Opioids

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Opioids

- Naturally occuring: Morphine, Codeine
- Semi-synthetic:
  - Hydromorphone (Dilaudid)
  - Diacetylmorphine (Heroin)
  - Oxycodone (Percodan)
- Synthetics:
  - Methadone
  - Meperidine (Demerol)
  - Fentanyl (Sublimaze)

Opium Poppies in Northern Thailand
photo by John W. Allen

Opioid History

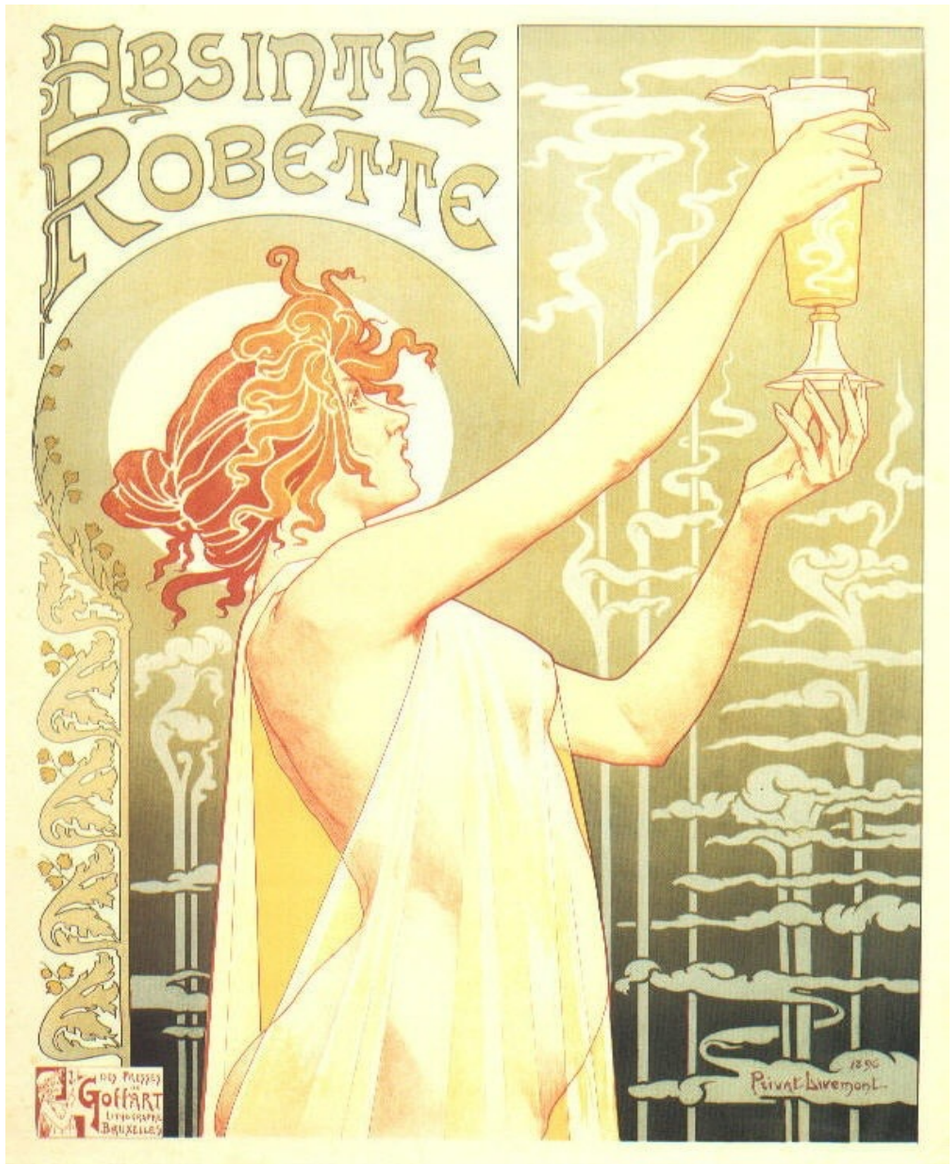
- 1300 B.C. Egyptians cultivate opium poppies.
- 330 B.C. Alexander the Great introduces opium to Persia and India.
- C. 1000 Opium is used medicinally throughout China and India.
- 1500 Opium is introduced to Europe by Paracelsus as Laudanum and used as a painkiller.

