Medical Interventions for Addiction in Primary Care Settings

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NIH Consensus on Drug Treatment

- Drug Addiction is a disorder of the brain and therefore a medical disorder
- Broader access to drug treatment
- Reduce federal and state barriers impeding access to treatment
- Stressed the importance of providing substance abuse counseling, psychosocial therapies, and other supportive services

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Summary Slide

- Just as medication can help with depression, medication can help in the treatment of alcohol dependence, opioid dependence, cocaine dependence, nicotine dependence, etc.

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Outline

- Neurobiology of addiction
- Medication assisted treatment
  - **Opioids - methadone, buprenorphine, naltrexone**
  - **Cocaine – disulfiram**
  - **Methamphetamine - buproprion**
  - **Alcohol – naltrexone, topiramate**
  - **Nicotine – NRT, buproprion, varenicline**

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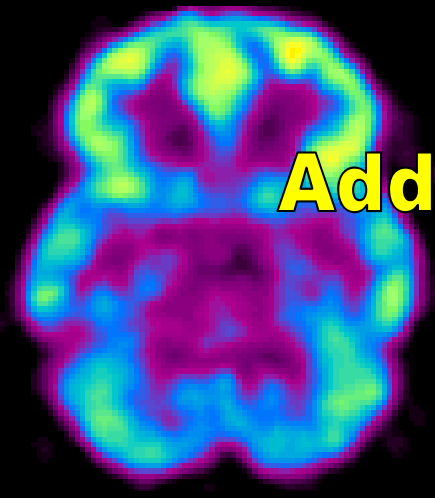
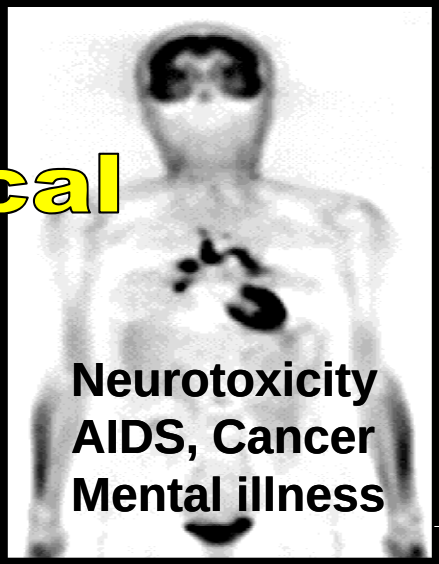


Addiction

Medical



Neurotoxicity
AIDS, Cancer
Mental illness

DRUGS

Social

Homelessness
Crime
Violence

Economic

Health care
Productivity
Accidents

If the societal cost is so high, why do people do drugs?

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Common Myths About Drug Abuse…

- Drug abuse equates to drug addiction
- Alcohol is not a drug
- Addiction is a moral weakness
- You have to hit rock bottom to recover
- You have to want treatment for it to be successful
- Drug abuse is more common among minorities

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Addiction

- A state in which an organism engages in compulsive behavior
  - **The behavior is reinforcing (that is, pleasurable or rewarding)**
  - **There is a loss of control in limiting the intake of the substance**

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Why Do People Take Drugs in The First Place?

To feel good

To have novel:
feelings
sensations
experiences
AND
to share them

To feel better

To lessen:
anxiety
worries
fears
depression
hopelessness

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Vulnerability

Why do some people become addicted while others do not?

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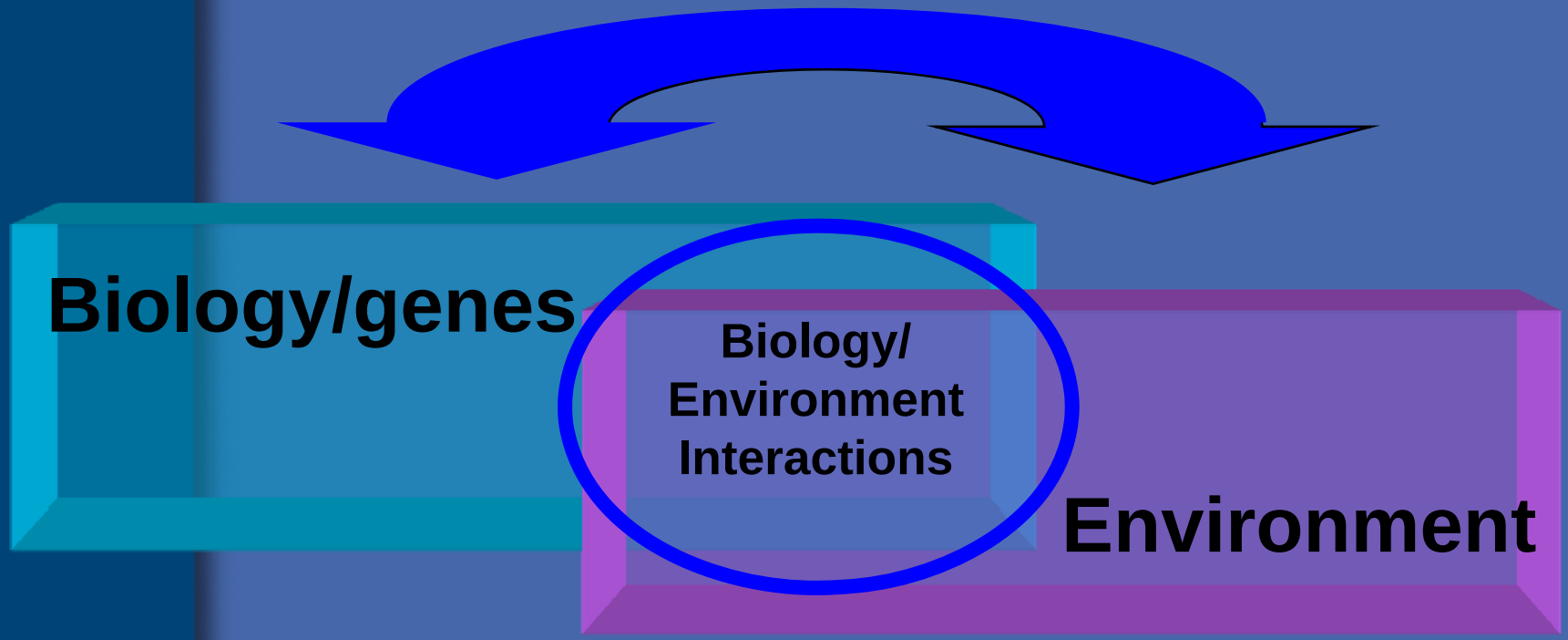

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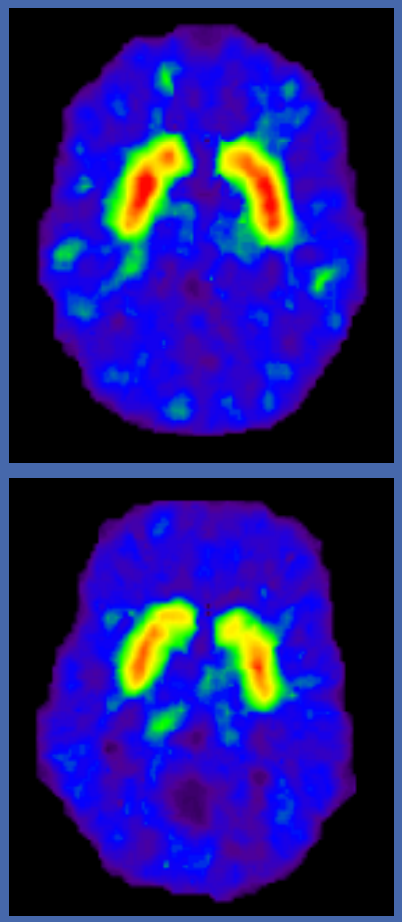
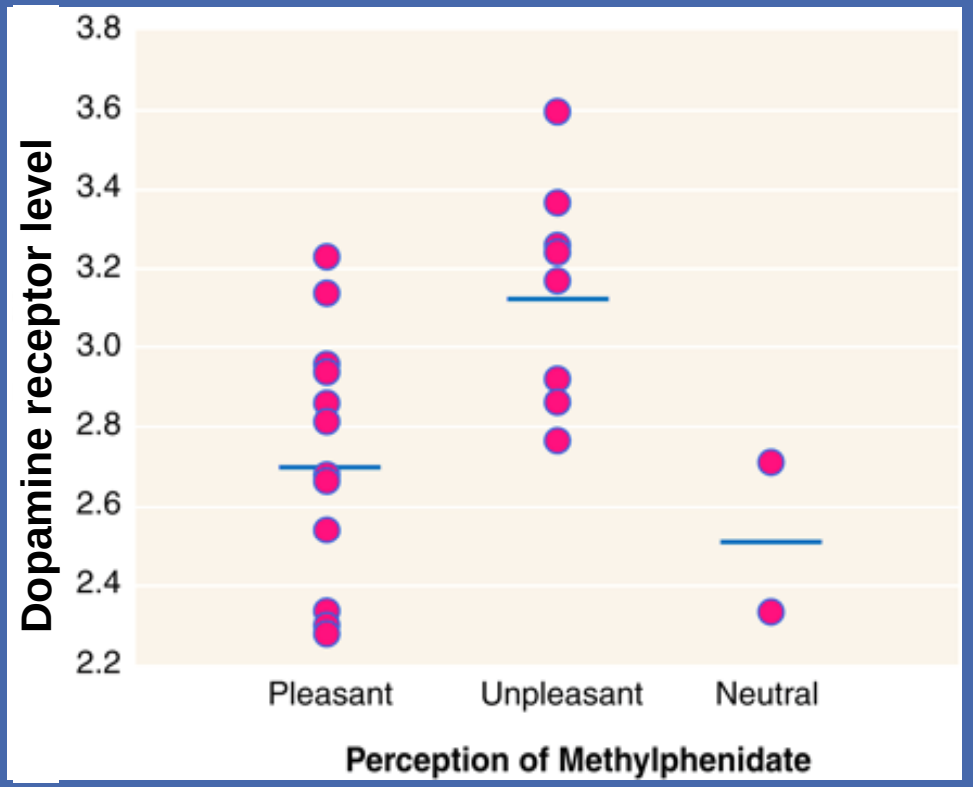
DA Receptors and the Response to Methylphenidate (MP)

