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

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Stephen Schmidt, PT, M.Phys, OCS, FAAOMPT

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New Orleans • February 21–24, 2018

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

Disclaimers…

We publish books on pain and receive an honorarium for the sales. These are not being promoted in the presentation. The intent is to share our research and not promote products

We teach for a seminar company offering continuing education for healthcare providers. The session is not designed to promote the attendance of the seminars

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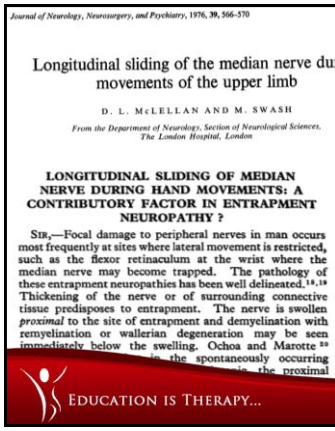
Let's start with a lab session...

BREAKING NEWS

McLellan 1975 & 1976

Accidentally found that nerves…move…

McLellan DL, Swash M. Longitudinal sliding of the median nerve during movements of the upper limb. *J Neurol Neurosurg Psychiatry.* Jun 1976;39(6):566-570.



Journal of Neurology, Neurosurgery, and Psychiatry, 1976, 39, 566-570

Longitudinal sliding of the median nerve during movements of the upper limb

D. L. McLELLAN AND M. SWASH

From the Department of Neurology, Section of Neurological Sciences, The London Hospital, London

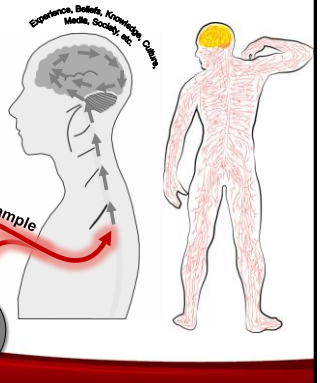
LONGITUDINAL SLIDING OF MEDIAN NERVE DURING HAND MOVEMENTS: A CONTRIBUTORY FACTOR IN ENTRAPMENT NEUROPATHY ?

SIR,—Focal damage to peripheral nerves in man occurs most frequently at sites where lateral movement is restricted, such as the flexor retinaculum at the wrist where the median nerve may become trapped. The pathology of these entrapment neuropathies has been well delineated.[18,19] Thickening of the nerve or of surrounding connective tissue predisposes to entrapment. The nerve is swollen *proximal* to the site of entrapment and demyelination with remyelination or wallerian degeneration may be seen immediately below the swelling. Ochoa and Marotte [20] in the spontaneously occurring ... the proximal

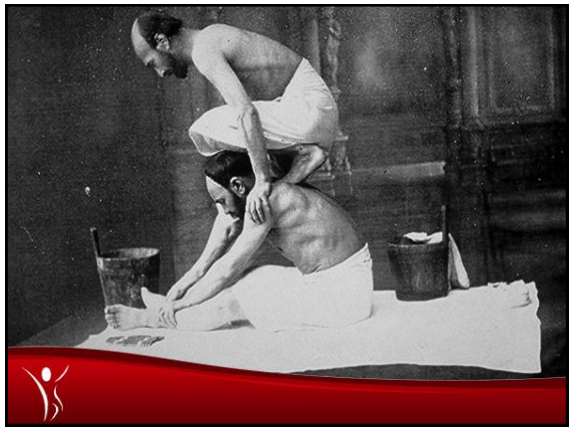
EDUCATION IS THERAPY...

In Partnership With EIM

The Body's Alarm System

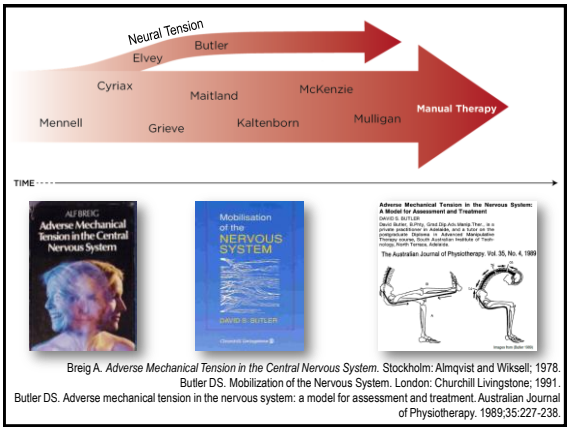


Gifford, L.S., *Pain, the tissues and the nervous system.* Physiotherapy, 1998. 84: p. 27-33.



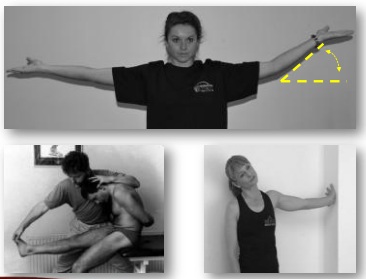
Actually…Imhothep 2800 BC

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

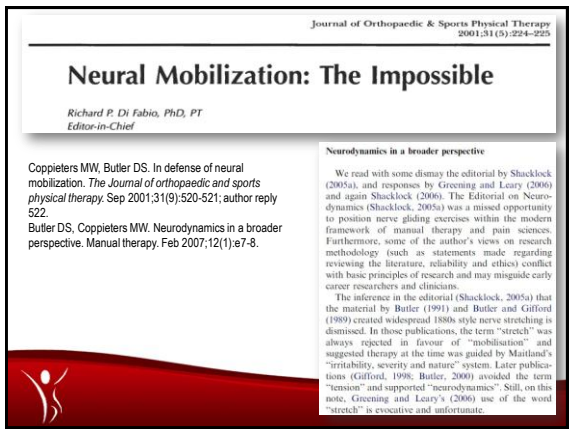


Breig A. *Adverse Mechanical Tension in the Central Nervous System.* Stockholm: Almqvist and Wiksell; 1978.
Butler DS. Mobilization of the Nervous System. London: Churchill Livingstone; 1991.
Butler DS. Adverse mechanical tension in the nervous system: a model for assessment and treatment. Australian Journal of Physiotherapy. 1989;35:227-238.

The Premise behind "Neural Tension"



Butler DS. Adverse mechanical tension in the nervous system: a model for assessment and treatment. Australian Journal of Physiotherapy. 1989;35:227-238.



Journal of Orthopaedic & Sports Physical Therapy
2001;31(5):224–225

Neural Mobilization: The Impossible

Richard P. Di Fabio, PhD, PT
Editor-in-Chief

Neurodynamics in a broader perspective

We read with some dismay the editorial by Shacklock (2005a), and responses by Greening and Leary (2006) and again Shacklock (2006). The Editorial on Neurodynamics (Shacklock, 2005a) was a missed opportunity to position nerve gliding exercises within the modern framework of manual therapy and pain sciences. Furthermore, some of the author's views on research methodology (such as statements made regarding reviewing the literature, reliability and ethics) conflict with basic principles of research and may misguide early career researchers and clinicians.

The inference in the editorial (Shacklock, 2005a) that the material by Butler (1991) and Butler and Gifford (1989) created widespread 1880s style nerve stretching is dismissed. In those publications, the term "stretch" was always rejected in favour of "mobilisation" and suggested therapy at the time was guided by Maitland's "irritability, severity and nature" system. Later publications (Gifford, 1998; Butler, 2000) avoided the term "tension" and supported "neurodynamics". Still, on this note, Greening and Leary's (2006) use of the word "stretch" is evocative and unfortunate.

Coppieters MW, Butler DS. In defense of neural mobilization. *The Journal of orthopaedic and sports physical therapy.* Sep 2001;31(9):520-521; author reply 522.
Butler DS, Coppieters MW. Neurodynamics in a broader perspective. Manual therapy. Feb 2007;12(1):e7-8.

Neurobiologically and Neurophysiologically…

1. Space
2. Movement
3. Blood

Louw A, Mintken P, Puentedura L. Neuophysiologic Effects of Neural Mobilization Maneuvers. In: Fernandez-De_Las_Penas C, Arendt-Nielsen L, Gerwin RD, eds. *Tension-type and Cervicogenic Headache*. Boston: Jones and Bartlett; 2009:231-245.
Nee RJ, Butler D, S. Management of peripheral neuropathic pain: integrating neurobiology, neurodynamics and clinical evidence. Physical Therapy in Sport. 2006;7:36-49.

http://drexel.edu/now/archive/2012/July/Harriet/

1. Space

Louw A, Mintken P, Puentedura L. Neuophysiologic Effects of Neural Mobilization Maneuvers. In: Fernandez-De_Las_Penas C, Arendt-Nielsen L, Gerwin RD, eds. *Tension-type and Cervicogenic Headache*. Boston: Jones and Bartlett; 2009:231-245.
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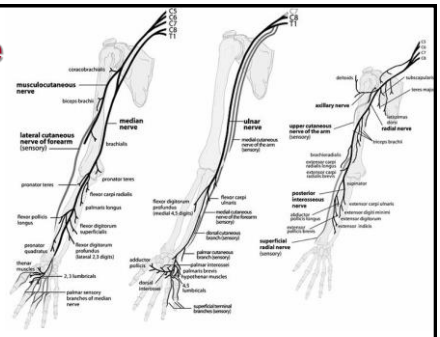
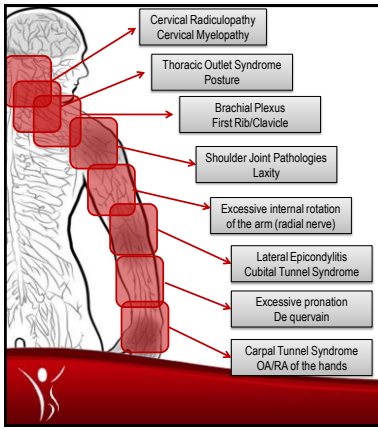


