

RECOVERY FROM ADDICTION

Neurobiology of Reward and Addiction

Norlien Foundation, 2010

Mark S. Gold, M.D.

**Donald R. Disney Eminent Scholar,
Distinguished Professor & Chairman
University of Florida, College of
Medicine, McKnight Brain Institute**



October 18, 2010 - October 22, 2010
Banff, Alberta



Norlien Foundation

Videos



- Baby Smoking Cigarettes
- SHS Fireman
- St Kitts Monkeys

Norlien Speech-Banff 2010



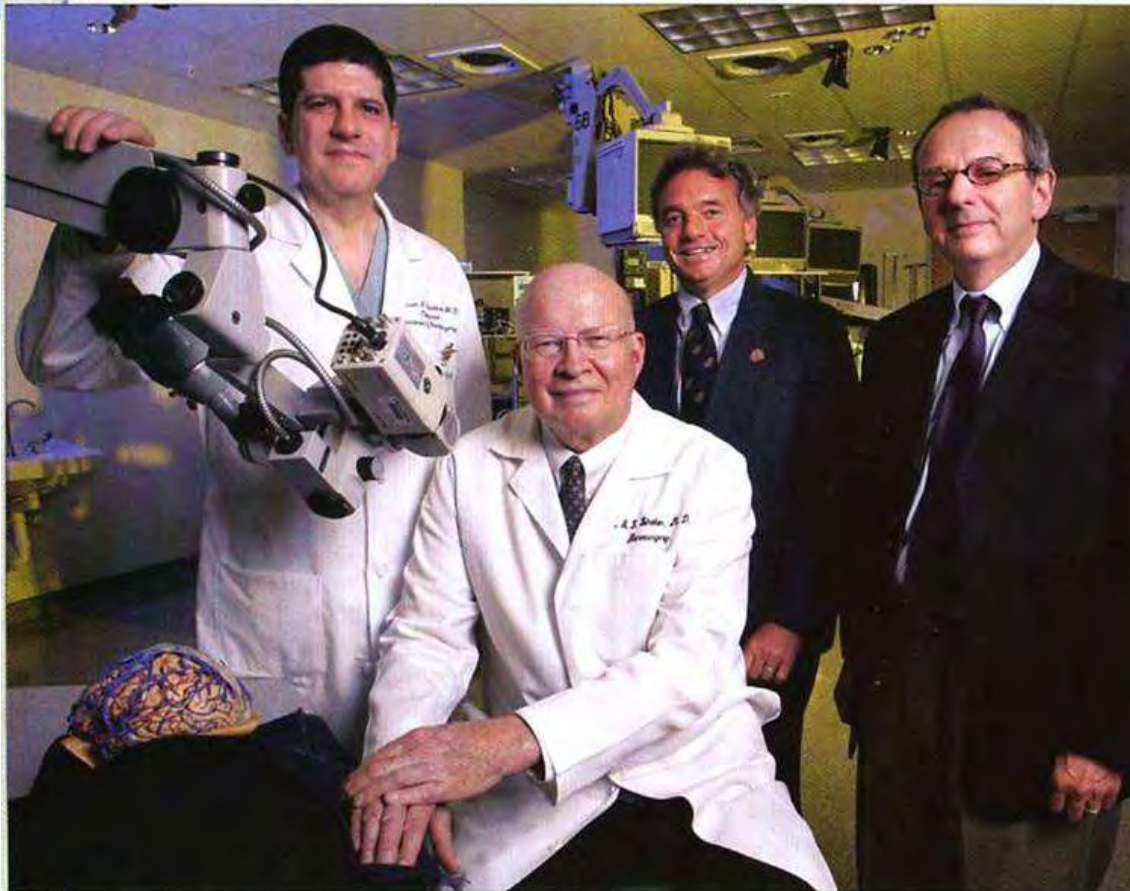
1. All periods are not created equally. First use at 50 is not very powerful brain-changer but the same exposure in utero or during childhood and adolescence is much more likely to cause changes in brain and behaviour .
2. Genes and genetics have been much hyped but have they helped us predict problem users or addicts ? Have identical twin studies or genes changed treatment ?
3. Meso-limbic neuroanatomy exists and has been studied in rats to humans and have helped us understand how use may become dependence, what withdrawal events might result from discontinuation, and how chronicity might result from repeated use. What is the difference between a rat and a human?
4. Drug, sex, food cravings are not destiny
5. If drugs, food, and sex work via the same neuroanatomy, addiction treatment should include treatment for sexual compulsivities and also for overeating.



I Have No Commercial Ties to Disclose

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Opening Founders McKnight Brain Institute, 1995



ROB C. WITZEL

FROM LEFT, PROFESSOR AND CHAIR OF NEUROSURGERY WILLIAM FRIEDMAN, PROFESSOR ALBERT RHOTON, PROFESSOR MARK GOLD AND EXECUTIVE DIRECTOR DENNIS STEINDLER.

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Current Research: 2010



- **Martin: Kabul and SH Opiates**
- **Bruijnzeel: ICSS and Drug Self Administration; SHS; Withdrawal from Fentanyl**
- **Goldberger: Caffeine in Decaffeinated Coffee and Withdrawal**
- **Lui: fMRI....Global Health, China, "Golden Arches"; delay, s/p surgery, provoked craving**
- **Cendan...Morbid Obesity & fMRI; Surgeryfor Obesity**
- **Kobeissey : Drugs and TBI proteomics**
- **Wang : Proteomics....MDMA (hippocampus), Methamphetamine (cortex)**
- **Baxter: Planeria , Neurogenesis & Club Drugs**
- **Melker: Naltrexone and Medications in Breath; Adherence**
- **Morey: Second hand Propofol and Fentanyl Levels in Anesthesiologist's Hair & Masks**
- **Rivenbark- PRN/State of Florida; 5year urine test confirmed outcomes for treatment ; Crack Doctors**
- **DuPont & McLellan- 50 State Analysis of MD Treatment Programs**
- **Carnes- Sexual Compulsivity; fMRI and co-morbidity**
- **Merlo: Overeating protection against drugs; Teen Surveys; Rebound hyperphagia and weight gain with abstinence**
- **Goldberger: Drug deaths & Accidents**
- **Noni Graham: Cocaine deaths; Methadone Deaths;**
- **Dennis- Nano-technology, Operating Room Second Hand Exposure; Air Testing**
- **Barry Jacobs-Stem Cell Repair of Drug-Related Cell Damage**
- **Avena: Food Addiction**
- **Hoebel : Sugar Binges as an Addiciton**
- **Sumner- SHS and Cardiac Cell Injury**
- **Baron: Performance Enhancing Drugs and Medications**
- **Jean Lud Cadet & Henry Baker : Drugs of abuse & genomics**

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Some Examples of Our Recent Work



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The Addictive Potential of Decaffeinated Coffee

Brian S. Fuehrlein, Rachel R. McCusker, Bruce A. Goldberger, Mark S. Gold

Departments of Anesthesiology, and Psychiatry, University of Florida College of Medicine, Gainesville, FL, United States

ABSTRACT

The Addictive Potential of Decaffeinated Coffee

Brian S. Fuehrlein, Rachel R. McCusker, Bruce A. Goldberger, Mark S. Gold
Department of Anesthesiology and Psychiatry, University of Florida College of Medicine,
Gainesville, Florida 32610-2362

Introduction: Caffeine is the most extensively consumed psychoactive in the world. Its pharmacologic effects include diuresis, cardiac vasoconstriction, CNS stimulation, gastric and mucosal vasodilation, and elevation of free fatty acids and glucose. Caffeine stimulates movement and arousal, in part, by its blockade of adenosine triphosphate (ATP) and adenosine triphosphate (ATP)ase, in part, by its blockade of adenosine triphosphate (ATP) and adenosine triphosphate (ATP)ase, in part, by its blockade of adenosine triphosphate (ATP) and adenosine triphosphate (ATP)ase.

Methods: Twenty-two decaffeinated coffee and espresso samples were purchased and analyzed for caffeine content utilizing gas chromatographic techniques. Results were listed in Table 1.

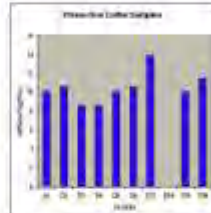
Results: Only one of the decaffeinated coffee samples was regular decaffeinated. The remaining three had a mean of 11.5 mg caffeine per 16-oz cup, 23.65 mg per 16-oz serving. The espresso samples had a mean of 5.4 mg and a range of 1.8 mg to 11.8 mg per 1-oz shot.

Conclusions: Caffeine-free samples of decaffeinated decaf are generally not caffeine-free. Caffeine-free samples range from 1 mg of caffeine to 23 mg of caffeine per 16-oz serving. Additionally, decaffeinated decaf is not a safe substitute for regular coffee because it contains caffeine. Decaffeinated decaf is not a safe substitute for regular coffee because it contains caffeine. Decaffeinated decaf is not a safe substitute for regular coffee because it contains caffeine.

