

Medication-Assisted Treatment and HIV/AIDS: Aspects in Treating HIV-Infected Drug Users.

R. Douglas Bruce, MD, MA, MSc
Assistant Professor
Yale AIDS Program

Medical Director
South Central Rehabilitation Center
(An Integrated Healthcare Center for Drug Users)
Cornell Scott-Hill Health Center

YALE UNIVERSITY



SCHOOL OF
MEDICINE

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

YALE UNIVERSITY



SCHOOL OF
MEDICINE

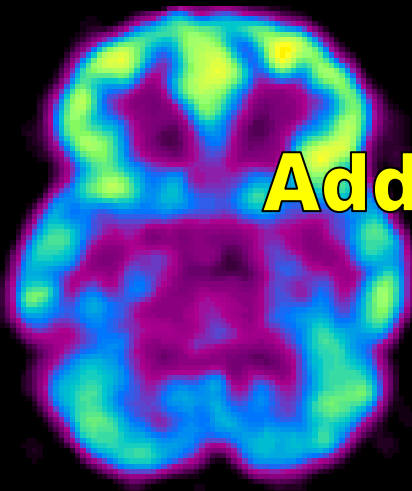
Summary Slide

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

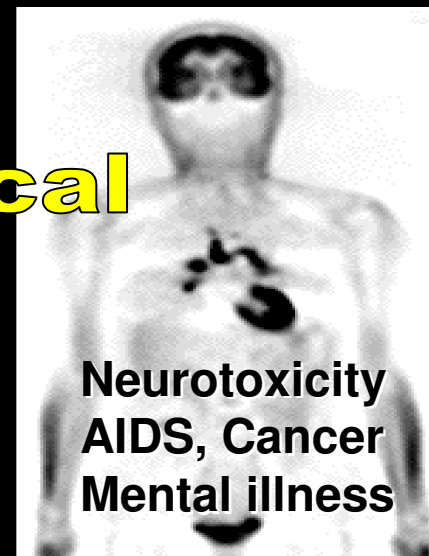
YALE UNIVERSITY



SCHOOL OF
MEDICINE



Addiction



Medical

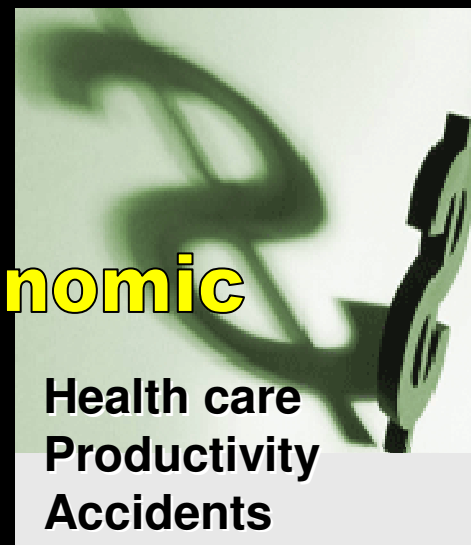
Neurotoxicity
AIDS, Cancer
Mental illness

DRUGS



Social

Homelessness
Crime
Violence



Economic

Health care
Productivity
Accidents

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

YALE UNIVERSITY



SCHOOL OF
MEDICINE

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**

YALE UNIVERSITY



SCHOOL OF
MEDICINE

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

YALE UNIVERSITY



SCHOOL OF
MEDICINE



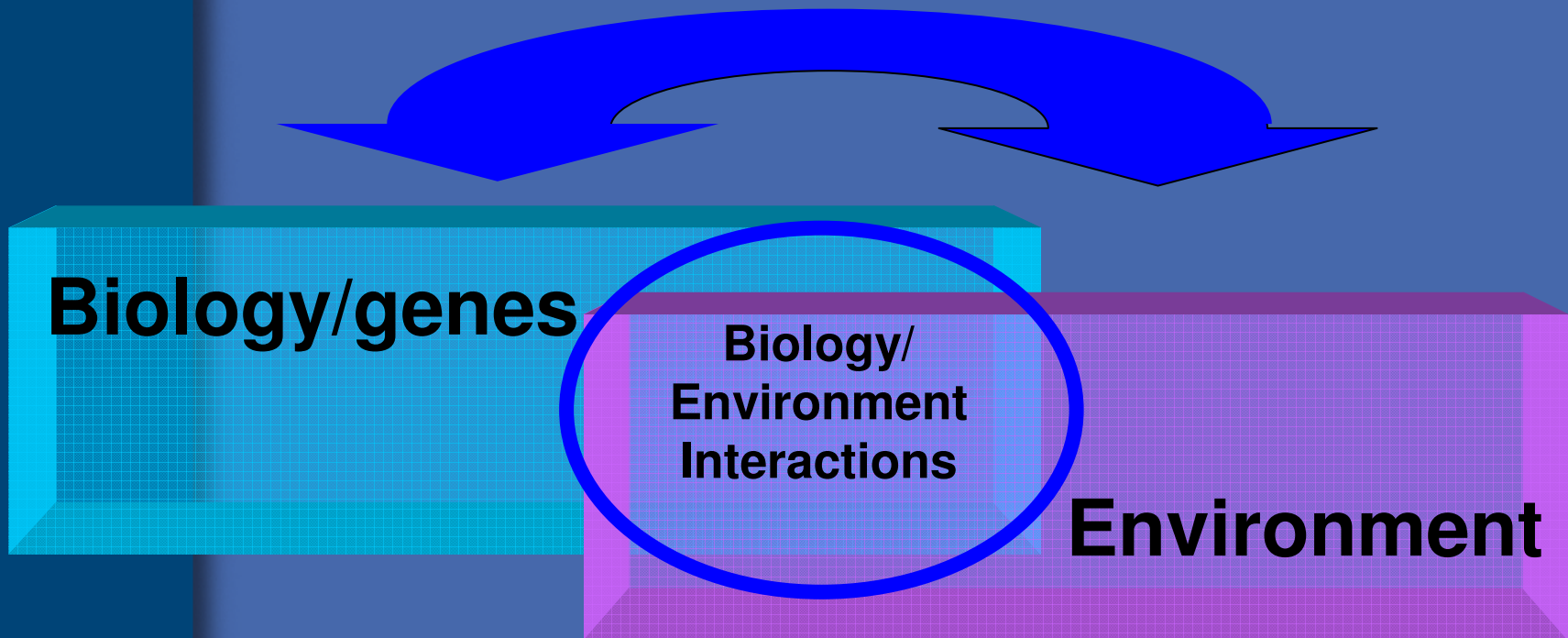
Vulnerability

Why do some people become addicted while others do not?

