Emerging options for neuropathic pain management

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April 9, 2025

WashU Medicine

the FOUNDATION for PERIPHERAL NEUROPATHY

Disclosures

- Continued medical education supported by Medtronic, Boston Scientific and SPR Therapeutics

Introduction

WashU Medicine

St. Louis, MO

Dedicated to understanding the mechanisms of chronic neuropathic pain and translating discoveries into novels therapies

Pain Physician

Researcher (Principal Investigator)

Outline

- Foundations
- Overview of Neuropathic Pain Management
- Advanced Neuromodulation Interventions
- Looking Ahead
- Research

Definitions

Peripheral neuropathy is defined as a disease or degenerative state of the peripheral nerves in which motor, sensory, or vasomotor nerve fibers are affected

Neuropathic Pain: Pain caused by a lesion or disease of the somatosensory nervous system[1]

Pain: An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage

Nociceptive Pain: Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors.

Definition and Clinical Manifestations of Peripheral Neuropathy

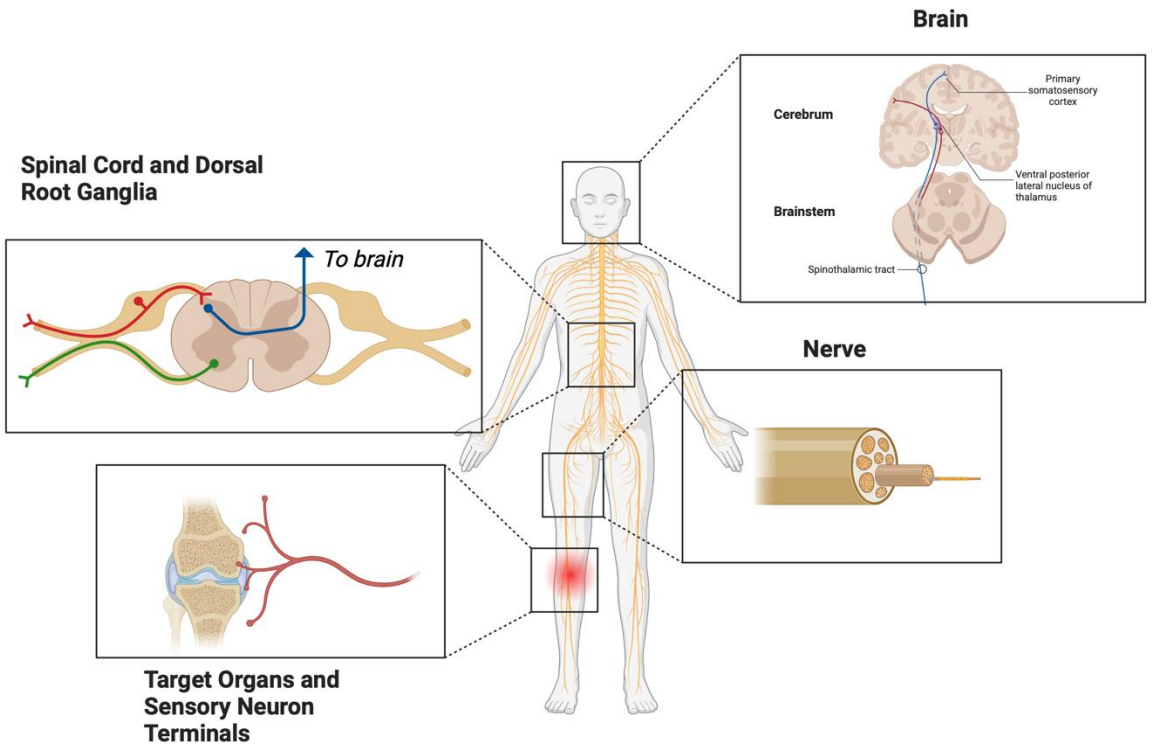
Peripheral neuropathy is defined as a disease or degenerative state of the peripheral nerves in which motor, sensory, or [autonomic] nerve fibers are affected

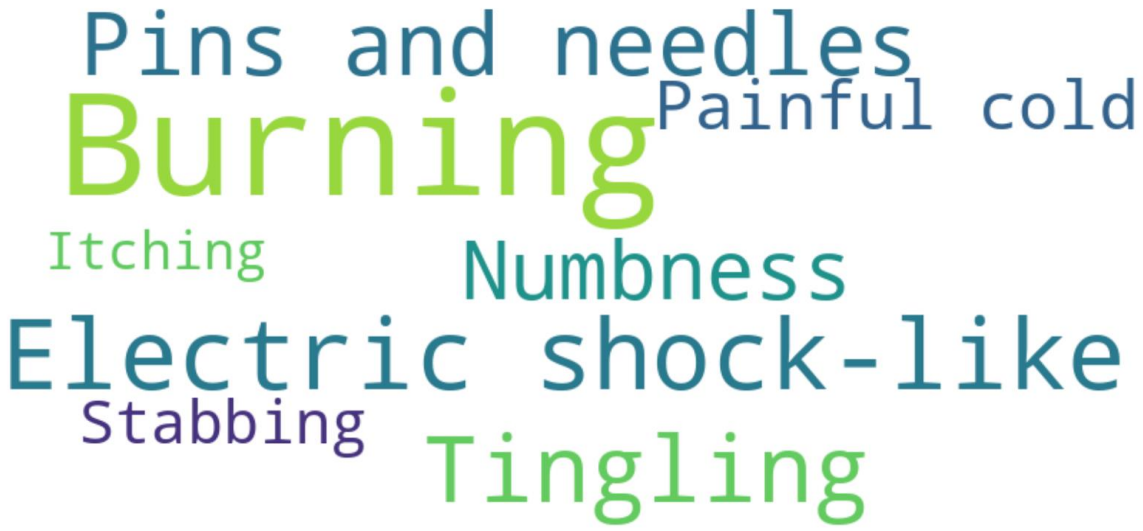
1.Rison, R. A. & Beydoun, S. R. *Bmc Neurol* **16**, 13 (2016).

Component	Gain-of-Function (Positive)	Loss-of-Function (Negative)
Sensory	Pain (Burning, Stabbing, Shocking), Paresthesias, Dysesthesia, Hypersensitivity, Allodynia	Diminished mechanical and thermal sensation, reduced vibration and proprioception, A/hyporeflexia, difficulty with object discrimination
Motor	Muscle cramps, Fasciculations, Myokymia	Weakness, Muscle Atrophy, A/hyporeflexia
Autonomic	Hyperhidrosis, Cardiovascular instability	Orthostatic hypotension, resting tachycardia, Anhidrosis, GI dysmotility, bladder dysfunction, sexual dysfunction, pupillary abnormalities

Neuropathic Pain

"Pain caused by a lesion or disease of the somatosensory nervous system[1]"



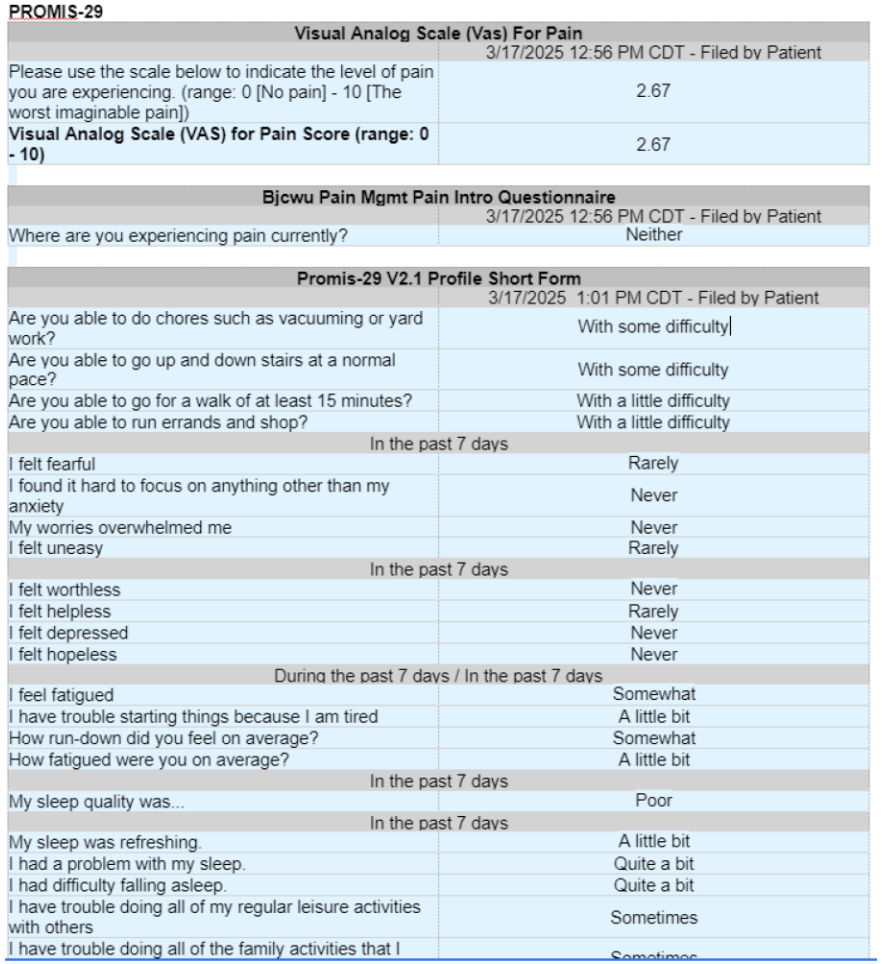


Etiology	Prevalence (U.S.)	Prevalence (Global)
Diabetic Neuropathy	~47% of diabetics	~50% of diabetics
Postherpetic Neuralgia	10–18% post-shingles	5–15% post-shingles
Chemotherapy-Induced Neuropathy	30–68% chemo patients	~41% chemo patients
HIV Neuropathy	~20% HIV patients	10–50% HIV patients
Idiopathic Neuropathy	~23% of neuropathy cases	20–30% of neuropathy cases

1. Finnerup, N. B. *et al. Pain* **157**, 1599–1606 (2016).
2. Finnerup, N.B., et al. (2021). Physiol Rev *101*, 259–301. 10.1152/physrev.00045.2019.

A Visit to my Pain Management Clinic

- Prior to Visit
  - Review of medical chart
  - Patient-reported outcome measures
- Encounter
  - History
  - Physical Examination
  - Diagnostics
  - Assessment and Plan



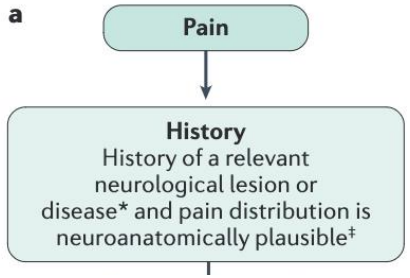
PROMIS-29

Visual Analog Scale (Vas) For Pain	3/17/2025 12:56 PM CDT - Filed by Patient
Please use the scale below to indicate the level of pain you are experiencing. (range: 0 [No pain] - 10 [The worst imaginable pain])	2.67
Visual Analog Scale (VAS) for Pain Score (range: 0 - 10)	2.67

Bjcwu Pain Mgmt Pain Intro Questionnaire	3/17/2025 12:56 PM CDT - Filed by Patient
Where are you experiencing pain currently?	Neither

Promis-29 V2.1 Profile Short Form	3/17/2025 1:01 PM CDT - Filed by Patient
Are you able to do chores such as vacuuming or yard work?	With some difficulty
Are you able to go up and down stairs at a normal pace?	With some difficulty
Are you able to go for a walk of at least 15 minutes?	With a little difficulty
Are you able to run errands and shop?	With a little difficulty
In the past 7 days	
I felt fearful	Rarely
I found it hard to focus on anything other than my anxiety	Never
My worries overwhelmed me	Never
I felt uneasy	Rarely
In the past 7 days	
I felt worthless	Never
I felt helpless	Rarely
I felt depressed	Never
I felt hopeless	Never
During the past 7 days / In the past 7 days	
I feel fatigued	Somewhat
I have trouble starting things because I am tired	A little bit
How run-down did you feel on average?	Somewhat
How fatigued were you on average?	A little bit
In the past 7 days	
My sleep quality was...	Poor
In the past 7 days	
My sleep was refreshing.	A little bit
I had a problem with my sleep.	Quite a bit
I had difficulty falling asleep.	Quite a bit
I have trouble doing all of my regular leisure activities with others	Sometimes
I have trouble doing all of the family activities that I	Sometimes

Diagnosing Neuropathic Pain



NeuPSIG Grading System for Neuropathic Pain				
		Status	Details	Comments
Possible	History of relevant neurological lesion or disease	☑	Diabetes, Sjogren's syndrome	
	Pain Distribution Neuroanatomically Plausible	☑	Bilateral feet	
Probable	Pain is associated with sensory signs the same neuroanatomically plausible distribution	☑	Pin gradient	
Definite	Diagnostic testing confirming a lesior or disease of the somatosensory nervous system explaining the pain	☑	Skin biopsy	
Final Grade:	Definite Neuropathic Pain			

Finnerup, N. B. et al. *Pain* 157, 1599–1606 (2016).

Finnerup, N. B. *et al* . *Pain* **157**, 1599–1606 (2016)
Colloca, L. *et al*. *Nature Reviews Disease Primers* **3**, 17002 (2017).

