# The Science of Opioid Addiction

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# Who am I?

- Medical doctor trained in mental health & substance abuse treatment
- Board-certified in:
  - General Psychiatry
  - Forensic Psychiatry
  - Adolescent Psychiatry

# Who am I?

- Medical Director, Fairbanks Community Mental Health Services
- Editor-in-Chief, Carlat Addiction Treatment Report
- No ties to the pharmaceutical industry
- About 70% of my patients have at least one substance use disorder.

# What does "Science" mean?

- Basic science—refers to drugs and receptors.

  *Heroin binds to opioid receptors, causing signal cascades within and between nerve cells.*

- Neuroscience—refers to brain structure and function.

  *Prefrontal cortex inhibits ventral tegmental area.*

- Social science—includes the psychology of addiction.

  *Walking past the bar increases alcohol craving.*

# What else does "Science" mean?

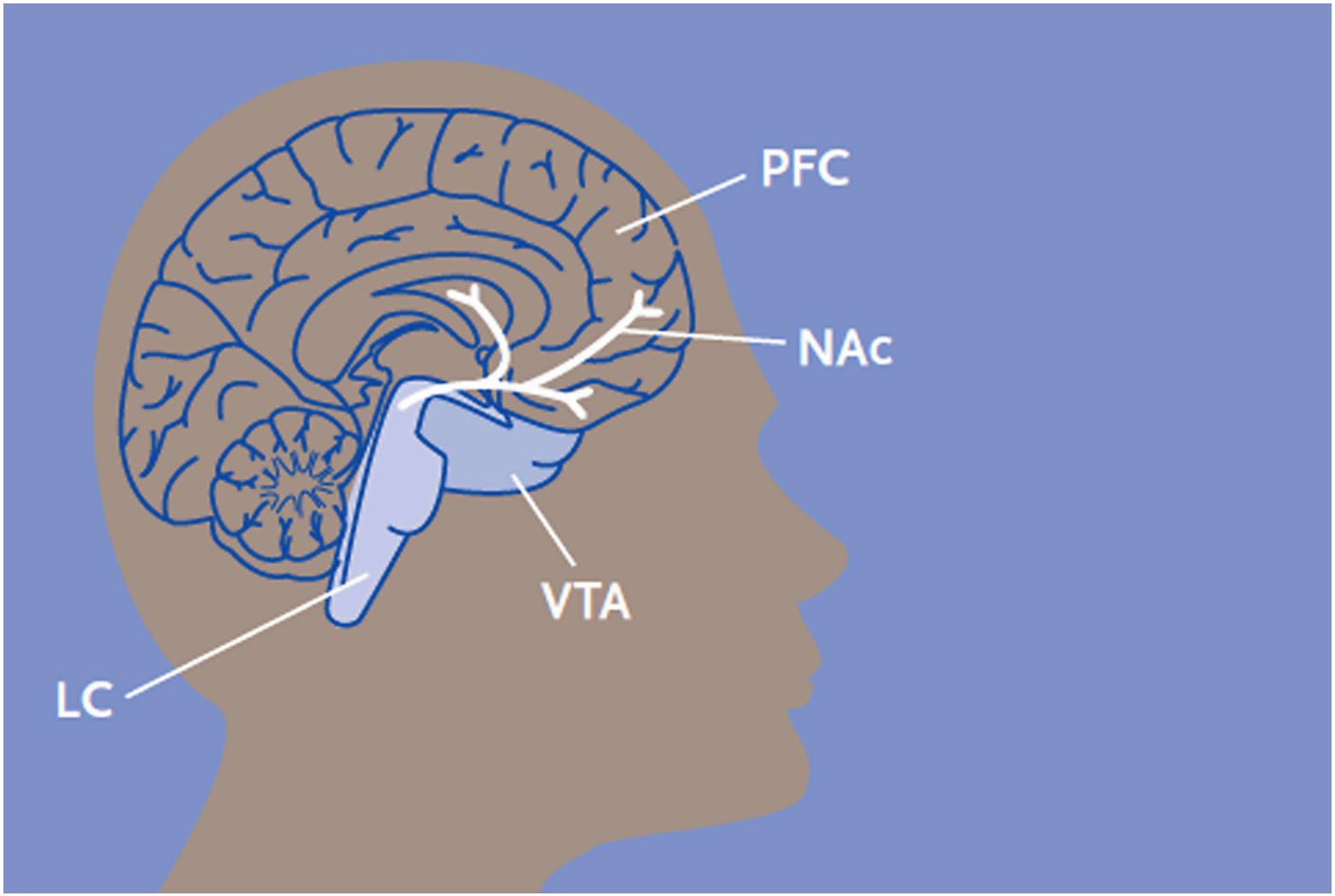
- Outcome research—shows which treatments work and which ones don't.