High DA receptor

Low DA receptor





As a group, subjects with low receptor levels found MP pleasant while those with high levels found MP unpleasant

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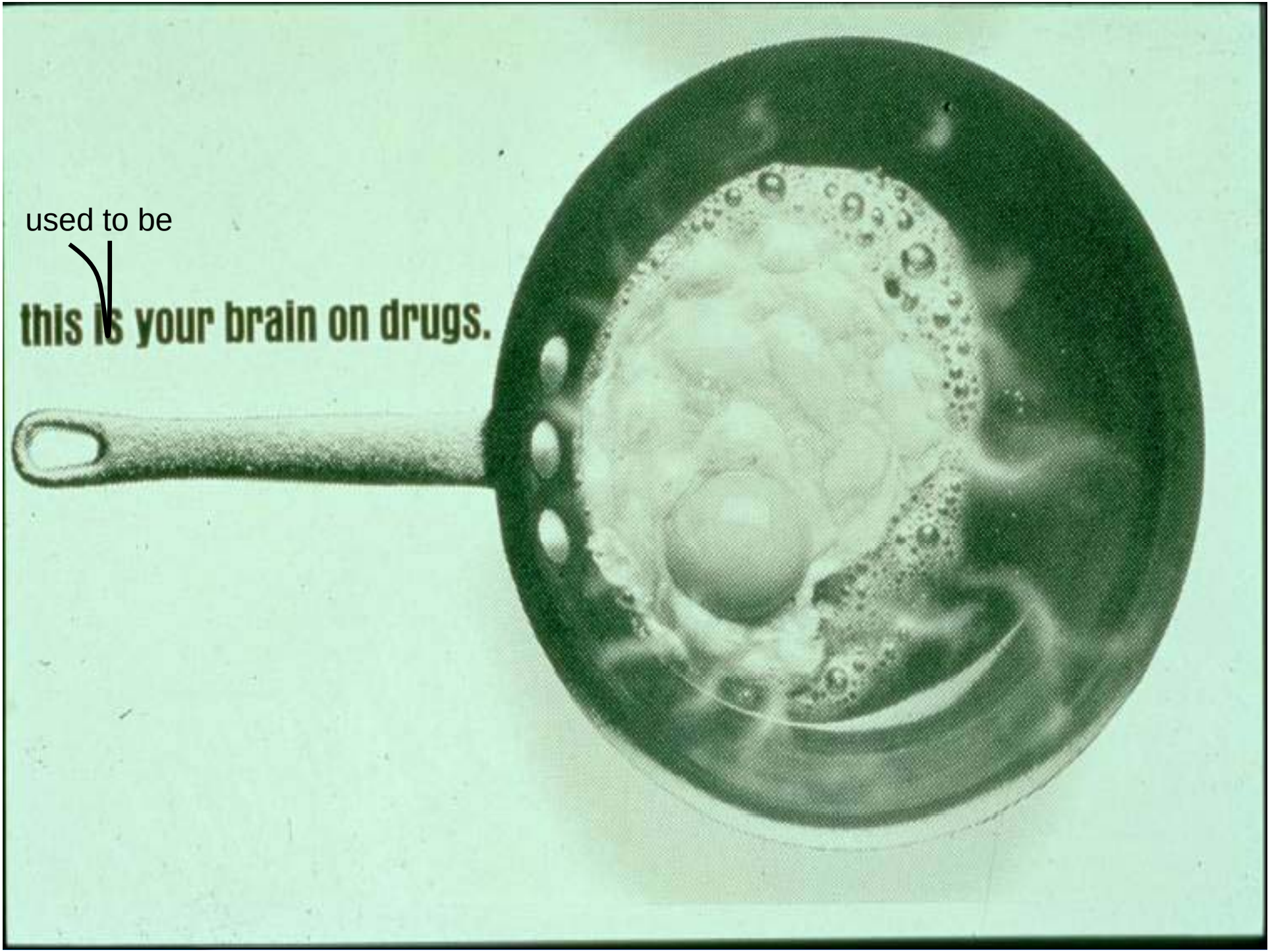
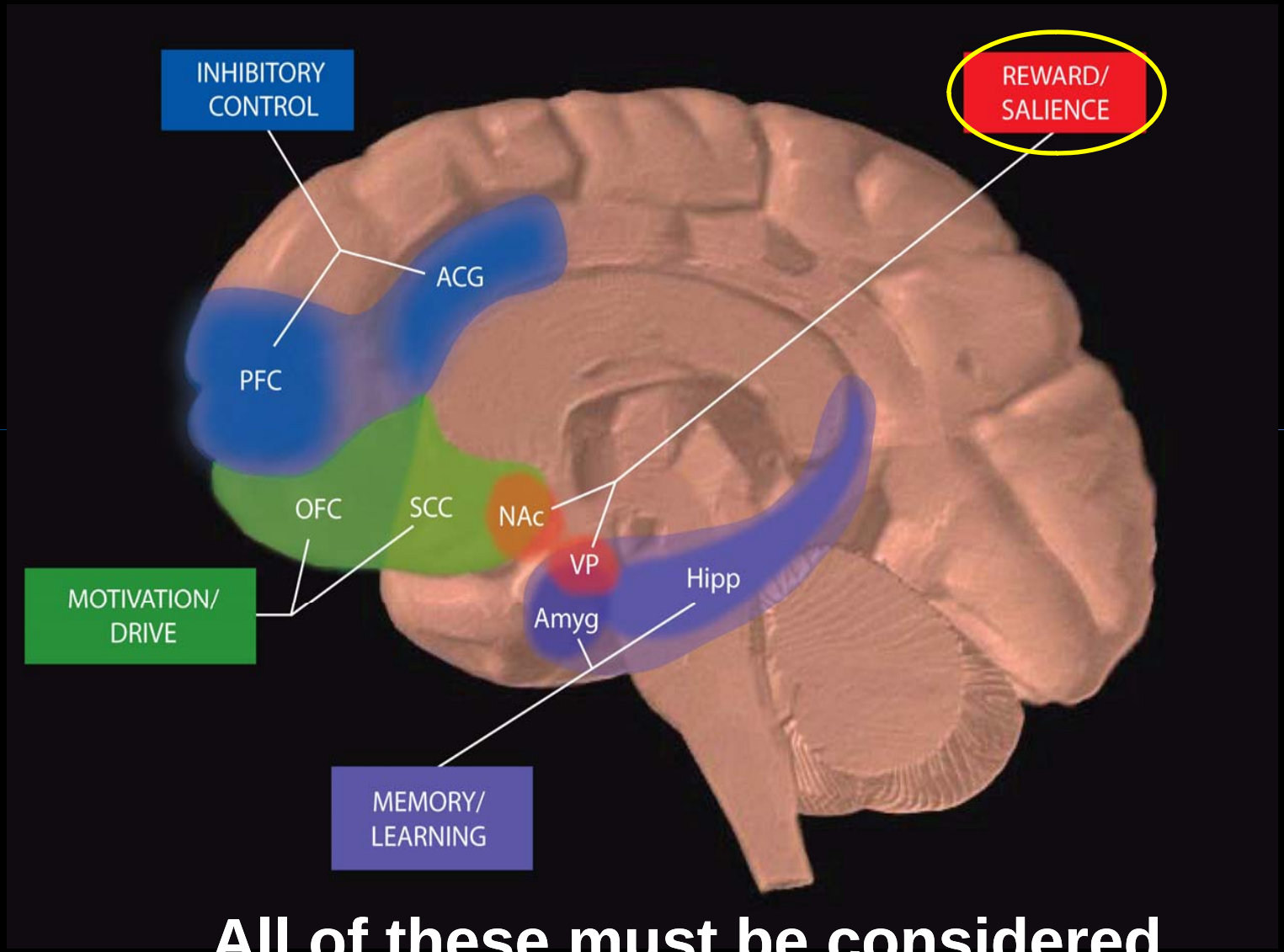
Adapted from Volkow et al., Am. J. Psychiatry, 1999.


used to be
this is your brain on drugs.

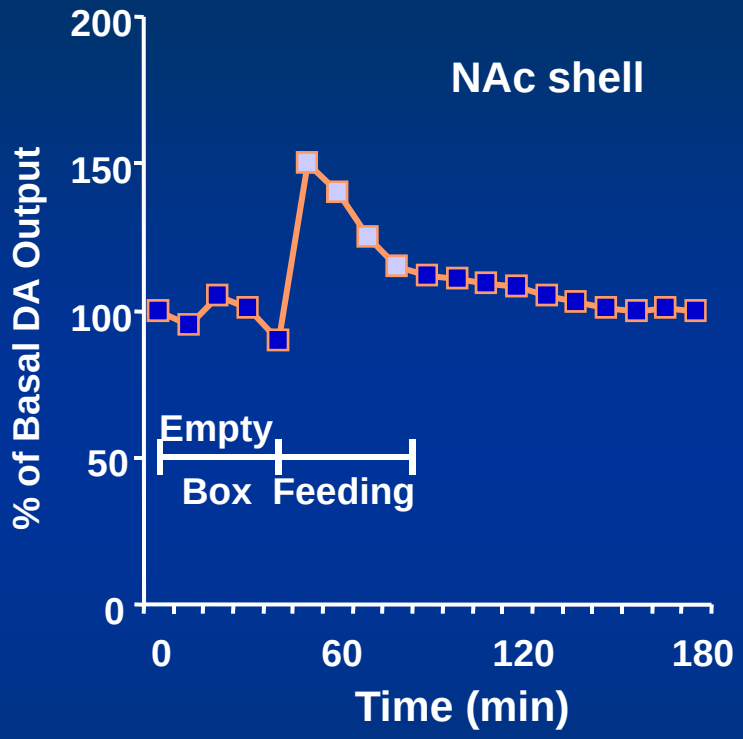
Circuits Involved In Drug Abuse and Addiction



