Multimodal approaches to pain management and potential synergies

Neuromodulation and Non-Pharmacological Approaches

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• Consultant to SPR Therapeutics, Inc.
Why Non-pharmacologic?

- Non-pharmaceutical treatments do not share equal status
- Drug side effects, interactions, or comorbid illness limit use for some
- Favorable risk-benefit ratios and evidence supports non-pharmacologic treatment
- Growth in non-pharmacologic treatment options including neuromodulatory devices
Neuromodulation Devices

• The alteration of nerve activity through targeted delivery of a stimulus to specific neurological sites

• Neural stimulus modulates abnormal neural pathways in CNS or PNS

• Stimulus – electrical current or chemical, non-invasive or invasive

• Goal- therapeutic pain reduction, improve function and QoL
Neuromodulation Options

- Spinal Cord Stimulation
  - Traditional, Burst, High Frequency
  - Dorsal Root Ganglion
Neuromodulation Options

• Spinal Cord Stimulation
  – Traditional, Burst, High Frequency
  – Dorsal Root Ganglion

• Peripheral Nerve Stimulation
  – Sensory
  – Motor
Neuromodulation Options

• Spinal Cord Stimulation
  – Traditional, Burst, High Frequency
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• Peripheral Nerve Stimulation
  – Sensory
  – Motor

• Brain Stimulation
  – Transcranial- Direct, Magnetic
  – Deep Brain Stimulation
## Evidence: Pain Relief

<table>
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<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Effect</th>
<th>Evidence</th>
<th>References</th>
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<td></td>
<td>Peripheral Nerve Stim vs. Sham</td>
<td>Moderate</td>
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<td>Chen, et al. 2015</td>
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<td>Phantom Limb Pain:</td>
<td>tDCS vs. Sham</td>
<td>Moderate</td>
<td>Low</td>
<td>Corbett, et al. 2018</td>
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<tr>
<td>Neuropathic Pain, SCI:</td>
<td>tDCS vs. Sham</td>
<td>Moderate</td>
<td>Low</td>
<td>Boldt, et al. 2014</td>
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<td>Chronic Pain (Various):</td>
<td>tDCS vs. Sham</td>
<td>Small</td>
<td>Low</td>
<td>O’Connell, et al. 2018</td>
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Non-pharma or NM Device?

• Based on evidence- which treatment?

• Evidence: no single treatment will suffice

• A better way?
Multimodal Treatment

• Use of separate therapeutic interventions with different mechanisms of action... aimed at different pain mechanisms – adapted IASP Task Force, 2017

• **Hypothesis:** Non-pharmacologic treatments and neuromodulation reduce pain different ways – KneeOA:
  – Exercise: improves biomechanics, alters endogenous pain mechanisms
  – tDCS: improves somatosensory function, encourages neuroplasticity

• Effects may be summative or synergistic

• Little evidence is available to guide multimodal practice
# Evidence: Multimodal Therapy

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<td>FM:</td>
<td>tDCS+AE vs. tDCS vs. AE</td>
<td>tDCS+AE &gt; tDCS or AE</td>
<td>1 RCT, Mendonca, et al. 2016</td>
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<td>CLBP:</td>
<td>tDCS + Exercise vs. sham-tDCS + Exercise</td>
<td>tDCS + Exercise &gt; sham-tDCS + Exercise</td>
<td>1 RCT, Straud, et al. 2018</td>
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An Example – PNS for HSP

Peripheral Nerve Stimulation – Level 1b Evidence

• Stimulation of **middle and posterior deltoids** through **single** lead
  – 12 Hz, 20 mA, individually tailored pulse width
• 6 hours per day, 3 wks (126h of stimulation)

Physical Therapy

• 8 hrs PT over 4 weeks
  – Proper positioning, handling, slings
  – ROM and strengthening
  – Task-specific therapy to improve ADLs
  – Home exercise program

MetroHealth

CASE WESTERN RESERVE UNIVERSITY
Results - Pain

Time $F(1,21) = 13.4$, $P=0.001$

Treatment x Time $F(1,62) = 4.4$, $P=0.04$

Multimodal Treatment?

- Multisite, RCT – Multimodal Therapy for HSP (NICHD, R01 HD084564)

96 Subjects
Chronic HSP

- PNS + PT
- PNS + shamPT
- shamPNS + PT

- Efficacy of multimodal treatment, and incremental differences between treatments
- Additional Outcomes- Mechanisms, Patient Selection
Multimodal Treatment for PLP

- F. Fregni– Optimizing Mirror Therapy + tDCS (NICHD, R01HD082302)

- Efficacy of multimodal treatment compared to sham, and incremental differences between treatments

- Additional Outcomes- **Mechanisms**

Ongoing Multimodal Research

• **R. Wilson** – Physical Therapy and Peripheral Nerve Stimulation for Subacromial Impingement Syndrome – MetroHealth Rehabilitation Institute, Cleveland, Ohio (R01 HD093661)

• **A. Oulette** – tDCS and Sensorimotor Retraining for CLBP – Western Sydney University, New South Wales, Australia

• **W. Chang** – tDCS and Exercise for Knee OA - Western Sydney University, New South Wales, Australia
Thank you

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