Understanding and Assessing Opioid Use Disorder in Patients with Chronic Pain

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Educational Objectives

At the conclusion of this activity participants should be able to:

• Describe a neurobiological framework/explanatory model for patients with chronic pain and opioid use disorder
• Recognize that differentiating opioid use disorder from pain is a complex task
• Identify key features of opioid use disorder
• Describe how to perform an opioid use disorder evaluation in primary care
Case

• 35 yo female with chronic daily migraine and diffuse myofascial pain who has been prescribed opioids for 5 years after the birth of her daughter. The patient has severe depression and anxiety, chronic nausea, history of adverse childhood experience (neglect as a child), and obesity. She is a stay at home mother to her 2 children, but frequently has to put the children in daycare because she can not care for them when she has severe migraines. She is also prescribed chronic high dose benzodiazepines by a psychiatrist.

• The patient has a history of losing her opioid prescription, obtaining opioids from another provider, being allergic to most other pain medication options, missing appointments, and frequently asking for opioid dose increases.
Case: Thought Questions

• Does this patient have pain?

• Does this patient have an opioid use disorder?

• What factors place this patient at risk for an opioid use disorder?

• What can you do to help this patient?
Whatever it’s cause, when pain persists, it often causes secondary problems that can in turn facilitate distress and pain.
As a chronic condition, OUD shares similar challenges as persistent pain.

- Secondary Physical Problems
- Sleep Disturbance
- Substance Misuse
- Anxiety
- Depression
- PTSD
- Functional Disabilities
- Cognitive Distortions
- Increased Stresses

Opioid Use Disorder (OUD)
When OUD and pain co-occur they may reinforce one another. Need to address both to successfully treat pain.
What is the underlying neurobiological mechanism that explains the complex interaction between pain and opioid use disorder?
Understanding Reward and Emotion in Chronic Pain

Reward learning processes may contribute to persistence and amplification of pain

SBP = subacute back pain
CBP = chronic back pain
Neurocircuitry of Substance Use Disorders

- Three stages of addiction that promote drug-seeking
  - #1: Binge/intoxication (basal ganglia)
    - Effects motivation for a substance via dopamine and opioid peptides
    - Plays a key role in pain-relief seeking also
Neurocircuitry of Substance Use Disorders

• Three stages of addiction that promote drug-seeking
  ▪ #2: Withdrawal/Negative Affect Stage (nucleus accumbens and amygdala)
    – Loss of reward
    – Dysphoria
    – Pain
    – anxiety

# Reward Transmitters Implicated in the Motivational Effects of Drugs of Abuse

<table>
<thead>
<tr>
<th>Positive Hedonic Effects</th>
<th>Negative Hedonic Effects of Withdrawal</th>
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<tbody>
<tr>
<td><strong>Dopamine</strong></td>
<td>Dopamine – “dysphoria”</td>
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<tr>
<td><strong>Opioid Peptides</strong></td>
<td>Opioid Peptides – pain</td>
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<tr>
<td><strong>Serotonin</strong></td>
<td>Serotonin – “dysphoria”</td>
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<tr>
<td><strong>GABA</strong></td>
<td>GABA – anxiety, panic attacks</td>
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Anti-Reward Transmitters Implicated in the Motivation Effects of Drugs of Abuse

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<td>Dynorphin – “dysphoria”</td>
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<tr>
<td>Corticotropin-Releasing Factor (CRF) – stress</td>
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<tr>
<td>Norepinephrine – stress</td>
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<td>These are ACTIVATED in amygdala and ventral striatum during withdrawal</td>
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Neurocircuitry of Substance Use Disorders

- Three stages of addiction that promote drug-seeking
  - #3: Preoccupation/craving (basolateral amygdala, hippocampus)
    - Loss of executive functioning and decision making
    - Impulsivity
    - Compulsivity
    - Sleep disturbances

The Reward System in Pain

A Quick Decision-Making Process:

1. Dopamine neurons* from Ventral Tegmental Area (VTA) estimate value of reward/relief-seeking opportunity
2. Nucleus Accumbens (NAc) listens, makes decision to proceed
3. Frontal cortex also receives information from VTA, can inhibit NAc, but is slow and may be impaired

* The larger the dopamine input, the more likely you are to do that behavior

Trafton, 2015
The reward system is crucial for survival; if out of balance, it takes over: impulsivity, search for immediate gratification, unable to tolerate distress.

