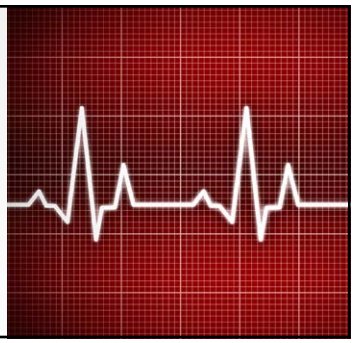
Pain

DEFINITIONS



Learning Objectives

- Understand and identify the types of pain fibers and classifications
- Understand and be able to explain current pain theories.
- Understand the neurophysiology in pain, as well as the pathophysiology in the development of chronic pain.

Learning Objective

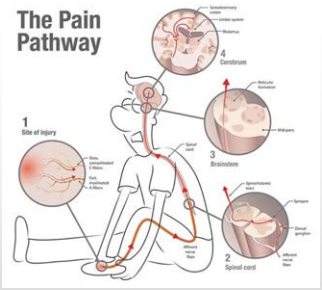
- Understand pathological concepts in pain and learn how to diagnose and manage these conditions early in their development / presentation

Definition of Pain

- McCaffery (1968)
  - Pain is "whatever the experiencing person says it is, existing whenever he/she says it does".
- IASP (1979)
  - Pain is "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."

Pain Classification

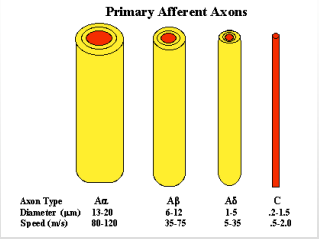
- Duration
  - Acute
  - Chronic
- Pathophysiology
  - Nociceptive
  - Inflammatory
  - Neuropathic



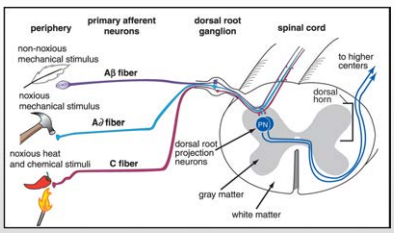
Types of Afferent Nerve Fibers

Type of Nerve Fibre	Information Carried	Myelin Sheath?	Diameter (micrometers)	Conduction Speed (m/s)
A-alpha	proprioception	myelinated	13 - 20	80 - 120
A-beta	touch	myelinated	6 - 12	35 – 90
A-delta	pain (mechanical and thermal)	myelinated	1 - 5	5 – 40
C	pain (mechanical, thermal, and chemical)	non-myelinated	0.2 - 1.5	0.5 - 2

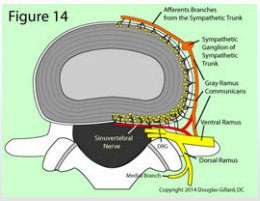
Types of Afferent Nerve Fibers

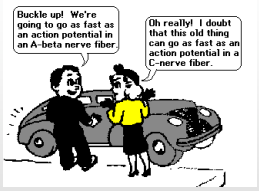


Types of Pain Fibers



Example: Innervation of IVD

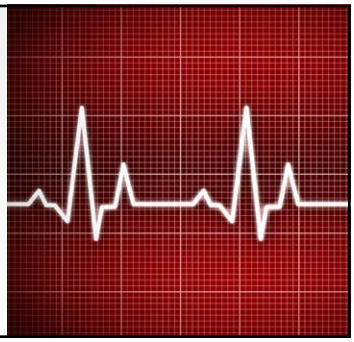




Nociceptors

- Sensitive to repeated or prolonged stimulation
  - Mechanosensitive
    - Excited by stress and tissue damage
  - Chemosensitive
    - Excited by the release of chemical mediators
      - Bradykinin
      - Histamine
      - Prostaglandins
      - Arachadonic Acid
- Primary Hyperalgesia – Due to injury (Nociceptive)
- Secondary Hyperalgesia – Due to spreading of chemical mediators (Inflammatory)

Neuropathic Pain



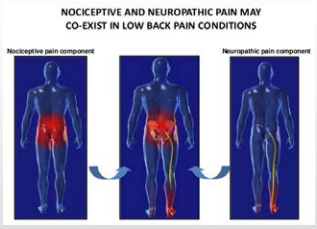
Definition

- Neuropathic pain involves the combination of positive and negative symptoms in patients in whom pain is due to pathologic changes of neural tissue (Devor et al)
  - Positive symptoms include pain, paresthesia, and spasm.
  - In contrast, anesthesia and weakness are negative sensory and motor symptoms.
  - Combination of positive and negative symptoms may broadly differentiate neuropathic pain from nonneuropathic; however, this may not always be the case, and so may be difficult to differentiate.
  - Some disorders may consist of "mixed" pain, whereby neuropathic and inflammatory pain mechanisms coexist (Walsh et al)

Neuropathic Pain

- Simply stated, neuropathic pain is present when the neural tissue itself is or becomes the primary pain generator.