METHODS

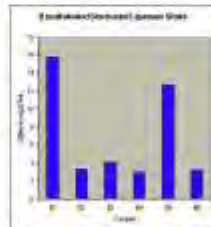
- Twenty-two decaffeinated coffee beverages were purchased and evaluated for caffeine content.
- In phase one of the study, six regular decaffeinated coffee beverages (D1-D6) were purchased from various coffee shops in Severna Park and Bethesda, MD.
- In addition, four regular decaffeinated beverages (D13-D16) were purchased from various restaurants in Gainesville, FL.
- In phase two of the study, six espresso decaffeinated coffee beverages (E1-E6) and six regular decaffeinated coffee beverages (D7-D12) were purchased from the same Starbucks® coffee shop in Gainesville, FL, on Day 1 and Day 2, respectively.
- Caffeine was quantitated in the coffee beverages utilizing a gas chromatographic technique previously reported.

RESULTS



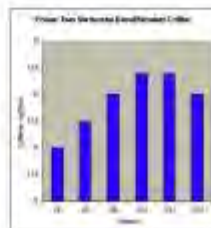
Sample	Name	Brand	Caffeine Content (mg/16oz)
D1	Starbucks®	Specialty	11.5
D2	Starbucks®	Specialty	11.5
D3	Starbucks®	Specialty	11.5
D4	Starbucks®	Specialty	11.5
D5	Starbucks®	Specialty	11.5
D6	Starbucks®	Specialty	11.5

Figure 1. Table 1. Regular Coffee Samples.



Sample	Caffeine Content (mg/1oz)
E1	5.4
E2	1.8
E3	1.8
E4	1.8
E5	11.8
E6	11.8

Figure 2. Table 2. Decaffeinated Espresso Samples.



Sample	Caffeine Content (mg/16oz)
D13	11.5
D14	11.5
D15	11.5
D16	11.5

Figure 3. Table 3. Other Than Starbucks® Decaffeinated Coffee Samples.

CONCLUSIONS

- Clinicians and patients should be aware that decaffeinated coffee frequently contains caffeine. Ingestion of multiple servings of decaffeinated beverages could result in doses of caffeine comparable to one cup of regular coffee or more.
- Since low doses of caffeine are present in decaffeinated coffee as was determined in the present study, the ingestion of these beverages may possibly demonstrate physical dependence. Physical dependence refers to behavioral and physiological changes that become evident when drug administration is discontinued after repeated exposure to a particular drug.
- People waiting in long lines to purchase decaffeinated coffee may be addicted to the caffeine, and not only desiring the taste.



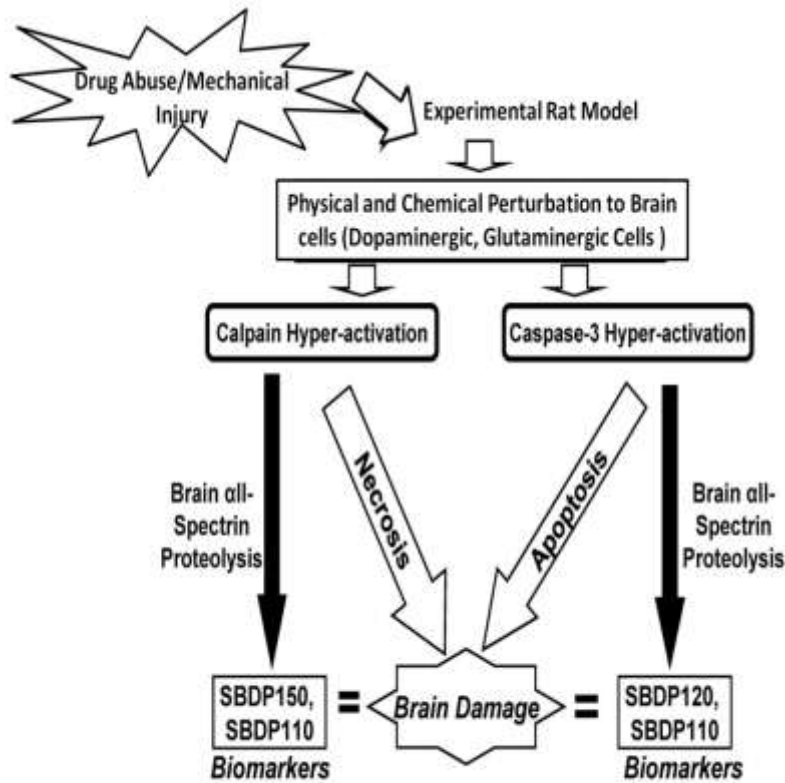
REFERENCES

1. McCusker RR, Goldberger BA, Cost EJ. Caffeine Content of Specialty Coffees. J Anal Toxicol 2003; 26:520-3.
2. Brady JV, Lottas SE. National Institute on Drug Abuse. Research Monograph Series 52. The Committee on Problems of Drug Dependence, Inc. Testing Drugs for Physical Dependence Potential and Abuse Liability, 1964.
3. Bonzetti MA. Methods of Assessing the Reinforcing Properties of Abused Drugs. Edited by Bonzetti MA, New York, Springer-Verlag, 1967, pp 635-638.

Methamphetamine- and Trauma-Induced Brain Injuries: Comparative Cellular and Molecular Neurobiological Substrates

Mark S. Gold, Firas H. Kobeissy, Kevin K.W. Wang, Lisa J. Merlo, Adriaan W. Bruijnzeel, Irina N. Krasnova, and Jean Lud Cadet

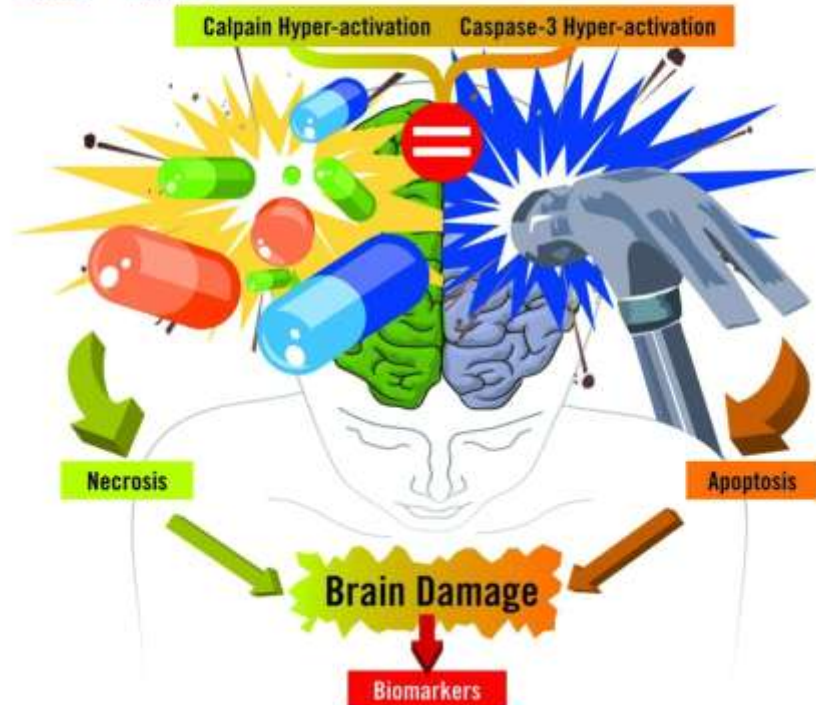
July Issue 2009



SBDP: Spectrin Break Down Product

Biological Psychiatry

Volume Number



The Difference Between Marijuana and Alcohol

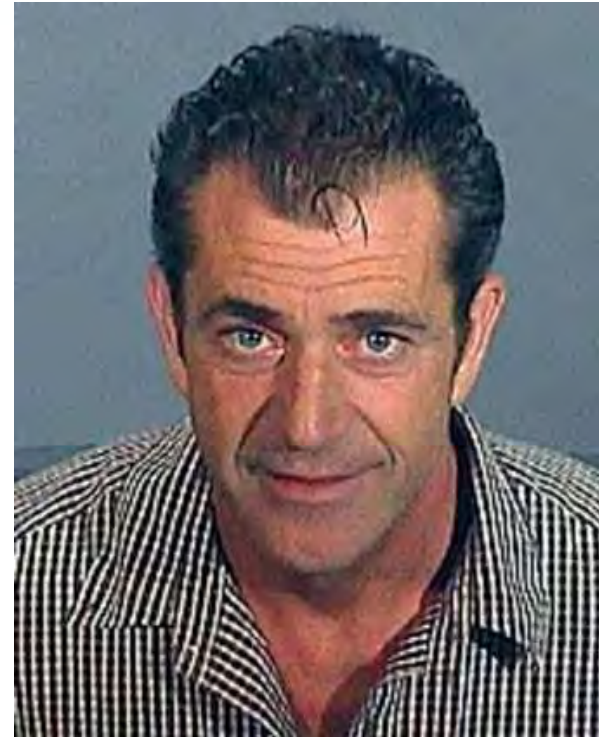


- When Willie Nelson was pulled over, he had only nice things to say about Jewish people
- Alcohol abusers go through yellow lights and MJ users wait for a while to go after a green light

Mel Gibson



- "Everything's f-----." "My life is f-----." — "I'm not going to get into your car." You motherf----- . . . I'm going to f--- you. You're going to regret you ever did this to me." — "I own Malibu and will spend all my money to get even with you." "F----- Jews." — "The Jews are responsible for all the wars in the world." "Are you a Jew?" What the f--- do you think you're doing?" "What do you think you're looking at, sugar tits?"