1. Space

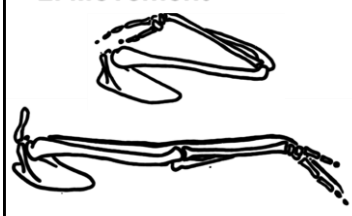
Louw A, Mintken P, Puentedura L. Neuophysiologic Effects of Neural Mobilization Maneuvers. In: Fernandez-De_Las_Penas C, Arendt-Nielsen L, Gerwin RD, eds. *Tension-type and Cervicogenic Headache*. Boston: Jones and Bartlett; 2009:231-245.
Nee RJ, Butler D, S. Management of peripheral neuropathic pain: integrating neurobiology, neurodynamics and clinical evidence. Physical Therapy in Sport. 2006;7:36-49.

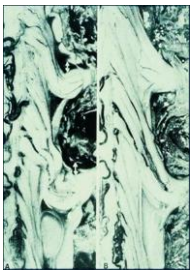


So What?

Lederman RJ. Peripheral Nerve Disorders in Instrumentalists. *Ann Neurol.* 1989;26:640-646.
Storm SA. Assessing the instrumentalist interface: modifications, ergonomics and maintenance of play. Physical medicine and rehabilitation clinics of North America. Nov 2006;17(4):893-903.
Bejjani FJ, Kaye GM, Benham M. Musculoskeletal and neuromuscular conditions of instrumental musicians. Archives of physical medicine and rehabilitation. Apr 1996;77(4):406-413.

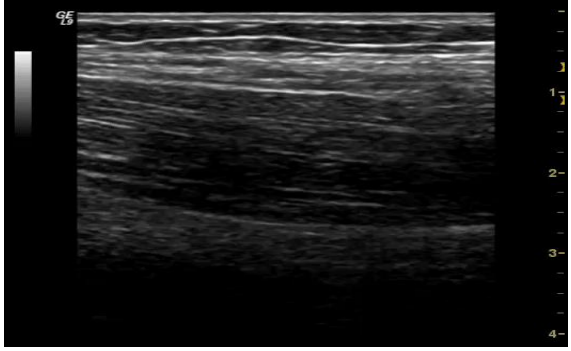
2. Movement



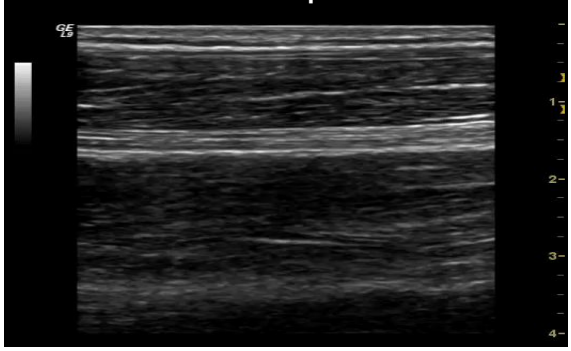


Millesi H, Zoch G, Reihsner R. Mechanical properties of peripheral nerves. Clin Orthop Relat Res. May 1995(314):76-83.
Greening J, Smart S, Leary R, Hall-Craggs M, O'Higgins P, Lynn B. Reduced movement of median nerve in carpal tunnel during wrist flexion in patients with non-specific arm pain. Lancet. Jul 17 1999;354(9174):217-218.
Breig A. Adverse Mechanical Tension in the Central Nervous System. Stockholm: Almqvist and Wiksell; 1978.

Median Nerve proximal to elbow during wrist flexion and extension



Median Nerve at the wrist during Shoulder Depression



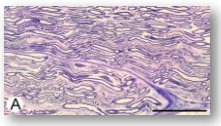
Carpal Tunnel Syndrome…

30% reduction in longitudinal movement of the nerve

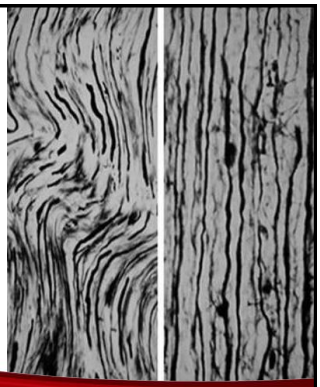
Hough AD, Moore AP, Jones MP. Reduced longitudinal excursion of the median nerve in carpal tunnel syndrome. *Arch Phys Med Rehabil*. May 2007;88(5):569-576.
Coppieters MW, Hough AD, Dilley A. Different nerve-gliding exercises induce different magnitudes of median nerve longitudinal excursion: an in vivo study using dynamic ultrasound imaging. J Orthop Sports Phys Ther. Mar 2009;39(3):164-171.

2. Movement

Nerves do not stretch
Axonal folding and unfolding

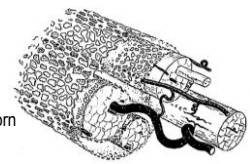


Breig A. *Adverse Mechanical Tension in the Central Nervous System*. Stockholm: Almqvist and Wiksell; 1978.
Li J, Shi R. A device for the electrophysiological recording of peripheral nerves in response to stretch. J Neurosci Methods. Jun 30 2006;154(1-2):102-108.



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



Dommisse GF, ed *The blood supply of the spinal cord and the consequences of failure*. 2nd ed. Edinburgh: Churchill Livingstone; 1994.
Boyling JD, Palastanga N, eds. Grieve's Modern Manual Therapy.
Lundborg G, Rydevik B. Effects of stretching the tibial nerve of the rabbit. A preliminary study of the intraneural circulation and the barrier function of the perineurium. J Bone Joint Surg Br. May 1973;55(2):390-401.
Ogata K, Naito M. Blood flow of peripheral nerve effects of dissection, stretching and compression. J Hand Surg [Br]. Feb 1986;11(1):10-14.

Tunnel Pressure

Positions similar to ulnar nerve biased ULNT cause at least 15% strain and **quadruple** intraneural pressure in this nerve at the elbow

Wright TW, Glowczewskie F, Jr., Cowin D, Wheeler DL. Ulnar nerve excursion and strain at the elbow and wrist associated with upper extremity motion. *J Hand Surg [Am]*. Jul 2001;26(4):655-662.
Pechan J, Julis I. The pressure measurement in the ulnar nerve. A contribution to the pathophysiology of the cubital tunnel syndrome. J Biomech. Jan 1975;8(1):75-79.

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

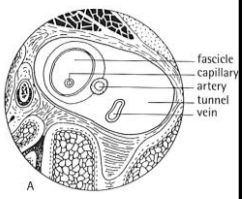


Image from Butler DS. *Mobilisation of the Nervous System*. Melbourne: Churchill Livingstone; 1991

P Arteriole > P Capillary > P Fascicle

Compartment Syndromes

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

- Once the nerve fascicle has nourished, it need to get out of the area
- Blood has to flow into the neighboring vein
- Ultimately the lowest pressure need to be in the tunnel

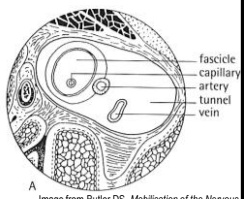
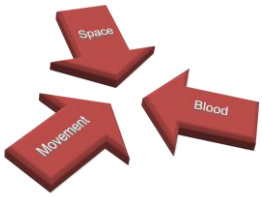


Image from Butler DS. *Mobilisation of the Nervous System*. Melbourne: Churchill Livingstone; 1991

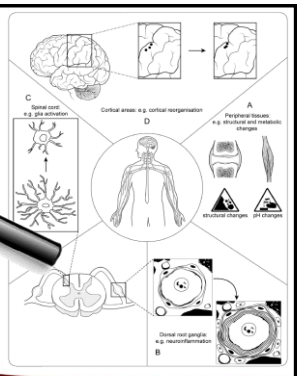
P Arteriole > P Capillary > P Fascicle > P Vein > P Tunnel

Entrapment Neuropathies



Schmid AB, Nee RJ, Coppieters MW. Reappraising entrapment neuropathies--mechanisms, diagnosis and management. *Manual therapy.* Dec 2013;18(6):449-457.
Oskay D, Meric A, Kirdi N, Firat T, Ayhan C, Leblebicioglu G. Neurodynamic mobilization in the conservative treatment of cubital tunnel syndrome: long-term follow-up of 7 cases. J Manipulative Physiol Ther. Feb 2010;33(2):156-163.

There is, however, more complexity...



Schmid AB, Nee RJ, Coppieters MW. Reappraising entrapment neuropathies--mechanisms, diagnosis and management. *Manual therapy.* Dec 2013;18(6):449-457.