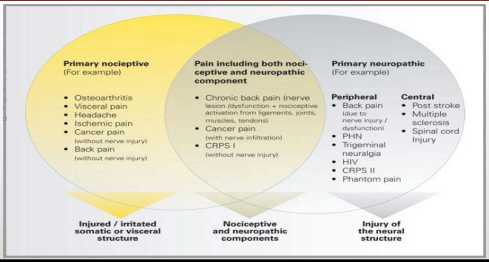
Neuropathic Pain: Common Perception



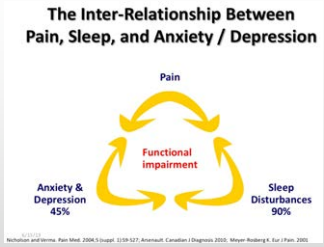
Neuropathic Pain: Symptoms

- Perception of spontaneous pain without identifiable stimulus.
- Hyperalgesia
  - Exaggerated responses to painful stimuli
- Allodynia
  - Pain with normally nonpainful stimuli

Pain Differentiation

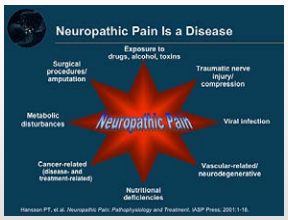


Neuropathic Pain: Perpetuating Factors

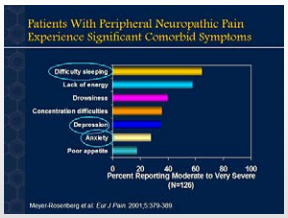


Neuropathic Pain: Etiology

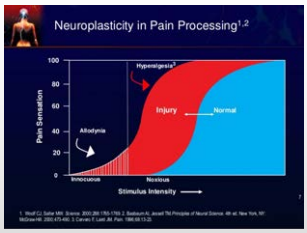
Neuropathic Pain Etiology



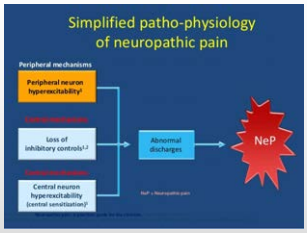
Neuropathic Pain Comorbid Symptoms



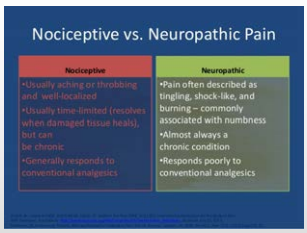
Graphing Hyperalgesia and Allodynia



Pathophysiology of Neuropathic Pain



Neuropathic Pain: DDx



Neuropathic Pain: Diagnostic Tools

Diagnostic Aids

- Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Scale (Bennett. Pain. 2001)
- DN4 Pain Questionnaire (Bouhassira et al. DN4)
- Neuropathic Pain Questionnaire (Backonja and Krause. Clin J Pain 2003)
- Neuropathic Pain Scale (Galer et al. Neurology 1997)

Pain Intensity / Characteristics

- VAS
- Pain Likert Scale
- McGill Pain Questionnaire
- Neuropathic Pain Symptom Inventory (Bouhassira et al. Pain 2004)

Neuropathic Pain: Screening Questionnaires

J Clin Epidemiol. 2015

- 37 studies were included.
- Evaluated measurement properties of:
  - DN4
  - LANSS
  - PainDETECT
  - Neuropathic Pain Questionnaire

Conclusion

- "DN4 and Neuropathic Pain Questionnaire were most suitable for clinical use."
- Should not replace a thorough clinical assessment.

Questionnaires for Neuropathic Pain Syndrome

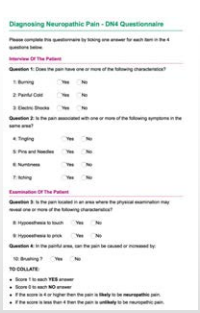
S-LANSS

- Leeds Assessment of Neuropathic Symptoms
  - S-LANSS score of 12 indicates neuropathic pain.
  - Questionnaire takes a few minutes and identifies up to 80%
- * Screening tests will fail to identify up to 20% of patients with neuropathic pain.

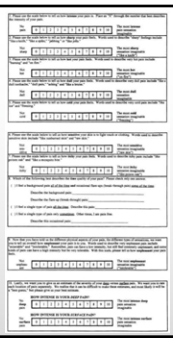
DN4

- Douleur Neuropathique 4 Questions
  - DN4 score of 4 or more indicates neuropathic pain.
  - Takes slightly longer due to clinical exam component.
  - 83% sensitivity and 90% specificity.
- * Clinical assessment remains the standard for diagnosing neuropathic pain.

S-LANSS Pain Score

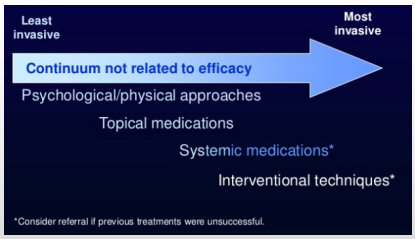


DN4 Questionnaire

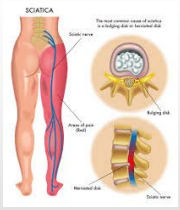


Neuropathic Pain Questionnaire

Pain Treatment Continuum



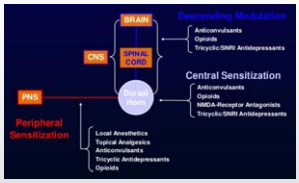
Neuropathic Pain: Conservative Treatment



Nonpharmacologic Options

- AMT
- Acupuncture
- TENS
- Biofeedback
- Relaxation Therapy
- Physical and Occupational Therapy
- Cognitive / Behavioral Strategies

Neuropathic Pain: Pharmacologic Agents



- Carbamazepine
  - trigeminal neuralgia
- Duloxetine
  - peripheral diabetic neuropathy
- Gabapentin
  - postherpetic neuralgia
- Lidocaine Patch 5%
  - postherpetic neuralgia
- Pregabalin
  - peripheral diabetic neuropathy
  - postherpetic neuralgia

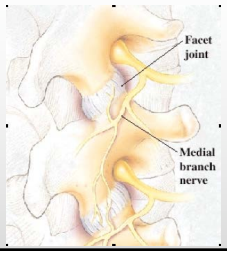
FDA-Approved Treatments for Neuropathic Pain

- Carbamazepine
  - trigeminal neuralgia
- Duloxetine
  - peripheral diabetic neuropathy
- Gabapentin
  - postherpetic neuralgia
- Lidocaine Patch 5%
  - postherpetic neuralgia
- Pregabalin
  - peripheral diabetic neuropathy
  - postherpetic neuralgia

Neuropathic Pain: Interventional Treatments

- Neural blockade
  - sympathetic blocks for CRPS-I and II (reflex sympathetic dystrophy and causalgia)
- Neurolytic techniques
  - alcohol or phenol neurolysis
  - pulse radio frequency
- Stimulatory techniques
  - spinal cord stimulation
  - peripheral nerve stimulation
- Medication pumps

Example: RF for Facet Mediated Pain



- Neuropathic Pain affecting the MBB resulting in chronic facet mediated pain.

