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Psychiatry and Addictions Case Conference
UW Medicine | Psychiatry and Behavioral Sciences

DIAGNOSING ANXIETY AND PTSD IN OUD

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4.24.2025

UW Medicine
UW SCHOOL OF MEDICINE

Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

SPEAKER DISCLOSURES

✓ No conflicts of interest

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

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OBJECTIVES

1. Epidemiology of comorbid OUD and anxiety/PTSD
2. Diagnosis considerations
3. Proposed mechanisms of comorbid interactions
4. Treatment for co-occurring disorders

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PATIENT CASE – J

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CASE

- J is a 42 year old male veteran who presents to clinic with goal of complete abstinence off fentanyl, requesting to be started on methadone
- SUD Hx:
  - Fentanyl: smoking 0.2g-0.5g powder/day ($20-50 worth) since 2021
  - Meth: using since 2015, about 0.1g-1g/day but not daily
  - Nicotine: ½ PPD cigarettes
  - Cannabis: “takes a couple hits off a joint” 1x/week

CASE

- Past Psychiatric Hx:
  - Past dx: OUD, stimulant use disorder, anxiety/panic, r/o PTSD
  - Hospitalizations: None
  - Medications:
    - Buprenorphine/Naloxone – reported precipitated withdrawal the first try; had successful induction during 2nd try, however reports it didn't have as strong of an effect as he was hoping and he returned to fentanyl use
    - Methadone – prescribed in 2024 during hospitalization, positive experience
    - Bupropion
    - Propranolol
    - Sertraline
    - Topiramat
  - Therapy: None
  - Denies past suicidal behavior

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CASE

- PMHx:
  - TBI in 2020: electrocuted fell 10ft
    - Hemicraniectomy to decompress
    - Cranioplasty
  - Cervical stenosis
- Military hx:
  - Army, 2000-2002

CASE

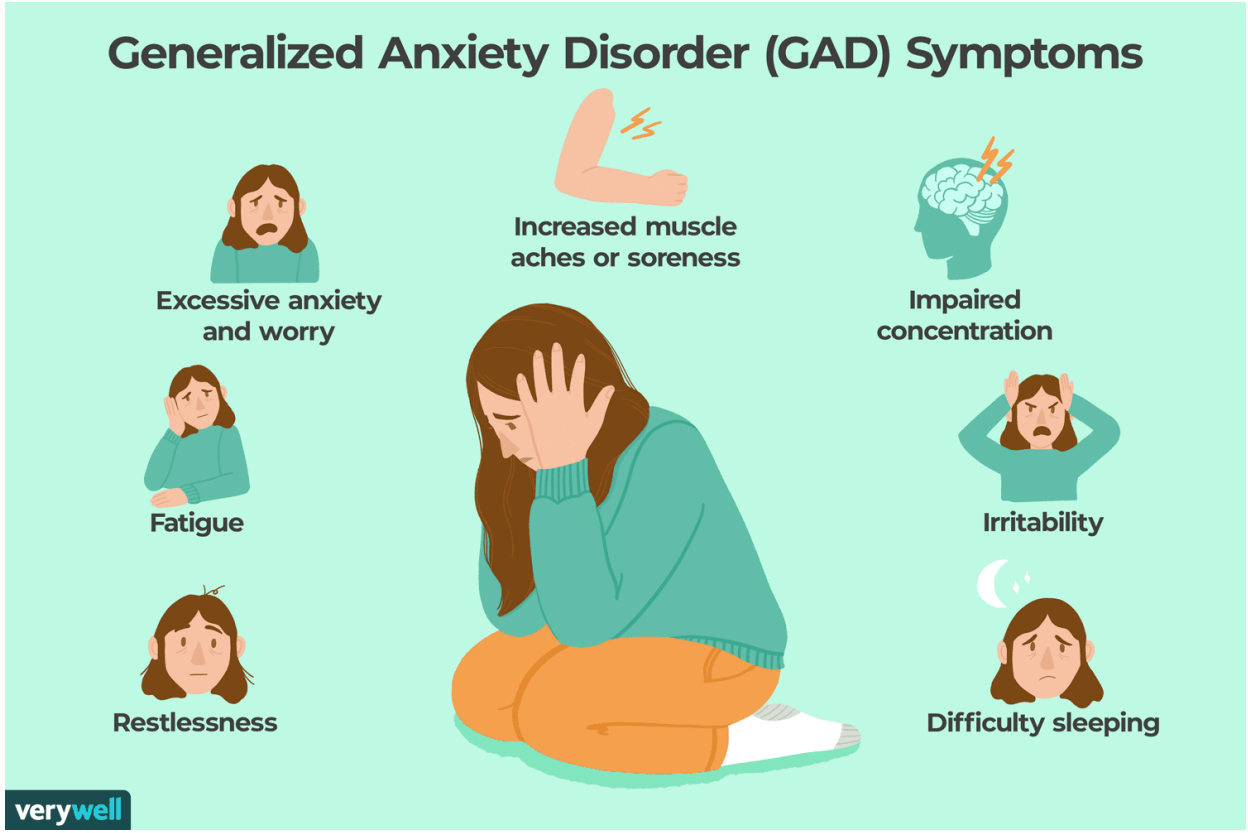
- Social Hx:
  - He is widowed, his partner of 17 years passed away 1 year ago due to heart attack
  - Housing: lives alone with dog, Bully at apartment
    - Partner died in this apartment, J says it is hard for him to be there as a reminder so he stays in his car 4 nights/week
  - Has two children with deceased partner but not in touch with them – were taken by CPS in 2010 for negligence
  - No local supports, family of origin lives in South Carolina – “I feel like the odd one out”
  - Income: SSDI, 10% VA benefits, he reports generating money by scrapping metal
  - Hx of military sexual trauma noted in chart, no further details. Denies combat exposure
    - Never reported nor received treatment, not service-connected for this
    - He is reluctant to talk about MST at intake
    - Has a lot of shame about it and didn’t even share with his partner when she was alive

