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Injured Workers and Opioid Use Symposium
March 1, 2017

Biology of Addiction

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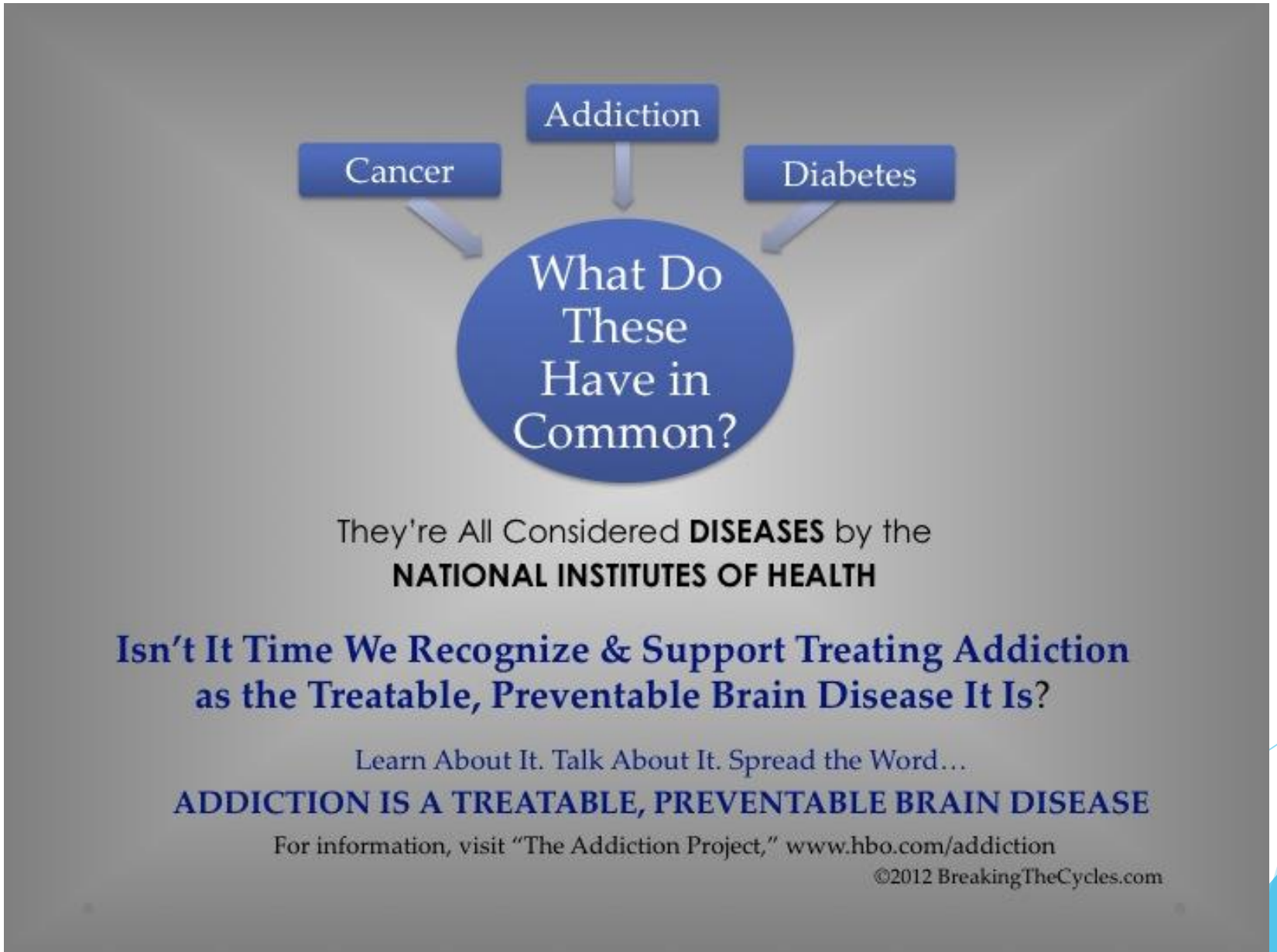

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Timing

Priming

Biology

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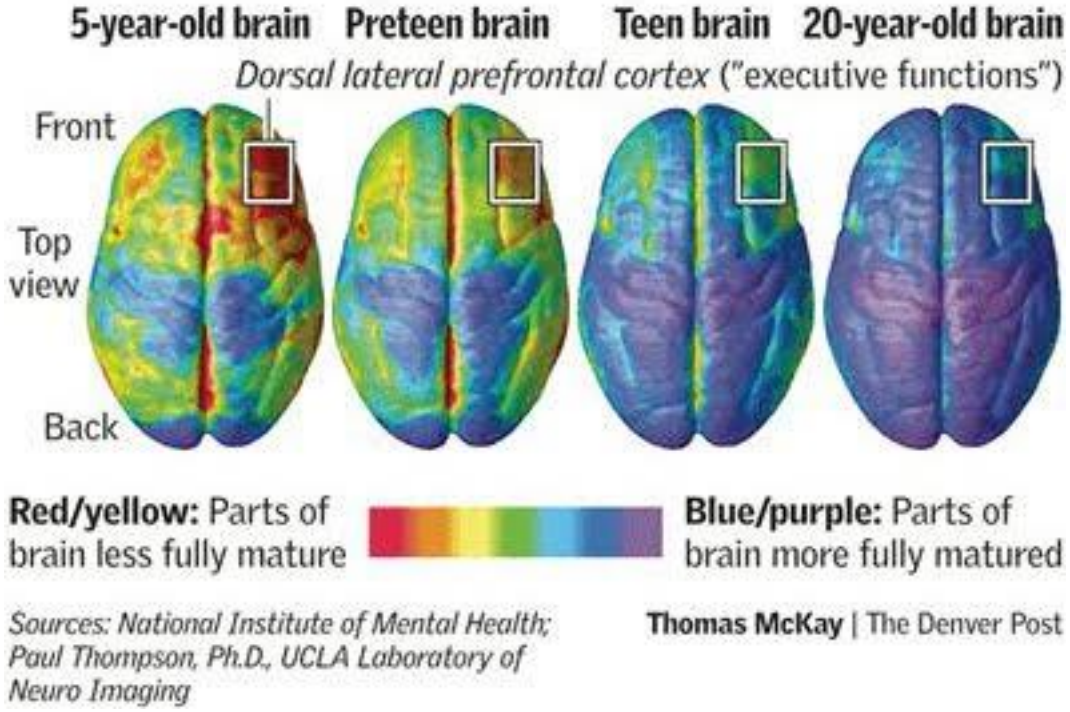
Early Exposure is Toxic



The Brain, particularly the decision making area does not finish developing until age 21

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National Center of Addiction and Substance Abuse

