

# Dorsal Root Ganglion Stimulation: Future Directions

Michael S. Leong, MD  
Director of Neuromodulation  
Clinical Professor  
Stanford University

# Dorsal Root Ganglion Stimulation: Future

- CONSULTANT: SORRENTO THERAPEUTICS – RESINIFERATOXIN
- GRANT/RESEARCH SUPPORT: WEX PHARMACEUTICALS – HALNEURON (TETRODOTOXIN)
- SPEAKER'S BUREAU: NONE
- SHAREHOLDER: NONE
- OTHERS:
  - Co-director of Advocacy and Legislative Fellowship, North American Neuromodulation Society
  - Board of Directors (Founding Secretary), Pacific Spine and Pain Society
  - Board of Directors, American Society of Pain and Neuroscience

**This presentation DOES contain off-label and/or investigational uses of drugs or products.**

# Dorsal Root Ganglion Stimulation

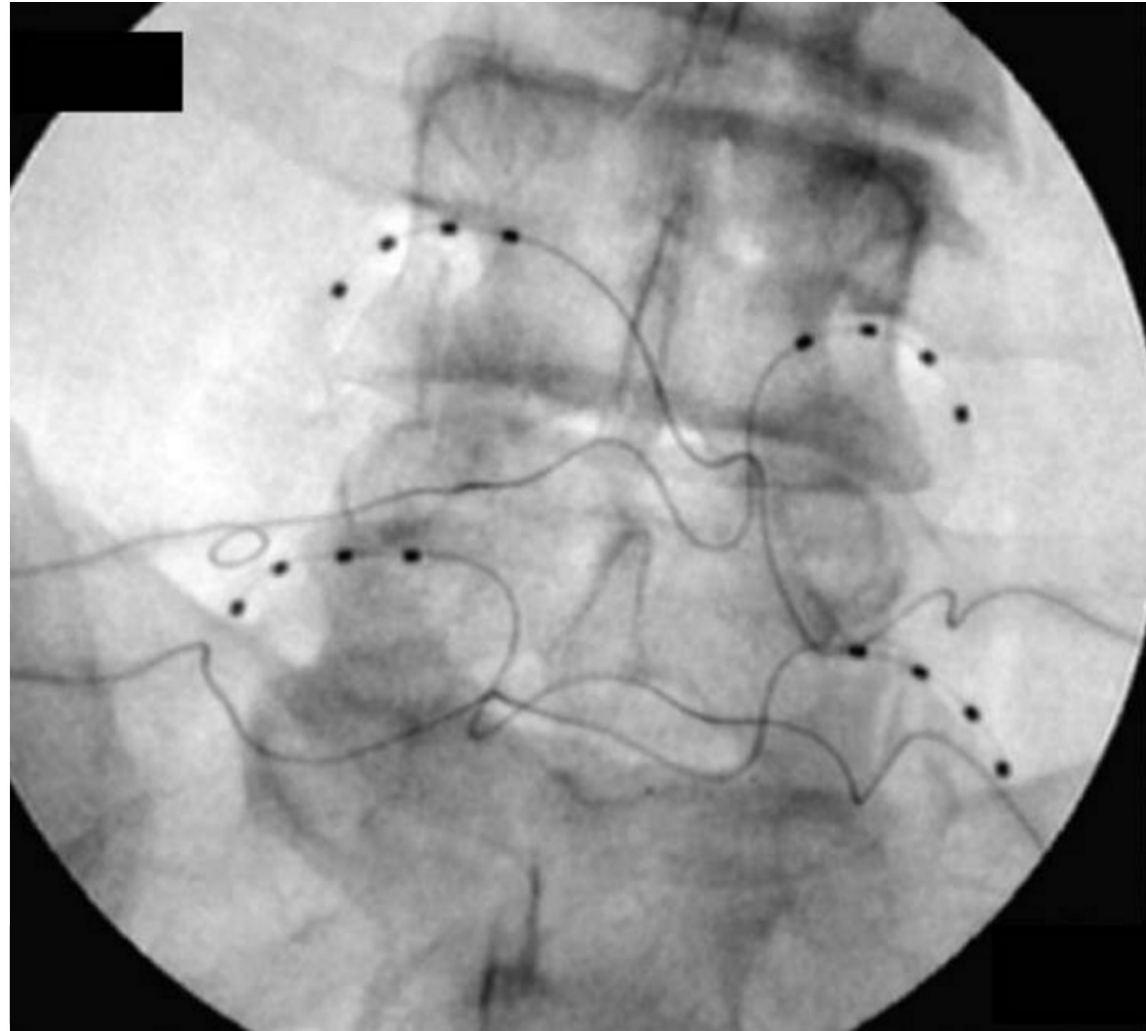
- Learning Objectives

- What is Dorsal Root Ganglion Stimulation?
- What are the Budapest Criteria for CRPS?
- How does DRG Stimulation change blood flow and blood pressure?