  *Psychosocial interventions, medical treatment or both?*
- Economic research—shows which interventions are cost-effective on a population basis.
- What can Alaska afford?

# Receptor Science

- Exogenous versus endogenous opioids
- Opioids bind to opiate receptors in the brain and spinal cord.
- Effects
  - Binds spinal cord receptors—decreasing pain
  - Decreases GABA—depressing neurologic function
  - Increases dopamine—causing pleasure

# The Reward Circuit




Kosten TR. The neurobiology of opioid dependence: implications for treatment. Sci Pract Perspect. 2002 Jul;1(1):13-20

# Why Do People Start Abusing Opioids?

- Exogenous opioids bind to receptors in the VTA.
- VTA sends dopamine to the NAc, causing pleasurable sensations the same as those that arise from pleasurable activities—but much more intense.
- This is what gets people started abusing opioids.

Kosten TR. The neurobiology of opioid dependence: implications for treatment. Sci Pract Perspect. 2002 Jul;1(1):13-20

# Why Do People Keep Abusing Opioids?

- Other areas of the brain create memories that associate opioid use with intense pleasure. These include conscious and unconscious associations that influence behavior.
- The other name for this is *learning*—people learn that opioids are pleasurable.

Kosten TR. The neurobiology of opioid dependence: implications for treatment. Sci Pract Perspect. 2002 Jul;1(1):13-20

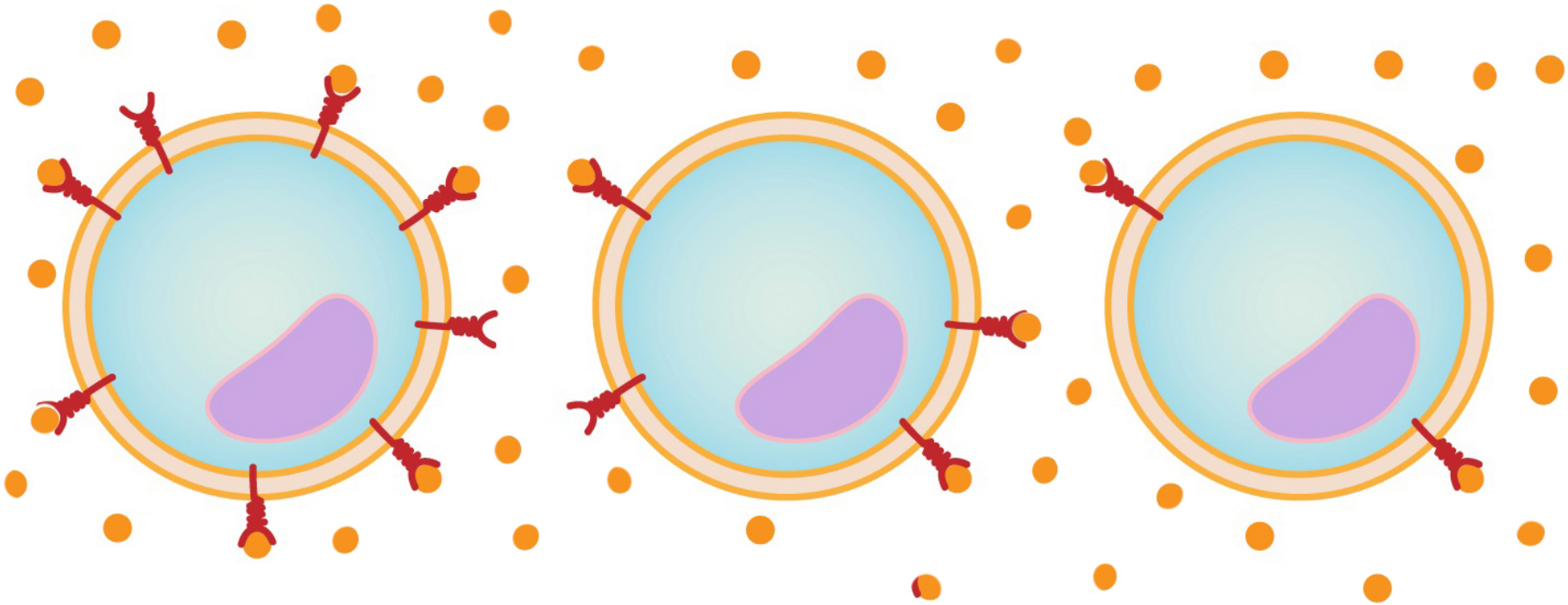
# Key Concept: Tolerance

- Tolerance is the need to take more of a drug to get the same effect.