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Priming

Adverse Childhood Experiences

Psychological Factors/Mental Illness

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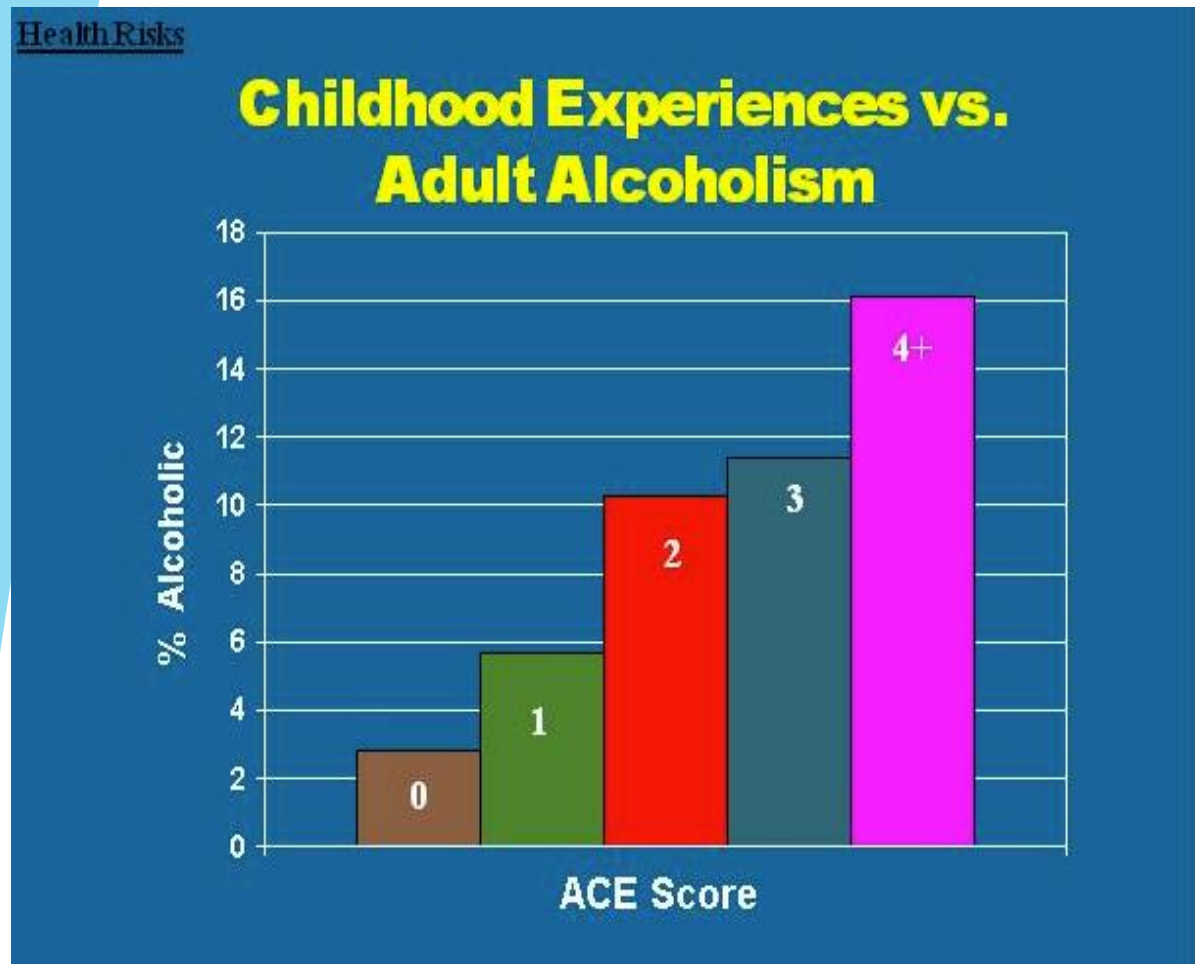
The Adverse Childhood Experiences Scale Score is Associated with Addiction

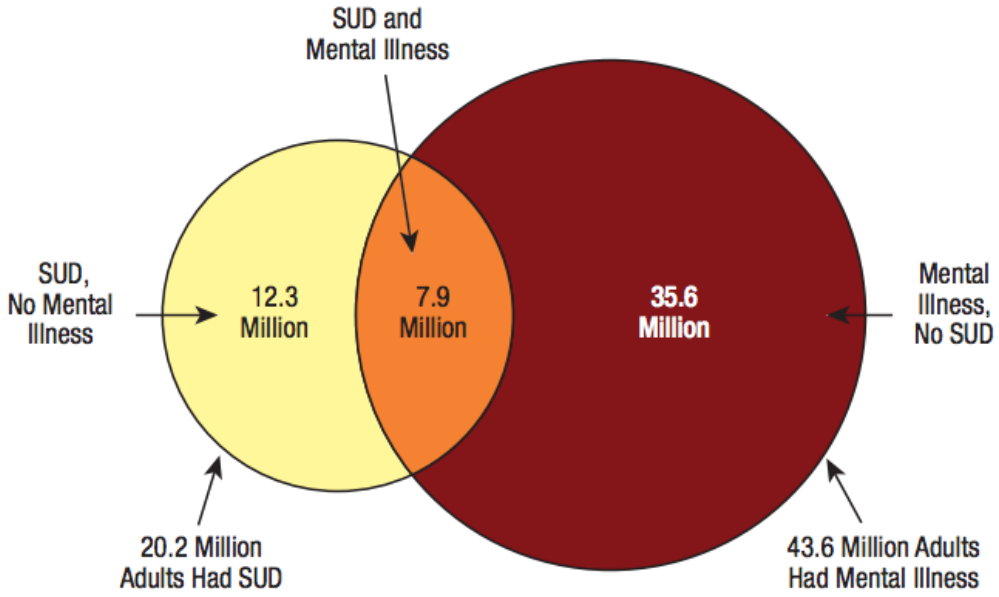


Childhood Abuse and Neglect as well as Parental Mental Illness and Addiction and Witnessing Violence increase risk of developing Addiction

https://acestoohigh.com/got-your-ace-score/

Mental Illness Increases Risk

Figure 48. Past Year Substance Use Disorders and Mental Illness among Adults Aged 18 or Older: 2014



SUD = substance use disorder.

Four childhood traits are associated with development of addiction:

Impulsiveness

Hopelessness

Anxiety Sensitivity

Sensation Seeking

J Am Acad Child Adolesc Psychiatry. 2013 Sep;52(9):911-20. doi: 10.1016/j.jaac.2013.05.020. Epub 2013 Jul 3

https://www.samhsa.gov/data/sites/default/files/NSDUH-FRR1-2014/NSDUH-FRR1-2014.pdf

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Biology

Genes

http://www.centeronaddiction.org/addiction/addiction-risk-factors

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Genetic Variants in Addiction

OPRMI codes for mu receptor- low levels of receptors tied to increase risk of addiction and severity of OD

Hancock DB, Levy JL, Gaddis NC, et al. *Cis*-Expression Quantitative Trait Loci Mapping Reveals Replicable Associations with Heroin Addiction in *OPRM1*. *Biological psychiatry*. 2015;78(7):474-484. doi:10.1016/j.biopsych.2015.01.003.

