Neurodynamics 2.0: Pain, Plasticity, and Desensitizing the Nervous System

Adriaan Louw, PT, PhD
Stephen Schmidt, PT, M.Phys, OCS, FAOMPT

Objectives

Upon completion of this educational session the participants will be able to:

• Recognize the advances in neurodynamics
• Develop a clinical knowledge of the various neurodynamic tests and treatments as it pertains to the advances in pain science
• Understand how a physical and psychologically unhealthy nervous system contribute to persistent pain
• Recognize various clinical conditions in which the altered neuroimmune responses contribute to persistent pain
• Immediately apply the information from the educational session into clinical practice

Let's start with a lab session...

McLellan 1975 & 1976

Accidentally found that nerves...move...

**The Body's Alarm System**


**Actually...Imhotep 2800 BC**

“When he extends (both legs), he contracts them both immediately, because of the pain he causes in the vertebra of his spinal column.”

**The Premise behind “Neural Tension”**


**Neural Mobilization: The Impossible**


1. Space
2. Movement
3. Blood


Breig A. Adverse Mechanical Tension in the Central Nervous System. Stockholm: Almqvist and Wiksell; 1978.


So What?

Cervical Radiculopathy
Cervical Myelopathy
Thoracic Outlet Syndrome
Brachial Plexus
First Rib/Clavicle
Shoulder Joint Pathologies
Lacunar Syndromes
Cubital Tunnel Syndrome
Lateral Epicondylitis
Carpal Tunnel Syndrome
OA/RA of the hands

2. Movement


Breig A. Adverse Mechanical Tension in the Central Nervous System. Stockholm: Almqvist and Wiksell; 1978.
Carpal Tunnel Syndrome...

30% reduction in longitudinal movement of the nerve


2. Movement

Nerves do not stretch
Axonal folding and unfolding


3. Blood Supply

- The brain and spinal cord are estimated to only account for 2% of the total body mass, yet they consume 20-25% of the available oxygen in the circulating blood
- If a nerve is "lengthened:"
  - 6-8%: Slow blood flow
  - 15%: Stop blood flow
  - 20%: Cells die in the dorsal horn: Demyelination


3. Blood Supply

- The brain and spinal cord are estimated to only account for 2% of the total body mass, yet they consume 20-25% of the available oxygen in the circulating blood
- If a nerve is "lengthened:"
  - 6-8%: Slow blood flow
  - 15%: Stop blood flow
  - 20%: Cells die in the dorsal horn: Demyelination


Compartment Syndromes
Where nerves run through tunnels they have pressure gradients to help nourish the nervous system

• Blood pressure is needed to "pump" blood to nerves
• Blood is diffused from the arteriole (PA) to the capillary (PA) and ultimately the nerve fascicle (PF)
• This allows nerves to have adequate blood supply

P Arteriole > P Capillary > P Fascicle


Entrapment Neuropathies


Compartment Syndromes
Repetitive motions...

Neuroinflammation
Tendon Swelling
Bony Changes

Increased Tunnel Pressure
Back up blood in the Venous
Back up blood in the Fascicle

Ischemia
Edema
Axonal Compression and Degeneration


Immune Changes and Nerve Sensitivity


Property of ISPI/Adriaan Louw – not to be copied without permission


• Mechanical
• Immune
• Chemical

Fig. 1.4 Schematic representation of a single sensory neurone highlighting ion channels and receptor proteins in the cell wall. Adapted from: Devor et al 1994
V+ channel; Ca2+ channel; Na+ channel; Adrenergic receptor = ligand gated ion channel sensitive to adrenaline; Mechano-receptor or Stretch activated receptor.
Vibration Sensitization

Dysfunction of A-beta fibers and Pacini corpuscles have shown increased sensitivity in neuropathic pain.


Neurogenic Inflammation

- Orthodromic impulses (to the CNS)
- Antidromic impulses (to the tissues)
  - Substance P (vasoactive)
  - Histamine
  - Cytokines, macrophages

Gifford LS. Pain, the tissues and the nervous system. Physiotherapy, 1998. 84: p. 27-33.

Identifying Neuropathic Pain in the Clinic

- Symptoms and sign clusters
- 150 times more likely to have a peripheral neurogenic pain state
  - Pain in dermatomal or cutaneous distribution
  - Positive neurodynamic and palpation (mechanical tests)
  - History of nerve pathology or compromise


Theoretically...

There is, however, more complexity...

Barrage into the CNS...


Remapping of the Spinal Cord...