All of these must be considered in developing strategies to effectively treat addiction

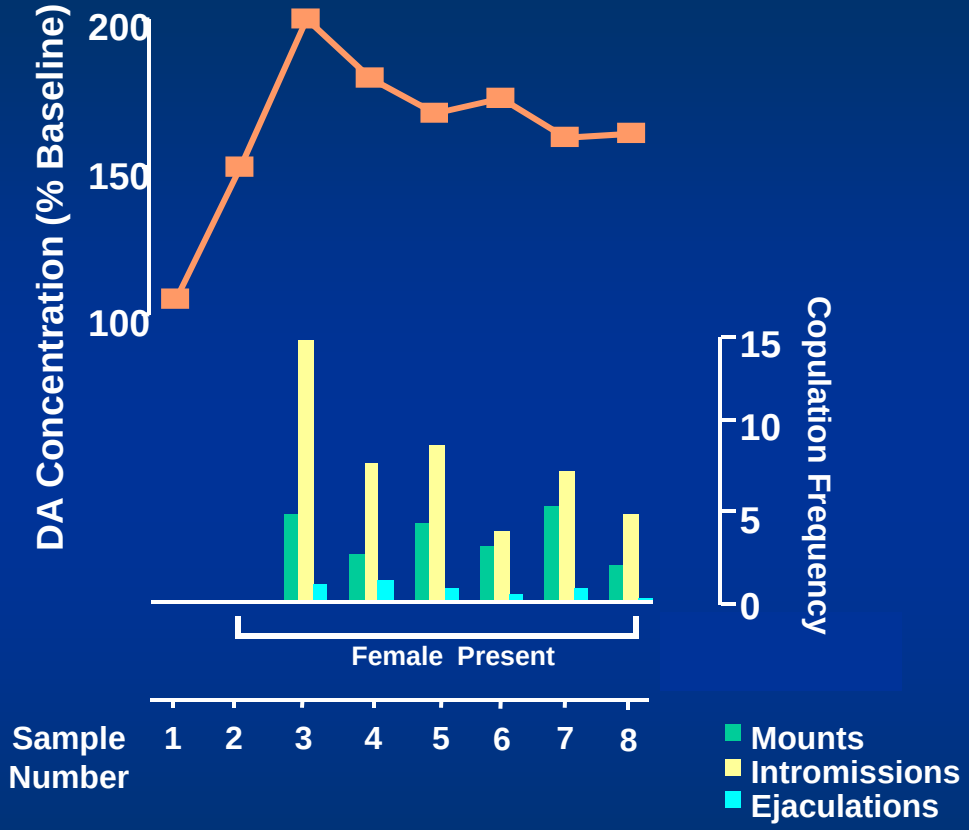
Natural Rewards Elevate Dopamine Levels

FOOD



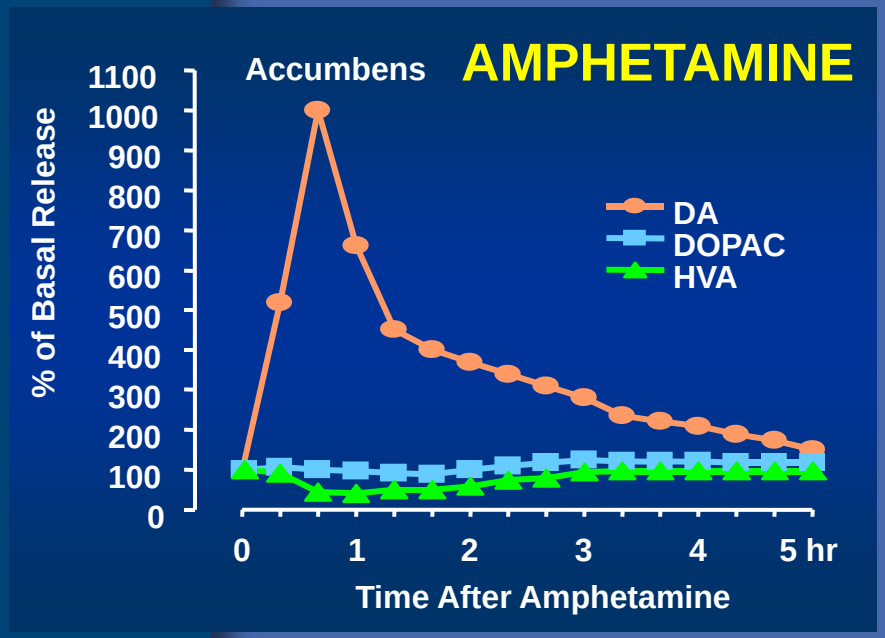
Di Chiara et al., Neuroscience, 1999.

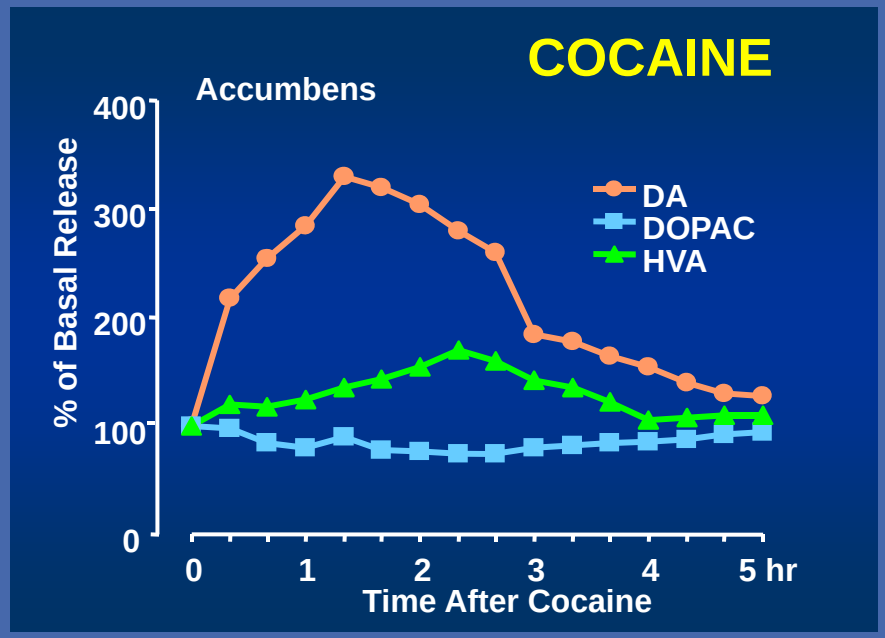
SEX

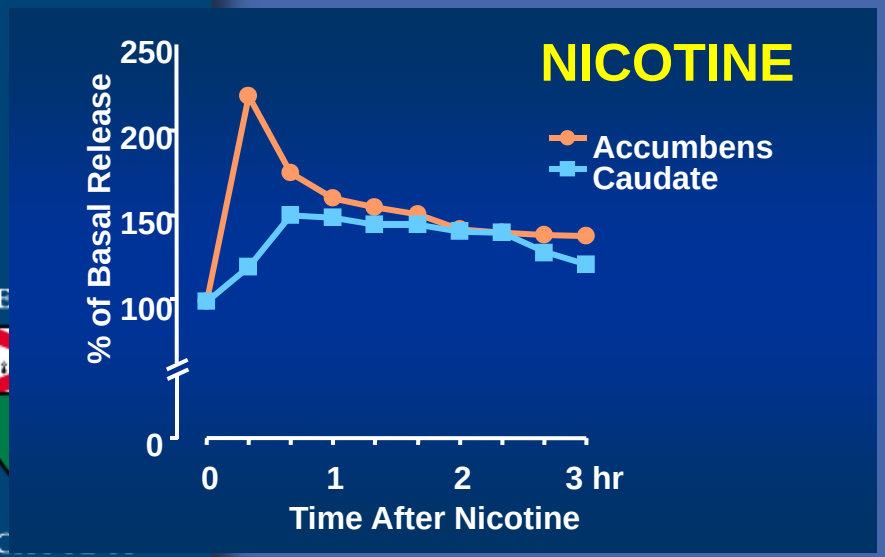


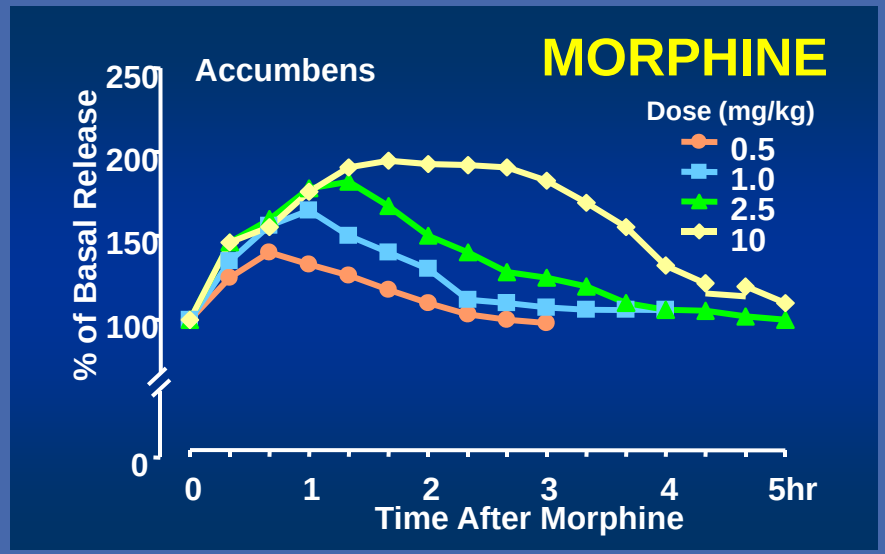
Fiorino and Phillips, J. Neuroscience, 1997.