CASE

- HPI:
  - Mood is “depressed”
  - Reports passive suicidal ideation, cites his dog and having hope for the future as reasons for living
  - Endorses nightmares, flashbacks about past traumatic experiences, avoidance of reminders

ANXIETY DISORDERS

- Anxiety:
  - Generalized Anxiety Disorder
  - Social Anxiety Disorder
  - Performance Anxiety
  - Panic Disorder



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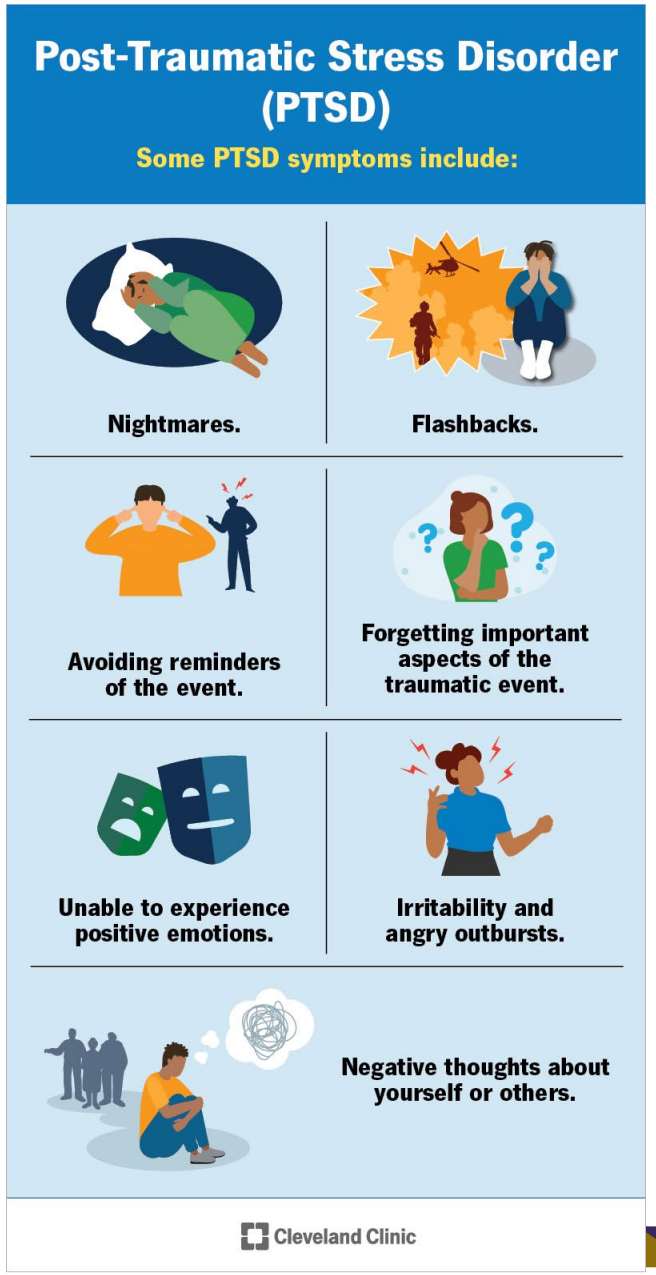
PTSD

- Persistent (1+ months) dysfunction after an index trauma as a result of several classes of symptoms:
  - Intrusive symptoms
  - Avoidance behaviors
  - Negative cognitions and mood
  - Hyperarousal/hyperreactivity



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CONCURRENCE OF OUD WITH PSYCH DX

- Prevalence meta-analysis of 104,135 pts with OUD over 345 studies (Santo et al 2022)
  - Concurrent prevalence:
    - Depression: 36.1%
    - Anxiety 29.1%
    - PTSD 18.1%
  - Not much data reported for lifetime prevalence
- Review of OUD and anxiety (Langdon et al 2018)
    - Anxiety lifetime prevalence: 60%
- Review of past studies reviewing OUD and PTSD (Ecker et al 2018)
    - PTSD current prevalence: 33%
    - PTSD lifetime prevalence: 41%

Santo T Jr, Campbell G, Gisev N, Martino-Burke D, Wilson J, Colledge-Frisby S, Clark B, Tran LT, Degenhardt L. Prevalence of mental disorders among people with opioid use disorder: A systematic review and meta-analysis. Drug Alcohol Depend. 2022 Sep 1;238:109551. doi: 10.1016/j.drugalcdep.2022.109551. Epub 2022 Jul 1. PMID: 35797876.