Opioid History

- 1700 Opium smoking begins in Asia.
- 1750 Britain assumes control of the opium trade.
- 1800s
  - Opium becomes widely available in medicinal preparations.
  - Laudanum cheaper than beer in England, addiction increases among working classes.

Opioid History

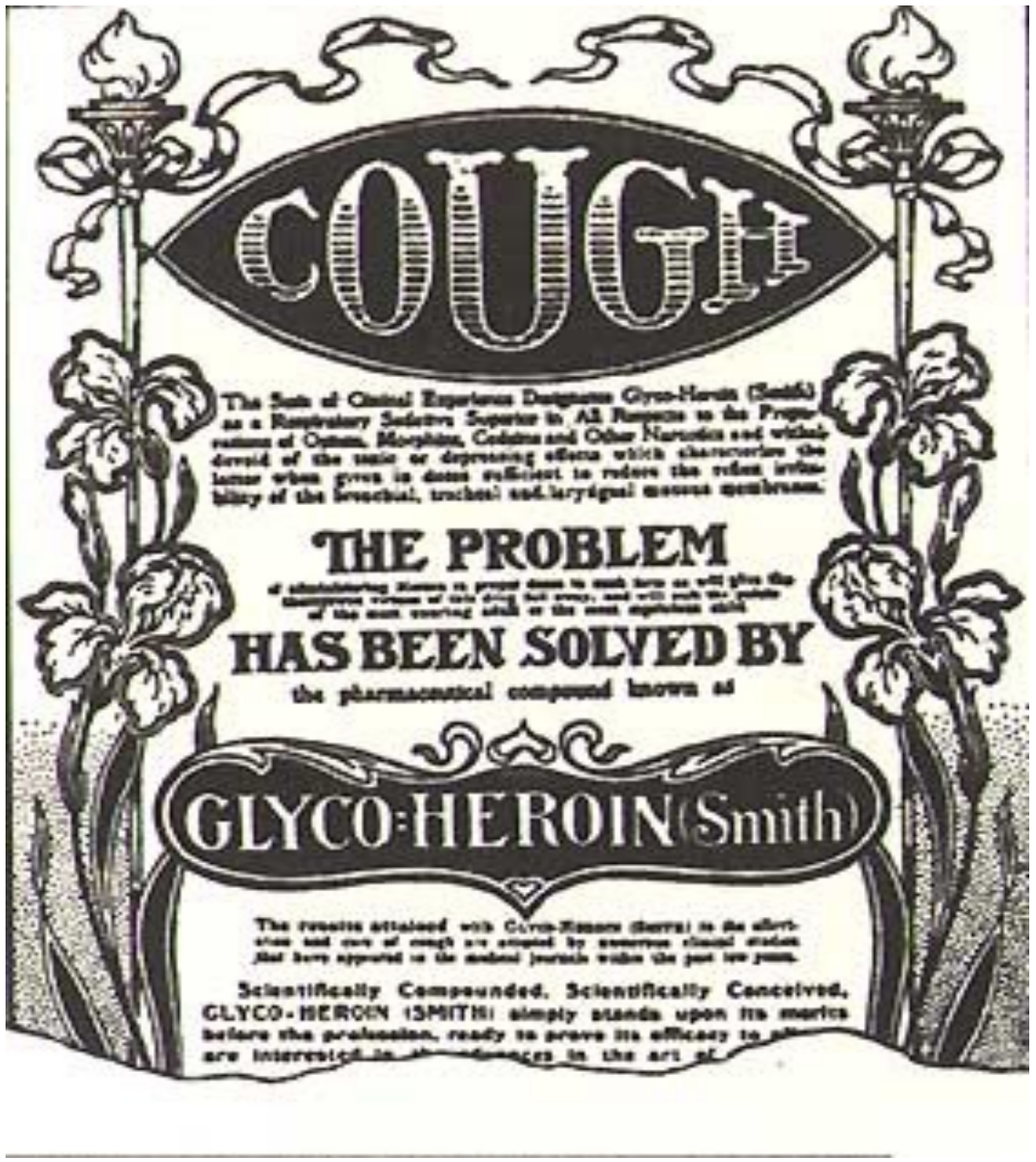
- 1800s
  - Some notable figures are known to use opium:
    - Byron, Shelley, Coleridge, Dickens
- 1803 Morphine is isolated from the poppy