- Literature References

- Deer TR, Levy R, Kramer J, et al. Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain syndrome and causalgia at 3 and 12 months: a randomized comparative trial. Pain 2017; 158: 669-681.
- Graham R, Sankarasubramanian V, Lempka S. Dorsal Root Ganglion Stimulation for Chronic Pain: hypothesized mechanisms of action. The Journal of Pain 2022; 23 (2); 196-211.

## Dorsal Root Ganglion Stimulation

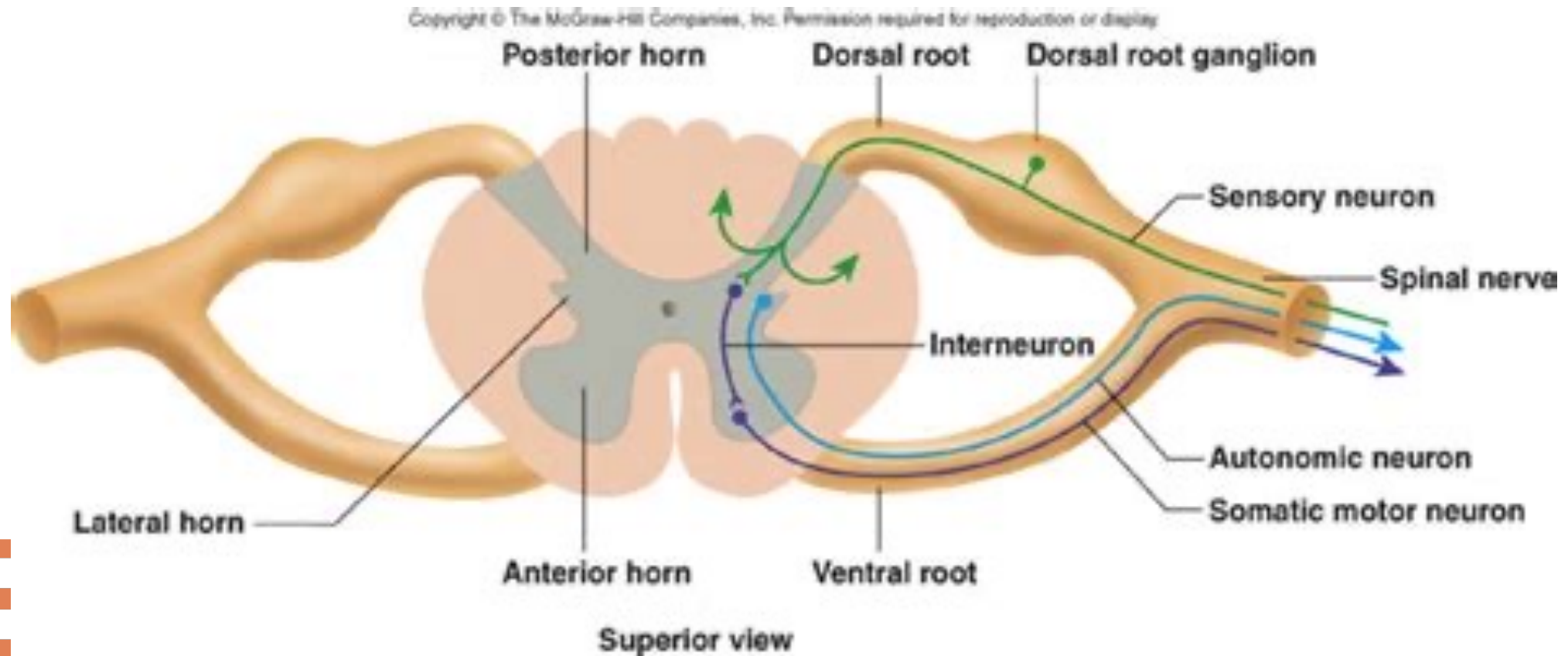




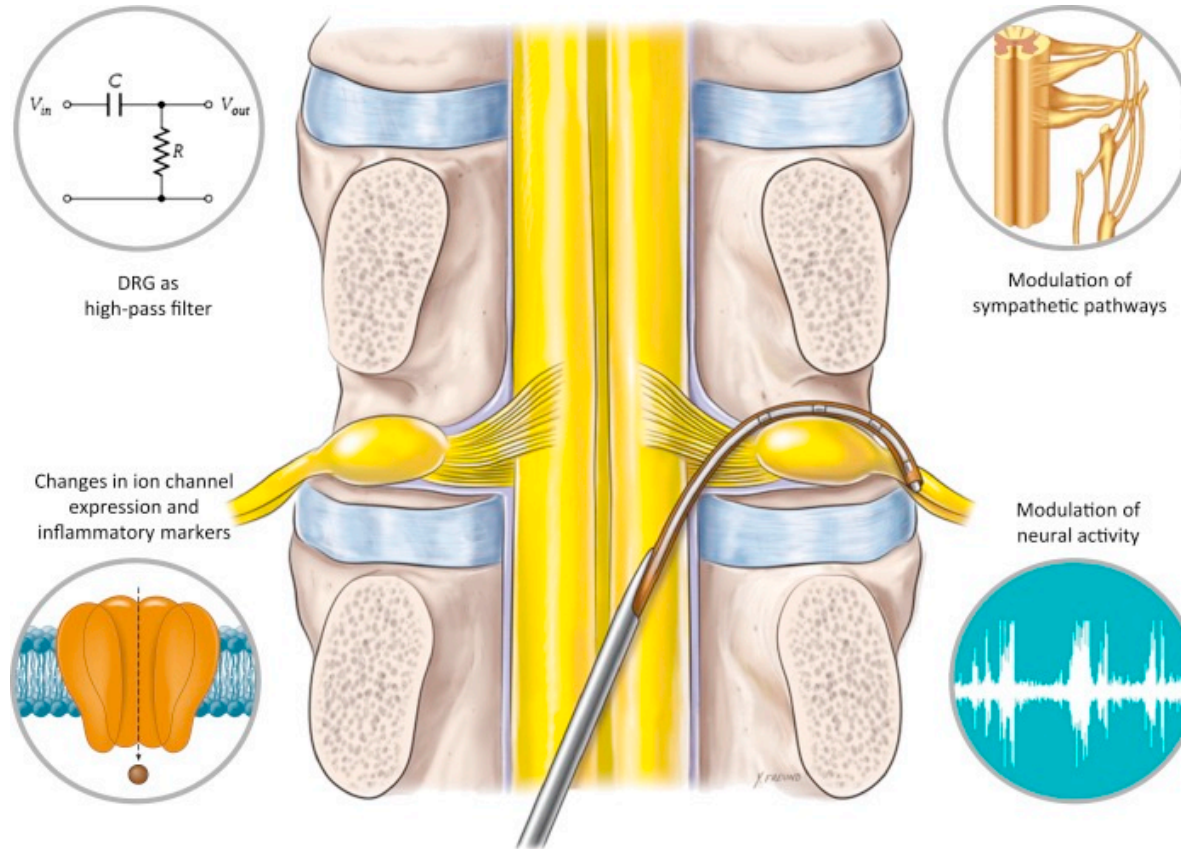
# What is Dorsal Root Ganglion stimulation?

- Definition: "the alteration of nerve activity through targeted delivery electrical stimulation to the dorsal root ganglion"
- Designed to address the lack of precision for SCS to treat chronic pain