OVERLAP OF SYMPTOMS

Opioid Use

- Analgesia
- Euphoria
- Constipation
- Sedation
- Confusion
- Respiratory depression
- Miosis (constricted pupils)

Opioid Withdrawal

- Lacrimation, rhinorrhea
- Piloerection "goose flesh”
- Diaphoresis
- Myalgia
- GI upset (diarrhea, nausea, vomiting)
- Mydriasis (dilated pupils)
- Photophobia
- Insomnia
- Autonomic hyperactivity (tachypnea, hyperreflexia, tachycardia, sweating, hypertension, hyperthermia)
- Yawning

OVERLAP OF SYMPTOMS

Opioid Use

- Analgesia
- Euphoria
- Constipation
- Sedation
- Confusion
- Respiratory depression
- Miosis (constricted pupils)

Many of these sx are seen in anxiety and PTSD!

Opioid Withdrawal

- Lacrimation, rhinorrhea
- Piloerection "goose flesh”
- **Diaphoresis**
- Myalgia
- GI upset (diarrhea, **nausea**, vomiting)
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- **Insomnia**
- **Autonomic hyperactivity** (tachypnea, hyperreflexia, tachycardia, hypertension, hyperthermia)
- Yawning

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SUBSTANCE-INDUCED MOOD DISORDER

- Mood symptoms that occur as a physiological consequence of the use of substances of abuse or medications
  - Can occur during use/intoxication or withdrawal
- Typically appropriate to use when a patient is currently using or recently used a substance
- 30 day rule

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SUBSTANCE-INDUCED MOOD DISORDER

- Differential dx includes primary mood disorder
  - Avoid definitively diagnosing with primary psychiatric conditions until at least **30 days of abstinence** from substance
- Sometimes can differentiate with time: ask the patient which came first, the mood symptoms or the substance use
  - However, there is enough interaction of the co-occurring disorders that it doesn't necessarily change your management decisions

OUD AND ANXIETY

- Landon et al. 2019:
  - 60% of people with OUD report lifetime anxiety-related disorder, compared with 31% of general population
  - Risk factors for co-occurrence include:
    - Earlier onset of opioid use
    - Rapid transition from use to use disorder
    - Premature discontinuation of substance use treatment
    - Higher rates of misusing other substances, ex. benzos
    - Female sex

Langdon KJ, Dove K, Ramsey S. Comorbidity of opioid-related and anxiety-related symptoms and disorders. Curr Opin Psychol. 2019 Dec;30:17-23. doi: 10.1016/j.copsyc.2018.12.020. Epub 2019 Jan 4. PMID: 30711906; PMCID: PMC6609499.

OUD AND ANXIETY

- Pts who receive rx opioids for pain:
  - w/ current anxiety: 50% screen positive for OUD
  - w/o current anxiety: 10% screen positive for OUD
  - There may be a specific risk factor in “pain-related anxiety” (worry about negative consequences of pain)
- Anxiety affects course of SUD treatment:
  - More likely to relapse and/or discontinue treatment prematurely if reporting sx of insomnia, nervousness, restlessness, feeling blah, depression, and anxiety
  - Anxiety results in higher levels of benzodiazepine use, which is contraindicated with methadone or buprenorphine therapy

Langdon KJ, Dove K, Ramsey S. Comorbidity of opioid-related and anxiety-related symptoms and disorders. Curr Opin Psychol. 2019 Dec;30:17-23. doi: 10.1016/j.copsyc.2018.12.020. Epub 2019 Jan 4. PMID: 30711906; PMCID: PMC6609499.

OUD AND PTSD

- Nelson et al 2006: Twin study for occurrence of childhood sexual abuse and SUD
  - Twin with childhood abuse had OR of 2.6 to develop OUD
  - Greater risk of OUD in DZ than MZ twins
  - Opioids was also the most common drug of abuse with adverse childhood experiences, along with sedatives

Nelson EC, Heath AC, Lynskey MT, Bucholz KK, Madden PA, Statham DJ, Martin NG. Childhood sexual abuse and risks for licit and illicit drug-related outcomes: a twin study. Psychol Med. 2006 Oct;36(10):1473-83. doi: 10.1017/S0033291706008397. Epub 2006 Jul 20. PMID: 16854248.
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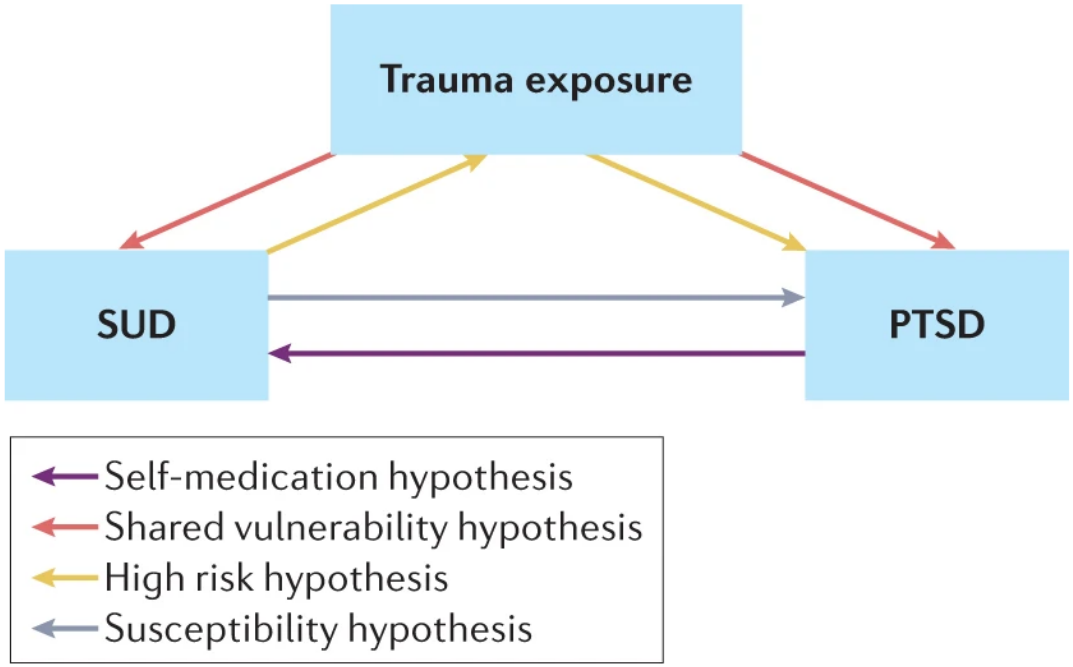
OUD AND PTSD