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Why So Many MD Addicts



- Access?
- Early Onset?
- Poor and traumatized
- Many Problems At Work
- Equal to Lawyers in Alcoholism and Abuse of Alcohol

Maybe It is that M.D.s like Drugs Themselves?



Second Hand Opioids: Addiction and Relapse

—So, How do you like working as an Anesthesiologist ?

Drugs Are Taken Voluntarily & As a Result of Environmental Exposure



"I'm starting to really like the smell of cocaine."

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Source of Second Hand Exposure



- Air
- Exposed Skin
- Hands
- Head-Hair

Study of SHS and MD addicts



- Renewed interest in clean air and water and effects of both , especially on the unborn and newly born

Want to Live Longer? Cut the Pollution



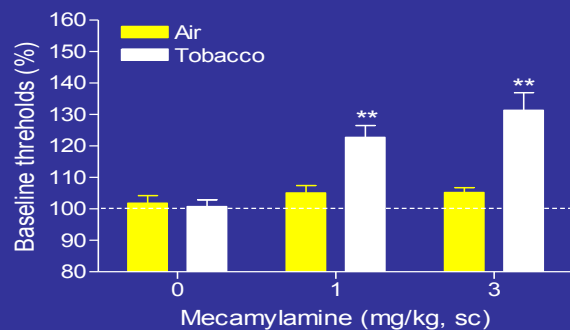
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Dependence from 2nd hand Smoke

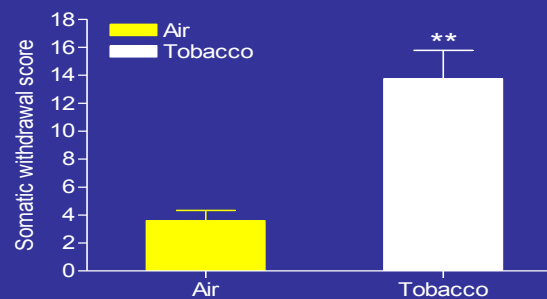


Passive exposure to tobacco smoke leads to nicotine dependence

Brain reward thresholds



Somatic signs



Bruijnzeel et al., in preparation

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Treating drug-addicted doctors is good medicine Filed under [Health](#), [Research](#) on Tuesday, February 24, 2009.



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- GAINESVILLE, Fla. — Doctors who become addicted to alcohol and other drugs can be treated successfully and returned to medical practice with the help of special programs that couple referral to treatment and monitoring with rapid responses to noncompliance, University of Florida researchers report.
- The study is the first national-level analysis of such Physician Health Programs, and confirms they are effective alternatives to simply punishing drug-addicted doctors. —“Treatment works,” said Dr. Mark Gold, psychiatry chairman at the UF College of Medicine and the McKnight Brain Institute. —“It has been shown now to be safe and effective and cost-effective.”
- But it’s not just for doctors, said Gold, who with UF colleagues pioneered evaluation and treatment for drug-addicted doctors. —“It should be a model for treatment of anyone with these diagnoses.”
- In general, rates of illicit drug use are lower among physicians than the general public, but rates of prescription misuse are five times higher among physicians, according to a 2008 review Gold co-authored in the Harvard Review of Psychiatry.
- Gold and others conclude that drug problems in doctors are related to medical specialties that put them in regular contact with drugs of addiction, ease of access to drugs, stress and lack of early detection. Addiction also appears linked to physician-suicide.
- Physician Health Programs aim to save the lives and careers of addicted physicians, and to protect the public by addressing substance use among doctors. They are also an effective way to remove noncompliant doctors from the practice of medicine.
- Doctors in the programs had to abstain from alcohol or other drugs, and were tested frequently at random for five or more years. If tests revealed they had returned to substance abuse, swift action was taken — doctors were reported to the medical board, which could lead to loss of their licenses.
- One-fifth of doctors were reported to their board during treatment and monitoring — some more than once with multiple disciplinary actions taken.
- But 78 percent of doctors in the programs had no positive drug tests during five years of intensive monitoring. And five to seven years after starting treatment, 72 percent were actively practicing medicine, without drug abuse or malpractice.
- Eighteen percent left medical practice, while others relapsed into drug use. Three percent of those who didn’t complete their programs had substance-related deaths or committed suicide. Although the programs employed a variety of approaches, the researchers found that success was not related to specific therapists or modes of therapy, but rather to the long-term nature of the treatment.
- Still, there are some “essential ingredients” that successful programs have in common, Gold said. Those include treatment
- extended over years — not weeks or months — and unambiguous success markers such as urine testing and
- return to work and normal family activities.

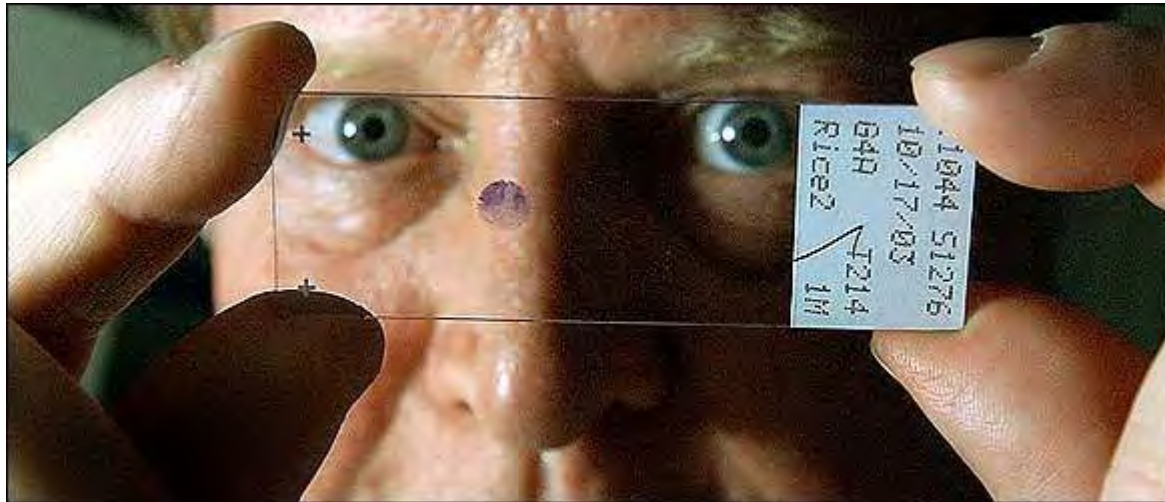
Relapse Rate



Specialty	Relapse Rate
All specialties	6

Anesthesiology	14.6

Nanotechnology



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Dr Gold's SH maternal-child research was supported by the
U.S. Department of State, Bureau for International
Narcotics and Law Enforcement.

Conflict of Interest

The authors have no conflicts of interest to disclose.



State Department Study Finds Alarming Rates of Opium Products in Afghan Children



BUREAU OF INTERNATIONAL NARCOTICS AND LAW ENFORCEMENT AFFAIRS

Fact Sheet

April 22, 2010

<http://www.state.gov/p/inl/rls/fs/140668.htm>

— . . The U.S. State Department contracted with a team of scientists in 2008 led by David M. Martin, PhD, Scientific Team Coordinator. Dr. Martin’s team includes two of the world’s leading experts on drug abuse, Mark S. Gold, MD and Bruce A. Goldberger PhD. . . ”

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Opium Den



Results



- We tested 30 homes, 20 smoking homes and 10 controls; each had five surface samples completed for a total of 150 surface samples
- Of the 20 smoking homes 19 had some positive surface test....95%. All the control homes were negative.
- Of the 20 smoking homes we obtained 13 air samples....12 were positive....92%.
- Of the 30 homes we obtained 69 hair samples from residents ranging in age from 50 years old to 9 months.
- Of the 20 smoking homes all but one home had at least one of the resident's hair positive for opiates
- We found not only opium but heroin in the hair, on surfaces and in the air at remarkable concentrations
- We also found synthetic opiates not routinely seen in hair samples.



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June 17, 2009

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WORLD

Drug Addiction, And Misery, Increase In Afghanistan

by Soraya Sarhaddi Nelson

Listen Now [5 min 40 sec] + add to playlist | download

First in a two-part series.



Hidden World Of Female Addicts

More In The Series

April 17, 2009
Treatment Lacking For Afghanistan's Addicts



Enlarge Holly Pickett for NPR

Surrounded by her children, Kari...

Morning Edition, April 16, 2009 - A growing number of Afghans — including children — are escaping the pain of war and poverty by using opium or heroin, for as little as a dollar a day.

A United Nations survey begun this month is widely expected to show that at least 1 in 12 people in Afghanistan abuses drugs — double the number in the last survey four years ago.

Experts say that the alarming trend is not being addressed by the Afghan government and its international partners, even though most officials acknowledge that the drug scourge threatens lasting stability in Afghanistan.

Many of the addicts, especially the women, feed their habit in secret, inside walled, mud-floor family compounds.