SNF804A is involved in Dopamine Release and Synthesis

Hancock DB, Levy JL, Gaddis NC, et al. Replication of *ZNF804A* gene variant associations with risk of heroin addiction. *Genes, brain, and behavior*. 2015;14(8):635-640. doi:10.1111/gbb.12254.

Infants with NAS have genetic variant

Wachman EM, Hayes MJ, Brown MS, Paul J, Harvey-Wilkes K, Terrin N, Huggins GS, Aranda JV, Davis JM. Association of *OPRM1* and *COMT* Single-Nucleotide Polymorphisms With Hospital Length of Stay and Treatment of Neonatal Abstinence Syndrome. *JAMA*. 2013;309(17):1821-1827. doi:10.1001/jama.2013.3411

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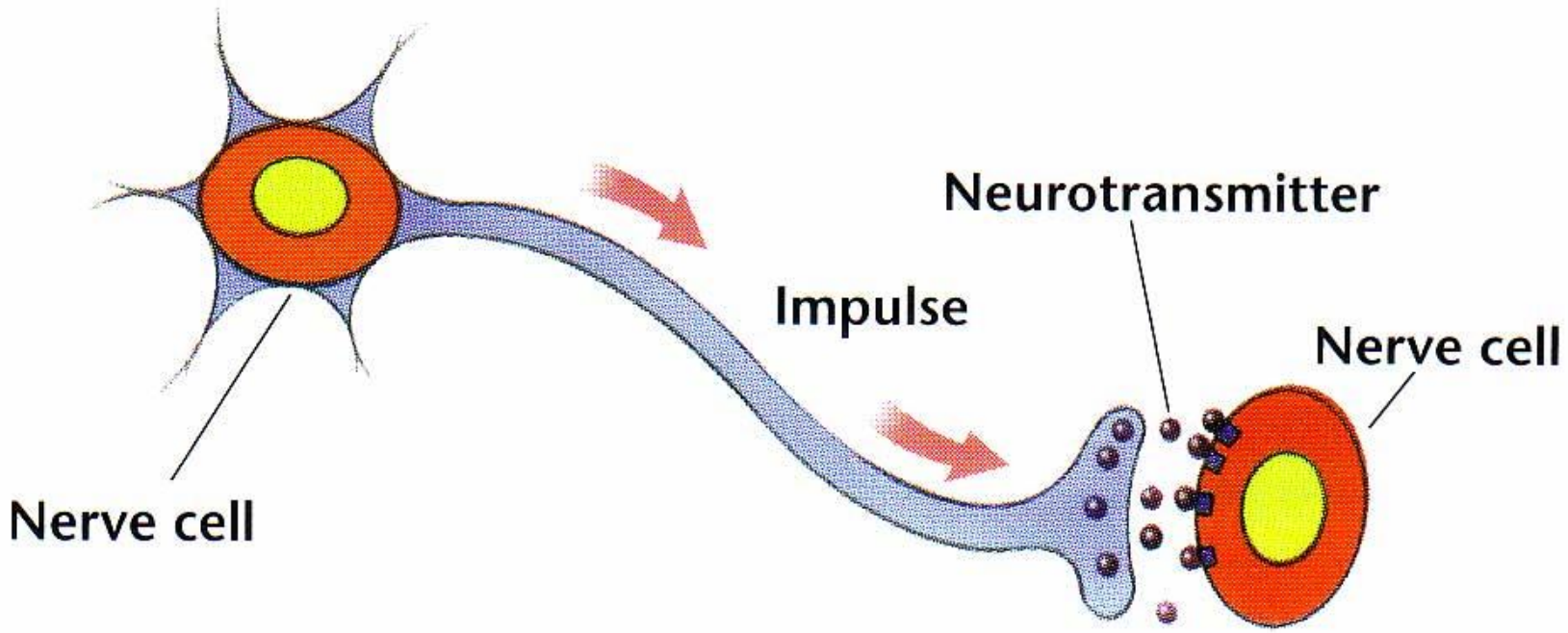
Opioids and the Reward System



http://grivina.com/diagram/brain-cell-diagram/

Opioid Receptors

Location	Action	Tolerance/Dependence
Reward Center	Euphoria	Yes
Pain Center	Analgesia	Yes
Brainstem	Respiratory Suppression	NO
GI tract	Constipation	Little to none

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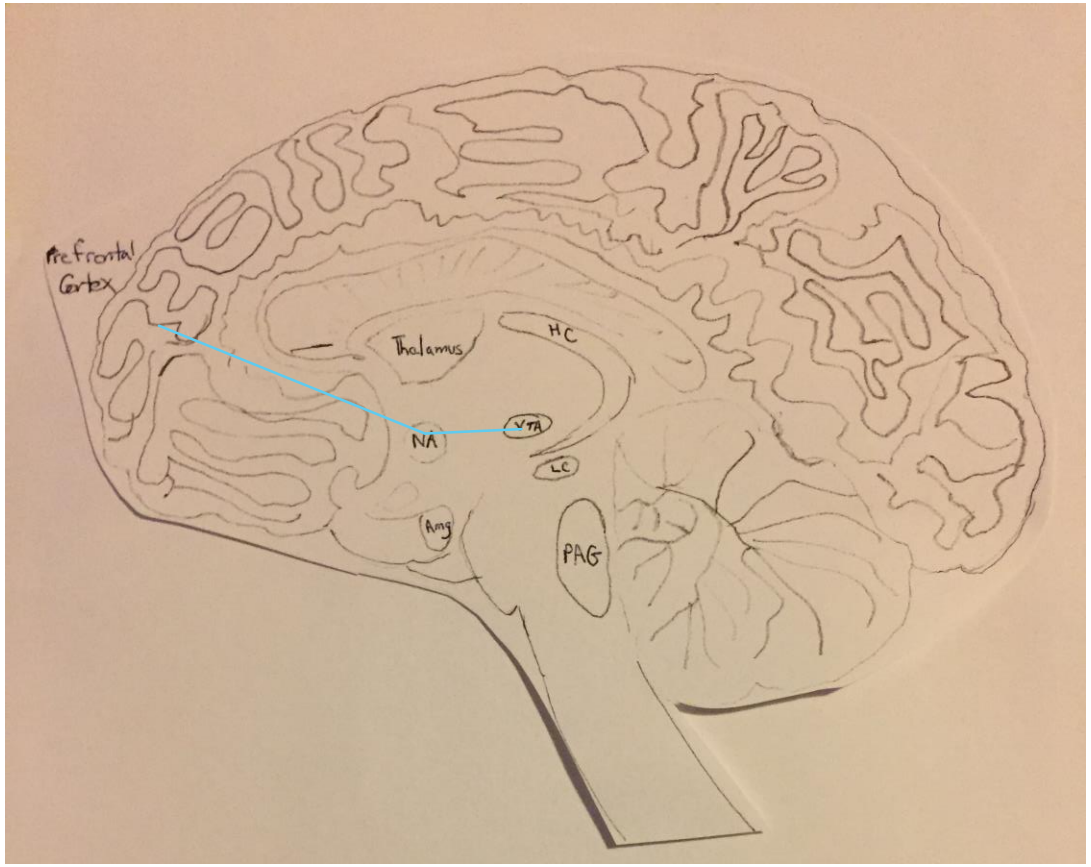
Neuroanatomy of Addiction



