Medicinal Cannabis & Pain: An Alternative to Opioids?

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Disclosures

- Nothing to disclose
Objectives

- Discuss with patients the evidence re cannabis and pain
- Educate patients regarding adverse effects of cannabis use
- Educate patients regarding the onset and duration for oral vs. inhaled delivery of cannabis
- Increase confidence answering having discussions with patients when they inevitably ask "what about marijuana"

Pre-Assessment Questions

- Which of the following is true about the effects of tetrahydrocannabinol (THC) on pain?
  A. Cannabidiol (CBD) has clinical evidence as an analgesic equivalent to that of THC
  B. THC reduces pain in a dose dependent fashion with no ceiling effect
  C. The strongest clinical evidence for analgesic effects of THC is in neuropathic pain
  D. The clinical evidence for the analgesic effects of THC is greatest for chronic low back pain

Pre-Assessment Questions

- Which is true regarding cannabis safety?
  A. There is no dependence or withdrawal associated with cannabis use
  B. Smoked cannabis has a strong association with lung cancer
  C. States with medical marijuana laws have higher rates of opioid overdose deaths
  D. High dose cannabis can induce paranoia and hallucinations
Pre-Assessment Questions

Which of the following is true regarding routes of administration for medicinal cannabis?

A. Enteral administration is the most commonly studied route of administration in clinical trials
B. Duration of effect for enteral administration is substantially longer than for inhaled route
C. Inhaled route of administration results in peak blood levels within 15-20 minutes
D. Topical administration has evidence for arthritis pain

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Which of the following is true regarding medicinal cannabis laws?

A. Cannabidiol (CBD) is a Schedule 1 drug
B. In order for a patient to obtain medicinal cannabis their physician must write a prescription
C. Cannabis products in dispensaries are regulated for purity and safety in the states with medical marijuana laws
D. A physician recommendation shields patients from being fired for cannabis use

Medicinal Cannabis

- History of cannabis as medicine
- Cannabis pharmacology
- Cannabis Safety
- Evidence for pain
- Clinical Practice & Legal Issues
History of Medicinal Cannabis

- China, 1st century: rheumatic pain, constipation...
- India: sedative, anxiolytic, anticonvulsant, analgesic...
- 1839: Dr. William O’Shaughnessy
- U.S. Dispensatory 1845; analgesic in place of opium
- Late 19th/Early 20th Century:
  - migraine, neuralgia, dysmenorrhea, acute rheumatism, dental pain
  - multiple patent medicines
- Removed from pharmacopeia in 1942
- Against advice of the AMA
- 1996: California prop 215

Cannabis Pharmacology

- Endocannabinoid system: CB1 and CB2
- Cannabis and opioid system interactions
- THC and CBD pharmacology
- Cannabis content of marijuana
- Cannabinoid pharmaceuticals
- Cannabis effects on tumors

Medicinal Cannabis: Pharmacology

Endocannabinoid System
- Cannabinoid receptors & endogenous cannabinoids
- Cannabinoid Receptors
  - G protein coupled receptors
- CB1: neuromodulatory
  - CNS & PNS
    - Reduced excitability - PNS
    - Pain processing centers: dorsal horn, amygdala, l grey, RVM
- CB2: immunomodulatory
  - macrophages, B/T-cells, mast cells
  - Inflammatory & immune mediator release
  - Immunotonicity
  - Localization of afferent terminals
Medicinal Cannabis: Pharmacology

Cannabis & Opioid Interactions

- Animal studies indicate a contribution of the opioid system in cannabinoid reward, reinforcement and dependence
- Opioid agonists facilitate while antagonist reduce self administration of cannabinoids
- Naloxone induces cannabinoid withdrawal while co-administration prevents dependence
- Opioids attenuate cannabinoid withdrawal
- Opioid modulation in humans less clear

Cooper ZV, Haney M. Int Rev Psychiatry, 2009, 104-112

Medicinal Cannabis: Pharmacology

- Cannabis contains > 400 compounds; > 80 are cannabinoids
- Delta-9-tetrahydrocannabinol (THC) – main psychoactive cannabinoid
  - Highly lipid soluble
  - High affinity for CB1 & CB2
  - Analog of the endogenous cannabinoid anandamide
- Cannabidiol (CBD) – non-psychoactive cannabinoid
  - Low affinity for CB1 & CB2 – possibly agonist/antagonist
  - Acts on TRPV-1 – inhibitor of cyclooxygenase
  - Has anticonvulsant, muscle relaxant, sedative, and anti-inflammatory activity
  - May attenuate the psychoactive properties of THC

Clinical Pharmacology of Marijuana

- THC & CBD concentration in marijuana varies greatly depending on cultivation, breeding, and processing
- Naturally occurring marijuana THC range 0.3-4%
- Dispensary marijuana THC range 10-30%
- Most common is low to minimal CBD
- "High CBD" marijuana is available

Medicinal Cannabis: Cannabinoid Pharmaceuticals

- THC (schedule 1)
- Nabilone (Cesamet) (schedule II)
- Dronabinol (Marinol) (schedule III)
- Nabiximols (Sativex)
- Not FDA approved

Canada & Europe:
- Cancer pain,
  spasticity

Medicinal Cannabis: Pharmacology

- Possible Anticancer Effects
  - Cannabinoids & cell signaling pathways
    - Cell survival
    - Invasion
    - Angiogenesis
    - Metastasis
  - Animal models
    - CBD inhibition of tumor progression
    - Cannabis extracts inhibition of tumor growth
  - Combined with chemotherapies
    - in vitro & animal models – no negative effects identified, possible synergism

Medicinal Cannabis: Safety

- Adverse effects: short-term and long-term
- Cannabis laws and opioid-overdose mortality
- Adverse effects in clinical use for pain
- Other safety issues and abuse/dependence
Medicinal Cannabis: AEs & Safety

- Short-Term AEs
  - Low Dose
    - Mild euphoria, relaxation, sociability, decreased anxiety, temporal slowing
  - Higher Doses
    - Agitation, anxiety, depersonalization
    - Dryness mouth & eyes, tachycardia
    - Psychomotor function impairment
    - paranoia, hallucinations, & psychosis

- Long-Term AEs
  - Large airway inflammation
  - Heavy use - smoking
  - Cancer Risks
    - Conflicting Studies
  - Cognitive Impairments
    - Verbal reasoning
    - Memory
    - Attention

COMPASS Study
- 1 yr prospective cohort; 531 chronic pain patients
- No difference serious AEs
- Cannabis grp > non-serious AEs
  - Nervous system; psychiatric; respiratory
- No difference: neurocognitive, heme, liver, renal, endocrine function
- Cannabis > Controls:
  - Pain intensity improvement
  - Symptom distress & mood disturbance
Medicinal Cannabis: Safety

- No Federal regulation: production, purity, potency
  - State oversight varies
  - Greater oversight/regulation in recreational states
- No way to clearly specify a dose
- Abuse & Dependence
  - Abuse potential lower than opioids
  - Regular/heavy users may experience withdrawal
- No clear lethal dose

Problematic Opioid vs Cannabis Use: Pain Patients

- Pre-Modern use for pain
- Experimental Pain
- Modern studies of pain
  - Limited & small studies
  - Best evidence: neuropathic pain
  - Wide variation in study product

Medicinal Cannabis: Evidence for Pain

Effects of Inhaled Cannabis on Experimental Pain

- Wallace et al, 2007
  - Healthy Volunteers: randomized, DB, PC, cross-over
  - 4 arms: placebo, low (1mg), medium (4mg), and high (7mg) dose smoked cannabis
  - Low dose no effect on pain
  - Medium dose reduced pain vs placebo
  - High dose increased pain vs placebo

- Abrams et al, 2007
  - 4% THC effect on capsaicin-induced pain in HIV patients
  - Sig reduction in experimental and neuropathic pain

RCTs of Smoked Cannabis in Pain

<table>
<thead>
<tr>
<th>N</th>
<th>Indication</th>
<th>Duration/type</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>HIV neuropathy</td>
<td>5 days/DB</td>
<td>Decreased pain and hyperalgesia (Abrams, 2007)</td>
</tr>
<tr>
<td>16</td>
<td>Diabetic Peripheral Neuropathy</td>
<td>Single dose/DB/Cross-over</td>
<td>Decreased pain (Wallace, 2015)</td>
</tr>
<tr>
<td>38</td>
<td>Neuropathic pain</td>
<td>Single dose/DBC</td>
<td>Decreased pain w/ highest dose, but significant psychoactive effects (Wilsey, 2008)</td>
</tr>
<tr>
<td>34</td>
<td>HIV neuropathy</td>
<td>5 days/DB</td>
<td>Improved pain vs placebo, (Ellis, 2009)</td>
</tr>
<tr>
<td>21</td>
<td>Chronic pain on opioids</td>
<td>5 days/DB</td>
<td>27% decrease in pain (Abrams, 2017)</td>
</tr>
<tr>
<td>42</td>
<td>Spinal cord injury</td>
<td>Single dose/crossover</td>
<td>Decreased pain, no difference between low and high dose (Wilsey, 2016)</td>
</tr>
</tbody>
</table>

RCTs of Synthetic Cannabinoids in Pain

<table>
<thead>
<tr>
<th>N</th>
<th>Agent</th>
<th>Indication</th>
<th>Duration/type</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>Apallic acid</td>
<td>Neuropathic pain</td>
<td>7 day crossover</td>
<td>Decreased pain (Karst, 2003)</td>
</tr>
<tr>
<td>24</td>
<td>Dronabinol</td>
<td>Neuropathic pain in MS</td>
<td>15-21 days/DBC</td>
<td>Median numerical pain and relief improved (Sendon, 2004)</td>
</tr>
<tr>
<td>40</td>
<td>Dronabinol</td>
<td>Postop pain</td>
<td>Single dose/DB</td>
<td>No Benefit (Begg, 2001)</td>
</tr>
<tr>
<td>30</td>
<td>Dronabinol</td>
<td>Chronic pain</td>
<td>3 doses, 1 day/DB</td>
<td>Total pain relief improved with 10 and 20 mg. AA prominent, (Voracek, 2008)</td>
</tr>
<tr>
<td>31</td>
<td>Nabilone</td>
<td>Fibromyalgia</td>
<td>2 weeks/DBC</td>
<td>No effect on pain, sleep improved (Ware, 2010)</td>
</tr>
<tr>
<td>96</td>
<td>Nabilone</td>
<td>Neuropathic pain</td>
<td>14 weeks/DBC or dihydrocodeine</td>
<td>DRC more effective with fewer AE (Frank, 2008)</td>
</tr>
</tbody>
</table>
### RCTs Cannabis-Based Medicines Neuropathic Pain