- Elman et al 2019: biological basis of comorbid OUD and PTSD
- **"Spiraling distress cycle"**
  - Increased opioidergic tone in PTSD
    - Increased sensitivity to pain
    - Increased responsiveness to opioids -> exaggerated CNS activity with exposure
  - Emergence of trauma sx can drive heavier opioid use which can lead to exposure/development of more stressors



Kline et al. 2023

Elman I, Borsook D. The failing cascade: Comorbid post traumatic stress- and opioid use disorders. Neurosci Biobehav Rev. 2019 Aug;103:374-383. doi: 10.1016/j.neubiorev.2019.04.023. Epub 2019 May 4. PMID: 31063739.
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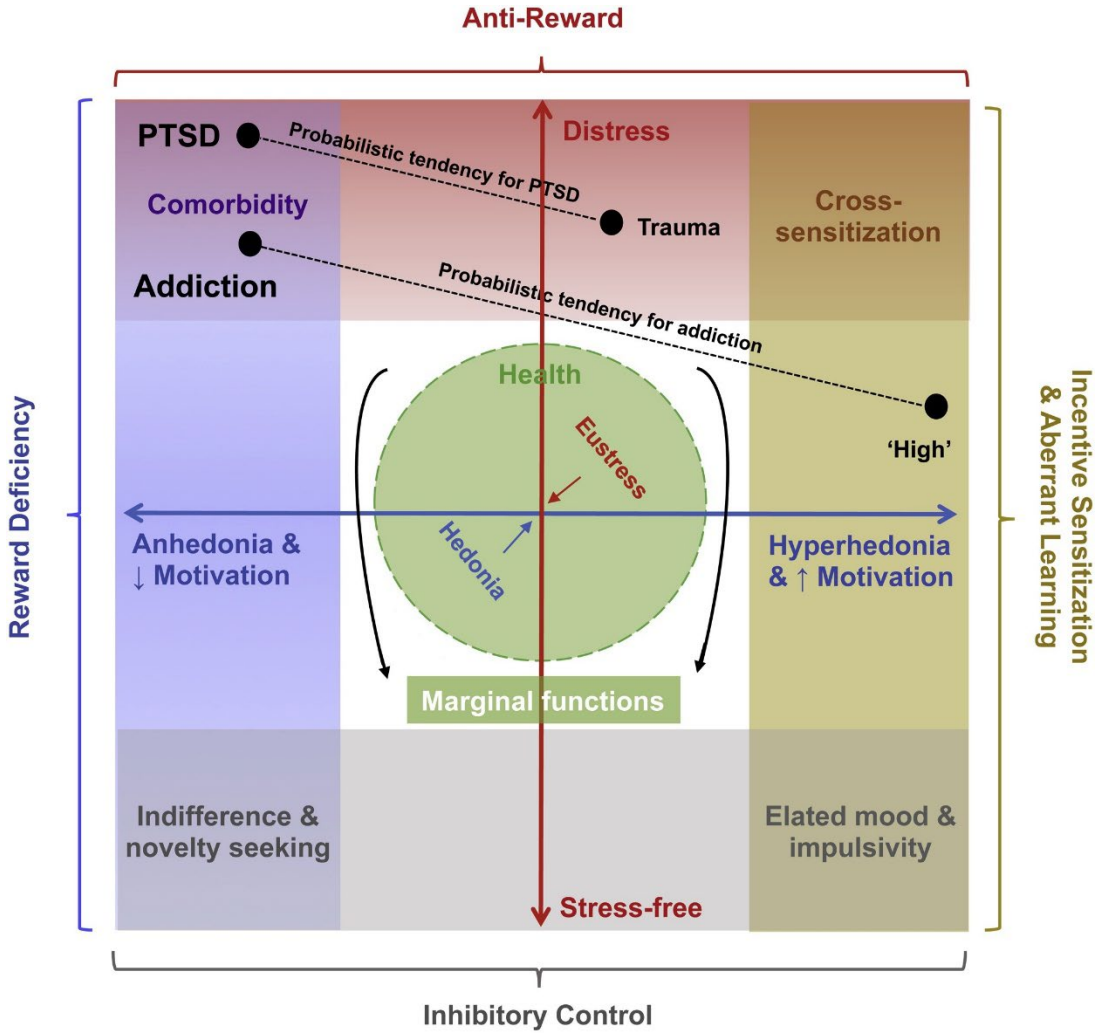
OUD AND PTSD

- Elman et al 2019: biological basis of comorbid OUD and PTSD
  - Both substances and stress cause excitation in dopaminergic pathways
    - Moderate stress can feel “rewarding” due to endogenous opioid release
  - After period of lengthy or repeated exposure, adaptation can occur so that the absence “feels” like deficiency/absence of reward
    - Emotional numbing
    - Anhedonia/amotivation
  - Deficiency drives more novel behavior, potentially chasing risky/high stress situations