Effects of Drugs on Dopamine Release









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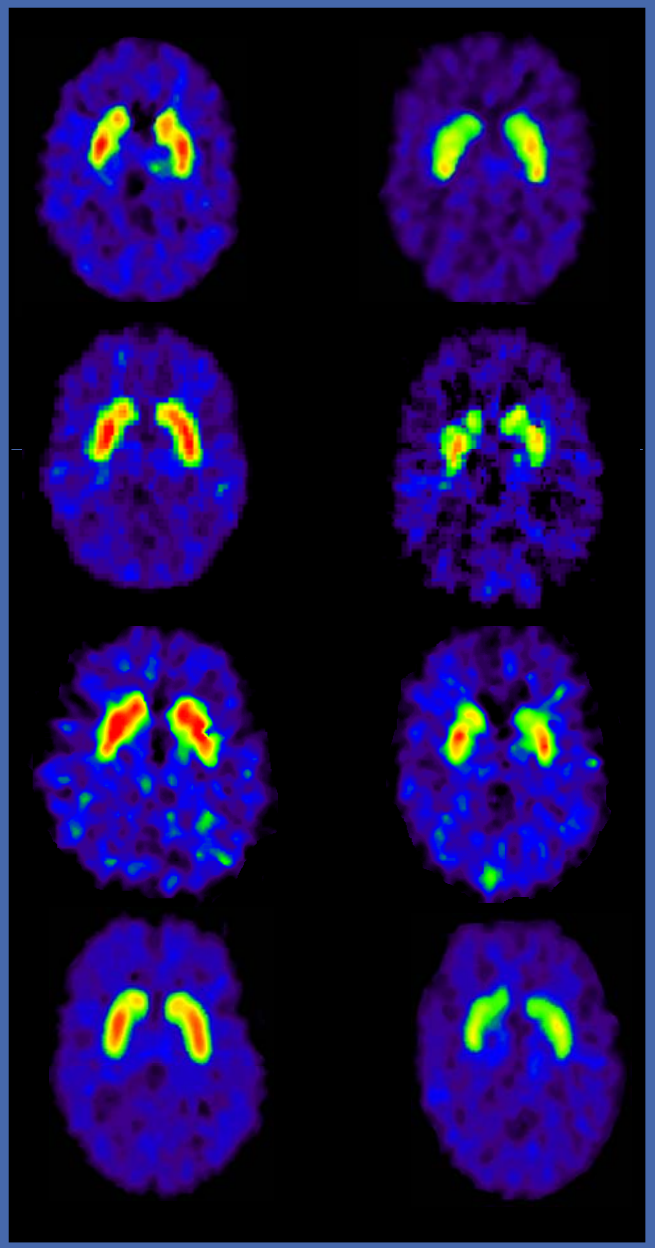
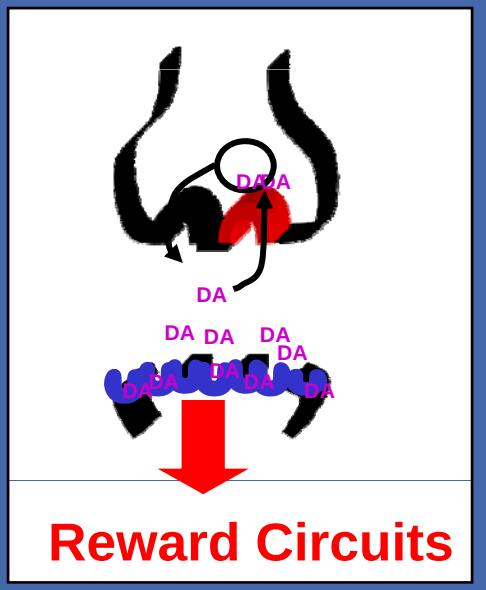
Di Chiara and Imperato, PNAS, 1988

Dopamine D2 Receptors are Lower in Addiction

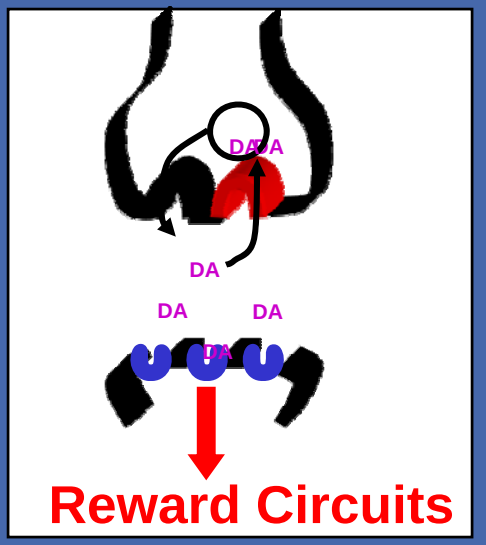
Control Addicted



DA D2 Receptor Availability

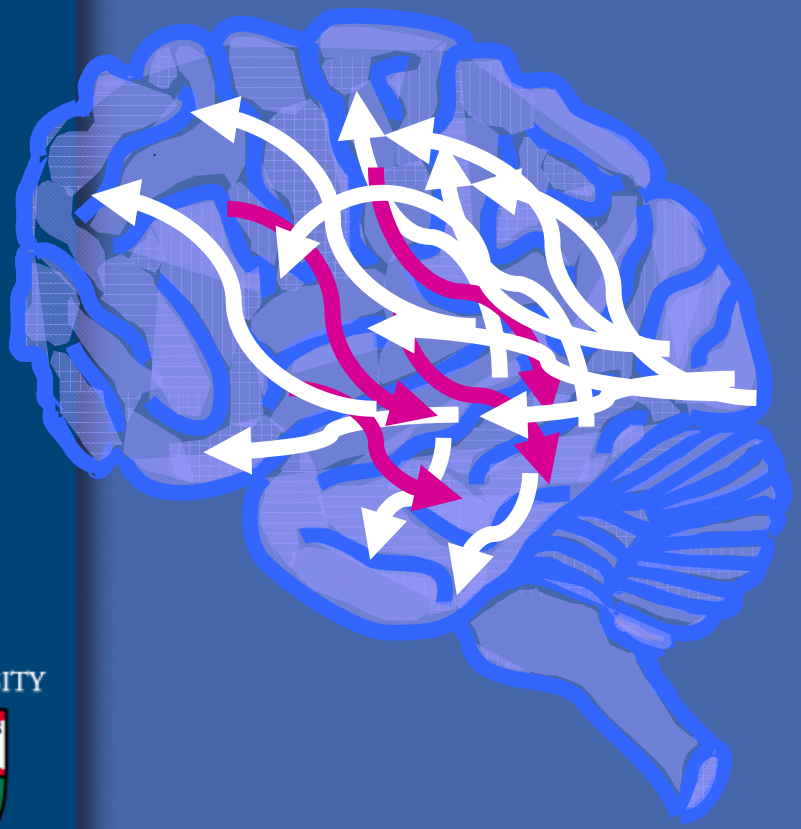


Non-Drug Abuser



Drug Abuser

Drugs Are Usurping Brain Circuits



and Motivational Priorities

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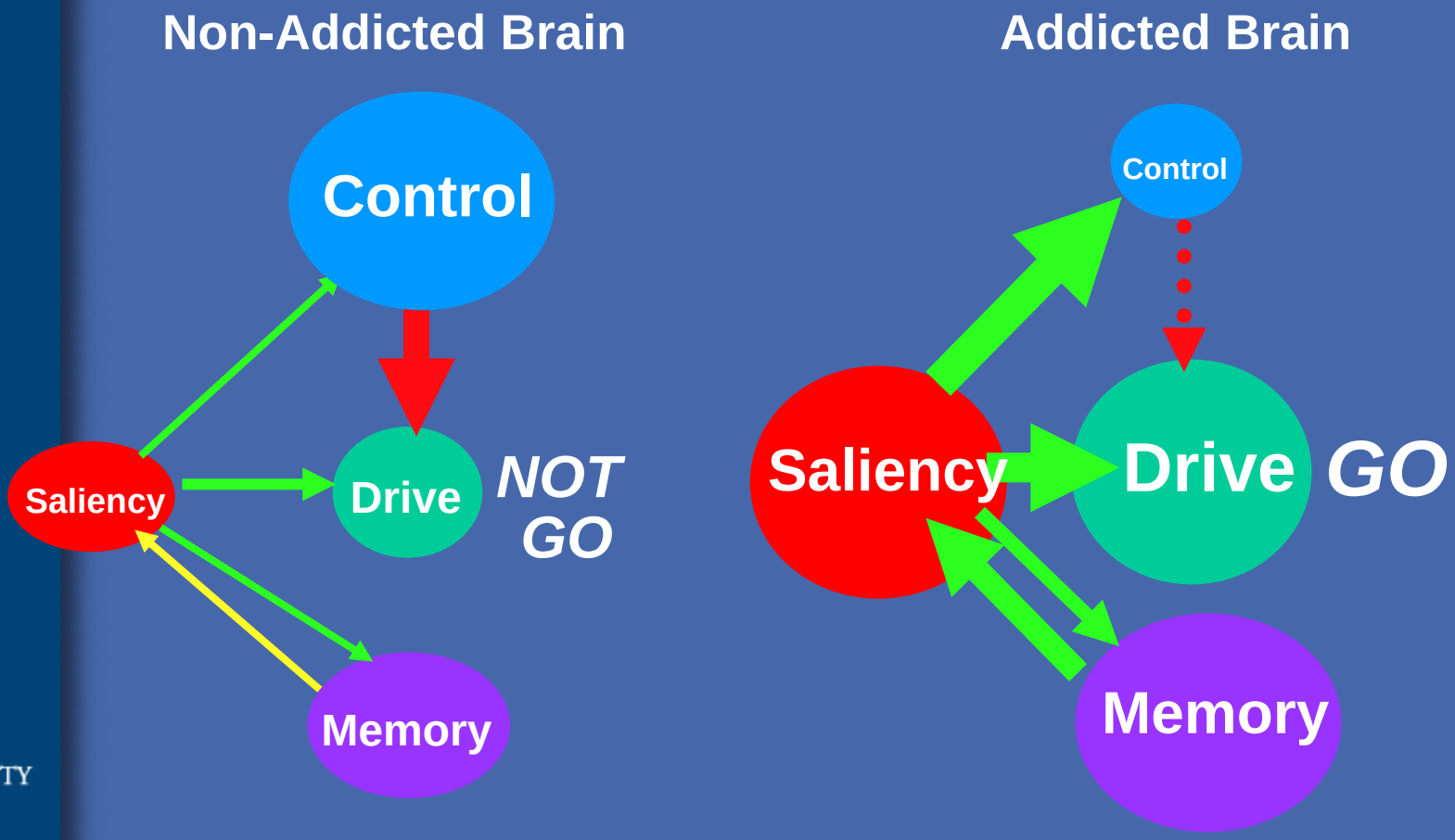
Addiction Changes Brain Circuits



Source: Adapted from Volkow et al., Neuropharmacology, 2004.