<table>
<thead>
<tr>
<th>N=</th>
<th>Agent</th>
<th>Indication</th>
<th>Duration/Type</th>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td>20</td>
<td>Nabiximols</td>
<td>Neurogenic pain</td>
<td>2 wk crossover</td>
<td>Decreased pain, (Wade, 2004)</td>
</tr>
<tr>
<td>117</td>
<td>Nabiximols</td>
<td>Spinal cord inj. pain</td>
<td>10 days</td>
<td>No effect on pain (unpublished)</td>
</tr>
<tr>
<td>44</td>
<td>Nabiximols vs THC</td>
<td>Brachial Plexus Avulsion</td>
<td>6 wk in 1 two-week arms</td>
<td>Decreased pain, (Berman, 113)</td>
</tr>
<tr>
<td>66</td>
<td>Nabiximols</td>
<td>Central neuropathic pain of MS</td>
<td>5 weeks</td>
<td>Decreased pain, (Rog, 2005)</td>
</tr>
<tr>
<td>125</td>
<td>Nabiximols</td>
<td>Peripheral neuropathic pain</td>
<td>5 weeks</td>
<td>Decreased pain and allodynia, (Nurmikko, 115)</td>
</tr>
<tr>
<td>65</td>
<td>Cannador</td>
<td>Post-Herpetic neuralgia</td>
<td>4 weeks</td>
<td>No benefit (Ernst, 2005)</td>
</tr>
<tr>
<td>419</td>
<td>Cannador</td>
<td>Pain in MS</td>
<td>15 weeks</td>
<td>Dose spouse-related pain, No-decr in Spans (Zakim, 2005)</td>
</tr>
</tbody>
</table>

### RCTs of Cannabis-Based Medicines in Cancer Pain

<table>
<thead>
<tr>
<th>N=</th>
<th>Agent</th>
<th>Indication</th>
<th>Duration/Type</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>Oral THC</td>
<td>Cancer Pain</td>
<td>Single dose vs codeine</td>
<td>Decreased pain similar to codeine; high dose cannabis &gt;AE than codeine, (Noyes, 1975)</td>
</tr>
<tr>
<td>117</td>
<td>Nabiximols</td>
<td>Cancer Pain</td>
<td>2 weeks</td>
<td>Decreased pain, (Johnson, 118)</td>
</tr>
<tr>
<td>360</td>
<td>Nabiximols</td>
<td>Cancer Pain</td>
<td>5 weeks/DB</td>
<td>Decreased pain in low and middle dose, (Portenoy, 2012)</td>
</tr>
</tbody>
</table>

### Medicinal Cannabis: Clinical Practice & Legal Issues
- Routes of Delivery and Pharmacokinetics
- Patient Selection and Monitoring
- Legality & Access
- State Level Medicinal Cannabis Laws
- Access to Medicinal Cannabis
Medicinal Cannabis: Delivery & Pharmacokinetics

- **Inhaled**
  - Smoked vs vaporized
  - Rapid (peak blood level 2-10 min)
  - Duration 2-4 hrs
  - Easier titration
  - 10-25% bioavailable

- **Ingested**
  - Onset 30-90 min
  - Duration 4-12 hours
  - 5-20% bioavailable
  - Simpler (safer?)


Medicinal Cannabis: Patient Selection & Monitoring

- **Risk Factors**
  - Psychiatric disorders: schizophrenia or psychosis
  - Substance abuse history
  - Legal difficulty – urine drug tests for work
  - Young age (adolescents)
  - Risk Tools??

- **Informed Consent (risks vs benefits)**
- **Monitor use and efficacy**
- **Consider UDS & PDMP review**
- **Cannabis naïve vs experienced**
Medicinal Cannabis: Legality & Access

• Federal vs State regulation practice of medicine
• DEA: all cannabinoids are Schedule 1
  • THC vs CBD
  • Limits ability to do studies
• No Prescriptions – "recommendations"

Map of U.S. Marijuana Legalization

• Medical:
  • 29 states & DC
• Recreational & Medical:
  • 8 states & DC
• CBD Only:
  • 15 states

As of May 2017

Medicinal Cannabis: Access

• Varies by State
  • Cultivation
  • Possession
  • ID Cards
  • Diagnosis restrictions
  • dispensaries
  • www.weedmaps.com
  • www.medicalmarijuana.procon.org
Post-Assessment Questions

Which of the following is true about the effects of tetrahydrocannabinol (THC) on pain?

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Conclusions

- Cannabis has a very long history in medicine
- Compared to opioids, cannabinoids have a good safety profile
- Evidence for pain exists but remains limited
- Federal legal status & limited/no regulation remains a major challenge
Next Generation Neuromodulation:

Paresthesia-Free Spinal Cord Stimulation,
Targeting of the Dorsal Root Ganglion,
and a brief look at what’s coming…

Ramana (Ramo) Naidu, MD.
Pain Physician and Anesthesiologist
Mt Tam Orthopedics
Medical Director of Pain Medicine at Marin General Hospital

Financial Disclosure

- Consulting honoraria with Abbott, Sonosite, & Halyard Health.

Pre-Test Questions

1. Which of the following forms of neurostimulation would be considered most appropriate for post-knee-arthroplasty pain syndrome?
   A. Tonic stimulation at 50Hz at T9-10
   B. Dorsal root ganglion stimulation at L3
   C. High frequency spinal cord stimulation at 10 kHz at T9-10
   D. Burst waveform spinal cord stimulation at T7-8

2. What is the current proposed mechanism behind the analgesic and anti-hyperalgesic effect of dorsal root ganglion stimulation?
   A. Gate Control Theory
   B. Increase in serotonergic tone
   C. T-junction filtering
   D. Sodium-channel blockade

3. A patient presents with severe pain from failed back surgical syndrome (post-laminectomy pain syndrome). You are deciding between a high-frequency spinal cord stimulator or a “traditional” tonic spinal cord stimulator system. Approximately what percentage of patients will prefer “traditional” tonic stimulation at 50Hz to “high-frequency” 10 kHz stimulation for their pain syndrome?
   A. 5%
   B. 20%
   C. 35%
   D. 50%
History

1965 - The Gate Theory proposed by Melzack & Wall

1967 - Shealy places a unipolar SCS in the intrathecal space (A&A)
Prior to 2012, with the primary indication being FBSS, the adage was:

- “Spinal cord stimulation works for lower extremity radicular pain, and don’t do it if it is just axial back pain.”
- The trial-to-perm ratio was 45-55%.

Since 2012, with regards to FBSS:

- “Spinal cord stimulation works for axial back pain and lower extremity radicular pain”
- The trial-to-perm is 60-90%.

So what changed?

- Frequency
- Waveforms
- Targets
Conductivity of Intraspinal Elements, from Oakley & Prager

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Conductivity</th>
</tr>
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<tbody>
<tr>
<td>CSF</td>
<td>1.7</td>
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<tr>
<td>White Matter Longitudinal</td>
<td>0.6</td>
</tr>
<tr>
<td>Gray Matter</td>
<td>0.23</td>
</tr>
<tr>
<td>White Matter Transverse</td>
<td>0.08</td>
</tr>
<tr>
<td>Epidural Fat</td>
<td>0.04</td>
</tr>
<tr>
<td>Dura Mater</td>
<td>0.03</td>
</tr>
<tr>
<td>Vertebral Bone</td>
<td>0.02</td>
</tr>
<tr>
<td>Electrode Insulation</td>
<td>0.002</td>
</tr>
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</table>

Anatomical Considerations for the Spinal Cord

Parameters: Frequency

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Traditional&quot;</td>
<td>50Hz [2-1200Hz]</td>
</tr>
<tr>
<td>Nevro</td>
<td>10 kHz</td>
</tr>
<tr>
<td>Boston Scientific</td>
<td>1kHz, 4kHz, 7kHz</td>
</tr>
<tr>
<td>(High Frequency)</td>
<td></td>
</tr>
<tr>
<td>Gimer</td>
<td>50 kHz [3Hz-800kHz]</td>
</tr>
</tbody>
</table>

Parameters: Frequency

EVIDENCE: SENZA-RCT (Nevro HF10 vs Boston Scientific Tonic)

Parameters: Waveforms

Tonic

Burst

TONIC STIMULATION (TRADITIONAL):

BURST STIMULATION:

Parameters: Waveforms

EVIDENCE: SUNBURST Trial
Parameters: Location of Stimulation

Foot, Lower Leg (L5)
Leg, Ankle (L4)
Upper Leg, Lower Leg, Knee (L3)
Upper Leg, Groin (L2)
Hip, Waist, Groin (L1)
Abdomen, Groin (T12)

Parameters: Location of Stimulation

EVIDENCE: ACCURATE Trial

Next Frontier: Feedback Mechanisms

Parameters: Feedback Mechanisms

Key for ECAP amplitudes:
- Within the subject’s therapeutic window
- Below the subject’s perception threshold
- Above the subject’s maximum tolerable limit

Russo M et al, INS 2017
Russo M et al, INS 2017

80% pain reduction at 6 months

77% pain reduction at 6 months

MEAN PAIN SCORES REMAIN STABLE OVER TIME

LOW BACK PAIN

LEG PAIN

64% OF SUBJECTS ARE HIGH RESPONDERS
(≥80% LOW BACK PAIN RELIEF)

Gross Comparison of SCS Systems

<table>
<thead>
<tr>
<th>Medtronic</th>
<th>Boston Scientific</th>
<th>Abbott (St Jude)</th>
<th>Nevro</th>
<th>NuvecIna</th>
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</thead>
<tbody>
<tr>
<td>MRI Percutaneous (2016)</td>
<td>MRI Conditional 1.5 T</td>
<td>MRI Conditionality-Head Only</td>
<td>MRI Conditional 1.5 T (below T6)</td>
<td>MRI Conditional 1.5 T</td>
</tr>
<tr>
<td>MRI Paddle (2016)</td>
<td>Head Only 1.5 T</td>
<td>MRI Conditionality-Head Only</td>
<td>MRI Conditionality-Head</td>
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<tr>
<td>Contacts</td>
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<td>32 contacts</td>
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<tr>
<td>IPG</td>
<td>Zero-Charge IPG</td>
<td>Primary Cell (5 years) and Rechargeable</td>
<td></td>
<td></td>
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<tr>
<td>I vs V</td>
<td>Voltage</td>
<td>Multiple Independent Current Control</td>
<td>Current</td>
<td></td>
</tr>
<tr>
<td>Patterns</td>
<td>Tonic</td>
<td>Tonic HIFreq 1200 Hz Burst, PRISMA</td>
<td>Tonic BurstDR</td>
<td>Proprietary 10k Hz</td>
</tr>
</tbody>
</table>

MRI Conditionality

All of the companies realize the importance of MRI conditionality.

Their challenge is having the technology that is cost-effective, and then seeking FDA approval which can be a time-consuming and costly process.
**Gross Comparison of DRG System(s)**

<table>
<thead>
<tr>
<th>MRI Percutaneous (2017)</th>
<th>Abbott DRG Stimulation (Spinal Modulation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI Paddle (2017)</td>
<td>1.5T Head and Ext (ProclaimDRG)</td>
</tr>
<tr>
<td>Contacts</td>
<td>N/A currently</td>
</tr>
<tr>
<td>IPG</td>
<td>up to 4 quadphodes, FDA approved for T10 and below</td>
</tr>
<tr>
<td>I vs V</td>
<td>ProclaimDRG (Primary Cell)</td>
</tr>
<tr>
<td>Patterns</td>
<td>Current</td>
</tr>
<tr>
<td></td>
<td>Tonic</td>
</tr>
</tbody>
</table>

**So many options… what to choose for what?**

**Spinal Cord (Dorsal Column) Stimulation**
- Neuropathic Conditions
- Ischemic Conditions

**Dorsal Root Ganglion Stimulation**
- CRPS
- Persistent Post-Surgical Syndromes
- Mono/Oligoneuropathy

**Burst Stimulation**
- Axial Back Pain
- Failed Back Surgical Syndrome

**HF10 Stimulation**
- Axial Back Pain
- Failed Back Surgical Syndrome

**Education: Improvement in Training, Guidelines, Dissemination of Information**

- International Neuromodulation Society
- North American Neuromodulation Society
- Centers of Excellence in Neuromodulation
- Neuromodulation
- NACC Guidelines
Summary

Neurostimulation is an effective method to manage pain.

