential to normal life. Deficits in recognition memory are a major symptom of the classical amnesic syndrome and early Alzheimer's disease. Many of the same neurotransmitter receptors and intracellular signaling cascades that give rise to synaptic plasticity (i.e., long-term depression) in the perirhinal cortex are also required for perirhinal cortex-dependent recognition memory.

Recognition memory for the familiar object is intact. These spontaneous object memory tasks do not require reinforcement or motivation. In object recognition memory tasks, rodents are allowed to explore an object for a certain length of time in the sample phase, and in a subsequent test phase, the animals are presented with the familiar object and a novel object. In the test phase, normal rodents preferentially explore the novel object, thus exhibiting a change in synaptic strength provides the neural mechanism by which the familiarity of an object may be encoded within the perirhinal cortex. The role of the perirhinal cortex in memory, and the links between recognition memory and synaptic plasticity, have been demonstrated by way of pharmacological infusion studies (see below). The following experimental data are from rodent models.

**In Vivo Mechanisms of Recognition Memory**

Recognition memory may be tested in rodents using single trial object memory tasks. Rodents are allowed to explore an object for a certain length of time in the sample phase, and in a subsequent test phase, the animals are presented with the familiar object and a novel object. In the test phase, normal rodents preferentially explore the novel object, thus exhibiting a change in synaptic strength provides the neural mechanism by which the familiarity of an object may be encoded within the perirhinal cortex. The role of the perirhinal cortex in memory, and the links between recognition memory and synaptic plasticity, have been demonstrated by way of pharmacological infusion studies (see below). The following experimental data are from rodent models.

**Perirhinal Cortex**
The perirhinal cortex is contained within the medial temporal lobe and it is thought to play an integral role in recognition memory, as well as perception and object association. Studies have shown that up to 50% of perirhinal cortex neurons show a reduction in their response to a visual stimulus when it is presented for a second or subsequent time. Neuronal modeling and experimental evidence have suggested that this reduction in synaptic strength provides the neural mechanism by which the familiarity of an object may be encoded within the perirhinal cortex. The role of the perirhinal cortex in memory, and the links between recognition memory and synaptic plasticity, have been demonstrated by way of pharmacological infusion studies (see below). The following experimental data are from rodent models.

**Pharmacological Intervention**
Pharmacological intervention may be used to assess the role of different neurotransmitters in recognition memory. Antagonists are delivered directly into the perirhinal cortex of the rodent via indwelling cannulae. As illustrated in the figure, administration of the muscarinic receptor antagonist scopolamine (0.05 ng/μl) impairs recognition memory at a 20 min delay, but not 24 hour delay (p<0.05). Conversely, administration of the nicotinic antagonist MLA impairs recognition memory at a 24 hour delay, but not 20 min delay. The discrimination ratio is an index of memory performance, and is calculated as the difference in the amount of time spent exploring the novel and familiar objects as a proportion of total exploration time. This graph has been adapted from Tinsley et al. (2011).

**Elucidating the Mechanisms of Long-term Depression**
Scopolamine also prevents the induction of long-term depression (LTD) in the perirhinal cortex. Synaptic plasticity is assessed using electrophysiological recordings from slices of perirhinal cortex. Below (left) is a graph showing the avoidance of evoked synaptic responses. LTD is experimentally induced using conditioning stimulation (indicated by two upward arrows). Application of scopolamine (right) prevents this induction; thus, it is thought to be a close relationship between recognition memory and LTD. The traces below are representative EPSCs taken from the time points indicated (1 and 2). These graphs have been adapted from Cho et al. (2000) and Warrington et al. (2003).

**Cellular Mechanisms of Recognition Memory**
Many neurotransmitters and intracellular signaling cascades have been identified to be involved in both LTD and recognition memory; these are illustrated in this schematic. The release of glutamate and acetylcholine from presynaptic afferents activates a range of postsynaptic receptors. Activation of cholinergic receptors (mACHR and mAChR) and glutamate receptors (mGluR, NMDAR, AMPAR) prompts an influx of Ca2+ ions, as does the activation of TrkB receptors and L-type VGCC. The resultant increase in intracellular Ca2+ concentration prompts the activation of calcium-calmodulin related kinases (CaMKs), resulting in the phosphorylation of both AMPA and NMDA receptors (leading to endocytosis and LTD), and the transcription factor CREB. CREB is also phosphorlated as a result of a MAPK signaling cascade initiated by BDNF/TrkB. CREB can upregulate the immediate early gene c-Fos, and regulates the production of the microRNA miR-132, though the mechanisms by which they sustain LTD are not known. It is thought that the Ca2+ increase also activates neutral nitric oxide synthase (nNOS), resulting in the synthesis of nitric oxide (NO), which in turn inhibits the release of glutamate and constitutes a form of negative feedback. Expression of LTD can be mediated through intracellular signaling of synaptic AMPA receptors, a process that is reliant on the interaction between AMPA receptors and the AP2 protein, an adaptor protein involved in clathrin-mediated endocytosis. KAR activation also results in a change in synaptic strength, potentially as a consequence of its involvement in AMPAR endocytosis. Pharmacological inhibition (in red) of cholinergic or glutamatergic receptors has been shown to impair either long- or short-term recognition memory.