



ESRA Italian Chapter

XXVIII
CONGRESSO
NAZIONALE

PRESIDENTE
DEL CONGRESSO
Luciano Calderone

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ICSMAugeri, Pavia

Peripheral neuromodulation: From the ganglion to the peripheral nerve



PALERMO 5-7 Ottobre

XXVIII

**CONGRESSO
NAZIONALE**



European Society of
Regional Anaesthesia
& Pain Therapy

ESRA ITALIA

Disclosures

Consultant for

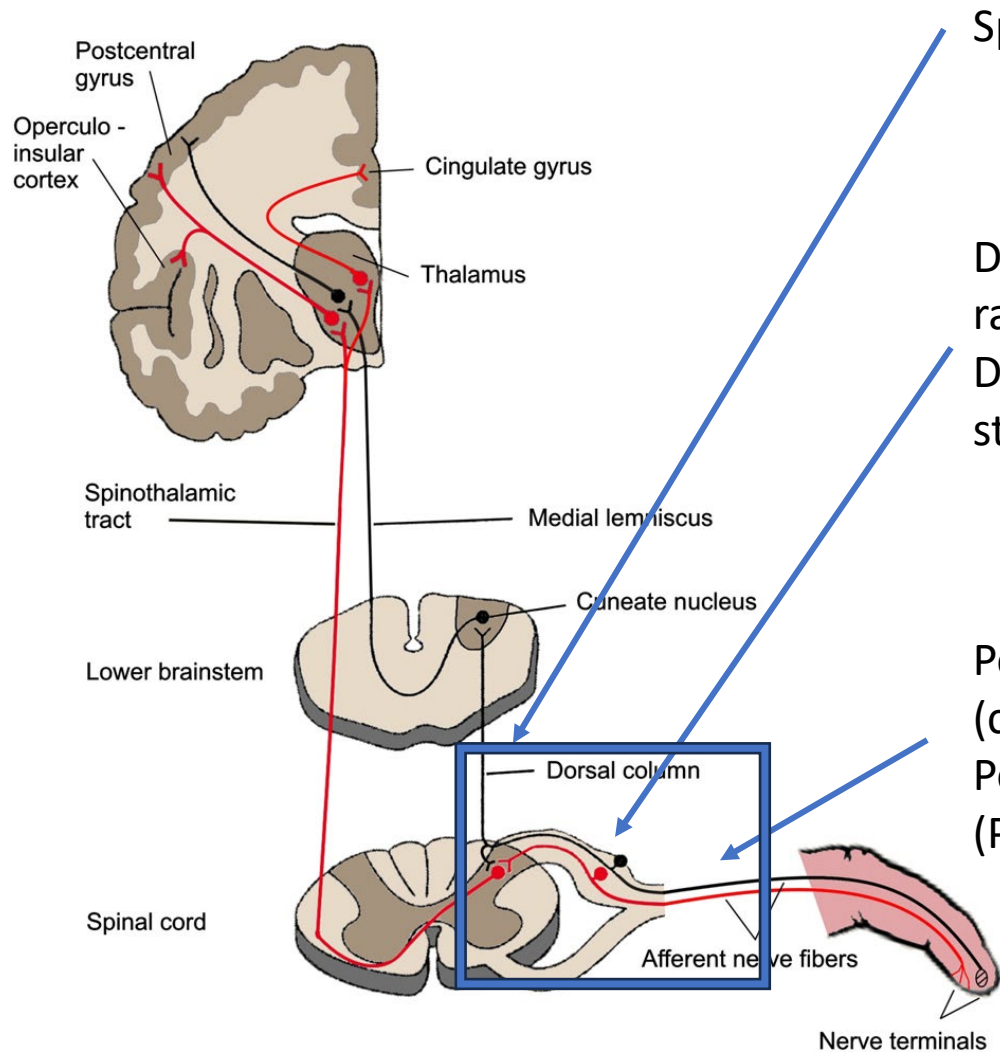
- Abbott
- Boston Scientific

What is neuromodulation?

The alteration of neuronal activity through a chemical or physical treatment applied to a neural target



Targets of neuromodulation

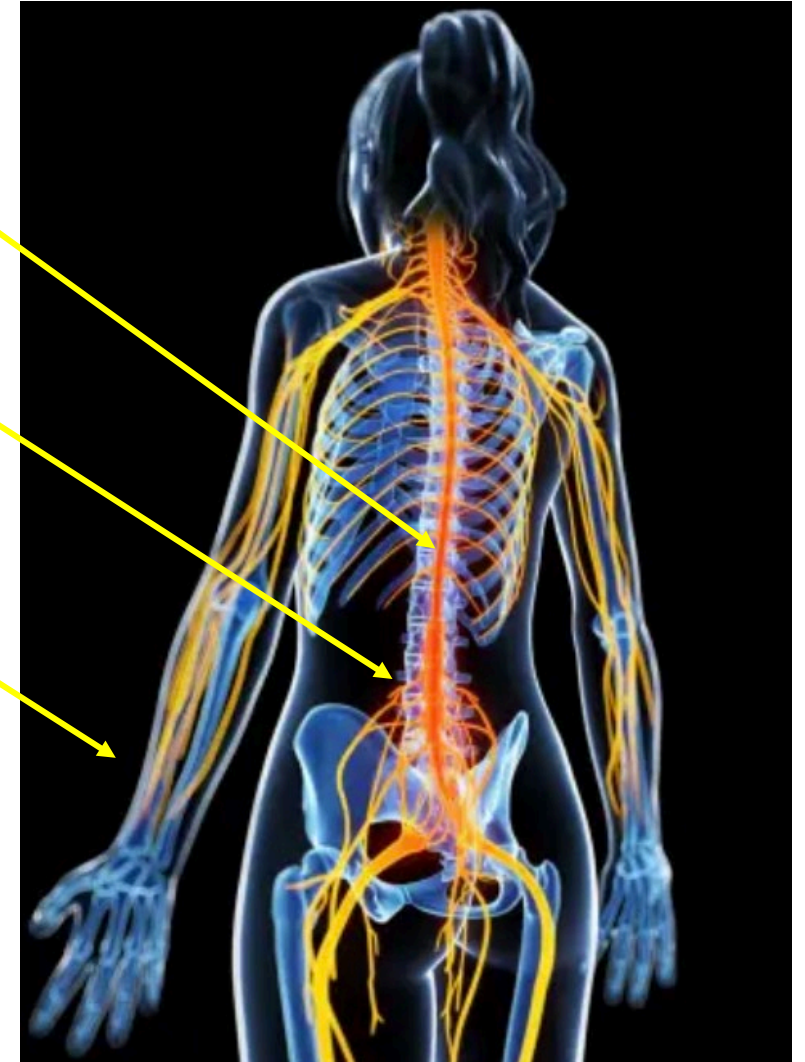


Cruccu et al, 2008

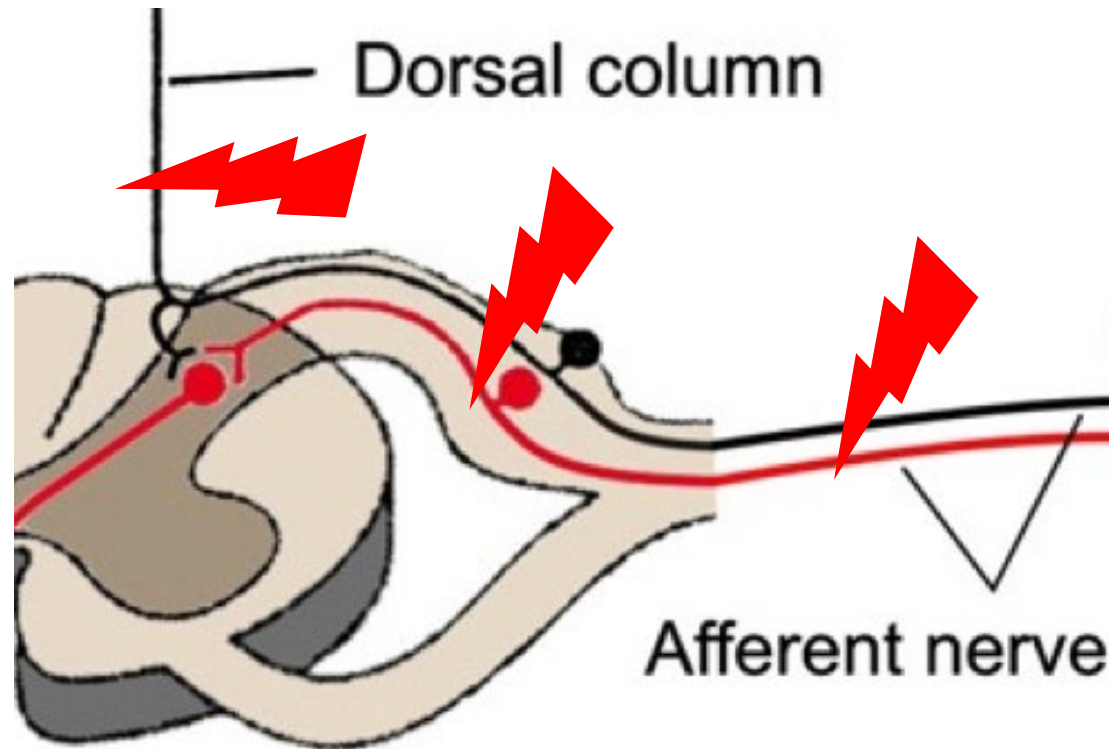
Spinal Cord Stimulation (SCS)

Dorsal Root Ganglion
radiofrequency modulation
Dorsal Root Ganglion
stimulation (DRGs)