With the current epidemic of opioids, other therapies need to be considered.

Goals of care are to improve function, reduce analgesic medication use, and improve quality of life.

Selection of candidates must be scrupulous

It is costly. Must demonstrate cost-effectiveness or reduce cost of implantation.

Technology continues to improve…

Bioelectrical Medicine for various conditions: OSA, Autoimmune Diseases, Epilepsy, GI Motility Disorders, Mental Health, etc.
Antoun Nader, M.D.
Professor of Anesthesiology and Orthopedic Section Chief, Acute Pain and Regional Anesthesiology Northwestern University

Disclosure

- None related to this topic

Objectives

- Recognize different classifications of orofacial pain and implications on treatment modalities
- Comprehend the sympathetic and parasympathetic modulation of orofacial pain and implications on treatment
  - Posterior cervical plexus: C2 dorsal root ganglion
  - Trigeminal complex: sphenopalatine ganglion
Pre-Assessment Questions: Case 1

- 37-year-old male presents with Severe Retro-orbital debilitating headache up to 8-10/day lasting up to 30 minutes. The pain is associated with ipsilateral conjunctival injection and lacrimation. Treatment options include:
  - Oxygen inhalation
  - Sumatriptan
  - Nasal local anesthetics
  - Occipital nerve blocks
  - All of the above

Case 2

- 55-year-old female presents with severe unilateral facial pain described like electric shocks lasting 2 sec up to 40/day. She is pain free between episodes and the physical exam is unremarkable. The pain can be triggered by applying pressure over the corner of the mouth. The most likely diagnosis is:
  - Trigeminal neuralgia
  - Temporal Brain tumor
  - Multiple sclerosis
  - Dental pain

Case 3

- 45-year-old female
- Multiple partial bowel obstructions
- Repeat nasogastric tube placements
- Severe burning constant facial pain
- Pregabalin, Carbamazepine
Orofacial Pain

<table>
<thead>
<tr>
<th>Type of orofacial pain</th>
<th>One-month period prevalence (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain in the jaw joint(s)</td>
<td>5.7</td>
<td>[4.8, 6.7]</td>
</tr>
<tr>
<td>Pain in area just in front of the ear/s</td>
<td>6.0</td>
<td>[5.1, 7.0]</td>
</tr>
<tr>
<td>Pain in or around the area</td>
<td>11.7</td>
<td>[10.5, 13.0]</td>
</tr>
<tr>
<td>Pain when opening the mouth wide</td>
<td>3.5</td>
<td>[2.8, 4.3]</td>
</tr>
<tr>
<td>Shooting pains in the face or cheeks</td>
<td>2.8</td>
<td>[2.2, 3.4]</td>
</tr>
<tr>
<td>Pain in the jaw joint when chewing food</td>
<td>3.8</td>
<td>[3.1, 4.7]</td>
</tr>
<tr>
<td>Pain in and around the temples</td>
<td>0.6</td>
<td>[0.5, 1.0]</td>
</tr>
<tr>
<td>Tenderness of muscles at the side of the face</td>
<td>3.3</td>
<td>[2.7, 4.3]</td>
</tr>
<tr>
<td>A prolonged burning sensation in the tongue or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>other parts of the mouth</td>
<td></td>
<td></td>
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<tr>
<td>Any OFP</td>
<td>1.2</td>
<td>[0.8, 1.7]</td>
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Disability

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of participants</th>
<th>No. with OFP</th>
<th>One-month period prevalence (%)</th>
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<tr>
<td>Age group (years)</td>
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<tr>
<td>18–25</td>
<td>277</td>
<td>73</td>
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<td>26–35</td>
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<td>36–45</td>
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<tr>
<td>56–65</td>
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<tr>
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<td>1129</td>
<td>253</td>
<td>22.4</td>
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<tr>
<td>Female</td>
<td>1385</td>
<td>413</td>
<td>30.2</td>
</tr>
<tr>
<td>Overall</td>
<td>2514</td>
<td>466</td>
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Disability associated with pain

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<td>466</td>
<td>18.5</td>
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</table>

Pain Characteristics

- Duration
  - Less than 3 months ago: 32.8%
  - 3 or more months ago: 62.3%

- Pain now
  - Yes: 11.8%
  - No: 88.2%

- Pain frequency during past month
  - Every day: 16.3%
  - 4–5 times a week: 6.3%
  - 2–3 times a week: 24.4%
  - Once a week: 14.4%
  - Less than once a week: 38.6%

- How long does the pain last?
  - Less than half-an-hour: 28.9%
  - About an hour: 11.0%
  - 1–4 h: 26.4%
  - 5–8 h: 11.1%
  - 9–12 h: 4.6%
  - More than 12 h: 16.1%

Retro-Orbital Pain: Common

- Eye pain, periorbital and retro-orbital pain, and headache or facial pain referred to the orbital region are common presenting complaints

- Unfortunately, in many patients, no etiology for the pain syndrome is discerned
  - Atypical facial pain

Eyes and Headaches

- Inextricable link between the eyes and headaches
  - Visual disturbances are often neurologic in origin

- Many primary headache disorders have ophthalmic features

- Many secondary causes of headache frequently involve the visual system
Eye: Most Sensitive Tissues in the Body

- More than 1000 small axons terminate as free nerve endings in the corneal stroma and epithelium
- Most sensitive tissues in the body
- Branches of the trigeminal nerve (V1) innervate the eye and orbital tissues.
  - Frontal nerve
    - Conjunctiva of the lateral upper eyelid
  - Nasociliary nerve
  - Sol sensory supply to the eye
- The lens, vitreous, and retina do not contain pain fibers

Facial Pain Referred to the Orbital Region

- Pain Syndromes with a normal Neuro-Ophthalmologic Examination
  - Primary short-lasting headache syndromes
    - With autonomic features
    - Without autonomic features
  - Primary long-lasting headache syndromes
  - Pain referred to the eye (Secondary)

Short-lasting Headache

With autonomic features
- Cluster headache
  - Cluster-tic syndrome
- Paroxysmal hemicranias
  - Chronic paroxysmal hemicrania
- SUNCT (short-lasting unilateral neuralgiform pain with conjunctival injection and tearing) syndrome
Short-lasting Headache

Without autonomic features

- Trigeminal neuralgia
- Sphenopalatine neuralgia
- Idiopathic stabbing headache (jabs and jolts syndrome, ice-pick headache, “needle-in-the-eye” syndrome)
- Valsalva maneuver headache
- Exertional headache
- Headache associated with sexual activity
- Cold stimulus (ice cream) headache
- Hypnic headache

Long-lasting Headache

Primary long-lasting headache syndromes

- Migraine
  - With aura
  - Without aura
- Tension headache and eye strain
- Hemicrania continua (episodic and chronic)
- Idiopathic eye pain (includes atypical facial pain and psychogenic pain)

Pain Referred to the Eye (Secondary)

- Sinus disease
- Diseases of the teeth, jaw
- Vascular disease
- Eye pain with neck disease
  - Cervicogenic headache or eye pain
- Face pain with lung cancer

Convergence: Referred Cervicogenic Headache

- Convergence between nociceptive afferents of the first division of the trigeminal nerve and nociceptive afferents of the C1, C2, and C3 spinal nerves
- Second-order neurons in the C1-C3 segments


Referred Pain: Cervicogenic

- The convergence largely involves Aδ and C fibers
  - Onto neurons in laminae I, II, V, and VI of the dorsal horn at C2
  - Stimulation of trigeminal afferents sensitizes the response to cervical input, and stimulation of cervical afferents sensitizes trigeminal input.

Bartsch T. et al.: Stimulation of the greater occipital nerve induces increased central excitability of dural afferent input. Brain 2002; 125: pp. 1496-1509

Retro-orbital: Cervicogenic Headache

- Pain from C2-3 tends to be perceived across the lateral occipital region and into the forehead and orbital region
- Pain from C1-2 also tends to gravitate to the orbital region but otherwise more often occurs in the vertex or around the ear.

Retro-orbital: Referred Pain

In human volunteers, pain in the head has been evoked experimentally by

- Electrical stimulation of the dorsal rootlets of C1
- Noxious stimulation of the greater occipital nerve or the suboccipital muscles of the neck


Referred Pain: Cervicogenic Headache

- The C2-3 zygapophysial joint is the most common source, followed by the lateral atlantoaxial joint and occasionally, the C3-4 zygapophysial joint
- In patients with suspected cervicogenic headache, headache can be relieved by anesthetizing the C2-3 zygapophysial joint


Cervicogenic Headache

- Any of the structures innervated by the C1-C3 spinal nerves could be a source of headache
  - Posterior neck muscles
  - C2-3 and C3-4 zygapophysial joints
  - Atlantoaxial joints
  - C2-3 and C3-4 intervertebral disks
  - Dura mater of the upper cervical spine
  - Vertebral artery

Cervicogenic Headaches

- C2-3 zygapophysial joint
  - Most extensively, and rigorously, studied
  - Mediated by the third occipital nerve
    - Third occipital headache.
- Submaximal strain injuries
  - Whiplash

Occipital Neuralgia

- Poorly defined entity that was a popular, anecdotal diagnosis of occipital headache in the past.
  - Deep, dull, aching pain
  - Cutaneous nerve
  - No pathology has been proved
  - No controlled studies of diagnosis or treatment have been published

Headache Disorders and Facial Pain

- Primary headaches
- Secondary headaches
- Painful cranial neuropathies, other facial pains and other headaches
Primary headaches

- Migraine
- Tension-type headache
- Trigeminal autonomic cephalalgias
  - Cluster headache
  - Paroxysmal hemicranias
  - Short-lasting unilateral neuralgiform headache attacks
  - Hemicrania continua
  - Probable trigeminal autonomic cephalalgia
- Other primary headache disorders

Migraine

- At least five attacks fulfilling criteria B–D
- B. Headache attacks lasting 4–72 hours
- C. Headache has at least two of the following four characteristics:
  - 1. unilateral location
  - 2. pulsating quality
  - 3. moderate or severe pain intensity
  - 4. aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)
- D. During headache at least one of the following:
  - 1. nausea and/or vomiting
  - 2. photophobia and phonophobia
- E. Not better accounted for by another diagnosis.