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TREATMENT

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TREATMENTS FOR STANDALONE CONDITIONS

OUD

- Medications
  - Methadone
  - Buprenorphine
  - Naltrexone
  - Sx support meds
- Therapy:
  - Motivational Interviewing
  - Contingency management
  - Recovery model
  - 12-step

Anxiety, PTSD

- Medications:
  - SSRIs/SNRIs
  - Atypical antidepressants
  - Anxiolytics
    - Don’t combine benzos with opioids!
- Therapy:
  - CBT
  - ACT
  - Mindfulness
  - CPT
  - Prolonged Exposure
  - EMDR

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TREATMENT OF OUD/ANXIETY

- Targets include:
  - Pain-related anxiety
  - Distress tolerance
- Methods used:
  - CBT
  - ACT
  - I-CBT

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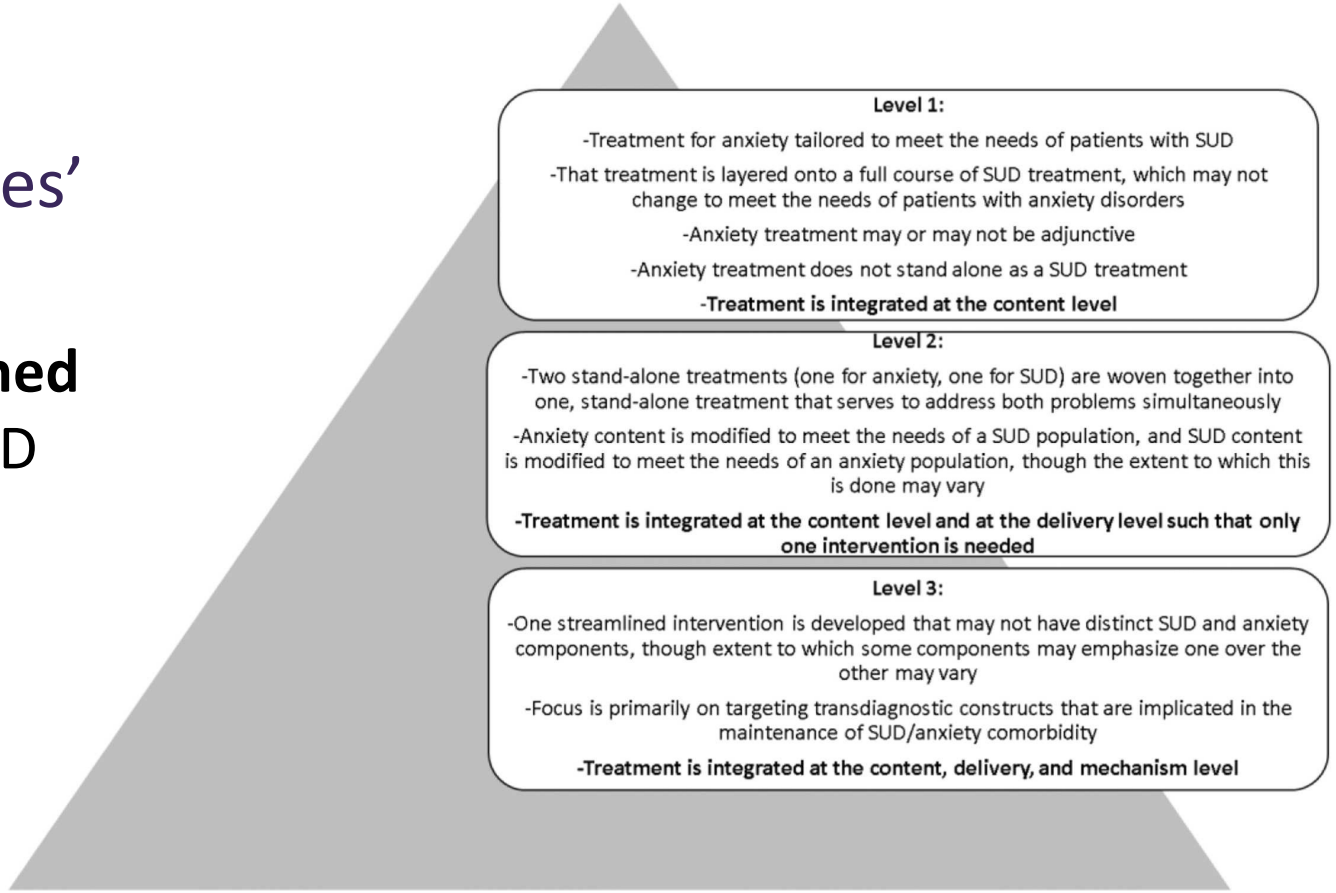
INTEGRATED CBT (I-CBT)

- Utilizes treatment elements that target interaction of shared symptoms/processes
- Conceptualizes these as single disorder
  - i.e. skills training addresses negative reinforcement feedback loop of behaviors (substance use) that provide relief from distress (anxiety) in short term

INTEGRATED CBT (I-CBT)

- Wolitzky-Taylor 2023: Meta-analysis of integrated therapies' mechanism and efficacy
  - Integrated therapy **outperformed** solo SUD treatment in both SUD and anxiety
  - Small to moderate effect



