



Presentation Abstract

Program#/Poster#: 617.28/XX60

Presentation Title: In Vivo Optical inhibition of peripheral neurons after intrathecal administration of viral vector and neuronal expression of the optically active proton pump ArchT in rat.

Location: Hall A-C

Presentation time: Tuesday, Nov 15, 2011, 11:00 AM -12:00 PM

Authors: ***M. BOADA**^{1,2}, D. RIRIE², T. J. MARTIN², E. BOYDEN³, J. C. EISENACH²;
¹Advance, NC; ²Anesthesiol., Wake Forest Baptist Med. Ctr., Winston-Salem, NC; ³MIT, Cambridge, MA

Abstract: Selective targeting and inhibition of afferent subtypes would allow control of nociceptive input to the spinal cord while potentially maintaining other sensory modalities and motor function. Optically active proton pumps provide precise temporal control of neuronal inhibition (Chow et al, 2010). Here we tested whether intrathecal viral vector delivery of the optically active proton pump ArchT could successfully result in neuronal transduction and expression of spinal cord or afferent neurons and whether peripheral afferent neurons could be inhibited using optical activation in vivo.

After Animal Care and Use Committee approval, 10 uL of replication deficient self complimentary AAV8 vector containing ArchT with a GFP tag were injected at L3-4 in male Sprague Dawley rats as described (Ririe et al, 2004). Eight weeks later, primary afferent electrophysiology was evaluated using intracellular recording at L5(Boada et al, 2010). After intracellular electrode placement, the receptive field (RF) and membrane electrical properties of 15 mechano sensory afferents were characterized (5 LTMR-Hair; 1 SAI, 2 LTMR-RA, 4 AHTMR, 1 CHTMR) followed by examination of the effect of exposure to green laser light (520 nm). Preliminary results showed 4/15 cells were optically sensitive. Of the 4 neurons inhibited, all were fast nociceptors (A-high threshold mechanoreceptors (AHTMR) with mechanical thresholds between 15-99 mN and CV in the A δ / β range (10-14 m/s)). In 4/4 cells, there was a rapid (\pm 0.02 sec) hyperpolarization of membrane potential (average 4.5 \pm 0.5 mV). After optical activation all RF and action potential

(AP) characteristics returned to baseline. Optical activation produced complete electrical block of AP propagation in response to skin incision in the RF. Sensitization within the RF from skin incision was also reduced; both cellular RF mechanical sensibility and size remained at normal levels. Active electrical properties, AP amplitude and duration (D50), appeared to be unaffected.

This is the first report of optical inhibition of peripheral sensory afferent neurons in vivo. The lack of expression of the channel in motor neurons is beneficial, but the etiology of the specificity is unclear. Further studies will focus on understanding the specificity of nociceptor efficacy of optical inhibition with ArchT. These techniques will be valuable for exploring afferent activity in pain circuits and may lead to therapeutic interventions utilizing light, possibly patient controlled, for spatial and temporal control of afferent nociceptive input to the spinal cord to control pain.

Disclosures: **M. Boada:** None. **D. Ririe:** None. **T.J. Martin:** None. **E. Boyden:** None. **J.C. Eisenach:** None.

Keyword(s): IN VIVO
PAIN
INTRACELLULAR RECORDING

Support: NIH grant GM48085

[Authors]. [Abstract Title]. Program No. XXX.XX. 2011 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, 2011. Online.

2011 Copyright by the Society for Neuroscience all rights reserved. Permission to republish any abstract or part of any abstract in any form must be obtained in writing by SfN office prior to publication.