YALE UNIVERSITY

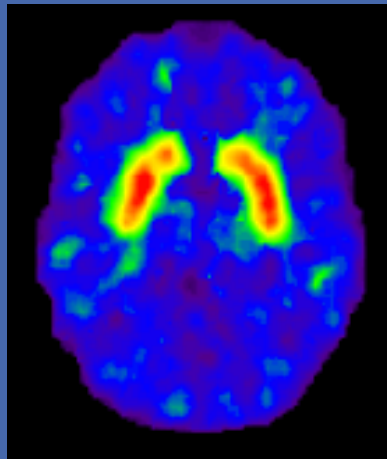


SCHOOL OF
MEDICINE



DA Receptors and the Response to Methylphenidate (MP)

High DA
receptor

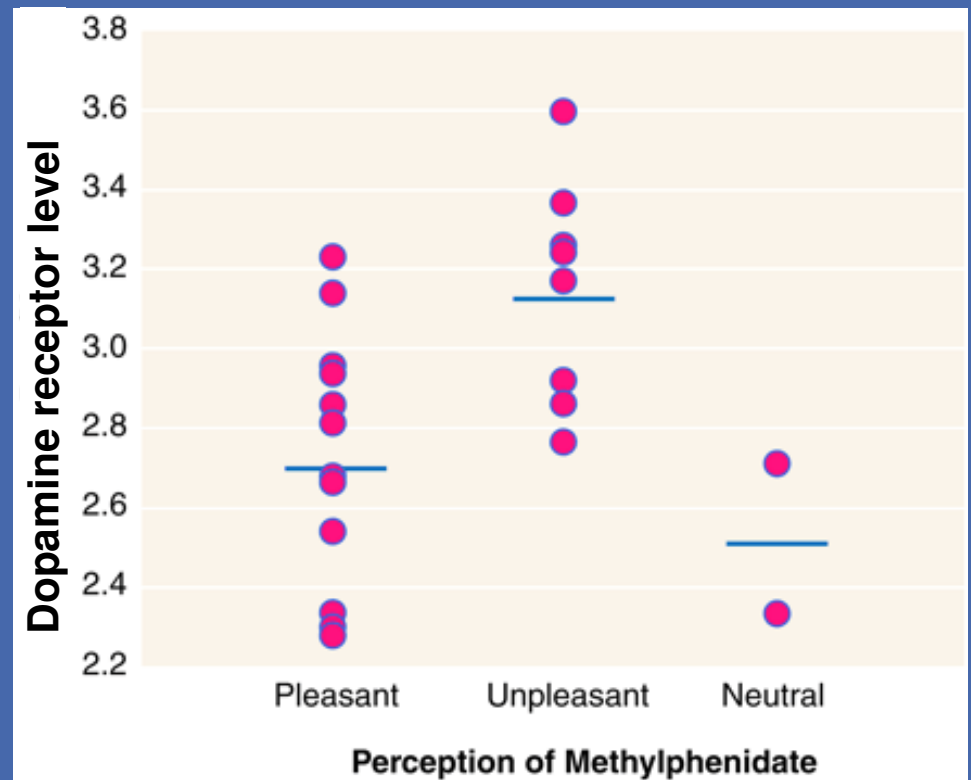
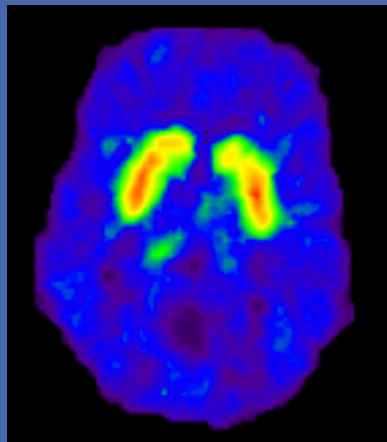


high



low

Low DA
receptor



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

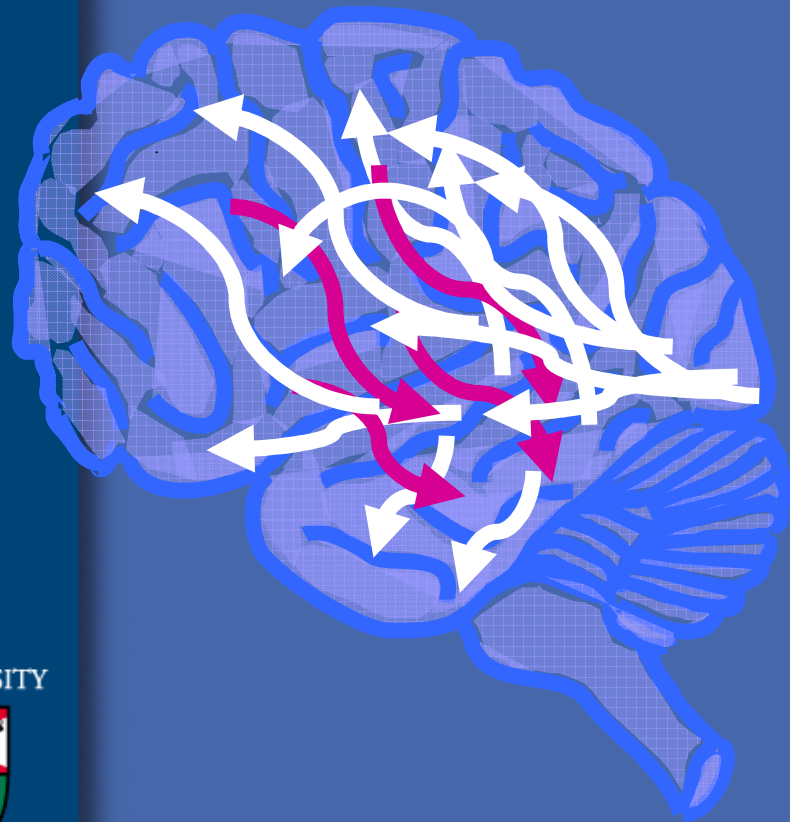
Adapted from Volkow et al., Am. J. Psychiatry, 1999.

YALE UNIVERSITY



SCHOOL OF
MEDICINE

Drugs Are Usurping Brain Circuits



and Motivational Priorities

YALE UNIVERSITY



SCHOOL OF
MEDICINE

This is why addicts can't just quit

This is why treatment is essential

YALE UNIVERSITY



SCHOOL OF
MEDICINE

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

YALE UNIVERSITY



SCHOOL OF
MEDICINE

Pharmacology in Primary Care: Opioids = Buprenorphine

YALE UNIVERSITY



SCHOOL OF
MEDICINE

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.

