

# **Neuromodulation and Neuropathy**

**a match made in heaven**

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# Objectives

- Identify 3 treatment options for neuropathy
- Explain the Mechanism of Action with Spinal Cord Stimulation.
- Understand the talking points for patient education on neuropathy and neuromodulation

# What is neuropathy?

Neuropathic pain

“pain arising as a direct consequence of a lesion or disease of the somatosensory system”



Sensory deficits/dysesthesias

# WHY DO WE CARE

Neuropathic pain prevalence estimated at 15% in US

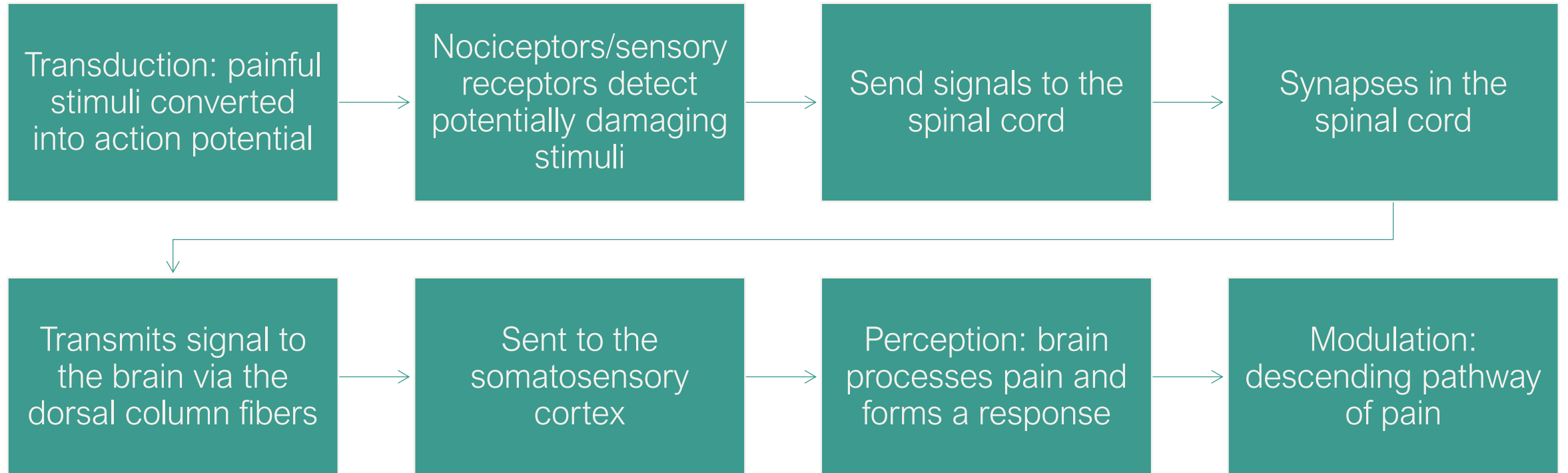
Diabetes affects 422 million adults worldwide (8% prevalence) and approximately 20% will develop Painful Diabetic Neuropathy (PDN) (Petersen et al., 2021)

Neuromodulation is a non-pharmacologic option (potentially opioid sparing)  
(Chakravarthy et al., 2018. Al-Kaisy et al., 2020. Pollard et al., 2019)

Spinal Pain (combined with low back pain and neck pain) ranks among the top 5 conditions of disability (Chakravarthy et al., 2018)



# How does it work?



**Each step provides a chance to intervene**

“It feels like getting hooked up to a car battery and getting shocked.”

“It is not a disease that you want to have- the pain is unbearable.”

“Every night is hell.”

“The pain is inconsolable.”