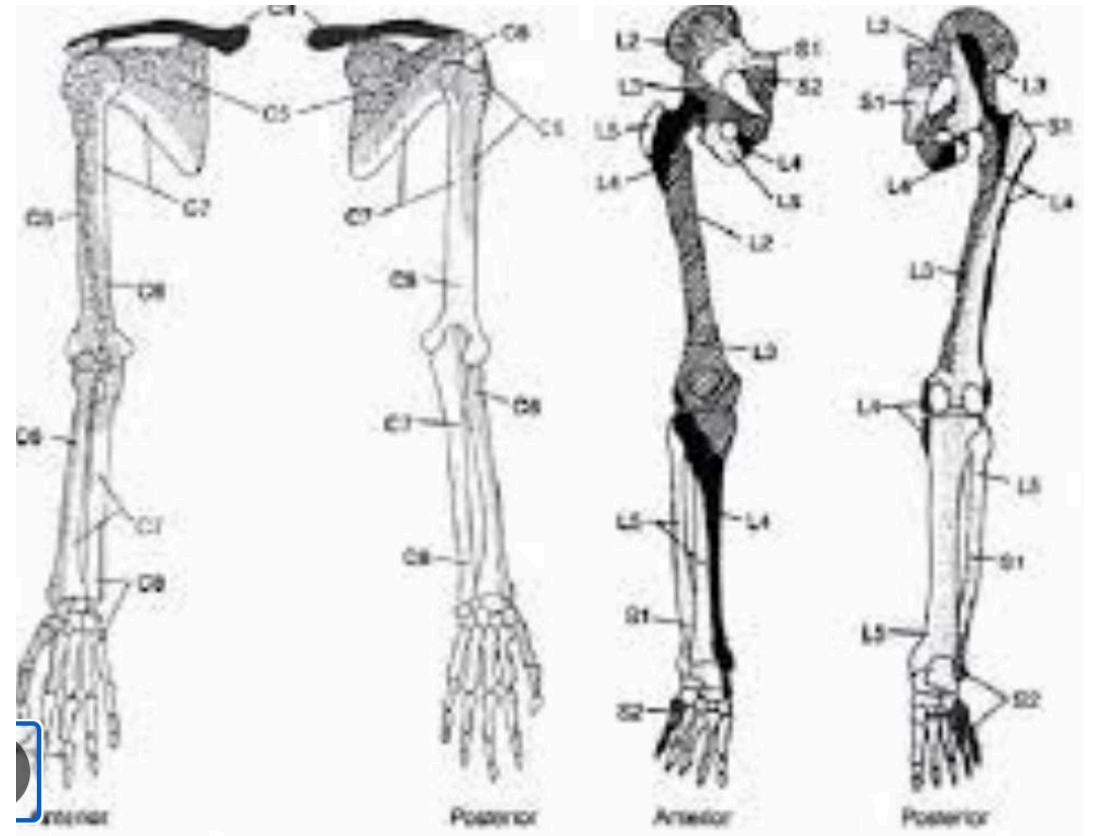
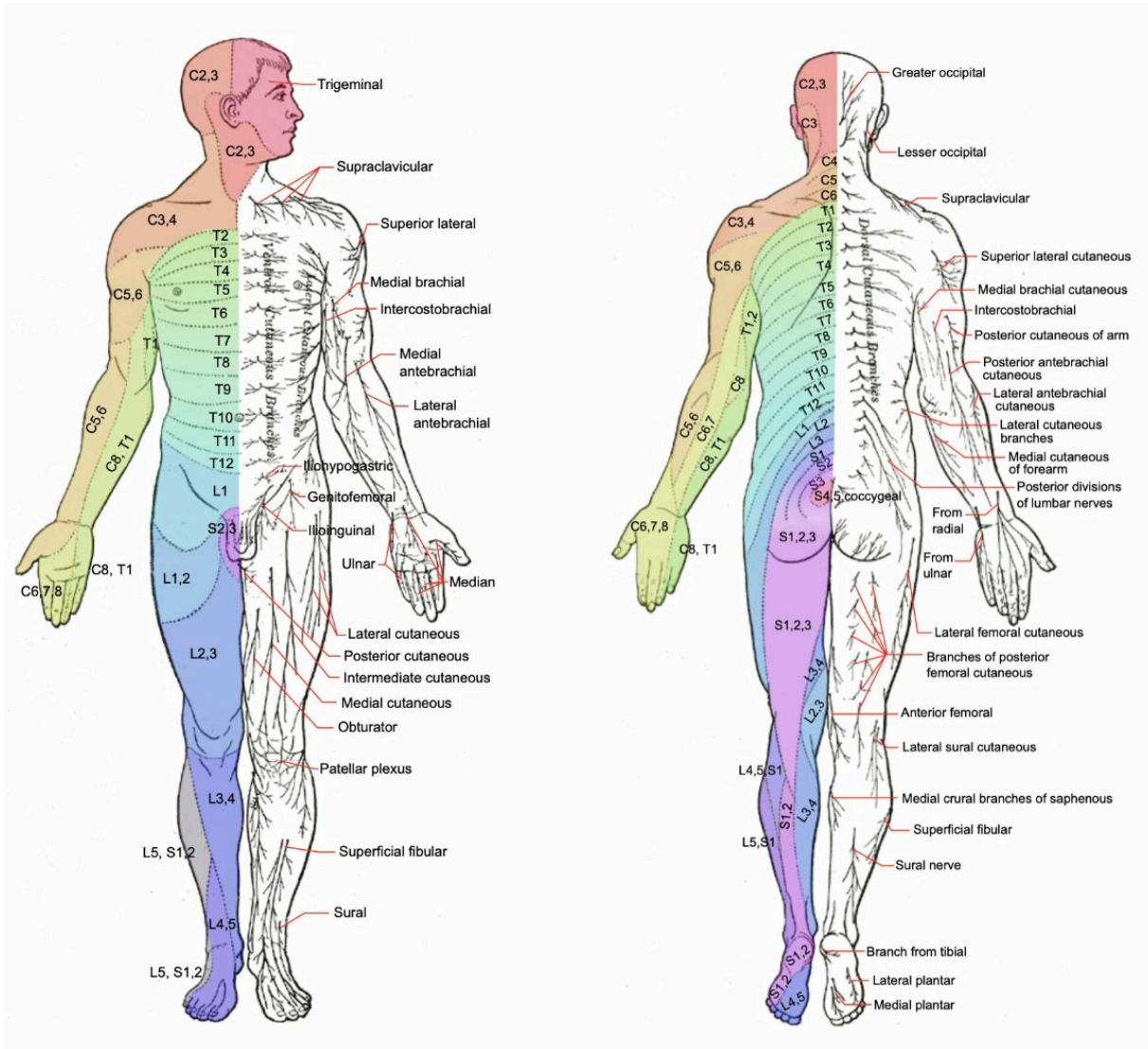
Peripheral nerve modulation
(cryo or RF)
Peripheral nerve stimulation
(PNS)



Which are the differences?



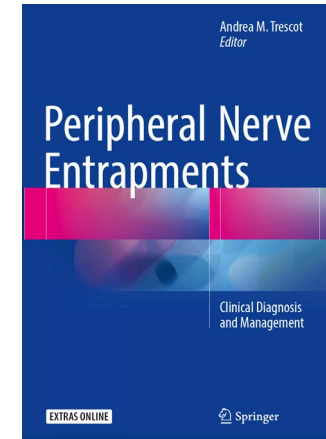
Anatomical distribution



Why modulate a peripheral nerve?

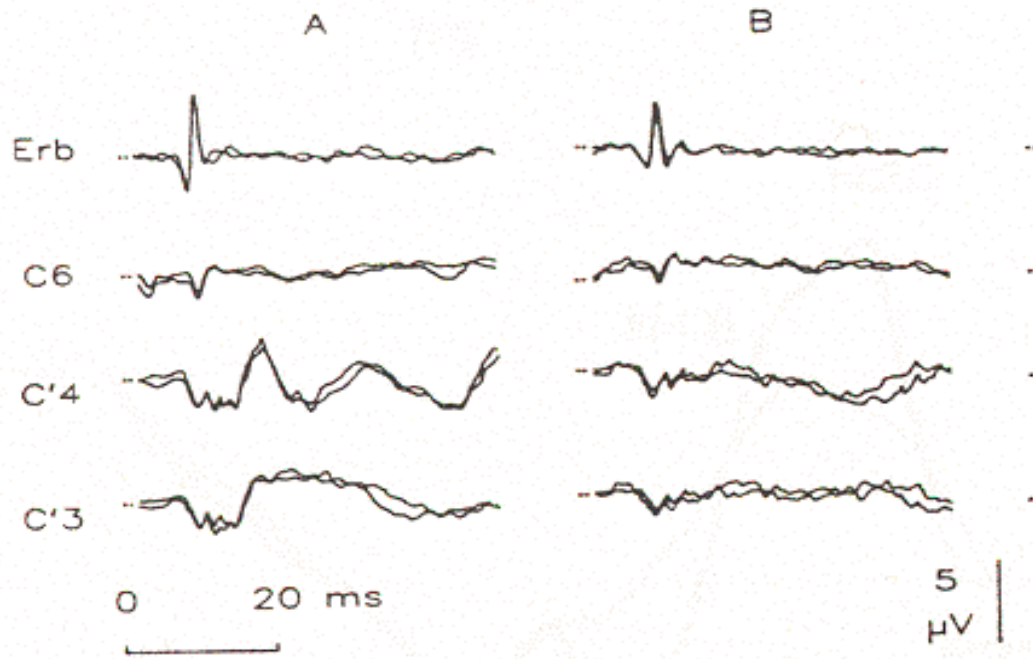
The nerve lesion is the cause of pain

- Traumatic nerve lesion
- Nerve entrapment

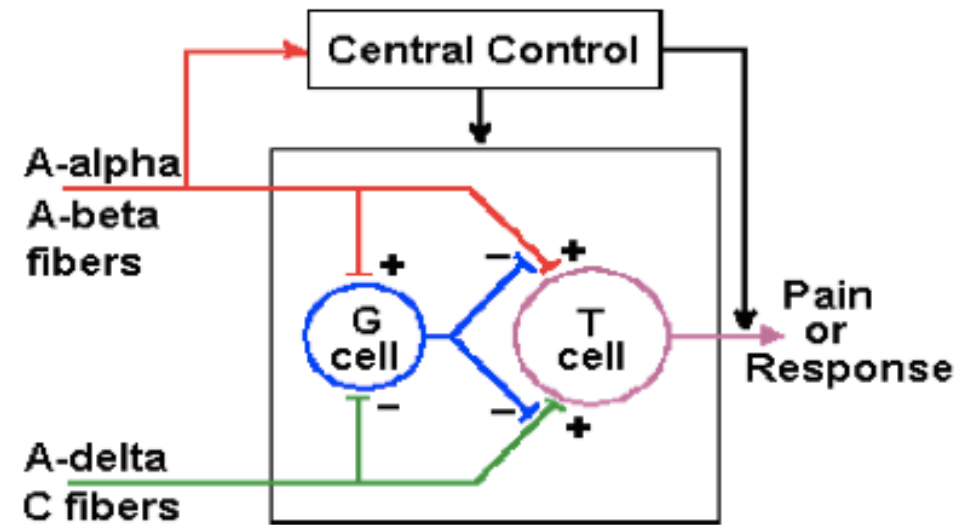
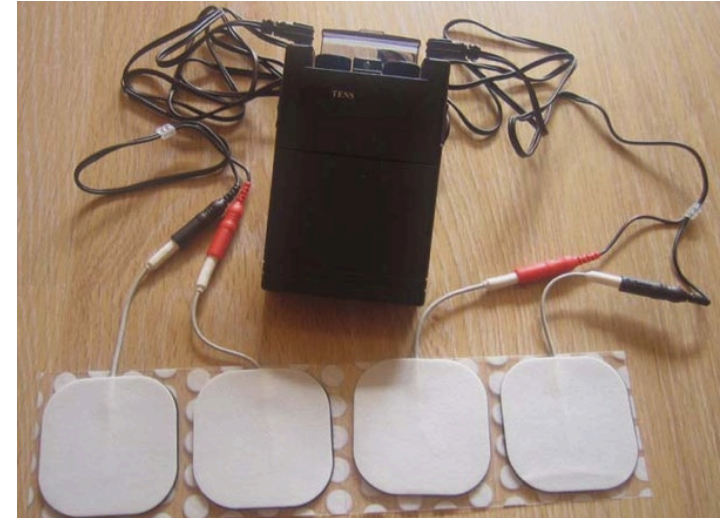


The nerve transports information from a painful area (eg.: joint)

Non invasive neuromodulation techniques



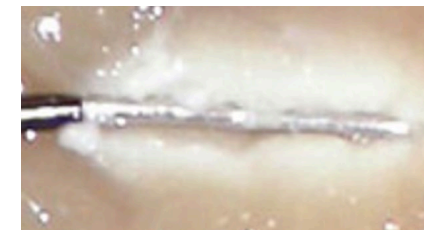
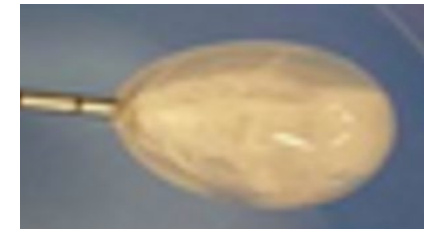
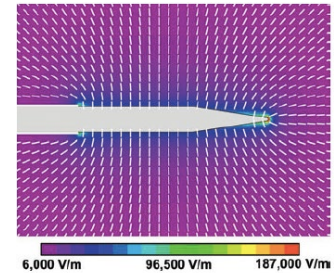
The electrical stimulation of a peripheral nerve reduces the amplitude of somato-sensitive evoked potentials obtained by the stimulation of that nerve. Nardone, Schieppati. 1989



Invasive, one shot techniques

- **Pulsed radiofrequency:** modulation of neural functionality with reduced excitability without conduction alteration
- **Cryomodulation:** lesion of nerve fibers without involving the epineurium; anatomical/functional restoration after 4-6 weeks
- **Continuous radiofrequency:** lesion of some fibers and perineural tissues; anatomical/functional restoration after months to years

NOT FOR PERIPHERAL NERVE LESIONS



Narrative Review

Pulsed Radiofrequency in Interventional Pain Management: Cellular and Molecular Mechanisms of Action – An Update and Review