Tension Headache

- At least 10 episodes of headache and fulfilling criteria B–D
- B. Lasting from 30 minutes to 7 days
- C. At least two of the following four characteristics:
  - 1. bilateral location
  - 2. pressing or tightening (non-pulsating) quality
  - 3. mild or moderate intensity
  - 4. not aggravated by routine physical activity such as walking or climbing stairs
- D. Both of the following:
  - 1. no nausea or vomiting
  - 2. no more than one of photophobia or phonophobia
- E. Not better accounted for by another diagnosis.
Cluster Headache

- A. At least five attacks fulfilling criteria B–D
- B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 minutes
- C. Either or both of the following:
  - 1. at least one of the following symptoms or signs, ipsilateral to the headache:
    - a) conjunctival injection and/or lacrimation
    - b) nasal congestion and/or rhinorrhea
    - c) eyelid oedema
    - d) forehead and facial sweating
    - e) forehead and facial flushing
    - f) sensation of fullness in the ear
    - g) miosis and/or ptosis
  - 2. a sense of restlessness or agitation
- D. Attacks have a frequency between one every other day and eight per day for more than half of the time when the disorder is active

Secondary headaches

- Headache attributed to trauma or injury to the head and/or neck
- Headache attributed to cranial or cervical vascular disorder
- Headache attributed to non-vascular intracranial disorder
- Headache attributed to a substance or its withdrawal
- Headache attributed to infection
- Headache attributed to disorder of homoeostasis
- Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structure
- Headache attributed to psychiatric disorder

Painful Cranial Neuropathies

- Painful cranial neuropathies and other facial pains
- Other headache disorders
Painful Cranial Neuropathies

- Trigeminal neuralgia
- Glossopharyngeal neuralgia
- Nervus intermedius (facial nerve) neuralgia
  - Attributed to Herpes zoster
- Occipital neuralgia
- Optic neuritis
- Headache attributed to ischaemic ocular motor nerve palsy
- Tolosa-Hunt syndrome
- Paratrigeminal oculosympathetic (Raeder’s) syndrome
- Recurrent painful ophthalmoplegic neuropathy
- Burning mouth syndrome (BMS)
- Persistent idiopathic facial pain (PIFP)
- Central neuropathic pain


Classical Trigeminal Neuralgia

- At least three attacks of unilateral facial pain
  - Occurring in one or more divisions of the trigeminal nerve, with no radiation beyond the trigeminal distribution
  - Pain has at least three of the following four characteristics:
    - recurring in paroxysmal attacks lasting from a fraction of a second to 2 minutes
    - severe intensity
    - electric shock-like, shooting, stabbing or sharp in quality
    - precipitated by innocuous stimuli to the affected side of the face
  - No clinically evident neurological deficit
  - Not better accounted for by another diagnosis


Trigeminal Neuralgia with Deficit

- Hypoesthesia or hypoalgesia in the affected trigeminal region always indicates axonal damage.
  - When either is present, there is trigeminal neuropathy and extensive diagnostic work-up is necessary to exclude symptomatic cases.
  - There are some patients with hyperalgesia in the painful region, which should not necessarily lead to a diagnosis of trigeminal neuropathy because it may reflect the patient’s increased attention to the painful side.

Trigeminal Neuralgia with Concomitant Persistent Facial Pain

- Referred to as atypical trigeminal neuralgia or, recently, as trigeminal neuralgia type 2.
  - Central sensitization may account for the persistent facial pain
  - Neurovascular compression on MRI is less likely to be demonstrated.
- Classical trigeminal neuralgia with concomitant persistent facial pain responds poorly to conservative treatment and to neurosurgical interventions.
  - It is less likely to be triggered by innocuous stimuli


Bilateral Trigeminal Neuralgia

- Symptoms are virtually always unilateral.
  - Bilateral TN is very rare
  - TN caused by multiple sclerosis (MS).
    - (~10%) with bilateral TN


Trigeminal Neuralgia/ MRI

- In about 15% of patients with TN, MRI reveals a major neurologic disease such as a benign tumor or MS

Trigeminal Neuralgia

- Pain does not extend to
  - Posterior third of the scalp
  - Back of the ear
  - Angle of the mandible
- These territories are innervated by cervical nerves


Gasserian Ganglion

The Gasserian ganglion lies in the middle cranial fossa within the Meckel’s cave


Trigeminal Nerve

- Gives rise to 3 branches which exit the skull through 3 distinct foramina
  - Ophthalmic (V1)
    - Superior orbital fissure
  - Maxillary (V2)
    - Foramen rotundum
  - Mandibular (V3)
    - Foramen oval

Nader et al, Pain Physician: 2013 Sep-Oct;16(5):
Branches (V2,3)

- Maxillary (V2)
  - Foramen rotundum
  - Anterior to lateral Pterygoid plate
- Mandibular (V3)
  - Foramen oval
  - Posterior to the lateral Pterygoid plate

Sphenopalatine Ganglion

Approach

- The foramen rotundum opens into the posterior part of the pterygoid palatine fossa which is located medial to the lateral Pterygoid plate.
- An injection anterior and medial to the lateral pterygoid plate into the upper part of the Pterygoid palatine fossa will place the injectate in close vicinity to the foramen rotundum.
The contents of the infratemporal fossa are partially exposed after the temporalis and lateral pterygoid muscles and bone flap have been removed. V3 = mandibular branch of the trigeminal nerve, IMA = internal maxillary artery, and MMA = middle meningeal artery.

The ramus of the mandible is removed, exposing the contents of the infratemporal fossa. The internal maxillary artery (IMA) passes medial to the mandibular branch of the trigeminal nerve (V3). The origin of the middle meningeal artery (MMA) from the IMA is also visible. V2 = maxillary nerve, BN = buccal nerve, LN = lingual nerve, IAN = inferior alveolar nerve, and MHN = mylohyoid nerve.

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Infratemporal Fossa


(A) Parasagittal, (B) coronal, and (C) axial illustrations of the infratemporal fossa on the left side. The superior border is formed by the squamous portion of the temporal bone and the greater wing of the sphenoid while the posterior boundary is defined by the tympanic and mastoid portions of the temporal bone. LPM = lateral pterygoid muscle, MMA = middle meningeal artery, MPM = medial pterygoid muscle, TM = temporalis muscle, MM = masseter muscle, CN VII = facial nerve, CN IX = glossopharyngeal nerve, CN X = vagus nerve, CN XI = accessory nerve, CN XII = hypoglossal nerve, IAN = inferior alveolar nerve, LN = lingual nerve, ATN = auriculotemporal nerve, V3 = mandibular branch of the trigeminal nerve, ICA = internal carotid artery, IMA = internal maxillary artery, IJV = internal jugular vein, and ET = eustachian tube.

Ultrasound Guidance

- Lateral pterygoid muscle
- Maxillary artery
- Maxilla
- Easily identifiable by ultrasonography

Nader et al: Anesthesiology 2013, 118(4), 957
Ultrasound Guidance

- Pterygopalatine fossa is small
- 2 ml of contrast produces a retrograde passage to reach the middle cranial fossa and allows visualization of the trigeminal ganglion

Nader et al, Anesthesiology 2013, 118(4), 857
Injection

- Following negative aspiration, the injectate was deposited deep to the lateral pterygoid muscle and plate
Needle Approach

- An echogenic needle is inserted in-plane
  - Parallel to the transducer probe
- Advanced from a lateral to medial and posterior to anterior direction
  - Toward the pterygopalatine fossa

Gasserian Ganglion
Gasserian Ganglion Block

Nader et al, Anesthesiology 2013, 118(4), 957

Treatment

Nader et al, Pain Physician 2013 Sep-Oct;16(5)

Treatment

Nader et al, Pain Physician 2013 Sep-Oct;16(5)
Gasserian Ganglion

- Classic approach
  - Through the foramen ovale
  - Needle in a direct line to the Meckel’s cave
  - Middle cranial fossa
- X-ray guided techniques
  - Bony anatomical landmarks
    - Maxilla, lateral pterygoid plate and foramen ovale
  - Difficult to interpret

Lateral Pterygoid Muscle

Chuang Y et al: Pain Physician 2015; 18:E933-E938 • ISSN 2150-114
Nader A et al: Pain Physician 2015; 18:E933-E938 • ISSN 2150-114

Lateral Pterygoid Muscle
Pulsed RF

- Pulsed Radiofrequency
- 42°C for 90 seconds

Nader, A et al: Pain Physician 2015; 18:E411-E415 • ISSN 2150-114

Pterygopalatine Fossa/Sphenopalatine Ganglion

Potential applications for neuromodulation at the pterygopalatine fossa (PPF)


C2 DRG

Acar F, Miller J, Golestani KJ, Israel ZH, McClenahan S, Burchiel KJ. Pain relief after cervical ganglionectomy (C2 and C3) for the treatment of medically intractable occipital neuralgia. Stereotact Funct Neurosurg. 2008;86(2)
C2 Neuralgia

- A. Unilateral or bilateral pain fulfilling criteria B-E
- B. Pain is located in the distribution of the greater, lesser and/or third occipital nerves
- C. Pain has two of the following three characteristics:
  - 1. recurring in paroxysmal attacks lasting from a few seconds to minutes
  - 2. severe intensity
  - 3. shooting, stabbing or sharp in quality
- D. Pain is associated with both of the following:
  - 1. dysaesthesia and/or allodynia apparent during innocuous stimulation of the scalp and/or hair
  - 2. either or both of the following:
    - a) tenderness over the affected nerve branches
    - b) trigger points at the emergence of the greater occipital nerve or in the area of distribution of C2
- E. Pain is eased temporarily by local anaesthetic block of the affected nerve
- F. Not better accounted for by another diagnosis.


C2 Spinal Nerve Pathology: Neck-Tongue Syndrome

Numbness of the tongue on rotating the head
- Caused by stretching of cervical afferents from the hypoglossal nerve by a subluxating lateral atlantoaxial joint
- Headache is caused by strain of the joint


Neck-Tongue Syndrome

- The condition can be caused by various disorders that affect the C2 spinal nerve
- Behind the lateral atlantoaxial joint.
- Inflammatory disorders of the joint may result in the nerve becoming incorporated in the fibrotic changes of chronic inflammation.


C2 Neuralgia

- Meningioma
- Neurinoma
- Anomalous vertebral arteries, and venous abnormalities
  - Surrounding the C2 spinal nerve and its roots
  - Compressing the C2 dorsal root ganglion


C2 Nerve

Occipital Triangle


C2 Ganglion

It is situated in the atlantoaxial interlaminar space.

Superiorly: posterior arch of the atlas,
Inferiorly: the lamina of the axis
Anteriorly: the lateral atlantoaxial joint and its capsule
Posteriorly: atlantoepistrophic ligament.

the obliquus capitis inferior muscle is noted posteriorly.