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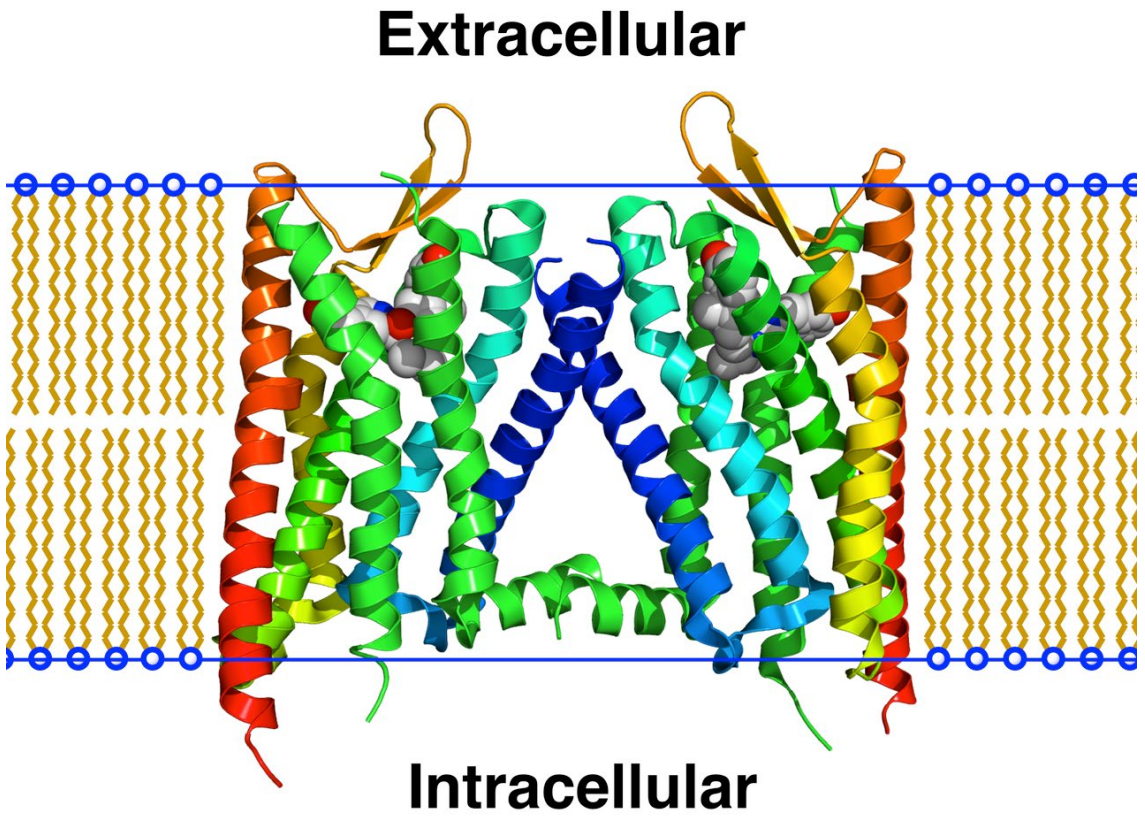
TREATMENT OF OUD/PTSD

- Kappa Opioid receptor:
  - One of the 4 subtypes of opioid receptors
  - Endogenous agonist dynorphin released in reaction to stress
    - May create withdrawal state afterwards -> motivation to seek out more agonism
  - With high activation/agonism, can cause dysphoria, hallucinations, cognitive issues
  - Antagonism may prevent stress rxn:
    - In mice, missing gene receptor or pre antagonism -> decreased learning/conditioning behaviors of aversive stimuli (Land et al 2008)
  - Antagonism is being explored as a way to treat SUD and other mood conditions



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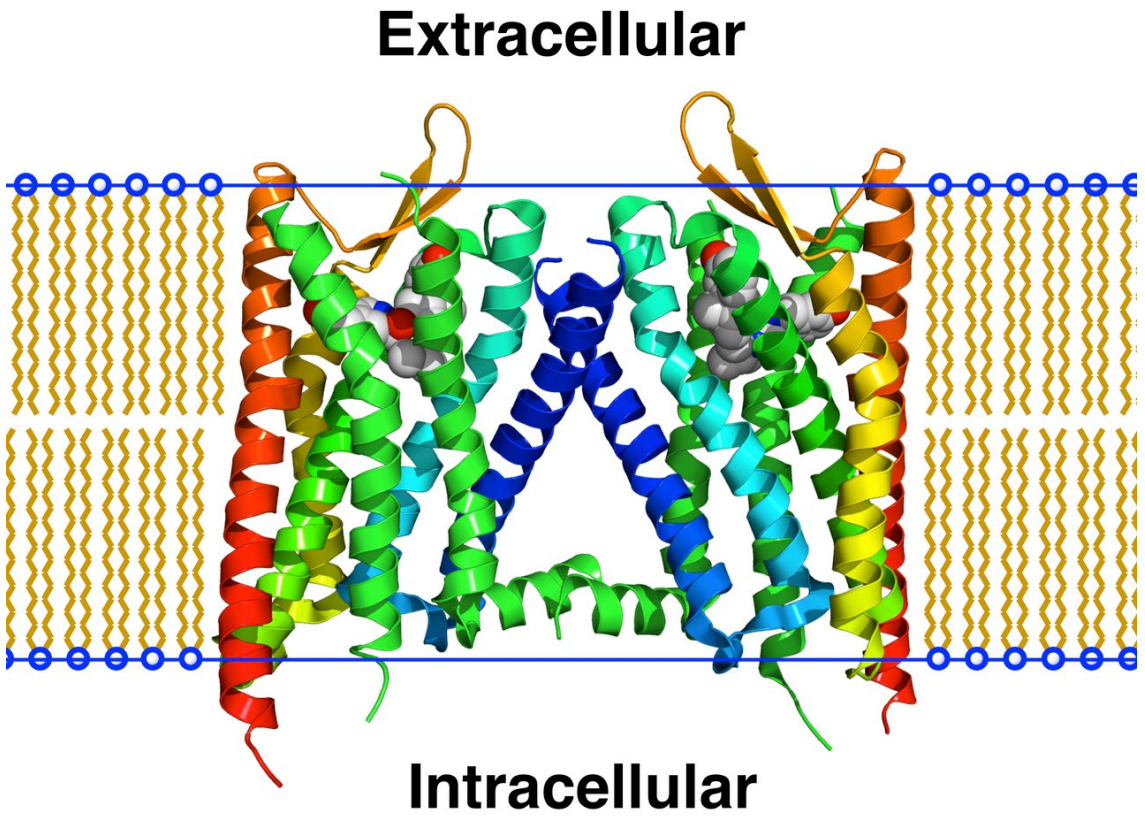
TREATMENT OF OUD/PTSD

