Mechanism of Persistent Pain and Evidence-based Treatment

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Disclosure

• No financial interests or affiliations with any pharmaceutical industry or manufacturer to disclose.
Objectives

- Sensory signal for tissue injury
- Pain as an output
- Peripheral mechanisms
- Central mechanisms
- Treatments

Tissue Damage = Pain Intensity
Rene Descartes - 1664
- Pain is a sensation coming from within the body itself
- Like a thread running from the skin to the brain

Perception
Transmission
Modulation
Transduction
Adaptive Model Applied to Persistent Pain

- Over the last 20+ years this approach has led to increased use of medications, injections and surgeries

Outcomes

According to a US Medical Expenditure Panel Survey, between 1997-2005:

- rise in injections, fusions & opioids
- increase in functional limitations, mental health disorders, work & social limitations

US - Public Health Crisis

Tissue Damage ≠ Pain Intensity

Compared to civilians with similar injuries:
- soldiers needed 5x less morphine
- fewer complaints

Fibromyalgia
- Pain in muscles and joints
- Negative tissue, laboratory and imaging findings
- Associated with poor sleep, depression and fatigue

Most persistent pain conditions correlate poorly with tissue damage
OA of Knee

- Poor correlation: x-ray and symptoms (1)
- Up to 50% of those with radiographic OA have no pain.
- 10% with mod-severe pain have normal x-rays.
- Psychological factors didn’t explain difference between symptoms and structure (2).
- NSAIDs, APAP, opioids have small effect size (3,4).
- Arthroplasty did not predictably relieve pain.
- 20% of hip and 25-30% of knee replacements don’t get improvement in pain (5).

Mature Organism Model
Louis Gifford

- Brain samples itself...
- Past experiences
- Knowledge
- Beliefs
- Culture
- Past successful behaviours
- Past successful behaviours observed in others

Output =
Altered behaviour
Altered physiology

The Neuromatrix
Ronald Melzack

Input
- Sensory
- Cognitive
- Limbic

Body-self neuromatrix

Output
- Pain
- Action
- Stress regulation
Pain is produced by coordinated patterns of nerve impulses - Neurosignatures/tags

- Subsignatures are impressed and transformed into larger neurosignatures
- Neurosignature produce a continually changing stream of awareness
- Neurosignatures are translated into movements that bring about a desired goal.
Cortical Areas Involved in Pain Processing

**Somatosensory cortex:**
- Discrimination and intensity
- Where is the message coming from? How bad is it?

**Insular cortex:**
- Integrates sensory, emotional and cognitive states
- Empathy for others' pain
- Involved in suffering aspect of pain (distress, fear)

**Anterior cingulate cortex:**
- Registers unpleasant feeling when things go wrong physically or emotionally

**Prefrontal cortex:**
- Processes pain signals rationally and plans action.

**Medial prefrontal gyrus:**
- Focuses on negative personal implications of pain.

**Right orbital frontal cortex:**
- Evaluates sensory stimuli and decides on response, particularly if fear is involved.

**Thalamus:**
- Receives pain signals from spinal cord and relays to the higher brain centers.


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Related content:
- [Cortical Areas Involved in Pain Processing](#)
- [Prefrontal cortex](#)
- [Medial prefrontal gyrus](#)
- [Right orbital frontal cortex](#)
- [Thalamus](#)
Persistent Pain – a different state of the brain

Somatosensory cortex and ACC
- become bigger
- metabolic activity
- neurotransmitter release
- widespread pain with variable intensity expression
- shift toward more emotional aspects pain
- cure responsiveness
- behavioral and cognitive changes
- contribute to allodynia and hyperalgesia

Neurons that wire together—fire together

Genetic Determinants
Pain Sensitivity in the general population

- Volume control - setting for how brain and spinal cord processes pain (1)
- Set by the genes (2-4), and modified by neurohormonal factors and neural plasticity
- The higher the volume control setting, the more the pain is experienced, irrespective of peripheral nociceptive input


Social Determinants

▲ Integration
▲ Activities
▲ Support
▲ Environmental Stressors
▲ Relationships
▲ Cognitive Decline
▲ Infectious disease
▲ Reoccurrence of CA
▲ Life stress
▲ Better prognosis for life-threatening disease
▲ Live Longer

Summary

1. Persistent pain poorly ≠ tissue damage

2. Neuromatrix and MOM theory of pain
   - Inputs - sensory, cognitive and emotions are cyclically processed
   - Produce outputs - pain perceptions including location, intensity and meaning
   - Outputs become new inputs

3. Genetic and Social factors

4. “Pain is then an unpleasant, conscious experience that emerges when the sum of all available information suggest a body part needs to be protected.”