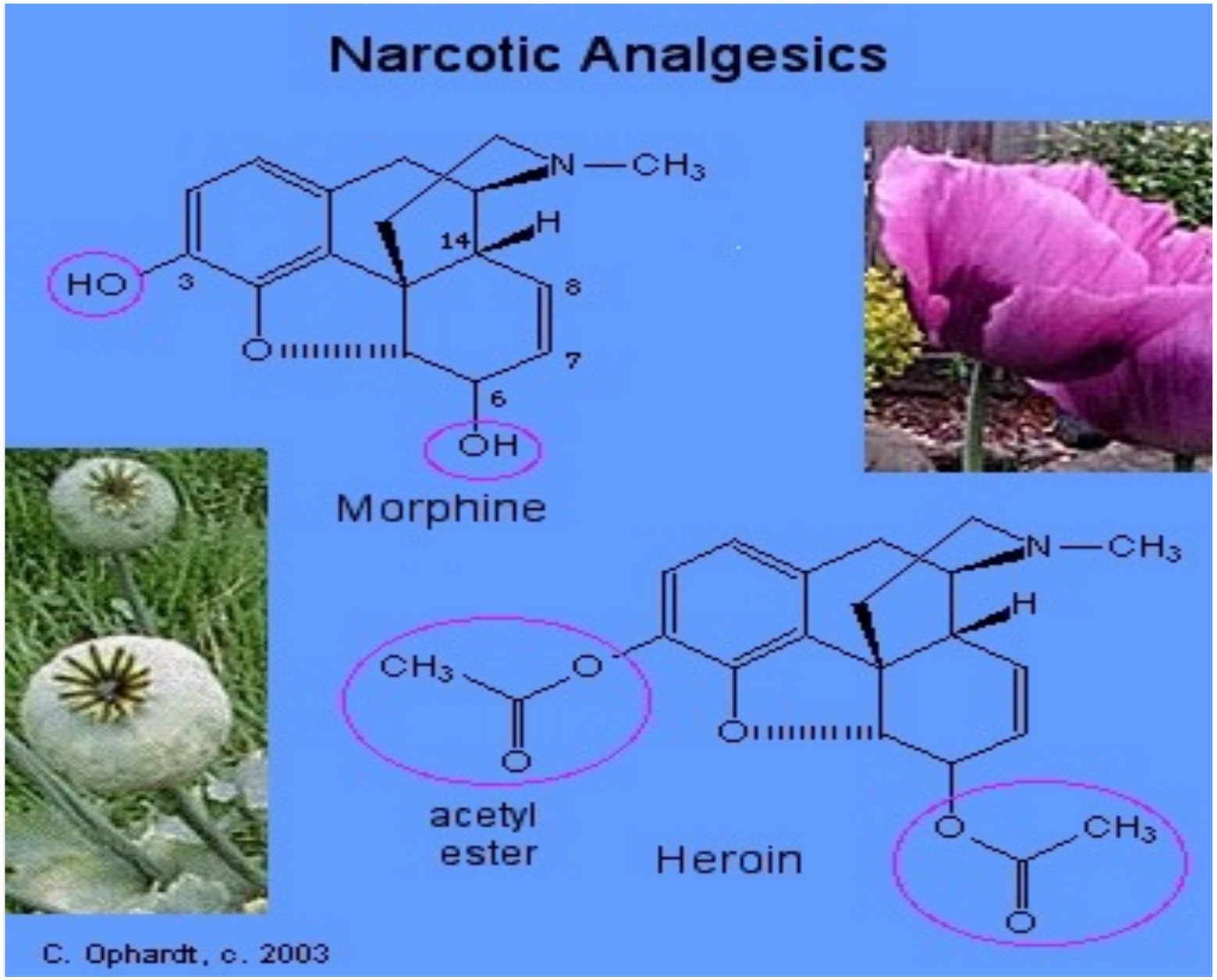
Opioid History

- 1853 First hypodermic needle invented by Pravaz and Wood. Morphine is the first injected substance.
- 1897 Heroin is synthesized by Felix Hoffman at Bayer Pharmaceutical. Bayer immediately recognized its potential and began marketing it heavily for the treatment of a variety of respiratory ailments.
- 1913 Bayer stops making heroin.