Curative (Disease Modifying) vs Symptomatic Treatment

Endpoint > Keep the Floor Dry

Fix the roof = Curative/Disease Modifying Treatment

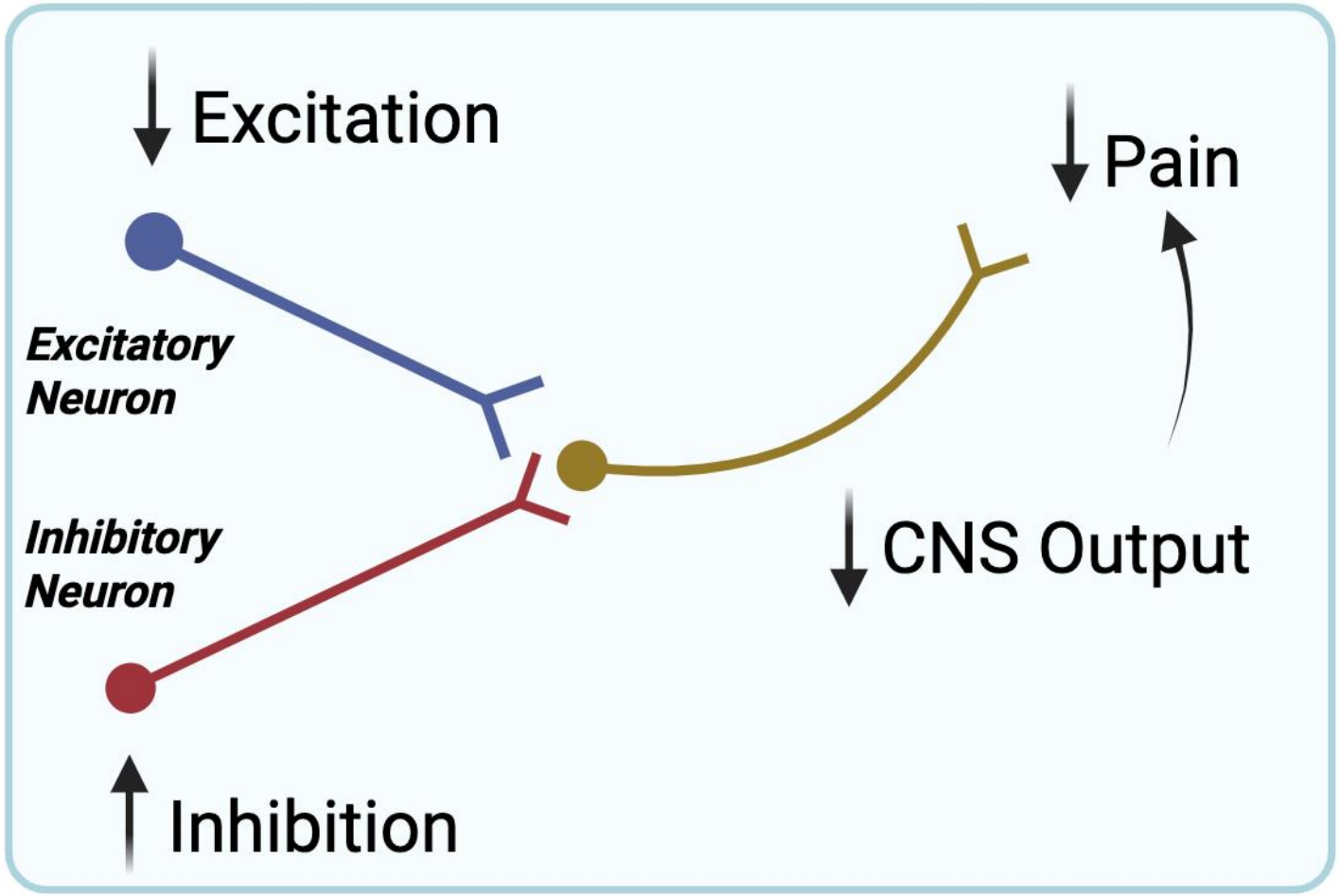
Catch Bucket = Symptomatic Treatment

Goals of Pain Management

- Significant Pain Reduction (≥50% decrease in pain intensity)
- Restore Specific Functions or Abilities
- Reduce Reliance on Opioids or High-Risk Medications
- Address Psychological and Social Factors that Contribute to or Exacerbate Pain
- Patient Education and Self-Management

Henry, S. G., Bell, R. A., Fenton, J. J. & Kravitz, R. L. *Clin. J. Pain* **33**, 955–961 (2017).

A Common Framework for Symptom-Reducing Pain Therapies



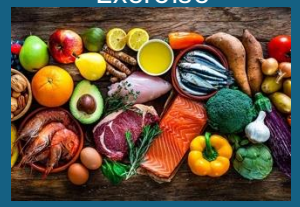
Neuropathic Pain Management Toolbox

Invasiveness/Risk

Exercise, Therapies, Lifestyle and Modalities

Exercise

Cognitive Therapy



Lifestyle

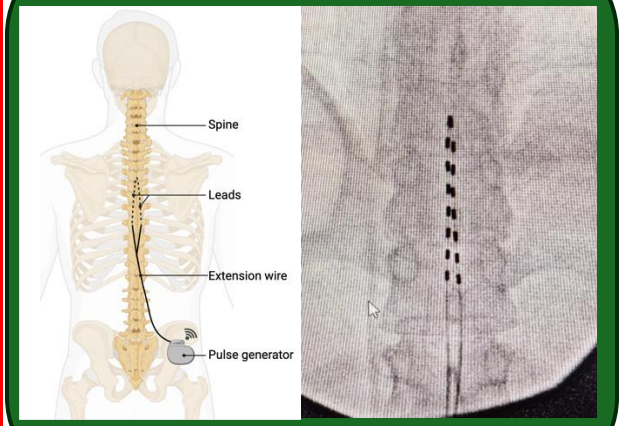
Modalities

Pharmacotherapy

Oral Medication

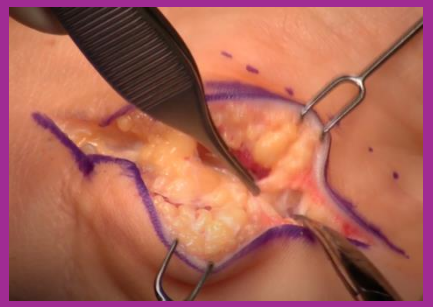
Topical Medication

Procedural Interventions



Spinal Cord Stimulation

Structural Modification (Surgery)



Nerve release

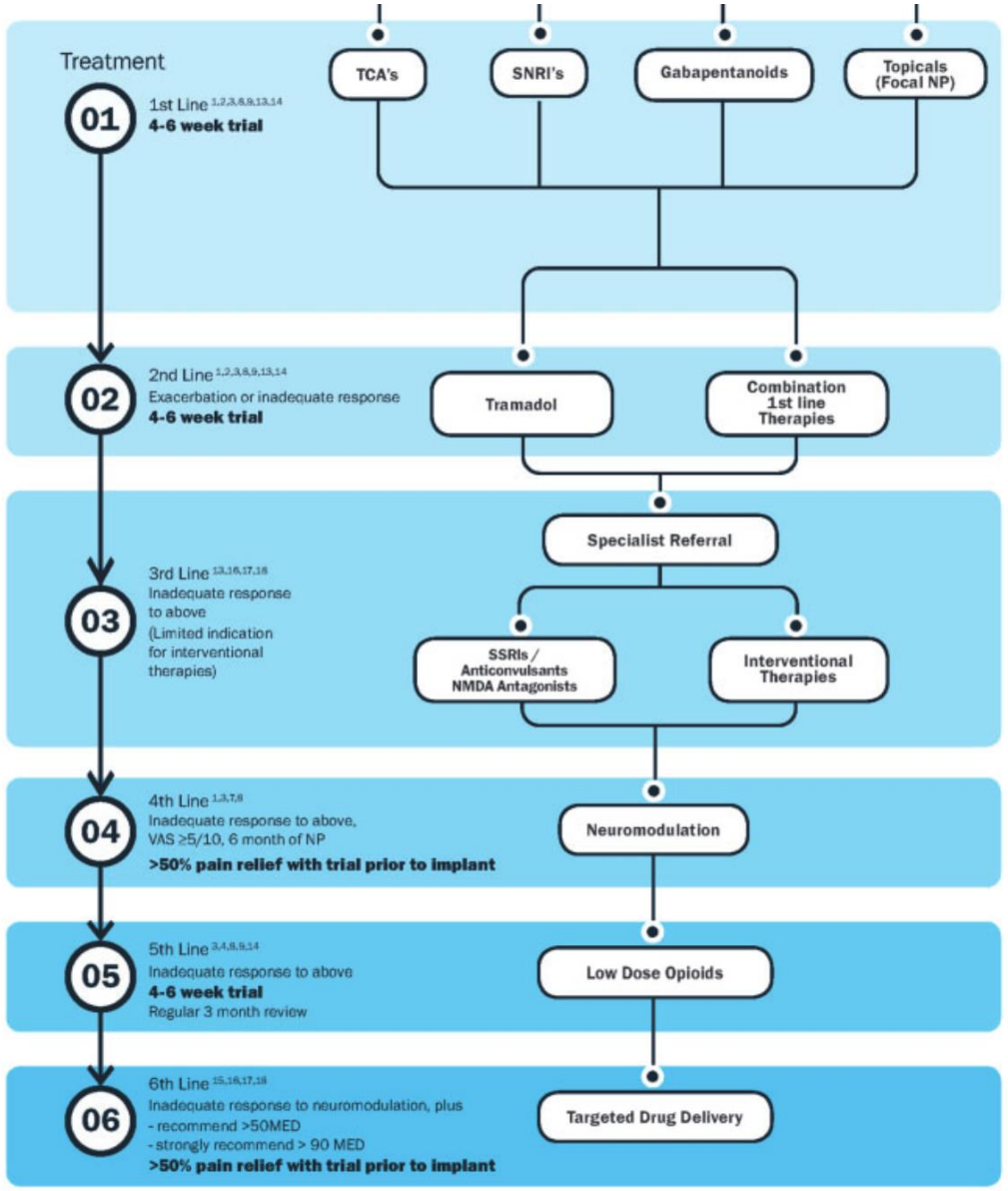
Core Tools for Pain Physician

Most Physicians and Allied Clinicians

Pain Medicine Specialists

Surgeons

Current Treatment Algorithms for Neuropathic Pain



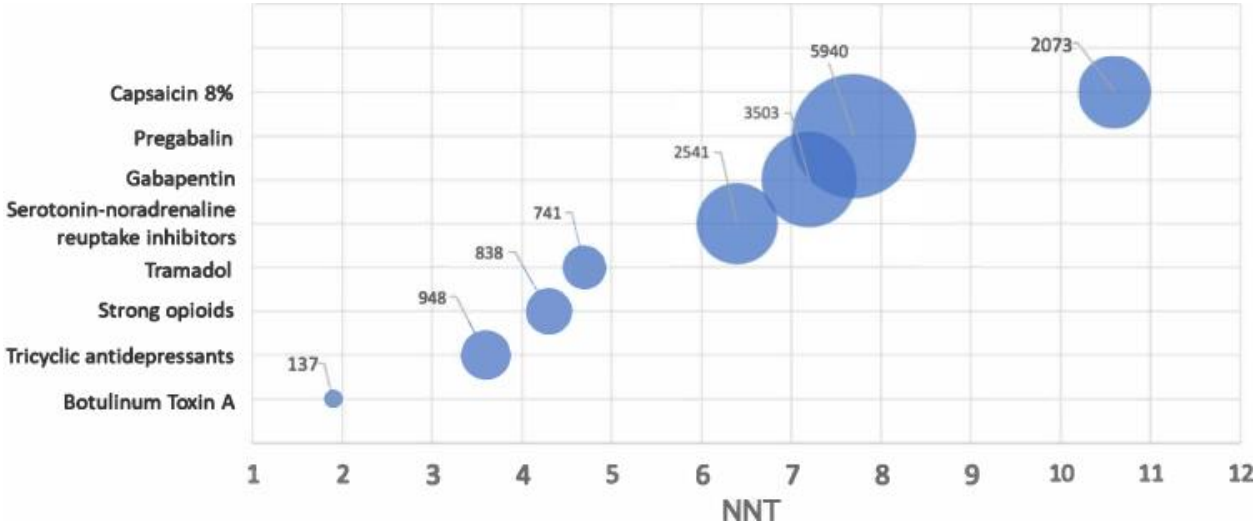
Bates, D. *et al*. *Pain Med* **20**, S2–S12 (2019).

Pharmacotherapy

	Total daily dose and dose regimen	Recommendations
Strong recommendations for use		
Gapabentin	1200–3600 mg, in three divided doses	First line
Gabapentin extended release or enacarbil	1200–3600 mg, in two divided doses	First line
Pregabalin	300–600 mg, in two divided doses	First line
Serotonin-noradrenaline reuptake inhibitors duloxetine or venlafaxine*	60–120 mg, once a day (duloxetine); 150–225 mg, once a day (venlafaxine extended release)	First line
Tricyclic antidepressants	25–150 mg, once a day or in two divided doses	First line†
Weak recommendations for use		
Capsaicin 8% patches	One to four patches to the painful area for 30-60 min every 3 months	Second line (peripheral neuropathic pain)‡
Lidocaine patches	One to three patches to the region of pain once a day for up to 12 h	Second line (peripheral neuropathic pain)
Tramadol	200–400 mg, in two (tramadol extended release) or three divided doses	Second line
Botulinum toxin A (subcutaneously)	50–200 units to the painful area every 3 months	Third line; specialist use (peripheral neuropathic pain)
Strong opioids	Individual titration	Third line§

Finnerup, N. B. *et al*. *Lancet Neurology* **14**, 162–173 (2015).