Approach to Treatments

Best outcomes use combination of treatments - multidisciplinary team or collaborative care models (1,2,3).

Patients need ongoing evaluation, education and reassurance.
   - Set reasonable expectations for treatment response.

Treatments on average result in 30% decrease in pain (4).
   - Even a partial response of 30% can be clinically significant and improve the patient's quality of life (5).

### Peripheral vs Central Pain Mechanisms

<table>
<thead>
<tr>
<th>Peripheral</th>
<th>Central</th>
</tr>
</thead>
<tbody>
<tr>
<td>location</td>
<td></td>
</tr>
<tr>
<td>• Mechanical</td>
<td>• CNS</td>
</tr>
<tr>
<td>• Inflammatory</td>
<td>• Amplification</td>
</tr>
<tr>
<td>• Amplification or processing problem</td>
<td></td>
</tr>
<tr>
<td>examples</td>
<td></td>
</tr>
<tr>
<td>• Surgical pain/trauma</td>
<td>• FM/HA/IBS/IC/LBP</td>
</tr>
<tr>
<td>• OA/RA</td>
<td></td>
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<tr>
<td>population</td>
<td></td>
</tr>
<tr>
<td>• Older</td>
<td>• Most common</td>
</tr>
<tr>
<td>• Younger</td>
<td></td>
</tr>
<tr>
<td>treatments</td>
<td></td>
</tr>
<tr>
<td>• Nondrug – PT</td>
<td>• Nondrug - sleep/activity</td>
</tr>
<tr>
<td>• Drug - NSAID’s/Opioids</td>
<td>• Drug – AntiSz/Antidep</td>
</tr>
</tbody>
</table>

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### Passive vs Active Treatments

<table>
<thead>
<tr>
<th>Passive</th>
<th>Active</th>
</tr>
</thead>
<tbody>
<tr>
<td>• surgeries/injections/SCS/ITP “Fix-it approach”</td>
<td>• body activity – activity, PT, HEP, sleep, diet</td>
</tr>
<tr>
<td>• medications</td>
<td>• mind activity – education, CBT, DBT, ACT, counseling, recovery</td>
</tr>
<tr>
<td>• complementary medicine</td>
<td>• slow (months – years)</td>
</tr>
<tr>
<td>• fast</td>
<td>• effort dependent</td>
</tr>
<tr>
<td>• independent of effort</td>
<td>• limited or no coverage</td>
</tr>
<tr>
<td>• covered</td>
<td>• lasting results</td>
</tr>
<tr>
<td>• temporary</td>
<td>• internal locus of control</td>
</tr>
<tr>
<td>• external locus of control</td>
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</tbody>
</table>
Medications

NMDA
- Brain/SC
- Glutamate gated Ca 2+ channels
- Learning, memory and neuroplasticity
- Overstimulation leads to neurodegeneration
- Memantine, dextromethorphan, ketamine (PCP), methadone
Medications Summary

Opioids:
- most effective of all medications
- Limited effectiveness for long term use d/t tolerance
- Most useful for acute pain (surgery/injury), end of life

NSAID’s:
- most effective for inflammation
- Limited effectiveness for long term use d/t toxicity
- Avoid long term use if ineffective

Antidepressants:
- Acts on CNS and SC to increase NE, 5HT, DA
- Neuropathic or central pain states

Antineuroleptics:
- Acts on CNS and SC
- Neuropathic or central pain states

Muscle Relaxants:
- Acts as CNS depressant
- Avoid long term use

Other:
- NMDA antagonist – Namenda, Ketamine
- Cannabinoids
- Neuropathic or central pain states

Physical Activity

- Improves conditioning
- Mobilizes joints
- Improves tissue health
- Promotes relaxation
- Reduces flare-ups
- Improves mood
- Reduces anxiety and depression
- Releases endorphins

**Exercise and Prevention**

Exercise is protective in transitioning from acute pain to chronic pain:

- Activation of opioid receptors in the descending inhibitory pathways
- Release of macrophages and increased IL-1- (anti-inflammatory cytokine) reducing nociceptor sensitization.

(1) Sluka KA, et. al., 2013 J Appl Physiol, 114 (6), (2) Leung, A., et. al., 2013, Pain, 14 (4)

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**Affect Regulation - Cognitive Treatments**

Pain education/information
- Alters beliefs and attitudes
- Pictures, examples and metaphors

Cognitive Behavioral Therapy
- Unhelpful thoughts and behaviors contribute to negative feelings increasing sensitivity to pain.
- Improve coping skills, increase confidence and self-efficacy, by changing how individuals behave in response to pain.