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This is why addicts can’t just quit

This is why treatment is essential

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Treatment for Addiction Includes:

1. Pharmacological (medications)
2. Behavioral Therapies
3. Medical treatment for the complications of addiction (e.g., HIV, HCV therapy)
4. Social Services

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Pharmacology in Primary Care: Opioids = buprenorphine

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Heroin

- Heroin is a short-acting, semisynthetic opioid produced from opium that can be smoked, sniffed, or injected

- Heroin euphoria begins shortly after injection and lasts ~ 1 hour, followed by 1-4 hours of sedation; withdrawal symptoms or craving begin several hours later.

- Most heroin dependent individuals inject 2-4 times per day. Many mediate sedating effects by injecting a small amount of cocaine, if available (not in Russia or Asia), known as a "speedball." Sometimes crack is smoked as a substitute.

- Unsterile use, unpredictable concentrations in street samples, adulterants in injection mixture, lifestyle necessary to procure drugs are responsible for most heroin-associated medical complications.

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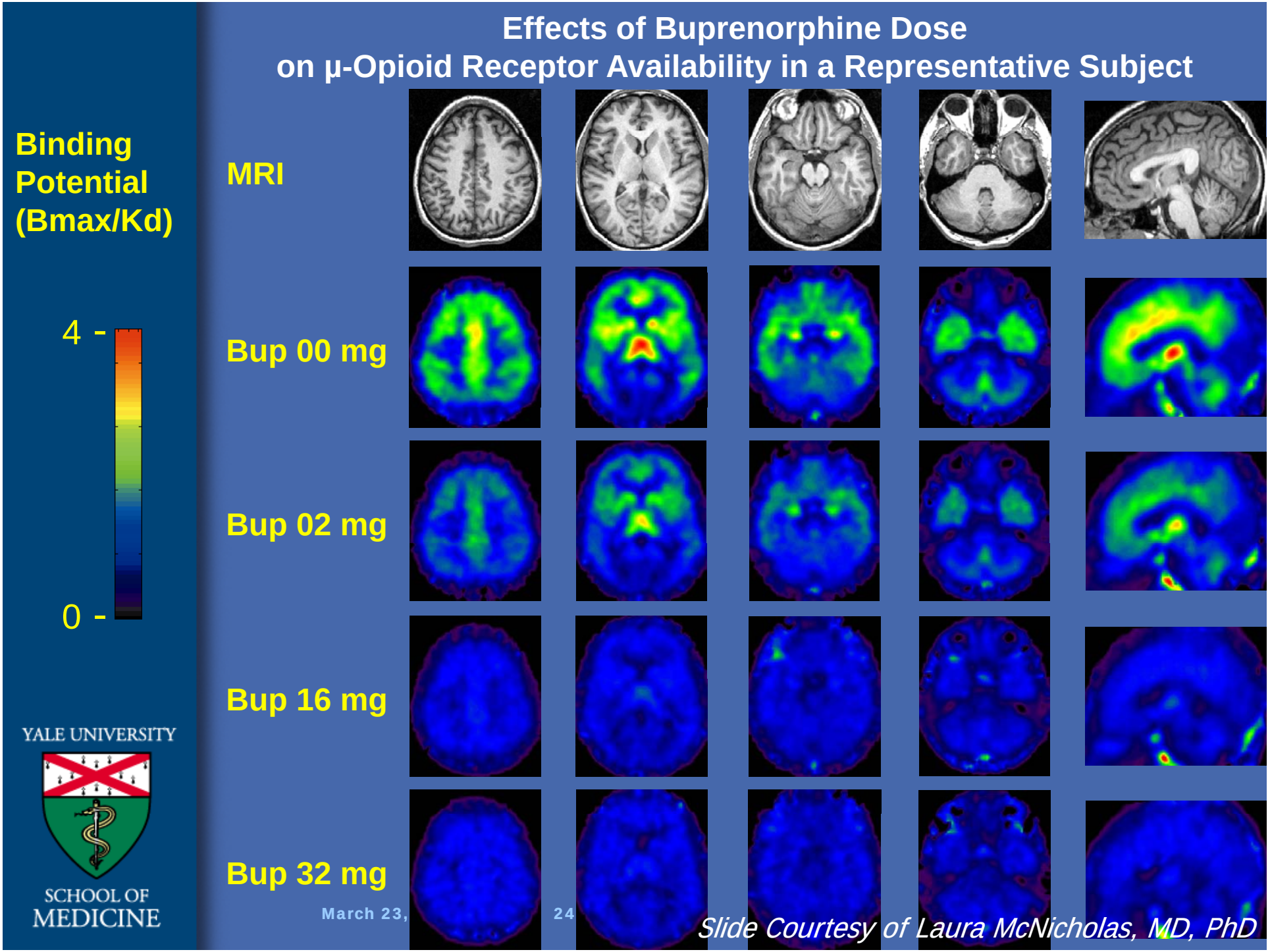
Effects of Buprenorphine Dose on μ-Opioid Receptor Availability in a Representative Subject



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Slide Courtesy of Laura McNicholas, MD, PhD

Medication Assisted Treatment - Opioids

- Rationale
  - **Cross-tolerance**
    - prevent withdrawal
    - relieve craving for opioids
  - **Narcotic blockade**
    - block or attenuate euphoric effect of exogenous opioids
- Pharmacotherapy
  - **Buprenorphine**
  - **Methadone**
  - **LAAM**
  - **Naltrexone**

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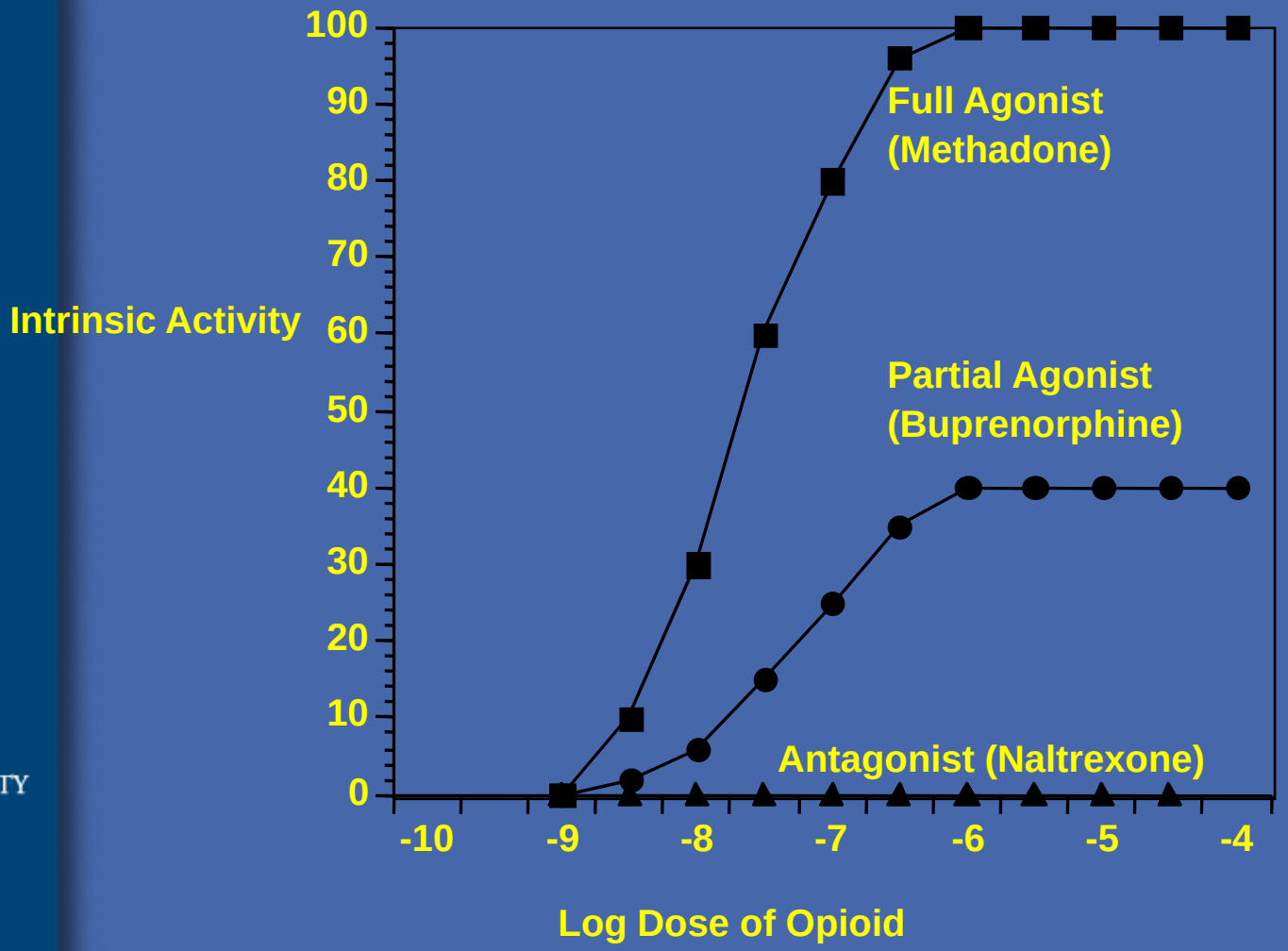
Intrinsic Activity