- How is DRG different from SCS
  - Targeted stimulation at the site of pain
  - Less energy for stimulation
  - Can be paresthesia-free
  - Less movement of leads with activity

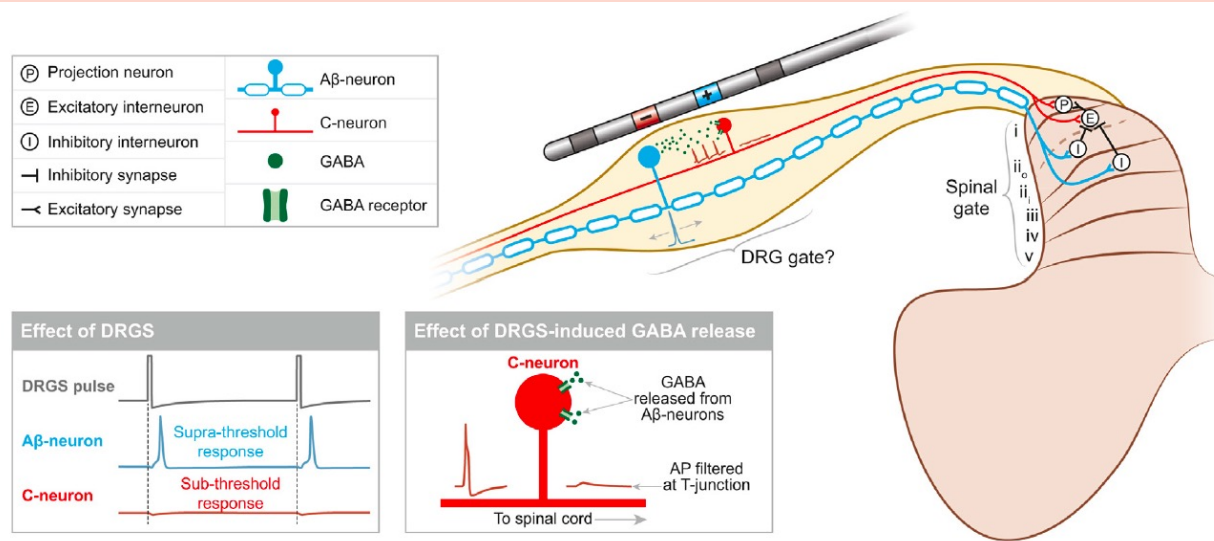
# Dorsal Root Ganglion from medical school



# Various mechanisms of action



# DRG Stimulation Mechanisms of Action



**Figure 2.** DRGS may drive pain-gating mechanisms in the spinal cord dorsal horn, the DRG, or both. DRGS applies trains of electrical pulses which induce APs in Aβ-neurons, which activate inhibitory interneurons in lamina ii, and iii in the dorsal horn. Concurrently, Aβ-neurons may release GABA within the DRG, which can act on C-neurons and potentially prevent ectopic APs from propagating to the spinal cord.