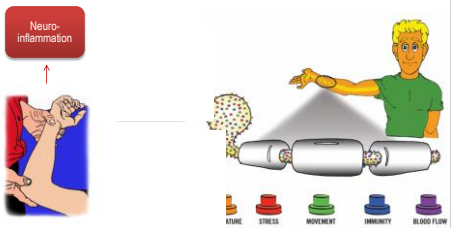
Compartment Syndromes

Repetitive motions…

Neuroinflammation Tendon Swelling Bony Changes	Increased Tunnel Pressure Back up blood in the Vein Back up blood in the Fascicle	Ischemia Edema Scarring Axonal Compression and Degeneration

Lederman RJ. Peripheral Nerve Disorders in Instrumentalists. Ann Neurol. 1989;26:640-646.
Dilley A, Odeyinde S, Greening J, Lynn B. Longitudinal sliding of the median nerve in patients with non-specific arm pain. Man Ther. Oct 1 2007.
van Tulder M, Malmivaara A, Koes B. Repetitive strain injury. Lancet. May 26 2007;369(9575):1815-1822.
Schmid AB, Nee RJ, Coppieters MW. Reappraising entrapment neuropathies--mechanisms, diagnosis and management. *Manual therapy.* Dec 2013;18(6):449-457.

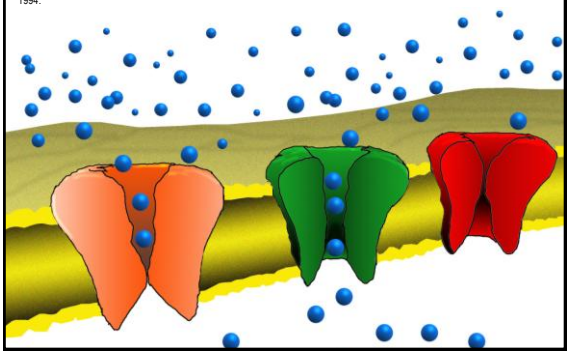
Immune Changes and Nerve Sensitivity



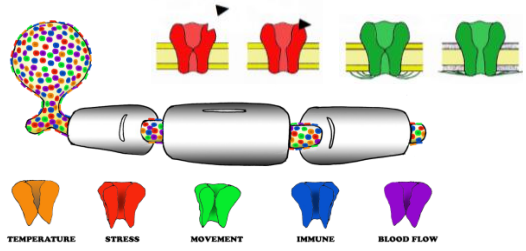
Thacker MA, Clark AK, Marchand F, McMahon SB. Pathophysiology of peripheral neuropathic pain: immune cells and molecules. *Anesthesia and analgesia.* Sep 2007;105(3):838-847.

Devor M. Sodium channels and mechanisms of neuropathic pain. *J Pain*. Jan 2006;7(1 Suppl 1):S3-S12.
Devor M. The pathophysiology of damaged peripheral nerves. In: Wall PD, Melzack R, eds. Textbook of Pain. 3rd ed. Edinburgh: Churchill Livingstone; 1994.

Ion Channels

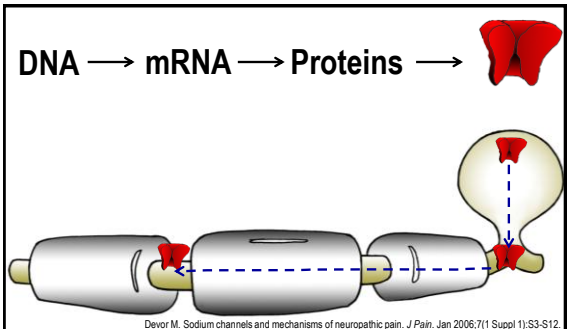


Various kinds of channels…



Devor M. Sodium channels and mechanisms of neuropathic pain. *J Pain*. Jan 2006;7(1 Suppl 1):S3-S12.
Devor M. The pathophysiology of damaged peripheral nerves. In: Wall PD, Melzack R, eds. Textbook of Pain. 3rd ed. Edinburgh: Churchill Livingstone; 1994.

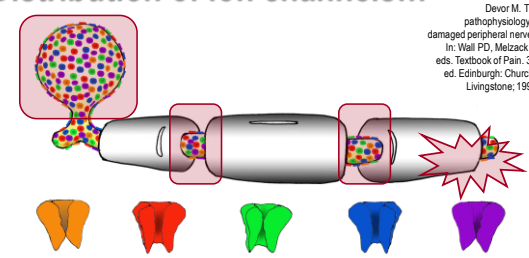
DNA ⟶ mRNA ⟶ Proteins ⟶



Devor M. Sodium channels and mechanisms of neuropathic pain. *J Pain*. Jan 2006;7(1 Suppl 1):S3-S12.
Devor M. The pathophysiology of damaged peripheral nerves. In: Wall PD, Melzack R, eds. Textbook of Pain. 3rd ed. Edinburgh: Churchill Livingstone; 1994.

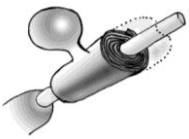
Distribution of ion channels…

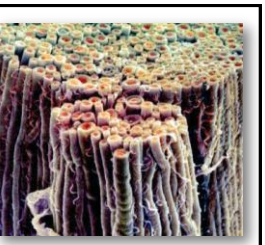
Devor M. Sodium channels and mechanisms of neuropathic pain. *J Pain*. Jan 2006;7(1 Suppl 1):S3-S12.
Devor M. The pathophysiology of damaged peripheral nerves. In: Wall PD, Melzack R, eds. Textbook of Pain. 3rd ed. Edinburgh: Churchill Livingstone; 1994.



Removing myelin

Devor M. The pathophysiology of damaged peripheral nerves. In: Wall PD, Melzack R, eds. Textbook of Pain. 3rd ed. Edinburgh: Churchill Livingstone; 1994.





- Mechanical
- Immune
- Chemical

Development of an Abnormal Impulse Generating Site

Devor M. The pathophysiology of damaged peripheral nerves. In: Wall PD, Melzack R, eds. Textbook of Pain. 3rd ed. Edinburgh: Churchill Livingstone; 1994.

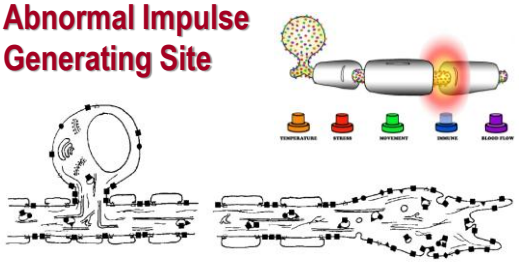
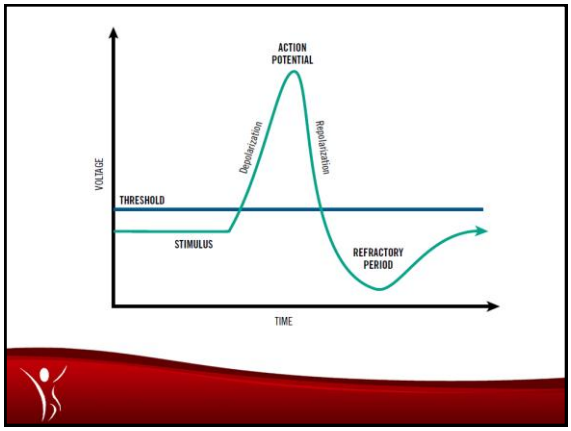


Fig. I.4 Schematic representation of a single sensory neurone highlighting ion channels and receptor proteins in the cell wall. Adapted from: Devor et al 1994
▽ K+ channel ● Ca++ channel
■ Na+ channel ▲ Adrenoreceptor = ligand gated ion channel sensitive to adrenaline.
◆ Mechaznoreceptor or Stretch activated receptor



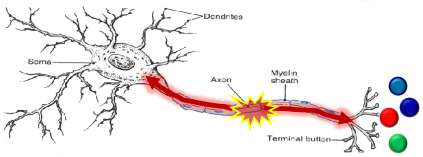
Vibration Sensitization

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

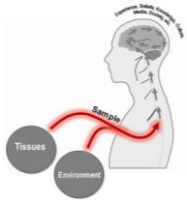
Greening J, Lynn B, Leary R. Sensory and autonomic function in the hands of patients with non-specific arm pain (NSAP) and asymptomatic office workers. *Pain.* Jul 2003;104(1-2):275-281.
Tyros I, Soundy A, Heneghan NR. Vibration sensibility of the median nerve in a population with chronic whiplash associated disorder: Intra- and inter-rater reliability study. Manual therapy. Sep 2016;25:81-86.