Heroin for your cough



Morphine v. Heroin



Opioid Mechanism

- Opioids bind to the opioid receptor.
- Opioid receptors are found in the CNS and PNS.
- There are several receptor subtypes, but the Mu 1 and 2 are most important:
  - Mu1: moderates euphoria and analgesia of opioids.
  - Mu2: modulates respiratory depression.

The Mu Receptor

- Types of Mu binding
    - Full Agonist: highly reinforcing, common in abuse
        - Heroin, methadone, oxycodone
    - Partial Agonist: activates at lower levels, less reinforcing, less abused.
        - Buprenorphine
    - Antagonist: occupies without activating, not reinforcing, blocks and displaces.
        - Naloxone, naltrexone

Opioid Tolerance

- Tolerance to opioids develops quickly.
- Changes in the number and sensitivity of opioid receptors are suspected.
- Many of the side effects of opioids decrease with increased use of the drug, save one…

Opioid Effects

- "Heroin: imagine the best orgasm you have ever had and multiply it by a thousand and you're still nowhere near it"
  'Mark Renton' in TRAINSPOTTING

Opioid Effect

- All opioids cause the following to a certain extent:
  - Euphoria
  - Analgesia
  - Pupilary constriction
  - Apathy
  - Drowsiness
  - Respiratory Depression
  - Constipation, Nausea

Opioid Intoxication

DSM 5 Criteria

- A. Recent use of an opioid.
- B. Clinically significant problematic behavioral or psychological changes
- C. Pupilary constriction (or dilation in severe OD) and one + of the following:
  - Drowsiness or coma
  - Slurred speech
  - Impairment in attention or memory.
- D. Symptoms not due to a general medical condition or other mental disorder.

Opiate Withdrawal

DSM 5 Criteria

- A. Either of the following:
  - Cessation of or reduction in opioid use that has been heavy or prolonged (weeks)
  - Administration of an opioid antagonist after a period of opioid use.

- B. Three or more of the following developing within minutes to days after A:
  - Dysphoric mood
  - Nausea/Vomiting
  - Muscle aches
  - Lacrimation or rhinorrhea
  - Pupillary dilation, piloerection, sweating
  - Diarrhea
  - Yawning
  - Fever
  - Insomnia

Opioid Withdrawal

DSM 5 Criteria (cont.)