# What Causes Tolerance?

- The brain makes adjustments so that it functions more or less normally when the drug is present, and abnormally when it is not.
- Think of tolerance like driving with the brakes on—the harder you push on the gas, the harder you have to push on the brake to stay under the speed limit.

# downregulation



time

# Key Concept:

- What happens when the gas pedal is all the way to the floor and you take your other foot off the brake?

# Key Concept: Withdrawal

**COWS**

| *Symptoms* | *Scores* | *Examples* |
|---|---|---|
| Resting pulse rate | 0-4 | 0=80 or less; 1= 81-100; 2=101-120; 4=120 or greater |
| Sweating | 0-4 | 0=none; 4=sweat streaming from face |
| Restlessness | 0-5 | 0=sits still; 5=unable to sit still (even for a few seconds) |
| Pupil size | 0-5 | 0=normal; 5=dilated (only iris rim visible) |
| Bone or joint aches | 0-4 | 0=none; 4=severe discomfort |
| Runny nose or tearing | 0-4 | 0=none; 4=constant |
| GI upset | 0-5 | 0=none; 5=multiple episodes of vomiting or diarrhea |
| Tremor | 0-4 | 0=none; 4=gross tremor |

# Key Concept: Dependence

Tolerance + Withdrawal

=

Dependence

Kosten TR. The neurobiology of opioid dependence: implications for treatment. Sci Pract Perspect. 2002 Jul;1(1):13-20

# Is Dependence the Same as Addiction?

No.

Think clonidine.  Nobody craves blood pressure medicine.

Think antidepressants.  Nobody builds a criminal lifestyle around Prozac.

# Key Concept: Addiction

*A primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.*

-American Society of Addiction Medicine

# Models of Addiction

- Moral—weak character
- Criminal—the war on drugs
- Recovery—a personal journey
- Social—learning theory
- Medical—addiction as disease

Each perspective is valid, but scientific basis increases moving down the list.

# A Note on Medical Models

- Biomedical Model—uses medications to treat diseases.
- Clinical Model—relies on the relationship between professional and patient.
- Public Health Model—refers to health policies designed to meet needs of a population

# Biomedical Models of Addiction

- Changed set point—Opioid use causes permanent structural and chemical changes that create a new biological and behavioral baseline for the addict.

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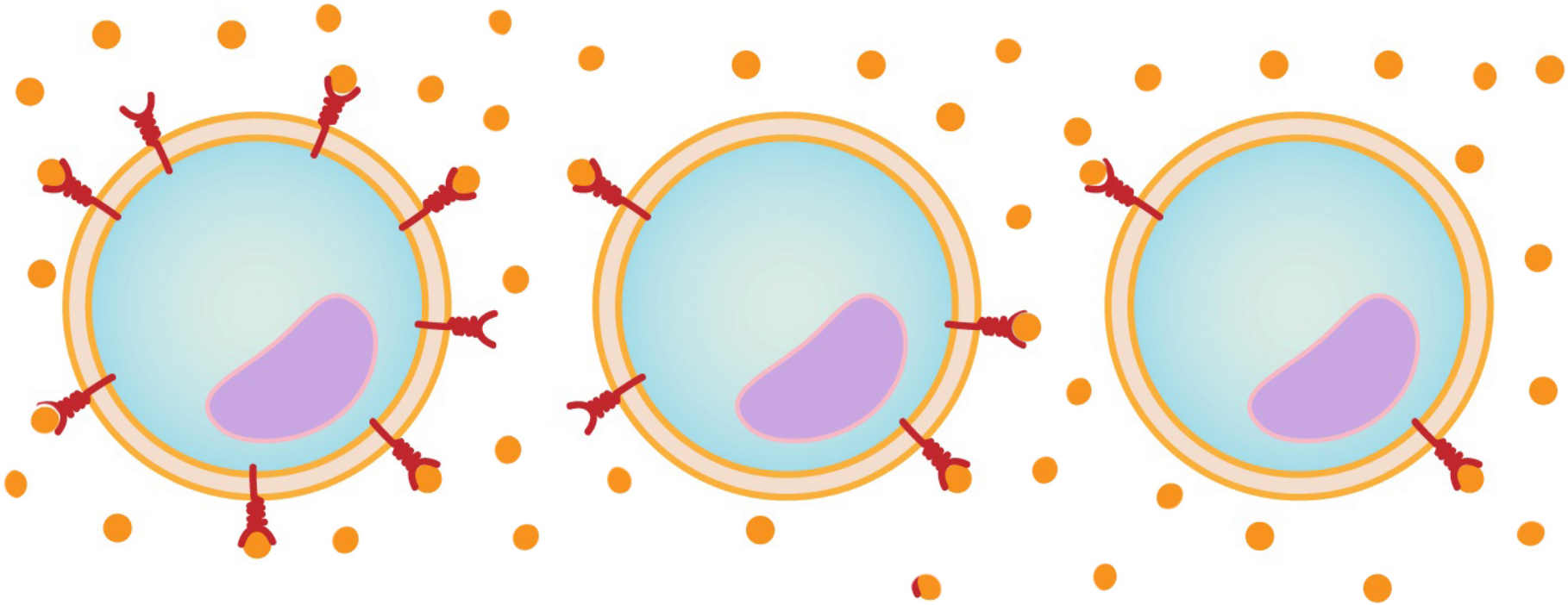
# downregulation



