Cannabis and Health

Module 6

Lecture 3: The Etiology (causes) of Opioid Use Disorder

What causes prescription opioid abuse/misuse?

- Limited research in this area
- Insights from qualitative research asking people about the "storylines" that led them to misuse opioids
- Self-reported reasons for initiating prescription opioid abuse
  - self-medication of emotional and/or physical pain
  - social influences
  - easy access to prescription opioids
  - recreation

Rigg & Murphy, 2014, *Qualitative Health Research*

What causes prescription opioid abuse/misuse?

- Rigg & Murphy, 2014 explored reasons for opioid abuse in 90 people (18-51 years old, 52 men, 38 women)
  - Substance-Abusing Families
    - 82% had close family member that abused drugs or alcohol
  - Escaping Hardships
    - adverse life events that caused longstanding and unpleasant emotional states such as childhood abuse
  - The “Male Influence”
    - Women typically introduced to opioids via close interactions with a prescription-opioid-abusing man
  - ”Prescribed Addiction”
    - requiring treatment that included a prescription painkiller

Rigg & Murphy, 2014, *Qualitative Health Research*

What causes non-prescription opioid abuse/addiction?

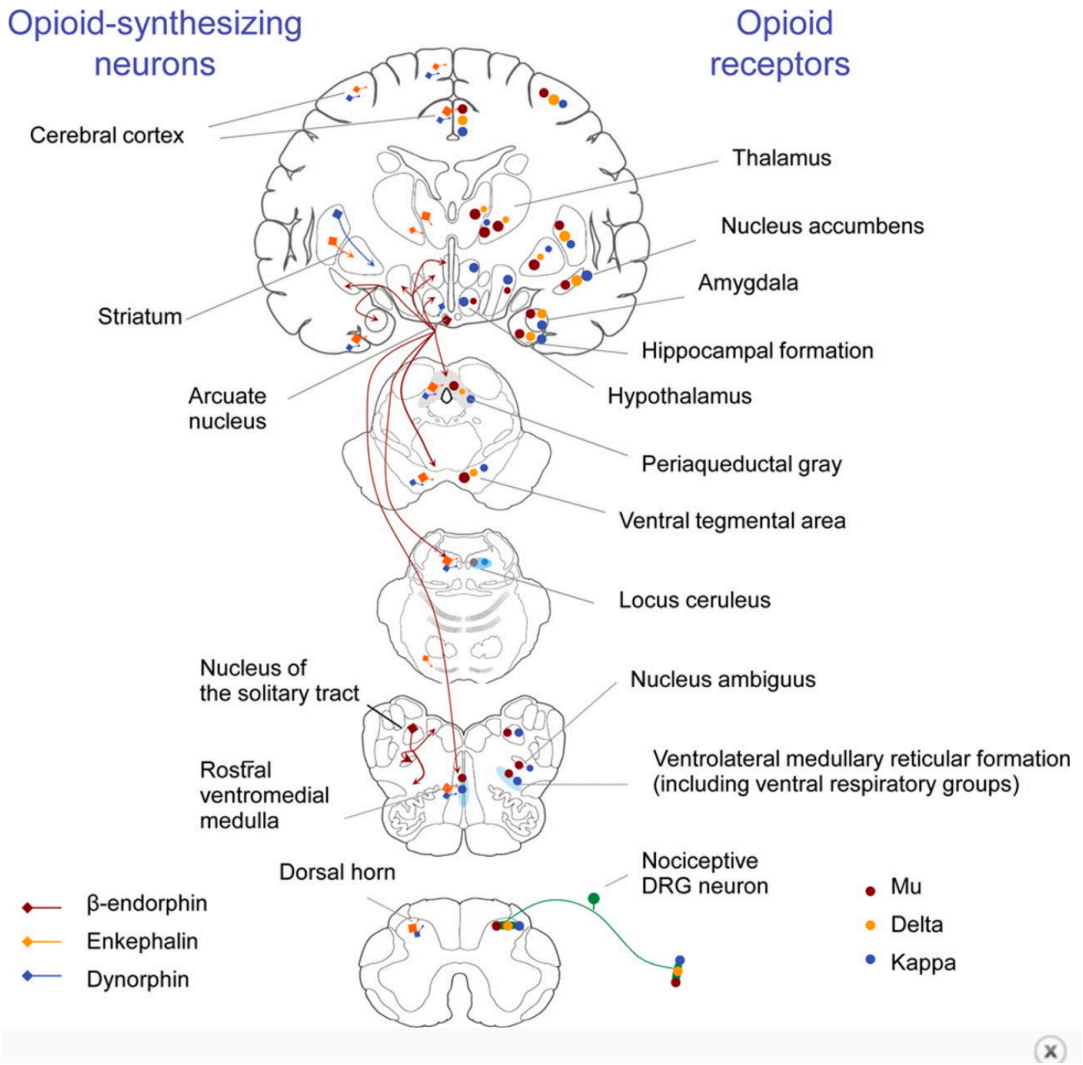
- Why do some people transition from prescription opioids to street drugs such as heroin?
  - Decrease in willingness of doctors to continue prescribing opioids after a certain period of time
  - Heroin is often cheaper than prescription opioids and relatively easy to obtain
  - Heroin is a highly addictive drug, due to various pharmacological properties
    - Some patients report being addicted after their first administration