THE REWARD CIRCUIT:

Opioids in the VTA (ventral tegmental area) lead to more Dopamine in the NA (nucleus accumbens) which connects to the PFC (prefrontal cortex) which registers pleasure

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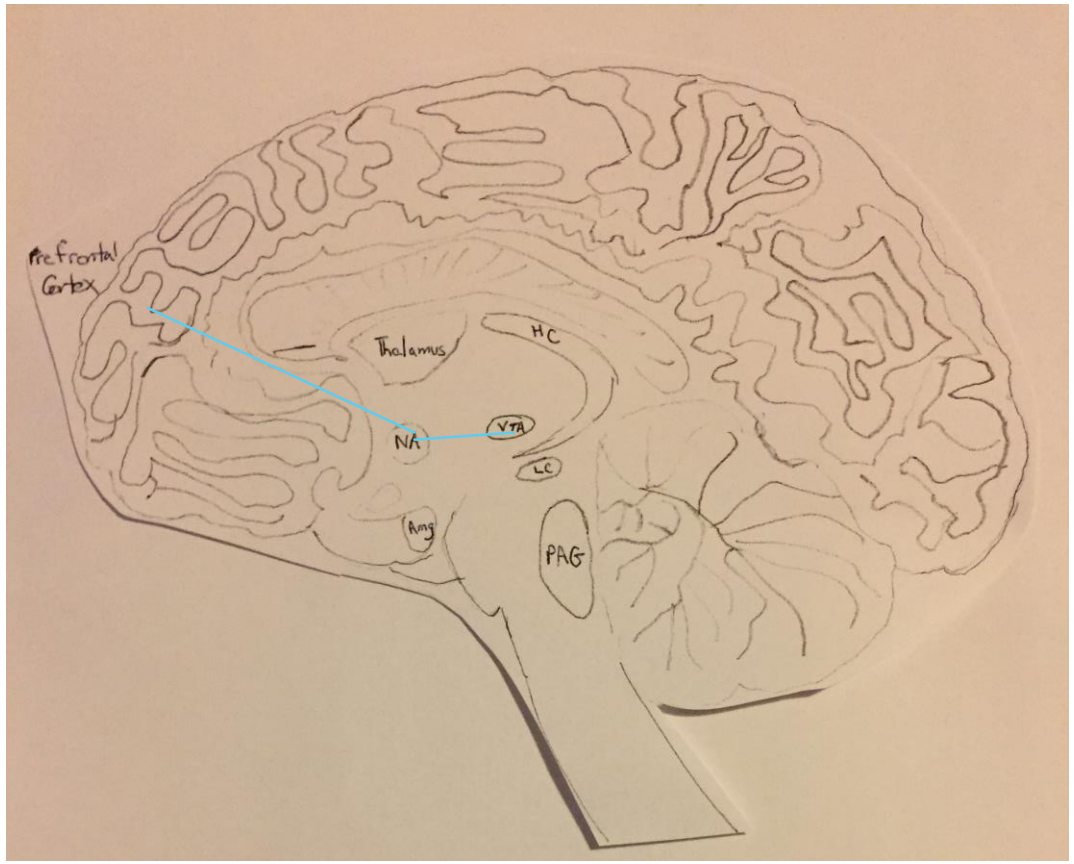
Neurological Basis of Addiction



There is something different about the reward circuit in people who go on to addiction:

Nothing moderates use and it becomes compulsive no longer responding to the judgement and decision making of the PFC.

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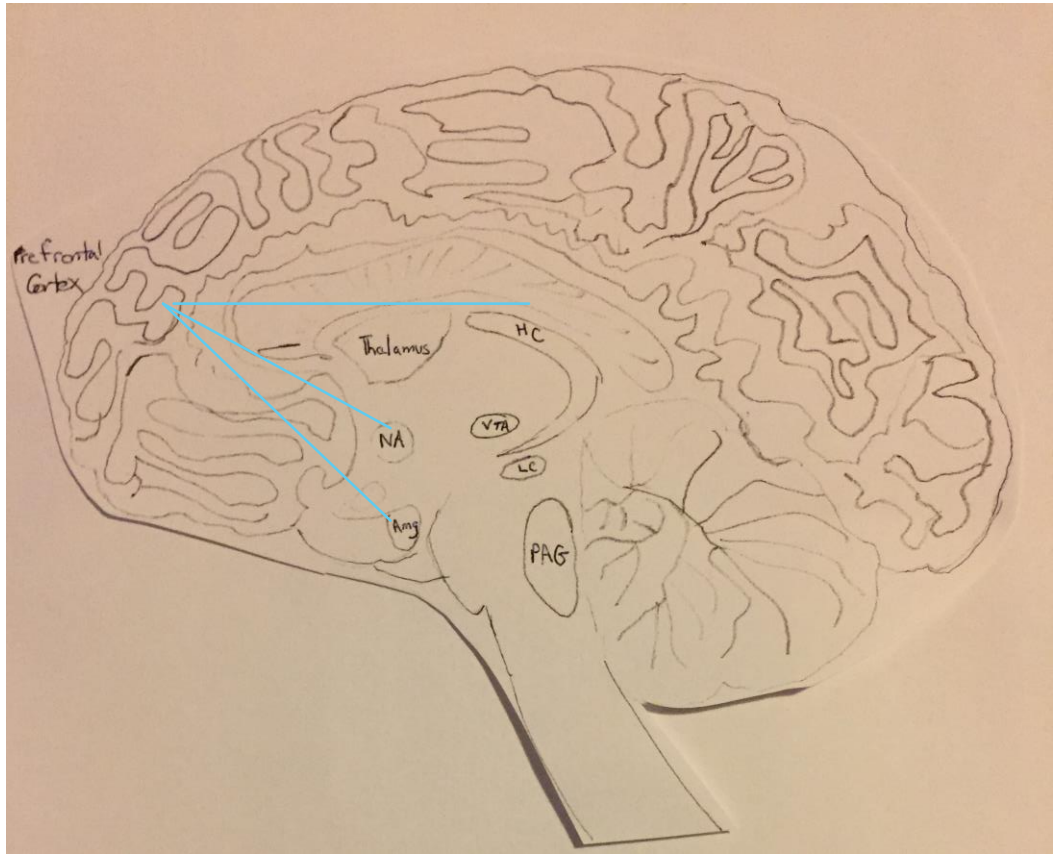
Neurological Basis of Addiction



The PFC is responsible for integrating information from the NA along with the HC (hippocampus) and the Amg (amgydala) which process emotion and memory. The PFC uses this information to form judgements and make decisions. This regulates use in healthy people.