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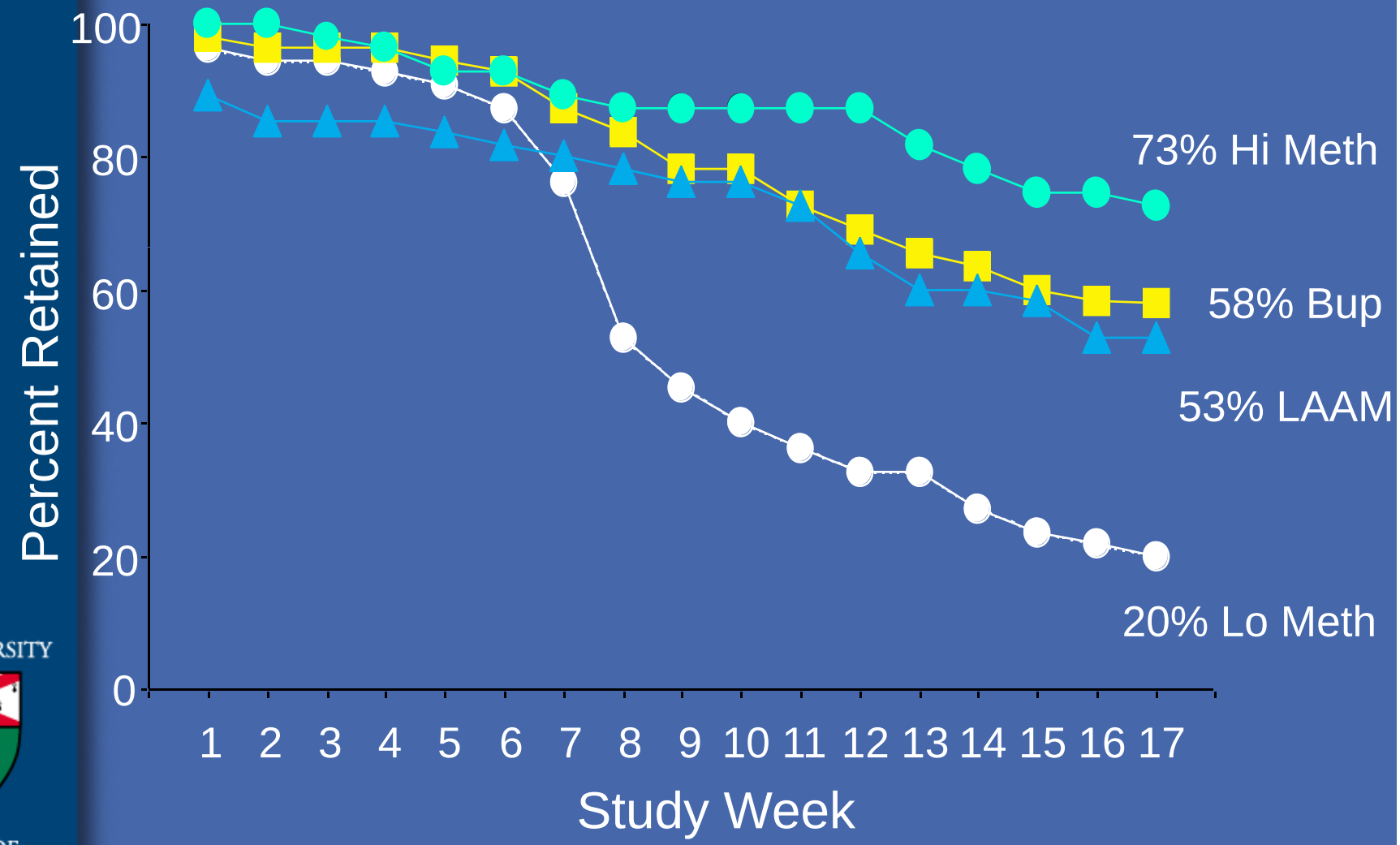
Buprenorphine, Methadone, LAAM: Treatment Retention



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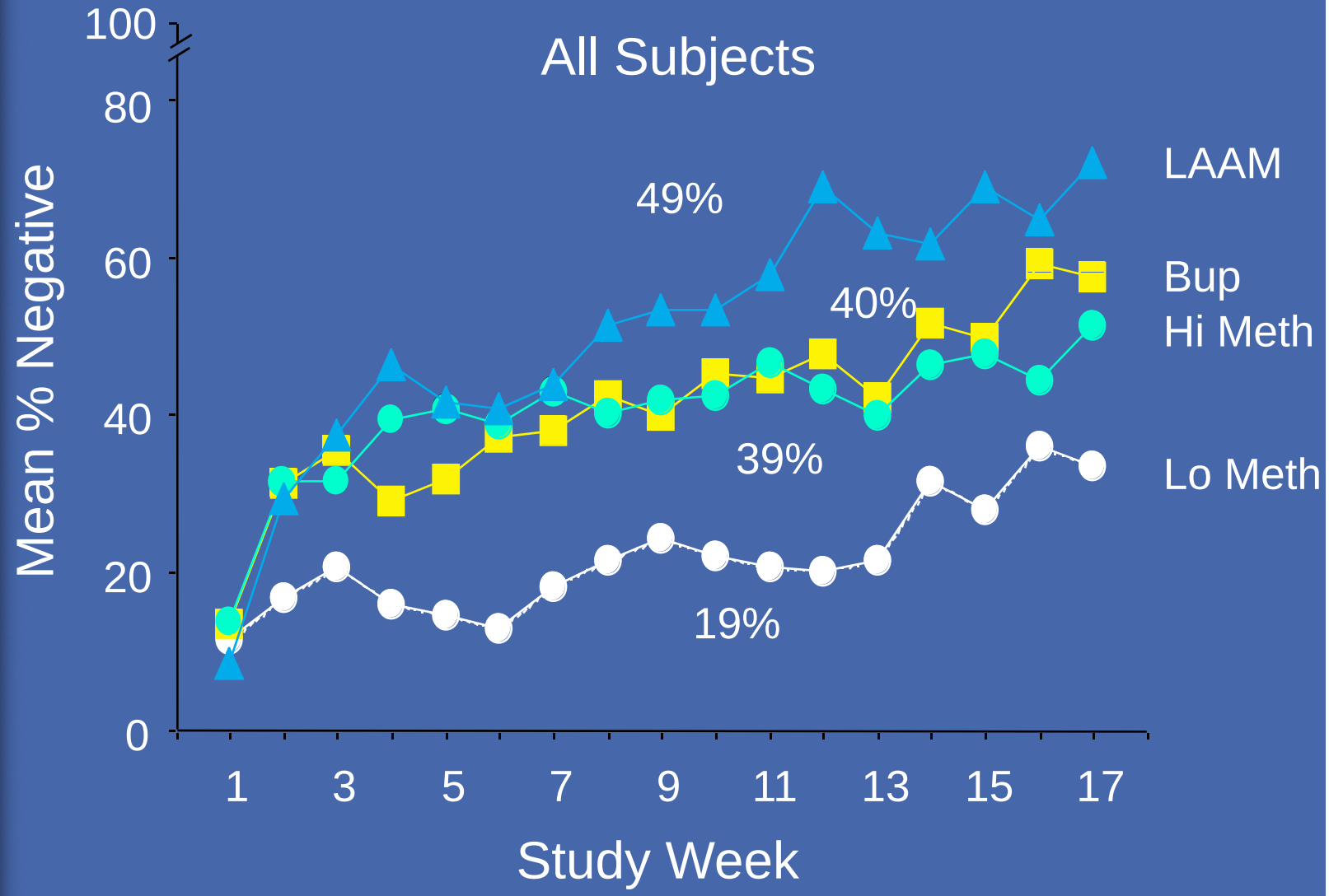
Buprenorphine, Methadone, LAAM: Opioid Urine Results



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Buprenorphine

- Every physician treating HIV-infected drug users should have an X waiver and be ready to prescribe.
- The 1, 2, 3 of BUP:
  - **1. It is easier than HIV/HCV treatment.**
  - **2. It is safer than prescribing oxycodone for pain or alprazolam for anxiety.**
  - **3. It is desperately needed to expand access to treatment.**

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Pharmacology in Primary Care : Cocaine = Disulfiram

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Cocaine

- Cocaine hydrochloride is a water-soluble salt which is injected or taken by nasal inhalation, “snorted”.

- Although cocaine hydrochloride is destroyed by heat, it may be chemically converted to a free-base ("crack") cocaine, which can be smoked. Pulmonary absorption of “crack” is as rapid as IV injection.

- Cocaine’s half-life is short, resulting in the need for frequent administration; active cocaine users may inject or inhale cocaine as many as 20 times a day.

- Cocaine induces feelings of elation, omnipotence and invincibility and with volatile behavior and rapid development of dependence.

- Cocaine use is associated with high risk sexual behavior.