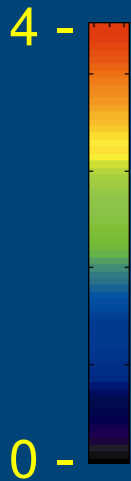
YALE UNIVERSITY

SCHOOL OF
MEDICINE

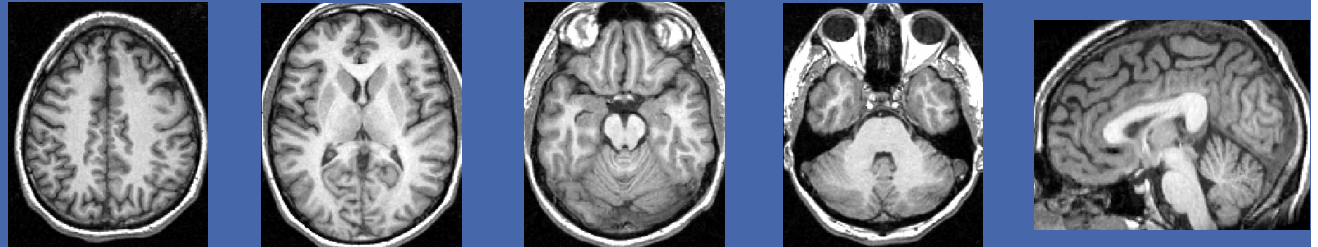
Effects of Buprenorphine Dose on μ -Opioid Receptor Availability in a Representative Subject

Slide #17

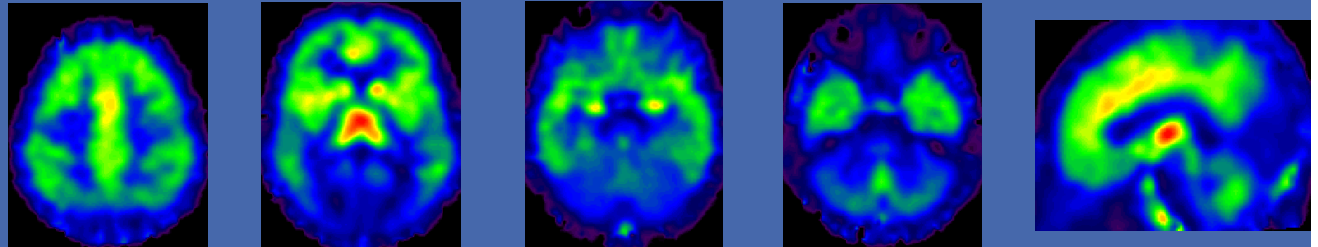
Binding
Potential
(B_{max}/K_d)



