



# Opioid Use in Patients with Mental Health and Substance Use Comorbidities

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# Outline



- What do opioids do?
- Who receives long-term opioid therapy for chronic pain, especially high-dose therapy?
- Once long-term opioid therapy is established (>90 days), who discontinues therapy?
- What can be done to support discontinuation in a patient addicted to prescription opioids?
- What can be done to support discontinuation in a patient NOT addicted to any drugs?



**“O just, subtle, and all-conquering opium!”**  
**-- Thomas De Quincey,**  
***Confessions of an English Opium Eater*, 1821**

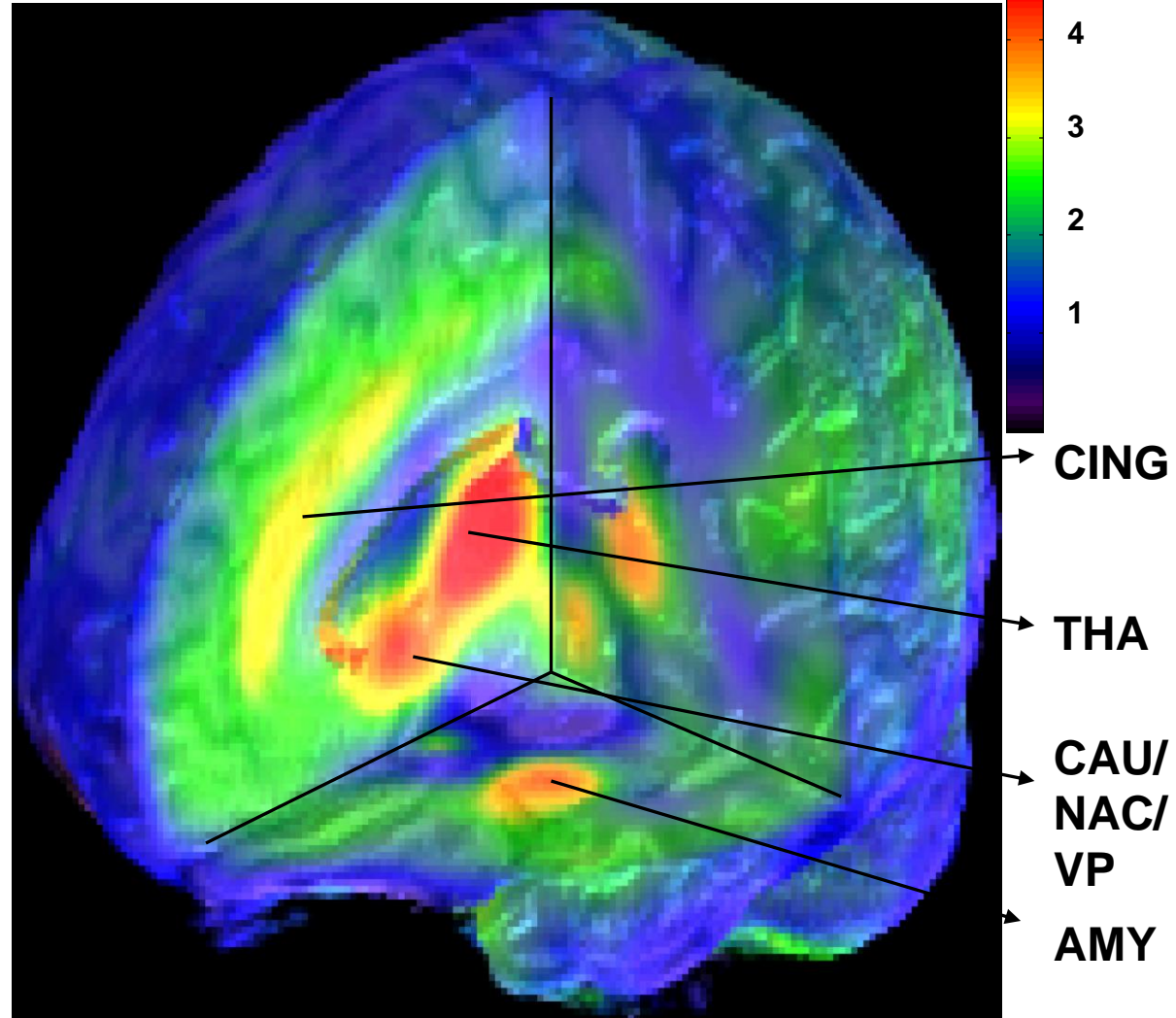
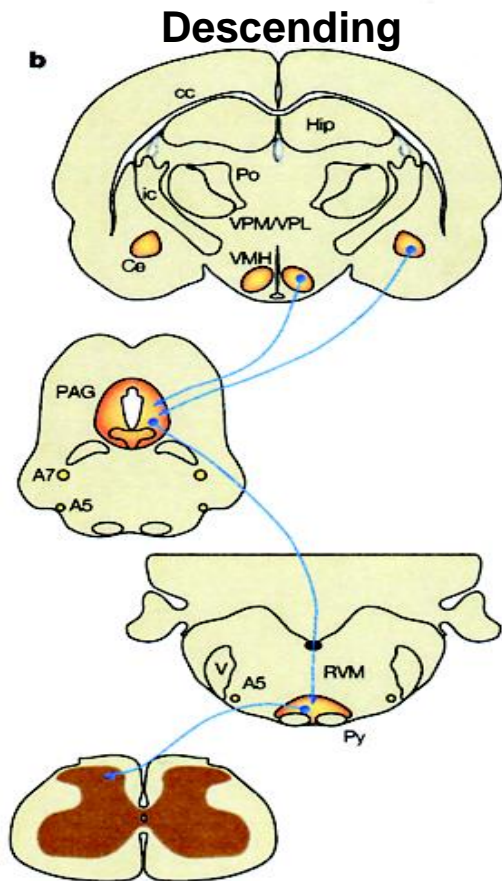
# Functions of the endogenous opioid system