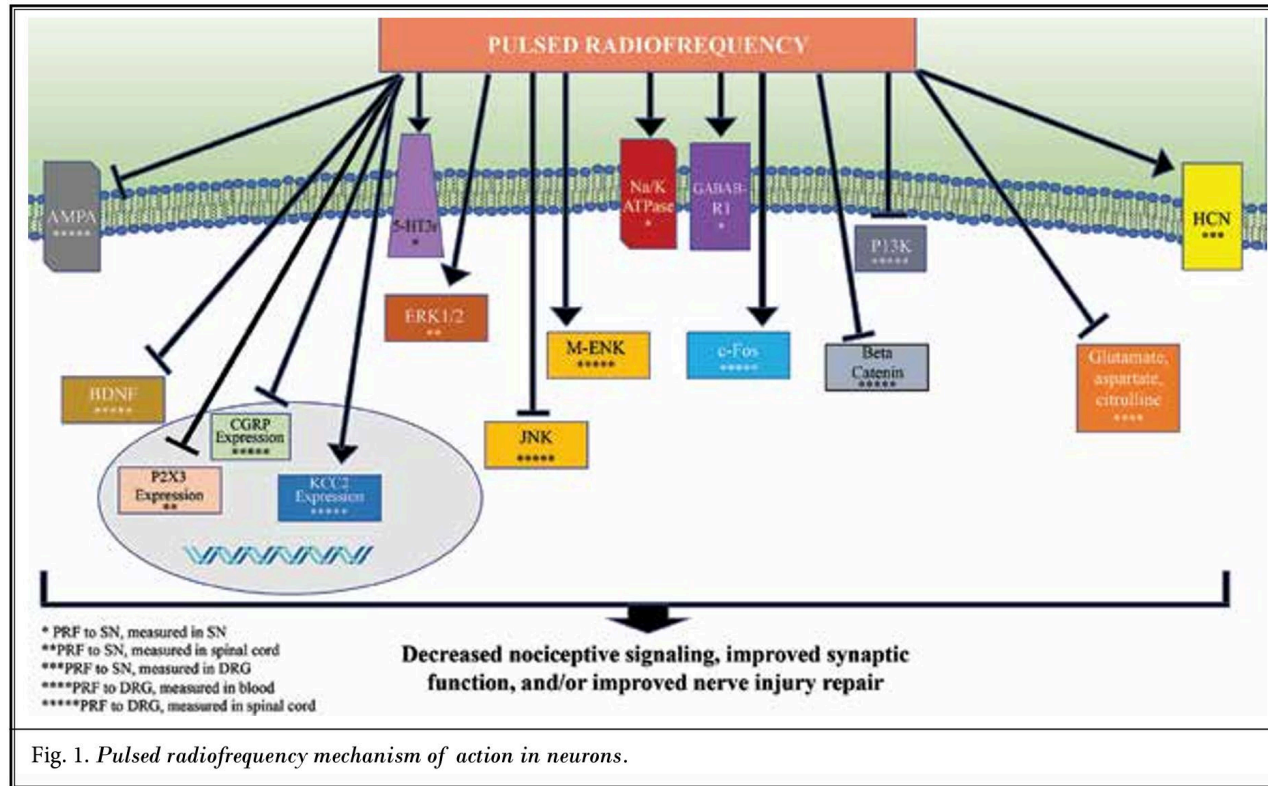


Fig. 1. Pulsed radiofrequency mechanism of action in neurons.

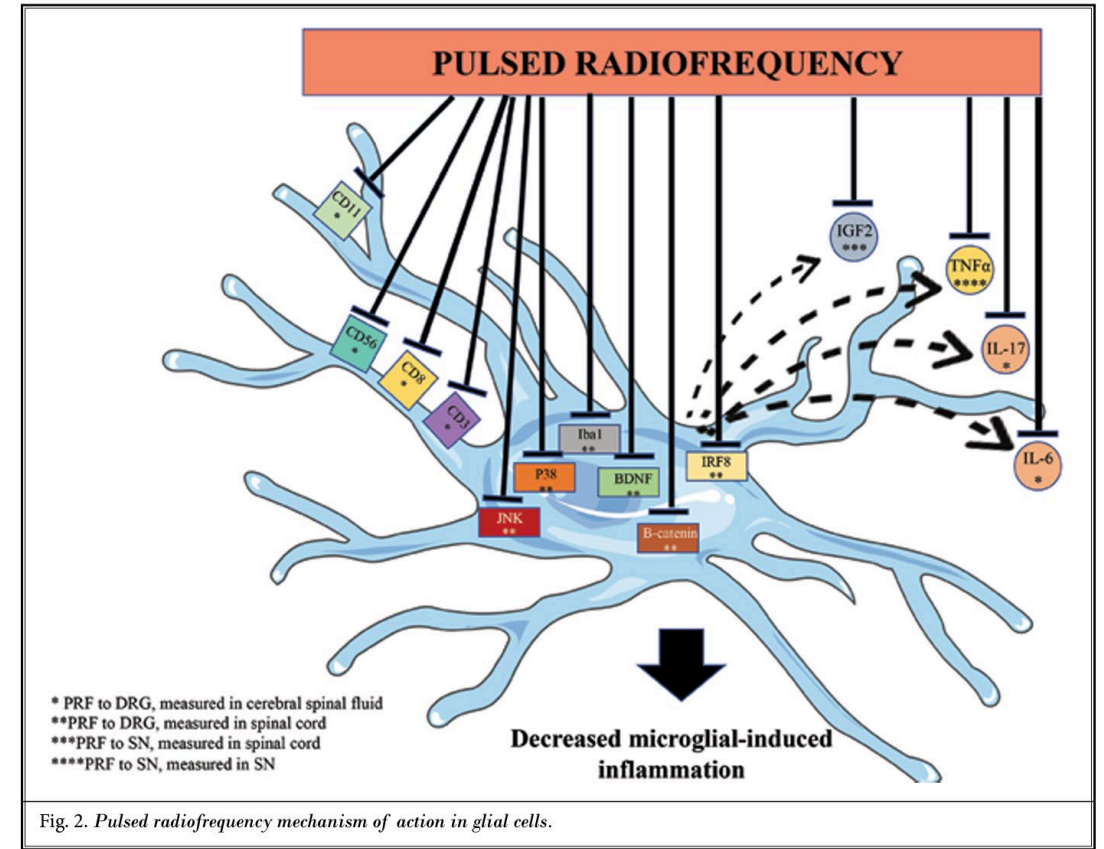
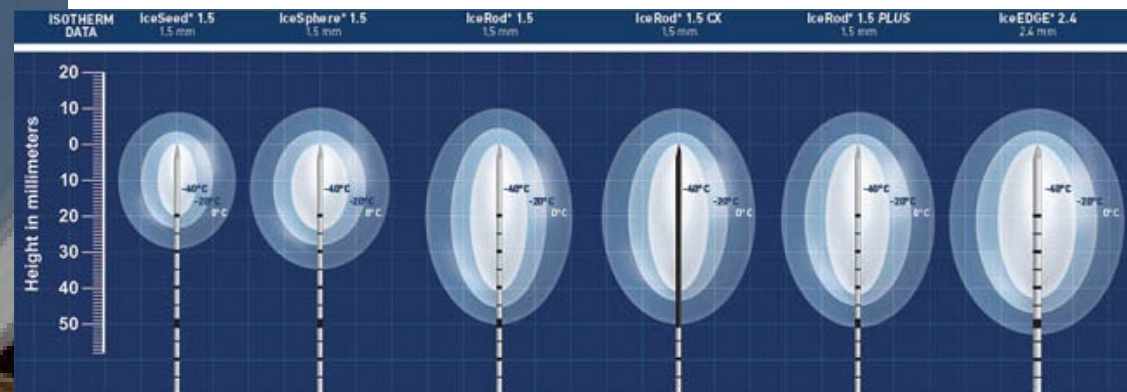


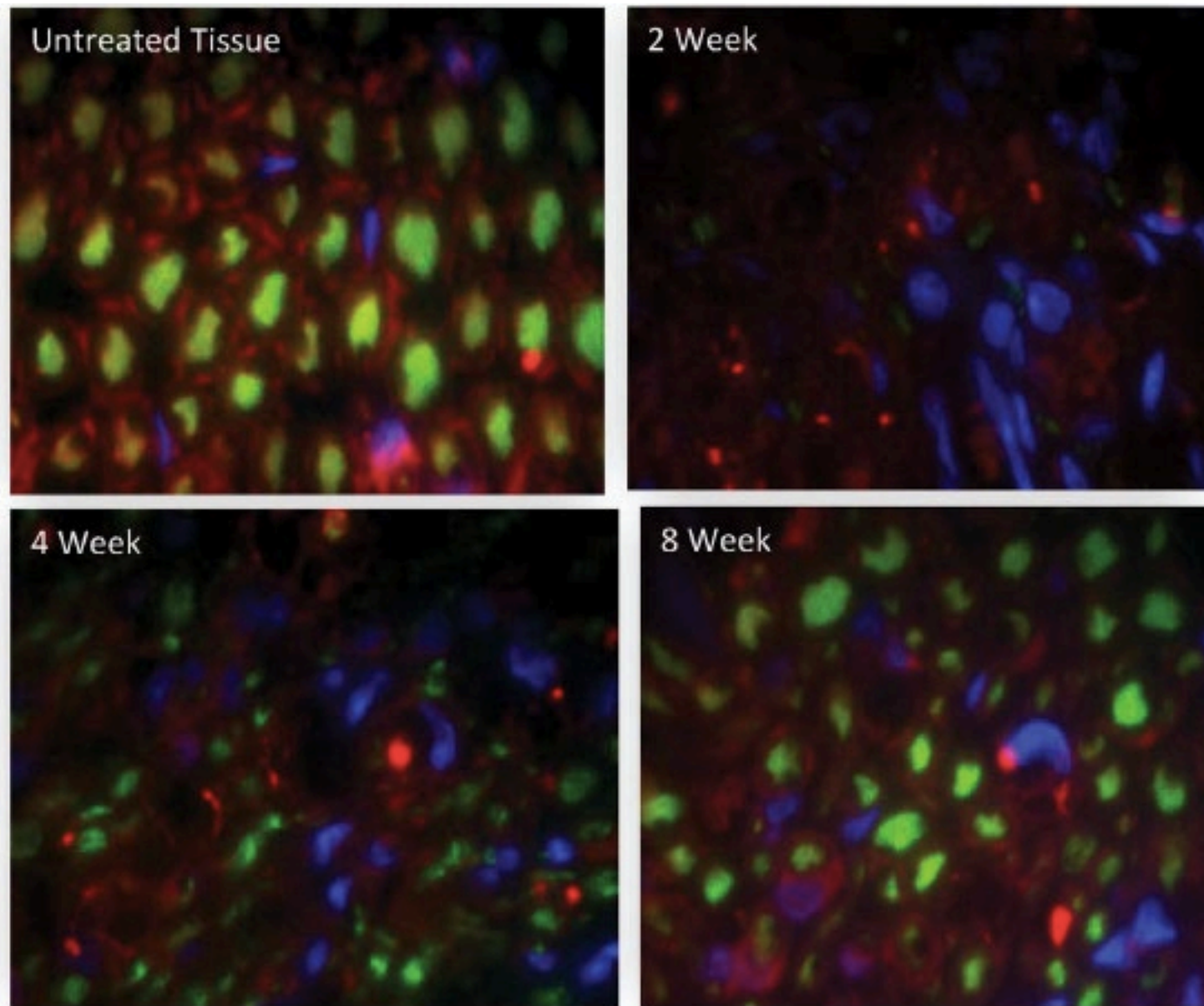
Fig. 2. Pulsed radiofrequency mechanism of action in glial cells.

