

2013 Pain Day Poster Competition

Basic Science:

Light-Induced Nociception: Remote Optogenetic Control Of Peripheral Pain Pathways In Freely Moving Mice

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Nociceptors are afferent neurons activated by noxious stimuli. Controlling the activity of nociceptors may lead to induction and/or inhibition of pain perception in vivo. Due to its high spatio-temporal precision, optogenetics is a powerful tool to selectively control neuronal activity. Using a tissue-restricted genetic strategy, we generated a transgenic mouse line expressing channelrhodopsin-2 (ChR2) in the subset of peripheral sensory neurons expressing Nav1.8 ion channels. Colocalization of ChR2 (fused to EYFP) with nociceptor-specific markers shows selective expression in peptidergic and non-peptidergic subpopulations. Electrophysiological recordings reveal a strong surface expression of ChR2 in DRG nociceptors with large photocurrents and action potentials evoked by pulses of blue laser light (473nm). Histological preparations show an efficient trafficking of ChR2 from cell soma to laminae I and II in the dorsal horn of the spinal cord, and throughout the sciatic nerve to nerve fibers in the skin. This strong and specific expression of ChR2 translated into robust behavioral responses to exposure of freely moving mice to blue light. As the light intensity increased, acute pain responses ranged from paw licking and withdrawal to escape, jumping and vocalization. Such nocifensive responses were absent after yellow light exposure. Blue light exposure rapidly produced place aversion, with ChR2-expressing transgenic mice avoiding blue-lit areas during and post-light application. Finally, transgenic mice were sensitized by blue light, displaying thermal and mechanical hypersensitivity following prolonged light exposure at intensities below the threshold for acute behavioral responses. We have thus developed a novel non-invasive pain model in which remote activation of peripheral nociceptive pathways in freely moving animals is achieved optogenetically, without any external noxious stimulus or injury.