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TRPV1 Modulation of Plasticity in the Hippocampus

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INTRODUCTION
Learning and memory are phenomena made possible via physical changes at neuronal synapses in the brain, a process known as synaptic plasticity. Dysfunction in synaptic plasticity can contribute to such diseases and disorders as Alzheimer’s Disease, Parkinson’s Disease, and retrograde amnesia (Bren et al., 2001). Recently, TRPV1 activation was shown to modulate synaptic plasticity in the hippocampus (Gibson et al., 2008). TRPV1 is a thermosensitive Ca²⁺ channel located throughout the CNS, including in the hippocampus. TRPV1’s channels are activated by the chemical capsaicin, which is responsible for producing the “hot” of red peppers. Several studies implicate a role for TRPV1 in contextual fear learning (March et al., 2007), recall of spatial memory (Li et al., 2008), and anxiety-related disorders (Santos et al., 2017), including depression (Kaskaew et al., 2020). Using field electrophysiological recordings in CA1 stratum radiatum we measured high frequency stimulation or theta burst-induced LTP in the presence and absence of TRPV1 agonist and antagonist. Our data suggest that TRPV1’s role in mediating increased LTP is not expressed at the CA1-CA1 synapses, but possibly at the CA1-interneuron synapses. Further, we propose a novel mechanism by which TRPV1 activation enhances hippocampal CA1 pyramidal cell LTP via modulation of inhibitory interneurons circuit.

QUESTION / OBJECTIVE
TRPV1 receptors have recently been demonstrated to mediate long-term depression of hippocampal CA1 stratum radiatum neurons in vivo (Santos et al., 2018). In addition, TRPV1 knock-out mice show enhanced LTP compared to wild-type mice (March et al., 2007) and application of high doses of the TRPV1 agonist capsaicin increased CA1 LTP in young Water rats (Li et al., 2008). However, the mechanism mediating TRPV1 increases in CA1 LTP are not known. We investigated whether interneuron LTP mediated by TRPV1 might play a role in modulating increases in LTP.

METHODS
Preparation of Brain Slices
Brain slices were obtained from 16-27 day old mixed male and female Sprague-Dawley rats. All experiments were performed in accordance with Institutional Animal Care and Use Committee (IACUC) protocols. Rats were anesthetized with isoflurane and quickly decapitated. The brain was rapidly removed and 400-μm thick coronal slices were obtained using a vibrating blade at room temperature for at least 1 h on a netting submerged in artificial cerebral spinal fluid (ACSF) containing 124 mM NaCl, 3 mM KCl, 1.3 mM MgSO₄, 2.5 mM CaCl₂, 13 mM NaHCO₃, and 11 mM dextrose, saturated with 10% O2:8% CO2 (pH 7.4). Slices were perfused with oxygenated ACSF (32-36°C, pH 7.4) above and below the slice at a flow rate of ~2-3 ml/min for the duration of the electrophysiological recordings. For experiments using picosecond, a surgical cut was made between the CA1 and CA2 regions.

Electrophysiological Field EPSP Recordings
The extracellular post-synaptic potentials (EPSPs) generated at the synapses between CA1 and CA3 pyramidal cells is in response to electrical stimuli of the CA3 Schaffer Collaterals were measured using field recording techniques. During field electrophysiological recordings, the EPSPs were recorded from the hippocampal stratum radiatum in 400 μm rat brain slices. A recording electrode filled with a 1 M NaCl was placed in the CA1 stratum radiatum and extracellular currents were induced using a bipolar stimulating electrode located 200-300 μm away from the stimulating electrode. The EPSP amplitude of control and without capsaicin (50 μM) was measured. The CA1 LTP was studied in hippocampal slices from rats treated with capsaicin (50 μM) for 30 min.

RESULTS
Capsaicin (100 μM) increased the CA1 LTP, which was blocked by capsaicin (100 μM).

SIGNIFICANCE
TRPV1 was first identified and described as a heat activated ion channel expressed in peripheral sensory neurons (Caterina et al., 1997), and the mechanism of TRPV1 has remained on the primary target of TRPV1 antagonists for modulation of pain. TRPV1 activity in the hippocampus is not well understood. Several studies suggest that TRPV1 is expressed in the hippocampus and plays a role in synaptic plasticity. In this study, we investigated the role of TRPV1 in synaptic plasticity in the hippocampus. The results show that TRPV1 activation increases CA1 LTP, which is blocked by capsaicin, a TRPV1 antagonist. This study provides evidence that TRPV1 activation enhances CA1 LTP and that picosecond-mediated blockade of GABAergic inhibition eliminates capsaicin-induced LTP. This suggests that TRPV1 receptors in enhanced hippocampal LTP are present on interneurons, rather than on CA1 pyramidal cells. This study suggests that TRPV1 activation may play a role in synaptic plasticity in the hippocampus.

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REFERENCES
Bren, V.H., et al. Retrograde amnesia for spatial memory induced by NMDA receptor-mediated long-term potentiation. The Journal of Neuroscience 2001; 21(11): 539-542;

Figure 1. Anatomy/stimulation of the hippocampal slices.

Figure 2. TRPV1 mediates depression of CA1 interneurons, but not of pyramidal cells.

Figure 3. TRPV1 receptor activation by capsaicin increases CA1 LTP, which is blocked by capsaicin.

Figure 4. TRPV1 activation liesopergiainferox in follows enhancement trend.

Figure 5. Picosecond blocks mediated enhancement of LTP.

Figure 6. Higher concentrations of capsaicin do not alter pyramidal cell EPSPs.