# Types of neuropathy

Metabolic

Toxic

Disease based

Idiopathic

# Chemo-induced neuropathy

- Taxanes: up to 100% incidence in pts treated with paclitaxel (Zeng, Alongkronrusmee & van Rijn, 2020)
- Paclitaxel causes abnormal microtubule accumulation; leads to demyelination and inhibits regenerative capacities of neurons
- Risk Factors: (Hammond et al., 2020)
  - Previous chemo
  - Exposure to toxins
  - Genetic causes
  - Pre-existing nerve health
  - Mechanical entrapment neuropathies



# Alcohol neuropathy

Occurs in 65% of pts with alcohol use disorder



Typically, symmetrical polyneuropathies in the lower distal extremities

- heavier abuse can progress to distal upper extremity symptoms

Cause may be multifactorial

- Nutritional: large-fiber neuropathy (vibration /proprioception) from thiamine deficiency
- Direct neurotoxic effect: acetaldehyde (neurotoxin formed when alcohol is metabolized) toxic effect on c-fibers (painful paresthesias, often in early disease)

# A note on alcohol neuropathy

“Abstinence for several months up to a few years have shown both clinical examination and electroneurographic improvements, with most patients showing complete regain of function.”

# Metabolic Neuropathy

- Can develop acutely
- Can include sensory ataxia, areflexia, variable muscle weakness, poor nutritional status, and weight loss, often with prolonged vomiting and normal cerebrospinal fluid protein
- Often low Vitamin B6 and Thiamin
- Improved with weight gain and vitamin supplementation



# Douleur Neuropathique 4 (DN4) diagnostic tool

Does the pain have the following characteristics?	YES	NO
1. Burning	1	0
2. Painful Cold	1	0
3. Electric Shocks	1	0
Does the area of pain also have the following	YES	NO
4. Tingling?	1	0
5. Pins & Needles?	1	0
6. Numbness?	1	0
7. Itching	1	0
Exam	YES	NO
8. Decrease in touch sensation (soft brush)?	1	0
9. Decrease in prick sensation (von Frey hair #13)?	1	0
10. Does movement of a soft brush in the area cause or increase pain?	1	0

## Scoring

Score 1 point for every YES

Test is positive if  $\geq 4$

$\geq 4$  sensitivity of 82.9% & specificity of 89.9%.

At score of 3, sensitivity and specificity are 84%

# **S-LANSS:** Leeds Assessment of Neuropathic Symptoms and Signs

**Total score: Score of 12 or more suggests pain of predominantly neuropathic origin**

**1. In the area where you have pain, do you also have “pins and needles”, tingling or prickling sensations?**

NO I don't get these sensations = 0

YES I get these sensations = 5

**2. Does the painful area change color (perhaps look mottled or more red) when the pain is particularly bad?**

NO The pain does not affect the color of my skin= 0

YES I have noticed that the pain does make my skin look different from normal=5

**3. Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations or pain when lightly stroking the skin might describe this.**

NO The pain does not make my skin abnormally sensitive to touch =0

YES My skin in that area is particularly sensitive to touch= 3

**4. Does your pain come on suddenly and in bursts for no apparent reason when you are completely still? Words like “electric shocks”, jumping and bursting might describe this.**

NO My pain does not really feel like this =0

YES I get these sensations often = 2

# LANSS cont.

- 5. Does your pain come on suddenly and in bursts for no apparent reason when you are completely still?**  
**Words like “electric shocks”, jumping and bursting might describe this.**  
NO My pain doesn't really feel like this= 0  
YES I get these sensations often= 2
- 6. In the area where you have pain, does your skin feel unusually hot like a burning pain?**  
NO I don't have burning pain= 0  
YES I get burning pain often= 1
- 7. Gently rub the painful area with your index finger and then rub a non-painful area (for example, an area of skin further away or on the opposite side from the painful area). How does this rubbing feel in the painful area?**  
The painful area feels no different from the non-painful area= 0  
I feel discomfort, like pins and needles, tingling or burning in the painful area that is different from the non-painful area=5
- 8. Gently press on the painful area with your fingertip and then gently press in the same way onto a non-painful area (the same non-painful area that you chose in the last question). How does this feel in the painful area?**  
The painful area does not feel different from the non-painful area= 0  
I feel numbness or tenderness in the painful area that is different from the non-painful area= 3

# Why wouldn't I **just** use medication?

## Gabapentin

(Wiffen et al., 2017)

- Doses 1200-3600mg: 38% had at least 50% improvement
- 68% had at least 1 adverse event: dizziness (19%), somnolence (14%), peripheral edema (7%), and gait disturbance (14%)
- Number needed to treat 6.6/ number needed to harm 7.5