- Analgesia
- Addiction: opioids, stimulants, alcohol, nicotine, cannabis
- Mental health: depression, stress, borderline PD, cognition, learning and memory
- Endocrine: fertility, sexuality, maternal-infant bonding, eating, drinking
- Gastrointestinal, renal and hepatic functions
- Cardiovascular responses, respiration, and immunological responses



# CNS Inhibitory Controls

## Mu Opioid Receptor-Mediated Neurotransmission



**Distributed in pain regions but also “affective / motivational circuits” - neuronal nuclei involved in the assessment of stimulus salience and cognitive-emotional integration.**

# Shared neural substrates for physical and social pain

- Physical pain and social pain use shared neural substrates.
- In primates, social attachment system borrowed the pain system, to prevent social separation (Eisenberger 2012)
  - Social pain (rejection, exclusion, loss) activates physical pain-related neural regions (anterior cingulate, anterior insula) (Eisenberger 2003)
  - Sensitivity to social or physical pain increase and decrease in parallel (Eisenberger 2006)
- Opioids decrease both physical and social pain
  - Opiates reduce distress of social separation (Panskepp 1978)
  - Opioid deficient mice show impaired maternal-infant bonding (Moles 2004)

# Who receives long-term high-dose opioid therapy?

- Rapidly increasing rates of long-term opioid therapy 2000-10
  - National peak of opioid use and abuse reached by 2012 (Dart, NEJM, 2015)
- The vast majority of opioid therapy is short-term. (Noble 2010, Furlan 2006)
  - Most “ideal” candidates for opioid therapy discontinue before reaching 90 days
  - Three-fourths of patients started on ER/LA opioids will not fill a second prescription.
- Of patients prescribed opioids for chronic pain, those who go on to long-term therapy are a highly self-selected group (Morasco 2011, Seal 2012, Edlund 2013)
  - SA and MH disorders much more common in long-term, high-dose users
  - COT cohort progressively enriched with high-risk patients.
- **'Adverse selection':**
  - combination of high risk patients with high risk med regimens
  - May link trends in use, abuse, and overdose



# Who discontinues long-term opioid therapy?

- TROUP study of 'daily' COT recipients (Martin 2011)
  - Sample: used at least 90 days, no 32 day gap
  - Outcome: 6 months without any opioid Rx
  - In two diverse samples (commercial and Medicaid), 70% of patients remain on opioids years later
  - COT continuation predicted by: high daily dose (>120mg MED) and opioid misuse
- Nationwide VA study: >70% continue opioids (Vanderlip, 2014)
  - Continuation predicted by: high opioid dose, multiple opioids, multiple pain problems, tobacco use, but NOT other SA, MH disorders
- Other prospective studies show similar findings (Franklin 2009, Thielke 2014)

