the plasticity block experiments, by comparing the fraction of infected neurons with conditioned fear responses, the authors estimated that blocking AMPA receptor insertion in about 20% of neurons was sufficient to prevent fear learning. Thus, synaptic modifications were widely distributed but with apparently limited redundancy.

Previous studies had already provided hints that fear conditioning led to the potentiation of a large number of synapses. Conditioning causes a large potentiation of AMPA-mediated synaptic transmission, which could have been observed only if a considerable percentage of synapses were involved[10,11]. This unexpectedly large commitment of amygdala memory space to single emotional memories may have significant implications for the understanding of emotional memory disorders such as post-traumatic stress disorder. Widely distributed representations of traumatic events may function as 'memory attractors' that inappropriately connect neutral stimuli with past traumatic experiences, potentially reinforcing those representations and the trauma associated with them.

The paper by Rumpel *et al.*[1] is representative of a growing trend in which molecular tools are used to address key questions that transcend traditional divisions in neuroscience. Indeed, a new field has emerged around studies such as this one that bridge molecular and cellular explanations of cognitive function (see http://www.molcellcog.org[2]). These studies are not only providing detailed information about molecular and cellular events involved in key aspects of cognitive function (such as insertion of AMPA receptors and potentiation of synapses as a result of learning), but they are also offering unique perspectives on important problems in systems and behavioral neuroscience. In this respect, the study by Rumpel *et al.* goes a long way toward resolving the hotly debated issue of whether the amygdala is a memory modulator, or whether this structure actually stores emotional information. These results do not refute the well-demonstrated role of the amygdala in memory modulation, nor do they eliminate the possibility that important facets of emotional experiences are stored in other sites, such as the neocortex. However, they demonstrate that synaptic changes in the lateral amygdala are triggered by learning and are required for emotional memory.

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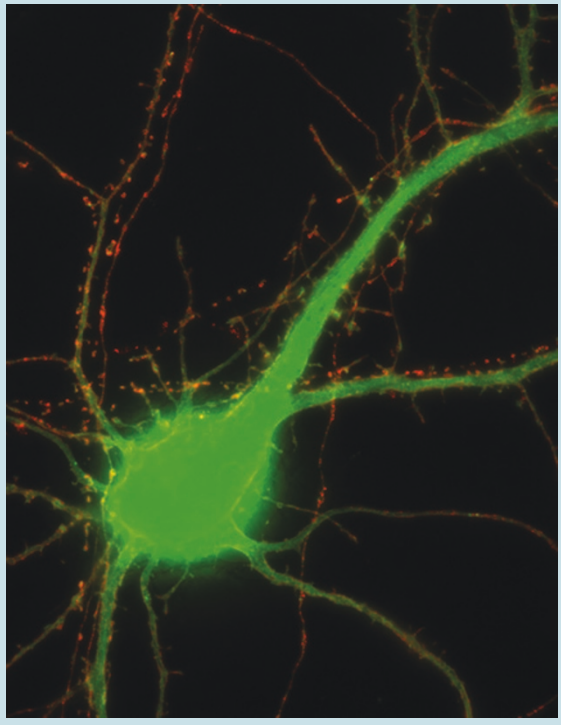
SK channels: a new twist to synaptic plasticity



The cellular mechanisms of long-term potentiation (LTP) have been widely studied because of the attractive idea that LTP may underlie learning and memory. In many parts of the brain, LTP depends on the NMDA receptor class of ionotropic glutamate receptors. Two independent groups show in this issue that NMDA receptors are negatively regulated by small-conductance, calcium-activated potassium channels (SK channels), and that this modulation can affect LTP.

NMDA receptors are normally subject to a voltage-dependent magnesium block, and so make a limited contribution to basal synaptic transmission. However, when the cell is depolarized, these receptors become active, allowing calcium to enter. Activation of NMDA receptors—and the resulting calcium influx—are required for LTP in many brain areas, including the hippocampus and lateral amygdala. The new papers show, however, that this calcium influx activates a negative feedback loop through SK channels that depresses the synaptic potential and turns off the NMDA-receptor response.

John Adelman and colleagues report on page 640 that in hippocampal pyramidal neurons (labeled with green fluorescent protein in the photo), NMDA receptors are colocalized with SK channels (labeled in red) at spines. Using two-photon laser scanning microscopy and two-photon uncaging of glutamate, the authors show that within individual spines, SK channels act to reduce the magnitude of a calcium transient evoked by NMDA receptor activation. During an excitatory postsynaptic potential (EPSP), calcium opens SK channels, which then provide a local shunting current to reduce the EPSP and promote a magnesium-dependent block of NMDA receptors. Blocking SK channels (with apamin, a component of bee venom) enhances NMDA receptor–dependent calcium signals and facilitates induction of long-term potentiation.

This intricate relationship between SK channels and NMDA receptors is not restricted to hippocampal neurons. In a related article, on page 633, Pankaj Sah and colleagues show that a similar mechanism operates in synapses in the lateral amygdala. In pyramidal neurons of the lateral amygdala, Sah and colleagues find that calcium influx via activated NMDA receptors also activates postsynaptic SK channels, and that activation of these SK channels depresses the synaptic potential. They also demonstrate that blockade of SK channels increases LTP of cortical inputs to lateral amygdala pyramidal neurons.

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