time

# Biomedical Models of Addiction

- Cognitive deficits—Opioid use degrades prefrontal cortical inhibition of the drive to use, undermining the addict's will at a neurological level.

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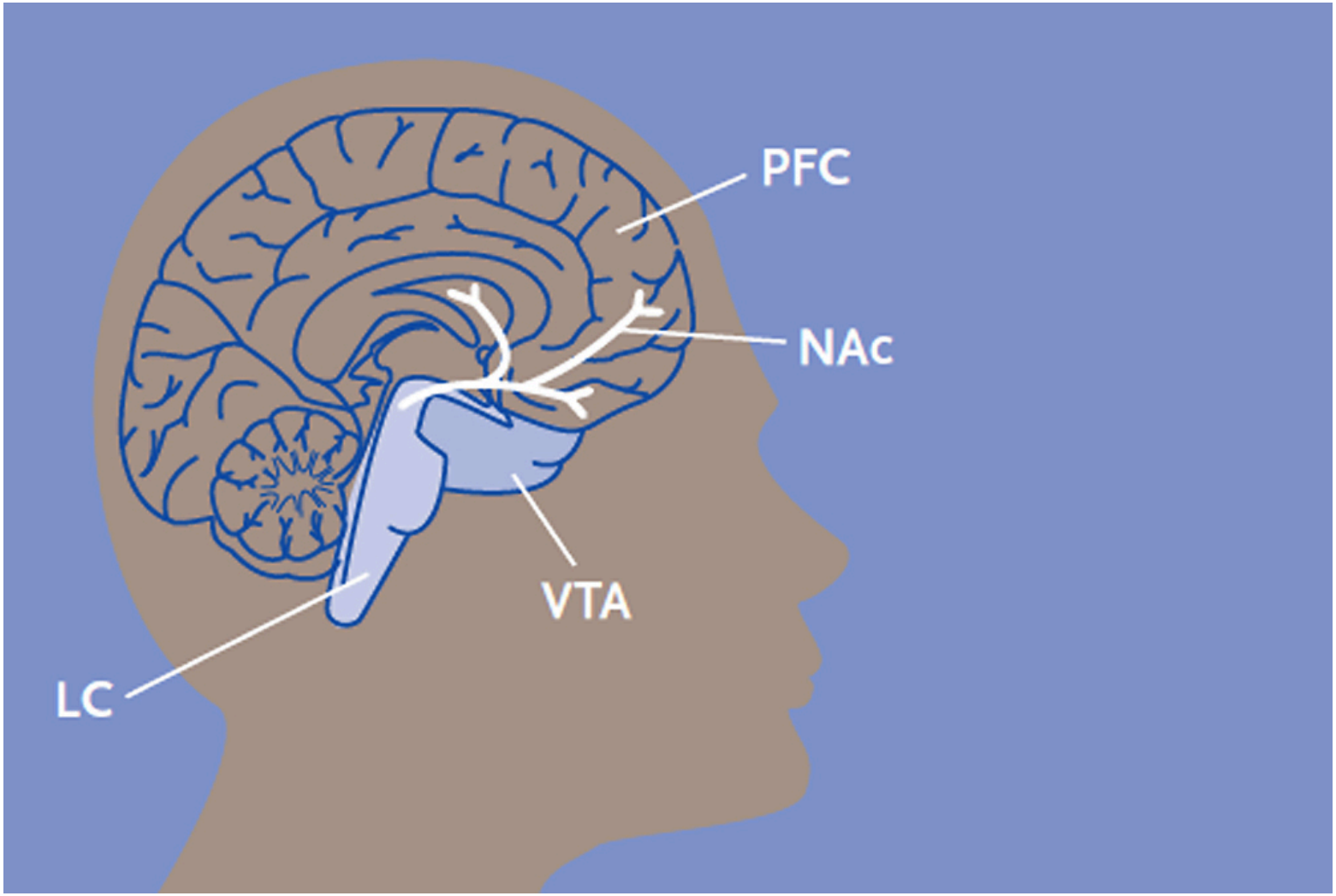
# Cognitive Deficit Model