Neurogenic Inflammation

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



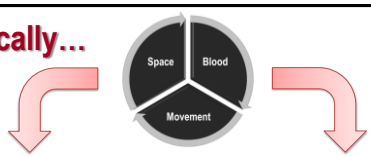
Identifying Neuropathic Pain in the Clinic



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

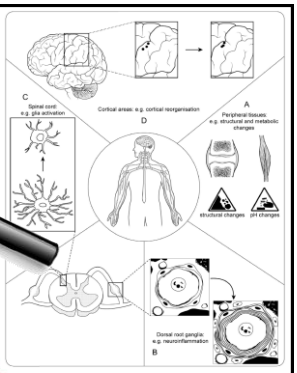
Gifford, L.S., *Pain, the tissues and the nervous system.* Physiotherapy, 1998. 84: p. 27-33.
Smart KM, Blake C, Staines A, Thacker M, Doody C. Mechanisms-based classifications of musculoskeletal pain: Part 2 of 3: Symptoms and signs of peripheral neuropathic pain in patients with low back (+/-leg) pain. Manual therapy. Aug 2012;17(4):345-351.
Smart KM, Blake C, Staines A, Doody C. Clinical indicators of 'nociceptive', 'peripheral neuropathic' and 'central' mechanisms of musculoskeletal pain. A Delphi survey of expert clinicians. Man Ther. Feb 2009;15(1):80-87.

Theoretically…



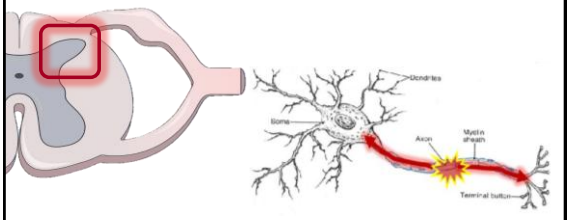
Neurodynamic Tests	Neurodynamic Treatment
• Can the nervous system move? • Does it have enough blood? • Is the container healthy? • Are there any familiar and/or unfamiliar symptoms? • How sensitive is the nervous system to move? • Active and passive tests • Upper limbs • Lower limbs • Trunk	• Explaining nerves to patients • Opening the containers • Unloading unwanted stress on the nervous system • Facilitating and normalizing nerve movements • Active, passive and home exercise • Calming the nervous system • Ensuring adequate blood flow for nerve and axoplasm

There is, however, more complexity…



Schmid AB, Nee RJ, Coppieters MW. Reappraising entrapment neuropathies--mechanisms, diagnosis and management. *Manual therapy.* Dec 2013;18(6):449-457.

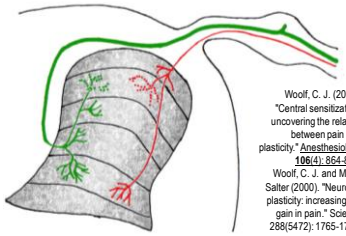
Barrage into the CNS…



Woolf CJ. Central sensitization: uncovering the relation between pain and plasticity. Anesthesiology. Apr 2007;106(4):864-867.
Vardeh D, Mannion RJ, Woolf CJ. Toward a Mechanism-Based Approach to Pain Diagnosis. *The journal of pain : official journal of the American Pain Society.* Sep 2016;17(9 Suppl):T50-69.

Remapping of the Spinal Cord…

C-fibers pull back and A-beta fibers grow in…



Woolf, C. J. (2007). "Central sensitization: uncovering the relation between pain and plasticity." Anesthesiology **106**(4): 864-867.
Woolf, C. J. and M. W. Salter (2000). "Neuronal plasticity: increasing the gain in pain." Science 288(5472): 1765-1769.

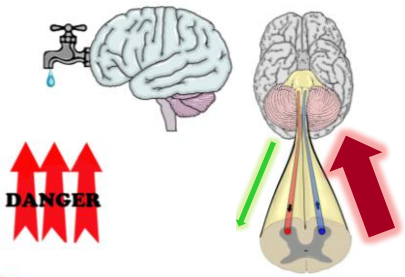
End-Result

Process	Consequence
• Death of the inhibitory neurons	• Decreased gating from the periphery
• C-fibers pull back; A-fibers grow in	• Allodynia
• Upregulation of second-order neurons	• Increased firing towards the brain
• Inappropriate synapsing – other levels	• Spreading pain
• Inappropriate synapsing – other fibers	• Sympathetic, immune, motor contributions
• Inappropriate synapsing – other side	• Bilateral "mirror" pains
• Decreased endogenous mechanisms	• Allodynia and Hyperalgesia

Woolf CJ. Central sensitization: uncovering the relation between pain and plasticity. Anesthesiology. Apr 2007;106(4):864-867.
Vardeh D, Mannion RJ, Woolf CJ. Toward a Mechanism-Based Approach to Pain Diagnosis. *The journal of pain : official journal of the American Pain Society.* Sep 2016;17(9 Suppl):T50-69.

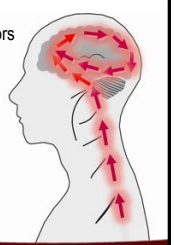
Central Sensitization

Woolf CJ. Central sensitization: uncovering the relation between pain and plasticity. Anesthesiology. Apr 2007;106(4):864-867.
Woolf CJ, Salter MW. Neuronal plasticity: increasing the gain in pain. Science. Jun 9 2000;288(5472):1765-1769.
Louw A, Puentedura E. *Therapeutic Neuroscience Education: Teaching patients about pain.* Minneapolis, MN: OPTP; 2013.



Identifying Central Sensitization in the Clinic

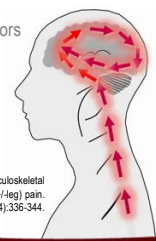
- Symptom and sign cluster (486 times) for CS
  - Disproportionate pain
  - Disproportionate aggravating and easing factors
  - Diffuse palpation tenderness
  - Psychosocial issues



Smart KM, Blake C, Staines A, Thacker M, Doody C. Mechanisms-based classifications of musculoskeletal pain: Part 1 of 3: Symptoms and signs of central sensitisation in patients with low back (+/-leg) pain. *Manual therapy.* Aug 2012;17(4):336-344.

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



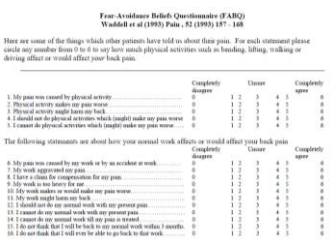
Smart KM, Blake C, Staines A, Thacker M, Doody C. Mechanisms-based classifications of musculoskeletal pain: Part 1 of 3: Symptoms and signs of central sensitisation in patients with low back (+/-leg) pain. *Manual therapy.* Aug 2012;17(4):336-344.

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

Fritz, J. M. and S. Z. George (2002). "Identifying psychosocial variables in patients with acute work-related low back pain: the importance of fear-avoidance beliefs." Phys Ther **82**(10): 973-983.
Poiraudeau, S., et al. (2006). "Fear-avoidance beliefs about back pain in patients with subacute low back pain." Pain 124(3): 305-311.



Fear-Avoidance Beliefs Questionnaire (FABQ)
Waddell et al (1993) Pain , 52 (1993) 157 - 168

Here are some of the things which other patients have told us about their pain. For each statement please circle any number from 0 to 6 to say how much physical activities such as bending, lifting, walking or driving affect or would affect your back pain.

	Completely disagree			Unsure		Completely agree
1. My pain was caused by physical activity	0	1	2	3	4	5	6
2. Physical activity makes my pain worse	0	1	2	3	4	5	6
3. Physical activity might harm my back	0	1	2	3	4	5	6
4. I should not do physical activities which (might) make my pain worse	0	1	2	3	4	5	6
5. I cannot do physical activities which (might) make my pain worse	0	1	2	3	4	5	6

The following statements are about how your normal work affects or would affect your back pain

	Completely disagree			Unsure		Completely agree
6. My pain was caused by my work or by an accident at work	0	1	2	3	4	5	6
7. My work aggravated my pain	0	1	2	3	4	5	6
8. I have a claim for compensation for my pain	0	1	2	3	4	5	6
9. My work is too heavy for me	0	1	2	3	4	5	6
10. My work makes or would make my pain worse	0	1	2	3	4	5	6
11. My work might harm my back	0	1	2	3	4	5	6
12. I should not do my normal work with my present pain	0	1	2	3	4	5	6
13. I cannot do my normal work with my present pain	0	1	2	3	4	5	6
14. I cannot do my normal work till my pain is treated	0	1	2	3	4	5	6
15. I do not think that I will be back to my normal work within 3 months	0	1	2	3	4	5	6
16. I do not think that I will even be able to go back to that work	0	1	2	3	4	5	6

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)

Sullivan, M. J. L., et al. (1995). "The pain catastrophizing scale: Development and validation." Psychological assessment **7**: 524-532.