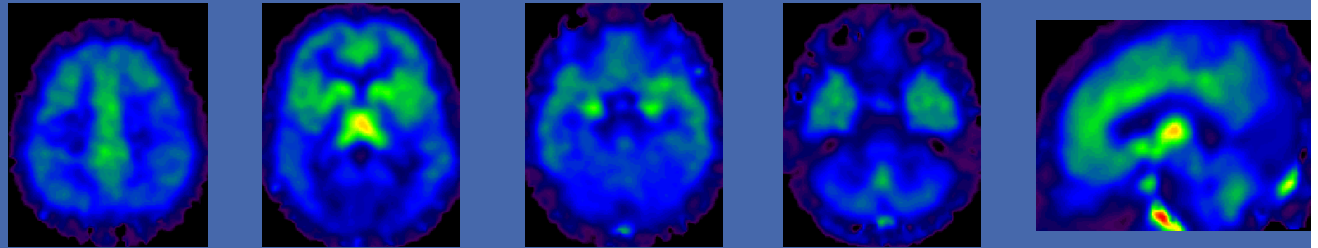
MRI



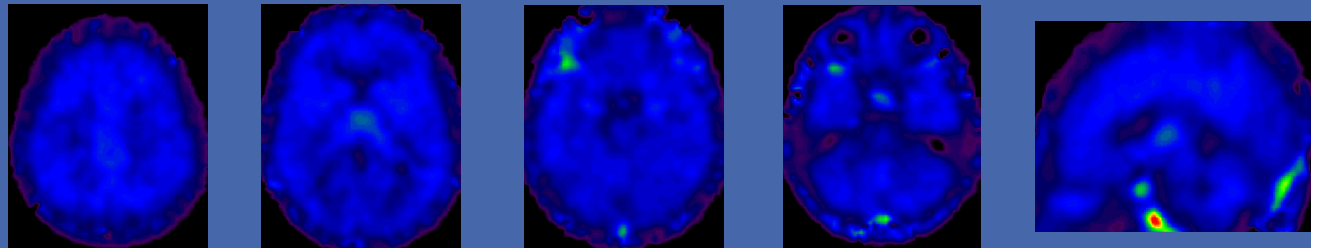
Bup 00 mg



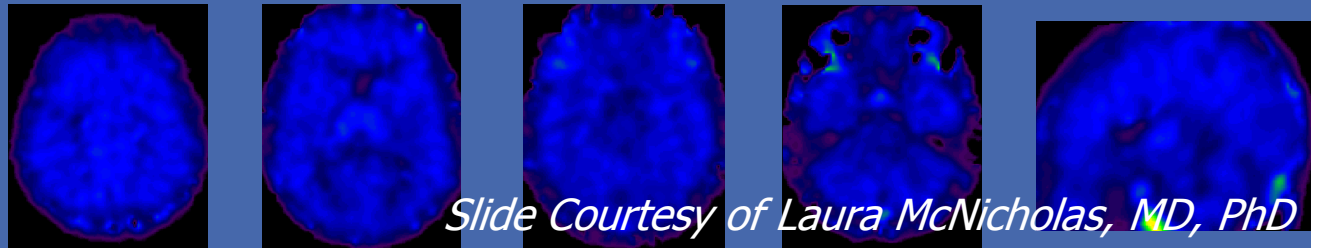
Bup 02 mg



Bup 16 mg



Bup 32 mg



Slide Courtesy of Laura McNicholas, MD, PhD

YALE UNIVERSITY



SCHOOL OF
MEDICINE

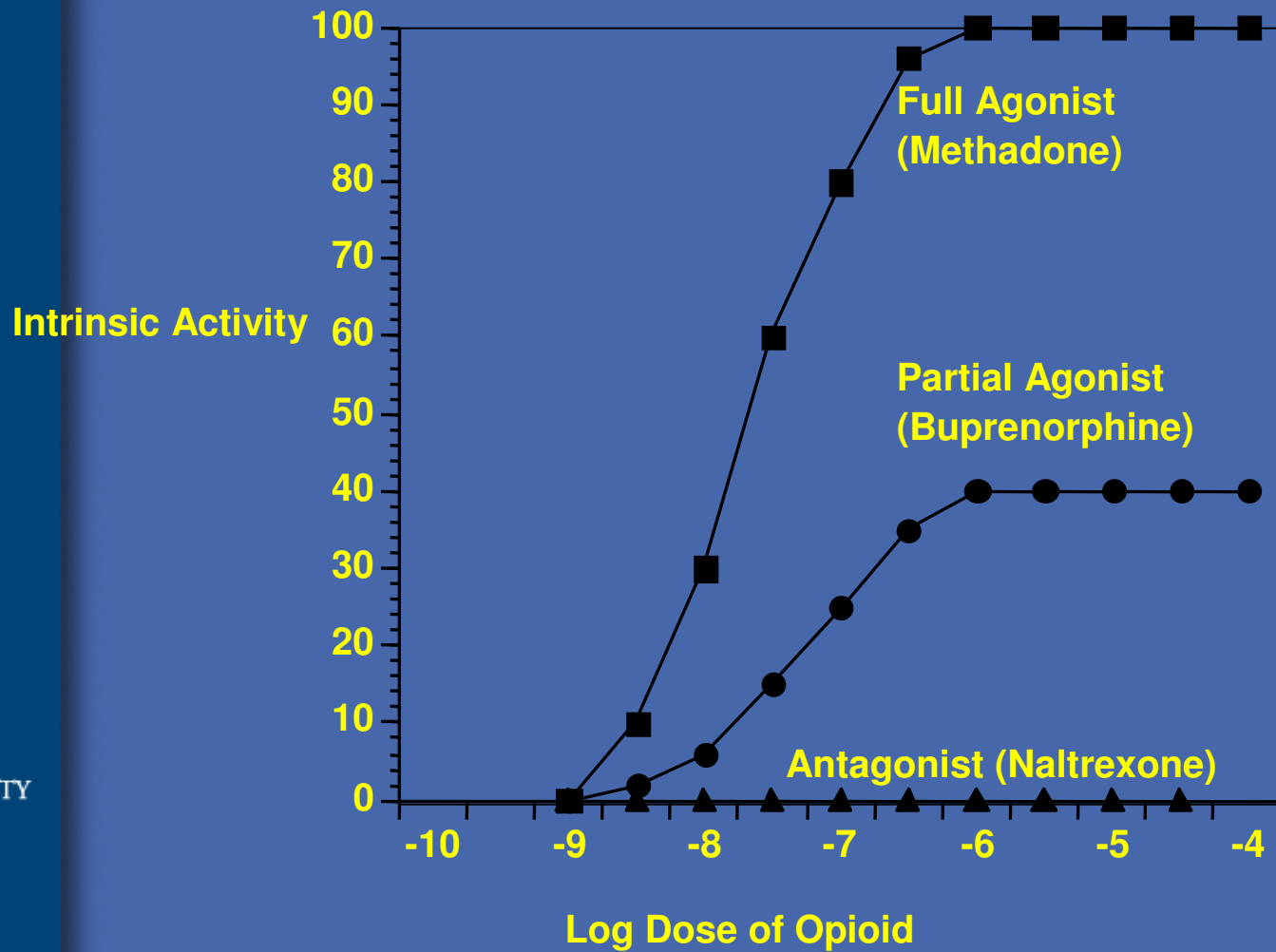
Medication Assisted Treatment - Opioids