- Obama OKs Equal Benefits For Some Federal Workers' Gay Partners 6:45 PM ET
- NPR-Themed Wedding Gets An NPR Assist 6:19 PM ET

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Environmental Hypothesis



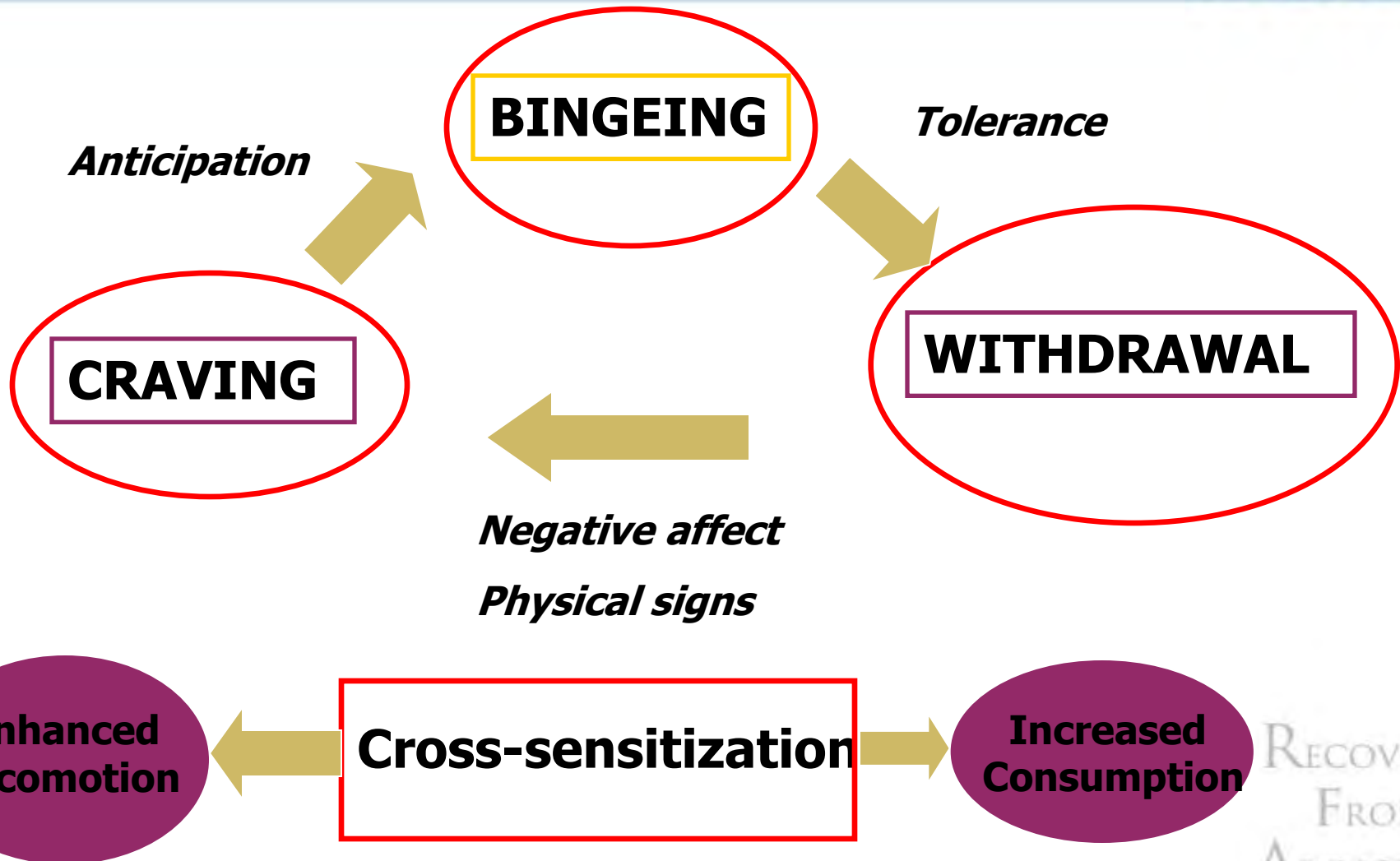
"We've got to pause and ask ourselves: How much clean air do we need?" --Lee Iacocca



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What is an “addiction”?

Look at criteria used to study
substance dependence

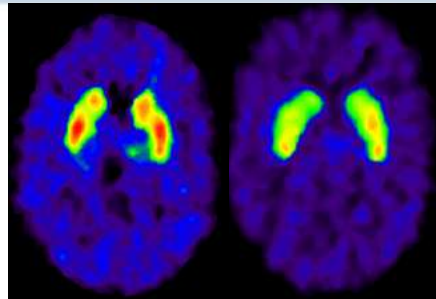




Dopamine D2 images of Drug Addiction



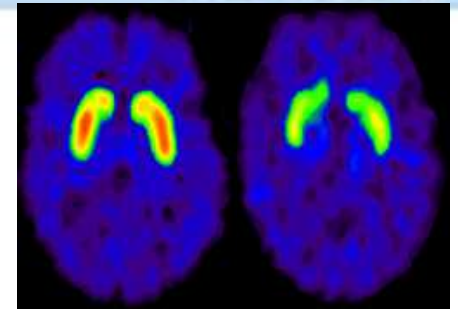
Cocaine



Control Abuser



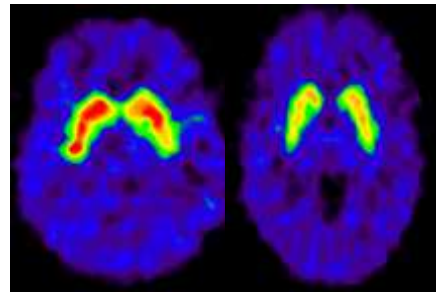
Heroin



Control Abuser



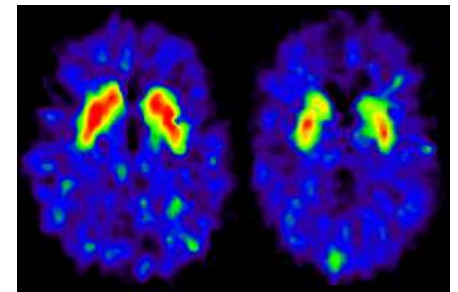
METH



Control Abuser



Alcohol



Control Abuser

Drug abusers have low brain dopamine activity indicating an under-stimulated reward system

[¹¹C]raclopride

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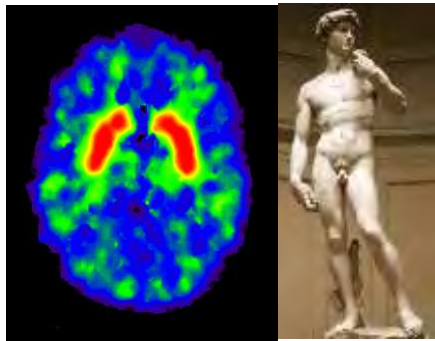
Decreased dopamine D2 receptors in obese human, monkey and rodent



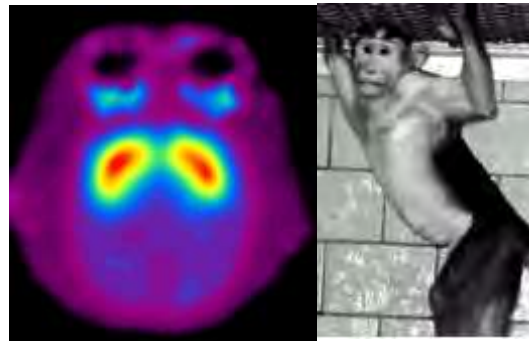
Human

Bonnet macaques

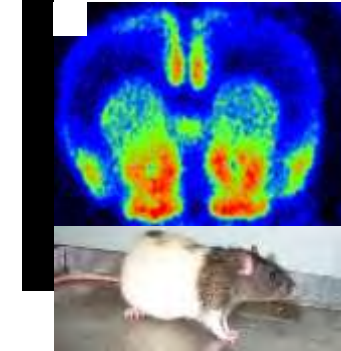
Zucker rat



BMI = 23



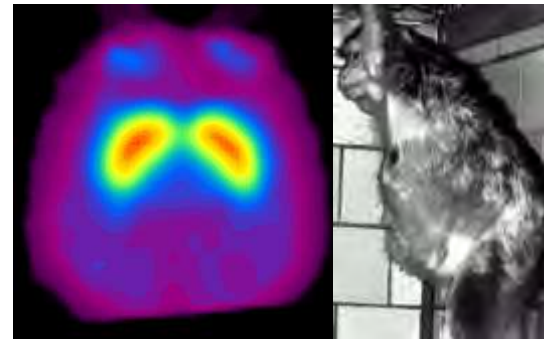
BMI = 23



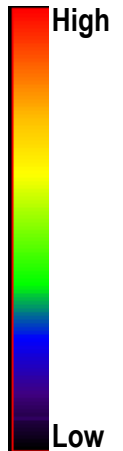
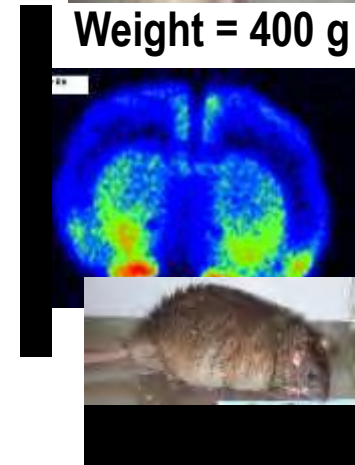
Weight = 400 g