C2 DRG

Acar F, Miller J, Goelthin KJ, Israel ZH, McCue J, Burchiel KJ. Pain relief after cervical ganglionectomy (C2 and C3) for the treatment of medically intractable occipital neuralgia Stereotact Funct Neurosurg 2008;86(2)
C2 Nerve

- Dorsal ramus
  - Splenius capitis and semispinalis capitis and finally becomes the GON
- Ventral ramus
  - Articular branches to the lateral C1/2 joint
  - Prevertebral muscles, SCM, and trapezius

Vertebral Artery: V3

Occipital Neuralgia/DRG C2

- Hypertrophy of the lamina or C1–C2 articulation
- Osteoarthritis (with bony spurs) and spondylosis
- ‘Whiplash’ injury with compression against soft tissue surrounding the nerve and ganglion
- Hypertrophy of the atlantoepistrophe ligament
- The C2/C3 ganglion is encased in a large vertebral venous plexus
  - Engorgement of this plexus is thought to contribute to the ON neuropathy observed
**C2 Nerve Block**
- Effective treatment for
  - Cervicogenic headache
  - Cluster headache
  - Occipital neuralgia
- Not Effective
  - Tension headache
  - Post traumatic headache
  - Hemicrania continua
  - Chronic paroxysmal hemicrania.

Tobin JI, Filman S. Occipital nerve blocks: when and what to inject? Headache. 2009 Nov-Dec;49(10):1521-33

**Myodural Bridges**

Rectus capitis posterior major (RCPma) and obliquus capitis inferior (OCI) muscles emitting dense connective tracts contributing to the atlantoaxial myodural bridge (MDB)

The myodural bridge (MDR) proceeds to communicate with the posterior aspect of the dura mater (Dura) between the atlas (C1) and the axis (C2).


**Cervicogenic Headache**

Pain referred from cervical structures due to convergence between trigeminal nerve and C1, 2, 3 nerves in trigeminocervical nucleus

Cruveilhier Plexus


C2 Nerve Block

- Effective treatment for
  - Cervicogenic headache
  - Cluster headache
  - Occipital neuralgia
- Not Effective
  - Tension headache
  - Post traumatic headache
  - Hemicrania continua
  - Chronic paroxysmal hemicrania.

Tobin J1, Flitman S. Occipital nerve blocks: when and what to inject? Headache. 2009 Nov-Dec;49(10):1521-33

Head and Neck Position Sense

- Very high densities of spindles have also been found in the three small muscles of the sub-occipital triangle (the superior and inferior oblique capitis, and rectus capitis posterior major and minor).
- These findings suggest that these muscles may act as sensors of the craniovertebral motion contributing to the fine control of head and neck position sense.

Trigeminal Reflex

- Bradycardia
- Hypotension
- Gastric hypermotility

C2 Nerve

C2 Nerve
Vertebral Artery
Headache Management and Recent Innovations

Mark Burish MD PhD
Neurologist and Interventional Pain Physician
Assistant Professor of Neurosurgery
Director, Will Erwin Headache Research Center

Midwest Pain Society
41st Annual Scientific Meeting
October 27-28, 2017
Chicago, Illinois

Disclosure
- Research support
  - American Headache Society
  - National Headache Foundation
  - Will Erwin Headache Research Foundation
- Consultant
  - none
- Speaker’s bureau
  - none
- Off-label use
  - Yes we will discuss

Objectives
- Migraine
  - Medical management
  - Non-pharmaceutical management of migraine
  - Procedural treatment (Onabotulinum toxin & Occipital nerve stim)
  - Recent treatments & treatment on the horizon
- Cluster headache
  - Neuromodulation
Pre-Assessment Questions
The most commonly used test to assess disability in migraine is the:

a) Short-form 36 (SF-36)  
b) Migraine Disability Assessment Test (MIDAS)  
c) Headache Impact Test (HIT-6)  
d) Brief Headache Screen

Four companies are currently in phase II or III testing of a new preventive treatment for migraine, which is expected to be available for patients by the year 2020. That treatment is:

a) Opioid/naloxone combination table  
b) Nerve growth factor  
c) Anti-calcitonin gene-related peptide (CGRP)  
d) Novel anti-depressant

Pre-Assessment Questions
Which of the following environmental factors may worsen the symptoms of a migraine?

a) Cold temperature  
b) Bright lights  
c) Humidity  
d) Quiet room

Case 1
38yo female
- Chief complaint: Headaches
- Screening forms
  - ID migraine screener™: positive for migraine
  - MIDAS = 2
**ID Migraine™ Screener**

During the last 3 months, did you have any of the following with your headaches?

1. You felt **nauseated** or sick to your stomach when you had a headache?  
   - □ Yes  □ No

2. **Light** bothered you (a lot more than when you don’t have a headache)?  
   - □ Yes  □ No

3. Your headaches limited your ability to work, study, or do what you needed to do for at least one day?  
   - □ Yes  □ No

A “yes” to 2 of the 3 questions has 81% sensitivity and 75% specificity for migraine

Lipton et al. 2002  
Neurology 61:375

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**MIDAS**

The Migraine Disability Assessment Test

Disability: 0-5: Little or None  6-10: Mild  11-20: Moderate  21+: Severe

Stewart et al. 1999  
Neurology 53(5):988

---

**Case 1**

38yo female

- Chief complaint: Headaches
- Screening forms
  - ID migraine screener™: positive for migraine
  - MIDAS = 2

---
AAN guidelines for acute migraine treatment

**ORAL MEDS**

**Class A evidence**
- Acetaminophen 1000mg
- Diclofenac 50-100mg
- Ibuprofen 200-400mg
- Naproxen 500mg
- Sumatriptan 25-100
- Stronger: Rizatriptan
- Weaker: Frovatriptan

**Class B evidence**
- Codeine + APAP
- Tramadol + APAP

**Class C evidence**
- Butalbital

Marmura et al. 2015
Headache 55:3

---

**Case 1**

38yo female

- **Chief complaint:** Headaches
- **Screening forms**
  - ID migraine screener™: positive for migraine
  - MIDAS ≥ 2
- **History**
  - No red flags for secondary headaches
  - Has tried acetaminophen without relief, not tried anything else
  - 2 headaches per month
- **Treatment options**
  - **Abortive**
    - Rescue abortive (to prevent from going to ED)
  - **Preventive (medications, Onabotulinum toxin A injections, neuromodulation)**

---

**Chronic migraine – non-prescription**

- **Pain psychology**
  - Biofeedback
  - Cognitive-behavioral therapy
- **Herbal/Neutraceutical**
  - Petasites (butterbur) 400mg daily (Vitamin B2)
  - Riboflavin 400mg daily (Vitamin B2)
  - Co-Q10 100 TID
- **MIG-99 (feverfew) 6.25mg TID**
- **Magnesium 300mg daily, 1:1 citrate:oxide**

Holland et al. 2012 Neurology 78:1346

---

- **Lifestyle changes**
  - Avoid triggers (alcohol)
  - Sunglasses (FL-41 lenses)
  - Migraine likes balance (sleep, exercise, food, caffeine)
Case 2

44yo female

- Diagnosis: Chronic migraine
- 20 days of headache per month
- Headaches last 4-12 hours

What treatment would you like to try next?

- Topiramate
- Amitriptyline
- Riboflavin
- Onabolutinumtoxin A
- Transcutaneous supraorbital nerve stimulation
- Occipital nerve stimulation

**Chronic migraine:**
15 or more days of headache per month

---

**Diagnostic criteria:**

A. Headache (unipolar-type like and/or migraine-like) on ≥15 days per month for ≥3 months and fulfilling criteria B and C.

B. Occurring in a patient who has had at least five attacks fulfilling criteria B-D for 1.1. Migraine without aura and/or criteria B and C for 1.2. Migraine with aura.

C. ≥15 days per month for ≥3 months, fulfilling any of the following:

1. Criteria C and D for 1.1. Migraine without aura
2. Criteria B and C for 1.2. Migraine with aura
3. Induced by the patient to be migraine at onset and relieved by a triptan or ergot derivative
4. Not better accounted for by another ICHD-3 diagnosis.

**Chronic migraine:**
15 or more days of headache per month

---

**ICHD-III beta criteria. Cephalalgia 2018;269**
Case 2

44yo female

- Diagnosis: Chronic migraine
- 20 days of headache per month
- Headaches last 4-12 hours
- Moderate disability (MIDAS score = 15)
- PMHx: anxiety, baseline bradycardia
- Current medications: venlafaxine
- Prior failed medications: topiramate

What treatment would you like to try next?

- Propranolol
- Amitriptyline
- Riboflavin
- Onabotulinum toxin A
- Transcutaneous supraorbital nerve stimulation
- Occipital nerve stimulation

PREVENTIVE

Level A evidence
- Anti-epileptics
  - Topiramate
- Beta-blockers
  - Propranolol

Level B evidence
- Antidepressants
  - Amitriptyline

Level C evidence
- ACEI
  - Lisinopril
- ARB
  - Candesartan

Silberstein et al. 2012
Neurology 78:1337

Chronic migraine - procedural treatments

- Onabotulinum Toxin A
- Occipital nerve stimulation
Onabotulinum – PREEMPT studies

Blumenfeld et al. 2010
Headache 50:1406

PREEMPT studies

Dinner et al. 2010
Cephalalgia 30(7):604

PREEMPT studies

Dwork et al. 2010
Headache 50(8):921
Onabotulinum Toxin A: Experimental data

- **Strong data**
  - Chronic migraine
  - Trigeminal neuralgia
  - Temporomandibular disorder

- **Modest data**
  - Episodic migraine
  - Post-concussive headache
  - Medication overuse headache
  - Nummular headache

- **Weak or limited data**
  - Occipital neuralgia
  - Tension headache
  - Cluster headache

---

Neuromodulation for headaches

- Miller et al. 2016
  - Pract Neurol 16:362

- Lipton 2009 (PRISM)
- Saper 2011 (ONSTIM)
- Silberstein 2012

---

Occipital nerve stimulation

- Miller et al. 2016 Pract Neurol 16:362
- Chen et al. 2015
  - PLoS ONE 10(3):e0116805

Adverse events:
- Serious: lead migration, infection
- Other: battery failure, hematoma, skin erosion
Patient selection – occipital nerve stimulation

- **Diagnosis:** Chronic migraine
- **Past medical history:** prior occipital surgery
- **Current medications:** anticoagulants
- **Prior treatment trials:** N/A

**Treatment**
- **Effectiveness:** modest
- **Side effects and risks:** lead migration, infection
- **Cost:** high

Migraine – recent innovations and treatments on the horizon

- **Abortives**
  - Old drug, new data
    - Simvastatin 20 BID + Vitamin D 1000 IU BID
  - Old drug, new formulations
    - Intranasal sumatriptan powder
    - Pulled off market: transdermal sumatriptan
  - Noninvasive single-pulse transcranial magnetic stimulation
  - Soon: lasmiditan (serotonin 1F receptor inhibitor)
    - Does not cause vasoconstriction like triptans (5HT 1B/1D inhibitors)

- **Preventives**
  - Noninvasive transcutaneous supraorbital nerve stimulation
  - Soon: Calcitonin gene-related peptide antibodies