Cryoanalgesia



The extension of the lesion depends on probe size, temperature (T) and time (t)



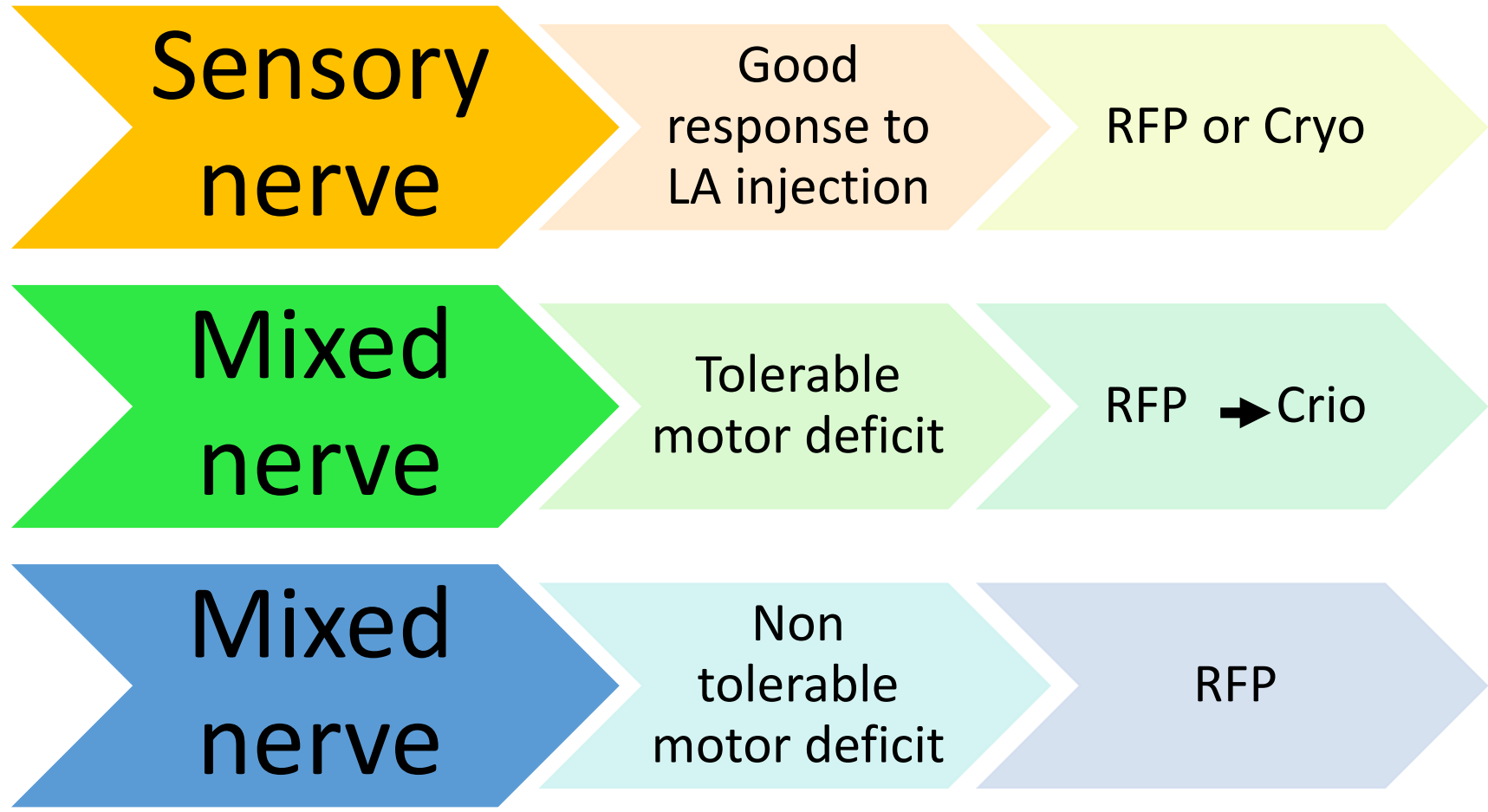


Immunofluorescence staining of tissue before and after cryoneurolysis (image courtesy of Myoscience).

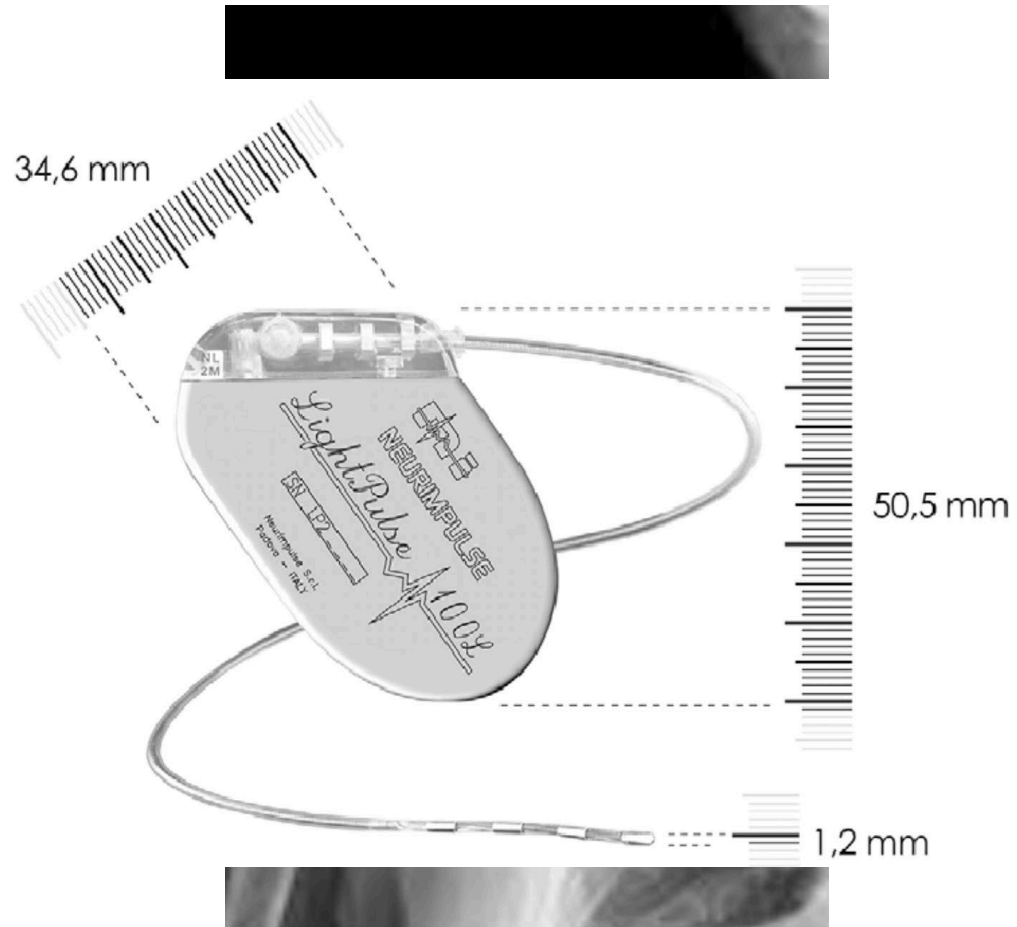
Ilfeld et al. Expert review of medical devices, 2016.

How can I choose in case of peripheral nerve lesion/entrapment?