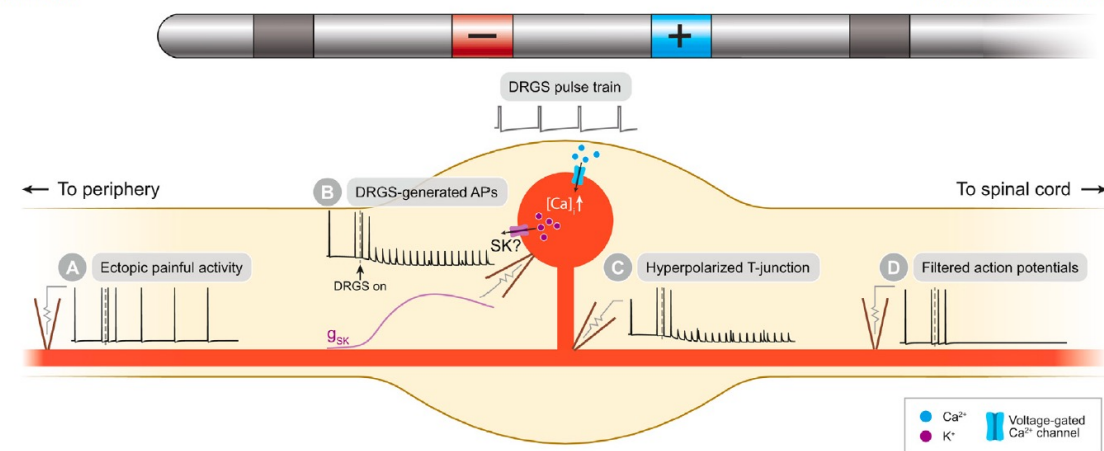
- Direct neural response to DRGS
  1. Driving pain-inhibition circuitry
  2. Augmenting low-pass filtering at T-junction of primary sensory neurons
  3. Suppressing hyperexcitability of PSNs in chronic pain states
- Indirect effects of DRGS
  - Spinal / segmental effects
  - Supraspinal
- Effects on Glia

# T-junction for Dorsal Root Ganglion

- T-junction is the region where the axon bifurcates spinally and peripherally
- T-junction is a large node of Ranvier; peripheral axon larger than spinal axon
- Can produce a ***low-pass filtering effect on action potentials***
- DRGS may provide analgesia by augmenting the filtering property in the DRG neurons responsible for pain pathophysiology

Graham et al

The Journal of Pain 201



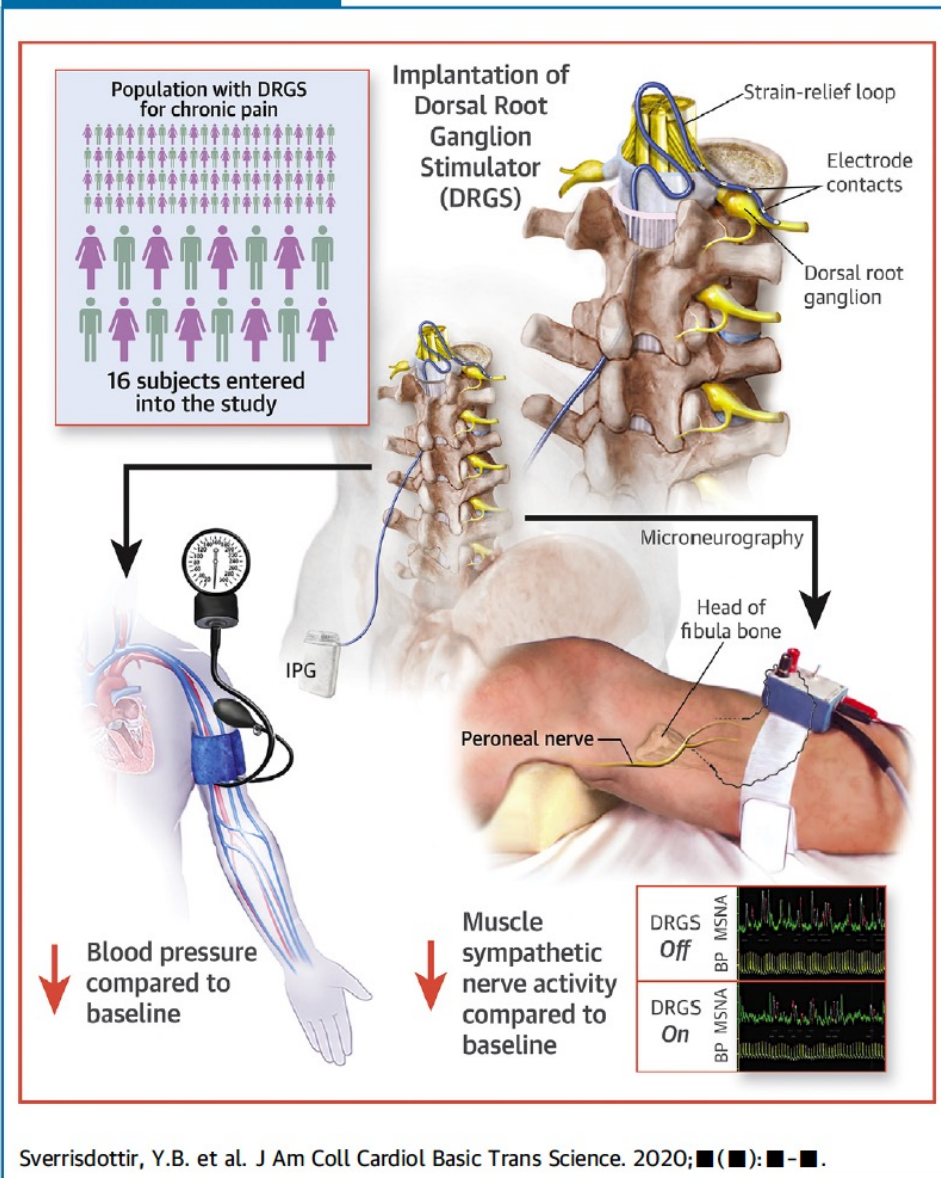
**Figure 3.** DRGS may augment the low-pass filtering properties of nociceptive C-neurons. A) Ectopic APs indicative of spontaneous pain propagate along the peripheral axons of C-neurons towards the central nervous system. B) The DRGS pulse train induces APs in or near C-neuron somata causing calcium influx through voltage-gated calcium channels, putatively triggering potassium efflux through calcium-activated SK channels. C) Potassium efflux hyperpolarizes the soma, which electrotonically hyperpolarizes the T-junction. D) Orthodromically propagating APs are unable to propagate passed the hyperpolarized T-junction into the spinal axon.