Central Sensitization


End-Result

<table>
<thead>
<tr>
<th>Process</th>
<th>Consequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Death of the inhibitory neurons</td>
<td>• Decreased gating from the periphery</td>
</tr>
<tr>
<td>• C-fibers pull back; A-fibers grow in</td>
<td>• Allodynia</td>
</tr>
<tr>
<td>• Upregulation of second-order neurons</td>
<td>• Increased firing towards the brain</td>
</tr>
<tr>
<td>• Inappropriate synapsing – other levels</td>
<td>• Spreading pain</td>
</tr>
<tr>
<td>• Inappropriate synapsing – other fibers</td>
<td>• Sympathetic, immune, motor contributions</td>
</tr>
<tr>
<td>• Inappropriate synapsing – other side</td>
<td>• Bilateral “mirror” pains</td>
</tr>
<tr>
<td>• Decreased endogenous mechanisms</td>
<td>• Aldyopia and Hypertagiasia</td>
</tr>
</tbody>
</table>

Identifying Central Sensitization in the Clinic

- Symptom and sign cluster (486 times) for CS
  - Disproportionate pain
  - Disproportionate aggravating and easing factors
  - Diffuse palpation tenderness
  - Psychosocial issues

Identifying Central Sensitization in the Clinic

- Symptom and sign cluster (486 times) for CS
  - Disproportionate pain
  - Disproportionate aggravating and easing factors
  - Diffuse palpation tenderness
  - Psychosocial issues
  - Fear-Avoidance
  - Pain Catastrophization

Fear-Avoidance

Presence of avoidance behavior is associated with increased risk of prolonged disability and work loss.

- FABQ-Work sub-scale scores >34
- FABQ-Physical Activities sub-scale scores >14


Central Sensitization Inventory

Scale range is 0-100
Answers and scoring method:
- Never = 0
- Rarely = 3
- Sometimes = 2
- Often = 3
- Always = 4


Clinical Examination of Central Sensitization

Clinical tests:
1. Assessment of pressure pain thresholds at sites remote from the symptomatic site
2. Assessment of sensitivity to touch during manual palpation at sites remote from the symptomatic site
3. Assessment of sensitivity to vibration at sites remote from the symptomatic site
4. Assessment of sensitivity to heat at sites remote from the symptomatic site
5. Assessment of sensitivity to cold at sites remote from the symptomatic site
6. Assessment of pressure pain thresholds during and following exercise
7. Assessment of joint end feel
8. Brachial plexus provocation test


Nerve Palpation: With/without pressure algometry...

Sensitive nerves

Nerve Palpation: With/without pressure algometry...

Nerve Palpation: With/without pressure algometry...

Pain Catastrophization Scale

Previous studies utilizing the PCS have shown a median score of 18 for healthy individuals and in patients with pain, the PCS is generally higher (>30 cut-off)


Nerve Palpation: With/without pressure algometry...

Nerve Palpation: With/without pressure algometry...

Nerve Palpation: With/without pressure algometry...

Combined Sections Meeting
Hand Therapy Section
February 2018


There is, however, more complexity...


But the CNS contains a lot more than just neurons

Microglia...

Glia in the Spinal Cord

- Neuroglia (Greek for “glue”), classically = cells that provide metabolic and structural support, but also:
  - Establish and maintain synapses
  - Regeneration and plasticity
  - Myelin formation and repair
  - Immune function
- Outnumber neurons >10 to 1


Cytokines

- Messengers of the immune system
- Produced by a broad range of cells, including immune cells (macrophages, B lymphocytes, T lymphocytes and mast cells)
- Participate in synaptic transmission in neurons and glial cells
- Cytokines regulate inflammation


Cytokine balance...

- A disproportion of pro-inflammatory and anti-inflammatory cytokines leads to a chronic peripheral sensitization of the nervous system.
- Release of chemokines and cytokines that elicit peripheral sensitization.

To test Neuropathic Pain:
Slow, progressive compression on the nerve...

Plastic tube around young rat nerve...as the rat grows, the nerve grows and steady, progressive pressure is added to the nerve – which mimics clinical scenarios.

Injury to a peripheral nerve and electrical stimulation of C-fibers each cause an increase in the permeability of the blood-spinal cord barrier and blood-brain barrier.

A cascade of immune changes start to occur...

Response of microglia in the spinal cord after peripheral nerve injury
**Various Neuroimmune responses are associated with Neuropathic Pain**

- a. Control
- b. One week after sciatic nerve transection
- c. Eleven weeks after sciatic nerve transection
- d. Additional glial cell activation


**Neuropathic Pain...? Widespread Pain**

Dermatomes and peripheral nerve textbook patterns do not correspond to real-world situations

Only approximately 1/3 of the clinical patterns match the textbook/articles


**Patients with FM display small fiber nerve pathology**

- Small fiber loss
- Demyelination
- Edema


**There is, however, more complexity...**


**In chronic pain there are structural and functional neuroplastic changes that occur in the Spinal Cord and Brain and it seems the immune system is a key player...**

**Plastic maps**

- Biologically coded
- Environmentally sculpted
- Changes occur in minutes...

Movement and use
Immobilization and limited use


It happens fast


Neglect and Pain

Neglect the tactile destruction in chronic back pain

The Brain: “Tell me more…”

Neuroplasticity Testing

Subjective
- Problems with left/right
- Dyslexia
- Different sensations?
- Different size?
- Missing body parts?
- Not belonging to you?
- Move different?
- In different place?
- Etc.