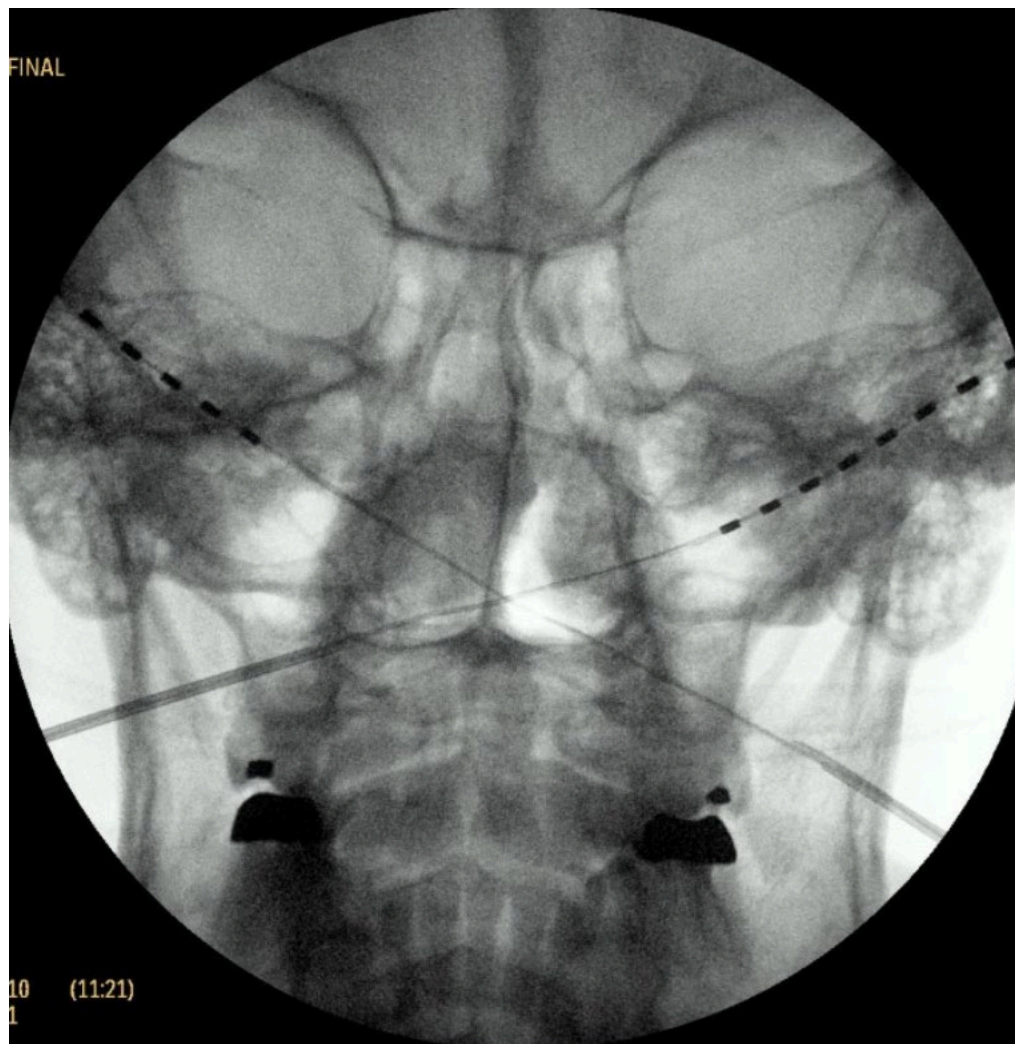




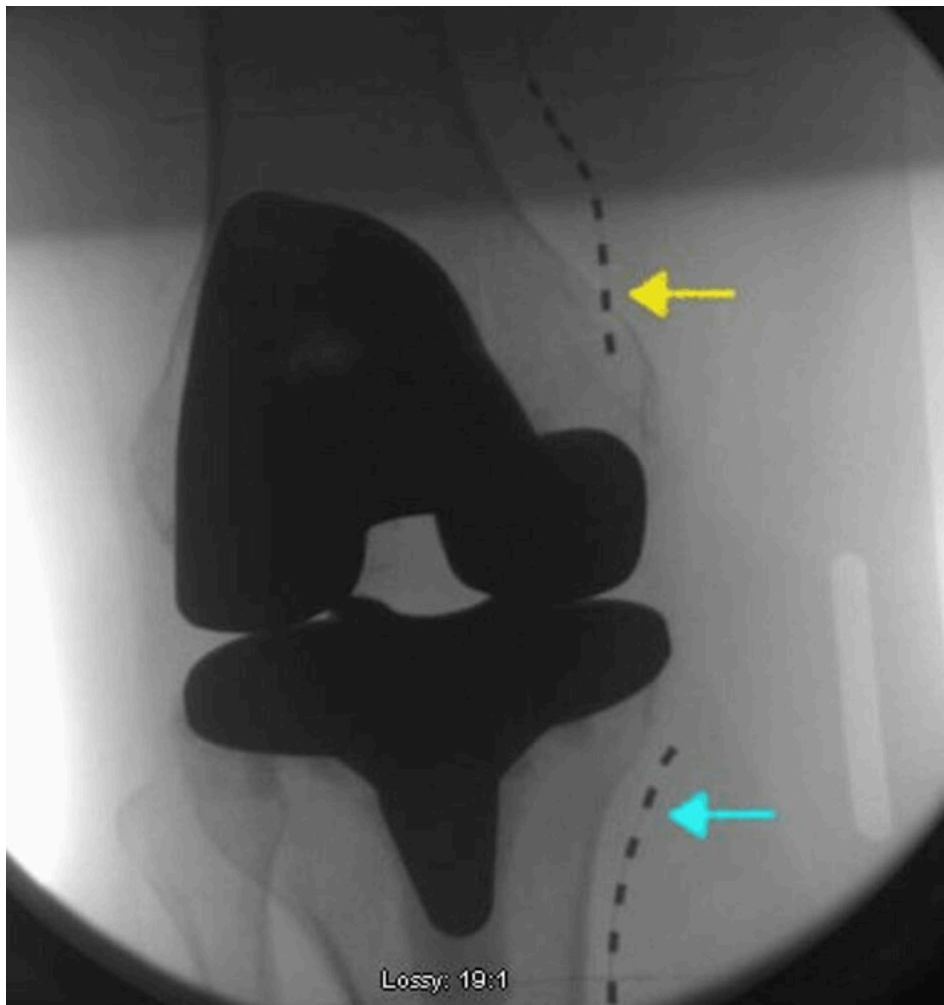
Peripheral neurostimulation



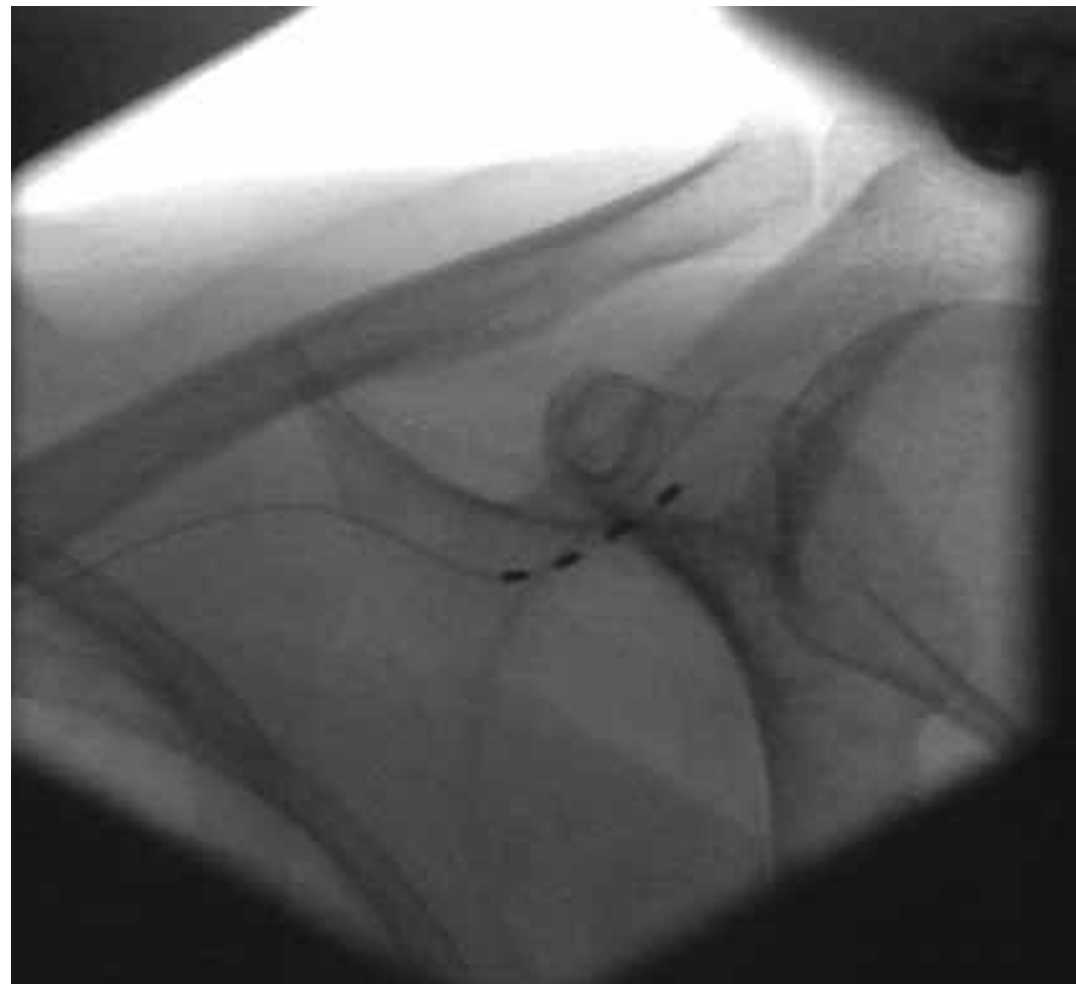
Occipital nerve stimulation for migraine



PNS for joint pain



Chauhan G. 2023



Kurt E. 2016



Regional Anesthesia and Pain Medicine

Volume 33, Issue 6, November–December 2008, Pages 558-565



Ultrasound and regional anesthesia

Feasibility of Ultrasound-Guided Percutaneous Placement of Peripheral Nerve Stimulation Electrodes and Anchoring During Simulated Movement: Part Two, Upper Extremity

Marc A. Huntoon M.D.^a  , Bryan C. Hoelzer M.D.^a, Abram H. Burgher M.D.^a, Mark
Friedrich B. Hurdle M.D.^{a, b}, Elizabeth A. Huntoon M.S., M.D.^a

When consider PNS?

- Less invasive than SCS or DRGs
- An option when SCS or DRGs are not recommendable for anatomical reasons
- The painful area should involve 1 or 2 peripheral nerve territory and the lead can be placed proximal to the lesion



[Brain Sci.](#) 2019 Feb; 9(2): 23.

Published online 2019 Jan 24. doi: [10.3390/brainsci9020023](https://doi.org/10.3390/brainsci9020023)

Neurostimulation for Intractable Chronic Pain

[Timothy R. Deer](#),^{1,*} [Sameer Jain](#),² [Corey Hunter](#),³ and [Krishnan Chakravarthy](#).⁴

There is evidence of the use of peripheral nerve stimulation in a variety of clinical indications that include plexus injuries, focal mononeuropathy, post-amputation pain, back pain, sacroiliac joint pain, headache, facial pain, arm and limb pain.

Prior studies have shown that there are good outcomes from PNS on median, ulnar, sciatic, ilioinguinal, and genito-femoral nerves, brachial plexus and lumbar plexus

Why modulate the DRG?

*Pain Medicine 2014; 15: 1669–1685
Wiley Periodicals, Inc.*

Review Article

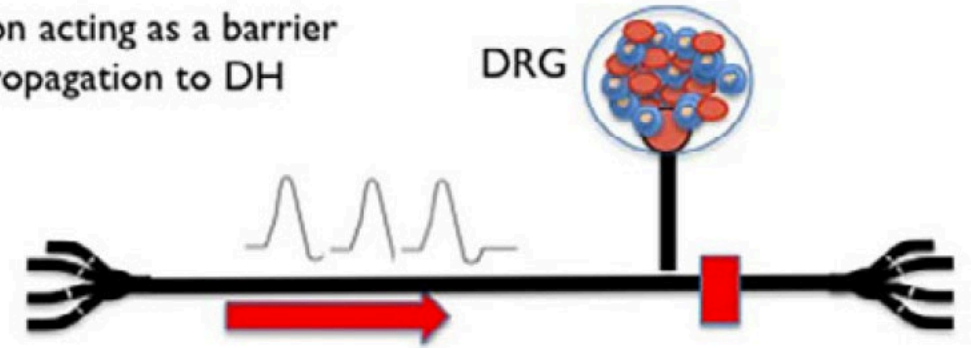
The Role of the Dorsal Root Ganglion in the Development of Neuropathic Pain

Physiological functions

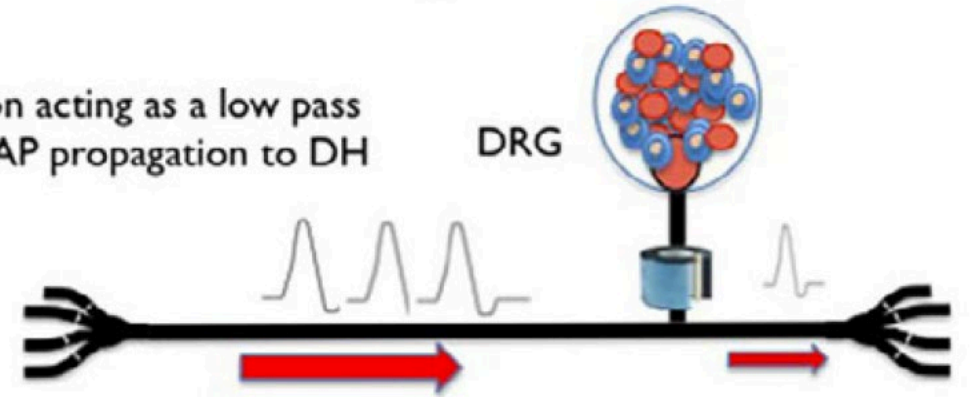
Nutrition

Production of neurotransmitters,
ionic channels, receptors

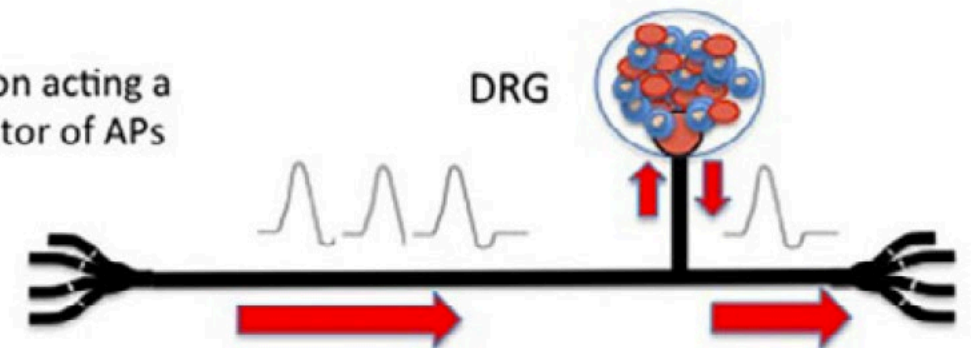
T-junction acting as a barrier
to AP propagation to DH