# PTSD and opioid use in veterans

- 141,029 Iraq/Afghanistan veterans with chronic pain, ~10% opioid tx.
- 6.5% of veterans w/o MH disorders
- 11.7% with non-PTSD MH disorder
- 17.8% of veterans with PTSD
  - higher-dose opioids, 2 or more opioids
  - receive sedative-hypnotics concurrently
  - obtain early opioid refills
  - Highest rates adverse clinical outcomes

# PTSD and opioid use in civilians

- Among indigent primary care pts, PTSD assoc w more pain, opioids
  - All PTSD sx related to pain, impairment
  - Only avoidance related to opioid use
- Among Af-Am MH patients, PTSD most strongly assoc w opioid use
- Violence exposure or PTSD predicts opioid abuse among teens

# Severity of PTSD and opioid use

- Severity of PTSD highly correlated with severity of opioid abuse
  - Heroin (Dell'Osso, 2014)
  - Prescription opioids and sedatives (Meier, 2014)
  - Medical cannabis and opioids (Bohnert, 2014)
- Prolonged opioid use after physical trauma (Helmerhorst, 2014)

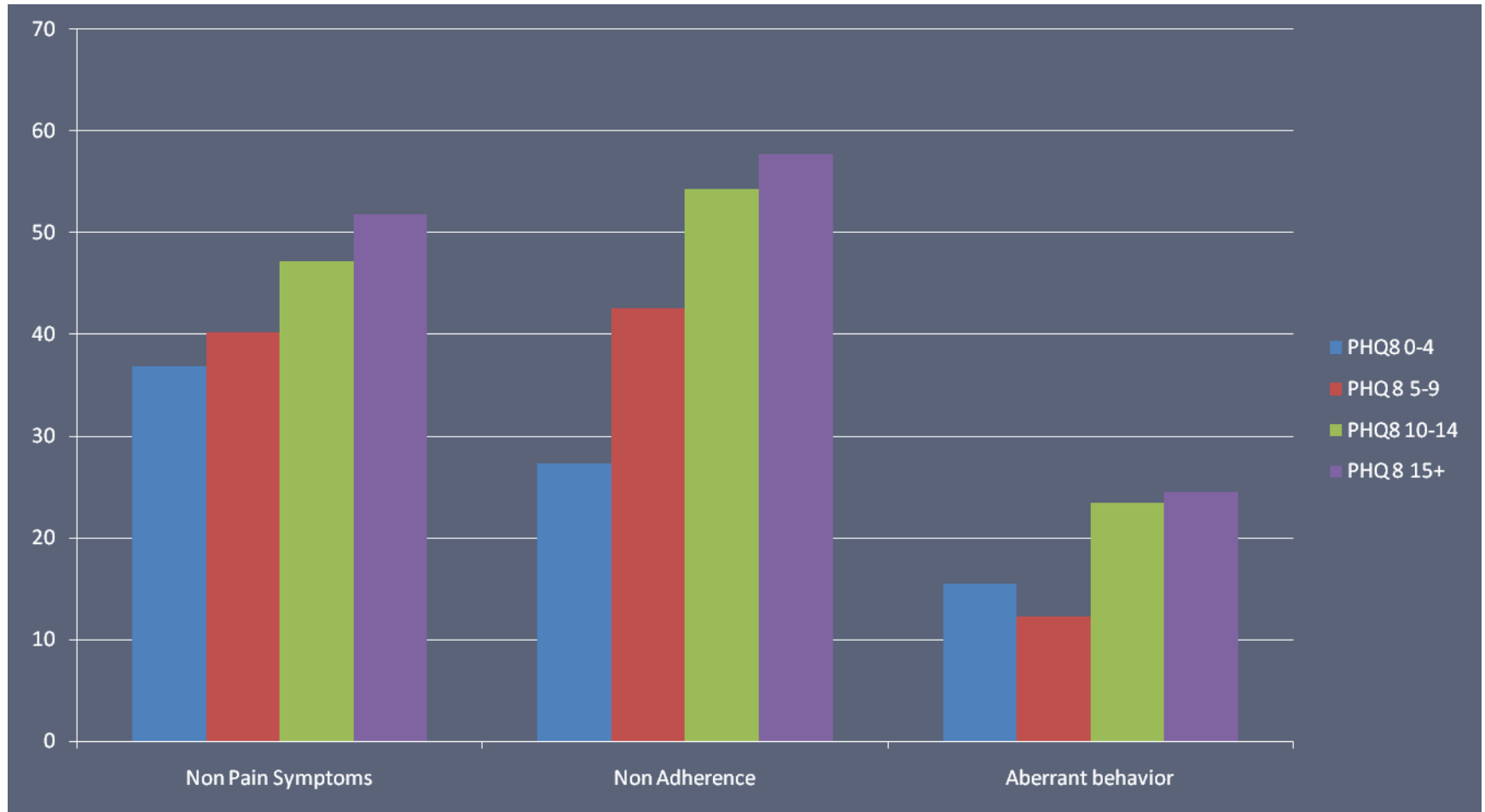
# What do opioids do for PTSD?