Quantitative Sensory Testing (QST)

EMG/NCV

- Neurophysiological examinations to support a proximal nerve root lesion include the distal motor latency and the F-wave latency of nerves, which receive their nerve fibers from the affected root. This examination will only show pathological values if motor fibers are involved in the damage. Sensory conduction studies are usually normal if the lesion is located proximal to the dorsal root ganglion; therefore, they do not help with the diagnosis. Somatosensory Evoked Potentials, which analyze the entire afferent conduction from the periphery to the brain, are used to detect a proximal damage of sensory fiber (eg., in the nerve root). However, it is important to understand that these conventional electrophysiological techniques only assess the function of myelinated peripheral axonal systems; the affection of small fibers, including noceceptors, are missed (Freynhagen et al. The Evaluation of Neuropathic Components in Low Back Pain. *Current Pain & Headache Reports* 2009, 13:188).

QST

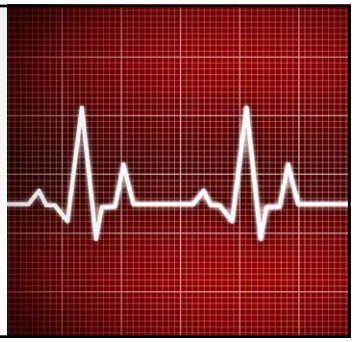
- Quantitiative Sensory Testing (QST), the standardized extension of the clinical neurological sensory examination, allows the complete assessment of all sensory submodalities, including the large and small fibers. It detects not only hypophenomena but also hyperphenomenon due to a disturbed pain processing in the periphery, spinal cord, or brain. QST is used to reveal pathological mechanisms involved in neuropathic pain and is recognized as a useful additional diagnostic tool (Freynhagen et al. The Evaluation of Neuropathic Components in Low Back Pain. *Current Pain & Headache Reports* 2009, 13:188-89).

Pain Classification

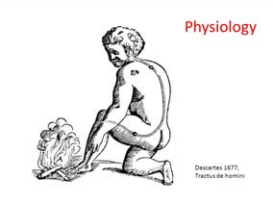
- Duration
  - Acute
  - Chronic
- Pathophysiology
  - Nociceptive
  - Inflammatory
  - Neuropathic

Pain Theories

CURRENT UNDERSTANDING

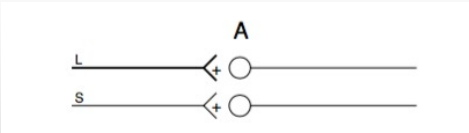


Descartes: Straight Through Sensory Projection (1664)



- Proposed 3 centuries earlier
- Concept of pain was a specific, straight-through sensory projection system.
- This rigid anatomy of pain in the 1950's led to attempts to treat severe chronic pain by a variety of neurosurgical lesions.
  - Melzack and Katz. Pain in the 21st Century: The Neuromatrix and Beyond

Specificity Theory (Decartes)



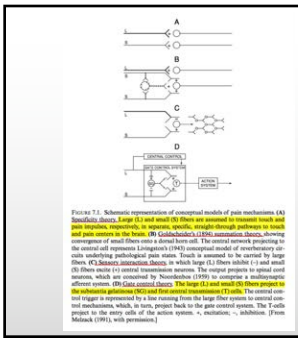


FIGURE 7.1. Schematic representation of conceptual models of pain mechanisms (A) Specificity theory. Large (L) and small (S) fibers are assumed to transmit touch and pain impulses, respectively, in separate, specific, straight-through pathways to touch and pain centers in the brain. (B) Goldscheider's (1894) summation theory, showing convergence of small fibers onto a dorsal horn cell. The central network projecting to the central cell represents Livingston's (1943) conceptual model of reverberatory circuits underlying pathological pain states. Touch is assumed to be carried by large fibers. (C) Sensory interaction theory, in which large (L) fibers inhibit (–) and small (S) fibers excite (+) central transmission neurons. The output projects to spinal cord neurons, which are conceived by Noordenbos (1959) to comprise a multisynaptic efferent system. (D) Gate control theory. The large (L) and small (S) fibers project to the substantia gelatinosa (SG) and first central transmission (T) cells. The central control trigger is represented by a line running from the large fiber system to central control mechanisms, which, in turn, project back to the gate control system. The T-cells project to the entry cells of the action system. +, excitation; –, inhibition. [From Melzack (1991), with permission.]

Development of Conceptual Models of Pain Mechanisms

Melzak and Wall Paper (1965)

19 November 1965, Volume 150, Number 3699

SCIENCE

Pain Mechanisms: A New Theory

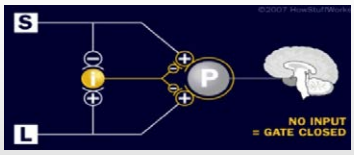
A gate control system modulates sensory input from the skin before it evokes pain perception and response.

Ronald Melzack and Patrick D. Wall

Gate Control Theory (Melzack & Wall, 1965)

- Gating mechanism exists within the dorsal horn of the spinal cord.
- Small nerve fibers (pain receptors)
- Large nerve fibers ("normal" receptors)
- These two fibers synapse on Projection Cells (P), which go up the spinothalamic tract to the brain, and inhibitory interneurons (I) within the dorsal horn.
- The interplay among these connections determines when painful stimuli proceed to the brain.