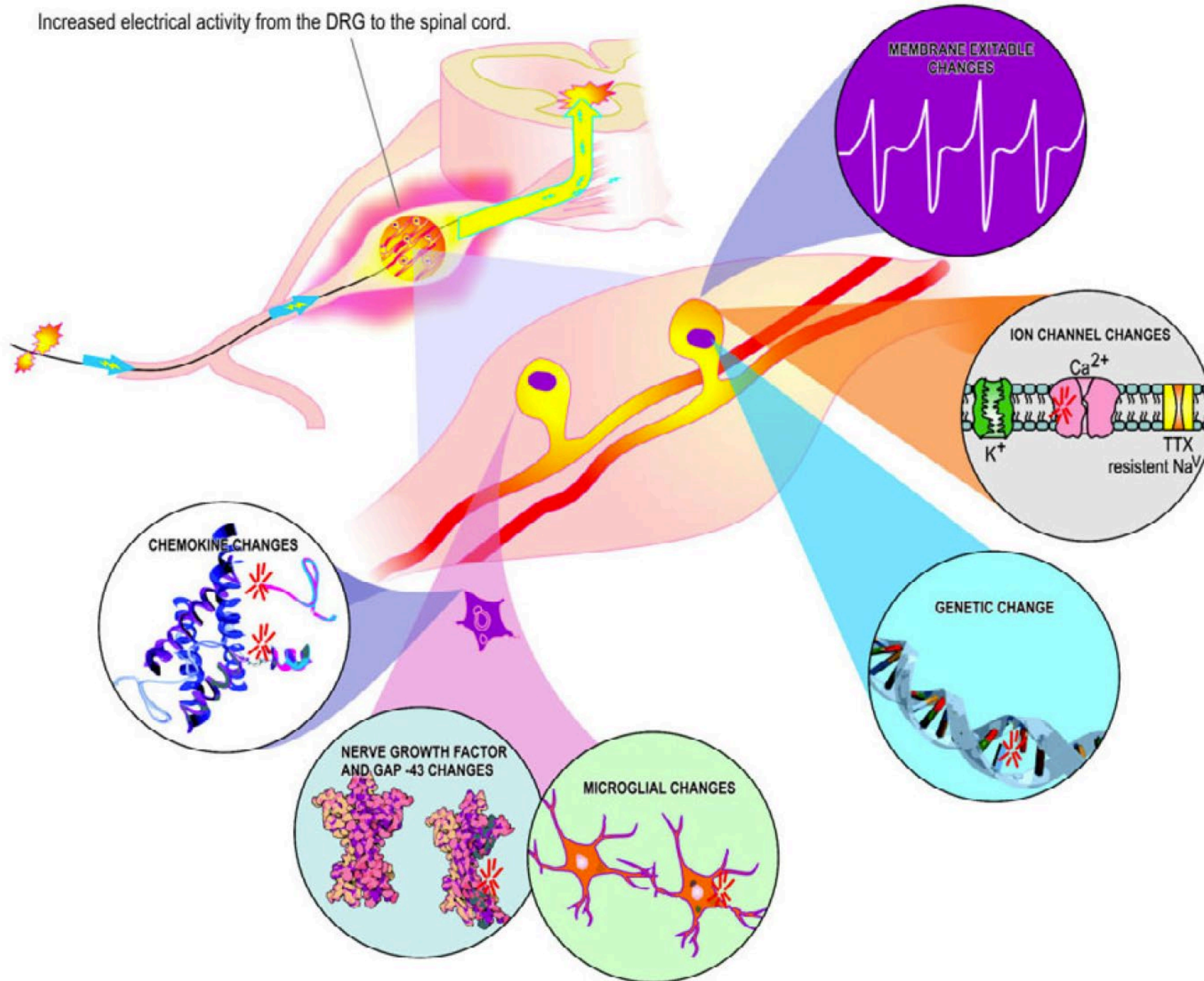


T-junction acting as a low pass
filter of AP propagation to DH



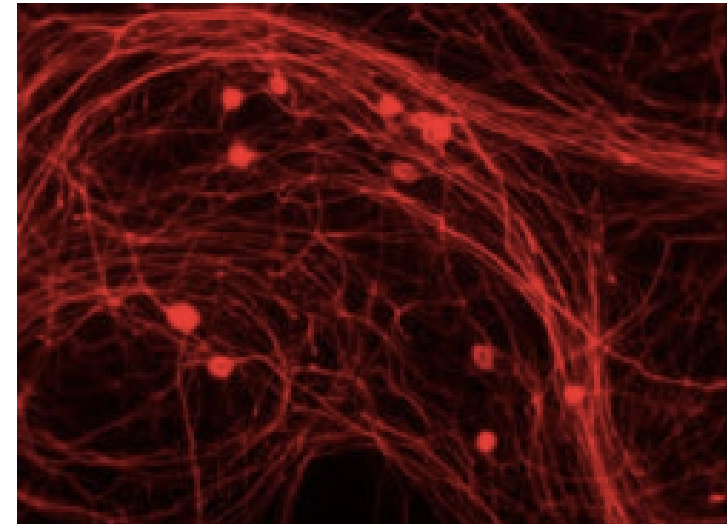
T-junction acting a
propagator of APs





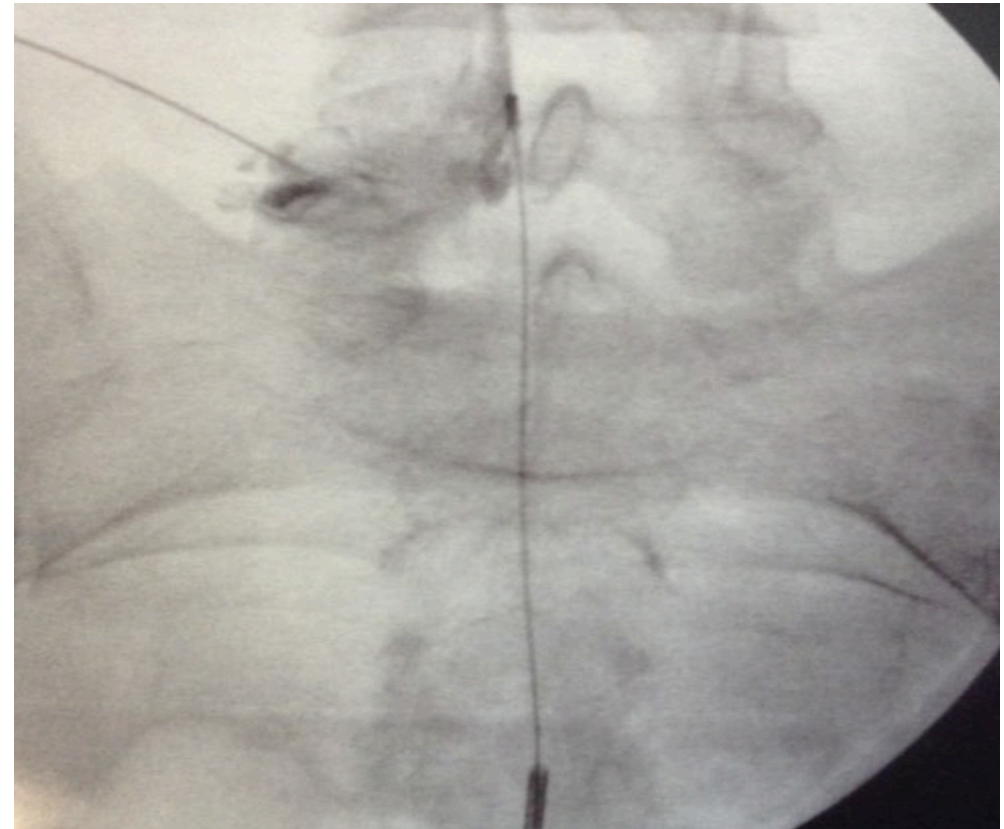
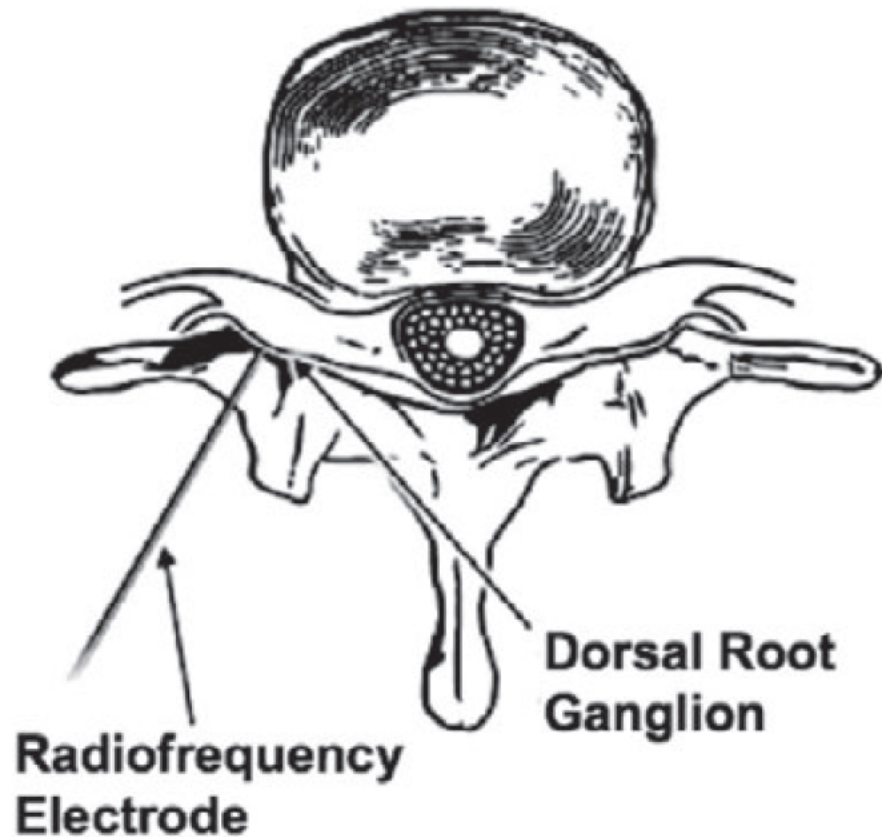
In response to a tissue inflammatory process or injury to a peripheral afferent fiber, the ganglion causes changes in glial cells with the release of chemokines, nerve growth factors, modifies the genetic expression and production of ion channels, in particular Na⁺, K⁺ channels, Ca⁺⁺

- DRGs are outside cerebro-blood-barrier, more susceptible to chemical transported through the blood flow (Devor, 1999)
- Easier to reach by electrical currents for neuromodulation (Deer, 2012)



Pulsed radiofrequency neuromodulation

The treatment typically uses currents at 50,000 Hz in bursts for 20 ms, at a frequency of 2/s, controlling that temperature remains under 42°C.



Mechanisms of action

- The mechanisms of action are poorly known. It seems that the electrical field modifies transiently the myelin along the fibers and the cellular structure in the ganglion: modified expression of Na⁺ channels (Hamann W et al. Eur J Pain. 2006)
- PRF seems to act selectively on A δ e C fibers (Hamann W et al. Eur J Pain. 2006)
- Immunomodulatory effect on CSF lymphocytes and inflammatory mediators (Das Be et al. Brain Behav Immune. 2018)



Brain, Behavior, and Immunity

Volume 70, May 2018, Pages 157-165



Human dorsal root ganglion pulsed radiofrequency treatment modulates cerebrospinal fluid lymphocytes and neuroinflammatory markers in chronic radicular pain

Basabjit Das^a  , Melissa Conroy^b, David Moore^a, Joanne Lysaght^b, Connail McCrory^a