- Release of  $\beta$ -endorphin in amygdala after stress inhibits overactivation of HPA axis
- Acute mu opioids after trauma decrease PTSD risk by inhibiting fear-related memory
- K- opioids initially promote escape but then induce anxiety, depression, drug craving
- Chronic opioid use associated with avoidance cluster of PTSD symptoms, but not with improved pain, depression, anxiety outcomes

# Depression and opioid misuse: CONSORT interviews

- Telephone survey 1334 COT patients from GHC KPNC with no hx SA
- Asked about three forms of opioid misuse: 1) self-medicating for non-pain symptoms, 2) self-increasing dose,
- 3) giving/getting opioids from family/friends
- Depression was evaluated by the PHQ8.

# Depression and opioid misuse: CONSORT interviews



Grattan A, et al, *Ann Fam Med*, 2012; 10:304-11.

# Evidence that long-term opioid therapy causes depression

- Among 50,000 veterans with no recent opioid use or depression, the risk of depression incr. significantly as duration opioid Rx incr.:  
HR=1.25 for 90–180d, HR=1.51 for > 180 days.  
(Scherrer et al, *J Gen Intern Med* 29:491–9, 2013)
- Among 355 patients with CLBP, opioid dose increase to >50mg MED incr. depr. OR= 2.65.  
Developing depression increased risk of opioid dose increase. OR= 2.13
  - Scherrer et al, *Pain*, 156 (2015) 348–355



# TROUP study: new opioid abuse diagnoses

- 3% of COT users got opioid abuse dx.  
Associated with : age, prev. SA, MH dxs.,  
more days supply, higher doses, Sched. II
- Among those with a new episode of CNCP  
and COT, opioid treatment >90 days predicts  
abuse dx more than dose:
  - OR= 3 acute, high dose
  - OR= 107 chronic, high dose

# What are we treating with COT?

- Most opioid therapy is brief, few progress to COT, fewer to long-term high dose COT
- This self-selected group has high rates of SA and MH comorbidity, especially PTSD
- We are essentially providing palliative or comfort care to these patients with 'total pain' resulting from both physical and psychological trauma

# Why does adverse selection occur?

- Providers want to help patients in pain and have few tools other than Rx pad
- Patients with MH and SA disorders
  - report higher pain levels
  - are more distressed and more persistent in demanding opioid initiation and dose increases
- Providers use opioid prescriptions as a “ticket out of the exam room”

# Need for psychiatric care of patients receiving long-term opioid therapy

The rise of chronic opioid therapy for chronic non-cancer pain with accompanying opioid overdoses, abuse and misuse has further highlighted the importance of psychiatric disorders in the population

Howe CQ, **Sullivan MD**, The Missing 'P' in Pain Management: How the Current Opioid Epidemic Highlights the Need for Psychiatric Services in Chronic Pain Care, *Gen Hosp Psychiatry*, 2014; 36:99-104. doi: 10.1016/j.genhosppsych.2013.10.003



# Conclusions

- Despite the fact that all treatment guidelines discourage prescribing high-dose long-term opioid therapy to patients with MH and SA disorders:
  - It is common in every health system
  - It is associated with high rates of adverse events
- Any patient being considered for high-dose long-term opioid therapy should have psychiatric consultation to make sure these disorders are addressed