

The Neurobiology of Opioid Addiction



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Neurobiology 101

- A neuron is a type of cell in central nervous system (CNS).
- Neurons communicate through receptors.
- Chemicals that bind receptors either stimulate or suppress neurons.



Endorphins

- Your body makes natural opioids called endorphins.
- Endorphins bind to receptors on neurons throughout the CNS.
- Endorphin binding gives you a sense of well being, blocks pain and helps control breathing.



Opioids

- Narcotic pain medications (morphine, codeine, oxycodone, vicodin, percocet, etc.) and illicit opiates (opium, heroin) all mimic endorphins and bind to opioid receptors.



Opioids are depressants

Normal mouse

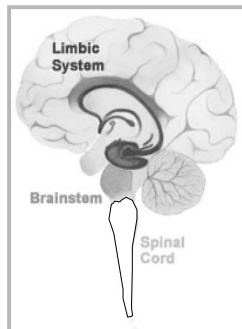


Mouse on opioids



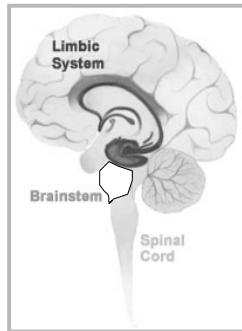
Where are opioid receptors?

- Spinal cord (transmits pain)
- Opioid binding here blocks pain messages
- Opioid receptors become available in response to tissue damage



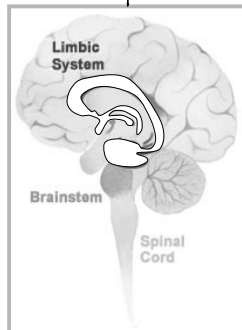
Where are opioid receptors?

- Brainstem (controls breathing)
- Opioid binding here slows respiration



Where are opioid receptors?

- Limbic system (controls emotions)
- Opioid binding here produces feelings of pleasure, relaxation and contentment.



- The brain adapts to high level of opioids by increasing the number of neuronal receptors.



- Once there are extra receptors, it takes more opioid binding to get an effect.

- This changed neurobiology makes it difficult for addicted patients to stay away from drugs.



Anhedonia

- The body normally produces natural opiates to help signal pleasure
- When the brain has too many opioid receptors, the natural opioid system is ineffectual
- Patients with opioid addiction can find it difficult to experience pleasure without drugs

Cravings

- The amygdala is part of the limbic system responsible for memory
- Just the *mention* of items associated with drug use turns on the amygdala
- When the amygdala is on, a craving occurs

When the Amygdala takes over ...

- Cravings are an *uncontrollable desire for drugs*.
- Once a craving has started, the brain ignores rational thoughts during cravings, and the person is no longer in control.
- This *changed brain* makes it almost impossible for drug addicts to stay drug-free without professional help.
- *Addiction is a brain disease*.

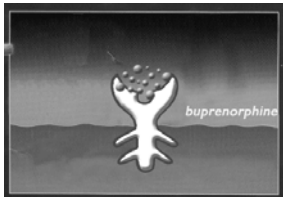
What is buprenorphine?

- Partial opioid agonist used for replacement therapy.
- Binds to the opioid receptor but only partially stimulates the neuron.
- Helps treat anhedonia and block cravings



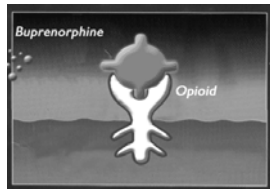
Buprenorphine blocks other opioids

- Buprenorphine has high affinity for opioid receptors.
- Other opioids cannot bind to the receptor if buprenorphine is there.



Buprenorphine can only be started when receptors are available

- Displaces other opioids
- Turns full stimulation from opioids to partial stimulation
- Can cause precipitous withdrawal



Common side effects of buprenorphine*

- Constipation
- Urinary retention
- Nausea/vomiting
- Fatigue
- Headache

* Should all be mild relative to effects of full opioids.



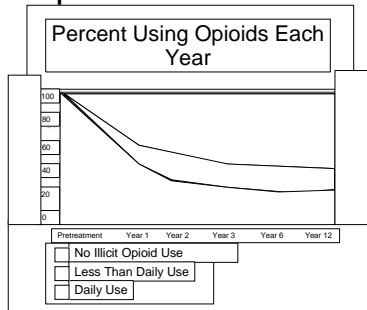
How long should teens stay on buprenorphine?

- Few published trials; all were studies of short term use of buprenorphine.*
- One study found that adolescents relapse in high rates when taken off replacement after 3 months.**
- Methadone patients often remain on replacement therapy for life.

*Marsch LA, Bickel WK, Badger GJ, et al. Comparison of pharmacological treatments for opioid-dependent adolescents: a randomized controlled trial. Arch Gen Psychiatry 2005;62(10):1157-64.

**Woody GE, Poole SA, Subramaniam G, et al.: Extended vs short-term buprenorphine-naloxone for treatment of opioid-addicted youth: a randomized trial. JAMA 300:2003-2011, 2008.

Relapse rates over time



Is buprenorphine addictive?

- Patients do not get high and do not develop compulsions to use buprenorphine
- Patients will have withdrawal if they stop taking buprenorphine suddenly
- Withdrawal is neither necessary nor sufficient to diagnose drug dependence

- Buprenorphine should always be discontinued under the supervision of a physician to avoid withdrawal.
- The usual method of ending treatment is a taper, which means a decreasing dose over a period of time.



Treating pain

- Patients taking buprenorphine can be treated with narcotics for pain if necessary
- For planned procedures: buprenorphine may be stopped the day before and another narcotic substituted
- In an emergency setting: a higher than usual dose of narcotics can overcome the buprenorphine blockade
- Buprenorphine may be taken safely with non-narcotic medications, which can give good pain relief in many situations.

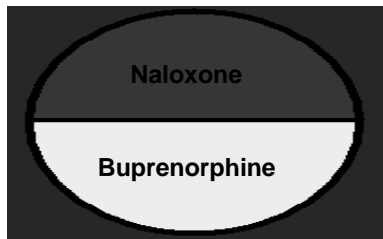
Ref: PCSS guidance

Depressants

- Alcohol, benzodiazepines, barbiturates and opioids are all depressants
- Depressants can suppress breathing
- Mixing depressants can lead to accidental overdose and should always be avoided

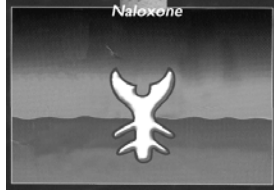
What Is Suboxone®?

- Brand name for a combination medication.



What is naloxone?

- Opioid antagonist
- Binds to the opioid receptor and turns the cell off
- Used to “reverse” overdose



Why is naloxone in Suboxone®?

- Naloxone is a safety feature
 - Not absorbed when taken sublingually
 - Prevents patients from injecting Suboxone® in attempt to get high from buprenorphine