Kosten TR. The neurobiology of opioid dependence: implications for treatment. Sci Pract Perspect. 2002 Jul;1(1):13-20

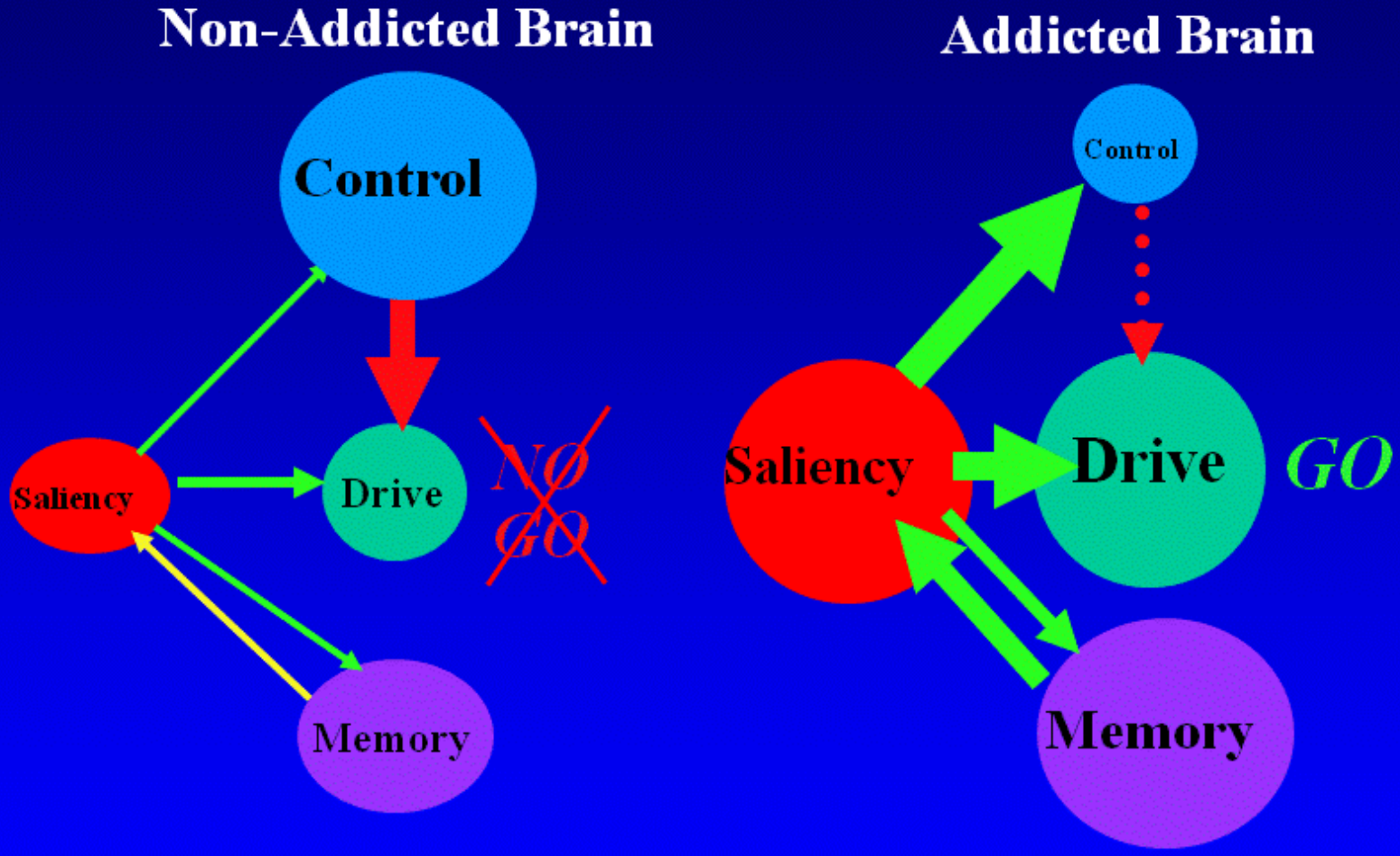
# So What is Addiction?