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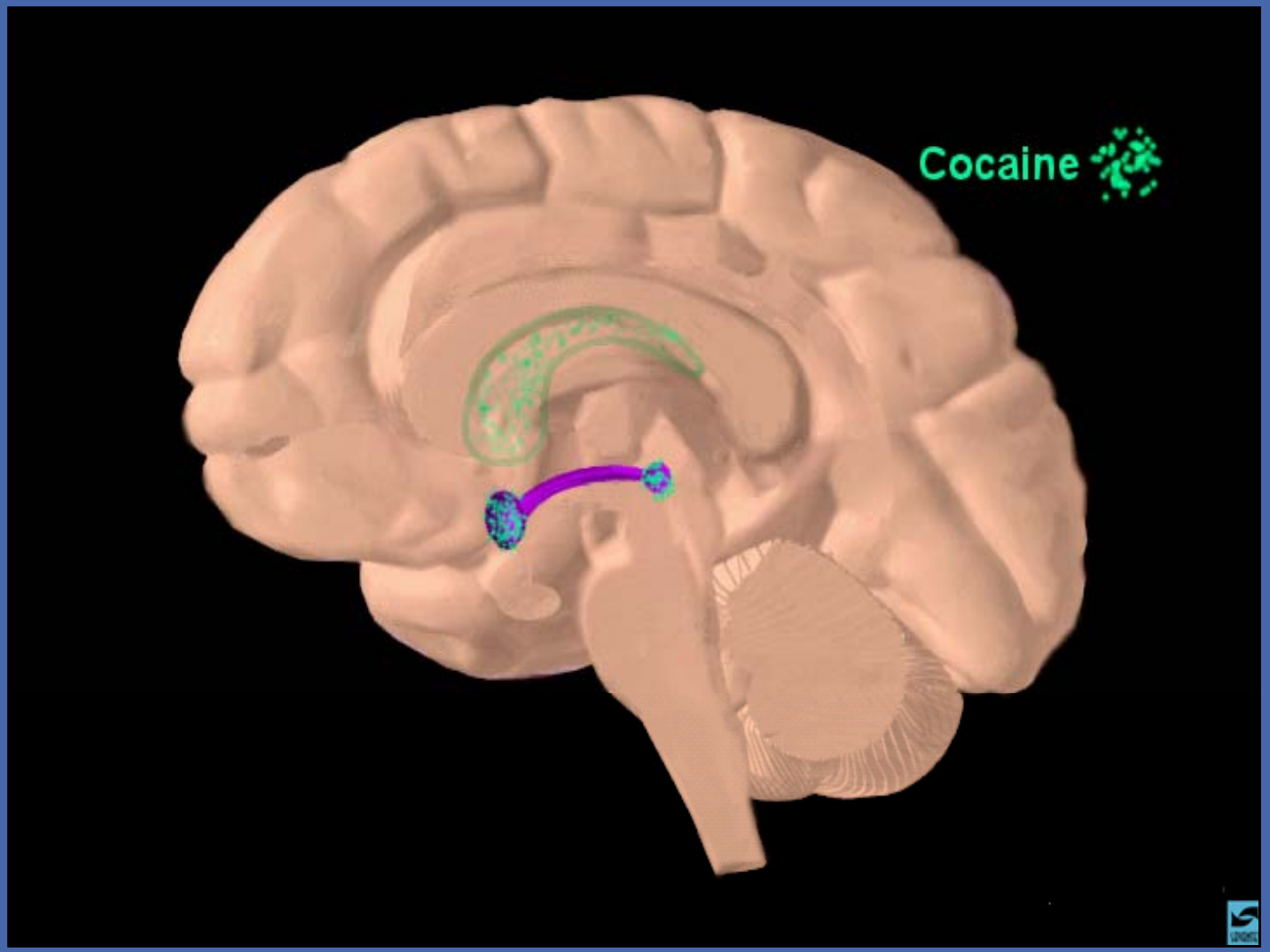
Site of Cocaine Binding



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Disulfiram

- Increases dopamine in the brain by inhibiting dopamine beta hydroxylase.
- 6 RCTs have demonstrated efficacy in treating cocaine dependence.
- Dosage: 250 mg/day
- No studies in HIV/HCV populations so need to watch AST/ALT
- Problem remains adherence. Works well with the motivated patient or the patient who is administered it with methadone.

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Pharmacology in Primary Care : Methamphetamine = Buproprion

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Methamphetamine (MA)

- MA is a psychostimulant similar in chemical structure to amphetamine with more profound effects on the CNS and can be smoked, snorted, injected, or administered rectally.
- Produces stimulation and feelings of euphoria and has a long duration of action (6 to 8 hours after a single dose)
- Tolerance develops rapidly and escalation of dose and frequency is required.
- As with cocaine, MA use is associated with high risk sexual behavior (especially in MSM)
- Neurocognitive effects of MA use worse in HIV positive patients..

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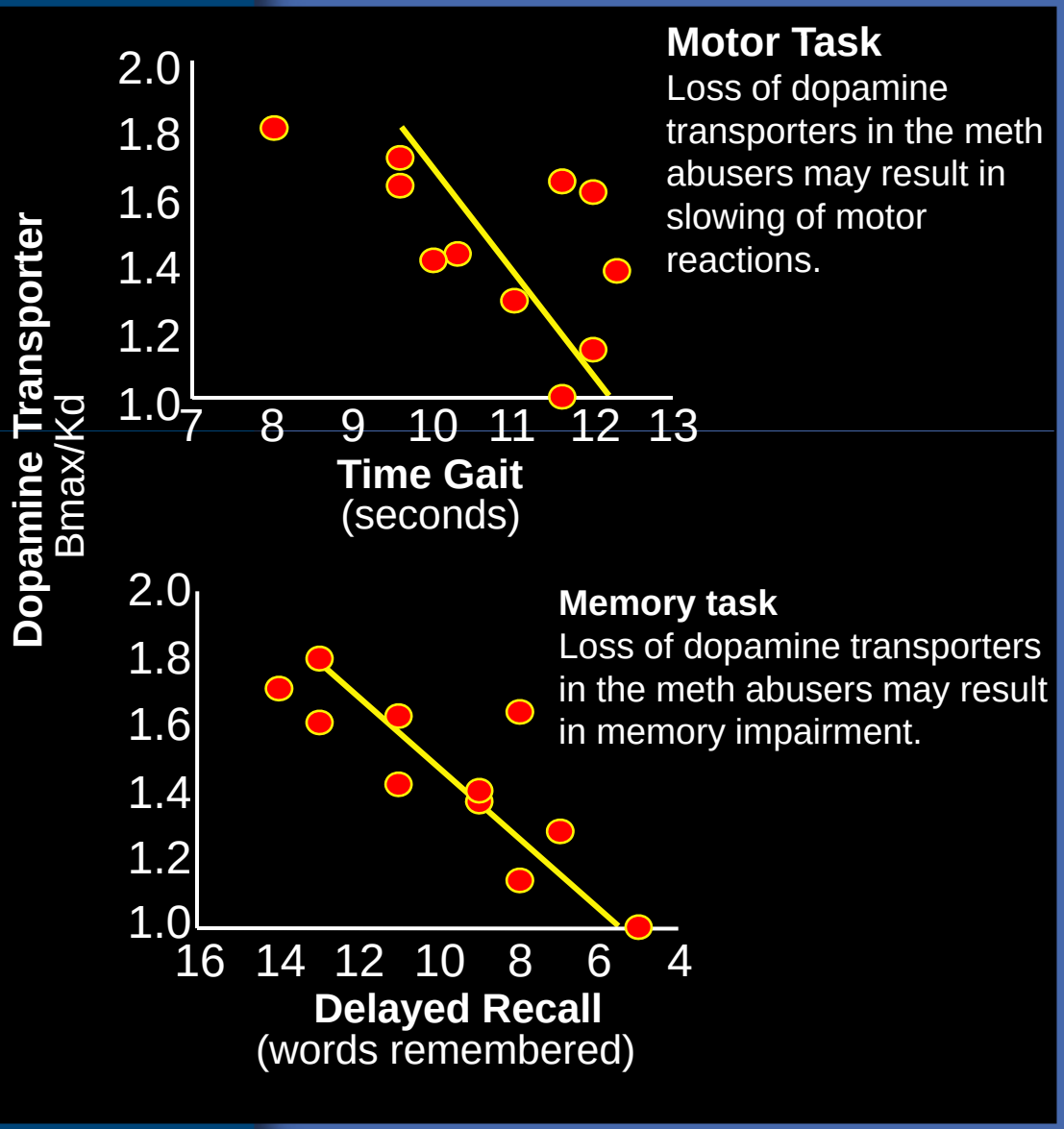
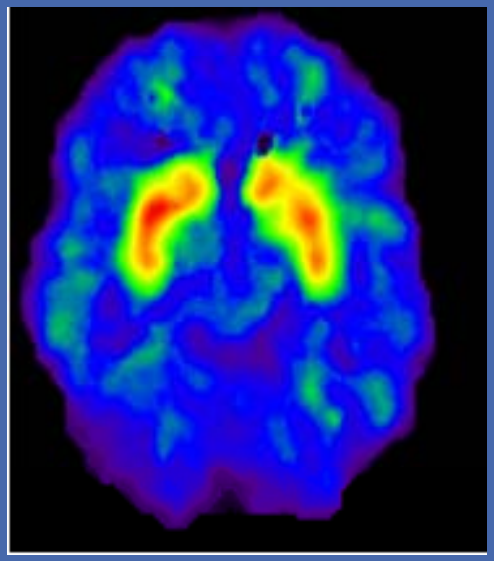
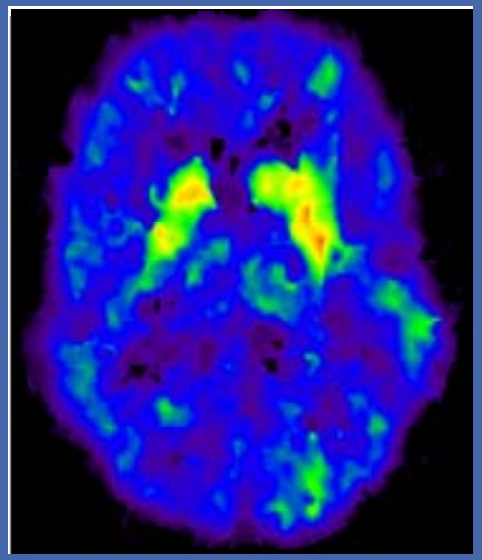
Dopamine Transporters in Methamphetamine Abusers





Normal Control



Methamphetamine Abuser

Volkow et al., Am. J. Psychiatry, 2001.

