PAIN SENSITIZATION

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DISCLOSURES

No conflicts of interest.

OBJECTIVES

1. Be able to explain how “chronic pain” differs from “acute pain”, including mechanisms of chronicization.
2. Know how abnormal descending modulation is key to the pathophysiology of central sensitization
3. Be able to describe several clinical pain conditions that often co-occur in central sensitization syndromes
4. Be able to quickly evaluate multidimensional domains to assess chronic pain
5. Know when to get help and how
When Pain is a symptom
• Cure is expected
• And this is a “reasonable” expectation

When Pain becomes a disease and no longer a symptom of an underlying disorder
• Physical, psychosocial, and environmental factors effect function and quality of life as defined by the patient and family
• Quality of life may not correlate with the severity of the pathophysiology, impairment, functional limitations, disability, or expectations of society
• Well-managed, not usually “cured”
ANATOMY OF THE PAIN PATHWAY

Basbaum A et al. 2010

THE LOESER ONION

What we observe during exam of our patients

Experience of diminished capacity

Pain transduction/transmission actively modulated multi-directionally throughout CNS = neuroplasticity

nociceptors

NOCICEPTIVE CASCADE

nociceptors selectively respond to noxious stimulation

Experience of diminished capacity

Pain transduction/transmission actively modulated multi-directionally throughout CNS = neuroplasticity
MECHANISMS OF PERIPHERAL SENSITIZATION

Hyperalgesia

Spontaneous pain

INHIBITORY INTERNEURONS

Normal transduction

Touch becomes pain....

From Woolf 2010

CENTRAL SENSITIZATION:
ROLE OF WIDE DYNAMIC RANGE NEURONS

Central sensitization leads to non-specific nerve impulses being perceived as painful (hyperalgesia).

Non-nociceptive neurons

Brain

WDR

Emerging Concepts in the Neurobiology of Chronic Pain
Department of Anesthesiology, University of Washington

MICROGLIA: MACROPHAGES OF THE CNS

Pro-inflammatory cytokine release after activation seen in peripheral nerve injury, MS, spinal cord injury, HNP, migraine

Ransohoff & Cordona Nature 2010

DORSAL HORN INTERNEURONS:
DUAL PATHWAYS OF NORADRENALINE RECEPTOR MODULATION

Facilitate inhibition

Inhibitory Interneurons (ININ)

Inhibit facilitation

NRADRENALINE

Bodnoff A et al. 2010
Millan MJ., Prog Neurobio 2002; 66: 375

PERIPHERAL AND CENTRAL SENSITIZATION
ANATOMY & PHYSIOLOGY

Dorsal horn
Dorsal root ganglion

Rexed laminae

Spinal Cord Descending pathways

Brain regional "connectomes"

From:
D’Mello 2006, Meredith 2003, O’Mara 2010
CASE 1

- 38 year old athletic woman with neck pain 2 years after whiplash
- Pain is deep, aching, and worsened with palpation and movement
- No radicular arm pain
- Exam with normal lordosis, pain inhibition to range, focal palpation tenderness with hyperalgesia in adjacent non-dermatomal pattern
- Imaging without significant findings

PERIPHERAL HYPERNOCICEPTION

MUSCLE HYPERALGESIA
“MYOFASCIAL PAIN DISORDER”
**THE FEELING OF WHAT HAPPENS**

**INTEROCEPTION**

*Interoception*: the sense of the physiological condition of the body (includes: pain, temperature, itch, sensual touch, muscular and visceral sensations, vasomotor, hunger, thirst, air hunger, emotional awareness)

**WHEN ABNORMAL:**
1. Hyper-reactivity of multiple brain regions
2. Increased neurotransmitters
3. Abnormal brain regional connections
4. Abnormal descending inhibitory pathways

Clauw, D. 2014; Craig AD. 2003; DamasioA. 1999; Giesecke T et al., 2004; Harris RE, et al. 2006

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**PSYCHOSOCIAL BURDENS OF CHRONIC PAIN**

- Performance of ADLs
  - Sleep disturbance
  - Work, Household chores
  - Leisure activities
  - Energy
- Marital & Family relations
- Intimacy
- Social isolation