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

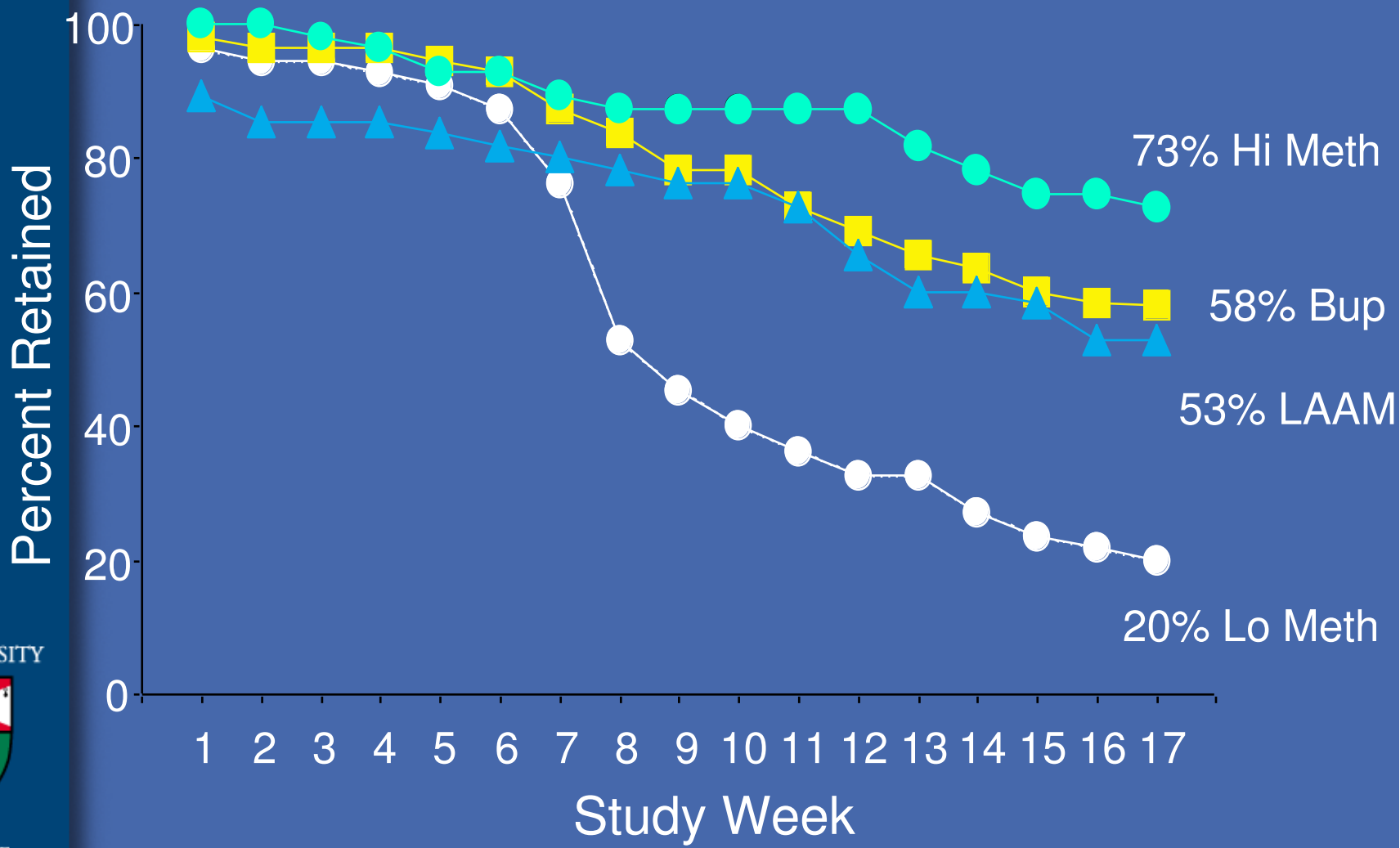
YALE UNIVERSITY

SCHOOL OF
MEDICINE

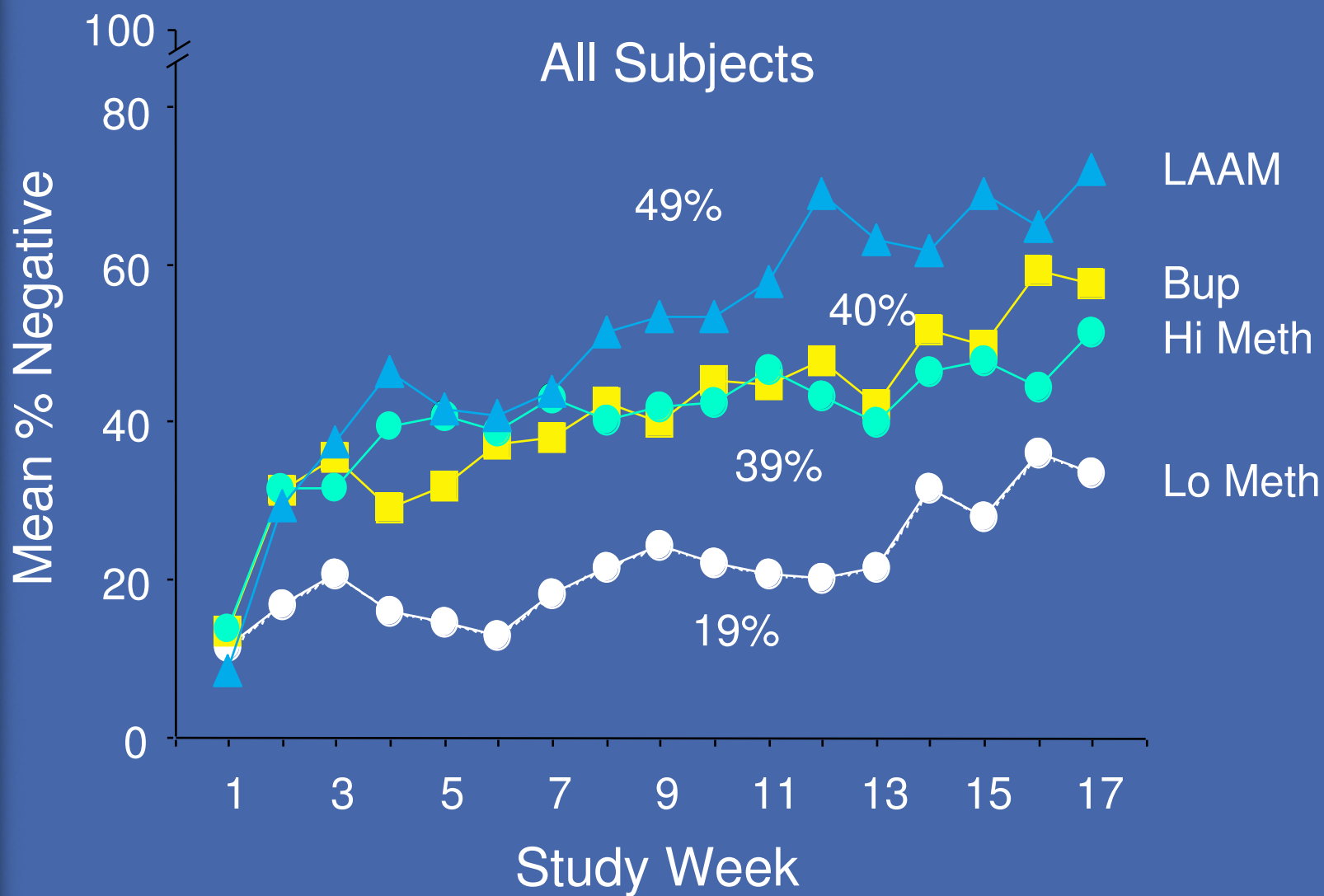
Intrinsic Activity



Buprenorphine, Methadone, LAAM: Treatment Retention



Buprenorphine, Methadone, LAAM: Opioid Urine Results



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.