Why are Opioids SO addictive?

- What makes a drug addictive?
  - A short time between administration to subjective experience of rewarding effects
    - Opioids produce euphoric effects almost right away, so people quickly “learn” to like the drug
  - The impact of the drug on the mesolimbic dopamine system in the brain
    - Exogenous opioids mimic powerful pain-relieving compounds produced by our bodies in times of stress
    - Thus, rewarding effects are extremely powerful
  - The development of tolerance and withdrawal symptoms
    - The strong effects of exogenous opioids cause the body to immediately work to counter these effects to maintain homeostasis
    - This produces tolerance and withdrawal quickly

A Quick Primer: The Endogenous Opioid System

- 3 families of opioid peptides: β-endorphin, enkephalins, and dynorphins
- 3 families of receptors: μ (MOR), δ (λ, DOR), and κ (KOR)
- Distributed in CNS areas that modulate pain, stress and reward



Benarroch, 2012, *Neurology*

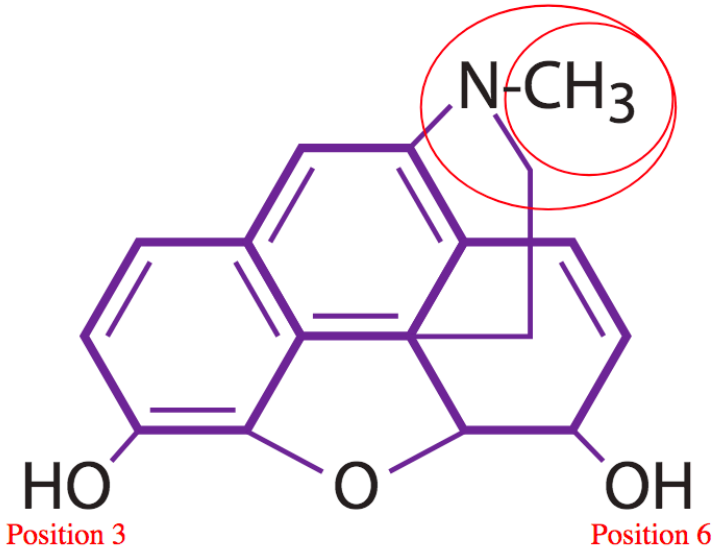
A Quick Primer: The Endogenous Opioid System