Addictive drugs and search for pain relief can dump tons of dopamine into these circuits.

Addictive drugs increase activity in these neurons, or prolong actions of neurotransmitters they release.

New research shows pain relief activates these neurons to drive habitual relief seeking.
Example: The Couch

Pain will shape reward learning circuits:

- VTA detects the couch as opportunity for relief, NAc says “go for it!”
- Back pain gets better, and your brain listens: “I got reward!”
- Your brain will refer that relief back to the laying down, reinforce its as new context
- However, the next time you lie down, you may not get as much reward
- If you try something else, you might get more dopamine the next time

People with pain are attracted to quick relief (lying down, guarding, help-seeking, self-medication), but not necessarily recovery.
What Happens Over Time?

Chronic dopamine firing reshapes these circuits, making them very fast and hard to control.

**Accelerator:**

D1 receptor

**D1 Receptors:** Dopamine in the receptors tells Nucleus Accumbens to say “Yes!”

**Brakes:**

D2 receptor

**D2 Receptors:** Activation of these receptors slows decision-making; allows frontal cortex time to step in

Trafton, 2015
Too Much Accelerator is a Bad Thing

- When DA neurons are chronically over-active, they activate D1 receptors:
  - D1 pathway becomes more efficient, speeding up decisions to seek relief
  - Activate anti-reward circuits (dynorphin, CRF, NE)
  - Increase stress response and worsen mood – both amplify pain signals
  - Pain severity increases and relief-seeking behaviors become compulsive
What Happened to the Brakes?

What happened to D2/Inhibitory Pathway?

- Big spikes in dopamine desensitize and internalize D2 receptors
- D2 receptor can’t work again until it is recycled (takes an hour) or a new receptor is synthesized

You may ultimately wind up with a system that has no brakes

Trafton, 2015
Summary – An Addiction-Like State

- Coupled with complex social, psychological, and biological stresses, certain people can be “primed” for development of severe chronic, complex pain and opioid use disorder.
- Both substance use disorder (SUD) and pain-relief seeking behaviors activate, and over-stress, the reward system.
- In both SUD and pain, when the reward system is over-activated, anti-reward neurotransmitters in the limbic system are enhanced, causing stress, negative affect, impulsivity, inducing compulsive behaviors to alleviate feeling lousy.
- In both SUD and chronic pain, the executive function of the pre-frontal cortex is impaired, unable to exert control over ventral striatum and limbic system, preventing activities that promote recovery.
Implications for Chronic Pain

- All about dysregulated dopamine
- In rats: increased place preference for opioids, more social anxiety, greater consumption of sugar water

  - People with dysregulated dopamine systems are more likely to develop chronic pain:
    - Acute injury $\rightarrow$ chronic pain
    - Drugs that increase dopamine $\rightarrow$ chronic pain
    - Smokers and people given high dose opioids after injury $\rightarrow$ chronic pain even after injury heals

Trafton, 2015
Other Implications for Chronic Pain

• The addicted brain may amplify pain to justify a substance it craves.
• Alternating withdrawal and intoxication can physiologically drive pain (sympathetic and psychomotor activation).
• Intoxication may mask pain and permit recurrent injury or overuse.
• Intoxication impairs adherence to treatment plan.
Which patients with chronic pain are at most risk to develop opioid use disorder?
Risk Factors for Opioid Use Disorder Development

- Published rates of abuse and/or addiction in chronic pain populations are 4-26%
- Suggests that known risk factors for opioid use disorder in the general population would be good predictors for problematic prescription opioid use
  - Lifetime history of substance use disorder
    - Past alcohol, tobacco, cocaine, or cannabis use
  - Family history of substance use disorder, a history of legal problems
  - Heavy tobacco use
  - History of severe depression, anxiety, or PTSD

References:
1. Ives T et al. BMC Health Services Research 2006
2. Reid MC et al JGIM 2002
Principle Risk Factors for Opioid Use Disorder

• Younger age, 13-45 years of age
• Previous substance use disorder
• Back pain, headache
• High dose chronic opioid dose > 90 mg morphine equivalents/day
Which Individuals are Most Likely to be Prescribed Opioids

• Those with greater number of pain diagnoses
• Those with mental health and substance use disorders
• Adverse selection – recipients of chronic opioid therapy are also most likely to develop opioid use disorder
Concentration of Opioid Use Among Patients with Chronic Pain

- Yearly total opioid use is highly concentrated
- 5% of CNCP patients use 70% of total opioids (in Morphine Equivalent Dosing)
- No other types of prescription medications show this degree of concentration among recipients

Why does Adverse Selection Occur?