Gate Theory



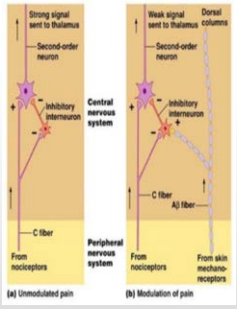
- When no input comes in, the inhibitory neuron prevents the Projection Neuron from sending signals to the brain (gate is closed).

Gate Theory

- Normal somatosensory input happens when there is more large-fiber stimulation (or only large-fiber stimulation).
- Both the Inhibitory Neuron and the Projection Neuron are stimulated, but the Inhibitory Neuron prevents the Projection Neuron from sending signals to the brain.
- Gate is closed.

Gate Theory

- Nociception (pain reception) happens when there is more small-fiber stimulation or only small-fiber stimulation.
- This inactivates the Inhibitory Neuron, and the Projection Neuron sends signals to the brain informing it of pain.
- Gate is open



Gate Theory Example

Bumping Elbow

- Initial trauma activates the A-delta and, eventually, C fibers.
- Rubbing the traumatized area stimulates the A-beta fibers, which activate the Inhibitory Neuron (I) to close the spinal gate.
- Results in inhibition of the transmission of painful stimulus.

Factors Which Can "Open the Gate"

- Physical Conditions
  - Extent of injury
  - Nature of injury
- Emotional States
  - Anxiety
  - Worry
  - Tension
  - Depression
- Cognitive States
  - Focusing on the pain
  - Boredom
- Lack of Activity
  - Minimal / No Fitness
  - Minimal / No Exercise

Group Activity: Devise & Justify Treatment Plan

History / Subjective

- Female 30 yoa with LBP from WC injury (one year earlier) while bending over to clean under a sink.
- Sharp, stabbing LBP belt line distribution
- Lt anterolateral thigh burning
- Pain equal with sitting/standing
- Ibuprofen no help
- Pain Scale: 7/10 (6/10 & 8/10)
- ROQ 70% Index
- Prior Treatment: Pharmacologic, PT, Declined TESI, Surgical Consult.

Objective / Diagnostics

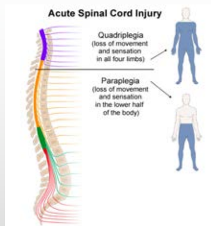
- 5'3", 160 lbs.
- Diffuse lumbar tenderness; all orthopedic testing positive (husband helped her change positions on exam table)
- Waddell's +5/5
- MRI: Mild bulges L3-4 & L5-S1 with mild IVF narrowing.
- EMG/NCV studies negative
- FCE Valid for Light Work

Gate Theory: Unanswered Questions

- Gate Theory
  - Has been widely accepted, but it leaves unanswered questions, such as:
    - Chronic Pain Issues
    - Sex-Based Differences
    - Effects of Previous Pain Experiences
    - Phantom Pain

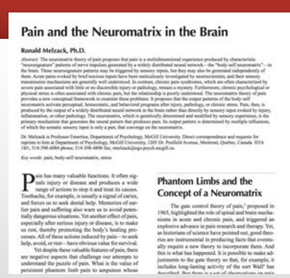
Phantom Limbs / Paraplegics

- Observations that don't fit the theory.
  - Peripheral and spinal processes are an important part of pain.
  - However, data on painful phantoms below the level of total spinal section (Melzack 1989), 1990) indicate that we need to go above the spinal cord and into the brain.



Neuromatrix Theory

- In 2001, Ronald Melzack came up with a newer theory of pain that answered some of these questions. This new theory, the Neuromatrix Theory, stipulates that every human being has an innate network of neurons that they named the "Body-Self Neuromatrix".
- Each person's matrix of neurons is unique and is affected by all facets of the person's physical, psychological, and cognitive traits, and also by their experience.



Pain and the Neuromatrix in the Brain

Ronald Melzack, Ph.D.

Abstract: The neuromatrix theory of pain proposes that pain is a multidimensional experience produced by characteristic "neurosignature" patterns of nerve impulses generated by a widely distributed neural network—the "body-self neuromatrix"—in the brain. These neurosignature patterns may be triggered by sensory inputs, but they may also be generated independently of them. Acute pains evoked by brief noxious inputs have been meticulously investigated by neuroscientists, and their sensory transmission mechanisms are generally well understood. In contrast, chronic pain syndromes, which are often characterized by severe pain associated with little or no discernible injury or pathology, remain a mystery. Furthermore, chronic psychological or physical stress is often associated with chronic pain, but the relationship is poorly understood. The neuromatrix theory of pain provides a new conceptual framework to examine these problems. It proposes that the output patterns of the body-self neuromatrix activate perceptual, homeostatic, and behavioral programs after injury, pathology, or chronic stress. Pain, then, is produced by the output of a widely distributed neural network in the brain rather than directly by sensory input evoked by injury, inflammation, or other pathology. The neuromatrix, which is genetically determined and modified by sensory experience, is the primary mechanism that generates the neural pattern that produces pain. Its output pattern is determined by multiple influences, of which the somatic sensory input is only a part, that converge on the neuromatrix.

Dr. Melzack is Professor Emeritus, Department of Psychology, McGill University. Direct correspondence and requests for reprints to him at Department of Psychology, McGill University, 1205 Dr. Penfield Avenue, Montreal, Quebec, Canada H3A 1B1; [illegible]

Key words: pain, body-self neuromatrix, stress

Pain has many valuable functions. It often signals injury or disease and produces a wide range of actions to stop it and treat its causes. Toothache, for example, is usually a signal of caries, and forces us to seek dental help. Memories of earlier pain and suffering also warn us to avoid potentially dangerous situations. Yet another effect of pain, especially after serious injury or disease, is to make us rest, thereby promoting the body's healing processes. All of these actions induced by pain—to seek help, avoid, or rest—have obvious value for survival.