PCS

Name:_____

Here are statements describing different thoughts and feelings that may be associated with pain. Using the scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

	Not at all	To a slight degree	To a moderate degree	To a great degree	All the time
I worry all the time about whether the pain will end	0	1	2	3	4
I feel I can't go on	0	1	2	3	4
It's terrible and I think it's never going to get any better	0	1	2	3	4
It's awful and I feel that it overwhelms me	0	1	2	3	4
I feel I can't stand it anymore	0	1	2	3	4
I become afraid that the pain will get worse	0	1	2	3	4
I keep thinking of other painful events	0	1	2	3	4
I anxiously want the pain to go away	0	1	2	3	4
I can't seem to keep it out of my mind	0	1	2	3	4
I keep thinking about how much it hurts	0	1	2	3	4
I keep thinking about how badly I want the pain to stop	0	1	2	3	4
There's nothing I can do to reduce the intensity of the pain	0	1	2	3	4
I wonder whether something serious may happen	0	1	2	3	4

Central Sensitization Inventory

Central Sensitivity Inventory

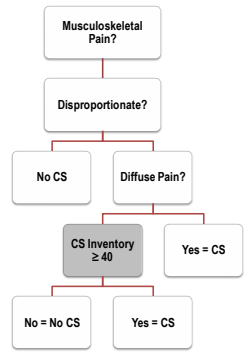
Scale range is 0-100
Answers and scoring method

- Never = 0
- Rarely = 1
- Sometimes = 2
- Often = 3
- Always = 4

1. I feel refreshed when I wake in the morning
2. My muscles feel stiff and achy
3. I have anxiety attacks
4. I grind or clench my teeth
5. I have problems with diarrhea and or constipation
6. I need help in performing my ADL's
7. I am sensitive to bright lights
8. I get tired very easily with physical activity
9. I feel pain all over my body
10. I have headaches
11. I feel discomfort in my bladder
12. I do not sleep well
13. I have difficulty concentrating
14. I have skin problems (dry, itchy, rashes)
15. Stress makes my physical symptoms worse
16. I feel sad or depressed
17. I have low energy
18. I have tension in my muscles
19. I have pain in my jaw
20. Certain smells make me dizzy/nauseated
21. I have to urinate frequently
22. My legs feel uncomfortable and restless at night
23. I have difficulty remembering things
24. I suffered trauma as a child
25. I have pain in my pelvic area

Nijs J, Van Houdenhove B, Oostendorp RA. Recognition of central sensitization in patients with musculoskeletal pain: Application of pain neurophysiology in manual therapy practice. Man Ther. Apr 2010;15(2):135-141.
Mayer TG, Neblett R, Cohen H, et al. The development and psychometric validation of the central sensitization inventory. Pain Pract. Apr 2012;12(4):276-285.

Nijs, J., et al. (2010). "Recognition of central sensitization in patients with musculoskeletal pain: Application of pain neurophysiology in manual therapy practice." Man Ther **15**(2): 135-141.



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

Nijs J, Van Houdenhove B, Oostendorp RA. Recognition of central sensitization in patients with musculoskeletal pain: Application of pain neurophysiology in manual therapy practice. Manual therapy. Apr 2010;15(2):135-141.

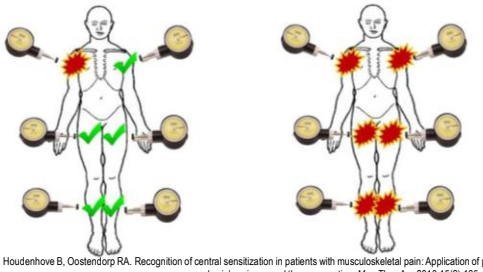
Nerve Palpation: With/without pressure algometry…

Sensitive nerves

Walsh, J. and T. Hall (2009). "Reliability, validity and diagnostic accuracy of palpation of the sciatic, tibial and common peroneal nerves in the examination of low back related leg pain." Man Ther **14**(6): 623-629.

Peripheral Sensitization

Central Sensitization



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Nerve Palpation: With/without pressure algometry…distal

Lower extremity: "away from the hot spot"

Walsh, J. and T. Hall (2009). "Reliability, validity and diagnostic accuracy of palpation of the sciatic, tibial and common peroneal nerves in the examination of low back related leg pain." Man Ther **14**(6): 623-629.

Lower Extremity Nerve Palption Quick Screen

Vibration Sensitization

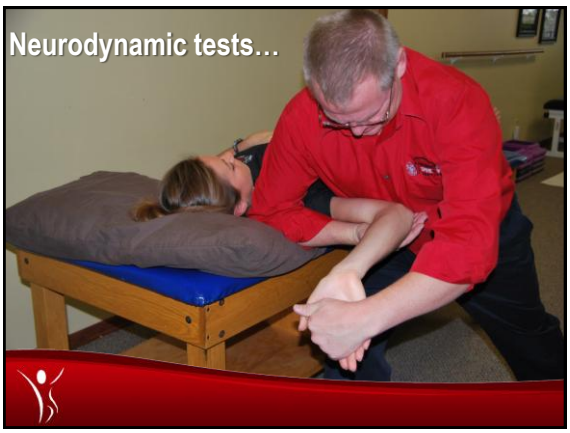
Dysfunction of A-beta fibers and Pacini corpuscles have shown increased sensitivity in neuropathic pain

Greening J, Lynn B, Leary R. Sensory and autonomic function in the hands of patients with non-specific arm pain (NSAP) and asymptomatic office workers. *Pain.* Jul 2003;104(1-2):275-281.
Tyros I, Soundy A, Heneghan NR. Vibration sensibility of the median nerve in a population with chronic whiplash associated disorder: Intra- and inter-rater reliability study. Manual therapy. Sep 2016;25:81-86.

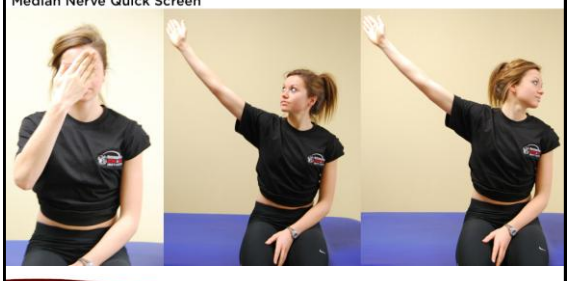
Heat and Cold…

Nijs J, Van Houdenhove B, Oostendorp RA. Recognition of central sensitization in patients with musculoskeletal pain: Application of pain neurophysiology in manual therapy practice. Manual therapy. Apr 2010;15(2):135-141.

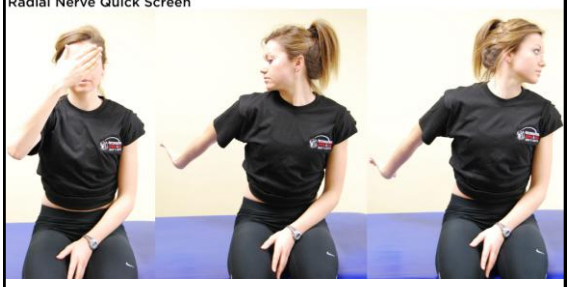
Neurodynamic tests…



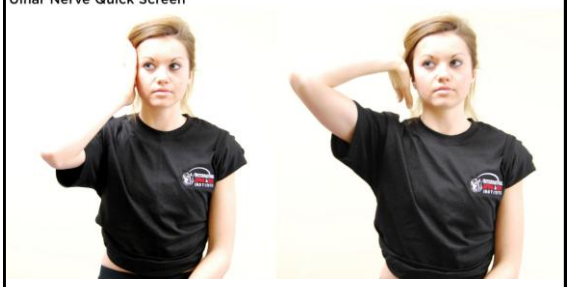
Median Nerve Quick Screen



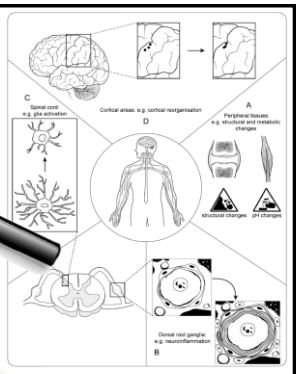
Radial Nerve Quick Screen



Ulnar Nerve Quick Screen

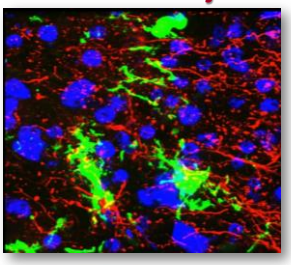


There is, however, more complexity…



Schmid AB, Nee RJ, Coppieters MW. Reappraising entrapment neuropathies--mechanisms, diagnosis and management. *Manual therapy.* Dec 2013;18(6):449-457.

But the CNS contains a lot more than just neurons

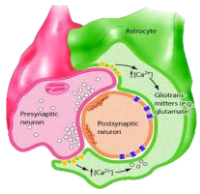


Microglia…

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

physiologyonline.physiology.org



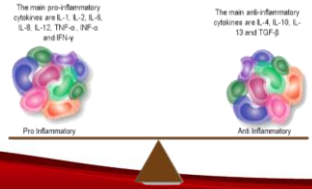
Watkins LR, Hutchinson MR, Milligan ED, Maier SF. "Listening" and "talking" to neurons: implications of immune activation for pain control and increasing the efficacy of opioids. *Brain Res Rev.* Nov 2007;56(1):148-169.

Watkins LR, Milligan ED, Maier SF. Immune and glial involvement in physiological and pathological exaggerated pain states. In: Dostrovsky JO, Carr DB, Kolzenburg M, eds. Progress in Pain Research and Management. Vol 24. Seattle: IASP Press; 2003:369-386.

Ji RR, Berta T, Nedergaard M. Glia and pain: is chronic pain a gliopathy? Pain. Dec 2013;154 Suppl 1:S10-28.

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**



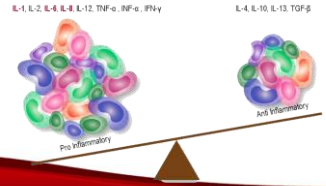
Menzies, V. and D. E. Lyon (2010). "Integrated review of the association of cytokines with fibromyalgia and fibromyalgia core symptoms." Biological research for nursing **11**(4): 387-394.