The **Number Needed to Treat (NNT):** Number of patients who need to be treated with a specific medication for one patient to experience a meaningful benefit, typically defined as a 50% reduction in pain intensity. A lower NNT indicates a more effective treatment.



Arthur, A., Kapural, L., Chiacchierini, R. P., Hargus, N. J. & Patterson, W. R. *J. Pain Res*. **17**, 3449–3453 (2024).

6 for improvement in diabetic neuropathy

☺	Benefits in NNT
6	1 in 6 was helped (diabetic neuropathy)
8	1 in 8 was helped (postherpetic neuralgia)

☹	Harms in NNT
8	1 in 8 was harmed (developed dizziness)
11	1 in 11 was harmed (developed somnolence)
13	1 in 13 was harmed (developed ataxia)
21	1 in 21 was harmed (developed edema)

https://thennt.com/nnt/gabapentin-chronic-neuropathic-pain/

Lidocaine Infusion

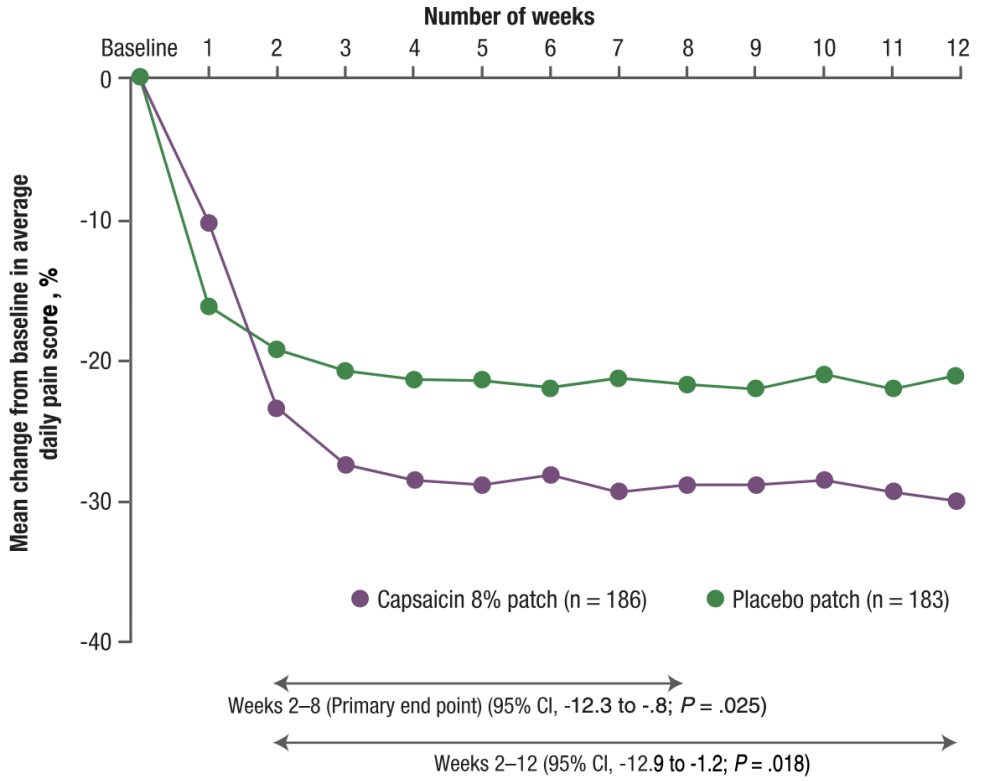
Lidocaine used to treat chronic pain at local hospital

By Russell Kinsaul

Published: Jan. 11, 2024 at 6:14 PM CST

High Concentration Topical Capsaicin (8%)

On-label indications (US):
Diabetic Peripheral Neuropathy
Post-herpetic Neuralgia



Weekly 95% CI	N/A	-10.4, 2.3	-13.1, -.4	-13.5, -.8	-13.6, -1.0	-12.6, .0	-14.4, -1.8	-13.5, -.8	13.2, -.6	-13.9, -1.2	-13.7, -1.1	-15.3, -2.7
Weekly *P* value	N/A	.208	.036	.027	.024	.051	.012	.026	.032	.020	.022	.005
Number of patients												
Capsaicin	186	186	186	186	186	186	186	186	186	186	186	186
Placebo	183	183	183	183	183	183	183	183	183	183	183	183

1.Simpson, D. M. *et al*. *J. Pain* **18**, 42–53 (2017).

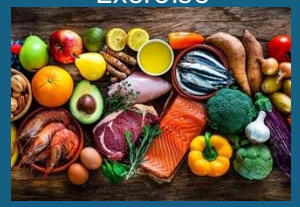
Neuropathic Pain Management Toolbox

Invasiveness/Risk

Exercise, Therapies, Lifestyle and Modalities

Exercise

Cognitive Therapy



Lifestyle

Modalities

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Oral Medication

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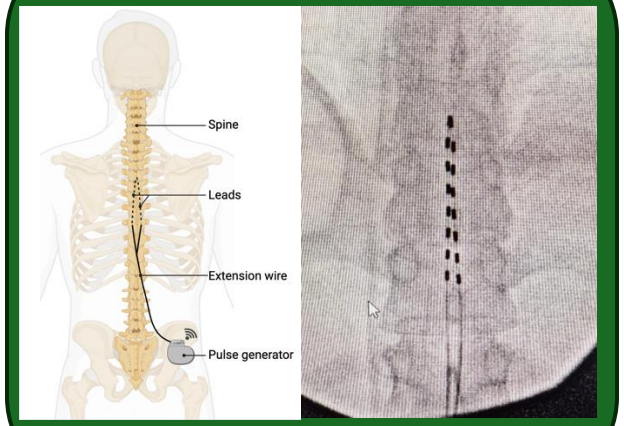
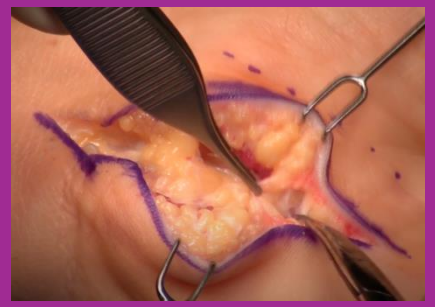
Procedural Interventions



Spinal Cord Stimulation

Structural Modification (Surgery)



Nerve release

Core Tools for Pain Physician

Most Physicians and Allied Clinicians

Pain Medicine Specialists

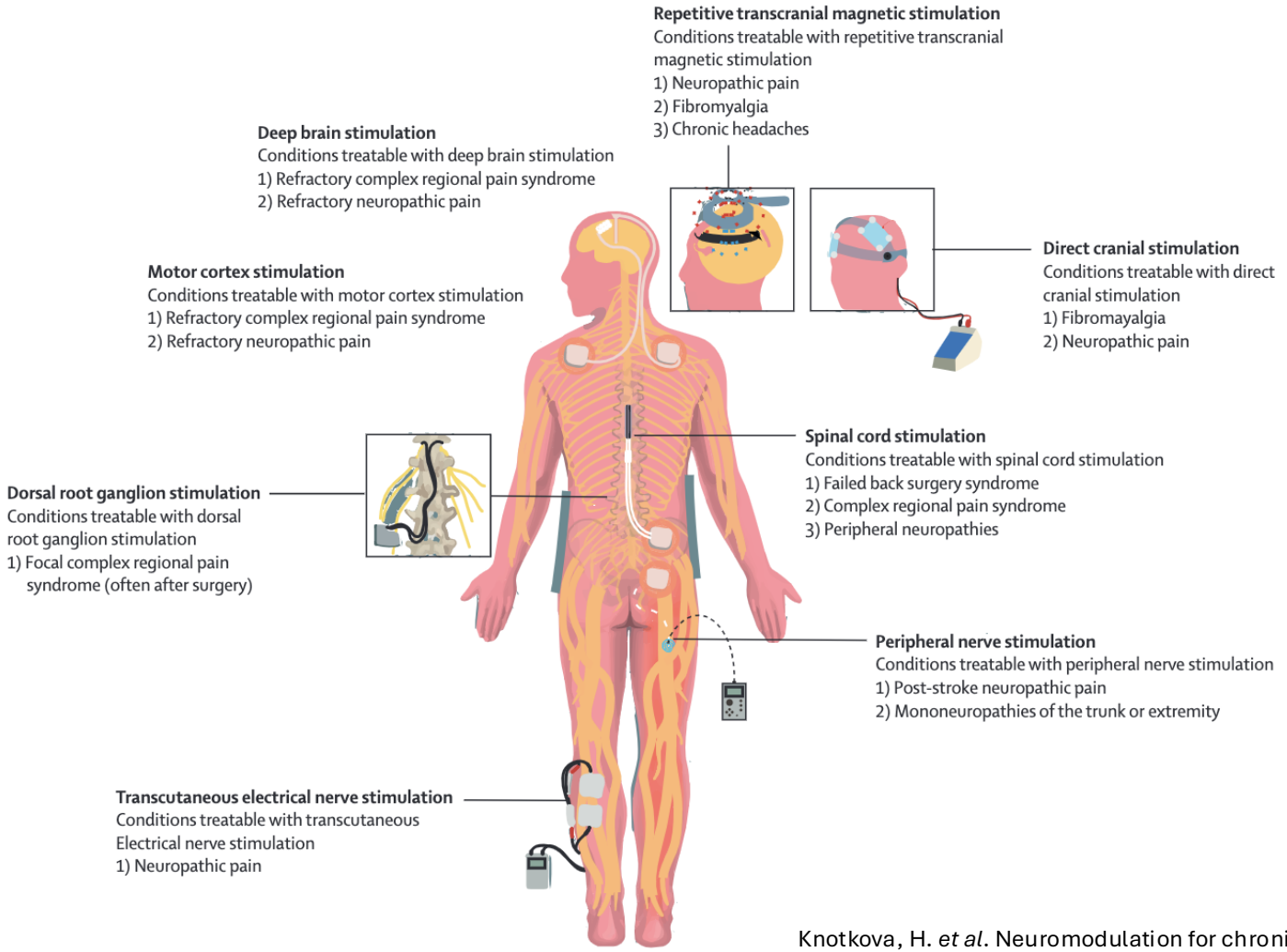
Surgeons

Procedural Interventions

Neuromodulation

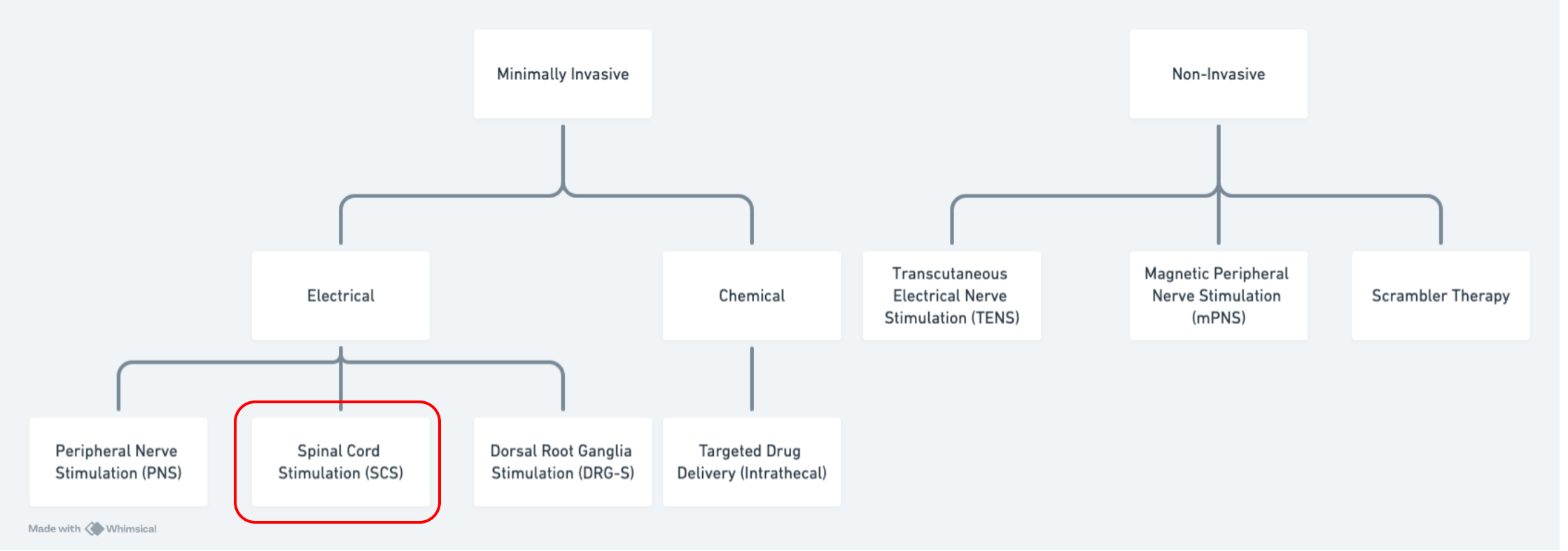
Neuromodulation

Neuromodulation: “the alteration of nerve activity through targeted delivery of a stimulus, such as electrical stimulation or chemical agents, to specific neurological sites in the body.”

