Electrical Tingles: Neuromodulation for the General Practitioner

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Title & Affiliation

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Disclosure

- Consultant: Nevro, Vertos, Camber Spine
**Learning Objectives**

- Explain the use of electrical signals to block pain
- Review the theory of how neuromodulation works
- Explore the different products that are currently on the market
- Review the application of the devices in clinical practice
- Review data supporting the role of products in decreasing opioid use
- Discuss the process of trial and implantation of devices
History of Neuromodulation

- First used to treat pain in 1967
- Gate theory was published in 1965
- Became more mainstream in 1980s
- 1989 FDA approved use of devices to treat chronic pain from nerve damage in trunk, arms or legs
- Year after year the devices continue to improve upon earlier iterations
Neuromodulation

- So what is it?
- Application of electrical signals to lessen pain complaints
- Drug/medication = electricity
- Types of neuromodulators
  - Spinal cord stimulators, dorsal column stimulators, dorsal root ganglion stimulators, peripheral nerve stimulators
Mechanism of Action

- Continues to be elucidated
- Current thought is that it increases firing of inhibitory neurons in the dorsal spinal horn
  - Decreases transmission/signaling of painful stimulus from reaching brain
  - Gate control theory
Gate Control Theory

- Published in 1965 in Science by Melzack and Wall
  - “Pain Mechanisms: A New Theory”
- Revolutionized theory of pain control


Gate Control Theory

Gate Control Theory

- Gating mechanism in spinal dorsal horn modulates transmission of nerve impulses from afferent fibers to spinal cord transmission cells
  - The gating mechanism is affected by the relative activity in large and small diameter fibers with the former inhibiting transmission (closing the gate) and the latter facilitating transmission (opening the gate)
  - Gating mechanism is also modulated by descending nerve impulses from the brain
  - Burn example

Neuromodulation and the Gate Control Theory

- Conventional SCS devices believed to relieve pain by:
  - Activation of Aβ fibers resulting in variable effects on sensory and pain thresholds
  - Potentiation of inhibition

Sdrulla, Guan, Raja. Spinal cord stimulation: clinical efficacy and potential mechanisms. Pain Practice. 2018;18 (8):1048-1067
Neuromodulation

- FDA approved
  - Alleviation of pain in trunk, arms or legs
  - Chronic regional pain syndrome
    • AKA RSD or causalgia

- Most common indication/usage
  - Failed back surgery syndrome
    • Post laminectomy pain syndrome
    • Chronic pain syndrome

- Pacemaker companies
  - Developed a lot of the initial technology
Amplitude, Frequency, Pulse Width

- Parameters we can change with SCS devices
  - Frequency is how often device delivers charge and depolarization
  - Amplitude is relative strength of charge delivered
  - Pulse width is duration of charge delivery

- Tonic or low frequency
  - 20-120Hz range
  - Patients perceive individual pulses

- High frequency
  - Pulses start to blend so no perception occurs
Amplitude, Frequency

Wavelength (\(\lambda\))
Distance between identical points on consecutive waves

Amplitude
Distance between origin and crest (or trough)

Frequency (\(\nu\))
Number of waves that pass a point per unit time

Speed
= wavelength x frequency
Traditional vs High Frequency vs DRG

- Traditional AKA “low frequency,” “tonic”
  - Tens unit sensation, paresthesia present, can go up to 1200Hz
- High frequency, paresthesia not present, 10,000Hz
- DRG (dorsal root ganglion) stimulators
  - Low frequency, used for focal pain locations
Electrodes

- Typically 8 electrodes per lead with two leads typically used
- Surgeons can place paddle leads with different configurations
- DRG 4 electrodes
Evidence for Neuromodulation

- **Kumar study**
- RCT conventional medical management (CMM) vs SCS for neuropathic pain
  - Primary outcome was patients reporting 50% or more relief of leg pain
  - Secondary outcomes were improvement in back pain, QOL, functional capacity, use of medication, patient satisfaction
- Compared with CMM group the SCS group saw
  - Improved back and leg pain, better QOL, greater treatment satisfaction

Evidence for Neuromodulation

- Deer study
- Multicenter, prospective RCT
  - Following successful trial 100 patients were randomized after implant to receive 12 weeks of tonic stim followed by 12 weeks of burst
  - Primary endpoint assessed the noninferiority of the within-subject difference between tonic and burst for mean daily VAS score
    - Burst stimulation is non inferior to tonic stim
    - Significantly more subjects 70.8% preferred burst over tonic; preference was sustained over 1 year

Frequency Matters

Responder Rate (50% Threshold)

- 0 Hz
  - KUMAR\(^1\)
  - SENZA-RCT\(^2\)
  - SUNBURST\(^3\)
  - HD\(^4\)
  - WHISPER\(^5\)

- 1 kHz
  - 48%
  - 51%
  - 39%
  - 47%
  - 39%

- 5 kHz
  - 79%
  - 79%

- 10 kHz
  - 79%
  - 79%

1,200 Hz: SCS Frequency Limit

Increasing Neural Inhibition

Legend:
- Traditional SCS
- Burst
- 1000 Hz
- HF10
Evidence for Neuromodulation

- SENZA Study
- Head to head study of low vs high frequency
- 24 month outcomes
  - Sustained, clinically superior outcomes
  - Long term, durable pain relief: 24 MONTHS
    - 76% responder rate
    - 2.4 cm VAS for both back and leg pain
  - Only device labeled as paresthesia-free
  - “Top Pain Paper of the Year”