*Fundamentally, addiction is a learning disability.*

-Nora Volkow, MD
Director, National Institute of Drug Abuse
National Institutes of Health

Volkow ND, Morales M. The Brain on Drugs: From Reward to Addiction. Cell. 2015 Aug 13;162(4):712-25.

# *Why Can't Addicts Just Quit?*




## *Because Addiction Changes Brain Circuits*



*Adapted from Volkow et al., Neuropharmacology, 2004.*

NIDA

# Treatment

- 12-step groups—NA, AA, etc.
- Detoxification—many varieties exist
- Psychosocial treatment—substance abuse counseling, intensive outpatient treatment, residential “rehab”
- Medication treatment—antagonist (naloxone, naltrexone) or medication-assisted treatment (MAT)

# Detoxification

- Useful as a bridge to psychosocial or methadone/buprenorpine maintenance treatment
- Very high relapse rates when used alone
- Elevated risk of overdose death within one month of any detox protocol

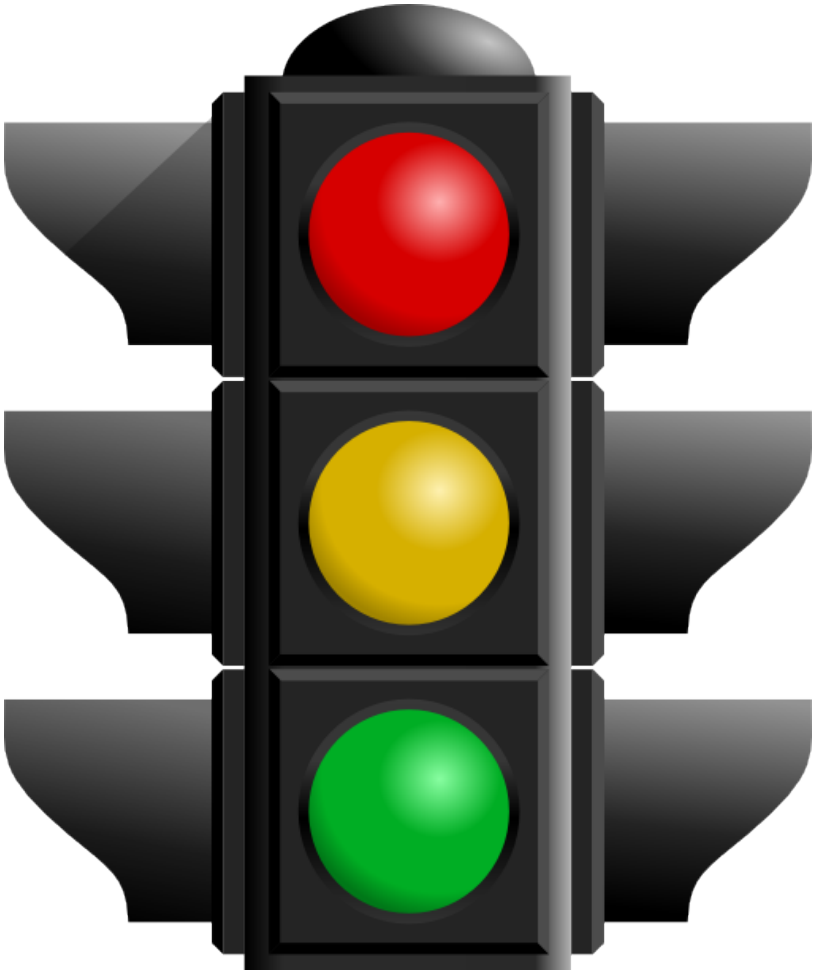
Nosyk B et al. A call for evidence-based medical treatment of opioid dependence. Health Aff (Millwood). 2013 Aug;32(8):1462-9.