BMI = 50



BMI = 42



PET
[¹¹C]raclopride

ARG
[³H]Spiperone

Thanos et al, Synapse 2008

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Drug Use Trends



- In 1962, only 2% of the U.S. population over the age of 12 years had tried an illegal drug
- By the mid 1980s, nearly 50% of the population had experimented with an illegal drug

National Survey Drug Use and Health (NSDUH) 2008. Available at <https://nsduhweb.rti.org>

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Incoming College Freshman Class

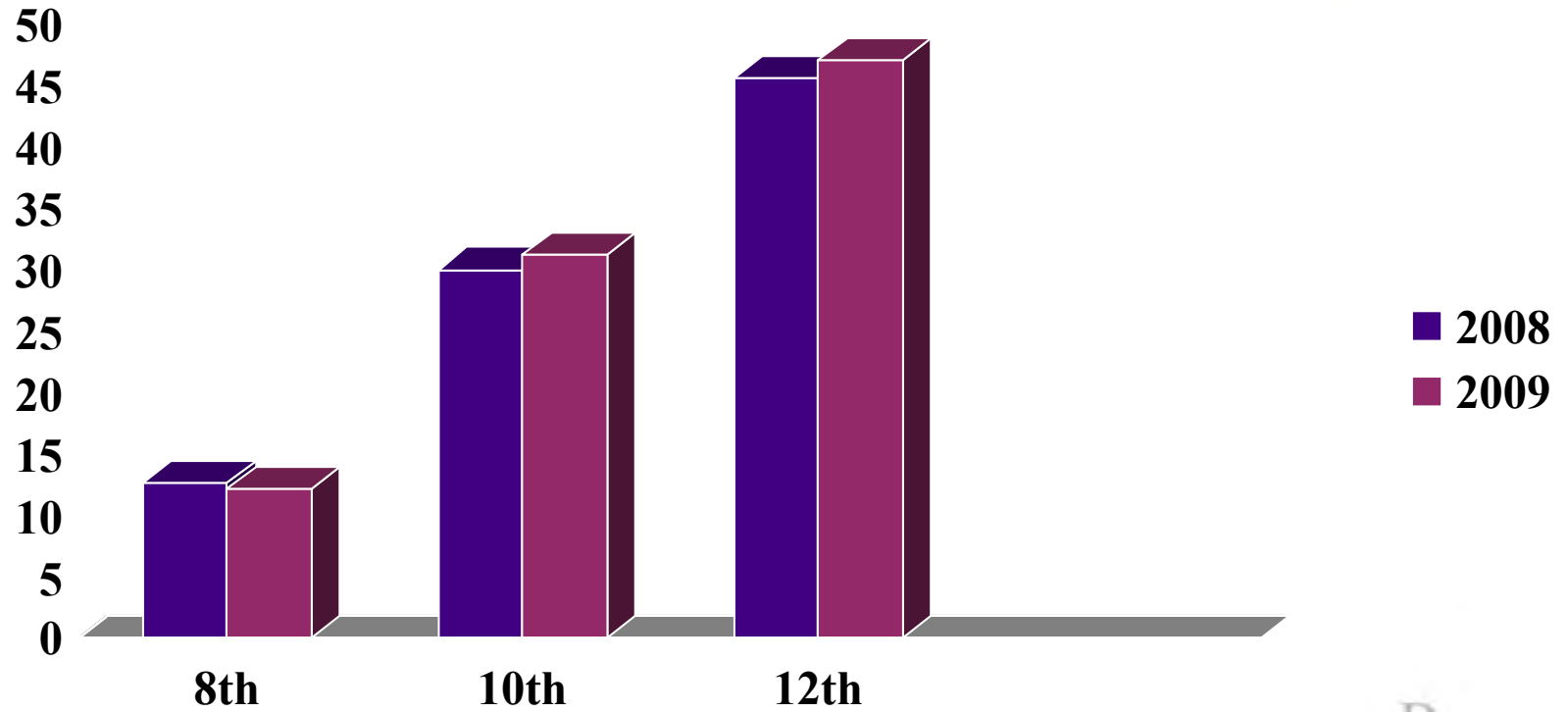


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High School Survey



Been Drunk in the Past Year



Bud

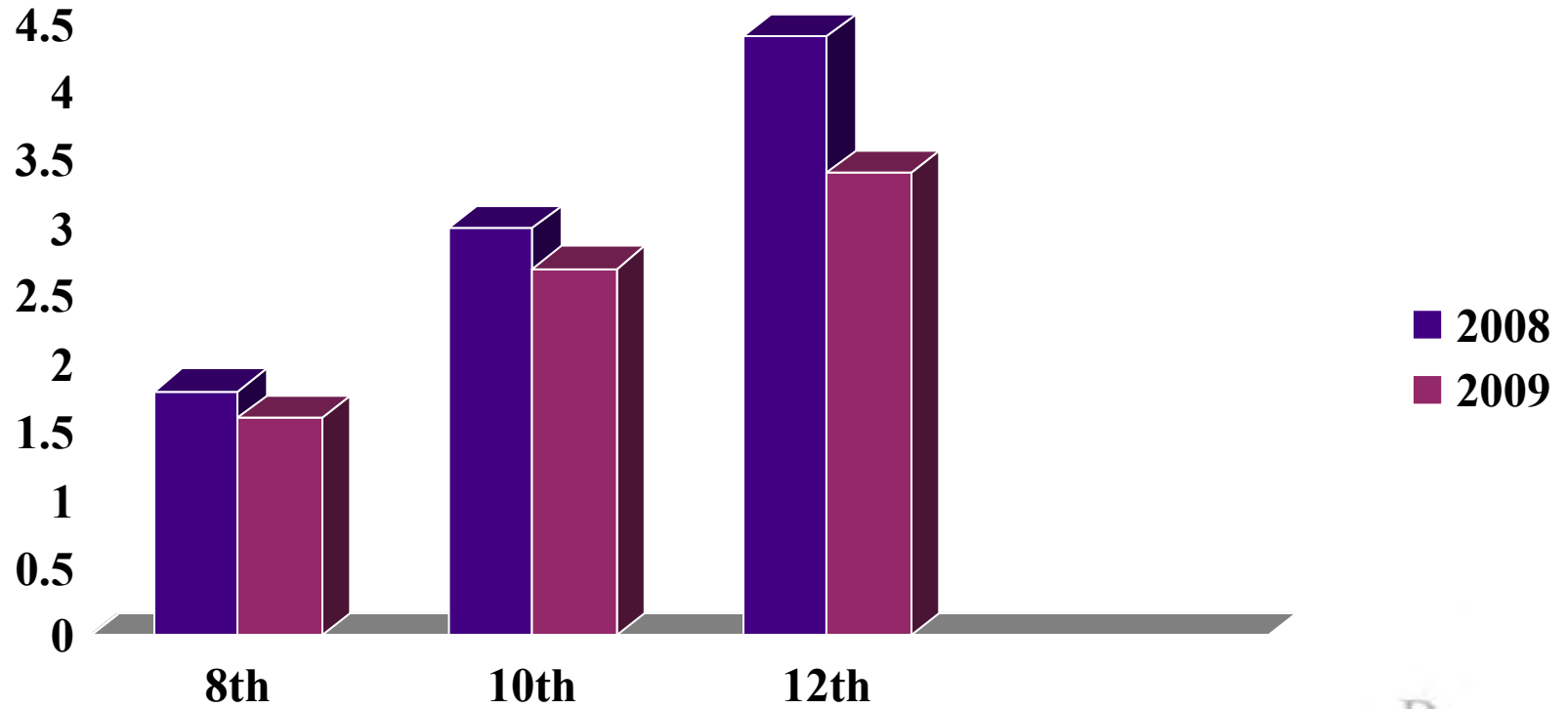


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Cocaine Use in the Past Year