Sturgill, J., E. McGee, et al. (2014). "Unique cytokine signature in the plasma of patients with fibromyalgia." Journal of immunology research **2014**: 938576.

Wallace, D. J. (2006). "Is there a role for cytokine based therapies in fibromyalgia." Current pharmaceutical design **12**(1): 17-22.

Cytokine balance…

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



Di Franco, M., C. Iannuccelli, et al. (2010). "Neuroendocrine immunology of fibromyalgia." Annals of the New York Academy of Sciences **1193**: 84-90.
Izquierdo-Alvarez, S., J. P. Bocos-Terraz, et al. (2008). "Is there an association between fibromyalgia and below-normal levels of urinary cortisol?" BMC research notes **1**: 134.
Rodriguez-Pinto, I., N. Agmon-Levin, et al. (2014). "Fibromyalgia and cytokines." Immunology letters **161**(2): 200-203.

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.

Schmid AB, Coppieters MW, Ruitenberg MJ, McLachlan EM. Local and remote immune-mediated inflammation after mild peripheral nerve compression in rats. *Journal of neuropathology and experimental neurology.* Jul 2013;72(7):662-680.

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

Three months later:

- Neural edema
- Demyelination and Wallerian degeneration
- Small fiber loss in the DRG (unmyelinated fibers)
- Axonal damage

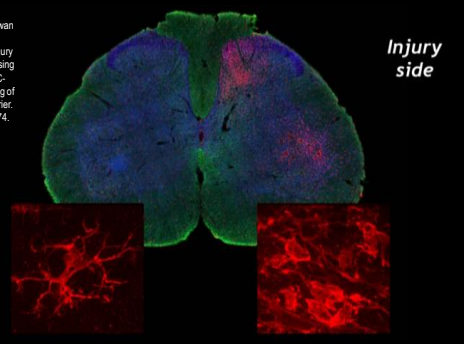
Schmid AB, Coppieters MW, Ruitenberg MJ, McLachlan EM. Local and remote immune-mediated inflammation after mild peripheral nerve compression in rats. *Journal of neuropathology and experimental neurology.* Jul 2013;72(7):662-680.

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

Beggs S, Liu XJ, Kwan C, Salter MW. Peripheral nerve injury and TRPV1-expressing primary afferent C-fibers cause opening of the blood-brain barrier. *Mol Pain.* 2010;6:74.

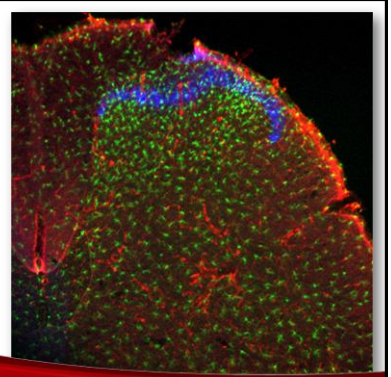
Response of microglia in the spinal cord after peripheral nerve injury

Beggs S, Liu XJ, Kwan C, Salter MW. Peripheral nerve injury and TRPV1-expressing primary afferent C-fibers cause opening of the blood-brain barrier. *Mol Pain.* 2010;6:74.



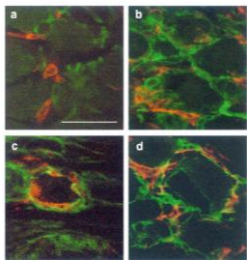
A cascade of immune changes start to occur…

Beggs S, Liu XJ, Kwan C, Salter MW. Peripheral nerve injury and TRPV1-expressing primary afferent C-fibers cause opening of the blood-brain barrier. *Mol Pain.* 2010;6:74.



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



Hu P, McLachlan EM. Macrophage and lymphocyte invasion of dorsal root ganglia after peripheral nerve lesions in the rat. *Neuroscience*. 2002;112(1):23-38.

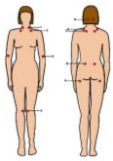
Neuropathic Pain…? Widespread Pain

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

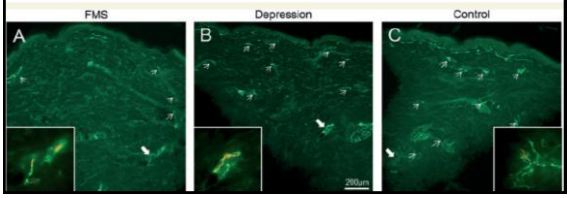
Anderberg L, Annertz M, Brandt L, Saveland H. Selective diagnostic cervical nerve root block--correlation with clinical symptoms and MRI-pathology. Acta neurochirurgica. Jun 2004;146(6):559-565; discussion 565.
Murphy DR, Hurwitz EL, Gerrard JK, Clary R. Pain patterns and descriptions in patients with radicular pain: does the pain necessarily follow a specific dermatome? Chiropractic & osteopathy. Sep 21 2009;17:9.
Nora DB, Becker J, Ehlers JA, Gomes I. Clinical features of 1039 patients with neurophysiological diagnosis of carpal tunnel syndrome. *Clinical neurology and neurosurgery*. Dec 2004;107(1):64-69.

Patients with FM display small fiber nerve pathology

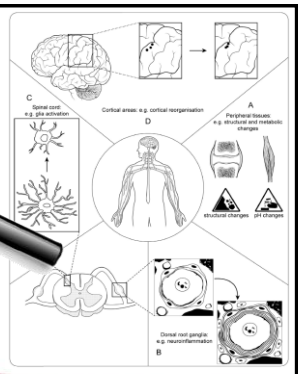


- Small fiber loss
- Demyelination
- Edema

Uceyler N, Zeller D, Kahn AK, et al. Small fibre pathology in patients with fibromyalgia syndrome. *Brain : a journal of neurology*. Jun 2013;136(Pt6):1857-1867.

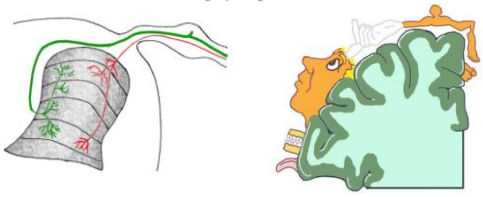


There is, however, more complexity…



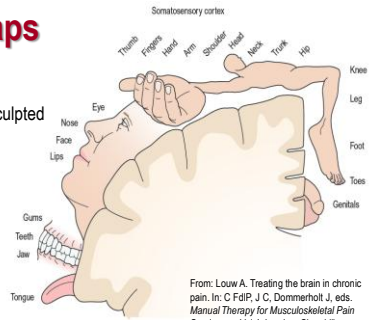
Schmid AB, Nee RJ, Coppieters MW. Reappraising entrapment neuropathies--mechanisms, diagnosis and management. *Manual therapy*. Dec 2013;18(6):449-457.

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

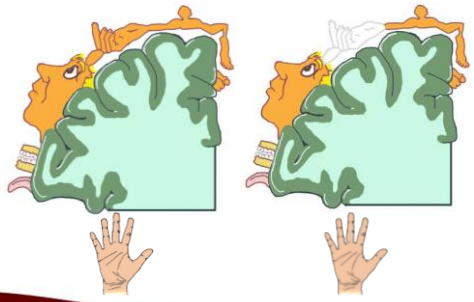
- Biologically coded
- Environmentally sculpted
- Changes occur in minutes…



From: Louw A. Treating the brain in chronic pain. In: C FdlP, J C, Dommerholt J, eds. *Manual Therapy for Musculoskeletal Pain Syndromes*. Vol 1. London: Churchill Livingston; 2015

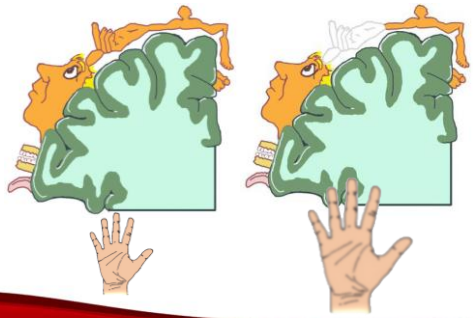
Maihöfner C, Handwerker HO, Neundörfer B, Birklein F. Patterns of cortical reorganization in complex regional pain syndrome. *Neurology.* December 23, 2003 2003;61(12):1707-1715. Flor H. The functional organization of the brain in chronic pain. Prog Brain Res. 2000;129:313-322.

Movement and use | Immobilization and limited use



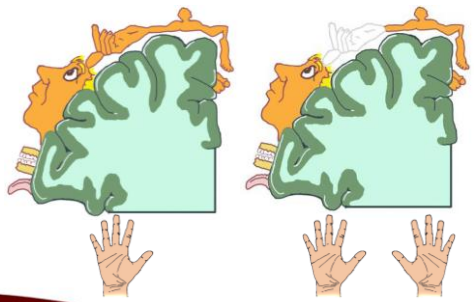
Maihöfner C, Handwerker HO, Neundörfer B, Birklein F. Patterns of cortical reorganization in complex regional pain syndrome. *Neurology.* December 23, 2003 2003;61(12):1707-1715. Flor H. The functional organization of the brain in chronic pain. Prog Brain Res. 2000;129:313-322.