Acceptance and Commitment Therapy

- Fundamental tenet: pain cannot be avoided.
- Struggling causes more suffering.
- A mindfulness based approach
  - observing thoughts and feelings without trying to change them.
  - then behaving in ways consistent with valued goals and life directions
- McCracken et al. (2004) - Chronic Pain Acceptance Questionnaire (CPAQ) showed two important aspects of pain acceptance
  1. willingness to experience pain
  2. engaging in valued life activities even in the face of pain.
- Acceptance of pain correlated with:
  - lower pain intensity,
  - less depression and pain related anxiety
  - greater physical and social ability
  - less pain avoidance
  - better work status.
- And that acceptance of pain was not related to pain intensity.


Sleep

- Essential for normal physiologic functioning.
- Common causes: primary insomnia, periodic limb movements, OSA or central sleep apnea.
- Pain worsens sleep and sleep deprivation/fragmentation increases pain perception.
- Addressed with medications (NSAIDS, opioids, Anti Sz, Anti-depressants) or cognitive therapies (CBT).

NKY Tang. CE Goodchild, LR Webster, Treatment of Chronic Pain by Integrative Approach, 2015
Integrated Approach

Basic components

• Medical
• Physical therapy
• Behavioral health

Summary

• Persistent pain
  - complex neurobiological phenomena
  - multidimensional (biopsychosocial)
  - best explained by the neuromatrix and mature organism model
  - changes treatment strategies

• Treatments
  - Reduce nociceptive input (may be a small part of the problem)
  - Medications and procedures are of limited benefit
  - Movement is essential: mind and body
  - Change environment, if possible (stress-reduce threat)
  - Integrated strategy is optimal
Pain and Trauma: A Behavioral Approach to Trauma Resolution

Anderson Rice, LPC, CADC1
Kaiser Permanente
Department of Addiction Medicine

Descriptions of Trauma

• “Trauma happens when the organism is strained beyond it’s adaptational capacity to regulate states of arousal.”

• “Humans possess regulatory mechanisms virtually identical to those in animals, these systems are often overridden by net-cortical inhibition (through the rational mind). This restraint leads to the formation of a constellation of symptoms including pain, patterns bracing and collapse, cognitive dysfunction, anxiety, and a sense of intrusion.”

- Peter Levine
“Traumatized people chronically feel unsafe inside their bodies: The past is alive in the form of gnawing interior discomfort. Their bodies are constantly bombarded by visceral warning signs, and, in an attempt to control these processes, they often become expert at ignoring their gut feelings and in numbing awareness of what is played out inside. They learn to hide from their selves.” - Bessel van der Kolk

For her project titled Marked, photographer Claire Felicie shot close-up portraits of the marines in the 13th infantry company of the Royal Netherlands Marine Corps before, during, and after their deployment from 2009-2010. She then arranged the portraits into haunting triptychs that show the toll war has on a person’s eyes and face.
A Healthy Nervous System – Observables

- The person will be relaxed and at ease
- The body and its senses will be relaxed, yet alert
- They are present through all layers of self (physical, emotional, psychological, spiritual)
- Physiology is appropriately responsive to a variety of circumstances
- Responses are fluid and resilient
- Available for connection, emotionally stable
- Experience of having choices and options
- Capacity for healthy relationships

Somatic Experiencing – Peter Levine, PhD

- Massive energy is mobilized as part of the survival system
- Animals spontaneously ‘discharge’ this energy
- Prey animals are rarely traumatized
- SE facilitates that completion of self-protective motor responses
- Not driven by content, or ‘re-telling’ of the story
- Slow and supported
**Fight** - sympathetic nervous system (SNS)

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**Freeze** – parasympathetic nervous system (PNS)  
(emergency shutdown)

**Social Engagement** – parasympathetic nervous system (PNS)

(Stephen Porges – Polyvagal Theory – Vagus Nerve)

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You have a tense interaction with somebody and voices are raised.  
**SNS arousal**  
You decide to take a break from the conversation and go for a walk to ‘clear your head’.  
**PNS response increases**
Traumatic event occurs, and traumatic stress is not discharged. System becomes dysregulated PTSD.