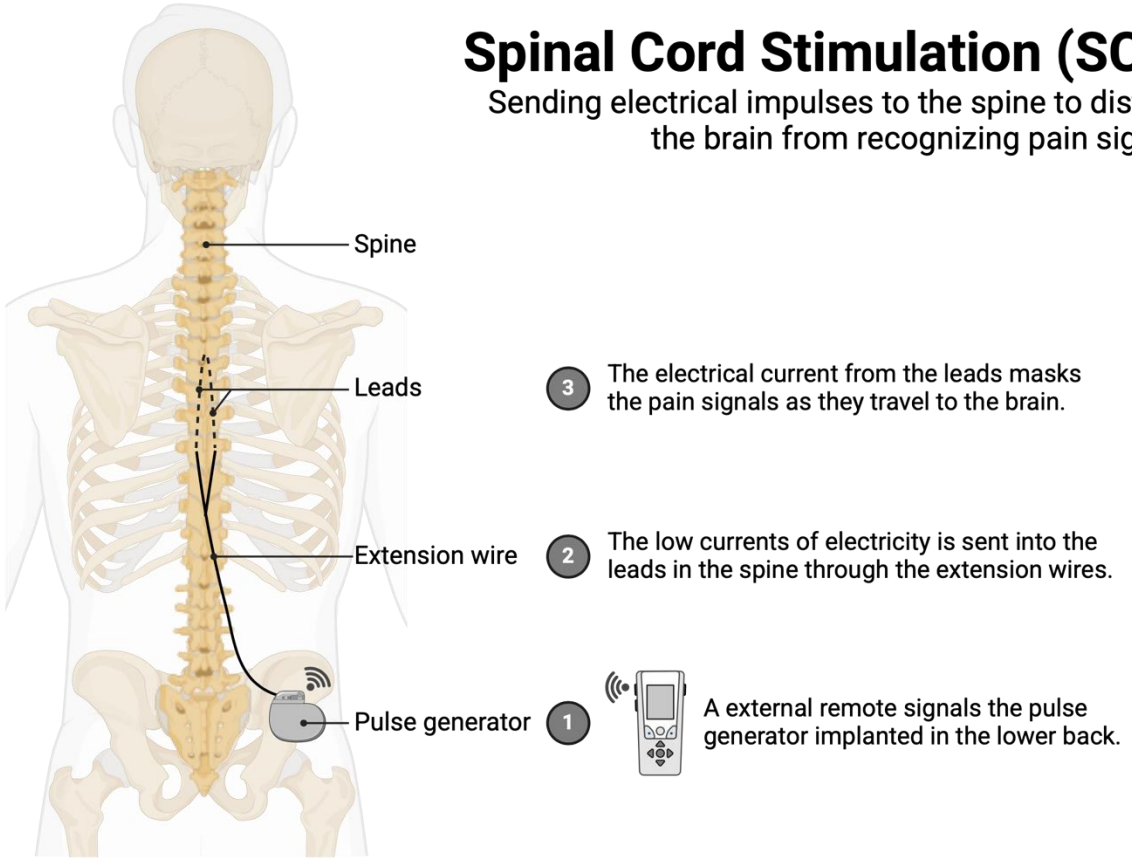


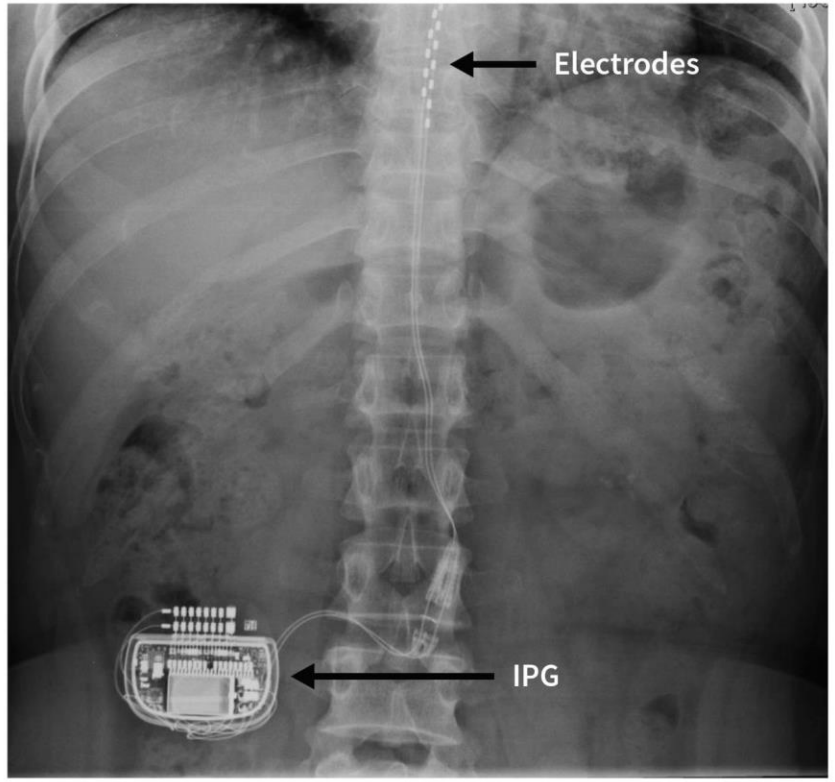
Knotkova, H. *et al*. Neuromodulation for chronic pain. *Lancet* **397**, 2111–2124 (2021).

Types of Neuromodulation Commonly Used in Pain Medicine for Neuropathic Pain



Spinal Cord Stimulation – What is it?





Spinal Cord Stimulation – Who is it for?

- **Approved 'on label' indications**[1]
  - Chronic low back pain from post-laminectomy syndrome
  - Lumbar stenosis without claudication
  - Neuropathic leg pain (i.e., radiculopathy)
  - Complex regional pain syndrome (CRPS)
  - **Painful diabetic peripheral neuropathy**

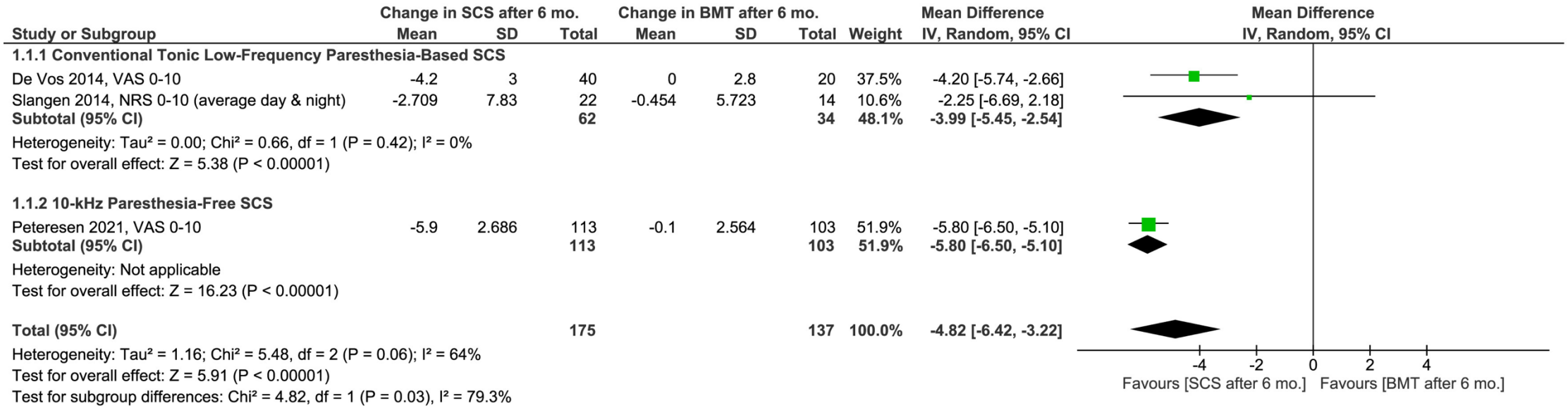
- Expanded 'off label' use[2]
  - Last resort treatment of moderate to severe (5 or more on a 10-point VAS scale) **chronic neuropathic pain of certain origins** (i.e., lumbosacral arachnoiditis, phantom limb/stump pain, peripheral neuropathy (including diabetic peripheral neuropathy), post-herpetic neuralgia, intercostal neuralgia, cauda equina injury, incomplete spinal cord injury, or plexopathy) that has been present for 12 or more months

1. Shirvalkar, P. Neuromodulation for Neuropathic Pain Syndromes. *Contin.: Lifelong Learn. Neurol.* **30**, 1475–1500 (2024).
2.https://www.aetna.com/cpb/medical/data/100_199/0194.html

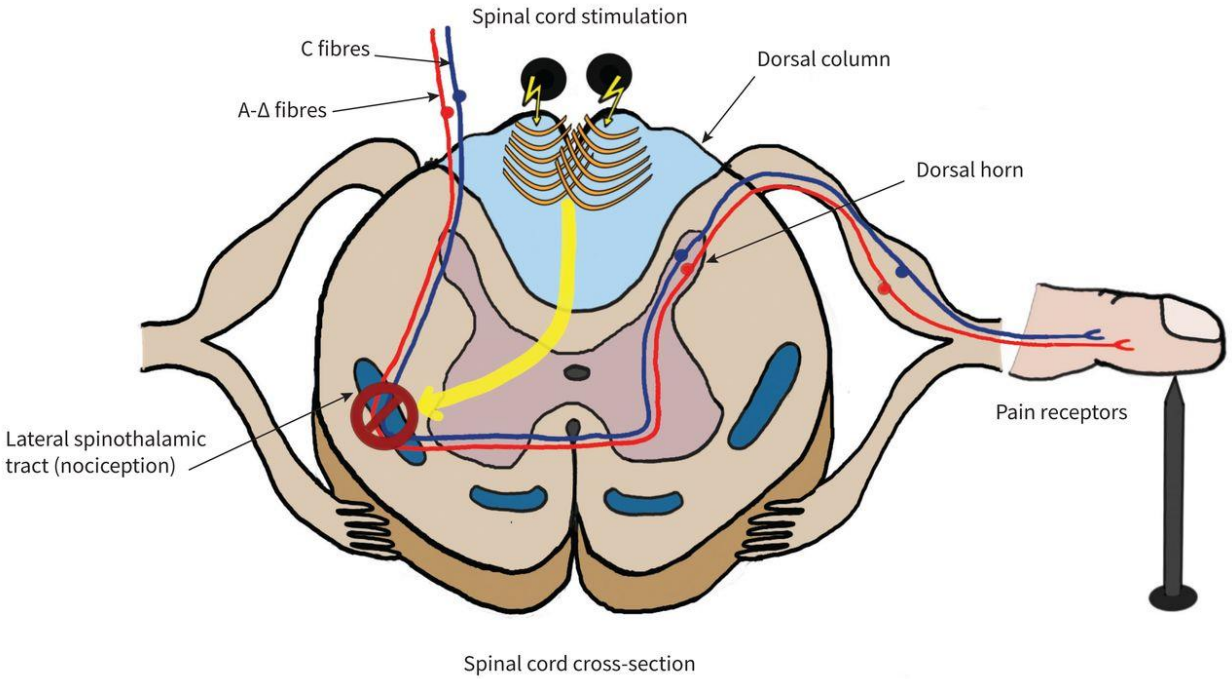
Spinal Cord Stimulation – Does it work?

Assessing the Efficacy of Spinal Cord Stimulation in Managing Painful Diabetic Neuropathy: A Systematic Review and Meta-Analysis

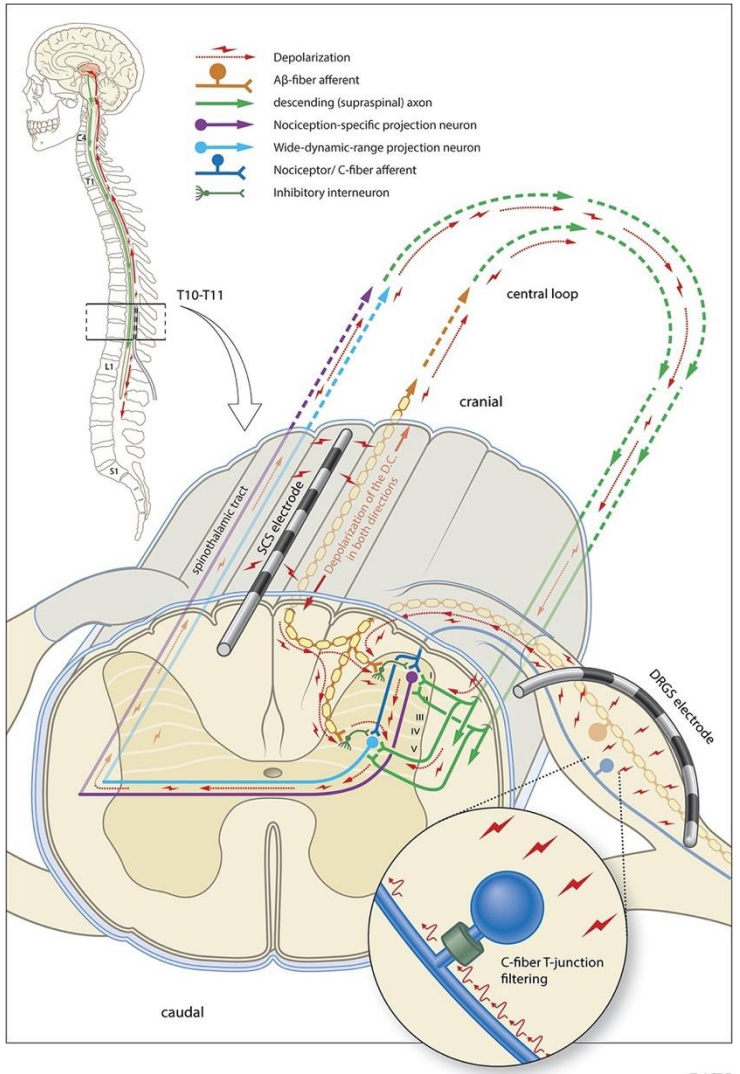
a



Spinal Cord Stimulation – How does it work?



