Leading from the Edge:
Opioids, Pain and Addiction
OSPA Conference "SEA-ME"
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Objectives

• 1. Understand more about how pain changes the brain.
• 2. Understand more about how opioids change the brain.
• 3. Understand more about how pain patients behave and what drives aberrant behavior.
• 4. Understand evidence-based approaches to caring for patients with pain who may or may not meet criteria for a substance use disorder.

Pain Changes the Brain

• "Glialopathic" Pain Generation

  • What Happens:
    • Chronic overstimulation of nociceptive neurons leads to CS remodeling via neuroplasticity.
    • Sessile microglial cells respond to high-level neuronal stimulation and become activated.
    • This activation becomes the signal for neuronal destruction.

  • Bottom Line: Persistent pain physically restructures the brain, and transforms the brain's perception of the body.
Microglial Cells Modulating CNS Transformation

Neuroimmunomodulatory dysfunction of inflammatory cytokines within the CNS

Chronic Back Pain: Gray Matter Loss in DLPFC and Thalamus

- Patients with CBP had 5%-11% less neocortical gray matter volume, equivalent to 10-20 years of normal aging 1
- Executive working memory areas have a role in pain inhibition 2

Complex Regional Pain Syndrome

Swelling and color changes
Increased sweating
Usually a single limb
Hair and nail growth changes
Thermal variance

Courtesy of Professor Candy McCabe, Consultant Nurse, Royal National Hospital for Rheumatic Diseases, Bath, UK
This piece represents my pain since sustaining severe spinal injuries. Sometimes the pain feels like my spine is rippling up and down like a broken electrical track full of electricity.

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How do opioids change the brain (and spinal cord)?

- Opioids bind to several sub-sets of receptors in the Brain and Spinal Cord.
  - Mu- Receptor → Primary analgesic pathway
  - Kappa- Receptor → Primary hyperalgesia/tolerance
  - Sigma-Receptor → Secondary analgesic pathway
  - Delta-Receptor → Accessory pathway

- Tolerance and hyperalgesia immediately begin with the first dose of opioid.
- G-protein linked Ca/Mg channel hyper-polarization
- Receptor down-regulation

- SALIENCE - The state of being prominent.
  - Analgesia is a novel experience
  - Reward → Imprint → Repeat

The “experience” of opioid analgesia

- Occurs as a potentially novel and unique experience for each patient with each exposure.
- Opioid analgesic → Mid-brain dopamine release
  - The SAME Survival-Based Reward/Reinforcement pathway that leads to addictive drive/behavior.

  The human midbrain is tasked with integrating the ‘intensity’ of the pain signal with the ‘intensity’ of the analgesic signal.

  Mismatch = Euphoria or Inadequate Analgesia

The importance of understanding tolerance/dependence
The importance of understanding tolerance/dependence

Opioid "Comfort" Zone

- Refers to the physiologic state of requiring the presence of opioids in order to maintain homeostasis of CNS dopamine levels.
- Withdrawal is the hallmark of "Opioid deficiency" in the setting of physiologic dependency.
- Severe emotional distress, Depression/Anxiety
- Autonomic Instability
  - Sweating, tremor, diarrhea, mydriasis, excessive tearing and rhinorrhea.
- PAWS "Post-acute withdrawal" symptoms persist for months.
- Deeply Traumatic experience

What is Opioid Dependence?
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What is (Opioid) Addiction?

- We now use the term:
  - "Opioid Substance Use Disorder"
- Mild, Moderate, Severe
- Fundamentally, ADDICTION is the following:

Compulsive Use Despite Harm
- Rooted in the concept of "Salience" ➔ That which is 'important'
  - Addiction ➔ Related to self-medication, chemical coping, regulation of emotions.
  - Physical Dependency ➔ Drives tolerance and behavior that can look like Addiction and transforms into Addictive behavior.

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Addiction: Moderate to Severe Substance Use Disorder

- TED Talk “Addiction: A disease of Self-will.” Meaning there is a total loss of volitional control over behavior. Dr. Nora Volkow, Director NIDA.
- A total loss of self-determination
- Drug seeking and repetitive use becomes a conditioned response.
This is Addiction

CEREBRAL ACTIVATION AND OPIATE CRAVING


CEREBRAL ACTIVATION AND OPIATE CRAVING

How do patients with access to C.O.T. Behave?

- 1. Est. 35% of patients taking C.O.T. meet criteria for Opioid Use Disorder.
- 2. 71% of claimants on C.O.T. > 3 months are not taking their medication as prescribed.
- 3. Among “chronic pain population” with sample of 939,000 urine drug screens;
  - 38% medication was absent
  - 29% non-prescribed opioid medication
  - 27% medication levels higher than prescribed
  - 11% illicit drugs

“Red flags” in Chronic Opioid Therapy

- 1. Undue focus on medications
  - Refusal of other modalities or non-opioid medications
- 2. Increasing reports of pain, decreasing function.
- 3. Prescription Drug Monitoring Reports
  - Multiple prescribers
- 4. Morphine equivalent >120mg/day
  - 9-fold increase in death doses above 120mg/day

The torment of daily migraine took away many things from my life, but it gave me a new way to express myself. My deepest hope is that my work could speak to others in a way that words—and prescriptions—cannot. ©2007 A. Heather Davulcu
What is Opioid Hyperalgesia?