Randomized Trial

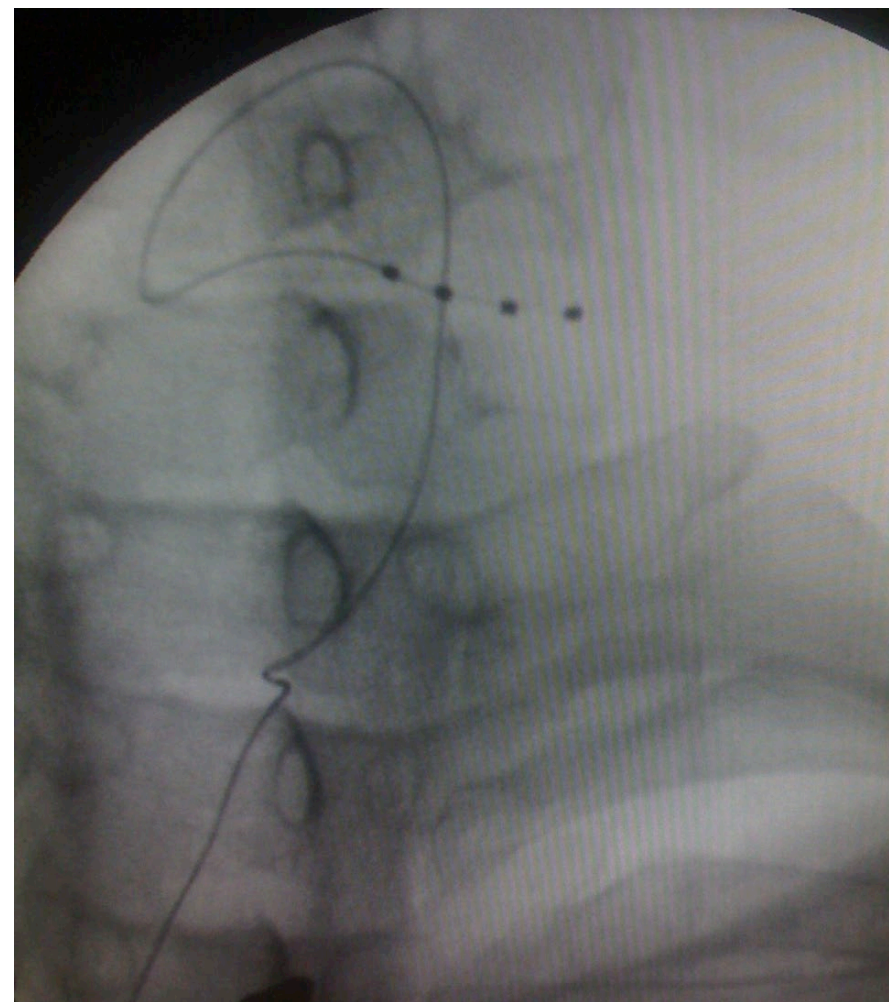
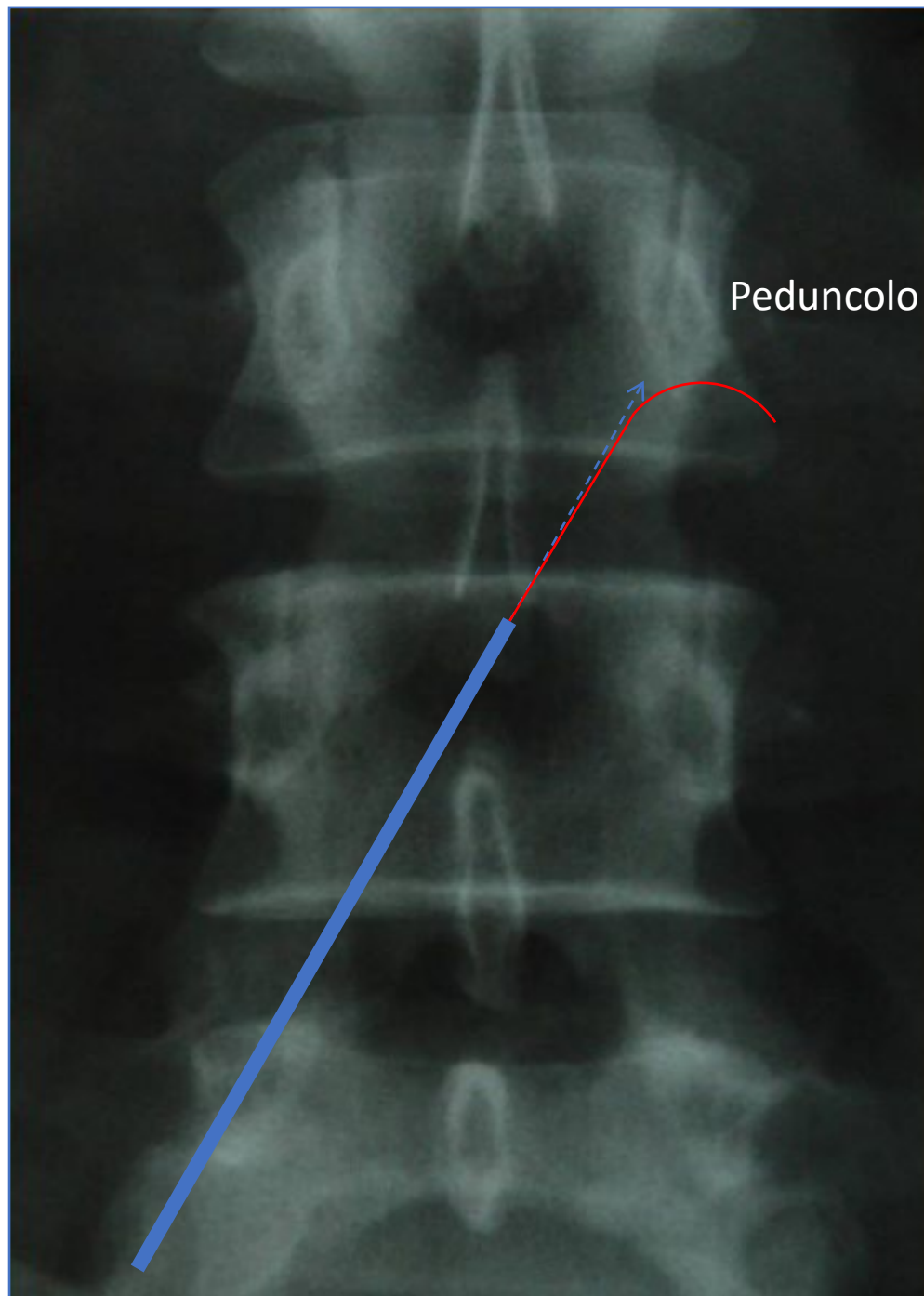
Pulsed Radiofrequency on Thoracic Dorsal Root Ganglion Versus Thoracic Paravertebral Nerve for Chronic Postmastectomy Pain, A Randomized Trial: 6-Month Results

Diab Fuad Hetta, MD¹, Sahar Abdel Baky Mohamed, MD¹, Kawser Hofny Mohamed, MD²,
Taha Abd Elrazek Mahmoud, MD¹, and Hanan Ahmed Eltyb, MD³

The percentage of patients who showed > 50% reduction in their VAS pain score was significantly higher in group DRG compared with group PVN when assessed at 4 and 6 months postprocedure (23/29: 79.3% vs. 13/29: 44.8%; $P = 0.007$) and (22/29: 75.9% vs. 7/29: 24.1%; $P < 0.001$), respectively, however, the 2 groups did not significantly differ at 1, 2, and 3 months postprocedure

During the 6-month follow-up period, the number of patients who discontinued the analgesics they received prior to the procedure were higher in group DRG compared with group PVN

DRG stimulation

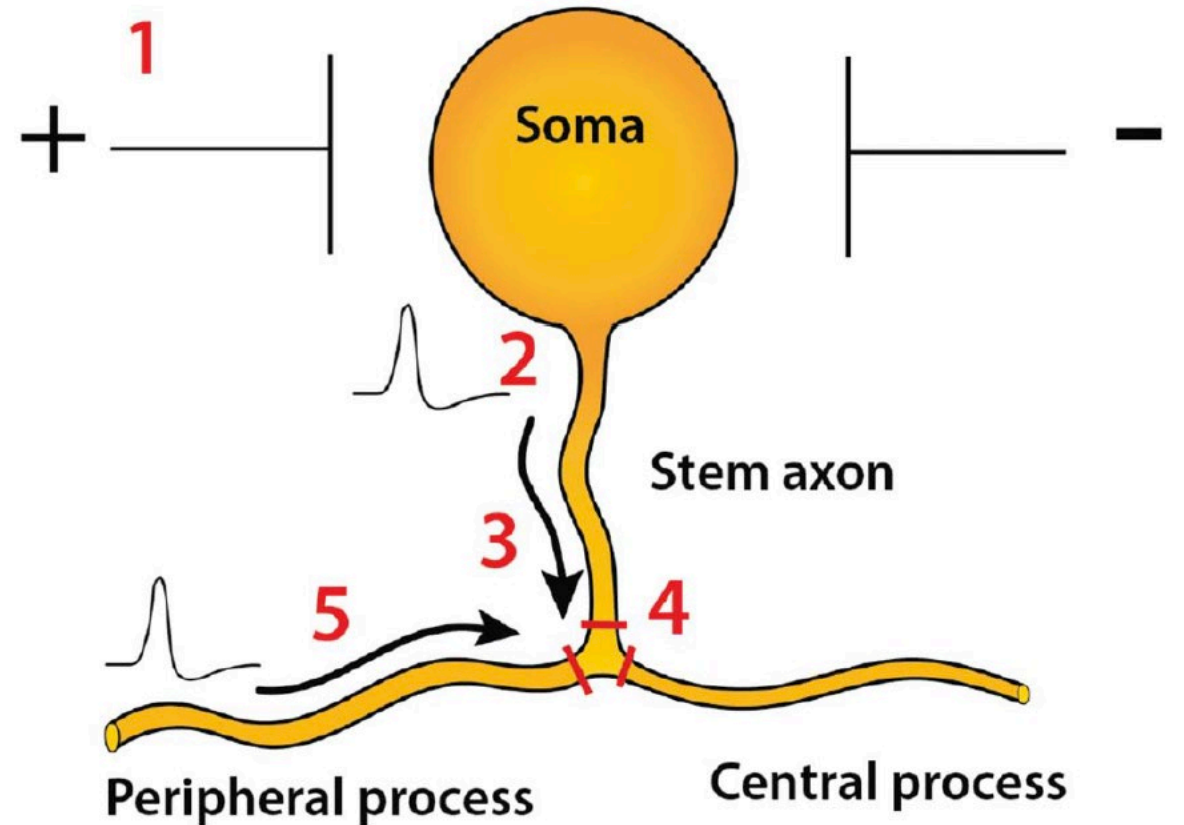


PAIN

Analgesic dorsal root ganglionic field stimulation blocks conduction of afferent impulse trains selectively in nociceptive sensory afferents

Dongman Chao^a, Zhiyong Zhang^{a,b}, Christina M. Mecca^a, Quinn H. Hogan^a, Bin Pan^{a,*}

The application of an electric field on the DRG (1) causes a cell depolarization that evokes an action potential (2) that propagating (3) provokes a reduction of the excitability at the T junction (4) inhibiting the action potential arriving from the periphery (5)

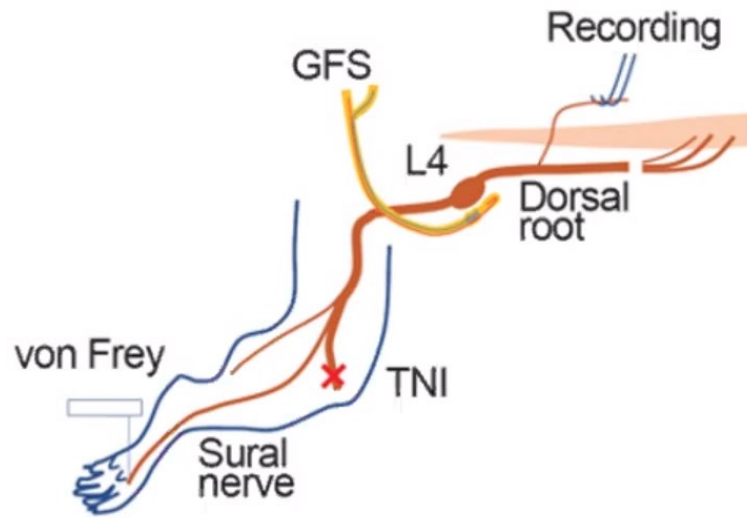


Analgesic dorsal root ganglionic field stimulation blocks conduction of afferent impulse trains selectively in nociceptive sensory afferents

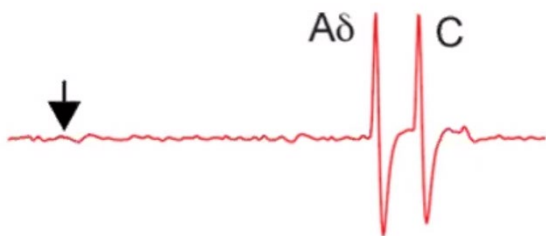
Chao, Dongman^a; Zhang, Zhiyong^{a,b}; Mecca, Christina M.^a; Hogan, Quinn H.^a; Pan, Bin^{a,*}

[Author Information](#)