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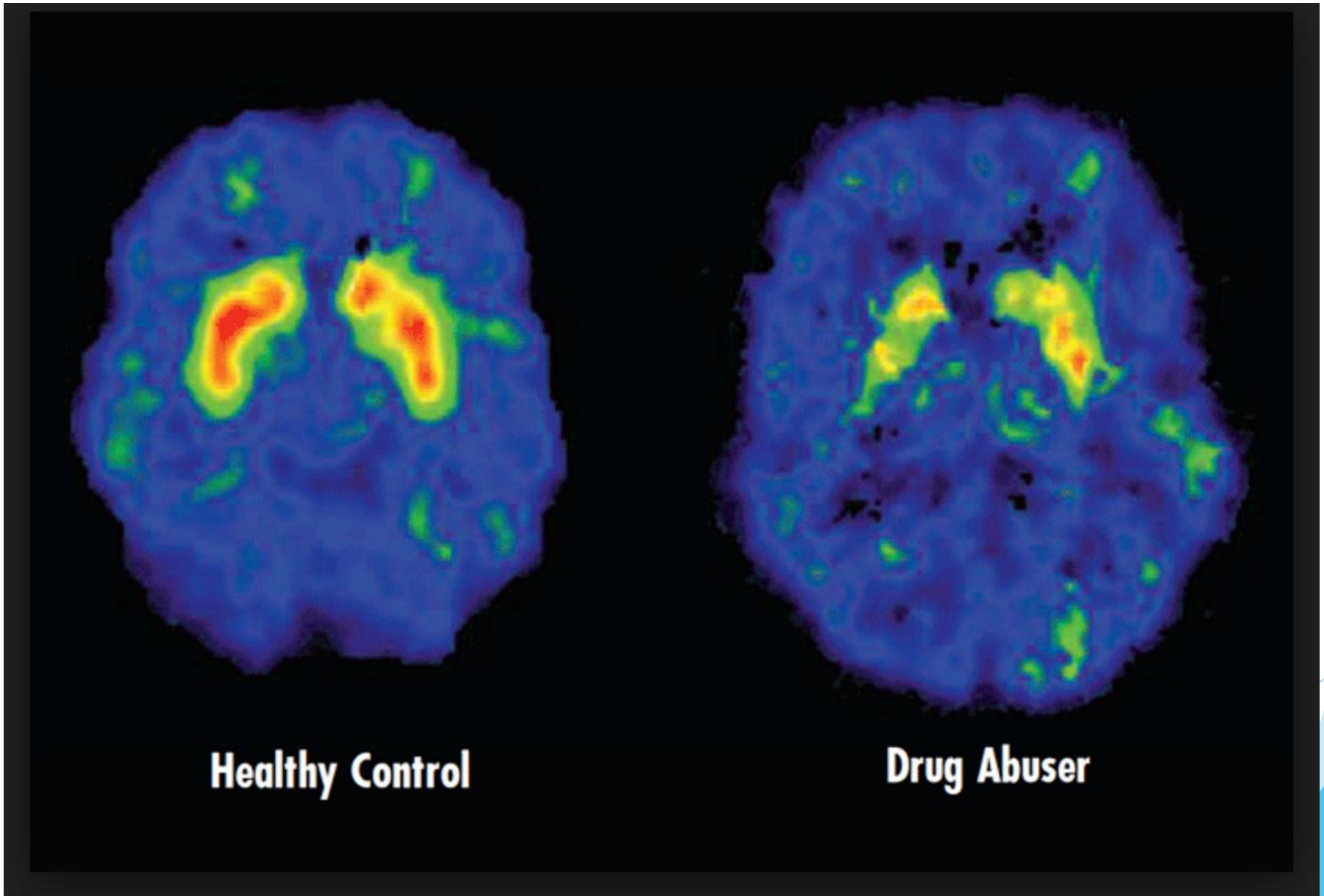