- Kappa Opioid receptor:
  - In healthy adults, administering low dose buprenorphine (0.2mg) led to less reactivity to negative social stimuli and more reactivity to positive social stimuli (Bershad et al 2016)
    - Also seen in mice, bup increases play behavior



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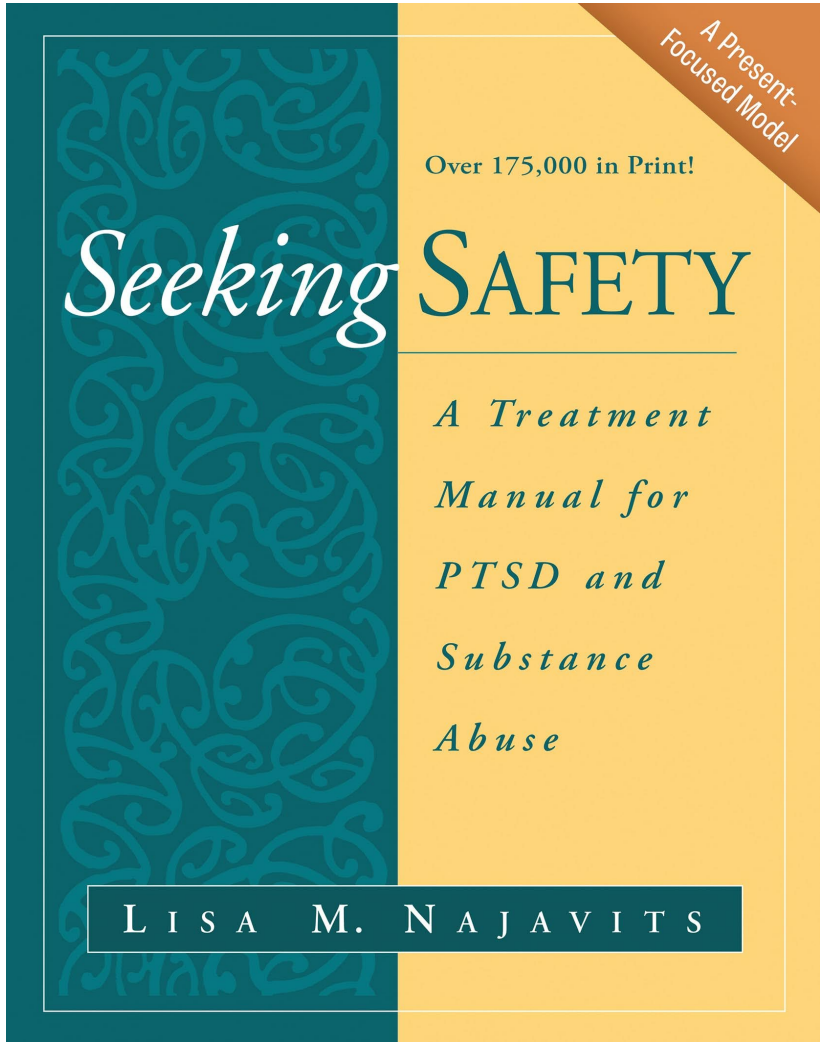
SEEKING SAFETY

- Skills-based CBT program that focuses on addressing **current** symptoms of PTSD and SUD
- Developed by Dr. Lisa Najavits in the 1990s
- Principles:
  1. **Safety** as the overarching goal (helping clients attain safety in their relationships, thinking, behavior, and emotions).
  2. **Integrated** treatment (working on both trauma and addiction at the same time if the person has both)
  3. **A focus on ideals** to counter the loss of ideals in both trauma and addiction
  4. **Four content areas**: cognitive, behavioral, interpersonal, case management
  5. **Attention to counselor processes** (counselors' emotional responses, self-care, etc.)