# Psychosocial Treatment

- Very effective for many types of addiction
- An essential component of any opioid addiction treatment program
- Not effective as a stand-alone treatment for opioid use disorders—except for doctors and pilots

Nosyk B et al. A call for evidence-based medical treatment of opioid dependence. Health Aff (Millwood). 2013 Aug;32(8):1462-9.

# Medical Treatment



- Antagonist
- Partial Agonist
- Agonist

# Antagonist Treatment

- Oral or long-acting injectable naltrexone (Vivitrol)
- Advantages:
  - Blocks high from opioids
  - Avoids stigma of MAT (doesn't "replace one addiction with another")
  - Appeals to people who favor abstinence
  - Can't be abused or diverted

# Antagonist Treatment

- Disadvantages:
  - Oral naltrexone no better than placebo

    Minozzi S et al, Cochrane Database Syst Rev 2011
  - Long-acting injectable naltrexone (Vivitrol) promising, but limited evidence

    Lee J et al. Extended-Release Naltrexone to Prevent Opioid Relapse in Criminal Justice Offenders. N Engl J Med. 2016 Mar 31;374(13):1232-42

    Krupitsky E et al.Injectable extended-release naltrexone (XR-NTX) for opioid dependence: long-term safety and effectiveness. Addiction. 2013 Sep;108(9):1628-37
  - Interferes with pain treatment
  - High treatment dropout rates

# Agonists and Antagonists

# Medication-Assisted Treatment

- Methadone
- Full agonist but long half-life
- Administered only in specially licensed methadone clinics when used for addiction treatment
- Can be used for pain treatment

# Medication-Assisted Treatment

- Buprenorphine (Suboxone)
- Partial agonist—harder to overdose
- Doctors need special training and DEA certificate, but in theory can be administered in any doctor's office.
- Can be used for pain treatment

# Partial Agonist

# Advantages of MAT

- Consistent evidence to support efficacy
- Better treatment retention
- Fewer overdose deaths
- Less hospitalization
- Cost effectiveness

Dugosh K. A Systematic Review on the Use of Psychosocial Interventions in Conjunction With Medications for the Treatment of Opioid Addiction. J Addict Med. 2016 Mar-Apr;10(2):91-101.

Mattick R. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev. 2008 Apr 16;(2).

Nosyk B et al. A call for evidence-based medical treatment of opioid dependence. Health Aff (Millwood). 2013 Aug;32(8):1462-9.

# Disadvantages of MAT

- Potential for abuse and diversion of medication
- Lifelong treatment for many—up to 95 percent relapse when taper attempted
- Some people see MAT as "substituting one addiction for another."

Nosyk B et al. A call for evidence-based medical treatment of opioid dependence. Health Aff (Millwood). 2013 Aug;32(8):1462-9.

# Economic Studies

## Multiple studies support cost-effectiveness of medication-assisted treatment.


Barnett P et al. The cost-effectiveness of buprenorphine maintenance therapy for opiate addiction in the United States. Addiction. 2001 Sep;96(9):1267-78.

Barnett P et al. Comparison of costs and utilization among buprenorphine and methadone patients. Addiction. 2009 Jun;104(6):982-92.

Nosyk B et al.Cost-effectiveness of diacetylmorphine versus methadone for chronic opioid dependence refractory to treatment. CMAJ. 2012 Apr 3;184(6).

Zarkin G et al. Benefits and costs of methadone treatment: results from a lifetime simulation model. Health Econ. 2005 Nov;14(11):1133-50.

# Economic Studies

MAT reduced hospital admissions and emergency department visits for Medicaid beneficiaries with opioid addiction compared with psychosocial treatment, abstinence, or detoxification.

Mohlman M et al. Impact of Medication-Assisted Treatment for Opioid Addiction on Medicaid Expenditures and Health Services Utilization Rates in Vermont. J Subst Abuse Treat. 2016 Aug;67:9-14. doi: 10.1016/j.jsat.2016.05.002. Epub May 2016.

# Take-Home Messages

- Addiction is a learning disorder with biological, psychological and social components
- Different addicts have different needs.
- For severe opioid addiction, psychosocial treatments alone usually fail.
- Best practice is combination of MAT with psychosocial treatment
- A spectrum of services is needed to address the needs of a population.