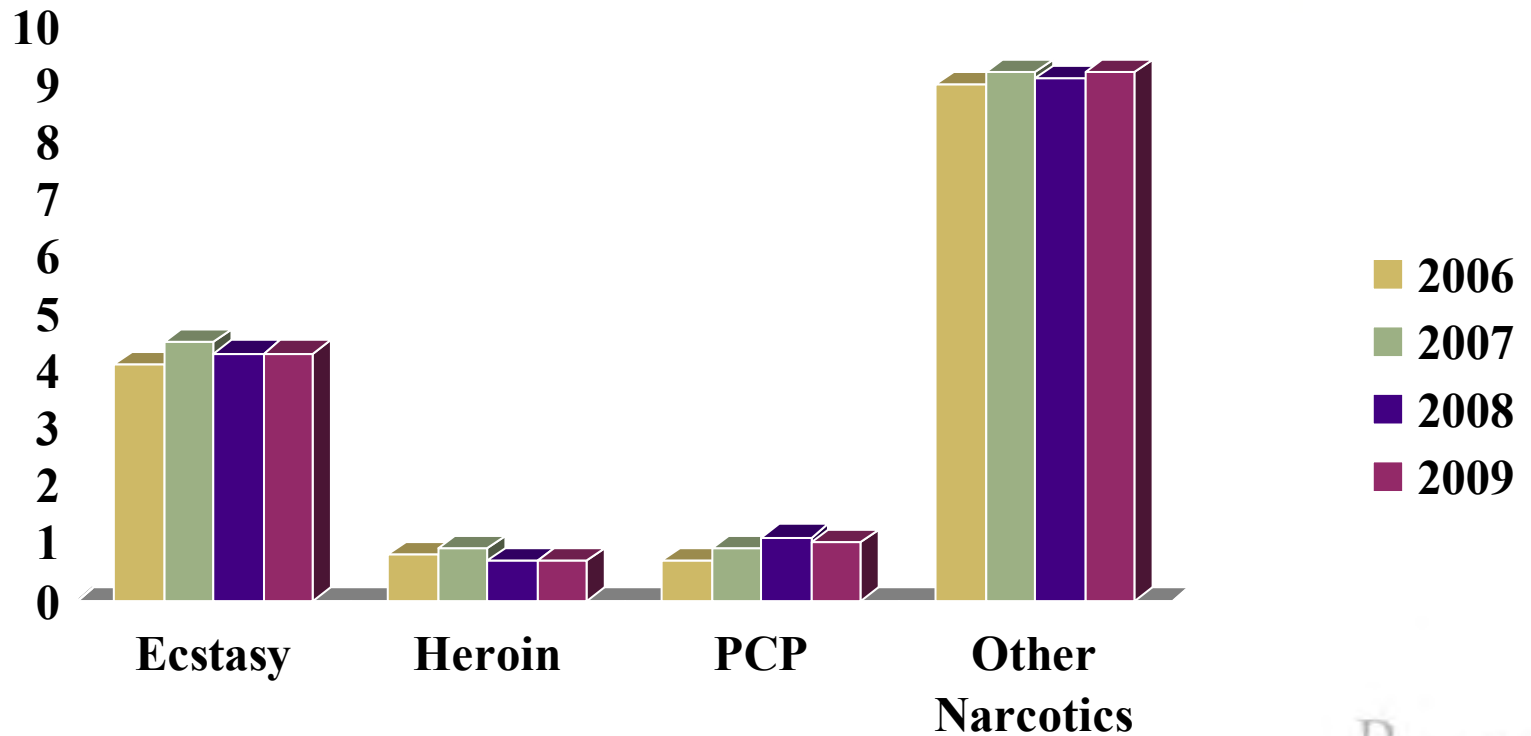
UM NIDA Monitoring the Future Study

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High School Survey



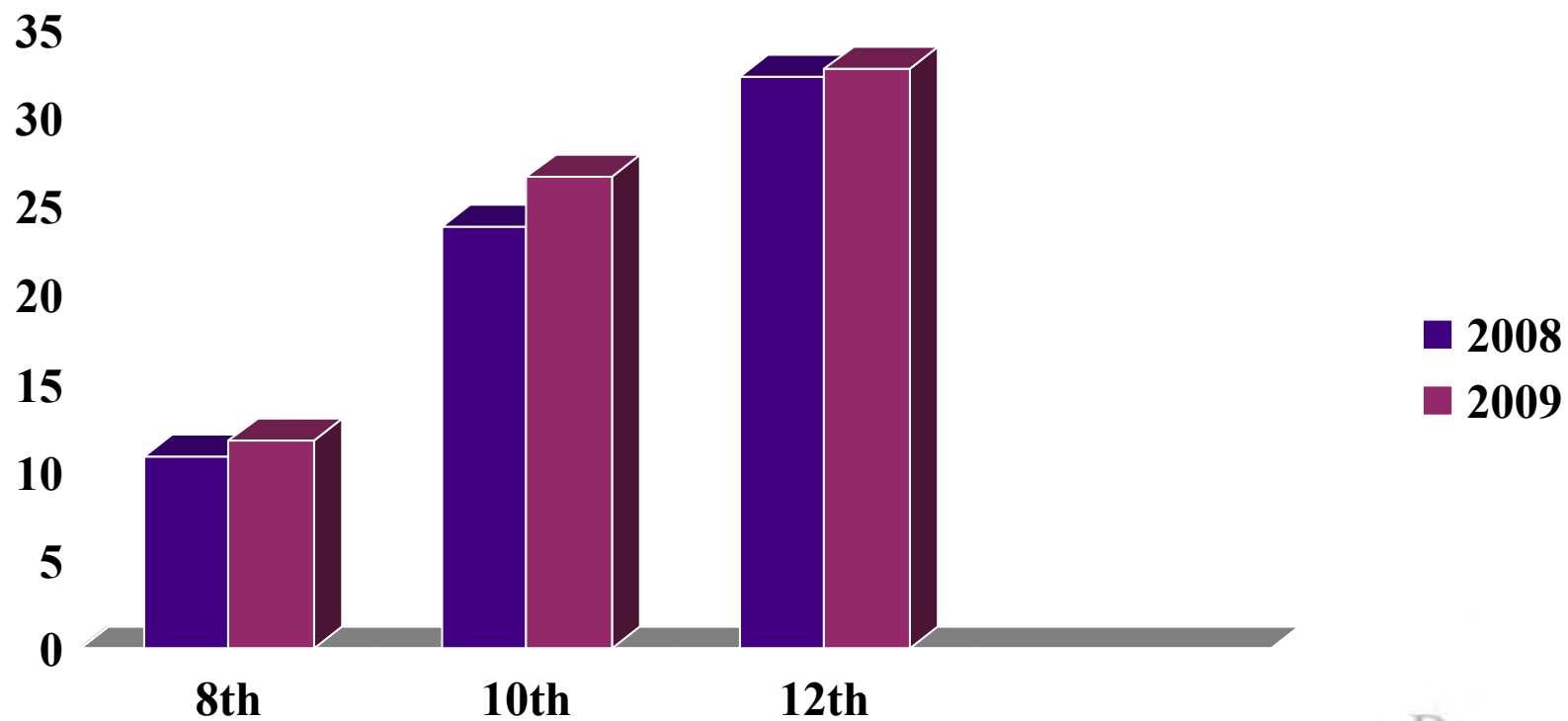
Used in the Past Year by 12th Graders



High School Survey



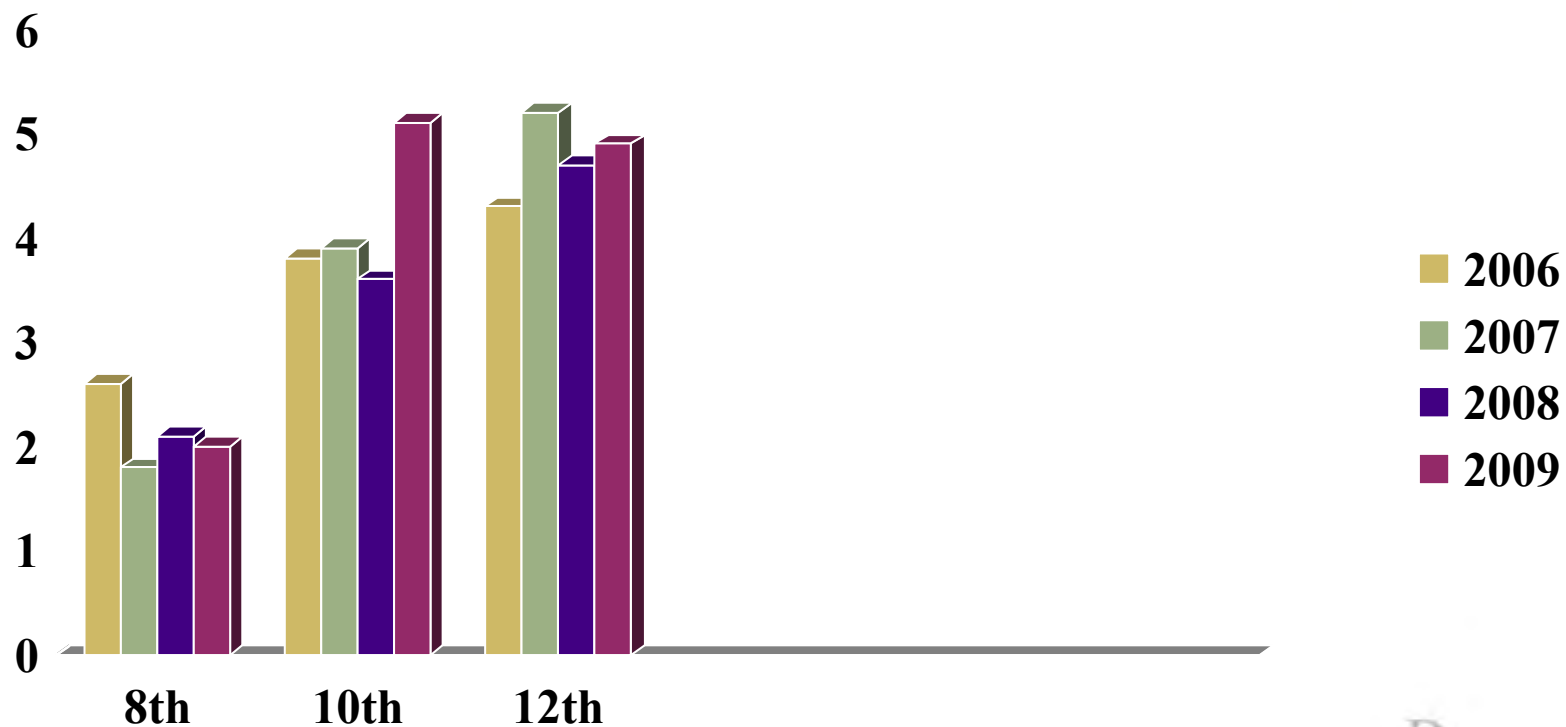
Marijuana Use



High School Survey



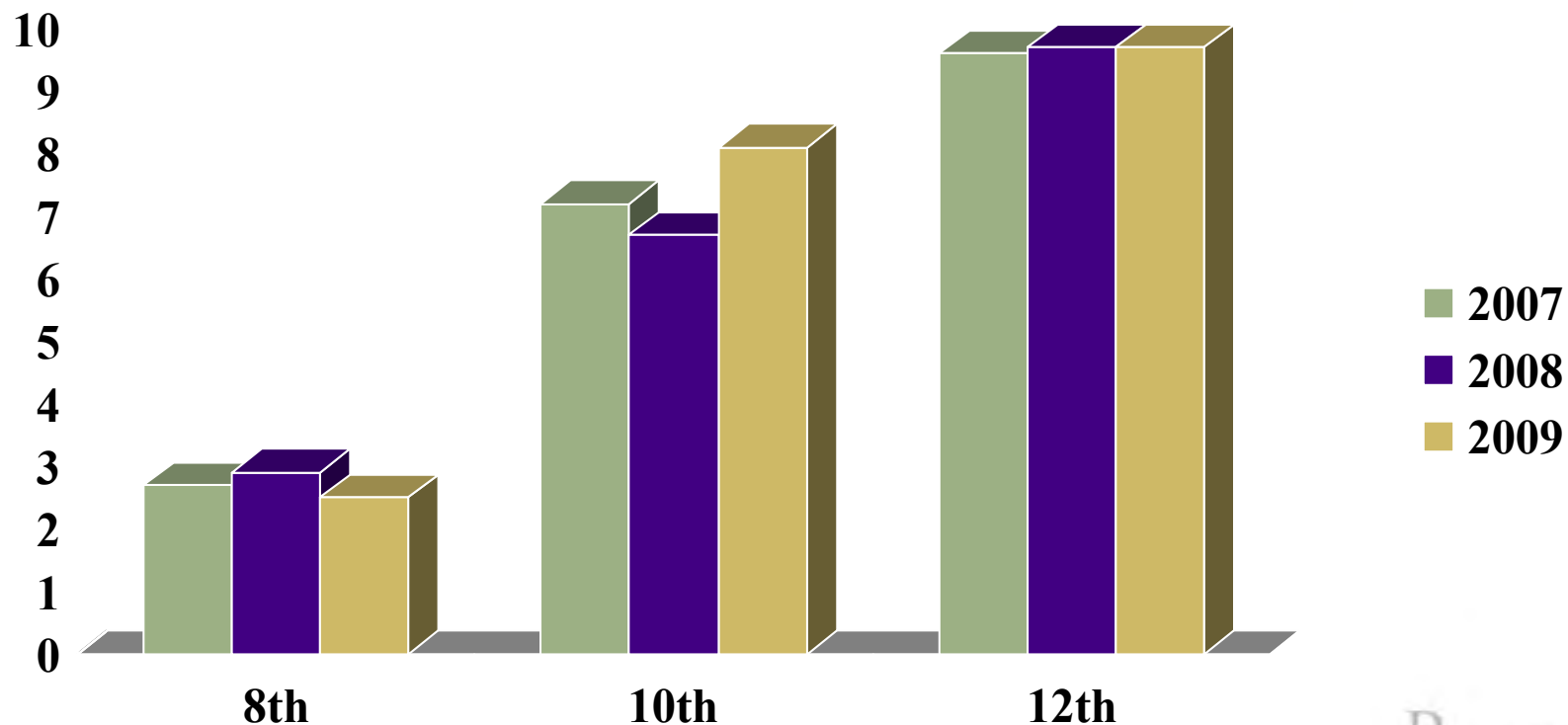