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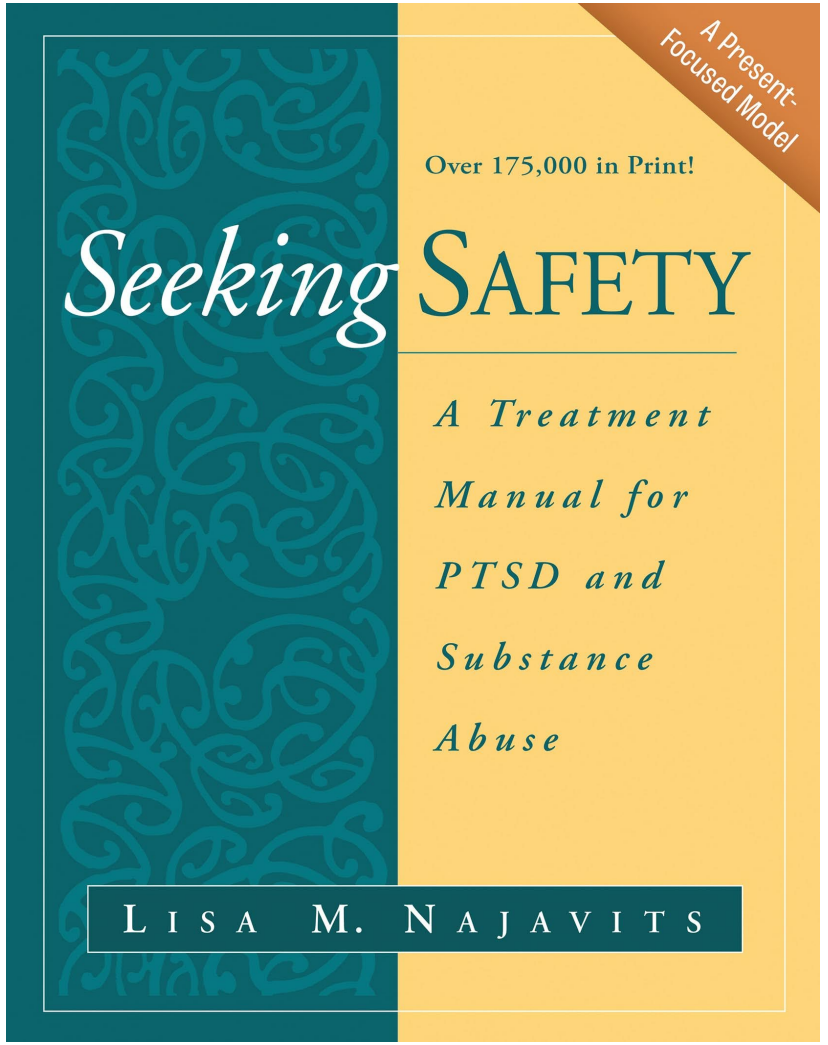
SEEKING SAFETY

- Highly flexible, lots of room for adjustment based on client needs
  - Individual or group settings
  - Can be delivered by professionals and paraprofessionals
  - Wide range of topics to explore, complete as many or as few as needed, no particular order



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SEEKING SAFETY

- Sherman et al 2023: Meta-analysis of evidence for Seeking Safety treatment protocol
  - In general, SS may be effective for reducing symptoms of PTSD and SUD, although tends to be more effective for PTSD
    - Theories about why this is include:
      - PTSD conceptualized as something that can respond to short-term treatment versus SUD which may be a chronic issue subject to relapses throughout life
      - SUD more susceptible to pt denial/lower insight than PTSD
      - Pts being more motivated to treat the PTSD than the SUD
  - No specific data on type of setting (individual vs. group), credentials of clinicians, number/length of sessions, or specific topics/content of sessions
    - Future studies should attempt to determine minimum "dose" of treatment to guide more effective delivery

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BACK TO THE CASE

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CASE

- Differential Dx:
  - OUD
  - Stimulant Use disorder
  - Nicotine dependence
  - PTSD
  - Prolonged Grief Disorder
  - MDD
  - GAD
  - Substance-Induced Mood Disorder
  - Mood Disorder due to a medical condition

CASE

- PTSD? (*= similar to OUD withdrawal)
  - Flashbacks
  - Intrusive thoughts
  - Nightmares*
  - Avoidance
  - Hypervigilance/exaggerated startle*
  - Emotional Lability/Reactivity*
- Has not experienced 30 days of sobriety yet
  - However his earliest index trauma predates opioid and stimulant use
  - Substance use leads to decisions that expose to further trauma or exacerbation of existing trauma
    - at this point they are both mediating the effect of the other

CASE

- At initial appointment, J wanted to focus on getting started on methadone
  - A discussion was had about relationship between SUD and mood conditions, and he seemed to accept that this is important to address in subsequent visits
  - Agreed to start contingency management for OUD
  - Declined groups/other programming

CASE

- 3 months of treatment in, J's adherence has been spotty
  - Has trouble making it to dosing hours and appointments due to the hours that he "works"
  - Difficult to reach by phone
  - Resulted in a several methadone restarts so far – he has not been able to reach therapeutic levels
  - "**Shame**" about missing appointments, **isolation**, **avoidance** of asking for help, inability to keep a structured life (i.e. benefit of housing, holding a job with daytime hours) due to avoidance of trauma **are obstacles in recovery**
  - *Subconscious avoidance of revisiting trauma?*
  - Now, he is now open to individual therapy--still declines groups

SUMMARY

- Co-occurring psychiatric diagnoses with OUD is common
  - Each likely increases the risk of the other
- Assessment can differentiate SIMD vs primary psychiatric disorder and drive management choices
- More severe mood symptoms → worse outcomes, including recovery from substances
- Better outcomes come from integrative treatments sensitive to the complex interaction between psychiatric conditions and OUD

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