Symptoms of Un-Discharged Traumatic Stress

**Sympathetic (SNS) “Fight/Flight”**
- Anxiety/Panic
- Hypersensitivity
- Exaggerated Startle Response
- Inability to relax
- Restlessness
- Hyper-vigilance
- Digestive Problems
- Emotional Flooding
- Chronic Pain
- Sleeplessness
- Hostility/Rage

**Parasympathetic (PNS) “Freeze”**
- Depression
- Flat Affect
- Lethargy/Deadness
- Exhaustion/Chronic Fatigue
- Disorientation
- Disconnection
- Dissociation
- Pain
- Low Blood Pressure
- Poor Digestion
**Fight** - sympathetic nervous system (SNS)

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Social Engagement – Creating Conditions

• **Ventral Vagus Nerve** – “getting the ventral vagal system online”

• **Social Engagement** – “down-regulates” the sympathetic (SNS), calming, often this is a first attempt to create safety. Unique to mammals.

• How does this impact how we interact with our patients?

• How do we start our sessions/appointments?

• What is the content of our patient discussions?

• Tone of voice? Body language?
• How do we roll with resistance?

• What are their interests?

• What is their body language telling us?

• How are the surroundings?

• What was going on in your life when the pain started?

• “I think this is important, but…”

• Many patients report that they don’t feel like their MD believes them
Common Symptoms:
Traumatic response coupled with physical injury

• Recovery may be slow
• Scars may appear that they’ve not healed properly
• General amnesia about that happened
• Fragmented reports of the experience
• Unrealistic fears associated with the experience
• General malaise
• Often ill
• Chronic inflammation
• Hypochondriasis

Syndromes

Examples of common syndromes with possible sympathetic/parasympathetic-mediated dynamics include:

• Migraines
• Fibromyalgia
• Autoimmune disorders
• Pain syndromes
• IBS
• Chronic fatigue
Other Approaches:

Trauma Treatment

Exposure Therapy:

Rooted in behaviorism

Gradual exposure to stimulus in order to minimize fear

Imaginal Exposure Therapy
EMDR – Eye Movement Desensitization and Reprocessing

CBT - Cognitive Behavioral Therapy with a trauma focus – recognizing negative thought patterns and beliefs in order to change behavior

DBT - Dialectic Behavioral Therapy – embraces the seemingly opposite ideas of acceptance and change with skills that are taught to modify behavior, feelings, thoughts and beliefs.

Distress tolerance
Emotional regulation
Mindfulness
Interpersonal effectiveness
The tension of opposites: acceptance/change
pleasure/pain  emotions/thoughts
Example: “I can receive negative feedback as a valued employee”

Other Therapeutic Modalities
Speaking of Mindfulness...what about pain? Depression? Anxiety?

**MBSR:** Mindfulness Based Stress Reduction

**ACT:** Acceptance and Commitment Therapy

Mindfulness means paying attention in a particular way: on purpose, in the present moment, without judgement.

- Jon Kabat-Zinn
Mindfulness Based Stress Reduction:

- Founded in 1979 by Jon Kabat-Zinn
- Began accepting referrals from MD’s at the Umass Medical School for pain patients
- While rooted in Zen Buddhism, MBRP is a secular form of mindfulness

**ACT: Acceptance and Commitment Therapy**

**Acceptance**
- Trying to get rid of your pain only amplifies it
- Distinguishes pain from suffering
- It is the struggle with pain that causes suffering

**Commitment and Values-based living:**
- Are you living the life you want to live?
• Development of an ‘observer-self’
• Building psychological flexibility in the context of the patient’s values
• Learn to notice thoughts rather than acting on them
• Is this even true?
  “I can’t do anything useful because of my pain.”
• The pain may still be there, but the patient’s relationship to it can change

www.psychologytoday.com

www.traumahealing.org

www.emdria.org

http://www.findcbt.org/xFAT/
Book Recommendations:

In an Unspoken Voice: How the Body Releases Trauma and Restores Goodness
  - Peter Levine, PhD

The Body Keeps the Score: Brain, Mind, and Body in the Healing of Trauma
  - Bessel van der Kolk, M.D.

The Body Bears the Burden: Trauma, Dissociation, and Disease
  - Robert Scaer, M.D.

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Pain and Trauma: Creating Safety in Patient Care

Role of Pain Education

NORA STERN, MS, PT
PERSISTENT PAIN PROJECT
PROVIDENCE HEALTH AND SERVICES
Disclosure

Providence Health and Services is packaging this pain education material for training and use to outside entities

Nora.stern@providence.org

Context and meaning

Childbirth vs. Trauma
PARADIGM SHIFT

PAIN IS AN OUTPUT FROM THE BRAIN AND NERVOUS SYSTEM

ALL PAIN IS REAL PAIN

NOCICEPTION IS NEITHER NECESSARY NOR SUFFICIENT FOR PAIN

PAIN ≠ HARM

adapted from material from G. Lorimer Moseley: Understand and Explain Pain course material 2010
What you say matters!!