- Functional Activities
- Socioeconomic consequences
- Health care costs
- Disability
- Lost productivity
- Energy
- Health care costs
- Disability
- Lost productivity
- Marital & Family relations
- Intimacy
- Social isolation

- Emotional Functioning
- Irritable
- Angry
- Anxious
- Depressed

Courtesy of Dennis Turk PhD, 2012

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**SUFFERING: EXPERIENCING DIMINISHMENT OF ONE'S CAPACITY**

- Negative affective response to unexpected consequence
  - Pain
  - Loss
  - Depression
  - Anxiety
  - Fear
  - Conflicts
- Accompanied by:
  - Negative misbeliefs
  - Catastrophic thinking
- Therapeutic Listener = Therapeutic Healer
  - Accompanies the patient
  - Offers Guidance/Counsel
  - Comforts in the therapeutic encounter

UW Medicine PAIN MEDICINE

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MIRROR NEURONS
CORTICAL AREAS RESPONDING TO OBSERVING MOTOR ACTS

Yellow = transitive distal movements
Purple = reaching movements
Orange = tool use
Green = intransitive movements
Blue = observation of upper-limb movements.

Cattaneo 2009

MIRROR NEURONS
RESPONDING TO AFFECTIVE STATES

Affective components of pain are activated during empathy.


EMPATHY = EMOTIONAL CONTAGION:
BRAIN ACTIVITY INCREASES WITH SUBJECT INTIMACY

Lamm, Derety, Singer 2011
**Maladaptive Response to Injury Can Be Preceded by Biopsychosocial Events**

Pre-existing disturbances of the central neural matrix increases pain intensity and interference

- Genetic predispositions
- Concurrent diseases
- Prior physical injury
- Prior psychosocial trauma
- Inactivity
- Social isolation & bereftness

**Adverse Childhood Events (ACE)**

**Significant Events:**
- Recurrent physical abuse
- Recurrent emotional abuse
- Contact sexual abuse
- An alcohol and/or drug abuser in the household
- An incarcerated household member
- Someone who is chronically depressed, mentally ill, institutionalized, or suicidal
- Mother is treated violently
- One or no parents
- Emotional or physical neglect

**Robust Correlation:**
- Depressed affect, suicide attempts
- Multiple sexual partners, sexually transmitted diseases
- Smoking & alcoholism
- Social, emotional, cognitive impairment
- Adoption of health/risk behaviors
- Disease, disability & social problems
- Early death

**Sensitization Promoters**

1. Chronic persistent nociception
2. Psychological distress, recent or remote
3. Sleep deprivation
4. Pain "catastrophizing" & "anticipation"
5. Opioids
6. Inactivity
CASE 2

- 42 yo woman with 8 years of widespread pain, headache, fatigue, and “brain fog.”
- Mood poor
- Sleep fitful and unrefreshed
- Imaging without specific pathoanatomy
- Exam: Muscle hyperalgesia above and below waist, bilaterally
- Assessment: ?

BRAIN IMAGING IN FIBROMYALGIA

BRAIN RESPONSE TO 4 KG/CM OF PRESSURE APPLIED ON THE RIGHT THUMB

- Fibromyalgia patients
- Healthy controls

ALTERED BRAIN CONNECTIVITY IN FIBROMYALGIA

Napadow et al. Arthritis Rheumatism 2010
THE PATIENT’S PAIN IS MOSTLY IN THE BRAIN

Correlation map between subjective pain scores and brain activations in fibromyalgia

"Pain is what a patient says it is."

Margo McCaffery, 2000

GENO-BIO-PSYCHO-SOCIAL DOMAINS OF CENTRAL SENSITIZATION

Yunus MB., 2007

CHRONIC OVERLAPPING PAIN CONDITIONS (COPC)

ACR DIAGNOSTIC CRITERIA FOR FIBROMYALGIA

Possible score ranges from 0 to 31 points; a score of 13 points is consistent with a diagnosis of fibromyalgia.