Neuromodulation for headaches
Single pulse TMS

Miller et al. 2016 Pract Neurol 16:362

Lipton et al. 2010 Lancet Neurol 9:373

Transcutaneous supraorbital nerve stim

Schamen et al. 2013 Neurology 80:697

Miller et al. 2016 Pract Neurol 16:362

Reported side effects
None in verum or sham groups

Cluster headache

<table>
<thead>
<tr>
<th>Treatment of choice</th>
<th>Therapy</th>
<th>Cluster Headache</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>100% oxygen, 15 L/min (A)</td>
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<tr>
<td></td>
<td>Naratriptan 2.5 mg sub. (A)</td>
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<tr>
<td></td>
<td>Rizatriptan 5 mg nasal (A,B)</td>
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<tr>
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<tr>
<td></td>
<td>Zolmitriptan 5 mg oral (B)</td>
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<td></td>
<td>Zalecetin 25 (B)</td>
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<tr>
<td></td>
<td>Ondansetron (B)</td>
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<td>Preventive</td>
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<td>Levetiracetam (B)</td>
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<td></td>
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<tr>
<td></td>
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<tr>
<td></td>
<td>Valsartan (C)</td>
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</tr>
<tr>
<td></td>
<td>Meloxicam (C)</td>
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<tr>
<td></td>
<td>Baclofen (C)</td>
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</table>

May et al. 2006 Eur J Neurol 13:1066
Neuromodulation for cluster headache

- Vagus nerve stim
- Occipital nerve stim
- Sphenopalatine ganglion stim
- Deep brain stim of hypothalamus

Cluster headache - guidelines

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuromodulation</td>
<td>Sphenopalatine ganglion stim</td>
</tr>
</tbody>
</table>
Thank you

mark.j.burish@uth.tmc.edu
**Vagus nerve stimulation**

Adverse events:
- Oropharyngeal pain
- Depression (1 subject only)


**Patient selection – vagal nerve stimulation**

**Diagnosis:** Chronic cluster headache

**Patient history**
- Past medical history: carotid / cardiac / vascular issues, brain tumor, brain hemorrhage, TBI
- Current medications: N/A
- Prior treatment trials: N/A

**Treatment**
- Effectiveness: moderate
- Side effects and risks: minimal
- Cost: not yet known

**Sphenopalatine ganglion stimulation**

Adverse events:
- Sensory disturbance
- Facial pain
- Rare: infection, mild nasolabial paresis

Patient selection – sphenopalatine ganglion stimulation

Diagnosis: Chronic cluster headache

Patient history
Past medical history: facial surgery, osteomyelitis, or recent facial XRT
Current medications: anticoagulants
Prior treatment trials: N/A

Treatment
Effectiveness: moderate
Side effects and risks: moderate
Cost: not yet known

Deep brain stimulation


Adverse events
Diplopia
Intracerebral hemorrhage


Deep brain stimulation

<table>
<thead>
<tr>
<th>Study</th>
<th>N of patients</th>
<th>N of patients diplopia</th>
<th>N of patients intracerebral hemorrhage</th>
<th>N of patients improved</th>
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<td>Mano et al. (2005)</td>
<td>10</td>
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</table>

Only 26 of the 28 patients were considered in the improvement evaluation.

Postoperative pain and dysesthesias.

By way of caution: and other gestures.

Dizziness, dizziness, and dizziness.

Sudden incontinence, sudden incontinence,

Sudden incontinence, sudden incontinence.
Patient selection – deep brain stimulation

**Diagnosis:** Chronic cluster headache

**Patient history:**
- Past medical history: brain tumor or other mass lesion
- Current medications: anticoagulants
- Prior treatment trials: should fail / not tolerate 2 good oral preventives

**Treatment:**
- Effectiveness: moderate
- Side effects and risks: high
- Cost: high

---

**Post-Assessment Questions**

The most commonly used test to assess disability in migraine is the:
- a) Short-form 36 (SF-36)
- b) Migraine Disability Assessment Test (MIDAS)
- c) Headache Impact Test (HIT-6)
- d) Brief Headache Screen

Four companies are currently in phase II or III testing of a new preventive treatment for migraine, which is expected to be available for patients by the year 2020. That treatment is:
- a) Opioid/naloxone combination table
- b) Nerve growth factor
- c) Anti-calcitonin gene-related peptide (CGRP)
- d) Novel anti-depressant

---

**Post-Assessment Questions**

Which of the following environmental factors may worsen the symptoms of a migraine?
- a) Cold temperature
- b) Bright lights
- c) Humidity
- d) Quiet room
EXERCISE: DOES IT HURT OR HELP?
UNDERLYING MECHANISMS AND CLINICAL IMPLICATIONS

Kathleen A. Sluka, PT, PhD, FAPTA
Professor
University of Iowa
Funding: NIH AR061371, AR052316, AR063381

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Valerie Kefalla, PhD
Steven P. Wilson, PhD
Maria Claudia Fusaro, PT
Nicholas Gregory, MD, PhD
Francine Bobinski, PT, PhD
Adair Santos, PhD
Claudia Carvalho, PT
Felipa da Silva, Inc.
Jill Williams, PT
Shintaro Takenaka, MD, PhD
Jonny Haskins
Sandeep Katar
Kerry Adesman, PhD
Sebastian F. Pesce, MD
Audrey Leung, MD
Nicholas Cooper, PT, PhD
Teelaye Yavarian, DDS, PhD
Lee Ann Allen, PT
Lucas Lima, PT
Ronaldo Sed, PT, PhD

Conflict of Interest

• Consultant Bayer, Inc.
• Research Grant, Medtronic
• Royalties, IASP Press

Objectives

• Understand the underlying mechanisms by which exercise increases and decreases pain
• Describe the clinical evidence showing that pain increases with exercise and pain decreases with exercise
• Design an exercise program to address pain, fear of movement, and pain catastrophizing


Pre-Assessment Questions

1. Exercise can both increase or decreases pain depending on the state of the immune system. The following is true regarding mechanisms for how exercise increases pain.

   a. Increased release of fatigue metabolites activates macrophages in muscle to release pro-inflammatory cytokines in sedentary individuals.
   b. In sedentary individuals there are a greater proportion of M2 macrophages leading to increased pain.
   c. Glial cells in the central nervous system enhance nociceptive transmission by increasing anti-inflammatory cytokines.
   d. ATP-receptors, like P2X4, are expressed on nociceptors and activated by fatigue metabolites.

Questions

2. The following is true regarding the use of exercise for pain control.

   a. There is weak evidence that regular exercise is effective for treatment of most musculoskeletal pain conditions.
   b. Use of localized strengthening exercises is more effective than aerobic exercise.
   c. The main barrier to exercise for people with chronic pain is depression and anxiety.
   d. Adherence to exercise can be improved by supervision, patient choice, and treating pain with activity.

3. Physical therapists are considered experts in exercise prescription, particularly when exercise involves patient populations with different diseases. Exercise in both acute and chronic pain conditions is commonly used by physical therapists as part of the treatment plan for a patient. Which of the following is TRUE regarding exercise?

   a. Exercise produces analgesia by activating endogenous opioid pathways, reducing nociceptor excitability, and altering immune function.
   b. People with the highest levels of physical activity are more likely to develop chronic musculoskeletal pain than those that are inactive.
   c. For patients with chronic low back pain, the type of exercise prescribed is critical for positive outcomes.
   d. Exercise increases pain in individuals with chronic pain by increasing activation of the motor cortex that subsequently excites nociceptive dorsal horn neurons.
Physical Inactivity is a Health Concern

HUNT STUDY
Increased risk for chronic musculoskeletal pain if inactive

Clinical Problem: Activity-Induced Pain

People with chronic pain
  - Report physical fatigue (80-90%)
  - Show increased pain with physical activity
  - Are physically inactive

Function, Pain, and Fatigue

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pain</th>
<th>Fatigue</th>
<th>Pain &amp; Fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIS-R</td>
<td>r=-.37</td>
<td>r=-.31</td>
<td>r=-.42</td>
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<tr>
<td>MAF-ADL</td>
<td>r=-.32</td>
<td>r=-.39</td>
<td>r=-.41</td>
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<tr>
<td>SF-36-PF</td>
<td>r=-.33</td>
<td>r=-.22</td>
<td>r=-.34</td>
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<tr>
<td>6MWT</td>
<td>r=-.40</td>
<td>r=-.38</td>
<td>r=-.42</td>
</tr>
<tr>
<td>STS</td>
<td>r=-.20</td>
<td>r=-.20</td>
<td>r=-.20</td>
</tr>
</tbody>
</table>

McGoughlin et al., 2011; Dailey et al., 2016; Merriweather et al., 2017
Chronic Pain Pathology

Exercise-induced pain: animal model

Animal Models of Exercise-Induced Pain

- Electrically-induced

- Activity-induced
Peripheral Mechanisms

Frey Law et al., 2008

Peripheral Mechanisms: Sedentary

Gregory et al., 2015; 2016
Peripheral Mechanisms: Sedentary

Gregory et al., 2015; Gong et al., 2016

Peripheral Mechanisms: Sedentary

Fusaro et al., unpublished

Peripheral Mechanisms: Physically Active

HUNT STUDY Decreased risk for chronic pain if physically active

Exercise Effective for Chronic Pain
Fibromyalgia
Osteoarthritis
Rheumatoid arthritis
Low back pain
Neck pain
Myofascial Pain
Tendinitis
Shoulder pain

Sarvestani and Skeie, 2005, 2016; Skars et al. 2015; Raffamond et al., 2016; Lanza et al., 2016; Lima et al., 2017; Brito et al., 2017; Bobinski et al., 2017
Peripheral Mechanisms: Physically Active

Exercise

Fatigue Metabolites

Anti-inflammatory Cytokines

Neuropathic Pain

Chronic Muscle Pain

IL-10

IL-4

Exercise - Control (IgG), n = 8
Exercise - aIL10R, n = 10
Sedentary - Control (IgG), n = 7
Sedentary - aIL10R, n = 8

pH 4.0

Antibody

Peripheral Mechanisms: Physically Active

Improves healing in animals
and reduces cytokines

Increases innervation people
with diabetic neuropathy

Bobinski et al., 2011; Kluding et al., 2012; Bobinski et al., 2017
Central Mechanisms

Enhanced Central Excitability

- Glutamate and NMDA
  - Increased glutamate
  - Blockade of NMDA receptors reverses hyperalgesia
  - Phosphorylation of NR1 enhances conductance and trafficking to synapse

- Spinal Cord and RVM
  - Altered neuron excitability
  - Changes in glutamate
  - Enhanced glial activation
  - Enhanced activation with activity
  - Enhanced activation with pain

Central Mechanisms: Excitability

Reduced neuron excitability
Reduced pNR1

Chronic muscle pain model
Increased pNR1

da Silva et al., 2011, 2012; Sluka et al., 2013
Exercise reduces psychological factors

Exercise improves:
- Depression
- Anxiety
- Pain Catastrophizing
- Fear of Movement (?)

Vincent et al., 2014; Naugle et al., 2014
Summary
Regular Physical Activity

Clinical Application

What is the clinical evidence?

- Exercise effective for chronic pain
- Type of exercise less important
  - Strengthening
  - Aerobic
  - Proprioceptive
  - Land-based, Water
- Combined with motivation more effective
- Supervision improves effectiveness
What type of exercise?

Given the evidence that MCE (motor control exercise) is not superior to other forms of exercise, the choice of exercise for chronic LBP should probably depend on patient or therapist preferences, therapist training, costs and safety.