Hong, A., Varshney, V., Hare, G. M. T. & Mazer, C. D. *CMAJ* **192**, E1264–E1267 (2020).



Joosten, E. A. & Franken, G. *Pain* **161**, S104–S113 (2020).

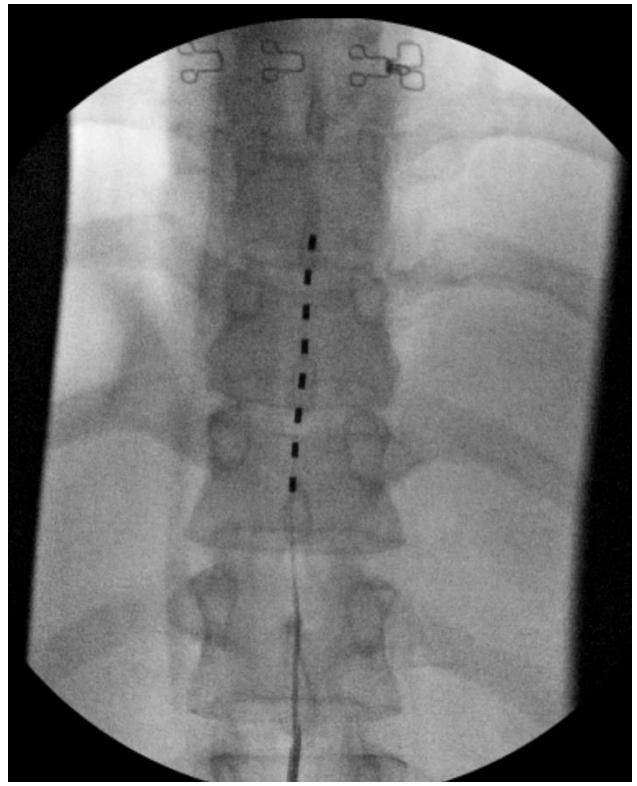
Spinal Cord Stimulation - Complications

Complication	SCS Mean Rate (%)
Lead Migration	15.49
Lead Fracture/Malfunction	6.37
Infection	4.89
Pain Over Implant	6.15
Device Removal	11

Eldabe, S., Buchser, E. & Duarte, R. V. *Pain Med.* **17**, 325–336 (2016).

SCS – The Process for the Patient

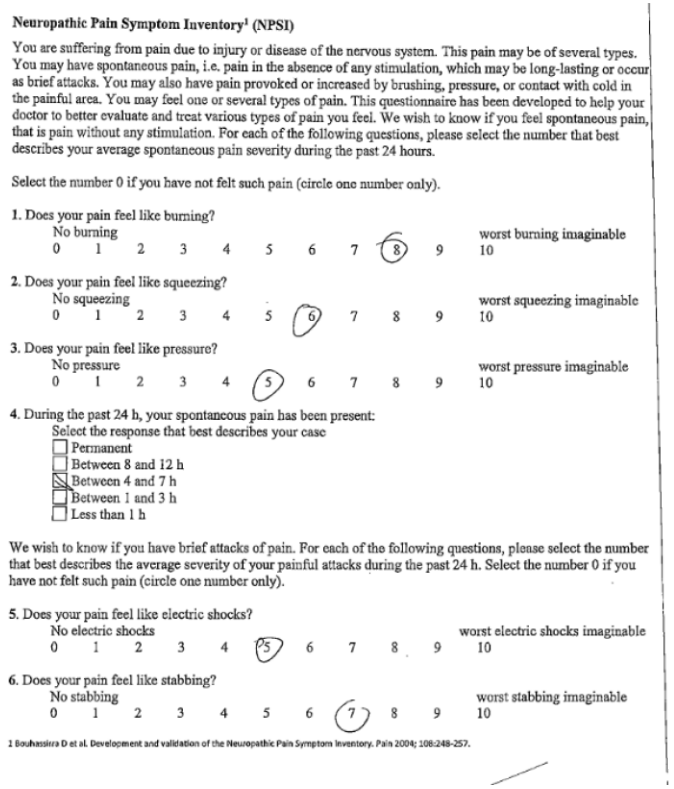
- Comprehensive evaluation
- Pain psychology evaluation
- Insurance pre-authorization
- Procedure
  - Trial
    - Office-based lead insertion
  - Permanent implant
    - Operating room, same day
- Post-procedure follow up



SCS for Small Fiber Neuropathy – A Case

- Young woman with FGFR3+ Small Fiber Neuropathy, with severe neuropathic pain
- Tried multiple pharmacologic agents with no benefits

She describes her pain as a 'rod on fire inside my bones'
"I feel like my shins are going to break"



Neuropathic Pain Symptom Inventory[1] (NPSI)

You are suffering from pain due to injury or disease of the nervous system. This pain may be of several types. You may have spontaneous pain, i.e. pain in the absence of any stimulation, which may be long-lasting or occur as brief attacks. You may also have pain provoked or increased by brushing, pressure, or contact with cold in the painful area. You may feel one or several types of pain. This questionnaire has been developed to help your doctor to better evaluate and treat various types of pain you feel. We wish to know if you feel spontaneous pain, that is pain without any stimulation. For each of the following questions, please select the number that best describes your average spontaneous pain severity during the past 24 hours.

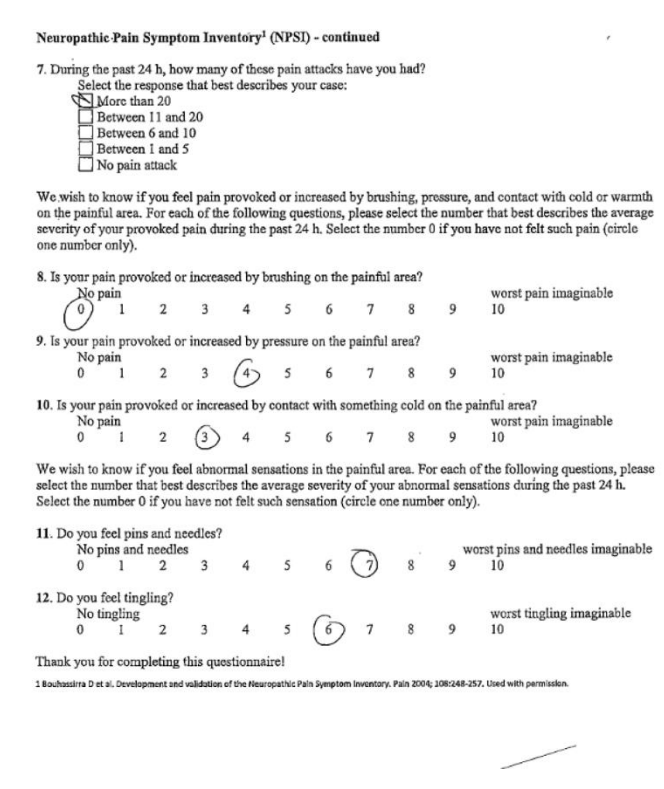
Select the number 0 if you have not felt such pain (circle one number only).

1. Does your pain feel like burning?
   No burning 0 1 2 3 4 5 6 7 (8) 9 10 worst burning imaginable
2. Does your pain feel like squeezing?
   No squeezing 0 1 2 3 4 5 (6) 7 8 9 10 worst squeezing imaginable
3. Does your pain feel like pressure?
   No pressure 0 1 2 3 4 (5) 6 7 8 9 10 worst pressure imaginable
4. During the past 24 h, your spontaneous pain has been present:
   Select the response that best describes your case
   - ☐ Permanent
   - ☐ Between 8 and 12 h
   - ☒ Between 4 and 7 h
   - ☐ Between 1 and 3 h
   - ☐ Less than 1 h

We wish to know if you have brief attacks of pain. For each of the following questions, please select the number that best describes the average severity of your painful attacks during the past 24 h. Select the number 0 if you have not felt such pain (circle one number only).

5. Does your pain feel like electric shocks?
   No electric shocks 0 1 2 3 4 (5) 6 7 8 9 10 worst electric shocks imaginable
6. Does your pain feel like stabbing?
   No stabbing 0 1 2 3 4 5 6 (7) 8 9 10 worst stabbing imaginable

1 Bouhassira D et al. Development and validation of the Neuropathic Pain Symptom Inventory. *Pain* 2004; 108:248-257.



Neuropathic Pain Symptom Inventory[1] (NPSI) - continued

7. During the past 24 h, how many of these pain attacks have you had?
   Select the response that best describes your case:
   - ☒ More than 20
   - ☐ Between 11 and 20
   - ☐ Between 6 and 10
   - ☐ Between 1 and 5
   - ☐ No pain attack

We wish to know if you feel pain provoked or increased by brushing, pressure, and contact with cold or warmth on the painful area. For each of the following questions, please select the number that best describes the average severity of your provoked pain during the past 24 h. Select the number 0 if you have not felt such pain (circle one number only).

8. Is your pain provoked or increased by brushing on the painful area?
   No pain (0) 1 2 3 4 5 6 7 8 9 10 worst pain imaginable
9. Is your pain provoked or increased by pressure on the painful area?
   No pain 0 1 2 3 (4) 5 6 7 8 9 10 worst pain imaginable
10. Is your pain provoked or increased by contact with something cold on the painful area?
    No pain 0 1 2 (3) 4 5 6 7 8 9 10 worst pain imaginable

We wish to know if you feel abnormal sensations in the painful area. For each of the following questions, please select the number that best describes the average severity of your abnormal sensations during the past 24 h. Select the number 0 if you have not felt such sensation (circle one number only).

11. Do you feel pins and needles?
    No pins and needles 0 1 2 3 4 5 6 (7) 8 9 10 worst pins and needles imaginable
12. Do you feel tingling?
    No tingling 0 1 2 3 4 5 (6) 7 8 9 10 worst tingling imaginable

Thank you for completing this questionnaire!

1 Bouhassira D et al. Development and validation of the Neuropathic Pain Symptom Inventory. Pain 2004; 108:248-257. Used with permission.

Pre-trial (SCS)

chores?

In the past 7 days	
How would you rate your pain on average?	6
PROMIS Physical Function T-Score (range: 10 - 90)	**29 (severe dysfunction) !!**
PROMIS Anxiety T-Score (range: 10 - 90)	54 (within normal limits)
PROMIS Depression T-Score (range: 10 - 90)	57 (mild)
PROMIS Fatigue T-Score (range: 10 - 90)	**69 (moderate) !**
PROMIS Sleep Disturbance T-Score (range: 10 - 90)	60 (mild)
PROMIS Ability to Participate in Social Roles & Activities T-Score (range: 10 - 90)	**39 (moderate dysfunction) !**
PROMIS Pain Interference T-Score (range: 10 - 90)	**70 (moderate) !**
PROMIS Pain Intensity (range: 0 - 10)	6

She describes her pain as a 'rod on fire inside my bones' "I feel like my shins are going to break"

Post-trial (SCS), 6 days

In the past 7 days	
How would you rate your pain on average?	2
PROMIS Physical Function T-Score (range: 10 - 90)	**37 (moderate dysfunction) !**
PROMIS Anxiety T-Score (range: 10 - 90)	51 (within normal limits)
PROMIS Depression T-Score (range: 10 - 90)	54 (within normal limits)
PROMIS Fatigue T-Score (range: 10 - 90)	57 (mild)
PROMIS Sleep Disturbance T-Score (range: 10 - 90)	48 (within normal limits)
PROMIS Ability to Participate in Social Roles & Activities T-Score (range: 10 - 90)	45 (within normal limits)
PROMIS Pain Interference T-Score (range: 10 - 90)	56 (mild)
PROMIS Pain Intensity (range: 0 - 10)	2

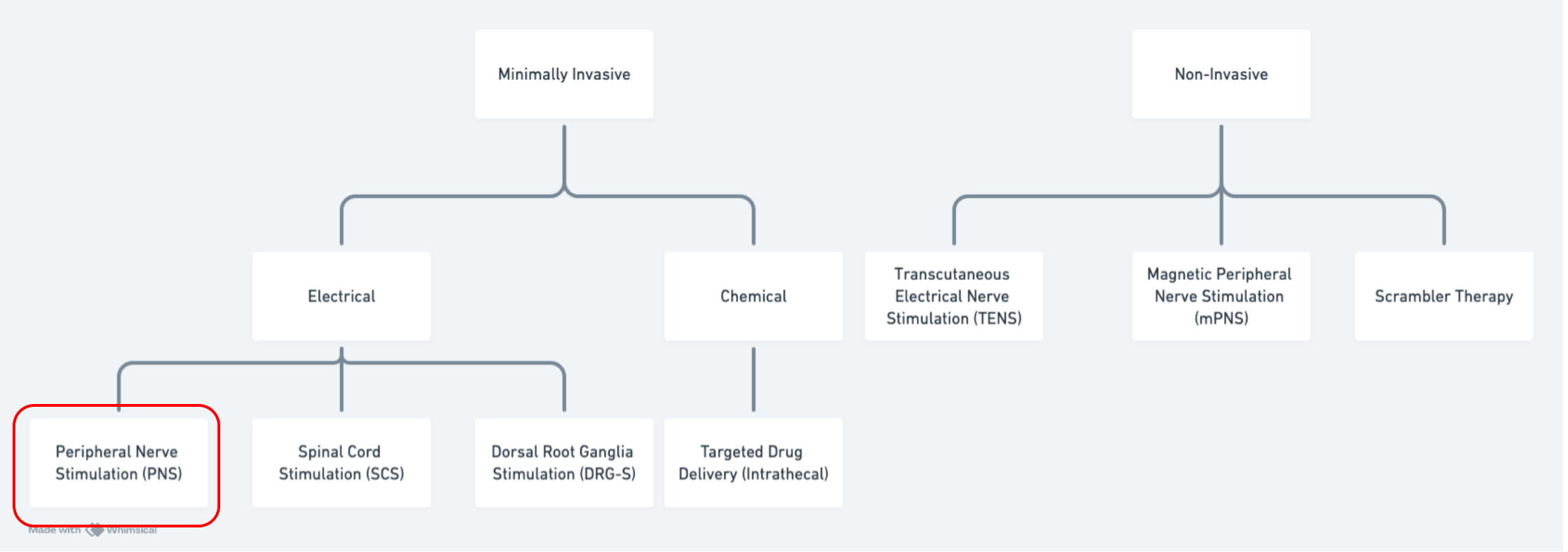
“My sleep definitely improved”