YALE UNIVERSITY



SCHOOL OF
MEDICINE

Pharmacology in Primary Care: Cocaine = Disulfiram

YALE UNIVERSITY



SCHOOL OF
MEDICINE

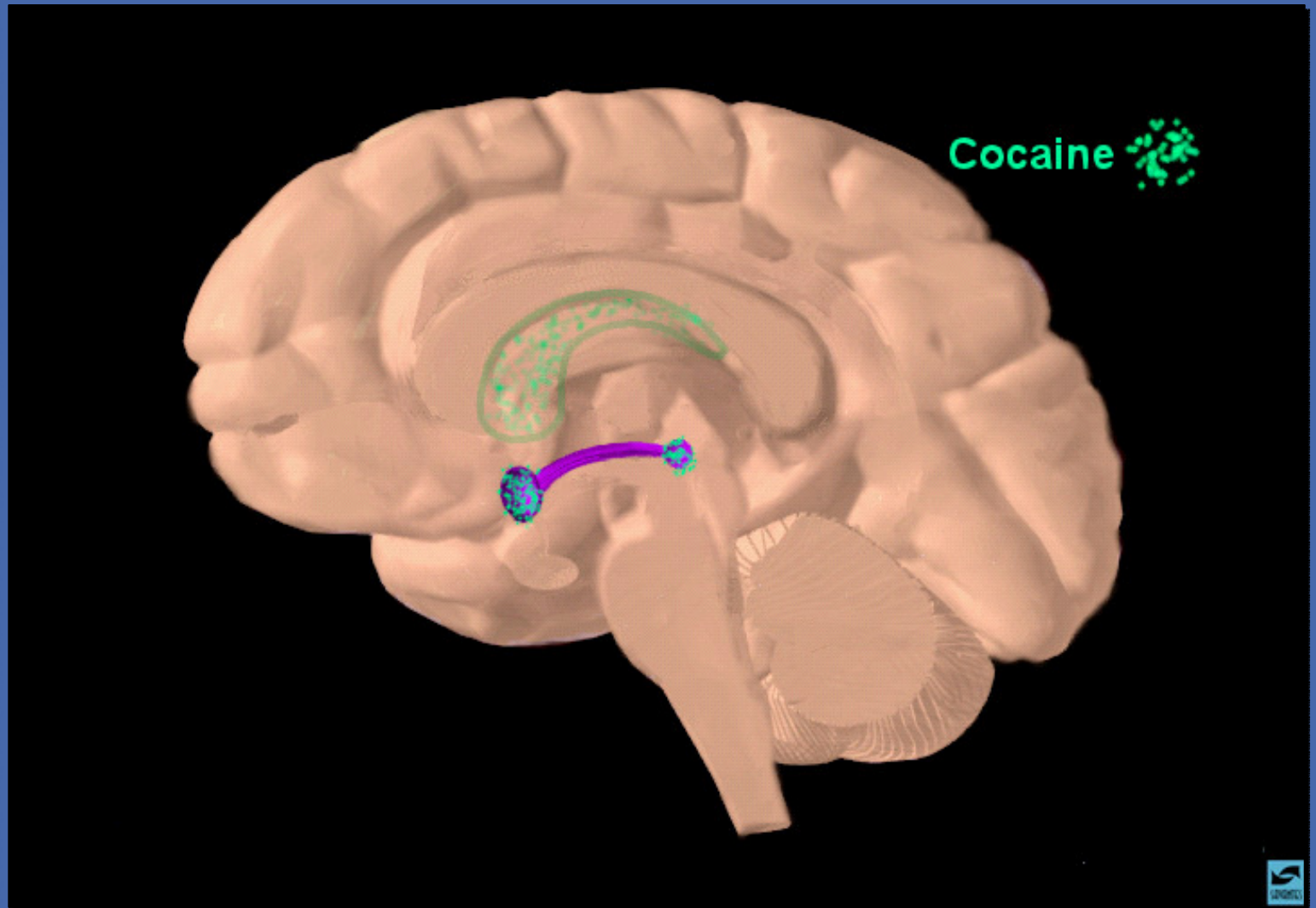
Cocaine

- 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.

YALE UNIVERSITY

SCHOOL OF
MEDICINE

Site of Cocaine Binding



YALE UNIVERSITY



SCHOOL OF
MEDICINE



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.

YALE UNIVERSITY

SCHOOL OF
MEDICINE

Pharmacology in Primary Care: Methamphetamine = Bupropriion

YALE UNIVERSITY



SCHOOL OF
MEDICINE

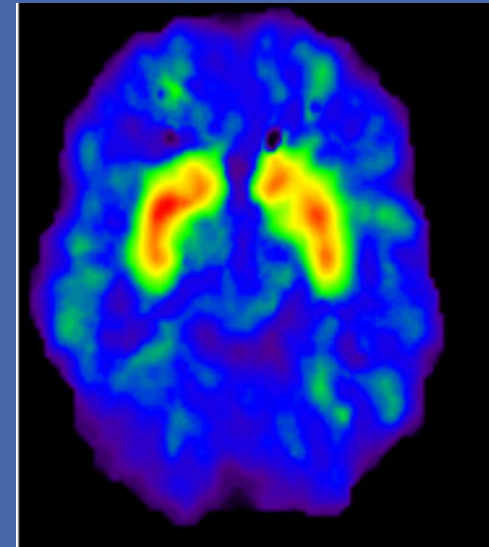
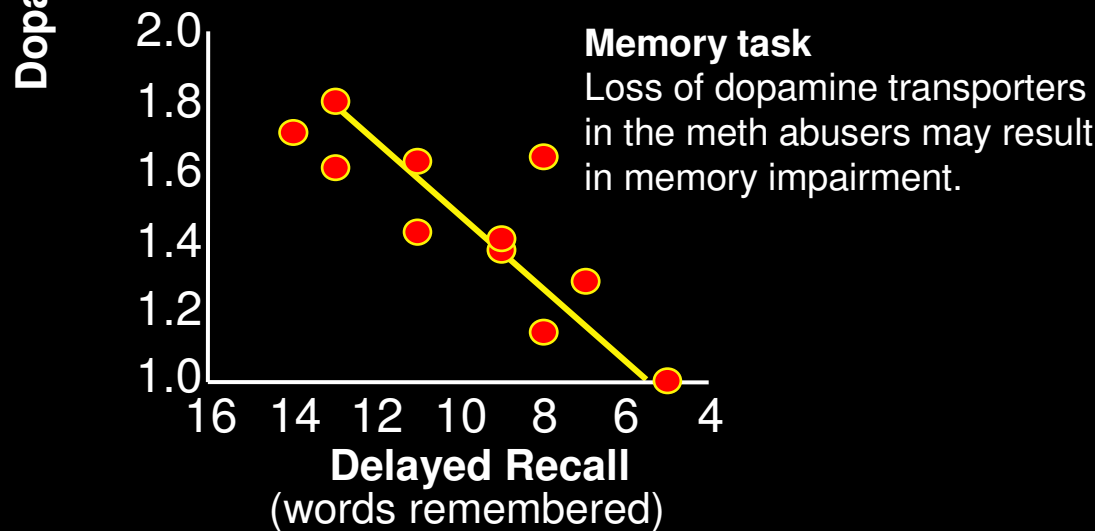
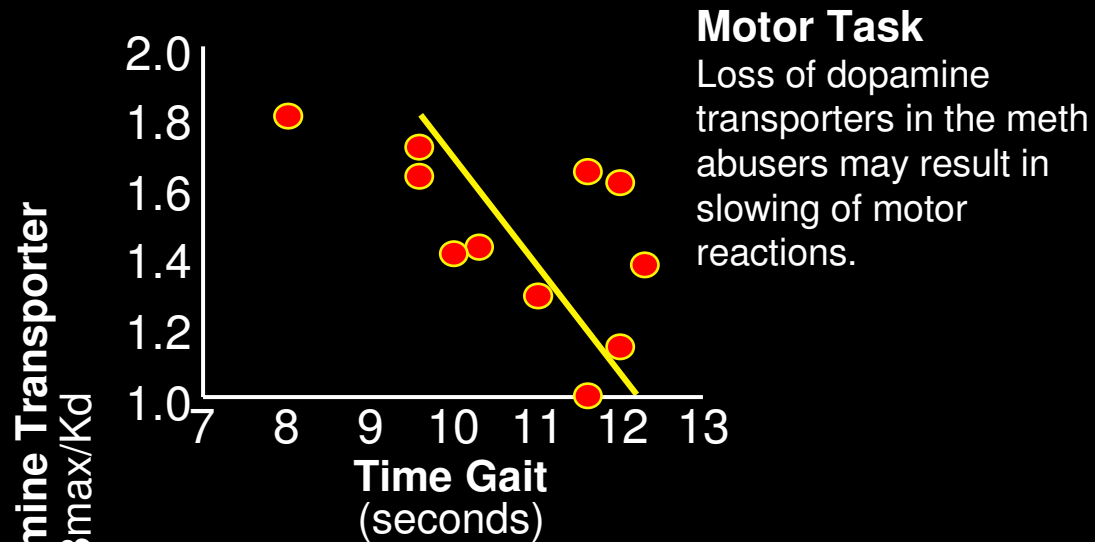
Methamphetamine (MA)

- 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..