-Cochrane review: Motor control exercise for chronic non-specific low back pain., 2016

Concerns with exercise

Up to 70% of patients non-adherent

What prevents adherence?
- Increased pain during exercise
- Low levels of physical activity

What improves adherence?
- Supervision
- Motivational interventions
- Individualization
  - Integrate into daily activities
  - Give patient a choice of exercise options
  - Family Involvement and Group Programs
  - Education
TENS reduces movement pain, not resting pain

Pain

TENS normalizes altered pain physiology

Pain Sensitivity
Conditioned Pain Modulation

A
Pressure Pain Threshold

B
Conditioned Pain Modulation

Summary

• Increased pain with acute exercise
• Fatigue metabolites
• Macrophage activation
• Central facilitation
• Treat with TENS
• Decreased pain with regular exercise
• Macrophage phenotype switch
• Decreased central facilitation
• Increased central inhibition
• Increased anti-inflammatory cytokines
• Improved healing
• Type of exercise not important
• Improve adherence
Post-Assessment Questions

1. Exercise can both increase or decrease pain depending on the state of the immune system. The following is true regarding mechanisms for how exercise increases pain.
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The Practical Application of Pain Science in the Clinic

Sandra Hilton PT, DPT
Entropy Physiotherapy and Wellness

Midwest Pain Society
41st Annual Scientific Meeting
October 27-28, 2017
Chicago, Illinois

Disclosure

• No relevant financial disclosures.

• A strong bias towards science based medicine.

• Clinical instructor for the treatment of pelvic pain and men’s health.

Objectives

• Participants will develop and implementation plan to utilize appropriate screening forms with all patients experiencing pain.

• Participants will integrate a biopsychosocial approach beginning with the initial patient encounter.

• Participants will demonstrate a choice of words that support the application of pain science in the clinic.
Pre-Assessment Questions

- The Pain Catastrophising Scale
  - A: Indicates if a person is telling the truth about their symptoms.
  - B: Is broken into subscales that provide insight for designing treatment.
  - C: Measures depression.
  - D: Has no relevance to pelvic pain
  - E: Is broken into subscales of Depression, Hopelessness, and Magnification

Pre-Assessment Questions

- Using a biopsychosocial approach for clinical care of pain involves a complete physical assessment and
  - A: Screening for psychosocial needs only if they are not progressing after 6 weeks.
  - B: Framing the results of your test in terms of strictly biomechanical terms.
  - C: Assessment of social needs and of their thoughts, beliefs, and expectations
  - D: Sending each patient for a full psychological work up.
  - E: Avoiding questions about partners, stressors, or life habits

Pre-Assessment Questions

- A 30 year old nulliparous woman is experiencing painful vaginal intercourse. She is able to tolerate a careful vaginal examination. Physical Therapy intervention should include:
  - A: Strictly following a set of exercises to increase core stability and pelvic alignment
  - B: Aggressive manual therapy regardless of the discomfort (pain) from the treatment
  - C: Education to avoid all aerobic activity
  - D: Sensory integration techniques including graded imagery and graded exposure (including the use of vaginal dilators).
  - E: Education on the use of adaptive techniques to avoid sitting
Theoretical Foundations
- Treating pain from a science-based perspective.
- What IS best evidence?
  - Levels of Evidence
  - Psychometrics for screening forms
    - Pain Catastrophizing Scale
    - Self-Efficacy

SBM, EBM, EBP, PBE?
- [https://sciencebasedmedicine.org/responding-to-dm-critics/](https://sciencebasedmedicine.org/responding-to-dm-critics/)
- “medical interventions that are safe and effective are inherently superior to interventions that are unsafe or ineffective”
- the best way to determine which interventions are safe and effective is by looking critically at all the available science
- there should be one, thoughtful, science-based standard that applies uniformly to all of health care

Waddell’s Non-organic signs

Training is biomedical

- Domenech et al (2011) looked at comparing biomedical training versus biopsychosocial training in LBP for 2nd year PT students and how it drove their beliefs

- OB/GYN residents at University of Toronto, Canada- 3 hours of training on the pain system in their entire residency

- Simmonds et al (2012): PT’s with a strong biomedical orientation and those with postgraduate training in manual therapy had:
  - More restrictive return to work recommendations that did not follow published practice guidelines (only 12% of PT’s were aware of practice guidelines)
  - More intolerant of uncertainty and made more restrictive activity recommendations

Words that hurt
Incorporating a Biopsychosocial Perspective into Practice

- Bio
- Psycho
- Social

This is not three words, it is one philosophical concept that underpins how a person is seen as a whole, existing and interacting in their life. (Hilton)

Assessment

- Ask the person in front of you what is wrong
- Listen to their answer and explanation

- Physical Examination is still important within a biopsychosocial framework.
- Determine: Biological triggers as well as thoughts, beliefs, and expectations.
Pain is produced when the body or a specific tissue is perceived to be in danger and a response is required.

What if: The treatment approaches you chose are laden with non-threatening and confidence building input?

- Words
- Movement
- Touch

“Rebecca”

PMH: Significant for C-sections and large surgical repair due to hemorrhage. Additional surgical repair of DRA with stitches that are beginning to work to the surface and are painful.

Patient has been to a variety of therapists and is under the impression that she won’t be able to return to her prior level of function due to risk of prolapse and problems associated with the abdominal and perineal scars.
"Rebecca"

- Her beliefs and expectations
  - Sex will be painful
  - Sex may rupture her surgery
  - Things will fall OUT
  - Scars will always hurt

Pain Catastrophizing Scale (PCS)

- Helplessness: a key indicator for suicide
- Rumination: stuck in a circle of thought
- Magnification: worsening thoughts and loss of confidence in ability to overcome
Treatment Options

- Magnification:
- Reframe pain
- Provide education and resources for self-efficacy
- Ruminations:
- Meditation (Patient workbooks: Lehman, Butler/Moseley)
- Affirmations
- Helplessness
- Social Support
- Minimize passive treatment and increase resiliency
- Patient-therapist handbook: increase self-efficacy
- CBT referral/ CBT self-help page on Healthskills

Where to start?

- Principles, not protocols
- Bring the team together to deliver a consistent message around pain.
- Minimize (eliminate) messages that imply danger/instability
- Maximize messages that encourage and support resiliency.

Treatment Philosophy

Identify the expectations of threat or inability and create a solution to confound the expectation and restore the person to at or beyond their prior level of function.
Conceptual Change Theory

- Offer evidence against their current concept or belief = \text{MULTIPLE TIMES}
- Provide an alternative concept to their belief
- Give stories/metaphors and new experiences
- Get emotions involved to make it stick
- Address all the threats

Reconceptualizing pain is as good an intervention as we have for treating persistent pain

Graded exposure

- Set functional goals
- Establish pain control strategies
- Break down goals into a safe starting point and build slowly from there

Supported Independence

- The good news
  - Maher et al. 2016 Systematic Review of NSLBP (ex that is liked is the preferred ex, equal possibility of success)
  - There’s no evidence that pain is unchangeable
  - There’s evidence that painful ex is not needed
  - Movement appears to be the key
    - All other treatments aim to make movement more likely
Sometimes when risk factors alone are considered, clinicians can fail to recognize that individuals bring strengths with them as well. After all, people who come to see a clinician have got themselves up, traveled to an appointment, and carried out the tasks of everyday even though they have pain: they have coped at least to a degree. If we only attend to risk factors, we probably don’t think about how well a person is doing, or what they can do to enhance their wellbeing, or build on what’s already working for them.

-Dr. Bronwyn Thompson
HealthSkills Weblog

Suggested Reading


Post-Assessment Questions

- The Pain Catastrophising Scale
  - A: Indicates if a person is telling the truth about their symptoms.
  - B: Is broken into subscales that provide insight for designing treatment.
  - C: Measures depression.
  - D: Has no relevance to pelvic pain
  - E: Is broken into subscales of Depression, Hopelessness, and Magnification

Post-Assessment Questions

- Using a biopsychosocial approach for clinical care of pain involves a complete physical assessment and
  - A: Screening for psychosocial needs only if they are not progressing after 6 weeks.
  - B: Framing the results of your test in terms of strictly biomechanical terms.
  - C: Assessment of social needs and of their thoughts, beliefs, and expectations
  - D: Sending each patient for a full psychological work up.
  - E: Avoiding questions about partners, stressors, or life habits

Post-Assessment Questions

- A 30 year old nulliparous woman is experiencing painful vaginal intercourse. She is able to tolerate a careful vaginal examination. Physical Therapy intervention should include:
  - A: Strictly following a set of exercises to increase core stability and pelvic alignment
  - B: Aggressive manual therapy regardless of the discomfort (pain) from the treatment
  - C: Education to avoid all aerobic activity
  - D: Sensory integration techniques including graded imagery and graded exposure (including the use of vaginal dilators).
  - E: Education on the use of adaptive techniques to avoid sitting
Exercise Prescription for Chronic Pain

Jason Silvernail DPT, DSc

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Disclosures

This certifies that I, Dr. Jason Silvernail, have not, nor has my spouse/partner or any immediate family member have had in the past 12 months or expect to have in the upcoming months, any financial relationship or gift-in-kind with industry that is relevant to the subject matter of the presentation.

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   b. 80% of maximum effort
   c. Enough to break a light sweat
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Exercise Prescription for Chronic Pain

Jason Silvernail DPT, DSc

Who has seen this patient?

- "Frequent Flyer"
- Multiple pain areas
- Failure to improve with care
- Out of work/school
- Poor health behaviors: smoking, inactive, overweight/obese, poor sleep
- Depression / anxiety

How can you help this patient?

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How About a Magic Pill?

- Reduces pain
- Improves overall physical function
- Reduces risk of future medical problems
- Improves symptoms of depression and anxiety
- Improves participation in social activities, work / school performance
- Improves cognitive performance

Exercise!

Sounds easy right? Everybody likes exercise

Clinical Guidelines vs My Patients
Prescribing Exercise for Chronic Pain

- Exercise, Pain, and Activity
- Tailoring Activity and Exercise for Patients
- Compliance and Adherence

Does Exercise Help Patients with Pain?
Exercise and Chronic Pain: Evidence / Effect Sizes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Aerobic</th>
<th>Strength</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Small</td>
<td>Large*</td>
<td>Large</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Small</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Global Health</td>
<td>Small</td>
<td>Large*</td>
<td>No change</td>
</tr>
<tr>
<td>Physical Function</td>
<td>Medium</td>
<td>Large*</td>
<td>Large CV Str</td>
</tr>
<tr>
<td>Depression</td>
<td>Small / Medium</td>
<td>Large*</td>
<td>No change</td>
</tr>
</tbody>
</table>

* Limited data

Adapted from Bruch 2011 In Rheumatology

Exercise and Pain: Tailoring by Pain Type

- Is all pain the same?
- Chronic / Acute / Sensitivity Issues??
- The kind of pain matters if we are going to use exercise...