- Providers want to help patients in pain and have few tools other than prescription pad.
- Patients with mental health and substance use disorders and multiple pain problems are more distressed (pain and psychological symptoms) and more persistent in demanding opioid initiation and dose increases.
- Providers write opioid prescriptions as a “ticket out of the exam room.”
How we think of addiction

How we think of dependence on pain medication

Are they biologically any different?
GRAY ZONE

ADICTED

Meets DSM criteria for opioid use disorder

NOT ADDICTED

• No lost prescriptions
• No ER visits
• No early prescriptions
• No requests for dose escalation
• No UDT aberrancies
• No doctor shopping (PMP)
Prescription Drug Misuse
(i.e. mild opioid use disorder)

Aberrant Medication-Taking Behaviors
(AMTBs)
A spectrum of patient behaviors that may reflect misuse

Total Chronic Pain Population

Severe Opioid Use Disorder

Daniel Alford, MD

Adapted from Steve Passik. APS Resident Course, 2007
Spectrum of Opioid Use Disorder

- Self medication (chemical coping)
  - Mood
  - Sleep
  - Traumatic memories
- Prevent withdrawal
- Reward (to get high)
- Opioid Use disorder
- Diversion for profit

Medication or substance misuse by persons with pain may occur for diverse reasons. Helps to identify and address the driver of misuse. Misuse may be self-limited or may be a sign of opioid use disorder in vulnerable people.
Continuum of Problematic Opioid Use

- Mild indiscretion
- Repeated misuse
- Opioid use disorder
- Severe Opioid Use Disorder (i.e. addiction)

Photo from http://mediad.publicbroadcasting.net/p/wnpr/files/styles/related/public/201603/PillBottle.jpg
Opioid seeking behaviors

依赖/成瘾通过疼痛治疗

- Pesterin reluctant doctors
- Using opioid to treat pain
- Predominant symptom of withdrawal - pain

依赖/成瘾通过娱乐性药物使用

- Need to procure opioid
- Often use paraphernalia
- Predominant symptom of withdrawal - anhedonia

DSM Criteria
- Social Disruption
- Loss of control over use
- Continued use despite knowledge of harm
- (Craving) (may not be manifest until off)

Accept that they have an opioid use disorder

Do not accept that anything is wrong other than pain
“Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment…Whether or not it is called addiction, complex persistent opioid dependence is a serious consequence of long-term pain therapy.”
From: DSM-5 Criteria for Substance Use Disorders (SUD): Recommendations and Rationale

<table>
<thead>
<tr>
<th>DSM-IV Abuse&lt;sup&gt;a&lt;/sup&gt;</th>
<th>DSM-IV Dependence&lt;sup&gt;b&lt;/sup&gt;</th>
<th>DSM-5 Substance Use Disorders&lt;sup&gt;c&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Hazardous use</td>
<td>–</td>
<td>X</td>
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<tr>
<td>Social/interpersonal problems related to use</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Neglected major roles to use</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Legal problems</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Withdrawal&lt;sup&gt;d&lt;/sup&gt;</td>
<td>–</td>
<td>X</td>
</tr>
<tr>
<td>Tolerance</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Used larger amounts/longer</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Repeated attempts to quit/control use</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Much time spent using</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Physical/psychological problems related to use</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Activities given up to use</td>
<td>–</td>
<td>X</td>
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Craving

≥1 criterion

≥2 criteria

DSM-5 Criteria: 2-3 = mild SUD, 4-5 = moderate SUD, >6 severe SUD

Date of download: 10/22/2013
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Opioid Use Disorder in Clinical Practice

• The 4 C’s
  - Loss of Control
  - Compulsive use
  - Continued use despite harms
  - Craving
Features of prescription OUD

- Inconsistent health care use patterns (e.g., missed appointments, lack of engagement with non-medication treatments)
- Signs/symptoms of drug use (e.g., intoxication, overdose, track marks)
- Emotional problems/psychiatric issues
- Illicit drug use
- Problematic medication behavior (escalating doses, early refills)
- Family concerns about use
- Functional stagnation, loss of roles
- Extreme difficulty with even a slow opioid taper