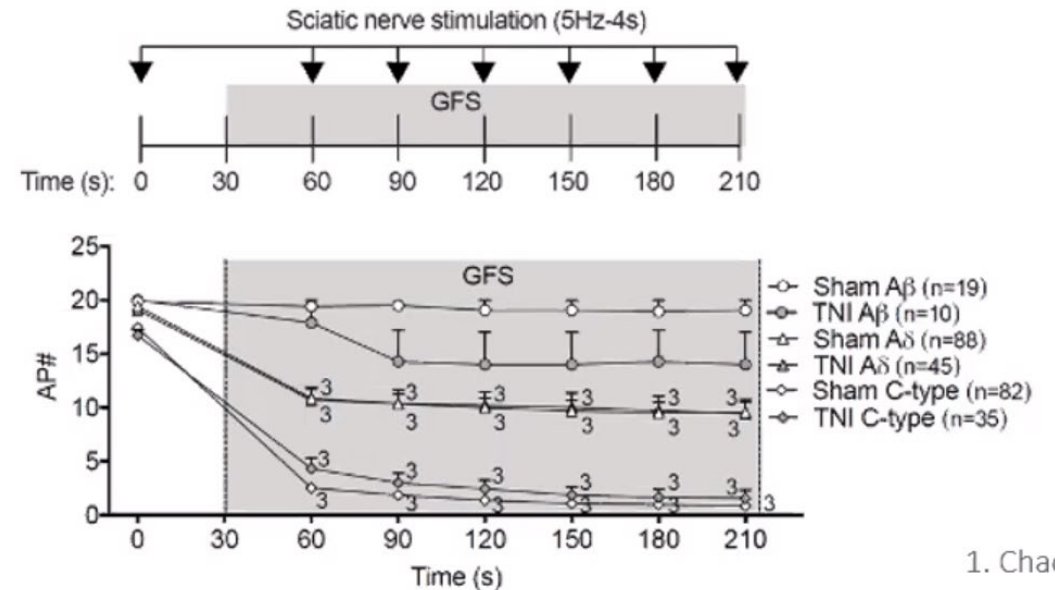
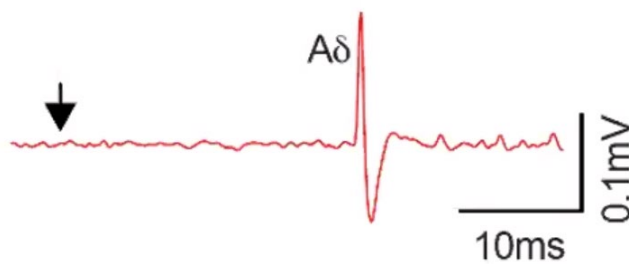
PAIN: December 2020 - Volume 161 - Issue 12 - p 2872-2886



Sciatic nerve stimulation
Before GFS



Sciatic nerve stimulation
During 20Hz GFS



ANESTHESIOLOGY



Dorsal Root Ganglion Stimulation Alleviates Pain-related Behaviors in Rats with Nerve Injury and Osteoarthritis

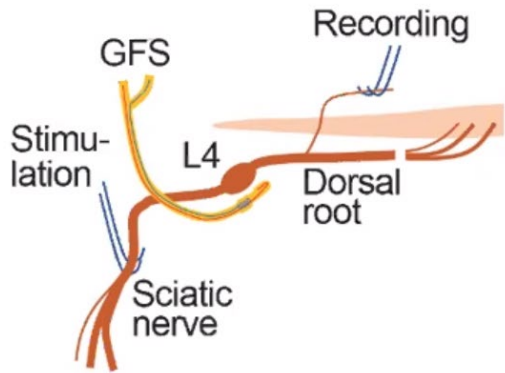
Guoliang Yu, Ph.D., Ian Segel, B.S.,
Zhiyong Zhang, M.D., Ph.D., Quinn H. Hogan, M.D.,
Bin Pan, M.D., Ph.D.

Anesthesiology 2020; 133:408–25

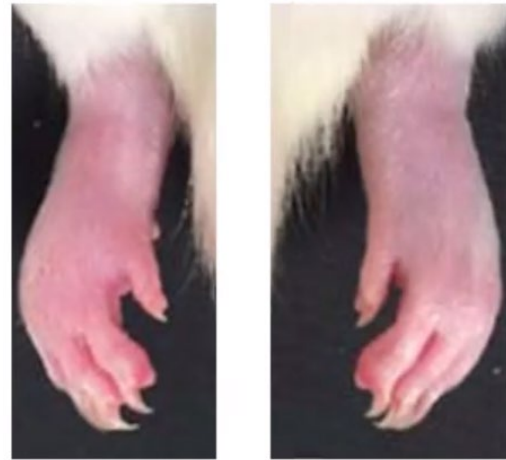
Review Article

Dorsal Root Ganglion Field Stimulation Prevents Inflammation and Joint Damage in a Rat Model of Rheumatoid Arthritis

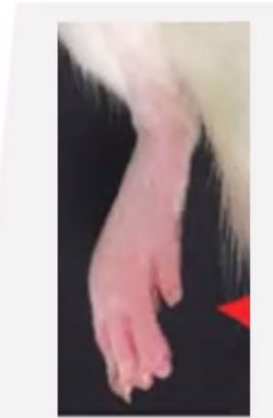
Bin Pan PhD, Zhiyong Zhang MD, PhD, Dongman Chao PhD, Quinn H. Hogan MD



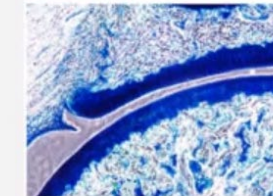
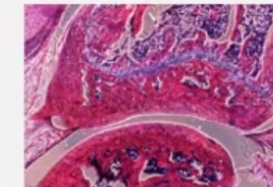
NO DRG STIMULATION



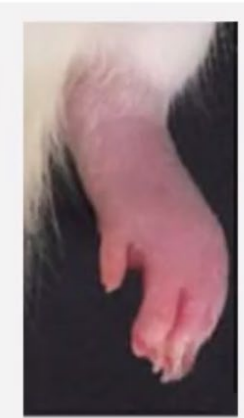
DRG STIMULATION



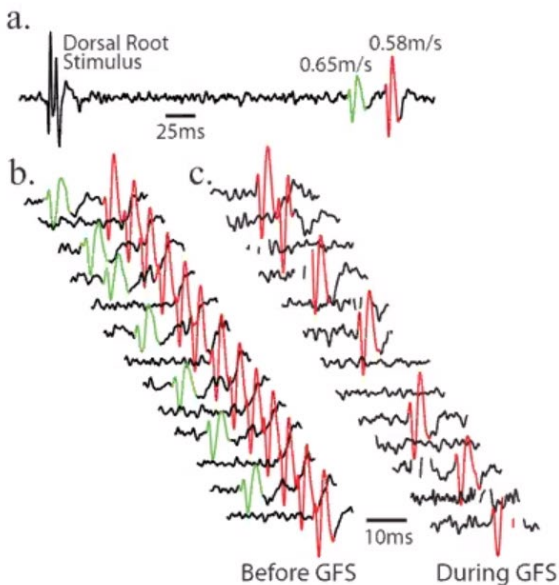
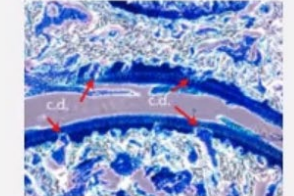
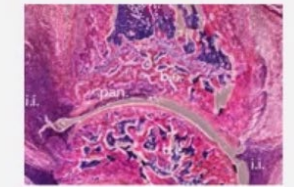
CIA + GFSipsi



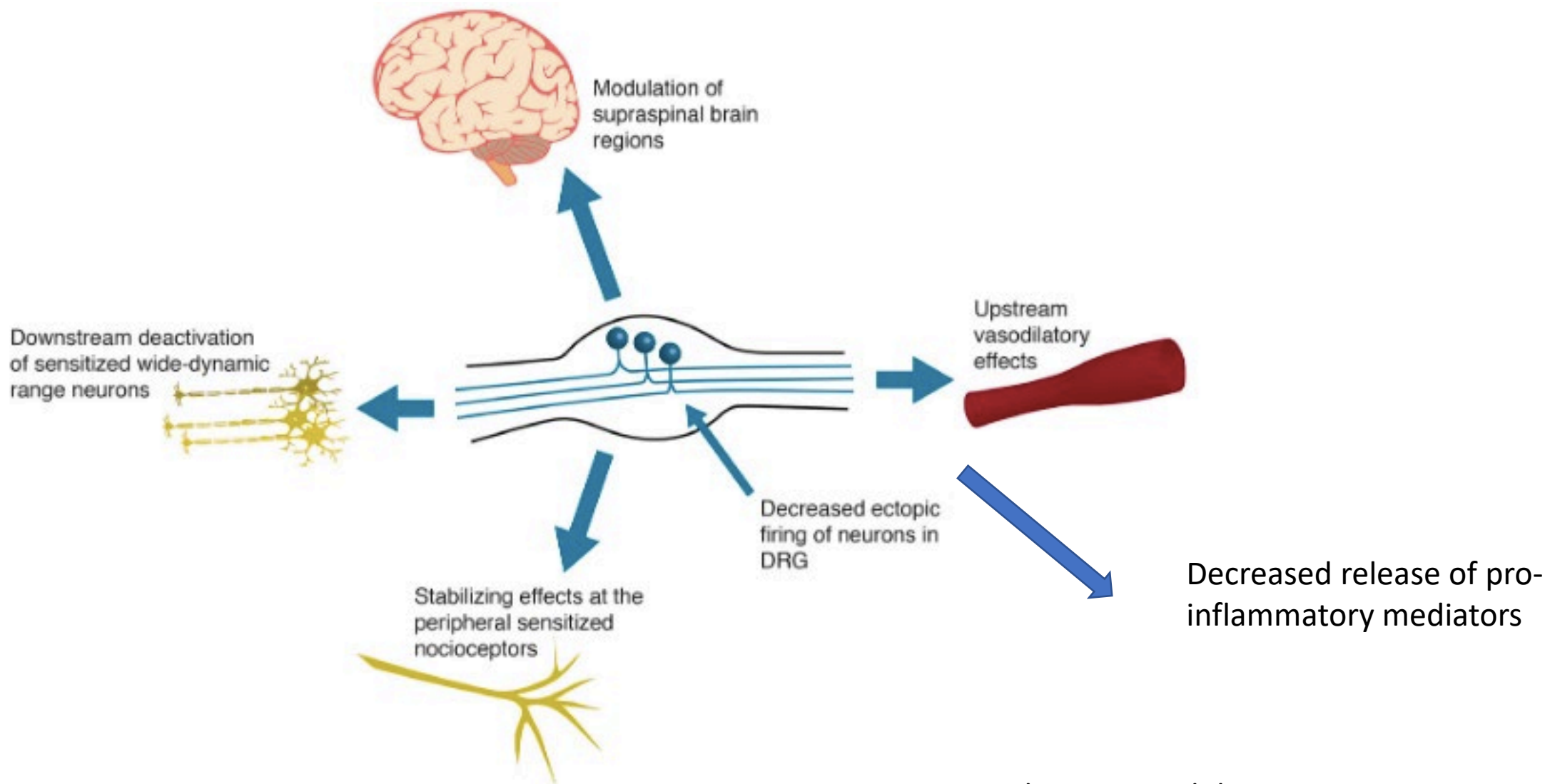
SHAM DRG STIMULATION



CIA + GFScontra



Possible effects of DRG stimulation



PRF stimulation before DRG implant

Neuromodulation: Technology at the Neural Interface

Received: June 5, 2013 Revised: July 5, 2013 Accepted: August 6, 2013

(onlinelibrary.wiley.com) DOI: 10.1111/ner.12113

LETTER TO THE EDITOR

Paresthesia Mapping: A Practical Workup for Successful Implantation of the Dorsal Root Ganglion Stimulator in Refractory Groin Pain

Neuromodulation: Technology at the Neural Interface

Received: November 25, 2016 Revised: January 10, 2017 Accepted: January 30, 2017

(onlinelibrary.wiley.com) DOI: 10.1111/ner.12595

Selective Radiofrequency Stimulation of the Dorsal Root Ganglion (DRG) as a Method for Predicting Targets for Neuromodulation in Patients With Post Amputation Pain: A Case Series

Corey W. Hunter, MD*; Ajax Yang, MD[†]; Tim Davis, MD[‡]

Take at home message

- PNS acts on the same first order neurons involved in SCS (in SCS other neurons and non neural cells can be involved) but paresthesia coverage is more precise
- DRGs acts on the soma with different mechanisms but first order neurons are involved with a different anatomical distribution from PNS and SCS