C. Symptoms in B cause distress or impairment in social, occupational, or other areas.

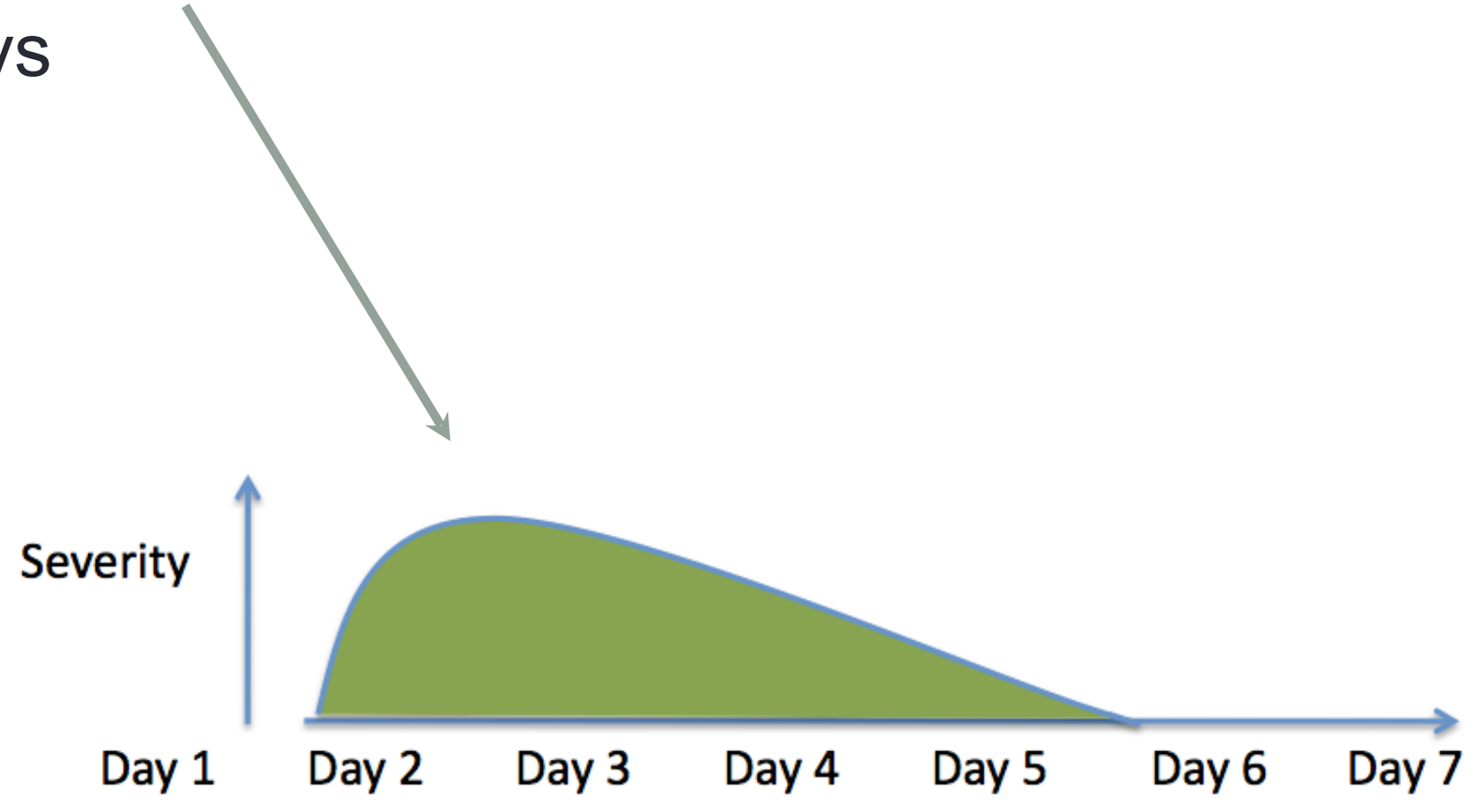
D. Symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

Opioid Withdrawal

- General rule:
  - Opioids with a short duration of action produce a short, intense withdrawal
  - Opioids with a long duration of action produce a prolonged withdrawal.
- Treatment:
- IV Naloxone if patient in respiratory distress.
- Methadone or Suboxone, if objective symptoms are present.

Opioid Withdrawal: Timing

- Short Acting
  - Heroin,oxycodone,hydrocodone
  - Begins: 12 hrs after last
  - Peak: 36-72 hrs
  - Duration: ~5 days
- Longer Acting
  - Methadone
  - Longer
  - Less severe



Methadone Maintenance

- What?
  - Use of a long acting medication in the same class as the abused drug. Dosed daily
  - Prevents withdrawal
- What it is not:
  - Substitution of “one addiction for another”
  - No longer an addict, but still dependent
- Who is appropriate?
  - >16 yo
  - 1 year hx of dependence
  - Medically compromised patients
  - Pregnant women