Yet despite these valuable features of pain, there are negative aspects that challenge our attempts to understand the puzzle of pain. What is the value of persistent phantom limb pain to amputees whose

Phantom Limbs and the Concept of a Neuromatrix

The gate control theory of pain,[1] proposed in 1965, highlighted the role of spinal and brain mechanisms in acute and chronic pain, and triggered an explosive advance in pain research and therapy. Yet, as historians of science have pointed out, good theories are instrumental in producing facts that eventually require a new theory to incorporate them. And this is what has happened. It is possible to make adjustments to the gate theory so that, for example, it includes long-lasting activity of the sort Wall[2] has described. But there is a set of observations on pain

Body Self Neuromatrix

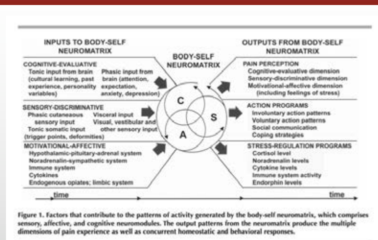
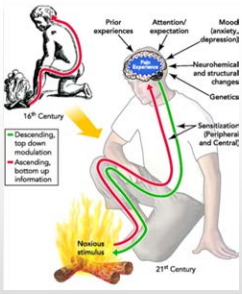


Figure 1. Factors that contribute to the patterns of activity generated by the body-self neuromatrix, which comprises sensory, affective, and cognitive neuromodules. The output patterns from the neuromatrix produce the multiple dimensions of pain experience as well as concurrent homeostatic and behavioral responses.

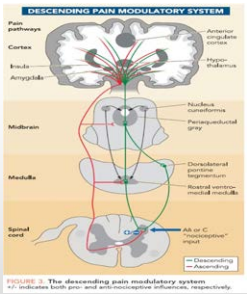
Neuromatrix Theory

- Essentially, the model of the Neuromatrix Theory states that the central nervous system (CNS), which is made up of the brain and spinal cord, is where pain is produced and that multiple parts of the brain and spinal cord work together in response to stimuli from the body and/or environment to create the experience of pain.
- This theory involves two important shifts in our understanding of pain:

1. The brain and spinal cord are what produce pain, not tissue damage.
2. Various parts of the CNS work together to produce pain.



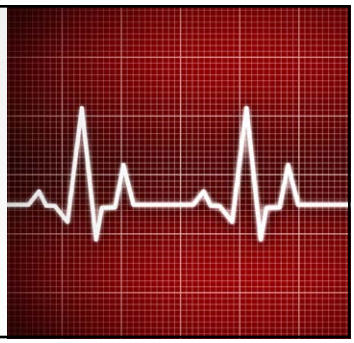
Descartes for the Modern Age



Descending Pain Modulatory System

Central Sensitization

CHRONIC "PSYCHOSOMATIC" PAIN MAY HAVE ORGANIC BASIS

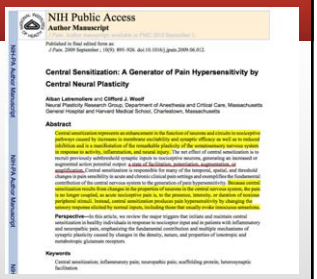


Definition

- Central Sensitization
  - Condition of the nervous system that is associated with the development and maintenance of chronic pain. When central sensitization occurs, the nervous system goes through a process called "wind-up" and gets regulated in a persistent state of high reactivity.

NIH: J Pain 2009

- Latremolier and Woolf
  - "Because CS results from changes in the properties of neurons in the CNS, the pain is no longer coupled, as acute nociceptive pain is, to the presence, intensity, or duration of noxious peripheral stimuli."
  - "Instead, CS produces pain hypersensitivity by changing the sensory response elicited by normal inputs, including those that usually evoke innocuous sensations."



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Author Manuscript

Central Sensitization: A Generator of Pain Hypersensitivity by Central Neural Plasticity

Alban Latremoliere and Clifford J. Woolf

Abstract

Woolf. Pain 152 (2011)S2-S15

- CS Contributes to the following clinical syndromes:
  1. Rheumatoid arthritis
  2. Osteoarthritis
  3. Temporomandibular disorders
  4. Fibromyalgia
  5. Misc Musculoskeletal Disorders
  6. Headache
  7. Neuropathic Pain
  8. Complex Regional Pain Syndrome
  9. Post-surgical Pain
  10. Visceral Pain Hypersensitivity