NIDA Drugs, Brains and Behavior

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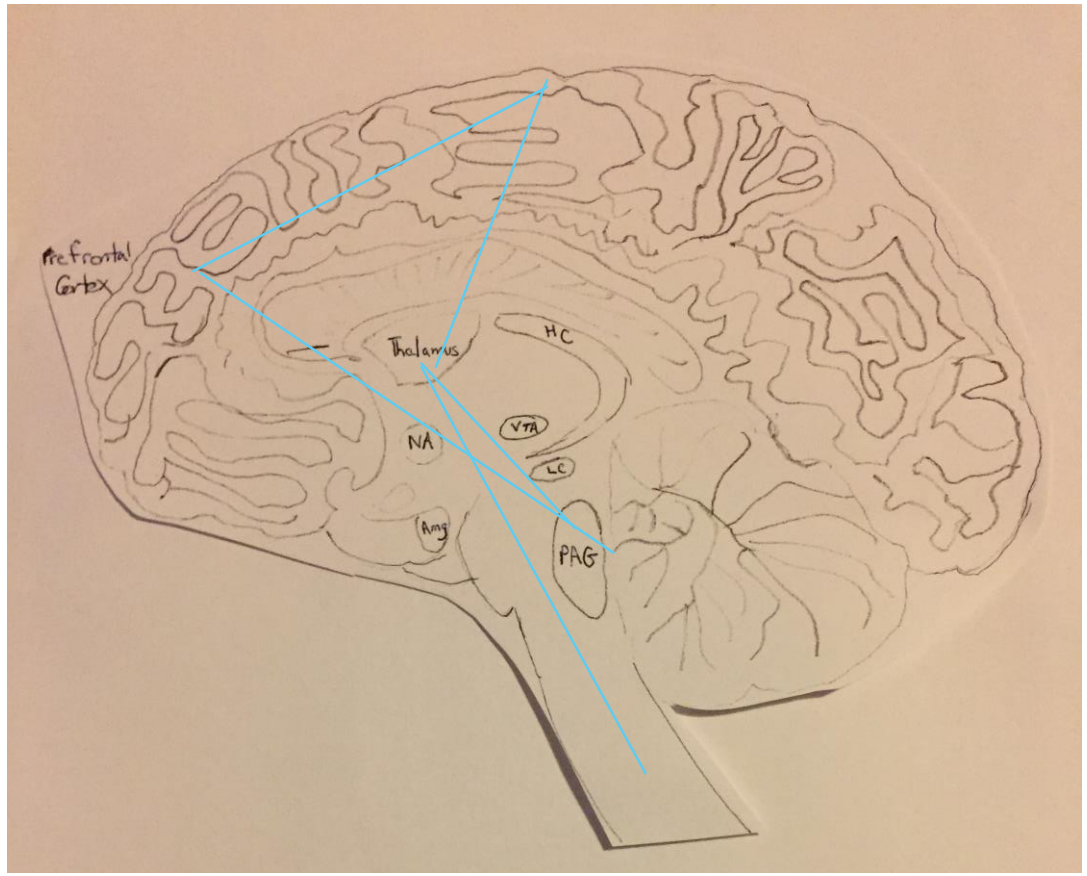
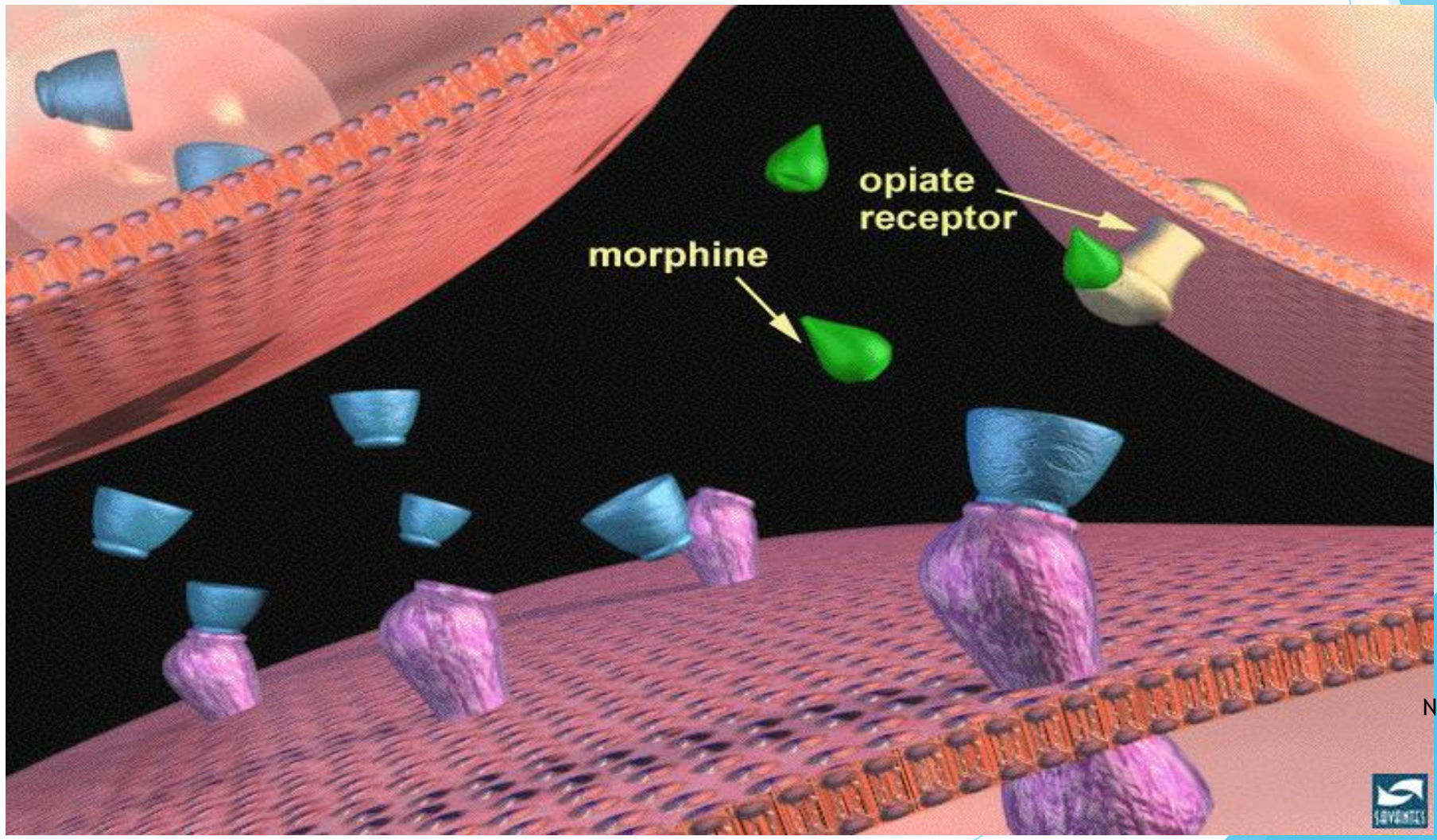
Neurological Basis of Pain



Pain signals from the body travel from the spinal cord to the Thalamus and then to the Sensory Cortex and the PFC. The PFC sends information to the PAG (periaqueductal gray) which then turns off the Thalamus

With Chronic Use Opioid Receptors Become Less Responsive



NIDA Drugs, Brain and Behavior

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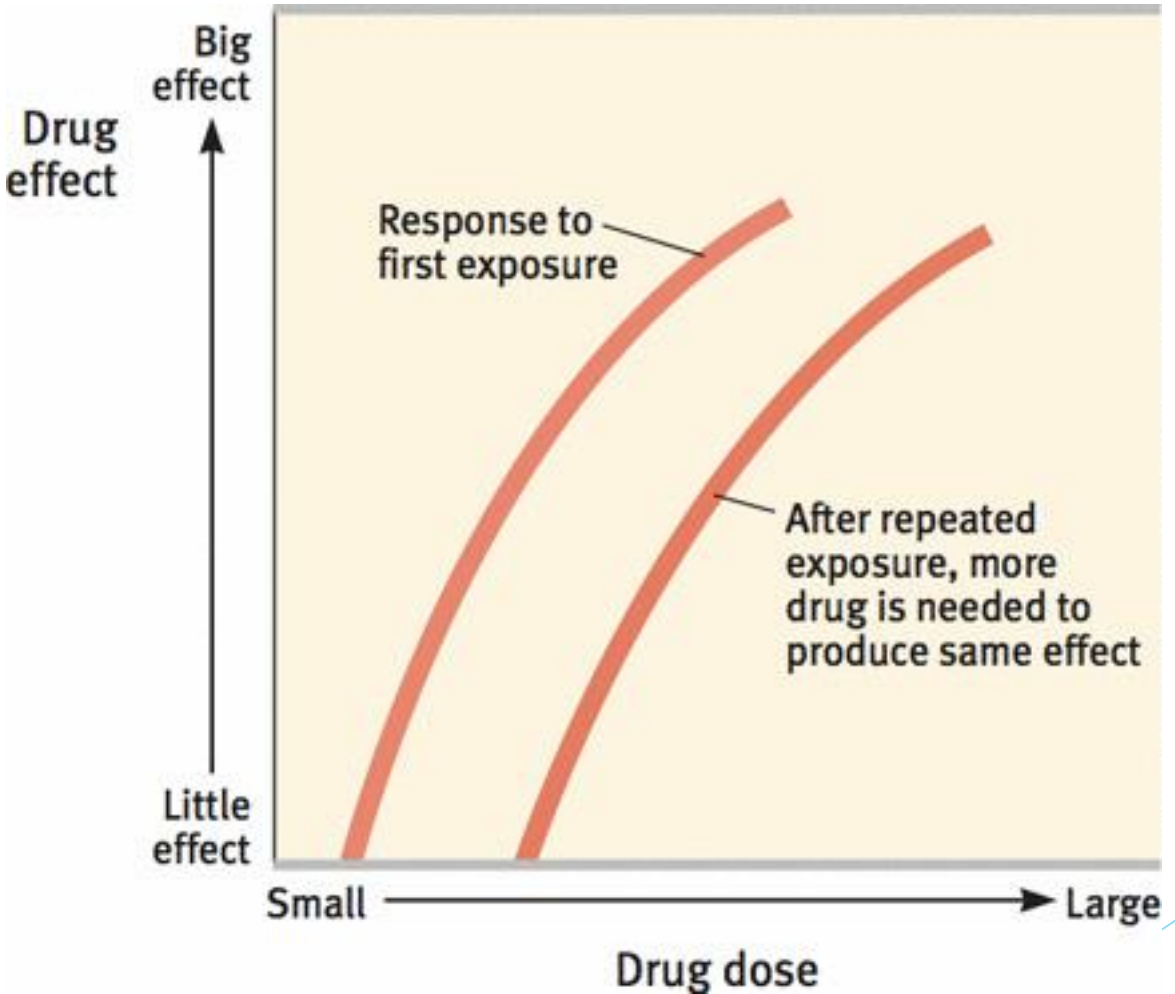
Tolerance