Implications
- Concern comes from the “pattern” or the “severity”
- Differential diagnosis
Concerning Behaviors for Opioid Use Disorder

Spectrum: Yellow to Red Flags

- Requests for increase opioid dose
- Requests for specific opioid by name, “brand name only”
- Non-adherence w/other recommended therapies (e.g., PT)
- Running out early (i.e., unsanctioned dose escalation)
- Resistance to change therapy despite AE (e.g. over-sedation)
- Deterioration in function at home and work
- Non-adherence with monitoring (e.g. pill counts, UDT)
- Multiple “lost” or “stolen” opioid prescriptions
- Illegal activities – forging scripts, selling opioid prescription

Does the patient with chronic pain who is prescribed opioids have an opioid use disorder?

1. Unable to fulfill role obligations – MAYBE
2. Social or interpersonal problems due to use – MAYBE
3. Hazardous use – MAYBE
4. Tolerance – DOES NOT APPLY*
5. Withdrawal/physical dependence – DOES NOT APPLY*
6. Taken in larger amounts or over longer period – MAYBE
7. Unsuccessful efforts to cut down or control – MAYBE
8. Great deal of time spent to obtain substance – MAYBE
9. Important activities given up or reduced – MAYBE
10. Continued use despite harm – MAYBE
11. Craving – MAYBE

*If opioids are prescribed, this criterion does not apply.
Initial Evaluation of Opioid Use Disorder for the PCP

• Normalize the process as part of Universal Precautions

• Appreciate the fear and stigma associated with opioid use disorder in patients with chronic pain
Initial Evaluation of OUD for PCPs

- Confirm and describe the chronic pain condition
  - Is a diagnosis possible?
  - Would further evaluation prove beneficial?

- Confirm functional improvement with pain medication
  - In the absence of functional improvements, the patient may be experiencing therapeutic failure of opioids
  - No functional benefit = lack of opioid benefit, so why would opioids be continued?

- Confirm and describe that appropriate treatment has been offered or failed
  - Are there treatments that could be optimized?
  - Have non-medication options been tried and/or failed?
Initial Evaluation of OUD for PCPs

- Describe patient’s side effects from the medication
- Describe patient’s relationship with healthcare providers and any concerning behavior
  - Describe prescription history: lost medications? Stolen medications? Frequent ED visits? Concerning reports from loved ones?
- Describe patient’s substance use disorder history or current substance use history
- Describe concomitant psychosocial factors
  - Depression, sexual use history, marital, financial or job stress
  - PHQ-9, GAD, Pain Catastrophizing Scale, Chronic Pain Self-Efficacy

Diagnostics

• Random Urine Drug Testing
  ▪ Including evaluation of alcohol use (ethyl glucuronide)
  ▪ See Risk Assessment, Mitigation, and Management Lecture

• Random Pill Counts

• Prescription Drug Monitoring Data

• Review of medical records

• Discuss case with other prescribers and/or family members
Questionnaires

• Current Opioid Misuse Measure (COMM™)
  • Helps to identify patients at high risk for current aberrant medication-taking behavior
  • A high score raises concern for opioid use disorder, but is **NOT** diagnostic

• Screening Tool for Addiction Risk (STAR)
  ▪ Self-report
  ▪ Corresponds to DSM-IV criteria

Butler SF, Pain. 2007; 130:144-156.
Diagnosis

• There is not one test or questionnaire that can confirm prescription opioid use disorder.
• The initial PCP evaluation will provide the basis for a risk/benefit determination
• This initial evaluation will place a focus not only on concerning behavior, but also on pain and pain care
  ▪ You can have pain and OUD
  ▪ Treating pain with opioids in the setting of OUD is risky
  ▪ Treating OUD without treating pain is also not likely to be effective
• Based on initial evaluation, consider referral for diagnosis of an OUD if you do not feel comfortable making it
• Ultimately, diagnosis made by DSM V criteria
What Next?

• Make a risk-benefit ratio judgement of the treatment, not the patient.