1 month post SCS permanent implant

In the past 7 days	
How would you rate your pain on average?	3
PROMIS Physical Function T-Score (range: 10 - 90)	39 (moderate dysfunction) !
PROMIS Anxiety T-Score (range: 10 - 90)	51 (within normal limits)
PROMIS Depression T-Score (range: 10 - 90)	54 (within normal limits)
PROMIS Fatigue T-Score (range: 10 - 90)	53 (within normal limits)
PROMIS Sleep Disturbance T-Score (range: 10 - 90)	48 (within normal limits)
PROMIS Ability to Participate in Social Roles & Activities T-Score (range: 10 - 90)	50 (within normal limits)
PROMIS Pain Interference T-Score (range: 10 - 90)	56 (mild)
PROMIS Pain Intensity (range: 0 - 10)	3

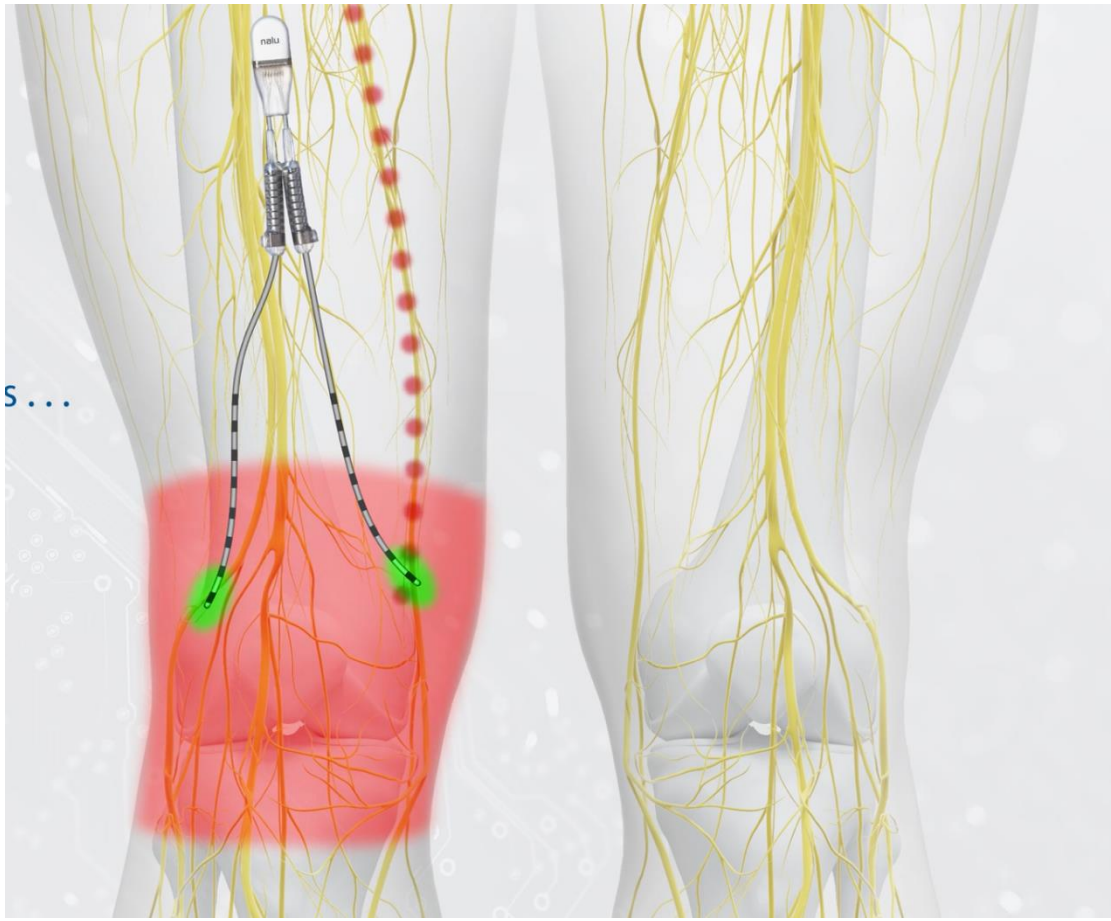
“I almost feel normal again”

Types of Neuromodulation Commonly Used in Pain Medicine for Neuropathic Pain



Peripheral Nerve Stimulation – What is it?

Peripheral nerve stimulation involves stimulating nerve axons by placing a fine electrode wire within 1 cm.



1.Shirvalkar, P. Neuromodulation for Neuropathic Pain Syndromes. *Contin.: Lifelong Learn. Neurol.* **30**, 1475–1500 (2024).

Peripheral Nerve Stimulation – Who is it for?

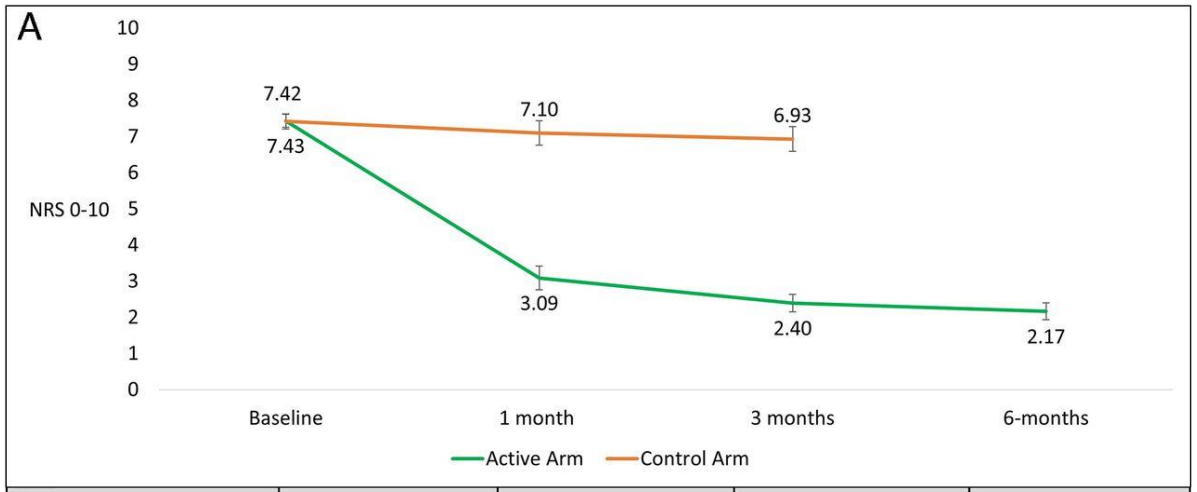
- Individuals experiencing pain in the distribution of one or two specific nerves, and who have not found relief through conventional care, could be considered for peripheral nerve stimulation.

- Studied Indications Relevant to Peripheral Neuropathy
  - Post-amputation pain (phantom limb)[2]
  - Post-traumatic/post-surgical neuralgia[3]
  - Nerve entrapment and mononeuropathy[3]
  - Case reports: Post-herpetic neuralgia, occipital neuralgia, tibial neuropathy

1.Shirvalkar, P. Neuromodulation for Neuropathic Pain Syndromes. *Contin.: Lifelong Learn. Neurol.* **30**, 1475–1500 (2024).
2.Gilmore, C. *et al*. Percutaneous peripheral nerve stimulation for the treatment of chronic neuropathic postamputation pain: a multicenter, randomized, placebo-controlled trial. *Reg. Anesthesia Pain Med*. **44**, 637–645 (2019).
3.Hatheway, J. *et al*. *Reg. Anesthesia Pain Med*. rapm-2023-105264 (2024) doi:10.1136/rapm-2023-105264.

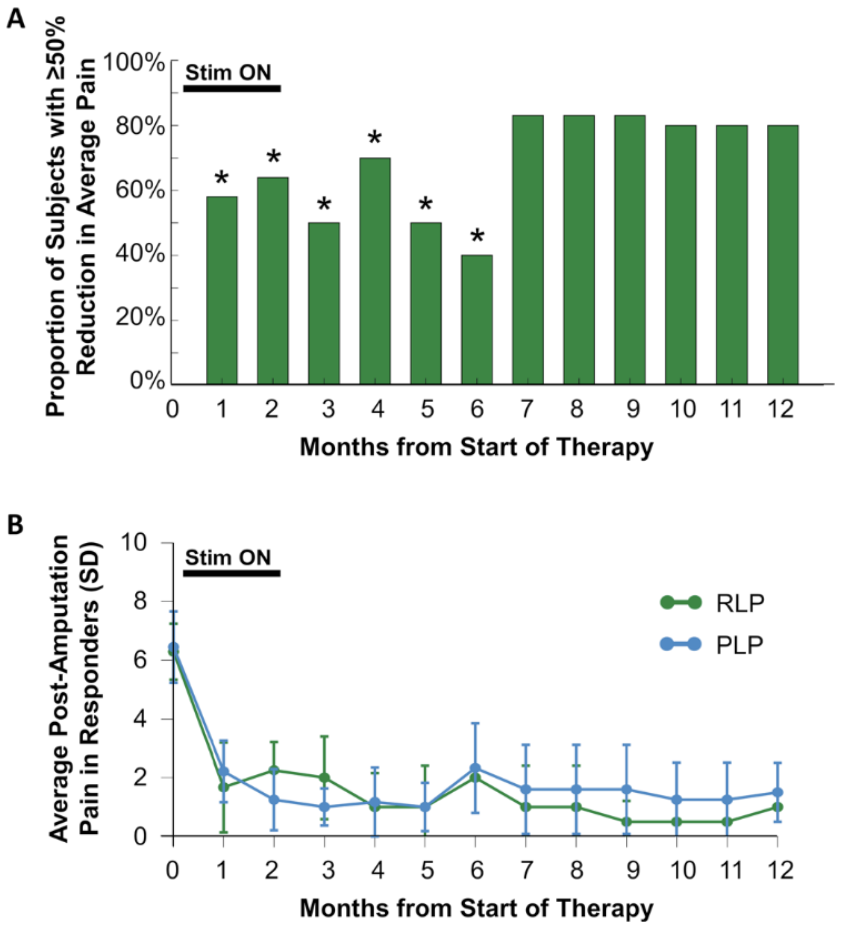
Peripheral Nerve Stimulation – Does it work?

Mixed Neuropathic Limb Pain[1]



B	Active Arm (43) 3-months	Control Arm (29) 3-months	p-value Active vs Control	Active Arm (42) 6-months
Responder Rate	84%	3%	$p < 0.001$	88%
% Pain Relief	67%	6%	$p < 0.001$	70%
High Responders	30%	3%	$p < 0.05$	36%

Post-amputation Pain[2]



1.Gilmore, C. *et al*. Percutaneous peripheral nerve stimulation for the treatment of chronic neuropathic postamputation pain: a multicenter, randomized, placebo-controlled trial. *Reg. Anesthesia Pain Med*. **44**, 637–645 (2019).

2.Hatheway, J. *et al*. *Reg. Anesthesia Pain Med*. rapm-2023-105264 (2024) doi:10.1136/rapm-2023-105264.