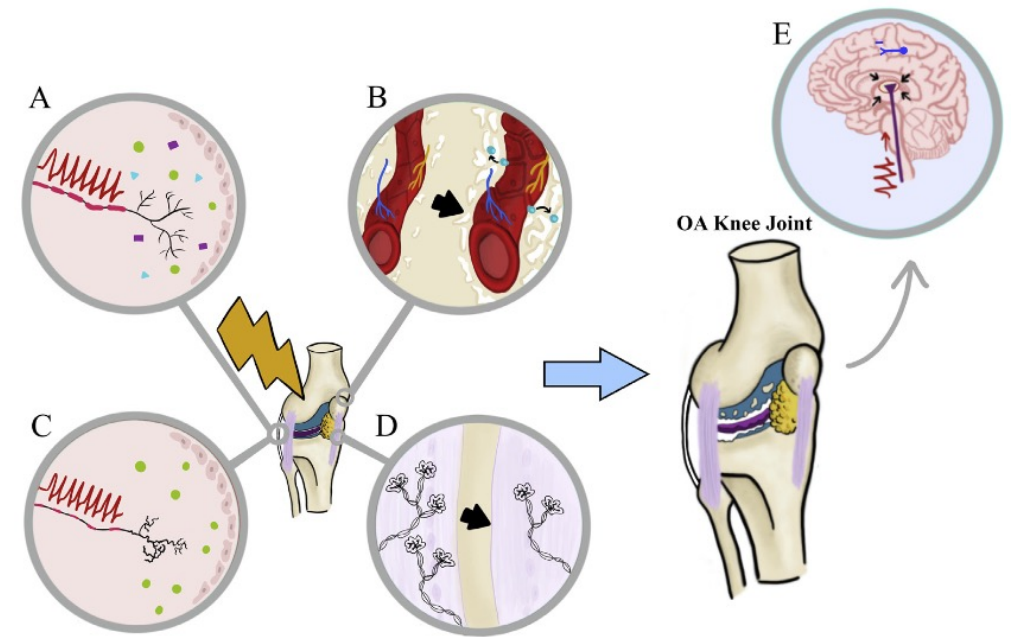
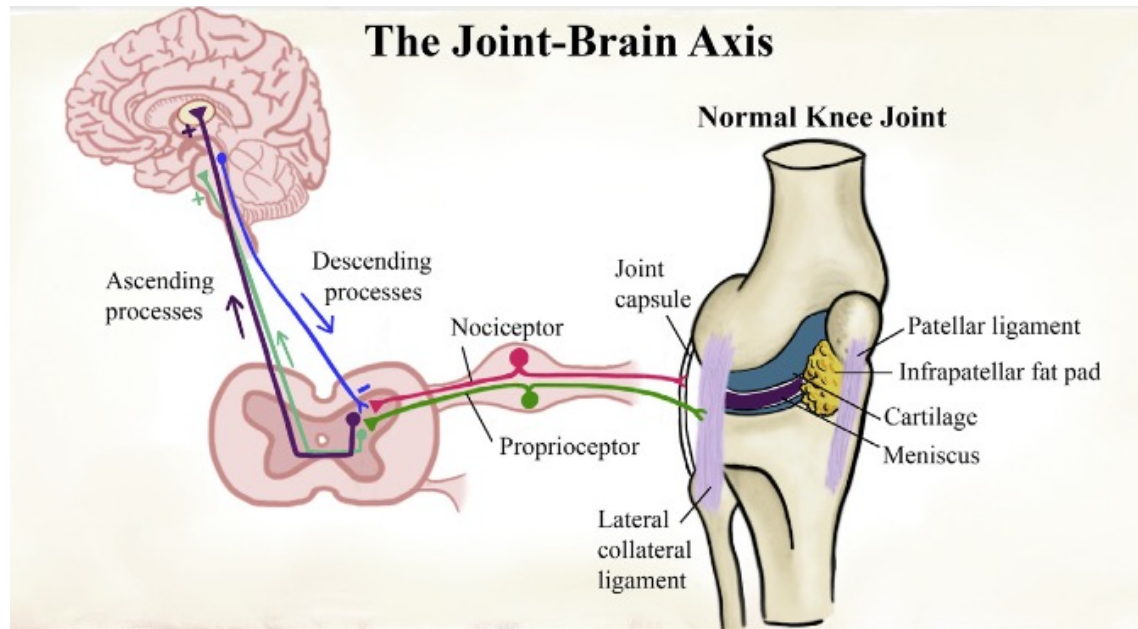
# Autonomic Neuromodulation