• If the risks outweigh the benefit, refer the patient and stop or taper opioids

• Continue to treat pain with non-opioid treatments

• Encourage the patient to seek medication assisted treatment for OUD
OUD Medication Treatments
See also **PCSS-MAT**

- **Naltrexone (oral or Intramuscular)**
  - Opioid antagonist
  - Possible pain relief at very low doses
  - May not work well for patients who have pain

- **Methadone**
  - Full opioid agonist
  - Analgesia for 4-6 hours
  - Only legally dispensed through a federally qualified opioid treatment program for treatment of OUD

- **Buprenorphine**
  - Partial opioid agonist
  - Analgesia for 4-6 hours, can be dosed BID or TID for improved pain management
  - Can be utilized to help patients taper off of opioids
  - Office based prescribing with DEA waiver or “X license” after completing online training
    - [Online Buprenorphine Training](#)
Patient undergoes a full opioid use disorder assessment and is determined to have a moderate opioid use disorder based on failure to fulfill roles, continued use despite harms, time spent procuring medication, and craving. She is reluctant and scared to consider alternative treatments or seek opioid use disorder treatment, but is appreciative of the honest assessment of her condition. She would like to think about the idea.

Two weeks later she makes an appointment to see you and seeks treatment for her OUD.

Three months after stabilizing and starting buprenorphine/naloxone along with cognitive behavioral therapy, she says “Thank you so much for helping me. I am myself again. I am finally enjoying my life with my kids and am thinking about starting a small business.”
Case: Thought Questions

- Does this patient have pain? YES

- Does this patient have an opioid use disorder? YES

- What factors place this patient at risk for an opioid use disorder?
  - Personality traits
  - Young age of opioid initiation
  - Concomitant use of benzodiazepines, possible synergism or cross addiction/dependency
  - Mental illness placing at greater vulnerability for chemical coping
  - Adverse childhood experiences
  - History of medication non-adherence (lost prescriptions, possible compulsive use or medication)
  - Possible frequent bouts of opioid withdrawal from overuse of opioids causing negative affective motivation and craving
Case: Thought Questions

- What can you do to help this patient?
  - Identify underlying biopsychosocial factors that are contributing to her pain
  - Identify neural processes that may be contributing to her behavior
  - Guide her toward activities and treatment modalities that increase D2 receptors (low level dopamine input)
    - Limit use of addictive drugs or medications, tobacco, fast-acting analgesics, etc.
    - Social reinforcement, problem-solving, effective emotional coping, small goal achievement, quality of life activities
  - Offer her safe and effective treatment for her pain and opioid use disorder
Conclusions

- Chronic pain and substance use disorders share many common features that can motivate a person’s behaviors.
- Diagnosing opioid use disorder during pain management is difficult and requires a thorough evaluation.
- Typical substance abuse risk factors probably apply to prescription opioid use disorder:
  - High risk groups include young individuals, cigarette smokers with comorbidity psychiatric conditions and high dose opioid analgesic treatment.
- Manage opioid use disorder by referring to substance use treatment and considering medication assisted treatment like buprenorphine or methadone.
References

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• Paulozzi, LJ. Congressional Testimony. CDC. 2007.
References

PCSS-O Colleague Support Program and Listserv

- PCSS-O Colleague Support Program is designed to offer general information to health professionals seeking guidance in their clinical practice in prescribing opioid medications.

- PCSS-O Mentors comprise a national network of trained providers with expertise in addiction medicine/psychiatry and pain management.

- Our mentoring approach allows every mentor/mentee relationship to be unique and catered to the specific needs of both parties.

- The mentoring program is available at no cost to providers.

For more information on requesting or becoming a mentor visit:  
www.pcss-o.org/colleague-support

- Listserv: A resource that provides an “Expert of the Month” who will answer questions about educational content that has been presented through PCSS-O project. To join email: pcss-o@aaap.org.
PCSS-O is a collaborative effort led by American Academy of Addiction Psychiatry (AAAP) in partnership with: Addiction Technology Transfer Center (ATTC), American Academy of Neurology (AAN), American Academy of Pain Medicine (AAPM), American Academy of Pediatrics (AAP), American College of Physicians (ACP), American Dental Association (ADA), American Medical Association (AMA), American Osteopathic Academy of Addiction Medicine (AOAAM), American Psychiatric Association (APA), American Society for Pain Management Nursing (ASPMN), International Nurses Society on Addictions (IntNSA), and Southeast Consortium for Substance Abuse Training (SECSAT).

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