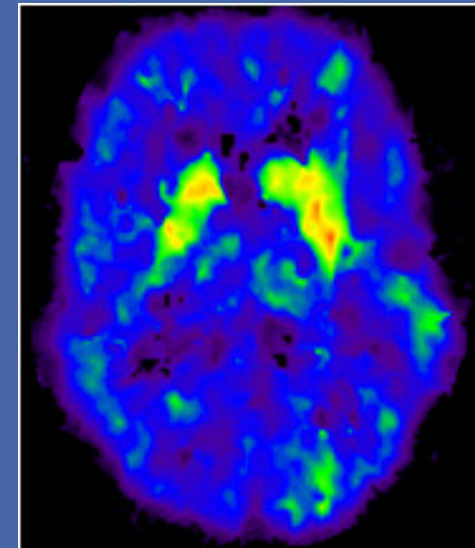
YALE UNIVERSITY

SCHOOL OF
MEDICINE

Dopamine Transporters in Methamphetamine Abusers



Normal Control



Methamphetamine Abuser

Treatments

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

YALE UNIVERSITY



SCHOOL OF
MEDICINE

Pharmacology in Primary Care: Alcohol = Naltrexone

YALE UNIVERSITY



SCHOOL OF
MEDICINE

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

YALE UNIVERSITY



SCHOOL OF
MEDICINE

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

YALE UNIVERSITY

SCHOOL OF
MEDICINE

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

YALE UNIVERSITY

SCHOOL OF
MEDICINE

Pharmacology in Primary Care: Nicotine = Nicotine

YALE UNIVERSITY



SCHOOL OF
MEDICINE

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!

YALE UNIVERSITY



SCHOOL OF
MEDICINE

Pharmacotherapy

- Nicotine replacement helps
- Bupropion 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 bupropion and nicotine in comparison trials – watch for suicidality and exacerbation of neuropsychiatric symptoms. Slow upward titration to minimize side effects.

YALE UNIVERSITY



SCHOOL OF
MEDICINE

Continuum of Interventions

Knowing the Pieces

YALE UNIVERSITY



SCHOOL OF
MEDICINE

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

YALE UNIVERSITY

SCHOOL OF
MEDICINE

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

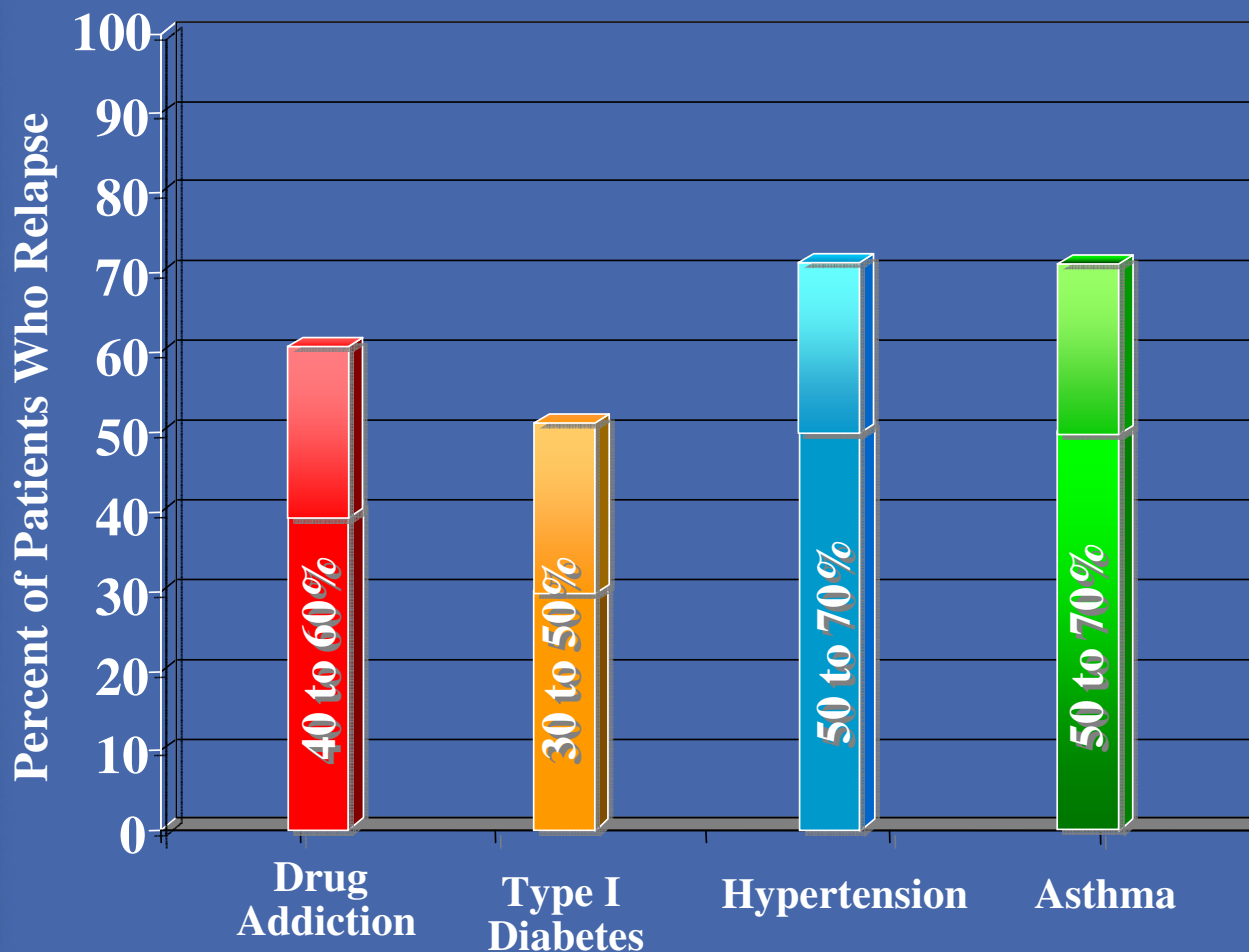
YALE UNIVERSITY



SCHOOL OF
MEDICINE

McLellan et al., JAMA, 2000.

Relapse Rates Are Similar for Drug Addiction & Other Chronic Illnesses



McLellan et al., JAMA, 2000.