- Parker Clinical Autonomic Research 2021
  - Modulation of sympathetic – vagal balance in blood pressure
  - Posture-dependent mobility associated pain
- Sverrisdottir J Am Coll Cardio Basic Trans Science 2020
  - Reduces sympathetic outflow and long term blood pressure
  - Only left-side stimulation; independent of pain; mostly lumbar L1, L2, L5, C6

## VISUAL ABSTRACT



# NEUROGENIC INFLAMMATORY REFLEX ARC<sup>1</sup>



1. Chiu 2012

Chiu I, et al. Neurogenic inflammation and peripheral nervous system in host defense and immunopathology. Nature Neuroscience 2012

# Lane Medical Library search for DRG

## ARTICLE

### Coccydynia Treated with **Dorsal Root Ganglion Stimulation**.

Giordano NL, van Helmond N, Chapman KB.

*Case Rep Anesthesiol.* 2018;2018:5832401.

[Preview Abstract](#)

Source: [PubMed](#)

[Get shareable link](#)

[Direct to PDF](#)



## ARTICLE

### A Case Series of Permanent **Dorsal Root Ganglion Stimulation**.

Lee T, Omosor E, Hussain N.

*Cureus.* 2022 Jan;14(1):e21193.

[Preview Abstract](#)

Source: [PubMed](#)

[Get shareable link](#)

[Direct to PDF](#)



## ARTICLE

### Neuromodulation: a focus on **dorsal root ganglion stimulation**.

Bremer N, Ruby J, Weyker PD, Webb CA.

*Pain Manag.* 2016;6(3):205-9.

Source: [PubMed](#)

[Get shareable link](#)



## ARTICLE

### **Dorsal root ganglion stimulator** for avascular necrosis of the hip.

Victor S, Burnett C, Lange R, Pohler K.

*Proceedings (Baylor University Medical Center).* 2018 Oct;31(4):532-533.

[Preview Abstract](#)

Source: [PubMed](#)

[Get shareable link](#)

[Direct to Full Text](#)



## ARTICLE

### **Dorsal root ganglion stimulation** for refractory post-herpetic neuralgia.

Kim JH, Apigo A, Fontaine C.

*Pain Pract.* 2021 09;21(7):794-798.

[Preview Abstract](#)

Source: [PubMed](#)

[Get shareable link](#)

[Direct to PDF](#)



## ARTICLE

### **Dorsal Root Ganglion Stimulation** for Chronic Groin Pain: A Review.

Char S, Barman RA, Deer TR, Hagedorn JM.