## Tricyclic antidepressants

(Gupta et al., 2021)

- In studies, relief over placebo did not reach statistical significance
- AE: gastrointestinal issues, orthostatic hypotension, dry mouth, urinary retention, and QTc prolongation
- NNT 3.6/ NNH 13.6 (Bardel et al., 2011)

## Duloxetine

(Gupta et al., 2021)

- Mean relief of 64-68% relief
- AE: nausea, somnolence, hyperhidrosis, and anorexia, black box warning for suicide risk
- NNT 5.8/ NNH 15 (Sultan et al., 2008)

# **Painful Diabetic Neuropathy**



“Stocking/glove”  
distribution

Electric Shocks

Allodynia:  
exaggerated pain  
response to  
normal stimuli.

Worse at rest

Burning

Numbness

Hyperalgesia:  
enhanced  
sensitivity to pain

Painful coldness



# Which leads to

- Decreased physical activity
- Increased fatigue
- Sleep problems
- Worsening quality of life
- Increased mortality



# Treatment

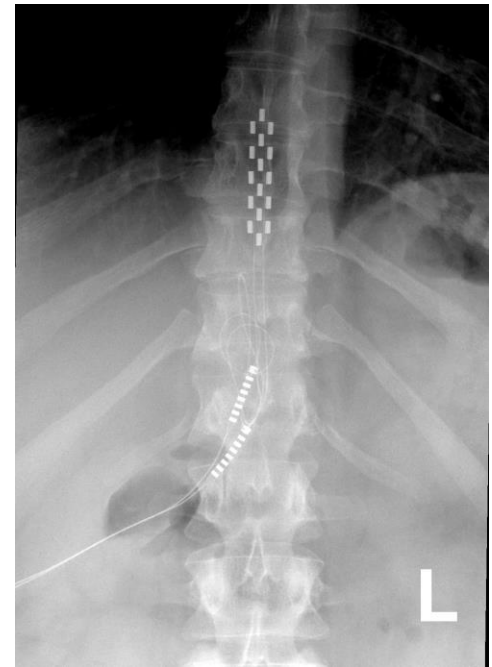
**“Any help is better than none”**

# WHAT IS 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

-the International Neuromodulation Society





**What does it look like**

# Which of my patients may benefit?



Neuropathic pain of trunk or limbs

Non-surgical refractory low back pain

Painful diabetic neuropathy

Do you know anyone with these issues?

# Varieties of stimulation

## Tonic SCS 45-1500 Hz

- Low frequency/ Tonic SCS: paresthesia vs. non paresthesia
- Indirect stimulation of dorsal horn
- MOA: gate control theory and enhanced release of GABA

## Burst SCS

- Mimics naturally occurring neural bursting patterns in the CNS
- stimulates sensorimotor cortex areas (localization and intensity of pain)
- stimulates the medial STT targeting limbic areas (cognitive motivational and emotional aspects of pain)

## High Frequency SCS/ 10,000 Hz

- Direct stimulation of dorsal column: no paresthesia
- Inhibitory signals electrochemical disturbance of dorsal horn and desynchronizing communication between C-fibers and/or depolarization blockade that blocks action potentials

# **The American Association of Clinical Endocrinology (AAACE) Guidelines Update 2022**

HIGH FREQUENCY (EG, 10 KHZ) SPINAL CORD STIMULATION IS A NONPHARMACOLOGICAL APPROACH THAT MAY BE EFFECTIVE IN PERSONS WITH PAINFUL DPN THAT FAILED AT LEAST ONE MEDICATION, AS SUGGESTED BY A RECENT LARGE RCT, LEADING TO FDA APPROVAL IN 2021.

LIFESTYLE INTERVENTIONS INCLUDING A COMBINATION OF REGULAR AEROBIC, STRENGTHENING, AND BALANCE EXERCISES, REDUCTION OF SEDENTARY BEHAVIOR, AND DIETARY MODIFICATION AIMED AT REDUCING CALORIE INTAKE AND INCREASING PLANT-BASED AND POLYUNSATURATED FATS ARE RECOMMENDED. NEUROMODULATORY TECHNIQUES SUCH AS HIGH-FREQUENCY SPINAL CORD STIMULATION AND COMBINING PHARMACOLOGICAL WITH NONPHARMACOLOGICAL.