Withdrawal

Severe Body Pain

Chills and Sweats

Nausea, Diarrhea and Vomiting

Inability to Sit Still

Runny Nose and Teary Eyes

Shaking and Tremors

Yawning

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Withdrawal fuels Ongoing Use Tolerance fuels Escalating Doses and Accidental Overdose

Opioid Receptors

Location	Action	Tolerance/Dependence
Reward Center	Euphoria	Yes
Pain Center	Analgesia	Yes
Brainstem	Respiratory Suppression	NO
GI tract	Constipation	No

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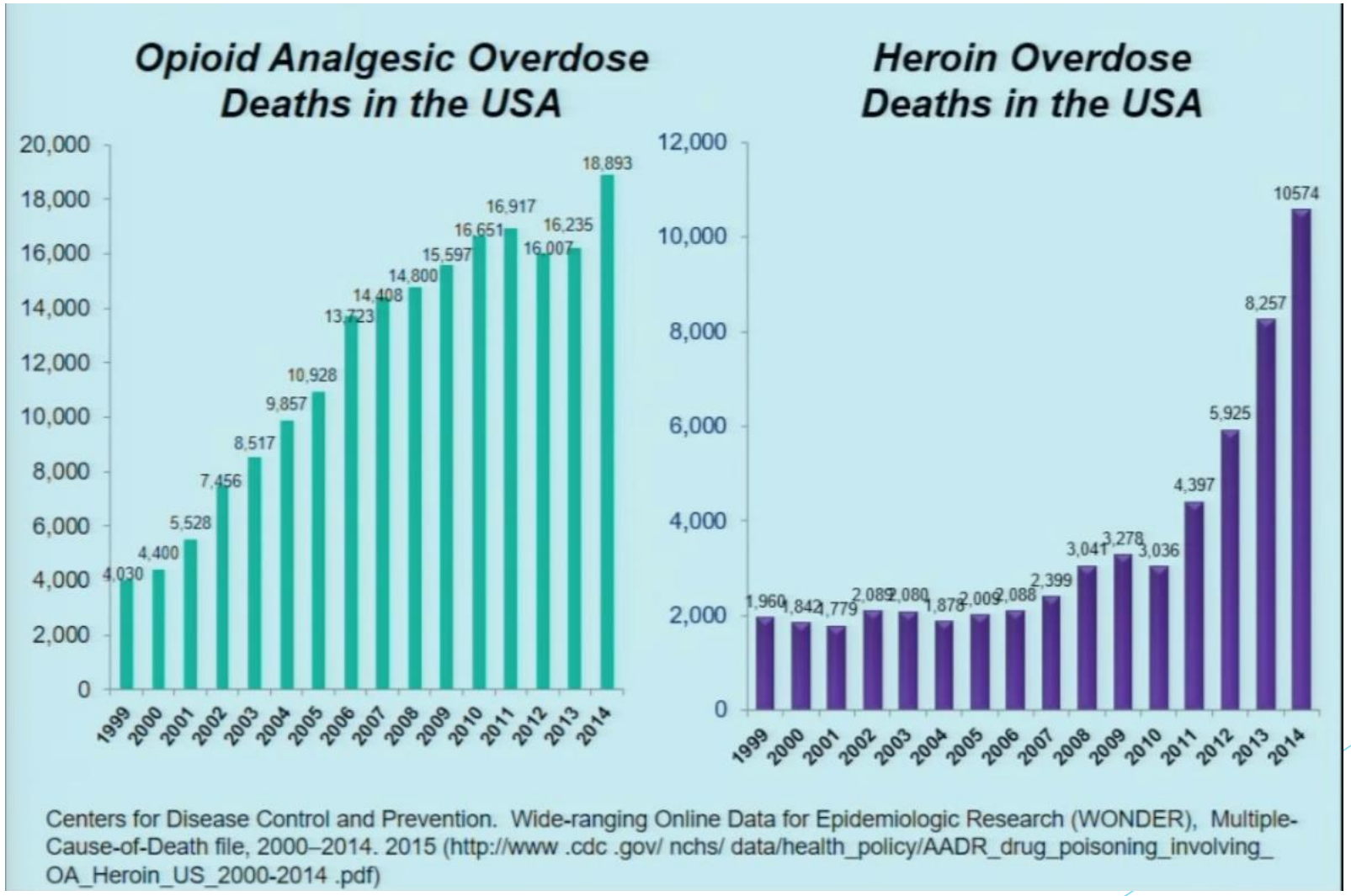
Overdose



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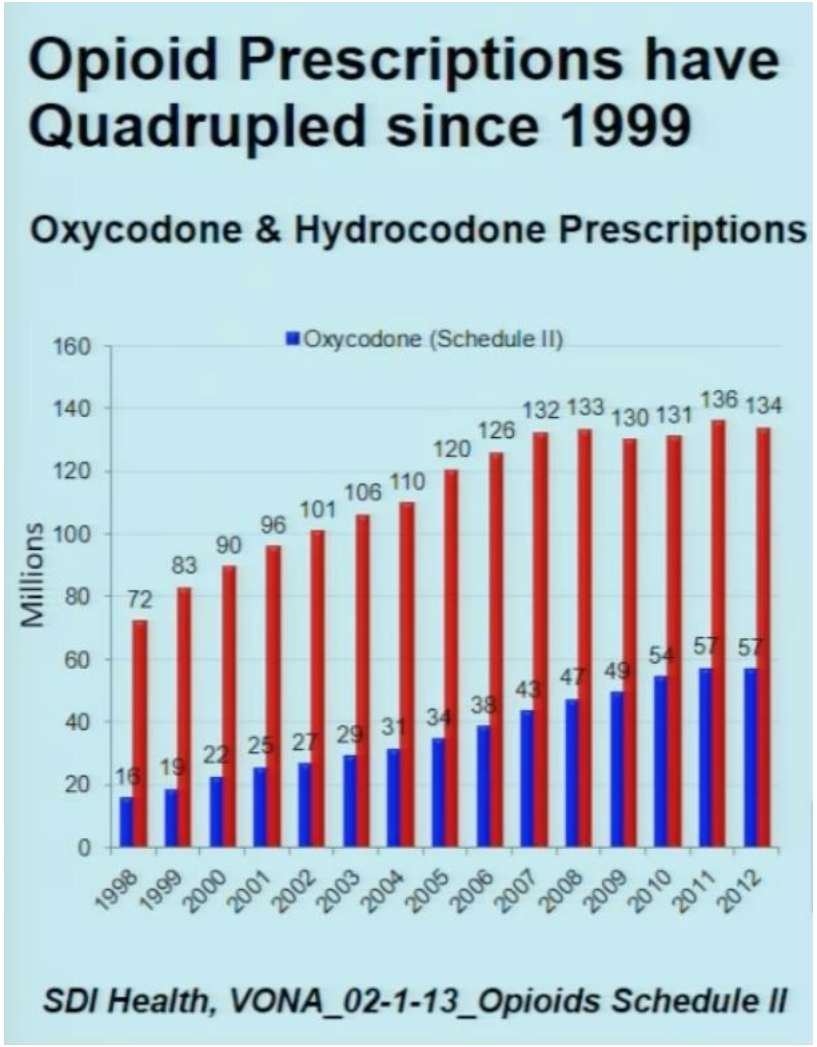
Prescriptions for Opioid Pain Medications have Skyrocketed