HEADACHE AND THE TRIGEMINAL NERVE

TRIGEMINAL NERVE: Facial structures
Blood vessels within head
Anterior tongue

OCCIPITAL NERVE: Posterior head and neck
Upper cervical structures

VISCERALLY SENSITIZED PAIN SYNDROMES

- Irritable Bowel Syndrome
- Pelvic pain syndromes
  - Interstitial Cystitis
  - Vestibulitis
  - Chronic prostatitis

Mayer, 2011
PREDICTORS OF ABNORMAL PAIN PROCESSING

- History and examination:
  - Demonstration of "non-anatomic" territory of pain
  - Depression or other preexisting mood disorder
  - Distressed socioeconomic status
  - Overall poor life coping status and satisfaction
- Active emotional distress
  - Particularly anxiety and fear (of the consequences or significance of an injury)

- Preexisting pain processing disorders:
  - "Fibromyalgia-ness"

- Prior surgical complications or failure to resolve pain after previous surgery

Carroll LJ, Pain 2004
Von KorffM, Pain. 2005
Carragee EJ, Spine J 2005
Clauw, D. JAMA 2014

THE JOURNEY:
ACUTE INTO CHRONIC SUFFERING

CHRONICIZATION TIMELINE:
ACUTE ➔ CHRONIC IN 90 DAYS

Persistent nociceptive activation alters peripheral and central pain processing
- "Wind-up"
  - Peripheral and spinal
- "Recruitment"
  - Viscero-somatic
  - Somatosensory-sympathetic
- "Neuroplastic" changes
  - Re-mapping via Connectivity changes
PHANTOM LIMB
“CORTICAL RE-ORGANIZATION”

Touching specific areas on the face of a person with an amputated arm will often evoke precisely localize sensations in the fingers.
Ramachandran 2005.

PHANTOM LIMB MIRROR TREATMENT

- Mirror visual feedback (MVF) in a patient with an amputated left arm

Ramachandran 2005

CASE 3

18 year old high school runner, twisted ankle
Avulsion ankle sprain injury
Week 2 intense pain
- Allodynia
- Erythema, mottling, and intermittent blanched cyanosis
- Hyperhidrosis
- Abnl skin temperature
CENTRAL SENSITIZATION:
COMPLEX REGIONAL PAIN SYNDROME (OR “RSD”)

Coupling somatic primary afferents with sympathetic neurons:
- Interneuronally
- Increased local blood flow
- Increased systemic output of epinephrine

Heightened pain sensitivity and response
Pain spatially correlated with signs of autonomic dysfunction
- Abnormal blood flow and sweating
- Skin and nail dystrophy

SENSORY DISCRIMINATION TRAINING

The effect of tactile discrimination training is enhanced when patients watch the reflected image of their unaffected limb during training.

"Tactile training imparted long-term improvement in tactile acuity when patients watched the reflected image of their unaffected limb in a mirror during training."

"In patients with phantom limb pain or complex regional pain syndrome (CRPS), sensory discrimination training increases tactile acuity, normalises cortical reorganisation and decreases pain."

Moseley GL, Wiech K. Pain 2009

CASE 3

43 year old man with back and bilateral leg pain
Axial, paravertebral aching; intermittent bilateral non-dermatomal leg pain
Sleep poor
Mood angry
s/p 3 spine surgeries: lam'y, revision, fusion
Exam: paravertebral tenderness, reduce ROM, no pathologic reflexes, pain inhibition
DX: ?
THE VALUE OF MAGNETIC RESONANCE IMAGING OF THE LUMBAR SPINE TO PREDICT LOW-BACK PAIN IN ASYMPTOMATIC SUBJECTS
A SEVEN-YEAR FOLLOW-UP STUDY
By David E. Robinson, MD, Kenji M. Ochi, MD, Mt. Asaaki, MD, Y. Ikuta, MD, Y. Ohtsuka, MD, T. Tsuchida, MD, and H. Nishino, MD

Results: Of the 115 subjects who returned the questionnaires, thirteen (5%) had no back pain. Low-back pain was present in ten subjects during the seven-year follow-up period. The MRI scans of these subjects demonstrated various degrees of disc degeneration, vertebral endplate fissure, annular fissure, and posterior longitudinal ligament. 