# YOU GET TO TRY IT FIRST!

It is reversible  
(unlike surgery)

Typical trial is about 1 week in duration

Trial procedure is similar to an epidural injection

Battery is external during trial

Important to set functional goals

Lumbar issues?  
Leads are placed well above problem area

Psych eval required prior per Medicare guidelines


## But what does it **FEEL** like?

# Outcomes with PDN with High Frequency SCS

SENZA study: high frequency SCS vs. conventional medical management

Primary endpoint  
 $\geq 50\%$  relief without  
worsening of baseline  
neurological deficits at 3  
months

SCS + CMM  $\geq 50\%$   
pain relief in 79% of pt  
(vs 5% with CMM alone)



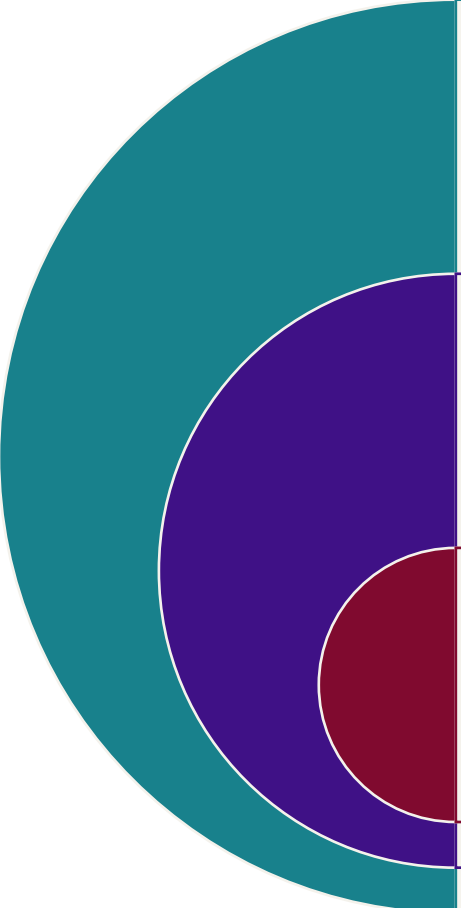
62% of pts had  
improvement in  
neurological exam

Avg 61.9%  
improvement in sleep  
disturbance

# Who were the patients in this study?

Measure	Inclusion Criteria	Study Participants
Hgb A1C	<10%	7.4%
BMI	45	33.7
Duration of Diabetes		10.9 years
Duration of Neuropathy	1 year	5.6 years
VAS	$\geq 5$	7.3
Daily opioid MME	<120	

# Outcomes in PDN with low-frequency/tonic SCS



69% responder rate (>50% relief) at 6 months:  
study of 36 pts (De vos et al., 2014)

56% responder rate at 6 months, 36 % responder  
rate at 5 years: study of 16 pts (Slagen et al., 2014)

No reported improvement in neurological symptoms  
in low frequency studies (Van Beek et al., 2018)



# **Medical Considerations**

Anticoagulated status

Psych Clearance

MRI compatibility

Diabetics: A1C < 10

Cognition/support systems

Shoulder mobility

Rechargeable vs. non-rechargeable battery



# What can I expect with implantation

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Outpatient procedure

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IPG device (battery) typically implanted in flank

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2 incisions: midline for anchor and flank for IPG

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Staples vs. glue

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Done under anesthesia

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Charging Frequency (for rechargeable)

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No twisting/reaching for 6 weeks

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Frequent follow up to maximize outcomes and programming

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# I'm scared to try it!

- Remember, it's an optional procedure.
- Continue with a multifactorial approach
- Medications can be tried first: gabapentinoids, TCA, SNRI, topical agents, cannabis
- Let's not forget about acupuncture.
- Down-regulate your nervous system with progressive relaxation and mindfulness meditation.



# conclusion

The pain of neuropathy does not have to be  
inconsolable.

We have options, we just need to let our patients  
know about them...

and stay the course.



# Let's connect

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