*Neuromodulation.* 2021 Jun 02





# Subcategories from Medline search

Abdominal pain

Avascular Necrosis  
of the hip

Cervical CRPS

Chemotherapy  
induced  
neuropathy

Knee pain

Pelvic Pain: groin  
pain, coccydynia

Post-herpetic  
Neuralgia

Supraspinal effects

Thoracic neuralgia  
post surgical

Ventricular  
arrhythmogenicity

1	<input type="checkbox"/>	Recruiting	<a href="#">Comparative Study in Patients With Refractory Chronic Lower Limb Neuropathic Pain and/or Back Neuropathic Pain.</a>	<ul style="list-style-type: none"> <li>Pain, Neuropathic</li> </ul>	<ul style="list-style-type: none"> <li>Other: Spinal Cord Stimulation, association of both (DUAL), Dorsal Root Ganglion stimulation</li> </ul>	<ul style="list-style-type: none"> <li>Poitiers University Hospital Poitiers, France</li> </ul>
2	<input type="checkbox"/>	Completed <a href="#">Has Results</a>	<a href="#">A Study to Confirm the Safety of High Frequency DRG Stimulator in Patients With Chronic Lower Limb Pain</a>	<ul style="list-style-type: none"> <li>Failed Back Surgery Syndrome</li> <li>Complex Regional Pain Syndrome (CRPS)</li> </ul>	<ul style="list-style-type: none"> <li>Device: GiMer Medical MN 1000 External Stimulator</li> </ul>	<ul style="list-style-type: none"> <li>China Medical University Hospital Taichung, Taiwan</li> </ul>
3	<input type="checkbox"/>	Active, not recruiting	<a href="#">TARGET Post-Approval Study</a>	<ul style="list-style-type: none"> <li>Complex Regional Pain Syndrome (CRPS)</li> </ul>	<ul style="list-style-type: none"> <li>Device: Dorsal Root Ganglion (DRG) Stimulation (Axiu™ Neurostimulator System)</li> <li>Device: Dorsal Root Ganglion (DRG) Stimulation (Proclaim™ Neurostimulator System)</li> </ul>	<ul style="list-style-type: none"> <li>Arizona Pain Specialists Scottsdale, Arizona, United States</li> <li>Spanish Hills Interventional Pain Specialists Camarillo, California, United States</li> <li>California Orthopedics &amp; Spine Larkspur, California, United States</li> <li>(and 42 more...)</li> </ul>
4	<input type="checkbox"/>	Active, not recruiting	<a href="#">Intermittent vs. Continuous Dorsal Root Ganglion Stimulation</a>	<ul style="list-style-type: none"> <li>Pain, Intractable</li> <li>Pain, Chronic</li> </ul>	<ul style="list-style-type: none"> <li>Device: Dorsal Root Ganglion Stimulation (DRG-S)</li> </ul>	<ul style="list-style-type: none"> <li>Spine and Pain Institute NY New York, New York, United States</li> </ul>
5	<input type="checkbox"/>	Unknown <sup>†</sup>	<a href="#">Study to Evaluate the Effectiveness of DRG Stimulation for Discogenic Low Back Pain</a>	<ul style="list-style-type: none"> <li>Discogenic Low Back Pain</li> </ul>	<ul style="list-style-type: none"> <li>Device: Dorsal Root Ganglion Stimulation</li> </ul>	<ul style="list-style-type: none"> <li>Rijnstate Ziekenhuis, Velp Velp, Arnhem, Netherlands</li> </ul>
6	<input type="checkbox"/>	Not yet recruiting	<a href="#">Intermittent Dosing of Dorsal Root Ganglion Stimulation as an Alternate Paradigm to Continuous Low-Frequency Therapy</a>	<ul style="list-style-type: none"> <li>CRPS (Complex Regional Pain Syndromes)</li> <li>Radiculopathy</li> <li>Peripheral Neuropathy</li> </ul>	<ul style="list-style-type: none"> <li>Device: DRG stimulation 20 Hz 30/90</li> <li>Device: DRG stimulation 5 Hz 30/90</li> </ul>	
7	<input type="checkbox"/>	Not yet recruiting	<a href="#">Prediction of Recruitment Potential of Participating Centers in Clinical Trials by Standardized Translation of Selection Criteria and Queries From DRG Database</a>	<ul style="list-style-type: none"> <li>Multicenter Clinical Study</li> </ul>		<ul style="list-style-type: none"> <li>Department of Public Health - Hôpital Ambroise Paré Boulogne-Billancourt, Hauts-de-Seine, France</li> </ul>

# Clinicaltrials.gov

- CRPS
- Discogenic Low Back Pain
- Failed Back Surgery Syndrome
- Neuropathic pain
- Peripheral Neuropathy
- Radiculopathy

# Budapest Criteria for CRPS

All of the following criteria must be met:

- Continuing pain that is disproportionate to the inciting event
- 1 sign in 2 or more of the categories below
- 1 symptom in 3 or more of the categories below
- No other diagnosis can better explain the signs and symptoms

Category	Signs/Symptoms
<b>Sensory</b>	Allodynia (pain to light touch or temperature sensation and/or deep somatic pressure and/or joint movement) and/or hyperalgesia (to pinprick)
<b>Vasomotor</b>	Temperature asymmetry and/or skin color changes and/or skin color asymmetry
<b>Sudomotor/Edema</b>	Edema and/or sweating changes and/or sweating asymmetry
<b>Motor/Trophic</b>	Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)

# Complex Regional Pain Syndrome

- NIH definition: a broad term describing excess and prolonged pain and inflammation that follows an injury to an arm or leg.
  - Historically, CRPS-1 (RSD) when there was uncertainty about the exact nerve injured
  - If a specific nerve is injured, diagnosis is CRPS-II (causalgia)
- Pain in CRPS and Causalgia (US label- which states in accordance with ACCURATE study causalgia does not need to meet Budapest criteria), many prospective studies, excellent outcomes
  - Post-surgical nerve pain: post-thoracotomy, post-mastectomy
  - Peripheral neuropathies: ilioinguinal

# Ongoing clinical studies

## Cohort Studies on:

- Discogenic low back pain
- Osteoarthritis
- Post-herpetic neuralgia /Polyneuropathy
- Peripheral vascular disease / Chronic limb ischemia
- Refractory Hypertension