Methadone Maintenance

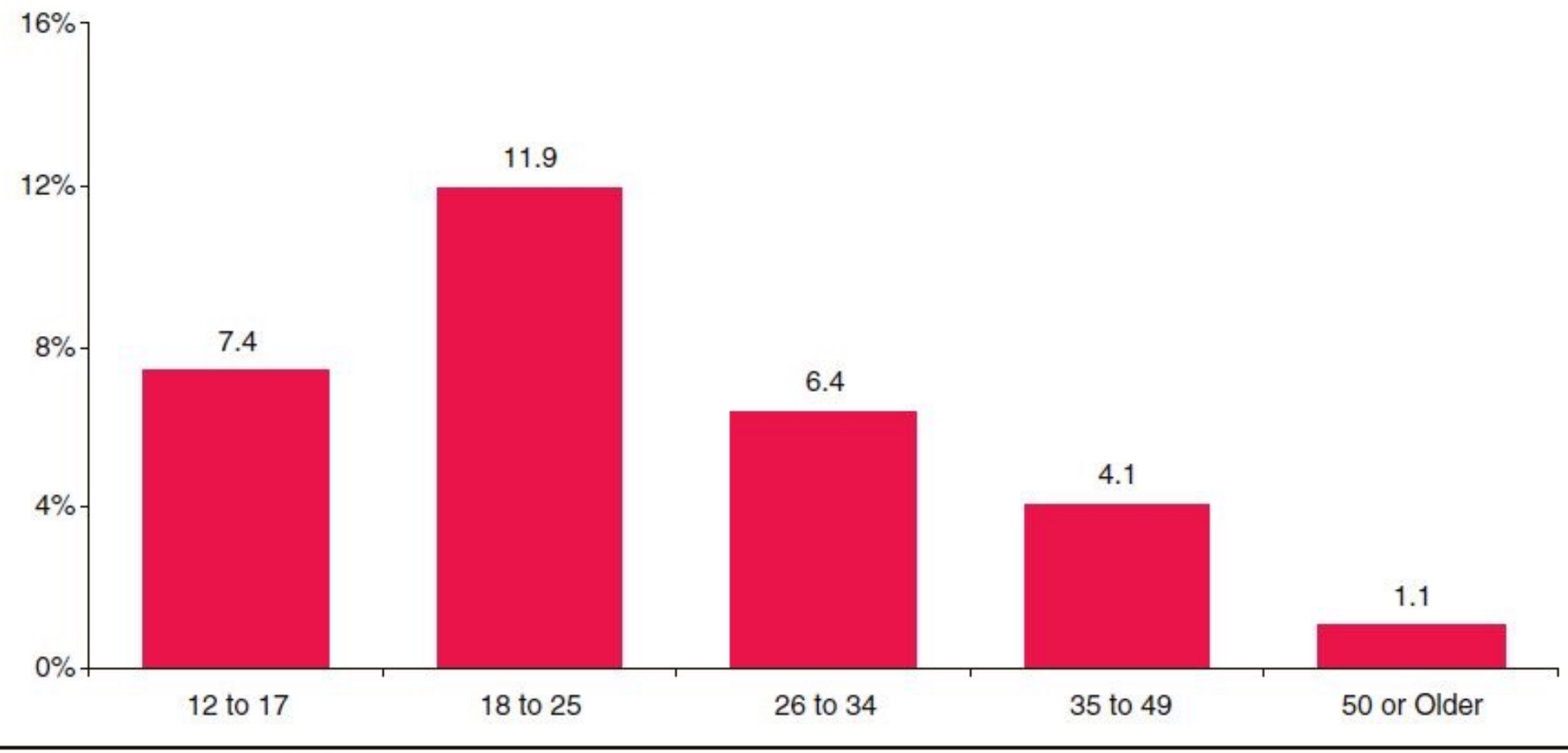
- Why?
    - Long half life (24-36 hours)
    - Regularly scheduled
        - Produces steady state
        - Alertness without craving
- Full agonist
- Steady state reached over weeks, 3-7 days on same dose.

Buprenorphine

- Mu partial agonist
- Pills
    - Suboxone: buprenorphine (4) + naloxone (1)
    - Subutex: buprenorphine only. Give in controlled settings
    - Long acting
- Wait until withdrawal starts
- 2-4mg first day, then increase over 3 days, avg 16-20mg

Prescription opioid abuse is a problem of young people.