Treatments

- Bupropion 150 mg twice daily has shown some reduction in use among mild methamphetamine users (Shoptaw DAD 2008)
- Counseling remains the mainstay

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Pharmacology in Primary Care: Alcohol = Naltrexone

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Alcohol Main Points

- Disinhibition that leads to increased risk taking behaviors and poor adherence to all treatments
- Withdrawal seizures
- The drug that really is frightening because it is neurotoxic and accelerates HCV disease progression
- CAGE Questions

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ETOH Treatment

- Naltrexone –
  - **FDA approved and standard of care**
  - **Watch for hepatotoxicity (black box warning)**
  - **Dosages: 100 mg per day (based on COMBINE study)**
- Acamprosate
  - **FDA approved, but inferior to naltrexone**
- Disulfiram
  - **FDA approved, but inferior to naltrexone**

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Topiramate

- Not FDA approved for ETOH dependence
- 8 papers showing efficacy of topiramate for ETOH dependence
- Doses varied by trial, but typically patients were started low (25 mg daily) and titrated up to a max of 300 mg over 6 weeks.
- Important choice because:

1. Can give to patients on opioids
2. Moderates symptoms of withdrawal

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Pharmacology in Primary Care: Nicotine = Nicotine

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The 5 A's

- *Ask* about tobacco use
- *Advise* smokers to quit
- *Assess* willingness to quit
- *Assist* with quitting
- *Arrange* follow-up
- Brief advice to quit does make a difference!

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Pharmacotherapy

- Nicotine replacement helps
- Buproprion doubles quit rates (but is metabolized by CYP 2B6 so possible interactions with NFV, RTV, and EFV). Doses 150 mg to 300 mg effective.
- Varenicline – better than buproprion and nicotine in comparison trials – watch for suicidality and exacerbation of neuropsychiatric symptoms. Slow upward titration to minimize side effects.

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Continuum of Interventions

Knowing the Pieces

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Range of Treatments

- Risk (Harm) Reduction
  - Decrease frequency of adverse events related to a behavior
  - Change in use behavior – e.g., Changing from injection use to sniffing
- Risk (Harm) Removal
  - Cessation of substance abuse
  - Abstinence based – 12 Steps
  - Agonist based – buprenorphine, methadone

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Harm reduction is critical because drug addiction is a chronic illness with relapse rates similar to those of hypertension, diabetes, and asthma

McLellan et al., JAMA, 2000.

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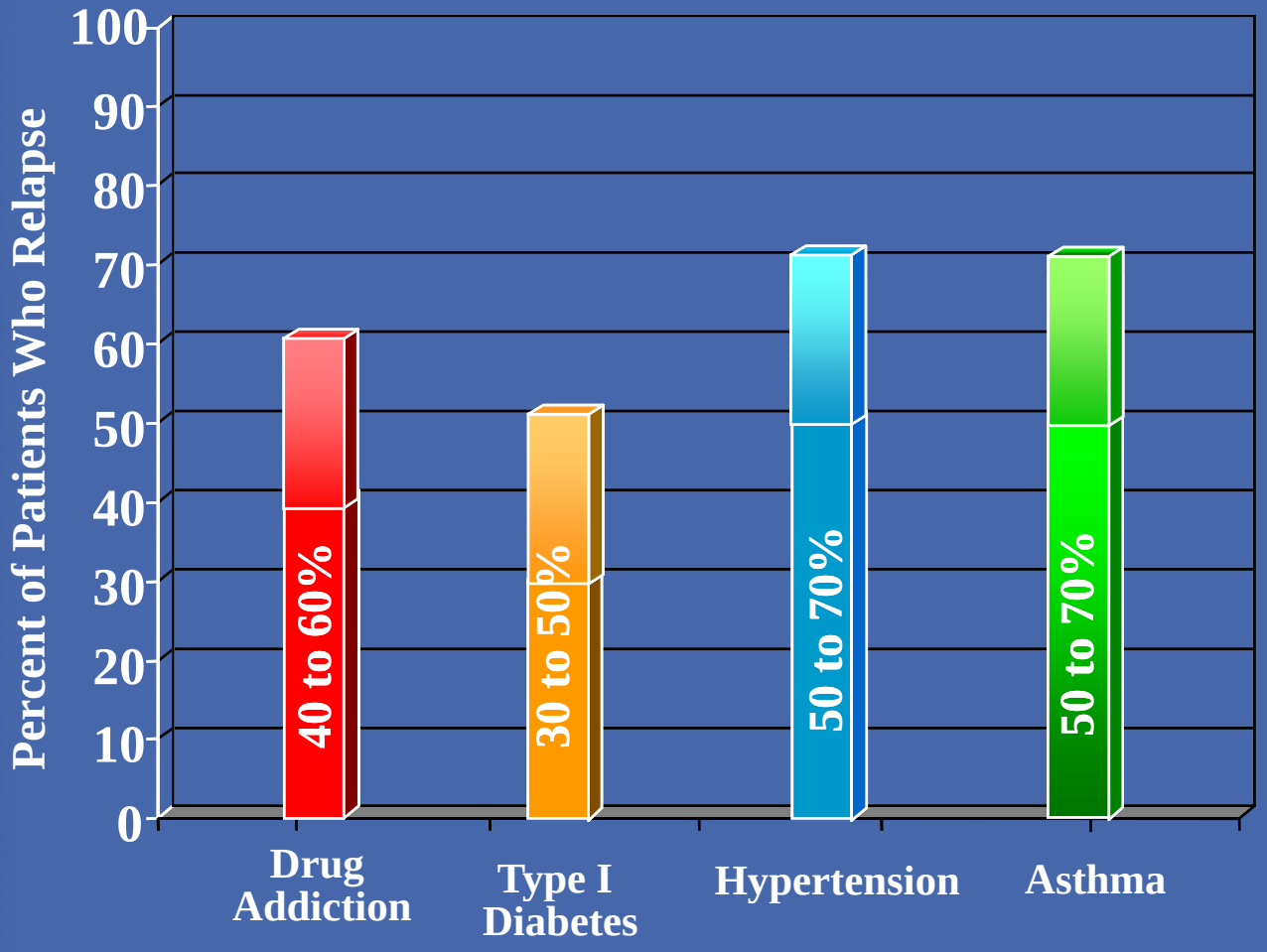
Relapse Rates Are Similar for Drug Addiction & Other Chronic Illnesses



McLellan et al., JAMA, 2000.

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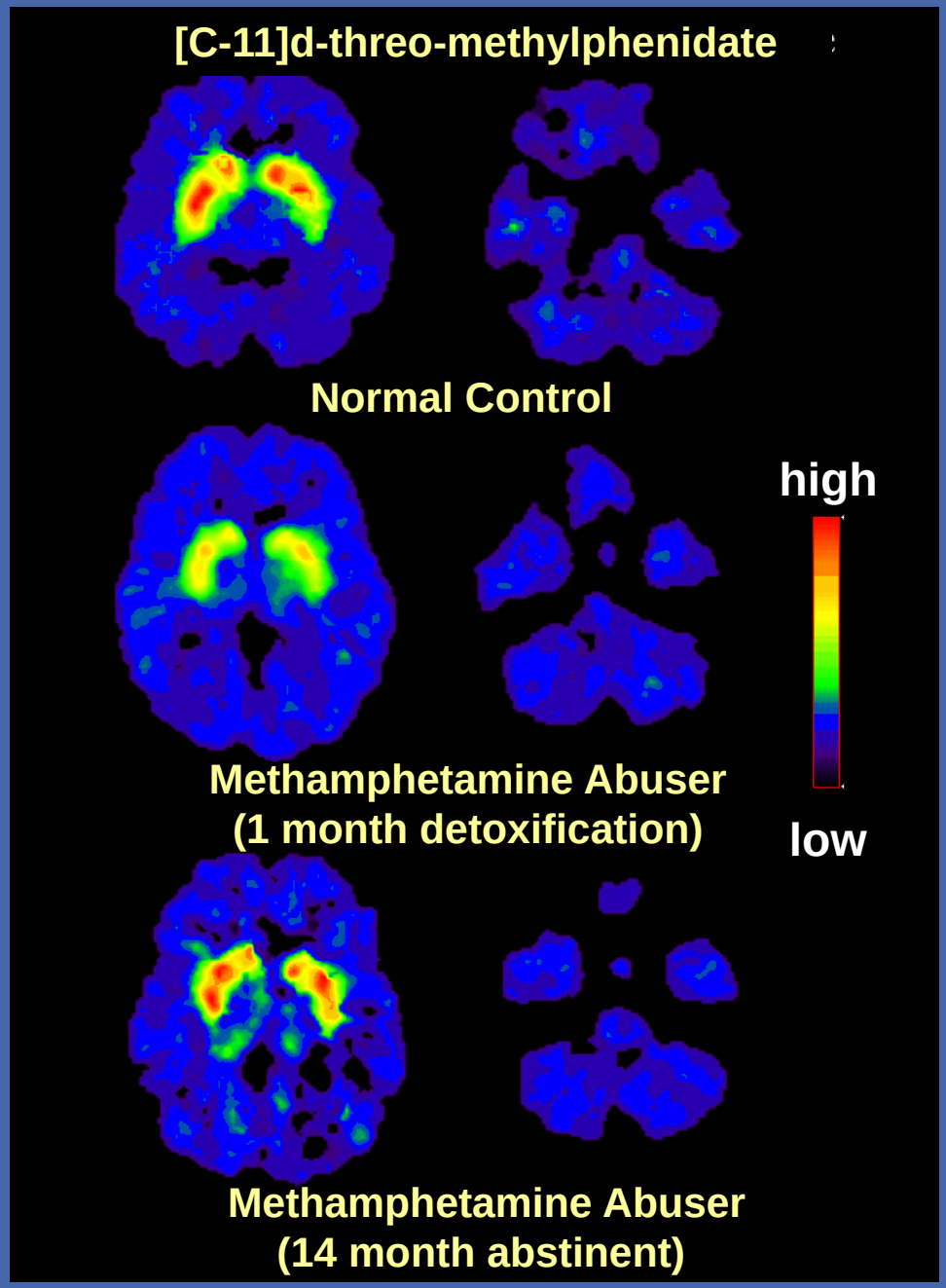
DAT Recovery with prolonged abstinence from methamphetamine

There is hope!!



Volkow et al., J. Neuroscience, 2001.

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Questions?

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