What kinds are there?
Exercise and Pain: Mechanisms / Prescription

- Nociceptive Pain Mechanism
  - Primarily about ascending danger signals – ankle sprains, arthritis

- Neuropathic Pain Mechanism
  - Primary lesion or injury to nervous tissue – neuropathy, radiculopathy

- Central Sensitization Pain Mechanism
  - Sensitization locally and at spinal cord, and reduced inhibitory processes
  - Allodynia
  - Hyperalgesia

Exercise and Pain: Nociceptive Mechanism

- Most common mechanism seen in clinic
- Driven by danger signals from tissue
- May or may not be related to tissue damage
- Local sensitivity present around the area

Pain and Tissue Damage: Fish and Bicycles

- Pain is VERY POORLY correlated to imaging studies of tissue problems
- Tissue degeneration /≠ Pain
- Pain /≠ Tissue degeneration
- Consistent Correct Clinical Correlation is Cey*
Tissue Issues: Relevance, please?

Did you know your MRI can be misleading?

If you take people without back pain and put them through a CT scan or MRI, you get some surprising results.

- 25% of 20-year-olds
- 80% of 30-year-olds
- 95% of 40-year-olds
- 85% of 50-year-olds

Nociceptive Mechanism

- Local origin danger signals to CNS
- Mechanical, inflammatory, immune processes
- Lowered thresholds in spinal cord quickly return to normal

Neuropathic Mechanism

- Primary injury or lesion to nerve tissue
- Mechanical, inflammatory, immune processes
- May or may not have changes in reflex activity, motor, sensation
Central Sensitization

- Sensitization along ascending tract - lowered thresholds, increased responses
- Inhibition along descending tract - decreased responses
- Result: more pain, more often, often disproportionate to stimulus

Clinically Recognizing Central Sensitization

- Generalized load and stress intolerance across a wide range of modalities
- Possible indicators of CS, generalized hypersensitivity:
  - Light, touch, sound, smells, temperature, pressure
- Possible indicators of CS, pain sensitization
  - Allodynia, hyperalgesia, hyperesthesia

Pain Sensitization Concepts

<table>
<thead>
<tr>
<th>Concept</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allodynia</td>
<td>Pain due to a stimulus that does not normally provoke pain</td>
</tr>
<tr>
<td>Hyperalgesia</td>
<td>Increased pain from a stimulus that normally provokes pain.</td>
</tr>
<tr>
<td>Hyperesthesia</td>
<td>Increased sensitivity to stimulation, excluding the special senses.</td>
</tr>
</tbody>
</table>
What does this tell us?

- Sensitized patients will often have pain flares when starting new exercise programs
- Careful dosing is important
- Long term changes > short term symptoms

OK, that’s Pain.

Let’s Talk about Exercise

Does This Sound Like Fun?

"planned, structured, and repetitive bodily movements that are performed to improve or maintain one or more components of physical fitness"

Howley 2001
**Exercise Dosage**

- **Aerobic training**
  - 150 min Moderate to Vigorous exercise
  - Moderate – 3 to 6 METs, "brisk walk"

- **Resistance Training**
  - 2-3 sessions per week, whole body

- **General Activity**
  - 7-11k steps per day, 10,000 is a good goal

---

**22% Drop Out Rate** in Aerobic Exercise Groups for Fibromyalgia Treatment

*In some trials it’s almost 30%*

---

**Exercise, Pain, and Activity**

- Exercise helps patients with chronic pain in many different ways

- Effect sizes are ok but not huge, probably not an easy sell for patients

- Known dosages of aerobic exercise, resistance, and general activity

- We need to find a better way to sell exercise
Prescribing Exercise for Chronic Pain

- Exercise, Pain, and Activity
- Tailoring Activity and Exercise for Patients
- Compliance and Adherence

Tailoring Exercise for Nociceptive Pain

- Generalized aerobic training clearly improves pain
  - Improved metabolic economy around injured area
  - Improved descending inhibitory function

- Activities that directly aggravate the problem area will be an issue

- "Training around" or finding less aggravating activities

- Starting a new exercise program does not* increase their pain

Tailoring Exercise for Nociceptive Pain

<table>
<thead>
<tr>
<th>Problem Area</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee Pain</td>
<td>Cycling, Walking, Swimming</td>
</tr>
<tr>
<td>Shoulder Pain</td>
<td>Careful with arm action on elliptical</td>
</tr>
<tr>
<td>Neck Pain</td>
<td>Cycling can be stressful</td>
</tr>
<tr>
<td>Back Pain - worse with sitting</td>
<td>Walking, Elliptical Trainer</td>
</tr>
<tr>
<td>Back Pain - worse with standing/walking</td>
<td>Cycling, Incline walking on Treadmill</td>
</tr>
<tr>
<td>Back Pain - improved by lying down</td>
<td>Swimming, Aqua Jogging</td>
</tr>
</tbody>
</table>
Tailoring Exercise for Neuropathic Pain

- Generalized aerobic training clearly improves pain
- Improved metabolic economy around injured area
- Improved descending inhibitory function

- Activities that directly aggravate the nervous tissue will be an issue
- “Training around” and avoid “neural tension” positions
- Starting a new exercise program does not increase their pain

What About Exercise for Sensitized Patients??

- Tailoring is much more complicated
- Easy decisions and cute (ugly?) charts will not help you
- Starting a new exercise program usually increases their pain
- Would you do something that reliably made you feel worse?

Threatening Places
Threatening Places

“planned, structured, and repetitive bodily movements that are performed to improve or maintain one or more components of physical fitness”

Getting Out of the Gym – Rebranding Exercise

- Do patients need to "Exercise" to experience gains?
- What if we can build patients’ capacity with non-exercise activity?
- How do you dose and manage this?
- How can you work toward established recommended dosages?

Lifestyle Physical Activity

- Activity not exercise
- Measured with accelerometers and activity diaries
- Walking most common but also gardening/yardwork, household chores, recreational activities
- Intensity still Moderate (3-6 METs)
Exercise vs Activity

<table>
<thead>
<tr>
<th>Option</th>
<th>Intensity</th>
<th>Duration</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td>Moderate (3-6 METs)</td>
<td>30 min/day</td>
<td>150 Min/Wk</td>
</tr>
<tr>
<td>Activity</td>
<td>Moderate (3-6 METs)</td>
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</tbody>
</table>

A Framework for Physical Activity Prescription

<table>
<thead>
<tr>
<th>Prescription</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 min/day target</td>
<td>Walking or Dancing</td>
</tr>
<tr>
<td>Moderate intensity</td>
<td>Yoga or home calisthenics</td>
</tr>
<tr>
<td>+5 minutes per week</td>
<td>Golf or doubles tennis</td>
</tr>
<tr>
<td>12 week program</td>
<td>Hiking flat ground</td>
</tr>
<tr>
<td>6 sessions</td>
<td>Walk down stairs</td>
</tr>
<tr>
<td>Include how to set intensity and deal with flares</td>
<td>Yardwork</td>
</tr>
</tbody>
</table>

Fontaine 2010
Education vs Activity Counseling
Activity Group More Active* - Is it enough?

Improving Fitness – Intensity

- Aerobic Fitness
  - 60-80% of maximum heart rate
  - 20-40 min per session, 2-4 sessions/week

- Strength Improvement
  - 60-80% of 1RM
  - 1-3 sets of 6-12 repetitions in general

To improve fitness, you need to work at about 60-80% of your maximum capacity, 2+ times/wk

Is this 60-80% of maximum capacity???
How much of a dose to improve pain?

- Improving pain?
- Improving function?
- Improving fitness parameters?
- Improving muscle performance?

Target Dosing and Progression

- We don’t need the kind of dosage that improves fitness
- Lower activity dosages can be effective for pain and function
- "Start low and go slow": 15 min/day, +5 min/wk

Tailoring Activity and Exercise for Patients

- Exercise is helpful and we have targeted dosages for health
- We don’t need to improve fitness to improve pain
- We can use Activity rather than Exercise to help patients improve
- Next step: compliance
Prescribing Exercise for Chronic Pain

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Improving Compliance and Adherence

- Linking Expectation and Outcome
- Expectation
  - The confidence that one can complete the task
  - Such as regular exercise or activity
- Outcome
  - Completing the task will result in the desired end point
  - Less pain, more function, better tolerating desired activities...

Self-Efficacy
Self-Efficacy

"having, or gaining, the confidence that one can complete a task, such as regular participation in exercise (efficacy expectation)" and "...believing that completing a task results in the desired effect, such as fitness or symptom control (efficacy outcome)"

Bandura 1977

Four Keys to Self-Efficacy: MVSM

1. Mastery
   - Patient should be involved in the prescription
   - Program should be REALISTIC – must fit their life
   - Program should be ACHIEVEABLE – something they can do
   - They should have a say in how it’s accomplished, what’s done, and what the options are for them

2. Verbal Persuasion
3. Symptom Reduction
4. Modeling

They are able who think they are able.
- Virgil

Self-Efficacy: Mastery

Jones & Lipton 2009
Barlow 1977
Self-Efficacy: Verbal Persuasion

- They must feel like their provider cares
- Express confidence in them and their capabilities
- Build their resilience and self-confidence
- Use as examples things from their past that demonstrate their toughness and capability

Jones & Lipton 2009
Bandura 1977

Verbal Persuasion Tips

- People with chronic pain are used to being discounted and disbelieved
- Express real confidence in them and their resiliency
- This is a lot easier if you actually like your patients

We Discount the Pain of Others When Pain Has No Medical Explanation

Journal of Pain

I know you can do this – you’ve done this before and I can help you do it again

You’ve been dealing with a lot of challenges – a lot of people would have given up, but you’re still here. You are tougher than you might think.

I have helped a lot of people just like you get their life back – even people who aren’t as strong as you are, who don’t have your grit.

You have an amazing dedication to your family – we can use that dedication to help you get better here so you can be the mother/father you want to be
Self-Efficacy: Symptom Reduction

- Early reduction of symptoms is important
- This might be related to ‘expectancy violation’
- You don’t need a huge effect here – just enough that’s noticeable and enough to challenge their ideas about their problem
- A “Quick Win” that helps improve buy-in

Self-Efficacy: Modeling

- Real life examples and stories are very powerful
- Group settings with at least one person who is successful
- Support groups or exercise groups can be very positive
- In person >>> Online

Self-Efficacy:

Builds resilience
Promotes self management
Enables Success
Our patients need you.

Exercise Prescription in Chronic Pain

- Exercise is helpful for chronic pain but compliance is difficult
- Think Activity rather than Exercise
- Understand dosage for fitness vs pain/function improvement
- Build Self-Efficacy with MVSM:
  - Mastery
  - Verbal Persuasion
  - Symptom Reduction
  - Modelling

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Case Example

- 48 y/o female
- Two children, school age
- Not working outside home
- Husband works
- No fitness background
- Wants to ride bike w/kids
- Chronic whole-body pains
- Unsuccessful medical treatment
Case Example: Exercise, Activity, and Dosage

- Are gym-based fitness programs likely to be successful here?
- Does she need 150 min/wk of aerobic ex and 2/wk strength training to feel better?
- Does she have an activity she likes that you can use to build her resilience?

Case Example: Build Self-Efficacy

- Mastery
  - Bike riding a useful place to start?
  - Playing with the kids?
  - When during the day can she fit this in?
- Verbal Persuasion
  - What are her strengths? Medical care experiences, family support, personal history
- Symptom Reduction
  - What early concrete action to reduce some symptoms she has?
  - What is her most bothersome symptom?
- Modelling
  - Local groups for support? Other patients in your clinic?

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