Commonly Available Prescription Opioids

codeine (only available in generic form)

fentanyl (Actiq, Duragesic, Fentora)

hydrocodone (Hysingla ER, Zohydro ER)

hydrocodone/acetaminophen (Lorcet, Lortab, Norco, Vicodin)

hydromorphone (Dilaudid, Exalgo)

meperidine (Demerol)

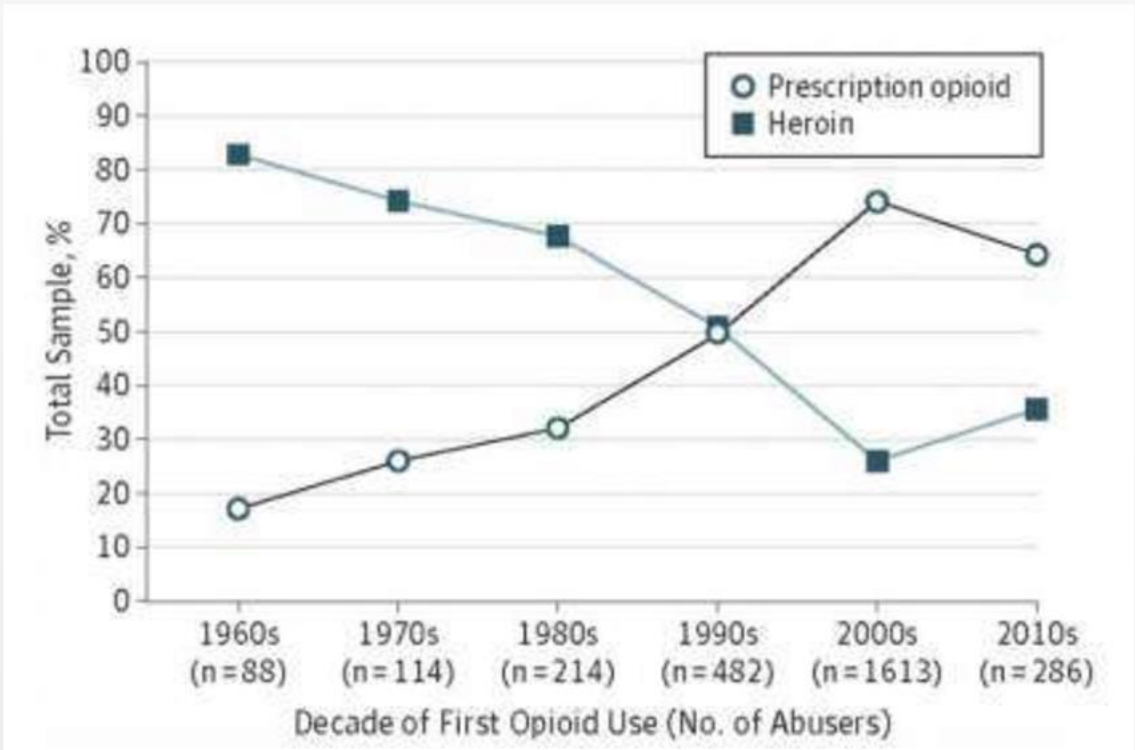
methadone (Dolophine, Methadose)

morphine (Astramorph, Avinza, Kadian, MS Contin, Ora-Morph SR)

oxycodone (OxyContin, Oxecta, Roxicodone)

oxycodone and acetaminophen (Percocet, Endocet, Roxicet)

Heroin is attractive because it is cheap and available…



Percentage of the total heroin-dependent sample that used heroin or a prescription opioid as their first opioid of abuse. Data are plotted as a function of the decade in which respondents initiated their opioid abuse. *Source: Cicero et al., 2014*

Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. *JAMA Psychiatry*. 2014;71(7):821-826.

SUMMARY

- Opioid Addiction is a multifactorial neurodevelopmental disease
- Early Use of ANY addictive substance increases risk
- Adverse Childhood Experiences increase risk
- Untreated Mental Illness increases risk
- Genetic Variants increase risk
- All these factors create the biological basis of addiction
- Anyone taking high doses is at risk for Overdose
- Opioid Prescription drugs are biochemically equivalent to Heroin
- Opioids produce tolerance and physical dependence in ALL, but only lead to addiction in SOME.

PREVENTION

- Reduce (STOP) Underage Drinking and Drug Use, including Nicotine
- Improve Mental Health and Access to Mental Health Treatment
- Design less addictive and more effective treatments for both acute and chronic pain
- Research the gene variants and learn make repairs

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Educate our Parents and Youth

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Mental Health Treatment Works

CMHA
Community Mental Health Affiliates

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Improve Treatments for Pain

Less Addictive Opioid Medication

Non-Opioid Medication

Non-Pharmacological Treatments

Treatment for Opioid Use Disorder

- Medication Is Essential
  - Methadone
  - Buprenorphine
  - Naltrexone

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Methadone

A Full mu receptor agonist
Shown to reduce use, reduce transmission of disease and save lives.

Buprenorphine

A Partial mu receptor Agonist

Can be prescribed in an office setting due to lower risk of misuse

Generally prescribed in fixed combination with Naloxone a short acting mu receptor antagonist to limit misuse and diversion

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Naltrexone XR

A long acting full mu receptor Antagonist

Increases adherence, decreases use and decreases cravings.

Sigmon SC, Bisaga A, Nunes EV, O'Connor PG, Kosten T, Woody G. Opioid Detoxification and Naltrexone Induction Strategies: Recommendations for Clinical Practice. *The American journal of drug and alcohol abuse*. 2012;38(3):187-199. doi:10.3109/00952990.2011.653426.

Addiction is both preventable and treatable; it is an illness as real as any other chronic disease.

No one ever chooses to be an addict.