MRIs don’t count
Asymptomatic
- HNP: 25-50%
- Extruded: 1-18%
- Degeneration of disc: 25-70%
- Vertebral endplate changes: 10%
- Annular fissure: 14-33%

From Carragee 2005

CLBP AND SPINAL PAIN SYNDROMES

THE FAILED SURGICAL SPINE PAIN STORY

- ≥ 1 surgeries to neck/back with poor pain outcome
- Hyper-Nociceptive Milieu
  - Hardware, pseudoarthroses, adhesions
  - Abnormal biomechanics by default
- Central Sensitization Syndrome
  - Neuropathic reorganization
- Abnormal biomechanics by default
- Pain overtakes life
REGIONAL GRAY MATTER DENSITY DECREASES IN CLBP

“THE CHRONIC PAIN BRAIN”

PAIN INJURES THE BRAIN: GRAY MATTER DECREASE COMPARED TO MATCHED HEALTHY CONTROL
**OPIOID TREATMENT GUIDELINES**

WA State Agency Medical Directors (AMDG) Opioid Treatment
Guideline
Published online in April 2007; updated 2010

[Image of the guideline cover]

Southern Oregon Opioid Prescribers Group
Published online May 2013

[Image of the guideline cover]

www.agencymedicaldirectors.wa.gov/or, Google: "AMDG Opioid"

**IMPROVED ACCESS TO PAIN SPECIALISTS**

**UW TELEPAIN**

Contact Information: Cara Towle RN MSN ctowle@u.washington.edu

or search: uw telepain

Sessions every Wednesday noon-1:30

**MULTIDIMENSIONAL PAIN ASSESSMENT**

- Assess Pain, Function, Mood, Sleep, and Risks at every relevant encounter

- 5 Quick Tools:
  1. Pain Intensity NRS
  2. Functional Interference NRS
  3. PHQ-4
  4. Sleep
  5. Opioid Risk Tool
  6. MED calculator
PAIN INTENSITY
PAIN INTERFERENCE WITH FUNCTION

**Pain Intensity (NRS)**

**Activity Interference**

From 2010 WA State AMDG Guidelines

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MEASURING MOOD

**PHQ-4**

Score ≥ 6 needs attention!

- Anxiety
- Depression

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POST TRAUMATIC STRESS DISORDER

**“PC-PTSD”: 4 QUESTIONS**

In your life, have you ever had any experience that was frightening, horrible, or upsetting, that in the past month you:

1. Have had nightmares or thought about it when you did not want to?
2. Tried hard not to think about it or went out of your way to avoid situations that reminded you of it?
3. Were constantly on guard, watchful, or easily startled?
4. Felt numb or detached from others, activities, or your surroundings?

½ yes = positive screen
OPIOID MISUSE RISK

Administration
- On initial visit
- Prior to LA Opioid Therapy

Scoring
- 0-3: low risk (6%)
- 4-7: moderate risk (28%)
- >8: high risk (> 90%)

TREATMENT ADHERENCE MONITORING
WHEN TO DO URINE DRUG TESTING

- Perform at initiation of all chronic opioid treatment
- ≤90 days of continuing opioid prescription
- Perform at intervals based on risk
  - low: ≤1-2/year
  - moderate: 2-4/year
  - high: monthly ± prn
- Document and track aberrancies

https://depts.washington.edu/anesth/education/forms/pain/UW-UDTinterpretationalgorithm.pdf

TREATMENT OUTCOME TRACKING
UW PAINTRACKER™
SUMMARY

1. “Chronic pain” differs from “acute pain”
2. Geno-bio-psycho-social events contribute to chronicization.
3. Abnormal descending modulation is key to the pathophysiology of central sensitization
4. Chronic overlapping pain conditions often co-occur and can help make the “syndromic” diagnosis of central sensitization.
5. Measure pain, function, mood, risk, and treatment adherence to assess chronic pain, especially when presents centralized.
6. Help is accessible through telemedicine platforms when pain is poorly controlled, poor pain outcomes, and/or high risks.