- Phenomenon that is different from opioid tolerance.
- Evolution of CNS to yield increased sensitivity to historically non-noxious stimuli (allodynia).
- Mechanism: NMDA receptor activation by opioids directly and indirectly via multiple membrane complexes.
  - May be antagonized by NMDA-R antagonists
    - Ketamine, dextromethorphan
    - Methadone has inherent NMDA-R antagonist properties
    - Buprenorphine is a potent Kappa receptor antagonist
- Take Home: Opioids making pain worse. More opioids are not the answer...

Opiate induced hyperkatifeia

- Neuroadaptation in brain reward systems which parallels opiate hyperalgesia and may indicate a transition to addiction vulnerability.
- Opiate misuse in the context of pain management produces a hyperactivity in reward pathways.
  - Mood changes linked directly to opiate therapy in the setting of a pain diagnosis.
- Continuous engagement of opponent processes leads to destabilization of homoeostasis.
  - Analgesia vs. “treatment of underlying emotional state.”
  - Pre-existing emotional state vs. one induced by the reward experience.

Opiate HYPERKATIFEIA

- OVER TIME......
The challenge(s) for the opioid dependent patient?

- 1. Cope with their legitimate pain experience.
- 2. Take medicine appropriately.
- 3. Not use other drugs or alcohol.
- 4. Cope with opioid side-effects.
  - Tolerance, Hyperalgesia, Hyperkatefia
  - Constipation, sleep-disturbance, loss/diversion risk
- 5. Get their refill always on-time.

**ALWAYS AVOID WITHDRAWAL**

The challenge(s) for the opioid prescriber?

- 1. Primum non nocare.
- 2. Patient/Family Expectations
  - Secondary gain?
- 3. DEA/State Compliance
  - Documentation (The Four A's)
  - Drug Screening, PDMP, Material risk consent forms
- 4. Practice demands ➔ "stuff" rolls downhill…
- 5. Making difficult decisions and confronting patients about the need to make changes.
  - MOST IMPORTANTLY in the patient that doesn’t have ‘issues’ with their opioids.
The challenge(s) for the medical provider?

1. Do something, anything other than prescribe an opioid...
   - Patient population in Oregon/Washington, ‘primed’
2. Traditional Physical Treatment modalities;
   - Acute vs. Chronic
   - Physical Medicine → TENS, PT, Hydrotherapy, Massage
3. Mental Health modalities;
   - Counseling, group therapy, Mindfulness-Based Meditation
4. Complementary Medicine;
   - Acupuncture, Naturopathy, Homeopathy

If you decide you are going to Rx Opioids....

1. Must ASSESS your patient completely.
   - Opioid Risk Tool- ORT
   - Substance Use/Abuse History
   - Urine Drug Screening
   - Past Medical History
     - Old Records
     - Prescription Drug Monitoring Report
     - Pharmacy
     - Imaging
2. Discuss the facts about opioids.
   - Grade C (at best) → Unlikely to be of benefit after 30 days.
   - Physical Dependency requiring difficult detoxification.

If you decide you are going to Rx Opioids....

3. Addiction Risk
4. Risk of Overdose Death if/when diverted or misused.
   - Security of medication
   - Pill counts
   - Urine Drug Screening with Ethyl Glucuronide (ETG)
5. EXPECTATION of abstinence from Alcohol.
6. Discuss how/why you will discontinue opioids.
   - Absence of evidence that they are helping functionality.
   - Aberrant behavior or evidence of a “shift in the relationship.”
   - Maximum MED of 90mg, define what that means.
   - You will refer back to these discussions in the future.
Identification of Substance Use Disorders-In Patients with Pain

1. SUDs may or may not be present.
   - Past history
   - Tobacco
2. Often the “leverage” used to change therapy.
   - Anecdotally, often used as an excuse to abandon patients.
3. Tools for identification;
   1. Prescription Drug Monitoring Reports
   2. Urine Drug Screening
   3. Pill counts
   4. Validated Scale- SOAPP-R

Changing Course in Opioid Therapy

• Follow-up evaluation and considerations for intervention.
  • Has salience for opioids changed?
  • Is there behavioral aberrance?
  • Affective change in patient?
  • Hyperalgesia?
  • Functionality?
  • Exploration regarding the resistance to change.
    • Secondary gain?
    • Substance Use Disorder?
    • Withdrawal avoidance?

Changing Course in Opioid Therapy

• 1. These medications change neurobiology profoundly.
• 2. Nearly all patients have been through a withdrawal experience at some point.
  • PTSD-like response for some patients
  • Programmed withdrawal avoidance
  • Resistance to change is default pathway
• 3. Introspective/perceptive impairment.
A spectrum of patients with pain.