Evidence for Neuromodulation....High Frequency

**Durable Back Pain Relief to 24 Months**

**Decreased Opioid Use in SENZA-EU Trial with HF10 therapy After 2 Years**

<table>
<thead>
<tr>
<th>% Of Patients Using Opioids</th>
<th>Mean Mg Morphine Equivalent Per Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (n=72)</td>
<td>Baseline (n=72)</td>
</tr>
<tr>
<td>86%</td>
<td>84</td>
</tr>
<tr>
<td>54%*</td>
<td>29*</td>
</tr>
<tr>
<td>57%*</td>
<td>27*</td>
</tr>
</tbody>
</table>

34% reduction in # of patients using opioids

68% reduction in dose

*p-value < 0.001 compared to Baseline

Opioid Reduction in Real World Practice

Results in My Permanent Implant Patients

Responder Rate (>= 50% pain relief)

Last Visit (n = 183)

78%

Last Visit Medication Change of IPG Patients

- Increase 2%
- Decrease 44%
- Same 55%

n = 172

Average number of months between IPG procedure and last visit is 17.3 (min=1.0, max=48.8)
Evidence for Neuromodulation

- New indication in 2021
- PDN
- Published in JAMA Neurology April 2021
- Compared traditional medical management vs high frequency spinal cord stimulation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No (%)</th>
<th>10-NIL/165 plus GMF</th>
<th>Standardized difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>80 (44.1)</td>
<td>39 (88.5)</td>
<td>0.84</td>
</tr>
<tr>
<td>Race</td>
<td>Black or African American 11 (12.6)</td>
<td>18 (35.6)</td>
<td>P = 0.04</td>
</tr>
<tr>
<td>Gender</td>
<td>Male 60 (42.5)</td>
<td>60 (91.3)</td>
<td>0.81</td>
</tr>
<tr>
<td>Sex</td>
<td>Female 20 (28.6)</td>
<td>7 (11.3)</td>
<td>0.84</td>
</tr>
<tr>
<td>Race</td>
<td>White 30 (36.5)</td>
<td>87 (172.0)</td>
<td>P = 0.04</td>
</tr>
<tr>
<td>Hispanic or other Pacific Islander</td>
<td>3 (3.7)</td>
<td>2 (3.7)</td>
<td>P = 0.14</td>
</tr>
<tr>
<td>流泪 (yes)</td>
<td>Eye 1 (1.2)</td>
<td>6 (10.0)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>College graduate 30 (28.6)</td>
<td>60 (36.5)</td>
<td>0.81</td>
</tr>
<tr>
<td>White (yes)</td>
<td>White 30 (36.5)</td>
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<tr>
<td>Asian</td>
<td>Asian 1 (1.2)</td>
<td>1 (1.7)</td>
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<td>American Indian or Other Asian</td>
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</tr>
<tr>
<td>Females</td>
<td>Females 57 (54.9)</td>
<td>43 (88.5)</td>
<td>0.84</td>
</tr>
</tbody>
</table>

**Table: Baseline Characteristics for All Donor Units**

**Notes:**

- All data are presented as counts and percentages unless specified otherwise.
- Standardized differences are calculated using the standard deviation of the difference between the two groups, and are presented as standardized differences. The 10-NIL/165 group is used as the reference group for all comparisons.

**References:**


**Footnotes:**

- Bolded values indicate a statistically significant difference between the two groups.
- All values are presented as mean ± standard deviation unless specified otherwise.
- All p-values are calculated using a two-tailed t-test for continuous variables and a chi-square test for categorical variables.
Procedure Overview (Trial)

- Only pain procedure that requires psychiatric/psychological clearance by insurance company
  - Patient is malingering or faking symptoms
  - Patient will call if there is infection or issues with device
  - Most of these patients have undergone previous spine surgery
  - Large scar present on back
Procedure Overview (Trial)

- Placement of percutaneous electrodes into epidural space
  - Just like performing an epidural. Done under xray
    - Rather than injecting medication electrodes are placed
    - Trial leads stay in place for 5-7 days and are connected to a battery
      - If >50% pain reduction
      - Implant can be performed
Procedure Overview (Trial)
Procedure Overview (Trial)
Procedure Overview (Permanent Implant)

- Leads are again placed into epidural space and then tunneled under skin to a battery
  - Battery, which powers the device, is placed in the flank
- Battery
  - Rechargeable vs Non-Rechargeable
Complications/Risks of Procedure

- **Infection**
  - Epidural abscess
    - Paralysis

- **Bleeding**
  - Epidural hematoma
    - Paralysis

- **Lead migration/lead fracture**
  - Loss of efficacy
Contraindications

- Severe uncontrolled psychological disorders
  - Schizophrenia, depression, bipolar disorder
- Bleeding disorder
- Use of blood thinners or NSAIDs
- Active infection
- Relative contraindication
  - Need for continued MRI studies
    - Most newer devices have MRI approval
Questions