Figure 2. Percentages of Past Year Nonmedical Prescription Pain Reliever Use among Persons Aged 12 or Older, by Age Group: 2002-2005



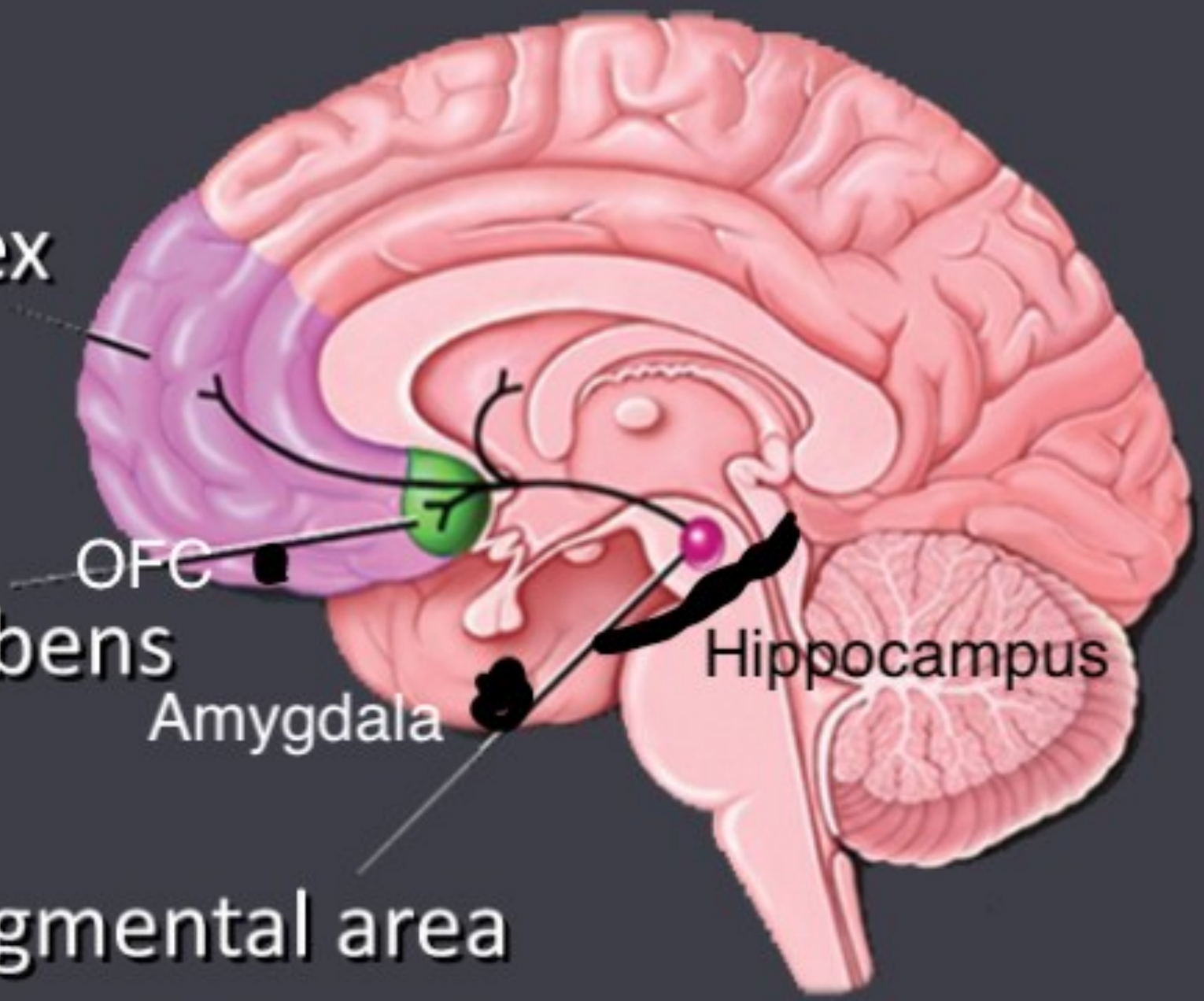
Source: SAMHSA, 2002-2005 NSDUHs.