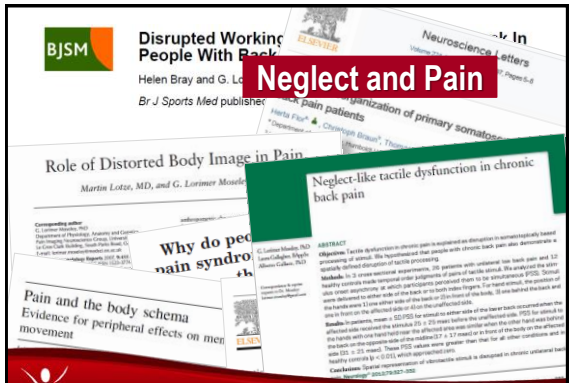
Movement and use | Immobilization and limited use



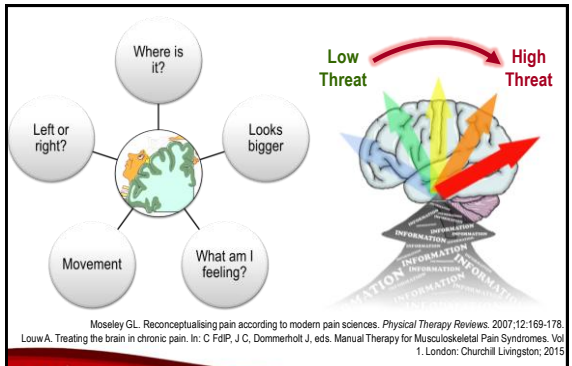
Maihöfner C, Handwerker HO, Neundörfer B, Birklein F. Patterns of cortical reorganization in complex regional pain syndrome. *Neurology.* December 23, 2003 2003;61(12):1707-1715. Flor H. The functional organization of the brain in chronic pain. Prog Brain Res. 2000;129:313-322.

Movement and use | Immobilization and limited use



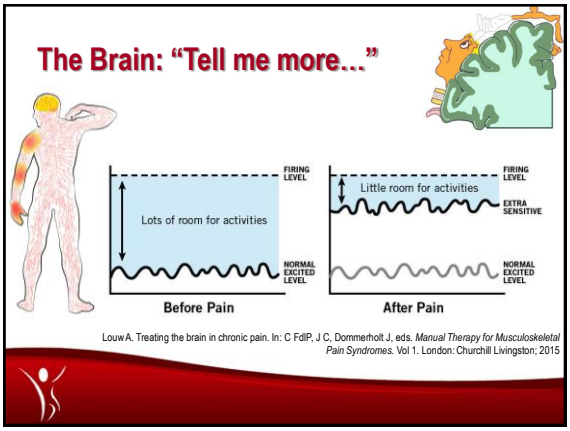


Moseley GL, Olthof N, Venema A, et al. Psychologically induced cooling of a specific body part caused by the illusory ownership of an artificial counterpart. *Proc Natl Acad Sci U S A.* Sep 2 2008;105(35):13169-13173. Stavrinou ML, Della Penna S, Pizzella V, et al. Temporal dynamics of plastic changes in human primary somatosensory cortex after finger webbing. Cereb Cortex. Sep 2007;17(9):2134-2142.



Moseley GL. Reconceptualising pain according to modern pain sciences. *Physical Therapy Reviews.* 2007;12:169-178.
Louw A. Treating the brain in chronic pain. In: C FdlP, J C, Dommerholt J, eds. Manual Therapy for Musculoskeletal Pain Syndromes. Vol 1. London: Churchill Livingston; 2015

The Brain: "Tell me more…"

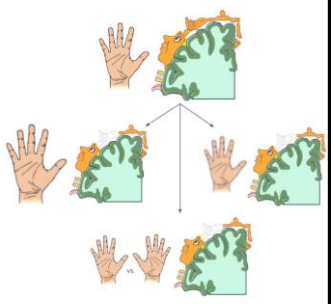


Louw A. Treating the brain in chronic pain. In: C FdlP, J C, Dommerholt J, eds. *Manual Therapy for Musculoskeletal Pain Syndromes.* Vol 1. London: Churchill Livingston; 2015

Neuroplasticity Testing

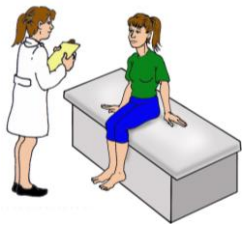
Subjective — Objective

- Smudging
- Laterality
- Shape

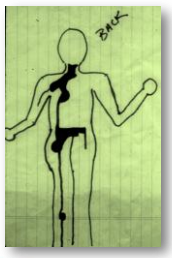


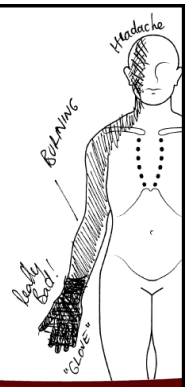
Neuroplasticity Testing: Subjective

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

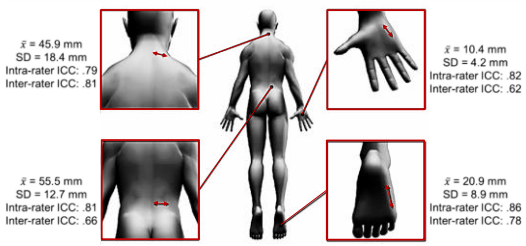


Smudging: Quick Screen





2 point discrimination norms



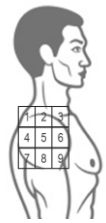
Catley, M. J., et al. (2013). "Assessing tactile acuity in rheumatology and musculoskeletal medicine--how reliable are two-point discrimination tests at the neck, hand, back and foot?" Rheumatology **52**(8): 1454-1461.

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

Upper lateral arm: 42.4	Mid medial forearm: 31.5	1st D. interosseous: 21.0
Finger pad: 2.5	Inf angle scapula: 52.2	Mid posterior thigh: 42.2
Distal lateral leg: 41.6	1-2 Met interspace: 23.9	Tip great toe: 6.6

Localization testing…

- Where was I touched?
- Stimulus from clinician then identification from patient
- Impaired tactile acuity relates to impaired motor control



Louw, A., et al. (2015). "Moving without moving: immediate management following lumbar spine surgery using a graded motor imagery approach: a case report." Physiotherapy Theory and Practice 31(7): 509-517.
Louw, A., et al. (2015). "Immediate effects of sensory discrimination for chronic low back pain: a case series." New Zealand Journal of Physiotherapy 43(2): 58-63.
Luomajoki, H. and G. L. Moseley (2011). "Tactile acuity and lumbopelvic motor control in patients with back pain and healthy controls." British journal of sports medicine 45(5): 437-440.

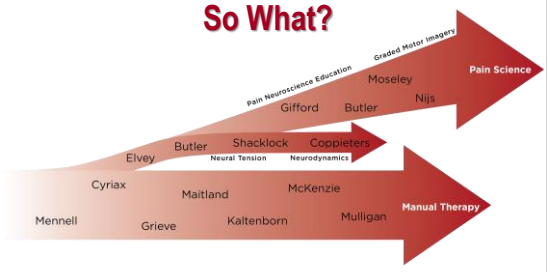
What's normal?

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

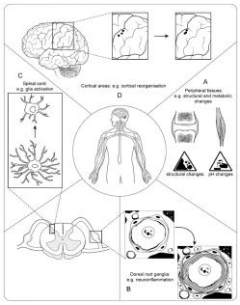
Moseley, G. L. (2004). "Why do people with complex regional pain syndrome take longer to recognize their affected hand?" Neurology **62**(12): 2182-2186.

Moseley, G. L., et al. (2005). "Experimental hand pain delays recognition of the contralateral hand--evidence that acute and chronic pain have opposite effects on information processing?" Brain research. Cognitive brain research 25(1): 188-194.

So What?



An Unhealthy Nervous System result in Immune Changes



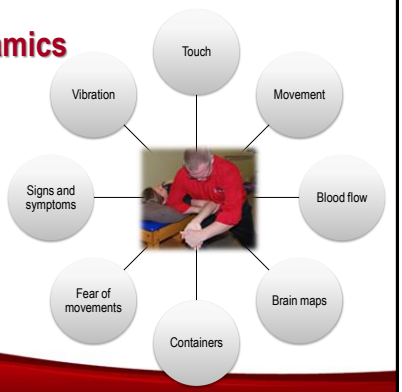
Schmid AB, Nee RJ, Coppieters MW. Reappraising entrapment neuropathies--mechanisms, diagnosis and management. *Manual therapy.* Dec 2013;18(6):449-457.

Neurodynamics

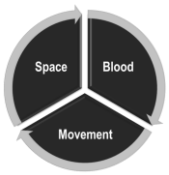
Butler DS, Coppieters MW. Neurodynamics in a broader perspective. *Man Ther.* Feb 2007;12(1):e7-8.

Coppieters MW, Kurz K, Mortensen TE, et al. The impact of neurodynamic testing on the perception of experimentally induced muscle pain. Man Ther. Feb 2005;10(1):52-60.