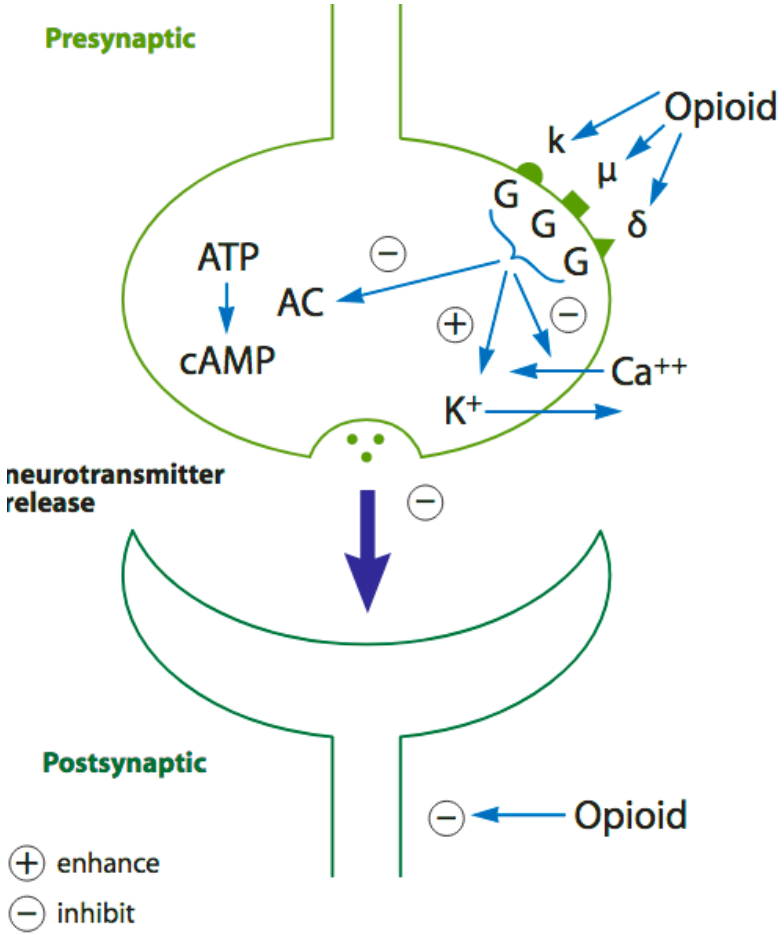
- Functional Consequences of Opioid Receptor Activation
  - Opioids exert various effects, depending on the pre-synaptic or postsynaptic distribution of their receptors in projection neurons and local neurons
  - In many brain regions, such as the PAG and VTA (which are associated with regulation of pain and reward), activation of certain opioid receptors facilitates neurotransmission by inhibiting GABA release from local inhibitory neurons

Benarroch, 2012, *Neurology*

Pharmacology of Opioids

- Majority of clinically relevant opioids have primary activity at the “mu” receptors, dubbed “morphine receptors”