PAIN 152 (2011) S2–S15

IASP PAIN

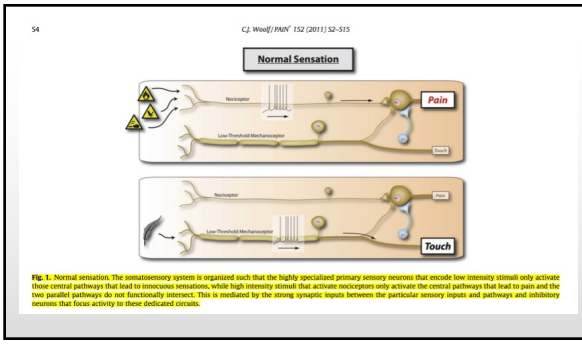
Review

Central sensitization: Implications for the diagnosis and treatment of pain

Clifford J. Woolf

ABSTRACT

1. Introduction


S4 C.J. Woolf / PAIN 152 (2011) S2–S15

Normal Sensation

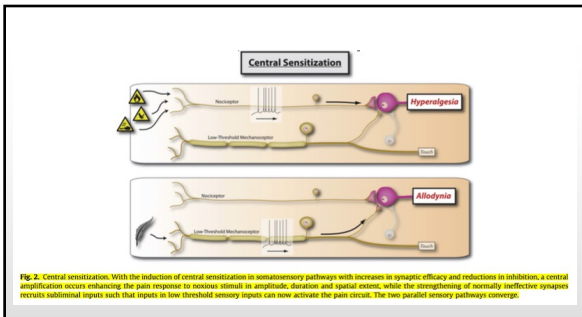
Nociceptor

Low-Threshold Mechanoceptor

Pain

Touch

Fig. 1. Normal sensation. The somatosensory system is organized such that the highly specialized primary sensory neurons that encode low intensity stimuli only activate those central pathways that lead to innocuous sensations, while high intensity stimuli that activate nociceptors only activate the central pathways that lead to pain and the two parallel pathways do not functionally intersect. This is mediated by the strong synaptic inputs between the particular sensory inputs and pathways and inhibitory neurons that focus activity to these dedicated circuits.


Central Sensitization

Nociceptor

Low-Threshold Mechanoceptor

Hyperalgesia

Allodynia

Fig. 2. Central sensitization. With the induction of central sensitization in somatosensory pathways with increases in synaptic efficacy and reductions in inhibition, a central amplification occurs enhancing the pain response to noxious stimuli in amplitude, duration and spatial extent, while the strengthening of normally ineffective synapses recruits subliminal inputs such that inputs in low threshold sensory inputs can now activate the pain circuit. The two parallel sensory pathways converge.

Has CS Been Received Well?

Accused and Labeled:

- Secondary Gain
- Opioid Drug Seeker
- Malingering
- Liar
- Hysterics
- Psychosomatic
- Somatoform Disorder

Woolf (2011)

- "We can now 30 years later, based on data from many studies in human volunteers and patients, address whether central sensitization, defined operationally as *an amplification of neural signaling within the CNS that elicits pain hypersensitivity*, is a real phenomenon or not and can assess its relative contribution to inflammatory, neuropathic and dysfunctional pain disorders in patients."

Central Sensitization: Two Main Components

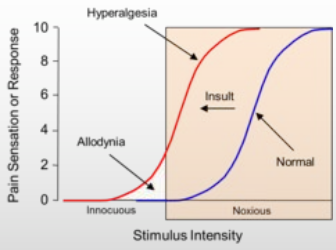
Allodynia

- Experience of pain with things that are normally not painful.
  - Light touch.
  - Massage
  - Jump Sign

Hyperalgesia

- Occurs when an actual painful stimulus is perceived as more painful than it should.

Pain Sensation / Response



Central Sensitization: Less Common Characteristics

- Can lead to heightened sensitivities across all senses, not just the sense of touch:
  - Photophobia
  - Phonophobia
  - Odor
  - Cognitive Deficits
    - Poor Concentration
    - Poor Short-Term Memory
  - Increased Level of Emotional Distress
    - Anxiety
  - Sick Role Behaviors
    - Rest / Malaise
    - Pain Behavior

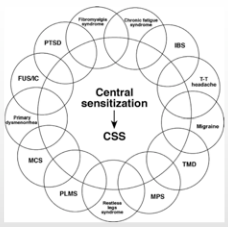
Central Sensitization: Associated Chronic Conditions

Peripheral

- Low Back Pain
- Chronic Neck Pain
- Whiplash Injuries
- Chronic Tension HA
- Migraine HA
- Rheumatoid Arthritis
- OA of Knee
- Endometriosis
- Post-Surgical

Central

- Fibromyalgia
- Irritable Bowel Syndrome
- Chronic Fatigue Syndrome
  - Common denominator of Central Sensitization



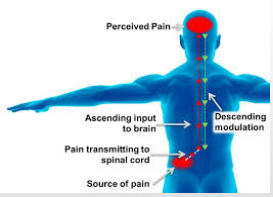
Central Sensitization Syndrome

Root Cause of Multiple Chronic Pain Conditions?

Central Sensitization: Causes in Peripheral Lesions

- Multiple Factors

1. Factors that are associated with the state of the CNS prior to the onset of original injury or pain condition (Predisposition)
2. Factors that are associated with the CNS following onset of original injury or pain condition (Antecedent Factors)



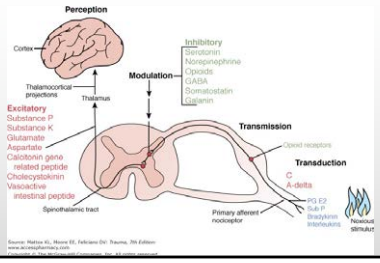
Central Sensitization: Predisposing Factors

- Psychophysiologic Factors
  - Stress
  - Anxiety
  - Psychological Trauma
  - Physical Trauma
  - Depression
- Genetic

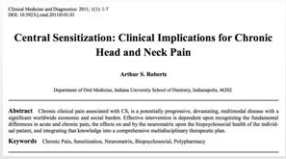
Central Sensitization: Antecedent Factors

- Subsequent development of:
  - Depression
  - Fear Avoidance
  - Anxiety
  - Poor Sleep
  - Operant Learning
    - Interpersonal Reinforcements
    - Environmental Reinforcements
    - Iatrogenic Reinforcement

Excitation vs. Inhibition



Central Sensitization: Two Distinctly Different Approaches



Central Sensitization: Clinical Implications for Chronic Head and Neck Pain

Arthur S. Roberts

Department of Oral Medicine, Indiana University School of Dentistry, Indianapolis, 46202

Abstract Chronic clinical pain associated with CS, is a potentially progressive, devastating, multimodal disease with a significant worldwide economic and social burden. Effective intervention is dependent upon recognizing the fundamental differences in acute and chronic pain, the effects on and by the neuromatrix upon the biopsychosocial health of the individual patient, and integrating that knowledge into a comprehensive multidisciplinary therapeutic plan.