Shacklock M. Improving application of neurodynamic (neural tension) testing and treatments: a message to researchers and clinicians. Manual therapy. Aug 2005;10(3):175-179.



Neurodynamics: Physical



Neurodynamics: Physical

- Neural mobilization helpful for cubital tunnel syndrome. (Oskay, Meric et al. ; Svernlov, Larsson et al. 2009)
- Development of a clinical prediction rule to identify initial responders to mobilization with movement and exercise for lateral epicondylalgia: Age (<49 years), pain free grip strength on the affected and unaffected side. (Vicenzino, Smith et al. 2009)
- A single cervical spine manipulation leads to immediate hypoalgesic and motor effects in subjects with lateral epicondylalgia.(Fernandez-Carnero, Fernandez-de-las-Penas et al. 2008)
- Neural mobilization helpful in a patient with lateral elbow pain.(Ekstrom and Holden 2002)
- Carpal tunnel syndrome (CTS) helped with neural mobilization (Nee, Vicenzino et al. 2012)
- Neurodynamics helpful in CTS (Tal-Akabi and Rushton 2000).
- Helpful in cervical radiculopathy (Coppieters, Stappaerts et al. 2003; Cleland, Whitman et al. 2005; Costello 2008; Young, Michener et al. 2009); Cleland, Whitman et al, 2005; Costello, 2008; Young, Michener et al, 2009)
- Lateral epicondylitis (Ekstrom and Holden 2002)
- Cubital tunnel syndrome (Coppieters, Batholomeeusen et al, 2004)
- Cervical lateral glide mobilizations to effect changes in neck and/or arm symptoms (Vicenzino, Collins et al. 1996; Cowell and Phillips 2002; Coppieters, Stappaerts et al. 2003; Cleland, Whitman et al. 2005) as this intervention has been shown to produce immediate reductions in mechanosensitivity and pain in patients with lateral epicondylalgia (Vicenzino, Collins et al, 1996) and cervicobrachial pain (Elvey, 1986; Cowell and Phillips, 2002; Coppieters, Stappaerts et al, 2003).
- CTS: Neural mobilization/tendon gliding reduced need for CTS surgery in 29.8% of patients (Rozmaryn, Dovelle et al. 1998)

Neurodynamics: Physical

Basson A, Olivier B, Ellis R, Coppieters M, Stewart A, Mudzi W. The Effectiveness of Neural Mobilization for Neuromusculoskeletal Conditions: A Systematic Review and Meta-analysis. *J Orthop Sports Phys Ther.* Sep 2017;47(9):593-615.

Systematic review

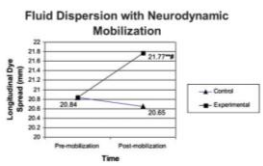
- Results:
  - For chronic neck-arm pain, pain improved following NM. For most of the clinical outcomes in individuals with carpal tunnel syndrome, NM was not effective (P>.11) but showed some positive neurophysiological effects (e.g., reduced intraneural edema).
  - Due to a scarcity of studies or conflicting 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

Brown CL, Gilbert KK, Brismee JM, Sizer PS, Roger James C, Smith MP. The effects of neurodynamic mobilization on fluid dispersion within the tibial nerve at the ankle: an unembalmed cadaveric study. *The Journal of manual & manipulative therapy.* Feb 2011;19(1):26-34.

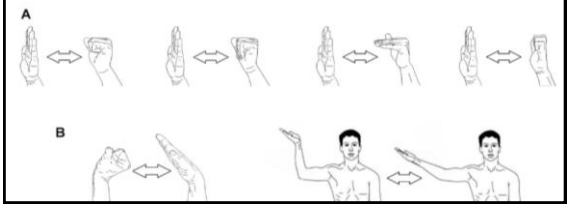
Gilbert KK, Smith MP, Sobczak S, James CR, Sizer PS, Brismee JM. Effects of lower limb neurodynamic mobilization on intraneural fluid dispersion of the fourth lumbar nerve root: an unembalmed cadaveric investigation. The Journal of manual & manipulative therapy. Dec 2015;23(5):239-245.



Neurodynamics: Intraneural Fluid

Intraneural edema reduction is a likely therapeutic mechanism of neural exercise

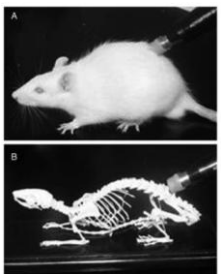
Schmid AB, Elliott JM, Strudwick MW, Little M, Coppieters MW. Effect of splinting and exercise on intraneural edema of the median nerve in carpal tunnel syndrome--an MRI study to reveal therapeutic mechanisms. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society.* Aug 2012;30(8):1343-1350.



Neurodynamics: Inflammation

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

Song XJ, Gan Q, Cao JL, Wang ZB, Rupert RL. Spinal manipulation reduces pain and hyperalgesia after lumbar intervertebral foramen inflammation in the rat. *Journal of manipulative and physiological therapeutics.* Jan 2006;29(1):5-13.



RA, Inflammation and Movement…

Growing body of evidence showing exercise:

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

Stenstrom CH, Minor MA. Evidence for the benefit of aerobic and strengthening exercise in rheumatoid arthritis. *Arthritis and rheumatism.* Jun 15 2003;49(3):428-434.

Hurkmans E, van der Giesen FJ, Vliet Vlieland TP, Schoones J, Van den Ende EC. Dynamic exercise programs (aerobic capacity and/or muscle strength training) in patients with rheumatoid arthritis. The Cochrane database of systematic reviews. Oct 07 2009(4):CD006853.

Wadley AJ, Veldhuijzen van Zanten JJ, Stavropoulos-Kalinoglou A, et al. Three months of moderate-intensity exercise reduced plasma 3-nitrotyrosine in rheumatoid arthritis patients. European journal of applied physiology. 2014;114(7):1483-1492.

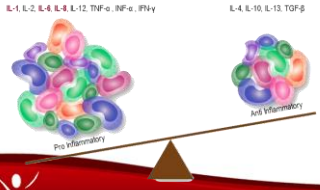
Neurodynamics: Immune

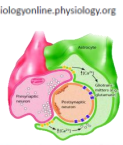
- Neural mobilization reverses behavioral and cellular changes that characterize neuropathic pain in rats
- Decreased neuroimmune activity, specifically glial cell activity

Santos FM, Silva JT, Giardini AC, et al. Neural mobilization reverses behavioral and cellular changes that characterize neuropathic pain in rats. *Mol Pain.* 2012;8:57.

Movement as Antigen?

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





Pedersen BK, Toft AD. Effects of exercise on lymphocytes and cytokines. *British journal of sports medicine.* Aug 2000;34(4):246-251.
Thacker MA, Clark AK, Marchand F, McMahon SB. Pathophysiology of peripheral neuropathic pain: immune cells and molecules. Anesth Analg. 2007;105:838-847.

Neurodynamics: Neuroplastic

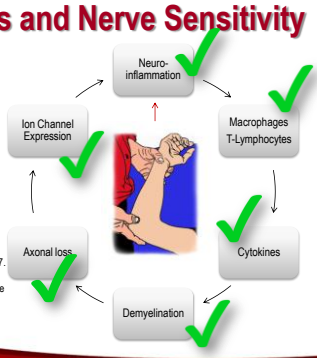
- Immobilization and neuroplastic changes…

Stenekes, M. W., et al. (2009). "Effects of motor imagery on hand function during immobilization after flexor tendon repair." Arch Phys Med Rehabil **90**(4): 553-559.
Toussaint, L. and A. Meugnot (2013). "Short-term limb immobilization affects cognitive motor processes." J Exp Psychol Learn Mem Cogn **39**(2): 623-632.
Meugnot, A., et al. (2014). "The embodied nature of motor imagery processes highlighted by short-term limb immobilization." Exp Psychol 61(3): 180-186.
Bassolino, M., et al. (2014). "Training the motor cortex by observing the actions of others during immobilization." Cereb Cortex 24(12): 3268-3276.
Meugnot, A. and L. Toussaint (2015). "Functional plasticity of sensorimotor representations following short-term immobilization of the dominant versus non-dominant hands." Acta Psychol (Amst) **155**: 51-56.
Meugnot, A., et al. (2016). "Selective impairment of sensorimotor representations following short-term upper-limb immobilization." Q J Exp Psychol (Hove) 69(9): 1842-1850.

There is, however, more complexity…

Schmid AB, Nee RJ, Coppieters MW. Reappraising entrapment neuropathies--mechanisms, diagnosis and management. *Manual therapy.* Dec 2013;18(6):449-457.

Immune Changes and Nerve Sensitivity



Schmid AB, Nee RJ, Coppieters MW. Reappraising entrapment neuropathies--mechanisms, diagnosis and management. Manual therapy. Dec 2013;18(6):449-457.
Thacker MA, Clark AK, Marchand F, McMahon SB. Pathophysiology of peripheral neuropathic pain: immune cells and molecules. Anesthesia and analgesia. Sep 2007;105(3):838-847.

Mobilizing the Immune System via Neurodynamics

Thank You

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

CSM APTA Combined Sections Meeting
New Orleans • February 21-24, 2018