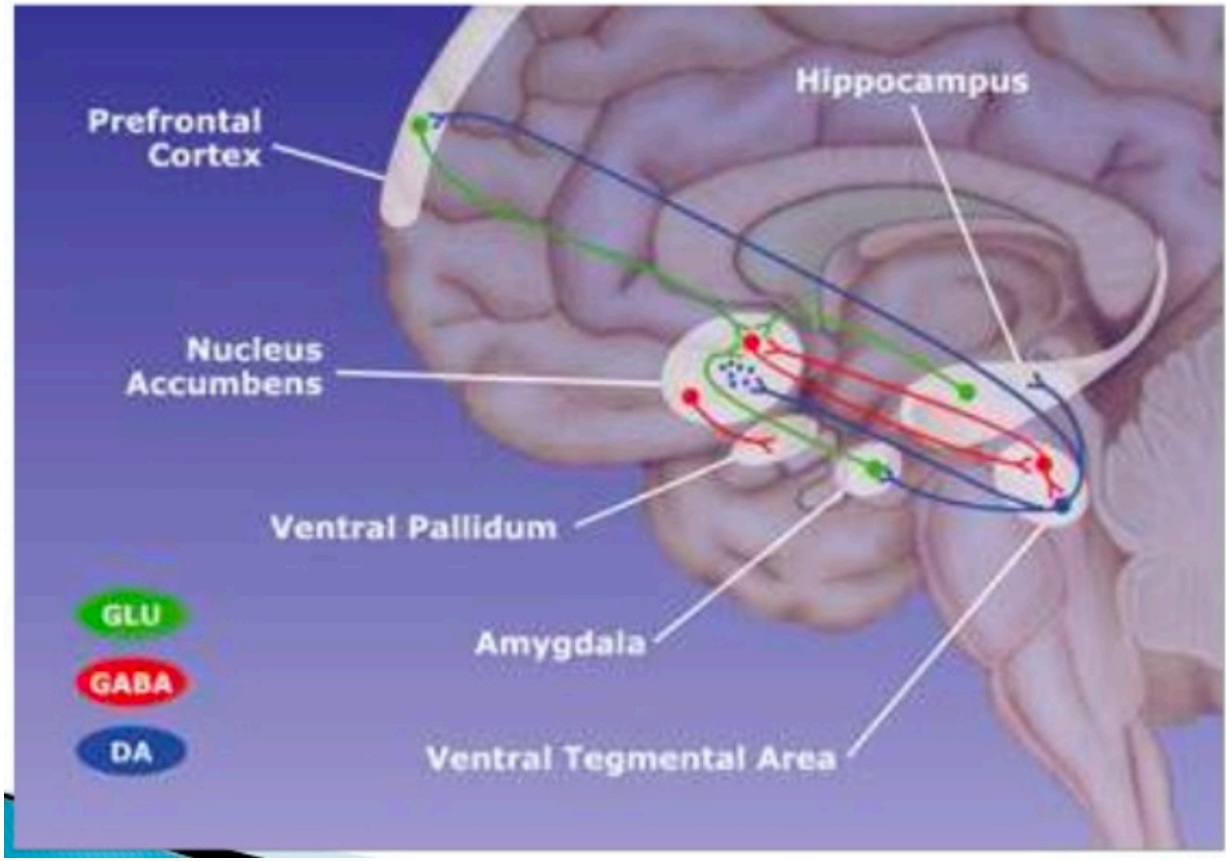




Trescot et al 2008, *Pain Physician*

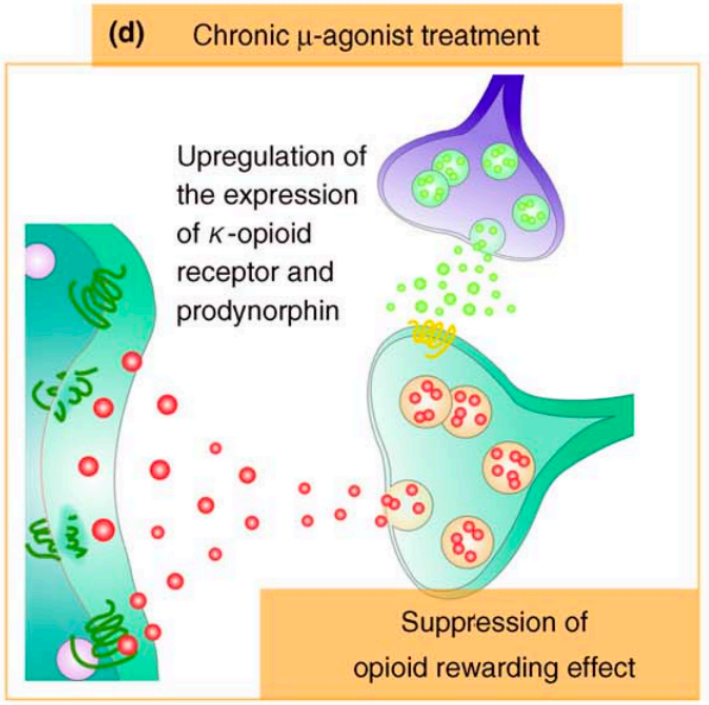
A Quick Primer: The Mesolimbic Dopamine System

- Originates primarily in the ventral tegmental area (VTA) and projects to the nucleus accumbens
- Part of complex **reward circuit** involving the amygdala, hippocampus, and the bed nucleus of the stria terminalis



Opioids and The Brain

- The critical CNS locus for opioid reward is the VTA
  - Mu opioid agonists activate Mu receptors
  - VTA contains dense concentrations of these receptors
  - Thus, numerous opioid synaptic actions within the VTA (especially dopamine neurons)
  - Some mechanisms and sites of actions are still unknown



Fields & Margolis 2015, *Trends in Neuroscience*

Some Important Remaining Questions

- Currently, we lack a complete picture of the acute and long-term effects of opioids on the brain and body
- How reversible or permanent are changes produced by long-term opioid use?
- Opioids may actually make chronic pain worse?
  - “sensitization” hypothesis
- What are the most effective treatments, and how can we match treatments with patients who will be most likely to respond?

Summary

- The pharmacology of opioids makes them highly addictive
  - Social and environmental influences are important for initiation of misuse/abuse
  - Target primarily mu opioid receptors in the brain, specifically in VTA that actives brain reward system
  - Repeated use produces long-term changes in these circuits
  - Repeated use produces tolerance and cutting back/quitting results in withdrawal – powerful incentive not to cut back or quit