Peripheral Nerve Stimulation – Complications

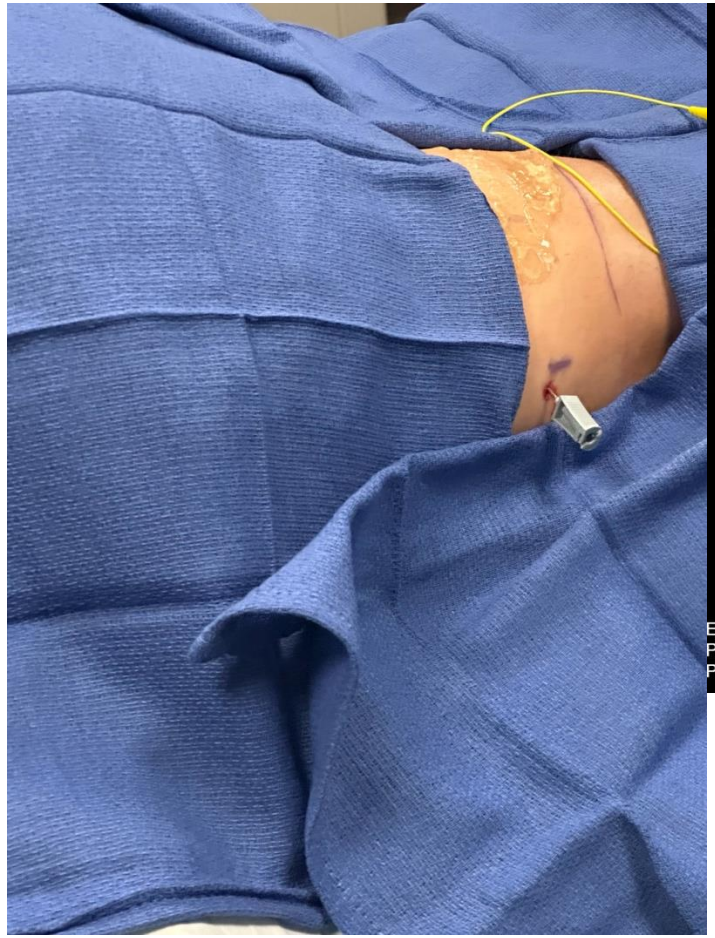
- Lead migration
- Lead fracture
- Infection
- Lack of efficacy

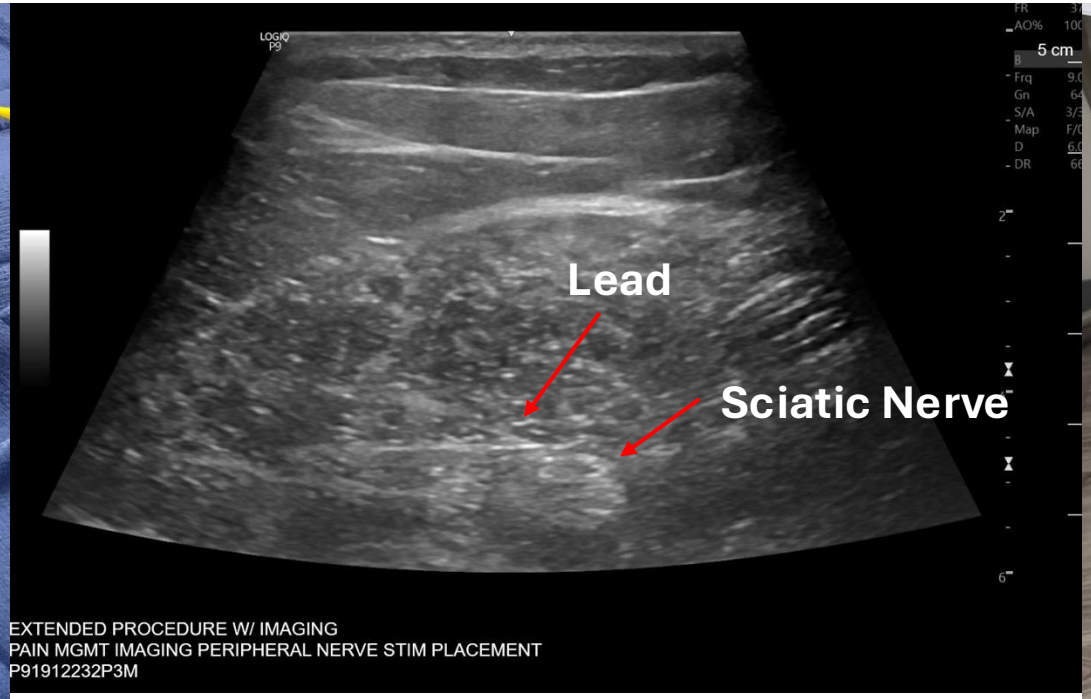
Peripheral Nerve Stimulation – The Process

- Comprehensive evaluation
- Pain psychology evaluation
- Insurance pre-authorization
- Procedure
  - Temporary devices
    - Office-based lead insertion
  - Permanent devices
    - Off-based trial (3-7 days)
    - Permanent implant (operating room)
- Post-procedure follow up

Terminal branches brachial plexus in upper arm

Peripheral Nerve Stimulation in a Patient with Phantom Limb Pain





Reports 50% relief for several weeks, ongoing.

Most helpful with spontaneous, paroxysmal ‘electric shocks’ at night.

Looking Ahead

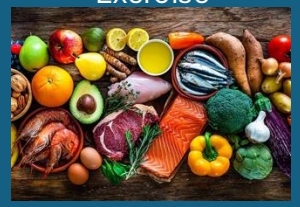
Neuropathic Pain Management Toolbox

Invasiveness/Risk

Exercise, Therapies, Lifestyle and Modalities

Exercise

Cognitive Therapy



Lifestyle

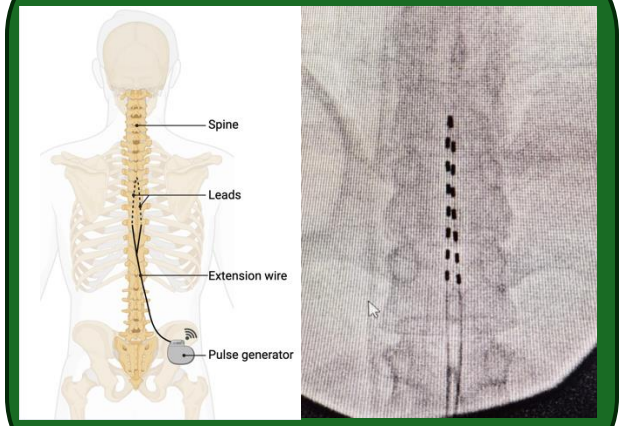
Modalities

Pharmacotherapy

Oral Medication

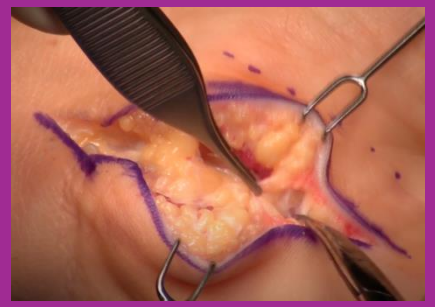
Topical Medication

Procedural Interventions



Spinal Cord Stimulation

Structural Modification (Surgery)



Nerve release

Core Tools for Pain Physician

Most Physicians and Allied Clinicians

Pain Medicine Specialists

Surgeons

Pharmacotherapy – In Development

Table 1 | Selected analgesics in clinical development

Drug	Company	Target	Lead indication	Status
$Na_V1.8$				
Suzetrigine	Vertex	$Na_V1.8$ inhibitor	Acute pain	NDA submitted
VX-993	Vertex	$Na_V1.8$ inhibitor	Pain	Phase I/II
JMKX-000623	Shanghai Jemincare	$Na_V1.8$ inhibitor	DPN	Phase II
ATX01	AlgoTherapeutix	$Na_V1.7$, 1.8 and 1.9 inhibitor, topical	CIPN and erythromelalgia	Phase II
LTG-305	Latigo Bio	$Na_V1.8$ inhibitor	Pain	Phase I
HBW-004285	Hyperway	$Na_V1.8$ inhibitor	Pain	Phase I
$Na_V1.7$				
OLP-1002	Olipass	$Na_V1.7$ ASO	OA pain	Phase II
ST-2427	SiteOne	$Na_V1.7$ inhibitor	Pain	Phase I
iN1011-N17	iN Therapeutics	$Na_V1.7$ inhibitor	OA pain	Phase I
Other targets				
Resiniferatoxin	Grunenthal	TRPV1 agonist	OA pain	Phase III
Cemdomespib	Biogen	HSP90 modulator	DPN	Phase II
Mazisotine	Lilly	SSTR4 agonist	Pain	Phase II
LY3857210	Lilly	P2X7 inhibitor	Chronic pain	Phase II
LY3848575	Lilly	Anti-epiregulin mAb	Chronic pain	Phase II
NA	Lilly	AT2R antagonist	Pain	Phase I
EC5026	EicOsis	sEH inhibitor	Pain	Phase I

ASO, antisense oligonucleotide; AT2R, angiotensin II type 2 receptor; CIPN, chemotherapy-induced peripheral neuropathy; DPN, diabetic peripheral neuropathy; HSP90, heat shock protein 90; mAb, monoclonal antibody; Na_V, voltage-gated sodium channel; NDA, new drug application; OA, osteoarthritis; sEH, soluble epoxide hydrolase; SSTR4, somatostatin receptor type 4.

https://www.nature.com/articles/d41573-024-00203-3

NaV1.8 Inhibition

Recruiting

Evaluation of Efficacy and Safety of Suzetrigine for Pain Associated With Diabetic Peripheral Neuropathy

ClinicalTrials.gov ID NCT06628908

Sponsor Vertex Pharmaceuticals Incorporated

Information provided by Vertex Pharmaceuticals Incorporated (Responsible Party)

Last Update Posted 2025-03-19

WashU Medicine

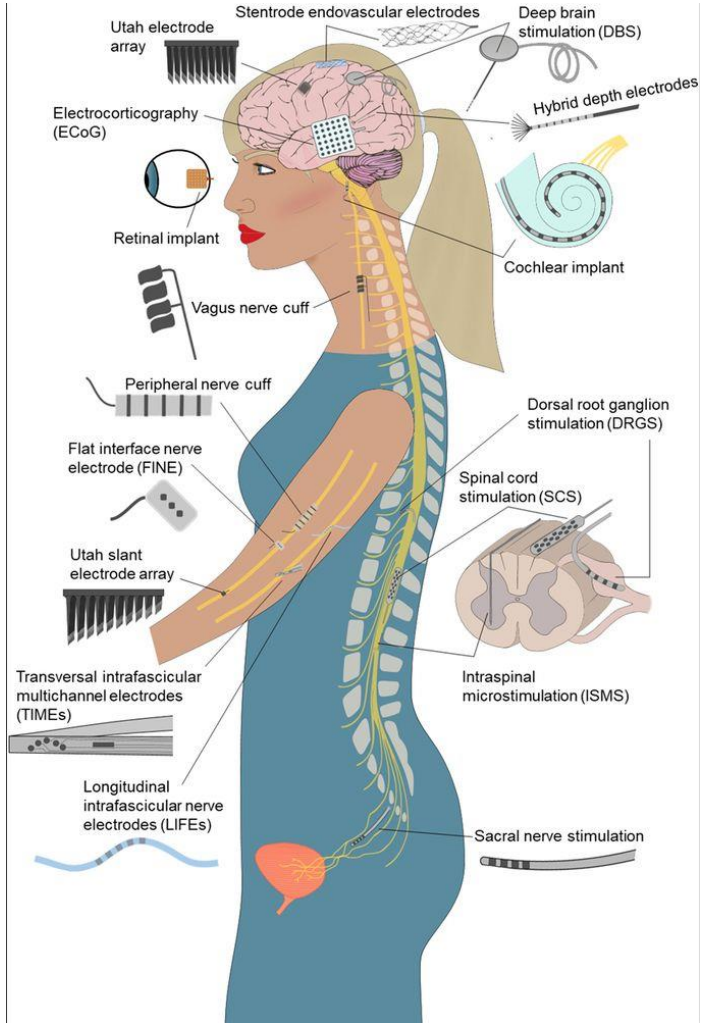
Clinical Site for Trial (PI: Chamessian)

https://clinicaltrials.gov/study/NCT06628908?intr=vx-548&rank=6

Neuromodulation

Growth of Non-Invasive Neuromodulation

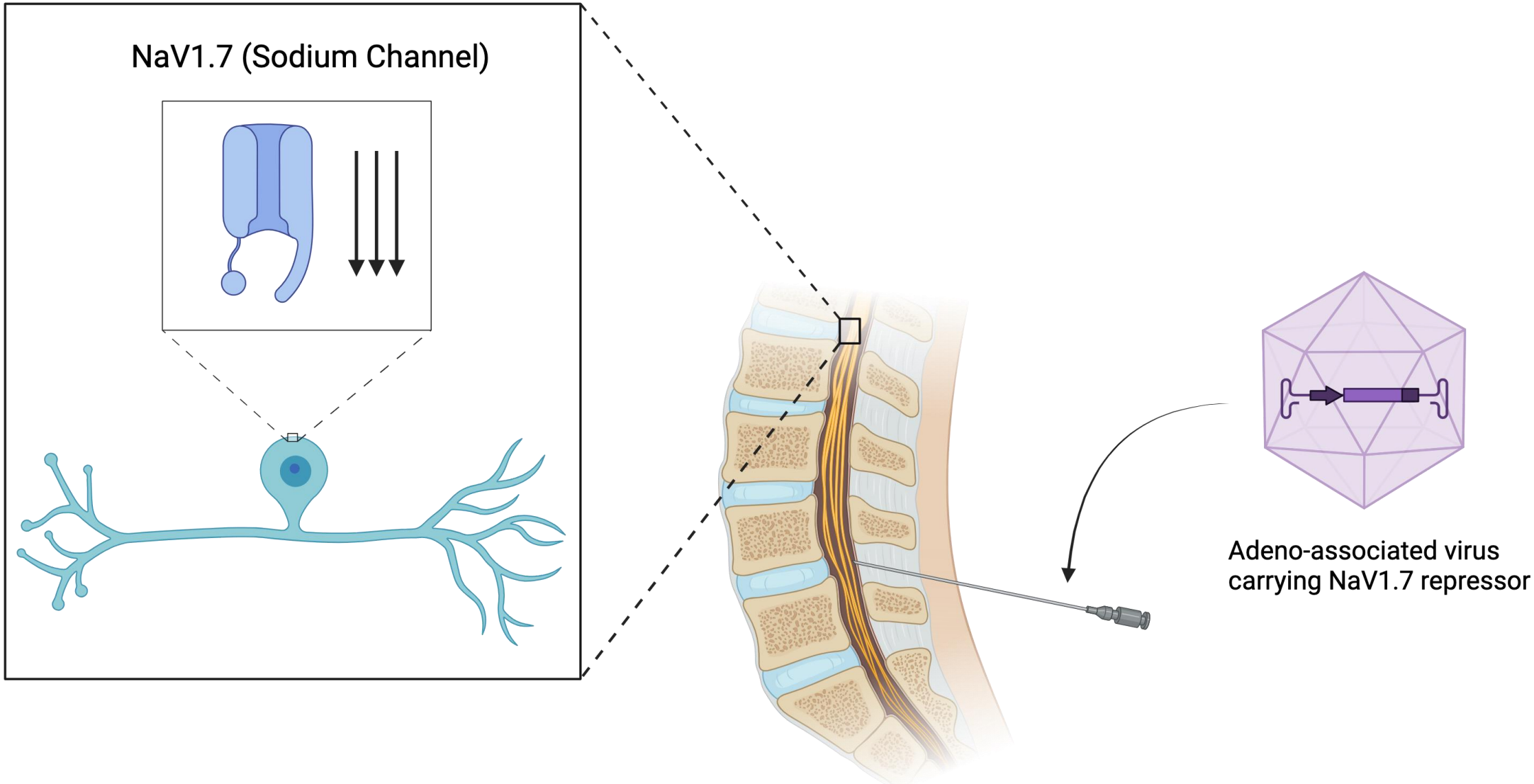
Magnetic Peripheral Nerve Stimulation



- New Device Hardware
- New Programming
- Expanded Neural Targets (Brain, Vagal Nerve, etc.)