- Disabled 58 y.o.
- Six spine surgeries: Cervical+ Lumbar
- Asperger’s syndrome
- Divorced 37 y.o. 2 kids
- L-Spine w a/p Fusion 4 level C bilat foramenotomies
- College-bound 26 y.o.
- 04-13 bilat laminectomies with posterior fusion of all levels

Who is the patient with Pain?

- Disabled 58 y.o.
- Six Cervical and Lumbar spine surgeries
- Asperger’s syndrome
- Axial spine pain
- Cervical and Lumbar Regions with radiculopathy

- 4 years of opioid acceleration: 100mcg/h fentanyl patch q48h
- 15mg oxycodone 1-2 q4h

The patient’s experience:

- Symptoms: Insomnia, Flushing, sweating and mood changes
- “I don’t like how I feel, I hurt and my memory is changing”
- “I want to try something different?”

Who is the patient with Pain?

- PDMP Report: Compliant
- Primary Care: Compliant
- Salience: None
- Withdraw: Yes
- Diagnoses: Cervical Spondylosis 722.10
- Lumbar Spondylosis 759.20
- Phys. Opioid Dependency

Medications Package:
- Buprenorphine 4mg sl bid
- Hydromorphone 4mg bid prn
- Lyrica 100mg bid
- Cymbalta 90mg qhs
- Tizanidine 4mg qhs
- Topical NSAID prn
Who has a substance use disorder?

College-bound 26 y.o.
C4-T2 bilat laminectomies with
Posterior fusion of all levels
Why?
Presented with fever and progressive dyspnea.....

6th month of IVDA → C4 Epidural Abscess
4 week hospitalization → 6 week SNF → 10 months of rehabilitation
Spastic quadriplegia – ambulatory, loss of all fine motor
- neurogenic bladder, and L. ext. spasticity

Who is the patient with Pain?

Divorced 37 y.o. 2 kids- Manages Retail Store
L-Spine w/ap Fusion- (total of 3 surgeries)
Previous medication package:
Hydrocodone/APAP 10/325 qid
Cyclobenzaprine 10mg bid
Divorce → Loss of insurance → medication access disruption
“I’m sick and by bad hurts, I can’t stand on my feet all day to go to
work”
“I am now uninsured.”

Who is the patient with Pain?

PDMP Report: Compliant
Primary Care: Compliant
Salience: Some (when stressed out)
Withdrawal Yes
Diagnoses:
Cervical Degenerative disc disease 722.10
Lumbar Spondylosis 752.20
Pys. Opioid Dependency

Initial Treatment Plan:
Buprenorphine 1mg q 12hr
Cyclobenzaprine 10mg bid
New Insurance → Butrans 20mcg/h, Lyrica 50mg bid, Trazodone 50mg
12 months later Arms/Hands go numb → DoSavens multi-level Cervical SSD/DID
Post-op → Back to same regimen → Insurance change → “initial plan”

Key Outcome is FUNCTIONALITY
Who is the patient with Pain?

College-bound 26 y.o.
C5-T2 bilateral laminectomies with posterior fusion of all levels.

Why?
C5 Epidural Abscess

Presented with fever and progressive dyspnea…….

4 week hospitalization → 8 week SNF → 12 months of rehabilitation

Spastic quadriplegia – ambulatory, loss of all fine motor
- neurogenic bladder, and L. ext. spasticity

Who is the patient with pain?

PDMP Report: Didn’t have one
Primary Care: Didn’t have one
Salience: Yes- Opioids, THC, Alcohol
Withdrawal: Yes
Diagnoses: Substance use disorder-Severe
- Opioid w physiological dep.
Quadriplegia

Reports persistent craving for opioids with extremity
painless/spasticity
ZERO pain at his operative site

Referred from SNF receiving Suboxone 2mg, Diazepam 10x3, Baclofen, Vistaril,

Month 29: Suboxone 2mg/8mg; Clonazepam 0.5mg qhs, escitalopram 20
Baclofen 10mg tid

Stressors → Month 39 Relapse, Methamphetamine, Psychosis, Lost to Follow-up….

Buprenorphine for pain

• In the setting of a Substance Use Disorder
  • Sublingual Buprenorphine or Buprenorphine/Naloxone 2-24mg
    • (60-720 MED): incomplete cross tolerance due to partial agonism at Mu

• In the setting of a primary pain diagnosis
  • Sublingual: Belbucca (very low MED 20-60)
  • Transdermal: Butrans (very low MED 20-60)
  • Off-label sublingual generic
    • Sublingual Buprenorphine or Buprenorphine/Naloxone 2-24mg
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Concluding Review

• All patients who take opioids are therapeutically dependent.
  • Most will be withdrawal avoidant.
  • Large percentage are addicted to opioids or other drugs/ETOH.
  • Many will eventually declare a need for medical detoxification.
    • MUST consider this therapeutic option in ALL patients.

• If you start opioids ➔ Be clear about WHY?
  • Acute vs. Chronic pain.
  • Analgesic Burden vs. Risk of Reinforcement/euphoria.
  • Recognize that for chronic pain the literature does not support this plan of action.

• Keep taking care of your patient, even if they have or develop a problem while receiving care from you.

THANK YOU

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