Talking about pain changes beliefs
Changing beliefs changes threat value
Changing threat value changes the pain experience

Managing and Coping with Chronic Pain

Understanding and Treating Persistent Pain

Reference: "Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research," Board of Health Science Policy, Institute of Medicine, of National Academies, Washington 2011
THREAT!

MRI and X-Ray results

Fear of movement

Struggles in living with pain

Medication is the only thing that can help me

Safety and Hope

Understand pain

Quiet your worry

Kisses of time

Sore, but safe

Bring some FUN back in your life!
Improvement in movement and function with pain education

Before Intervention:
10 degrees forward bend

After the 1st session: 72 degrees forward bend
<table>
<thead>
<tr>
<th>Patient says:</th>
<th>Threat</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>I’m worried about my xrays.</td>
<td>Your x-ray looks pretty bad.</td>
<td>Half of people with joint degeneration have no pain.</td>
</tr>
<tr>
<td>I can’t do _____.</td>
<td>You’d better avoid that then.</td>
<td>Because your system has gotten too good at protecting you, that pain does not mean that you are causing yourself harm. Let’s talk about slowly introducing activity a little at a time.</td>
</tr>
<tr>
<td>Medication is the only thing that will help me.</td>
<td>I have to stop your medication. There is nothing else I can do.</td>
<td>We now understand pain a bit differently. It turns out that there are a lot of things that produce pain, so I am thinking that if we explore together, we can find some things that will start to help you get back to the things you enjoy.</td>
</tr>
</tbody>
</table>

It’s not safe for me to be active?
Pain and Trauma: Creating Safety in Patient Care

Role of Rehab  
Best Practice

NORA STERN, MS, PT  
PERSISTENT PAIN PROJECT  
PROVIDENCE HEALTH AND SERVICES

Providence Rehab for sensitized pt:

- Pain Education  
  - Classes, videos, written material and phrasing

- Physiological quieting  
  - Mindfulness including videos for home use

- Pacing and Graded Exposure
Pain Education made easily accessible: Videos for inpatient, outpatient, home health, written material and classes

Physiological quieting (relaxation training)
Pacing

Ideal rehab experience for patient with trauma history

- Decrease threat
- Less information, more experience
  - Pacing focused on non-threatening activity w graded exposure
  - Physiological quieting
  - Communication w Behavioral Health and Primary Care
Prepping the patient and working together: Primary Care, Rehab, Behavioral Health

- Pain education: framework for care plan and for decreasing opiates
  - Using the same language, aligning the message
- Consider patient motivation
- Timing of rehab treatment with complex mental health needs. eg severe depression, anxiety, high catastrophizing, trauma
- Strongly endorse parts of your plan and ask about them at followup sessions

WHEN TO TAKE YOUR HANDS OFF THE PATIENT
New benefits through OHA

All back pain:

- 4 visits of chiropractic, PT, or acupuncture

If assessed as having psychosocial indicators of chronicity
- (eg STarT tool: medium to high risk):
  - Up to 30 visits of PT, chiropractic, acupuncture

Choosing Treatment Options and making a plan of care

Choosing what/when
Case discussion
38 year old Caucasian female, married, no children

History
- Physical and sexual abuse
  - Including torture and incest, with PTSD Dx.
- Multiple foster homes during pre-teen years.
- In recovery for Alcohol Use Disorder (severe)
  - Active member of AA
  - Support group, > 1 year of sobriety.

Symptomology:
- Cannot handle being in crowds
- Acute startle response
- High sympathetic and parasympathetic arousal simultaneously
- Emotionally labile
- Physical tightening in her chest, feels like she is being hit.

Chief complaints of pain:
- Low back pain x 10 years
- Spread in last 3 years to hips and up into upper back
- Hard to tell where it is sometimes.
- Also headaches and shoulder and neck pain.
- Entire body diagram black, with places circled at low back and neck, head, shoulders.
- 15 years of pelvic pain, which you learn on the second session.

Function:
- Not working.
- Feels like she needs to be doing more around the house, tries to, ends up in bed or watching TV because she is so painful.
- Is afraid of making her pain worse so does as little as possible.

Xrays:
- Multiple, shows moderate degeneration throughout spine.
Other important information:

- Used to ride her bike but is afraid of doing so because of pain.
- Wants to be able to return to walking her dog in the woods, but doesn’t walk much now.
- Spouse is supportive of the work she is doing.
  - Has pain with sex and avoids sex
  - Has a close group of friends and a supportive recovery community.

Discussion of case