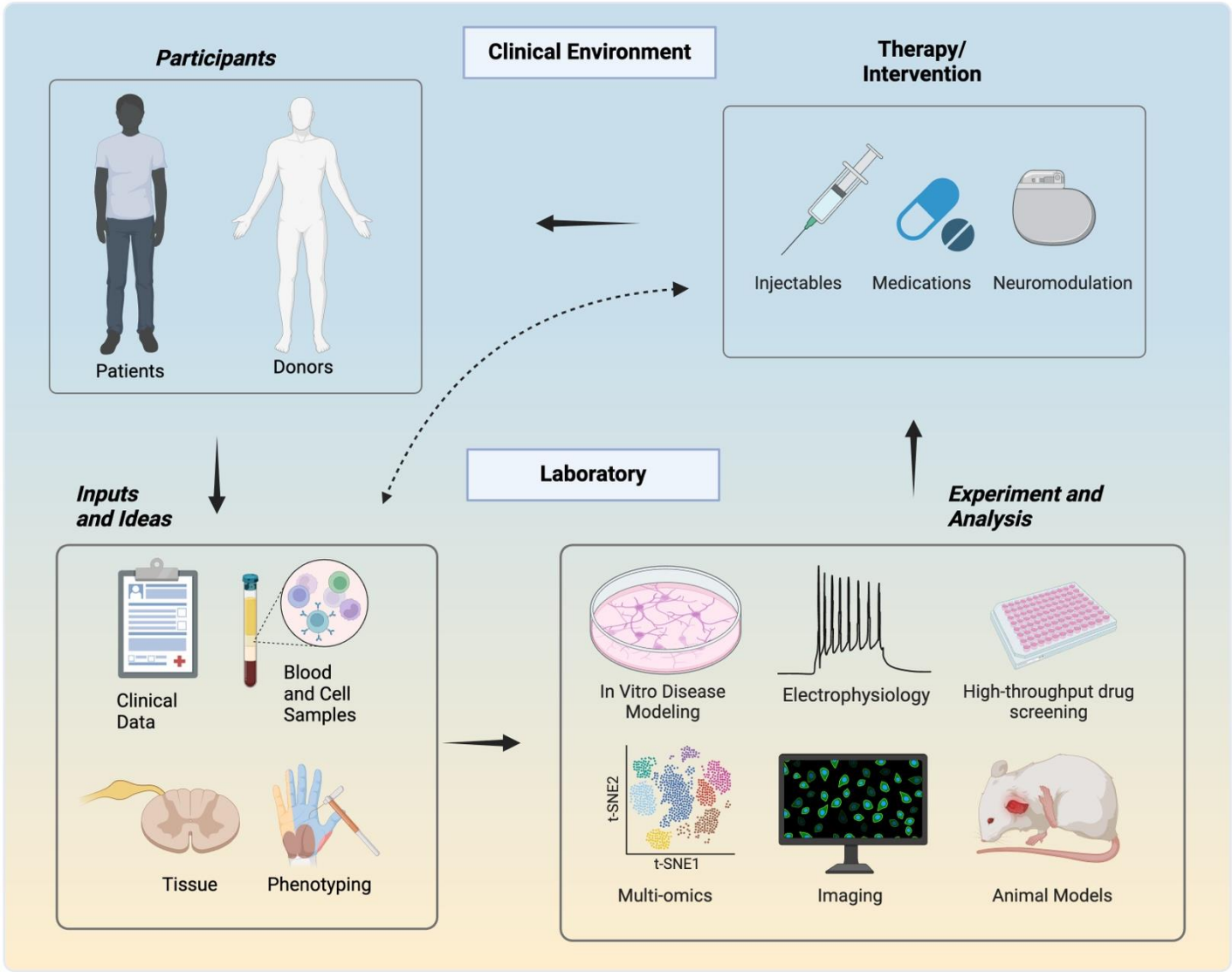
1.Dalrymple, A. N., Jones, S. T., Fallon, J. B., Shepherd, R. K. & Weber, D. J. *Bioelectronic Medicine* **11**, 6 (2025).

Gene Therapy

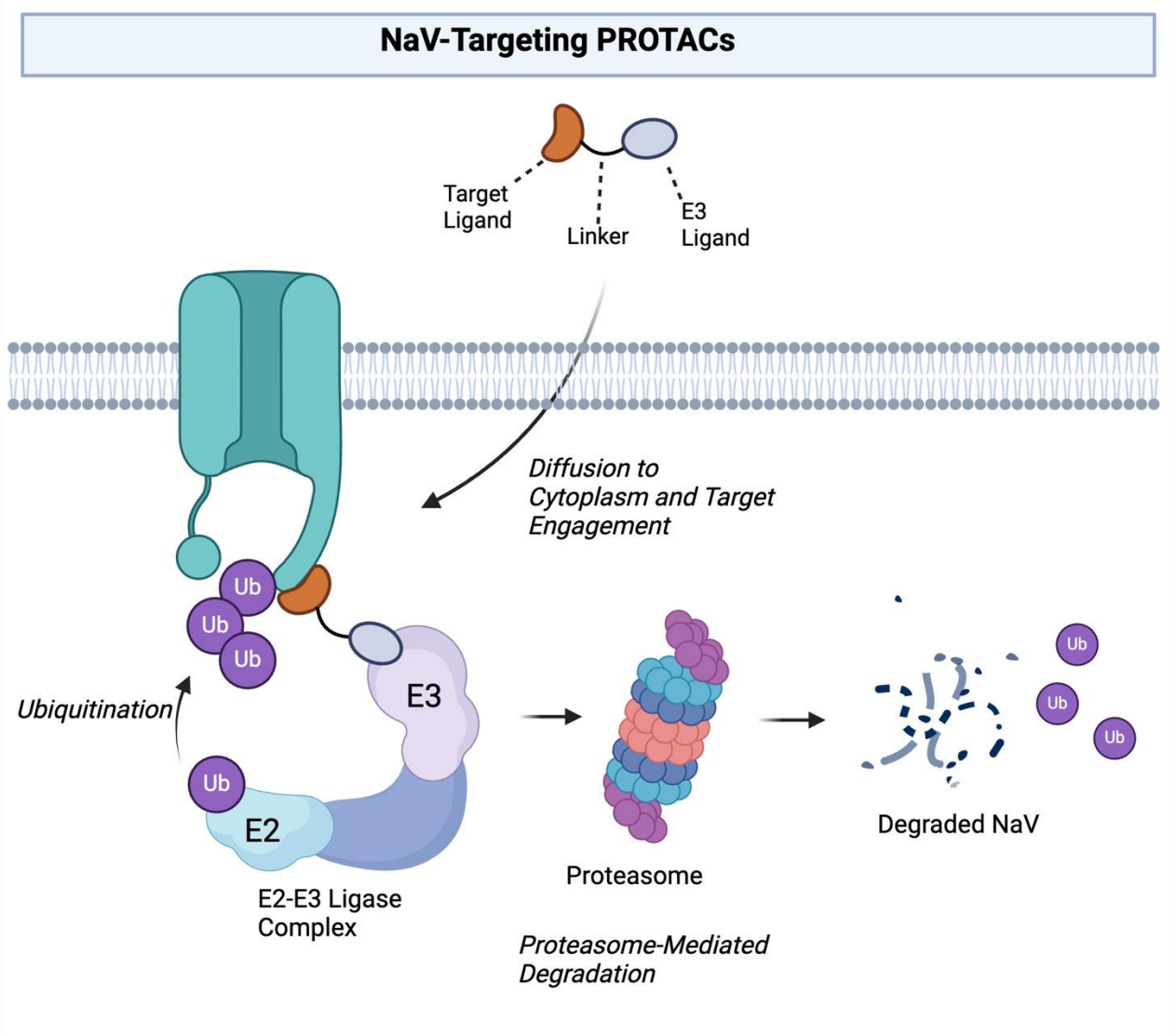


Research – Chamessian Lab

Approach


Participants
Clinical Environment
Therapy/
Intervention
Patients
Donors
Injectables
Medications
Neuromodulation
Laboratory
Inputs
and Ideas
Experiment and
Analysis
Clinical
Data
Blood
and Cell
Samples
Tissue
Phenotyping
In Vitro Disease
Modeling
Electrophysiology
High-throughput drug
screening
t-SNE2
t-SNE1
Multi-omics
Imaging
Animal Models

New Pharmacology – NaV1.8 Degrader Analgesics



New Results

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Small molecule-mediated targeted protein degradation of voltage-gated sodium channels involved in pain

Posted January 22, 2025.

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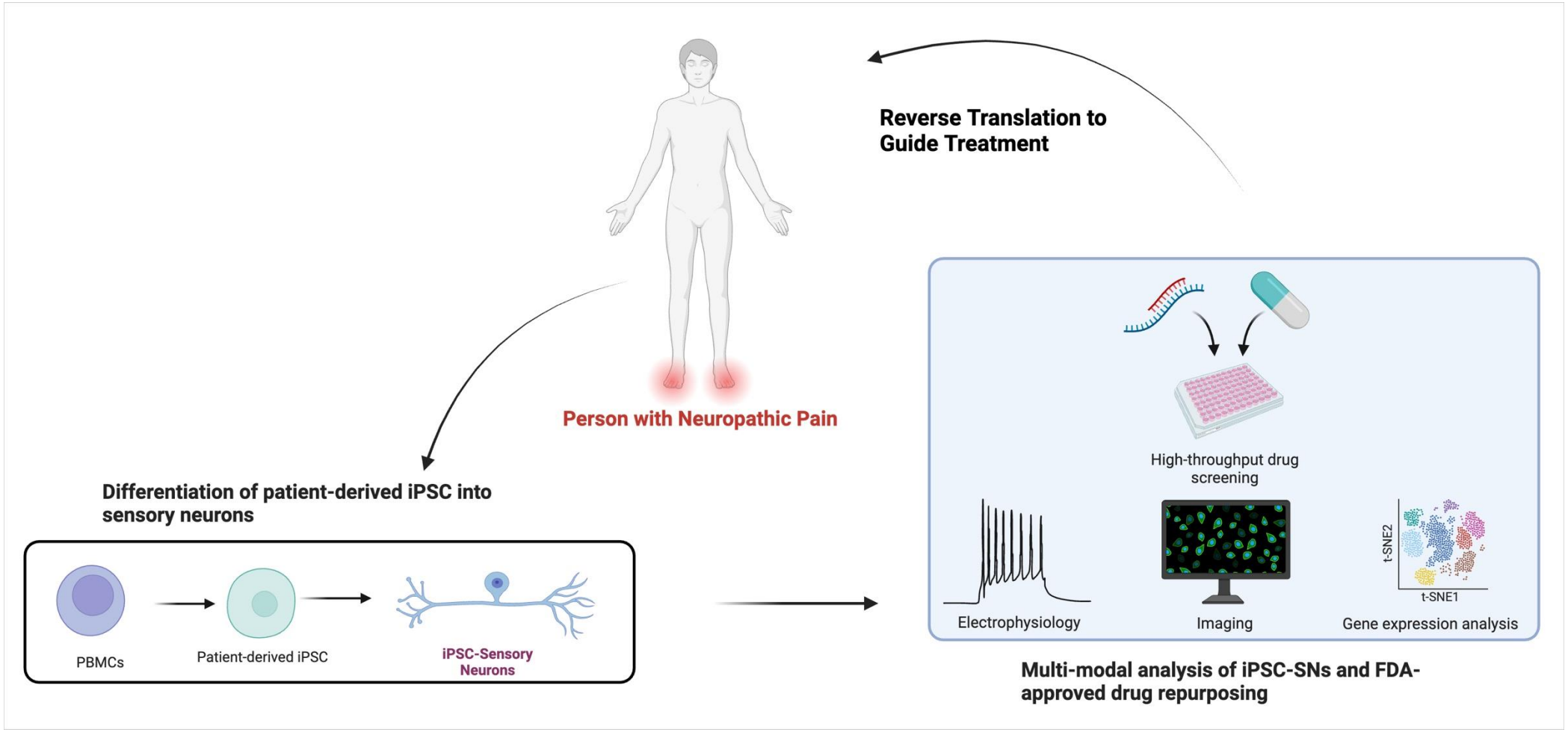
Alexander Chamessian, Maria Payne, Isabelle Gordon, Mingzhou Zhou, Robert Gereau IV

doi: https://doi.org/10.1101/2025.01.21.634079

Abstract | Info/History | Metrics | Preview PDF

Patient-Specific ‘Pain in a Dish’



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Questions?