Keywords Chronic Pain, Sensitization, Neuromatrix, Biopsychosocial, Polypharmacy

1. Address effects of CS after it has occurred.
2. Interrupt the CS and let the body's homeostatic mechanisms clear residual pathologic products.

- Within these two categories there are pharmacological and non-pharmacological therapeutic options.

Central Sensitization: Treatment Complications

1. "Polypharmacy is one of the problems attendant to CSS therapy, and is the result of approaching each of the varied presentations of CSS as a separate and distinct disease."
2. "…failure to differentiate acute pain from chronic pain."
3. "…essential to treat the pathways in chronic pain disease".

- Roberts. Clin Med and Diag. 2011

Figure 2. Adapted from Wallace and Clauw [2] MGN – Migraine, TTH - Tension-type headache, IBS – Irritable bowel syndrome, CFS - Chronic Fatigue syndrome, FMS – Fibromyalgia, MPS – Myofascial pain syndrome, TMD – Temporomandibular dysfunction, RLS - Restless leg syndrome, PLMD - Periodic limb movement disorder, MCS - Multiple chemical sensitivity, PTSD - Post traumatic stress disorder, DPSN – Depression, PD - Primary dysmenorrhea, AO - Atypical odontalgia, BMS - Burning mouth syndrome.

Central Sensitization: Non-Pharmacological Approaches

- Manual Therapy
- Percutaneous Electroneural Stimulation (PENS)
- Improving Stress Tolerance and Neuro feedback Training
- TENS
- Virtual Reality
  - Roberts. Clin Med and Diag. 2011

Central Sensitization: Pharmacological Approaches

Address Effects of CS

- Acetaminophen
- Serotonin (SSRI) and Norepinephrine (SNRI) reuptake inhibitors
- Tricyclic antidepressants (TCA)
- Opioids and Traumadol

Treat CS Itself

- N-methy-D-aspartate (NMDA) receptor blockers
- Calcium channel alpha(2) ligands
  - Gabapentin
  - Pregabalin

Central Sensitization: Treatment

- Interdisciplinary Chronic Pain Rehabilitation Program (CPRP)
  - Health Psychology
  - PT / Chiropractic
    - Must avoid too aggressive treatment (hypervigilant CNS)
    - Must show "Sensitivity to Sensitivity"
  - Medication
    - Target CNS (antiepileptics and antidepressants)
      - NSAIDS and other medications which target the peripheral tissues are ineffective

Interdisciplinary Pain Management

Focused Review

A Comprehensive Review of Opioid-Induced Hyperalgesia

Opioid-Induced Hyperalgisia (OIH)

Be wary of OIH...

Opiod-Induced Hyperalgesia

- State of nociceptive sensitization caused by exposure to opioids.
- Suspect OIH:
  1. Opioid treatment effects wane in the absence of disease progression.
  2. Unexplained pain reports or diffuse allodynia unassociated with the original pain.
  3. Increased level of pain with increased opioid dosages.

Table 2. Classes of Opioids

Phenanthrene Opioids	Nonphenanthrene Opioids
Codeine	Piperidine derivatives:
Hydrocodone	Fentanyl
Hydromorphone	Meperidine
Morphine	Sufentanil
Oxycodone	Other:
Oxymorphone	Buprenorphine
	Methadone
	Tramadol

Source: References 11, 14.

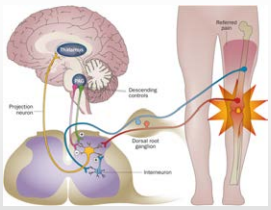
Placebo Effect

- Placebo is derived from the Latin work for "I shall please"
  - Used to describe pain reduction obtained from a mechanism other that those related to the physiological effects of the treatment.
  - All treatments have some degree of placebo effect
    - Most reputable studies utilize some type of "sham" treatment for comparison.
    - Ultrasound set at the intensity of 0 and an actual treatment have shown decreased levels of pain in each group.

These capsules are fabulous! When I look at the box, I stop coughing.

Common Knee Surgery No Better Than Placebo

- Study published in the New England Journal of Medicine (2002)
  - Patients with OA of knee who underwent placebo arthroscopic surgery were just as likely to report pain relief as those who received the real procedure, according to the Department of Veterans Affairs and Baylor College of Medicine.



Placebo Response and Neuromatrix Model

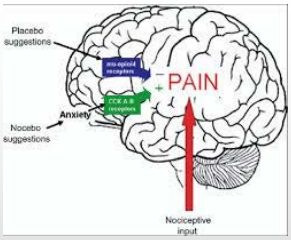
- Neuromatrix Model of pain puts what we know about the Placebo Response in a new light.
- Perhaps the Placebo Response is not so mysterious; nor should it be so "taboo"
- What if, all along, the Placebo Effect has been an unintentional cognitive behavioral intervention that changes the neuromatrix of the brain's responses and thereby reduces pain?

Nocebo Effect

- Placebo has an Evil Twin Named "Nocebo"
  - Just as expectations of a treatments effectiveness can influence the reaction to a placebo, an expectation of side effects can cause a patient to experience them as well.
  - Study on Finasteride for Enlarged Prostate
    - Half were told by the doctor that erectile dysfunction was a possible side effect and the other half were not.
    - Of the group told about ED, 44% reported ED compared to only 15% of that group that was not told.
- Do you know of any "physicians" taking advantage of the Nocebo Effect?

Nocebo:

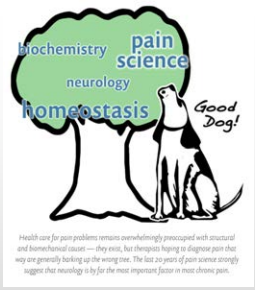
A harmless thing that causes harm because you believe it's harmful.