Oxycontin Use in the Past Year



High School Survey



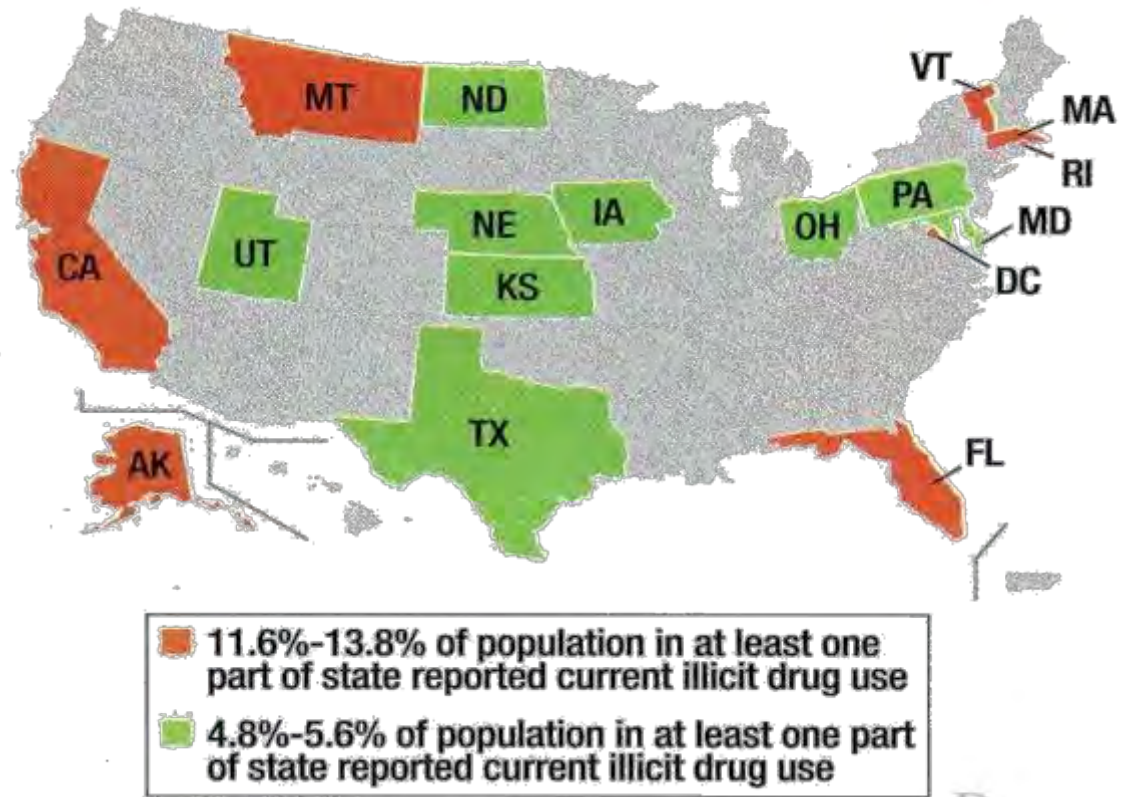
Used Vicoden in the Past Year



High rates of drug abuse spread throughout U.S.



Using 2004-2006 data, the National Survey on Drug Use and Health found that the eight highest rates of illicit drug use in the U.S. were in regions in the states highlighted and in the District of Columbia

