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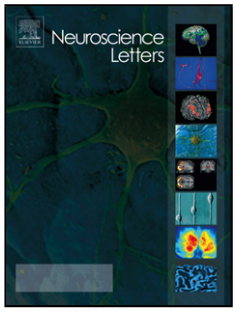

Title: Thermogenetic stimulation of single neocortical pyramidal neurons transfected with TRPV1-L channels

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Thermogenetic stimulation of single neocortical pyramidal neurons transfected with TRPV1-L channels.

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Highlights

- Functional TRPV1-L channels can be expressed in pyramidal cells of mouse neocortex using *in utero* electroporation.
- IR (infrared) radiation induces membrane depolarization in TRPV1-L+ pyramidal neurons in acute brain slices at near physiological temperatures.
- Stronger IR radiation evokes a consistent spiking response in TRPV1-L+ neurons.

Abstract

Thermogenetics is a promising innovative neurostimulation technique, which enables robust activation of single neurons using thermosensitive cation channels and IR stimulation. The main advantage of IR stimulation compared to conventional visible light optogenetics is the depth of penetration (up to millimeters). Due to physiological limitations, thermogenetic molecular tools for mammalian brain stimulation remain poorly developed. Here, we tested the possibility of employment of this new technique for stimulation of neocortical neurons. The method is based on activation gating of TRPV1-L channels selectively expressed in specific cells. Pyramidal neurons of layer 2/3 of neocortex were transfected at an embryonic stage using a pCAG expression vector and electroporation *in utero*. Depolarization and spiking responses of TRPV1L+ pyramidal neurons to IR radiation were recorded electrophysiologically in acute brain slices of adult animals with help of confocal visualization. As TRPV1L-expressing neurons are not sensitive to visible light, there were no limitations of the use of this technique with conventional fluorescence imaging. Our experiments demonstrated that the TRPV1-L+ pyramidal neurons preserve their electrical excitability in acute brain slices, while IR radiation can be successfully used to induce single neuronal depolarization and spiking at near physiological temperatures. Obtained results provide important information for adaptation of thermogenetic technology to mammalian brain studies *in vivo*.

Keywords

Thermogenetics, neurostimulation, neocortex, patch clamp, pyramidal neuron