Placebo vs Nocebo

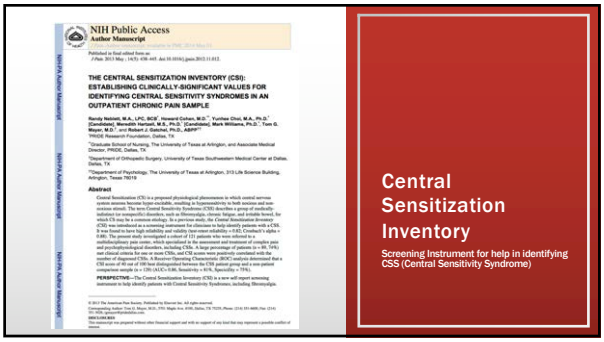
Central Sensitization: Thoughts

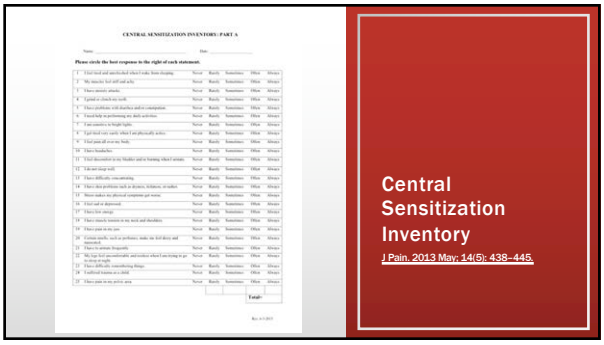
- Represents a "Neurologic Meltdown"
- Researchers now believe Central Sensitization is a major common denominator in most difficult pain problems.
- May be the universal factor that puts the "chronic" in chronic pain, giving all such problems characteristics regardless of how it got started – not the cause of the pain, but perhaps the cause of its chronicity.



Central Sensitization

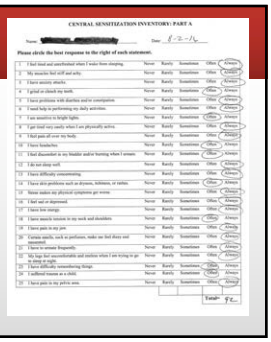
Have we been "Barking Up the Wrong Tree"?





Revisit Chronic LBP Patient

- After History & Evaluation
- Administered Central Sensitization Inventory
- Part A
  - Score equal or greater than 40 considered positive for Central Sensitization.
  - Patient scored 92
- Part B
  - Significant for Central Sensitization Syndromes



CSI Part B

- Significant for:
  - Migraine Headaches
  - Irritable Bowel Syndrome
  - Depression
- All diagnosed in 2015
- What's the significance?

CENTRAL SENSITIZATION INVENTORY: PART B

Name: [redacted]

Date: 8/2/16

Have you been diagnosed by a doctor with any of the following disorders?

Please check the box to the right for each diagnosis and write the year of the diagnosis.

		NO	YES	Year Diagnosed
1	Restless Leg Syndrome	X		
2	Chronic Fatigue Syndrome	X		
3	Fibromyalgia	X		
4	Temporomandibular Joint Disorder (TMJ)	X		
5	Migraine or tension headaches		✓	2015
6	Irritable Bowel Syndrome		✓	2015
7	Multiple Chemical Sensitivities	X		
8	Neck Injury (including whiplash)	X		
9	Anxiety or Panic Attacks	X		
10	Depression		✓	2015

WC Patient

DIAGNOSTIC IMPRESSIONS:

Related to Industrial Injury (07/25/15):

1. Lumbar Spine
   a. Strain (07/25/15)
   b. MRI (09/23/15), mild disc bulges at L3-L4 and L5-S1 result in mild neuroforaminal stenosis.
   c. Left lower extremity radiculitis (Dr. Vater, 09/30/15)
   d. EMG/NCV (02/19/16), normal study.
   e. MMI (04/04/16)
2. FCE (03/30/16), VALID.
3. Clinical development of Central Sensitization (08/02/16).

Pre-Existing:

1. Noncontributory.

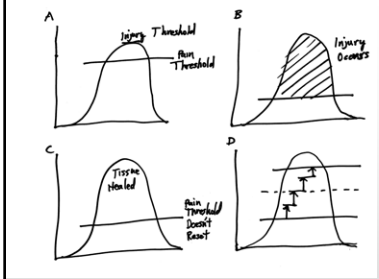
During the course of my history and examination, the patient exhibited strong evidence consistent with posttraumatic central sensitization. Therefore, at the conclusion of my history and evaluation I had the patient fill out The Central Sensitization Inventory (CSI) questionnaire.

Part A of the CSI assesses 25 health-related symptoms that are common to central sensitization syndrome, with total scores ranging from 0-100. Part be (which is not scored) and ask if I has previously been diagnosed with one or more specific disorders, including 7 separate CSSs (*Neblett et al. The central sensitization inventory (CSI): establishing clinically-significant values for identifying sensitivity syndromes in an outpatient chronic pain sample.J Pain. 2013 May;14(5):438-445*).

For Part A, a CSI score equal or greater than 40 is consistent with central sensitization. In this case, the patient scored 92. For Part B, the patient reported the following associated Central Sensitization Syndrome disorders: Migraine/tension headaches, irritable bowel syndrome, and depression (all reportedly diagnosed in 2015).

Central Sensitization is a condition of the nervous system that is associated with the development and maintenance of chronic pain. When central sensitization occurs, the nervous system gets regulated in a persistent state of high reactivity. This persistent, or regulated, state of reactivity subsequently comes to maintain pain even after the initial injury might have healed. Central sensitization has two main characteristics. both involve a heightened sensitivity to pain and the sensation of touch. They are called "allodynia" and "hyperalgesia". These characteristics were both present in this evaluation today.

Patient Explanation



Case Studies