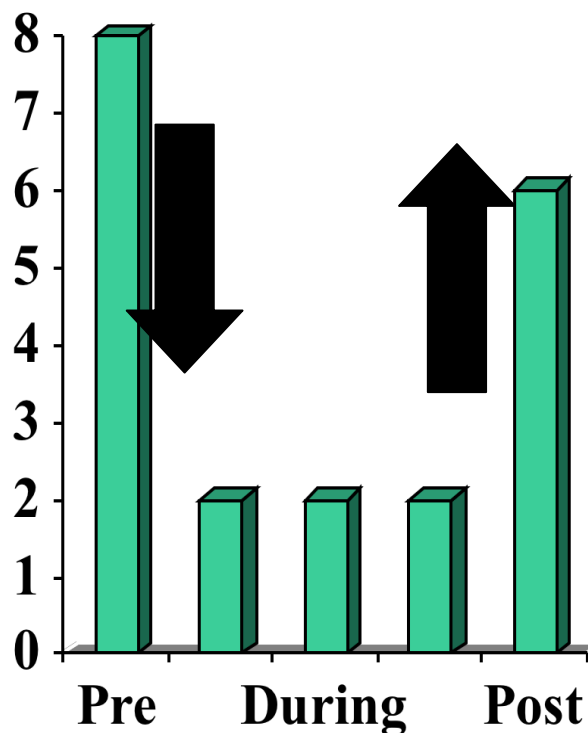
YALE UNIVERSITY



SCHOOL OF
MEDICINE

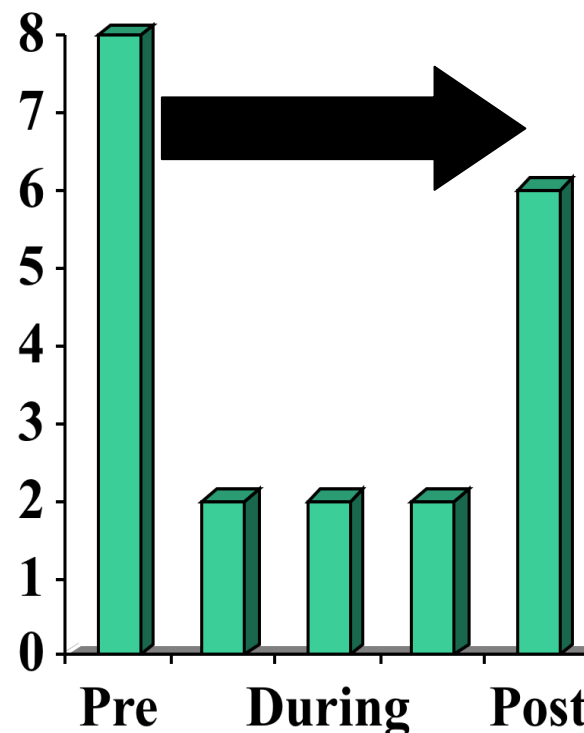
There is a right way and a wrong way to Measure the Outcome of Treating Chronic Illnesses like Addiction

Hypertension Tx



Stage of Tx

Addiction Tx

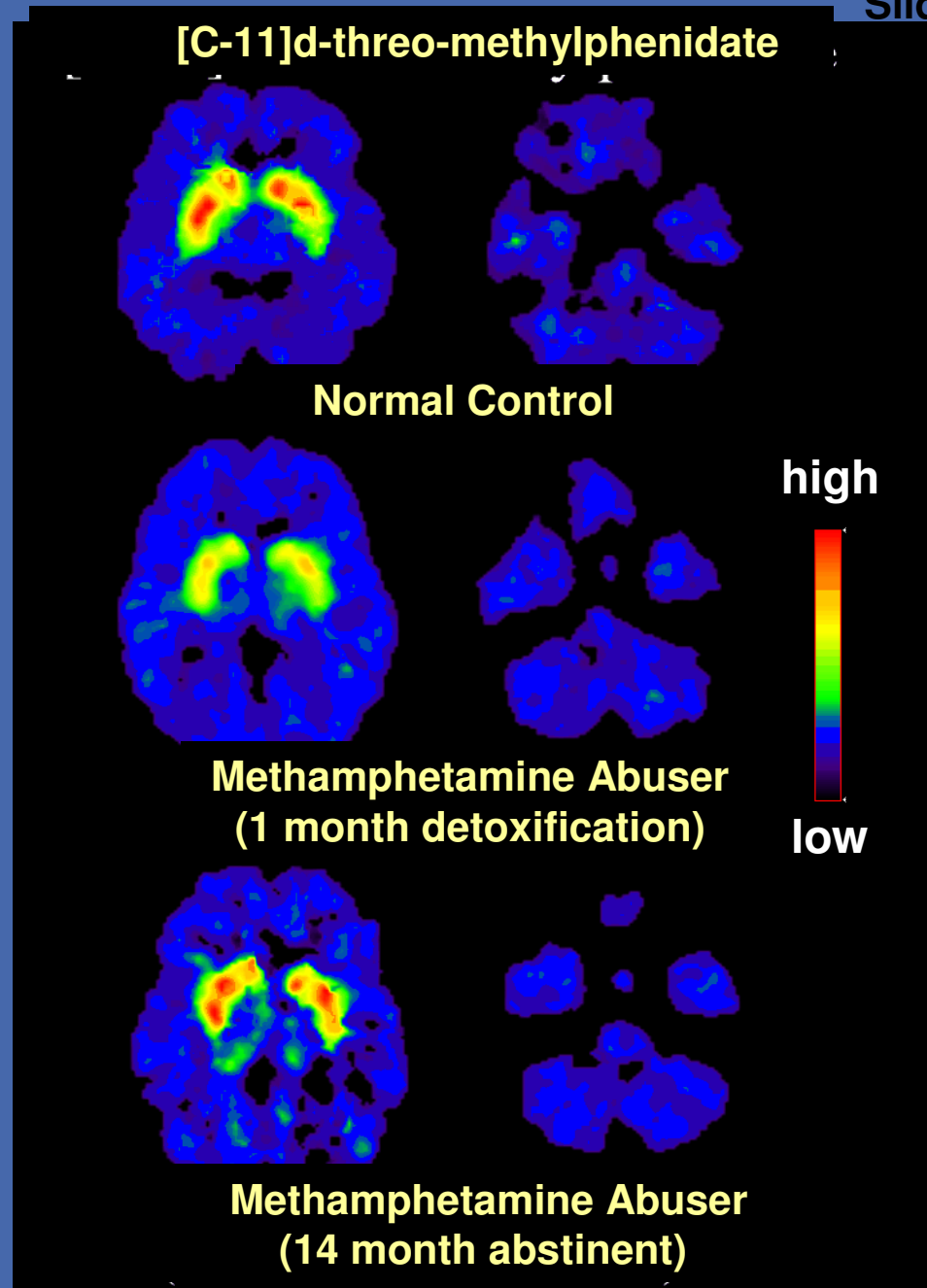


Stage of Tx



DAT Recovery
with prolonged
abstinence from
methamphetamine

There is hope!!



YALE UNIVERSITY



SCHOOL OF
MEDICINE

Questions?

Robert.bruce@yale.edu

YALE UNIVERSITY



SCHOOL OF
MEDICINE