Aberrant Behaviors

- Deterioration in work/home
- Resistance to change in therapy
- Use by injection, nasal
- Early refills
- Lost/stolen Rxes
- Doctor shopping
  - ISTOP
- Prescription forgery
- Abuse of other substances
- Frequent ED visits
- Unauthorized dose increases
- Seeks specific drug
- Refuses referral to specialist

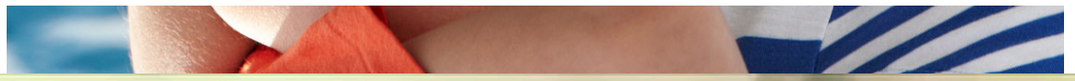
*not all behaviors equal

Prefrontal cortex



Ventral tegmental area

Training Sound



What if they get addicted?

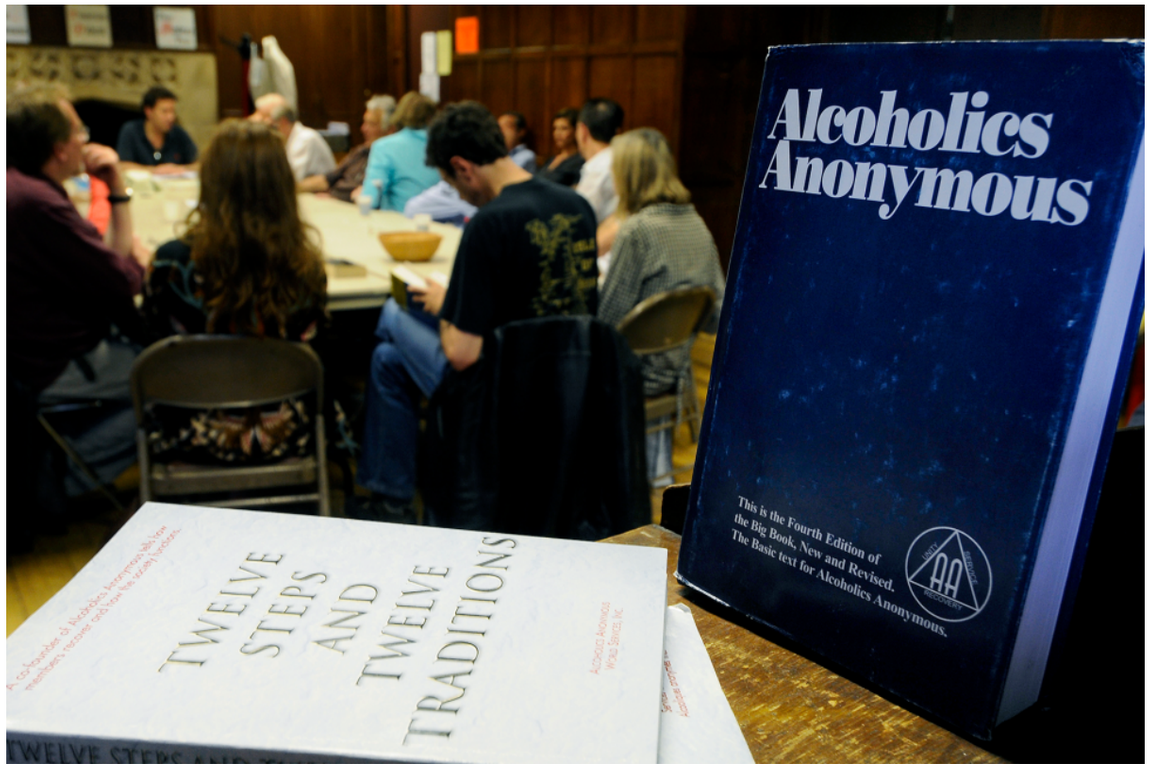
Levels of Treatment:

I: Outpatient
II: Intensive Outpatient & Partial Hospitalization
III: Residential & Inpatient
IV: Medically Managed Inpatient Treatment

**If they deny addiction, cutting them off won't help, they will get opioids from other sources. Outcomes are much worse if they don't self-admit addiction

Additional Treatment Components

- Psychosocial Services
  - Individual therapy
  - Group therapy
  - Family therapy
  - 12 Step/ Mutual Support Groups
  - Higher psychiatric severity patients more responsive to increased services
- Contingency treatments very useful-reward good behavior
  - Vouchers
  - Take homes
  - Prize Incentives



The Most Important Skill to Learn

- The most valuable skill you can learn in Medical School

- How to effectively communicate with your patients to help elicit change