

# Pain receptor in brain may be linked to learning and memory

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Scientists have long known that the nervous system receptor known as TRPV1 can affect sensations of pain in the body. Now a group of Brown University scientists has found that these receptors – a darling of drug developers – also may play a role in learning and memory in the brain.

In surprising new research, published in the journal *Neuron*, Julie Kauer and her team show that activation of TRPV1 receptors can trigger long-term depression, a phenomenon that creates lasting changes in the connections between neurons. These changes in the brain – and the related process of neural reorganization known as long-term potentiation – are believed to be the cellular basis for memory making.

“We’ve known that TRPV1 receptors are in the brain, but this is some of the first evidence of what they actually do there,” Kauer said. “And the functional role we uncovered is unexpected. No one has previously linked these pain receptors to a cellular mechanism underlying memory. So we may have found a whole new player in brain plasticity.”

The study findings have implications for drug development, Kauer said.

The research points out potentially effective new targets for drugs that could prevent memory loss or could possibly treat neural disorders such as epilepsy, Kauer said. The other implication may be cautionary. Drug makers already sell drugs – such as the weight-loss pill rimonabant, which is sold in Europe under the name Acomplia – that can block TRPV1 receptors. Other drugs aimed at reducing pain and inflammation

by blocking or activating TRPV1 receptors are in the research pipeline. But drugs that bind to TRPV1 receptors in the central nervous system are likely to influence more than just pain-related functions, Kauer said.

“Our findings suggest the possibility that some of the psychiatric side effects from rimonabant could be due to the blocking of TRPV1 receptors,” she said.

TRPV1, short for transient receptor potential vanilloid subtype, can be found all over the nervous system, including in skin, the spinal cord and the brain. These receptors can sense heat, trigger inflammation and transmit pain. TRPV1 receptors not only respond to heat but also to capsaicin, the compound that creates the spicy kick in chili peppers.

In her study, Kauer, professor of medical science in the Department of Molecular Pharmacology, Physiology and Biotechnology at Brown, treated rat brain tissue from the hippocampus, the brain’s seat of learning and memory, with capsaicin. The team found that this compound activated TRPV1 channels – which alone triggered long-term depression in the brain tissue. Further, rimonabant entirely blocked long-term depression by blocking TRPV1 channels.

The team then tested brain tissue from mice that lacked TRPV1 receptors and found that long-term depression was absent – and that applying capsaicin still couldn’t elicit the changes to the synapses.

Source: Brown University

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