IDE Pilot Study started on osteoarthritis on the knee (N=30) NCT05103527

# Wish list for the Future



Supraspinal effects as biomarker for neuropathic pain



Heart: blood pressure and arrhythmias

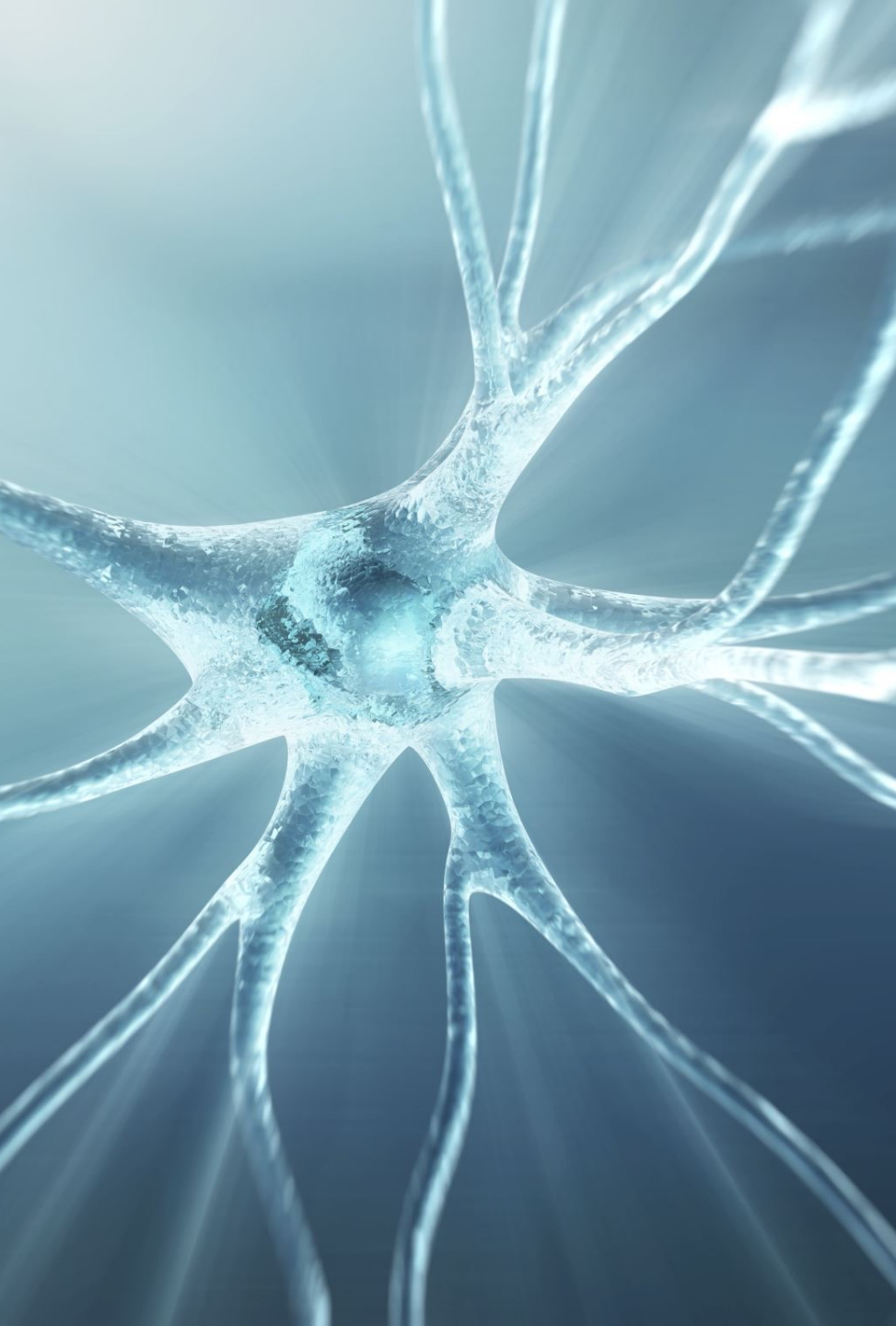


Back pain – ANYWHERE  
Joint pain – Knees and beyond



Wireless





# DRG Summary and Conclusions

---

- Dorsal Root Ganglion Stimulation approved for CRPS types 1 & 2
- DRG mechanisms of action
  - Direct neural effects of primary sensory neurons and t-junctions
  - Indirect supraspinal effects and at autonomic system (blood pressure and vasculature)
  - IDE study on joint (knee) pain and potentially others
- The Future of DRG for Pain Treatment
  - Beyond pain: blood pressure control, arrhythmias, vasculature
  - Dorsal Root Ganglion for specific back, trunk, and extremity regions
  - Simpler placement in spine with **wireless** stimulation

**Michael S. Leong, MD**

**[msleong@stanford.edu](mailto:msleong@stanford.edu)**

450 BROADWAY STREET  
PAVILION A, 1<sup>ST</sup> FLOOR  
REDWOOD CITY, CA 94063  
WORK: 650-723-6238