Objective
- Smudging
- Laterality
- Shape

Neuroplasticity Testing: Subjective

• Problems with left/right
• Dyslexia
• Different sensations?
• Different size?
• Missing body parts?
• Not belonging to you?
• Move different?
• In different place?
• Etc.

Smudging: Quick Screen

Other normative values reported in mm (see Nolan MF - 1982, 1983, 1985)

<table>
<thead>
<tr>
<th>Location</th>
<th>Normative Values</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper lateral arm</td>
<td>42.4</td>
<td>(see Nolan MF - 1982, 1983, 1985)</td>
</tr>
<tr>
<td>Lateral epicondyle forearm</td>
<td>31.5</td>
<td></td>
</tr>
<tr>
<td>Medial epicondyle forearm</td>
<td>21.0</td>
<td></td>
</tr>
<tr>
<td>Finger pad</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Distal lateral leg</td>
<td>41.6</td>
<td></td>
</tr>
<tr>
<td>Inf angle scapula</td>
<td>52.2</td>
<td></td>
</tr>
<tr>
<td>Mid posterior thigh</td>
<td>42.2</td>
<td></td>
</tr>
<tr>
<td>Tip great toe</td>
<td>6.6</td>
<td></td>
</tr>
</tbody>
</table>

2 point discrimination norms


What's normal?

- Accuracy of >80%
- 1.6 sec +/- 0.5 for necks and backs
- 2 sec +/- 0.5 for hands and feet


An Unhealthy Nervous System result in Immune Changes


Neurodynamics

- Neural mobilization helpful for cubital tunnel syndrome. (O’kay, Metcalf et al., Sventak, Larsson et al. 2009)
- Development of a clinical prediction rule to identify initial responders to mobilization with movement and exercise for lateral epicondylalgia. Age 149 years, pain-free grip strength on the affected and unaffected side.
- A single cervical spine manipulation leads to immediate hypalgesic and motor effects in subjects with lateral epicondylalgia (Fernandez-Camero, Fernandez-de-la-Peina et al. 2008)
- Neural mobilization helpful in a patient with radial elbow pain (Butler and Holden 2002)
- Carpal tunnel syndrome (CTS) helped with neural mobilization (New, Vicenzino et al. 2012)
- Neurodynamics helpful in CTS (Tri-Arab and Rushton 2004)
- Lateral epicondylitis (Biston and Holden 2002)
- Cervical lateral glide mobilizations to effect changes in neck and/or arm symptoms (Vicenzino, Collina et al. 1999, Cowell and Phillips 2000, Coppieters, Bimpoulas et al. 2005; Olsed, Whitman et al. 2005) as this intervention has been shown to produce immediate reductions in mechanical sensitivity, and pain in patients with lateral epicondylitis (Vicenzino, Collina et al. 1999) and carpal tunnel pain (New, 1999; Cowell and Phillips, 1999)
- CTS: Neural mobilization/ tendon gliding realized need for CTS surgery in 29.8% of patients (Rozmaryn, Drielle et al. 1998)

Neurodynamics: Physical

- Neural mobilization helpful for cubital tunnel syndrome
- Development of a clinical prediction rule to identify initial responders to mobilization with movement and exercise for lateral epicondylalgia.
- A single cervical spine manipulation leads to immediate hypalgesic and motor effects in subjects with lateral epicondylalgia.
Neurodynamics: Physical

Systematic review

• Results:
  – For chronic neck-arm pain, pain improved following NM. For most of the clinical outcomes in individuals with carpal tunnel syndrome, NM was not effective (P>.11) but showed some positive neurophysiological effects (e.g., reduced intraneural edema).
  – Due to a scarcity of studies or conflicting results, the effect of NM remains uncertain for various conditions, such as postoperative low back pain, cubital tunnel syndrome, and lateral epicondylalgia.

• Conclusion:
  – This review reveals benefits of NM for back and neck pain, but the effect of NM on other conditions remains unclear.


Neurodynamics: Intraneural Fluid

Passive neural mobilization induces dispersion of intraneural fluid


Neurodynamics: Intraneural Fluid

Intraneural edema reduction is a likely therapeutic mechanism of neural exercise


Neurodynamics: Inflammation

Spinal mobilization changes in inflammation around the nerve root and DRG...


RA, Inflammation and Movement...

Growing body of evidence showing exercise:

• Reduces disease process
• Anti-inflammatory effect
• Does not increase, but rather decrease pain


Neurodynamics: Immune

• Neural mobilization reverses behavioral and cellular changes that characterize neuropathic pain in rats
• Decreased neuroimmune activity, specifically glial cell activity

Movement as Antigen?

• Antigens stimulate immune responses
• Synapses are influenced by glial cells
• Vigorous movement/exercise – pro-inflammatory
• Moderate movement/exercise – anti-inflammatory


Neurodynamics: Neuroplastic

• Immobilization and neuroplastic changes...


Mobilizing the Immune System via Neurodynamics

Thank You

Stephen Schmidt, PT, M.Phys, OCS, FAAOMPT
Adriaan Louw, PT, PhD