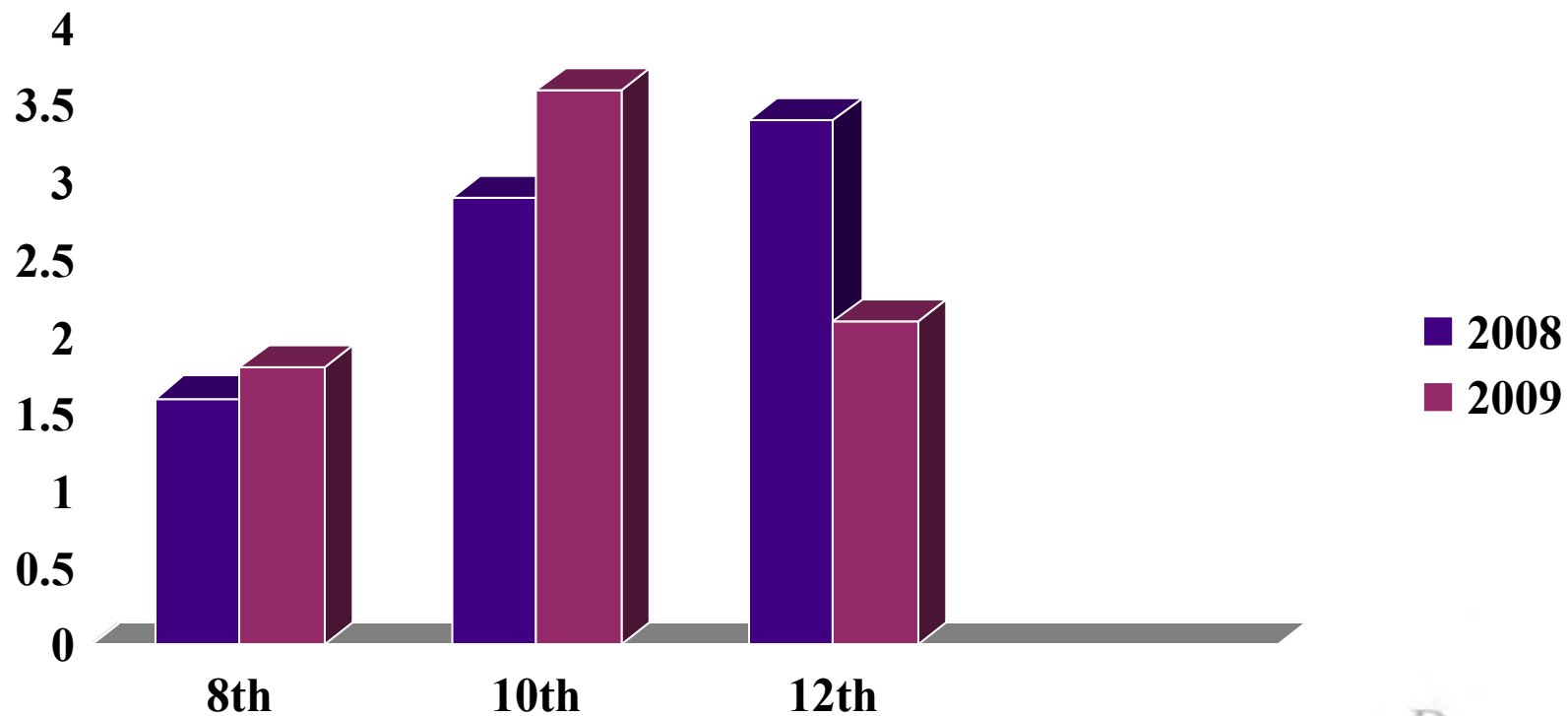


National Survey on Drug Use and Health 2007. Available at <http://www.oas.samhsa.gov>. Accessed August, 2010.

High School Survey



Ritalin Use in the Past Year





Signe

DRUG-FREE AMERICA

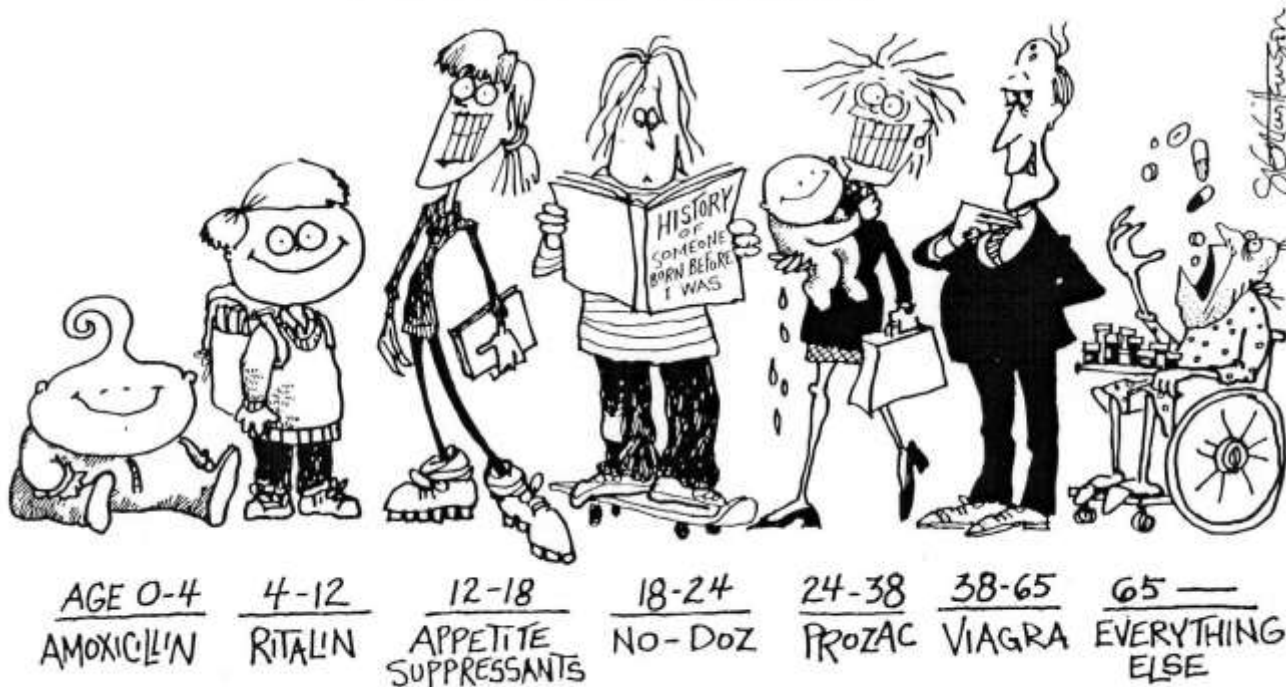
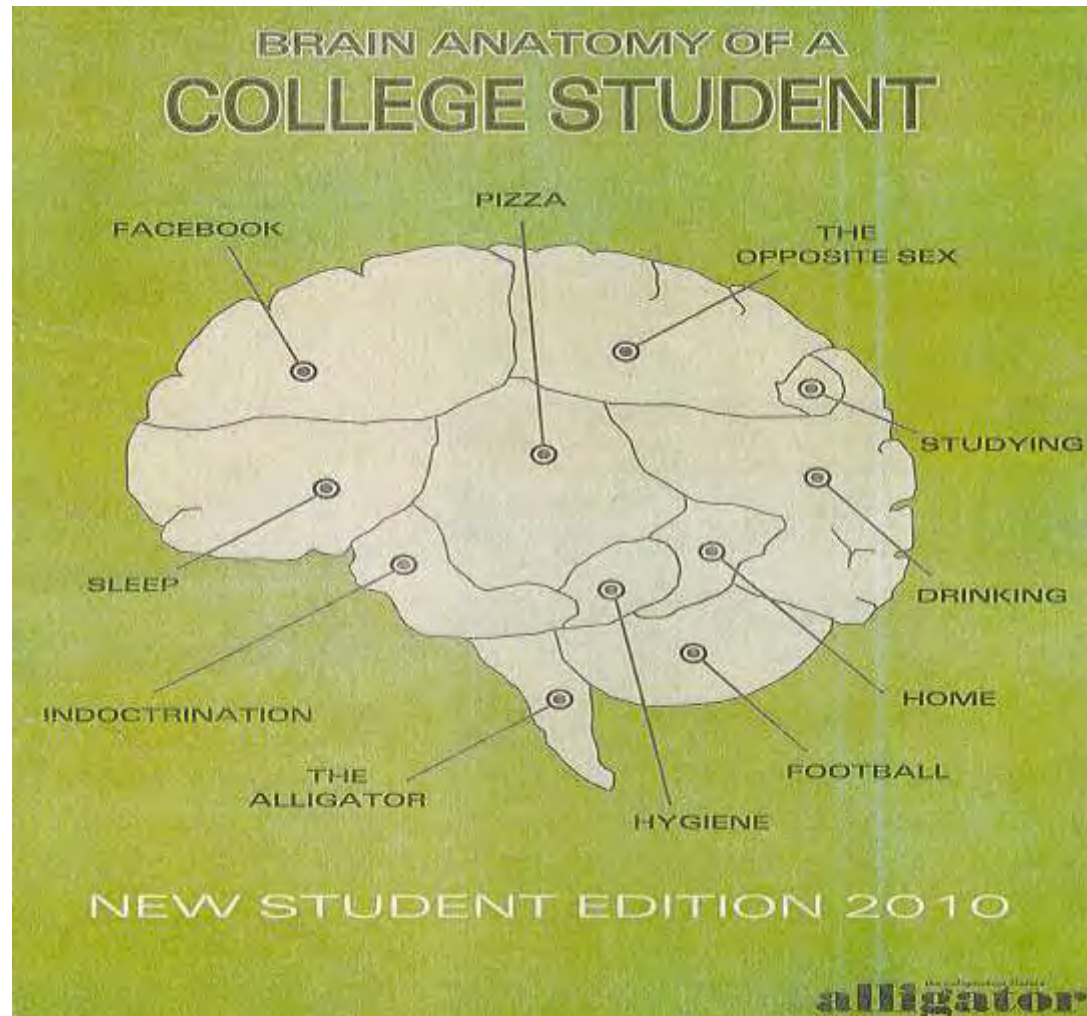


FIG. 1. Reproduced by permission of the publisher and courtesy of Signe Wilkinson/CWS.

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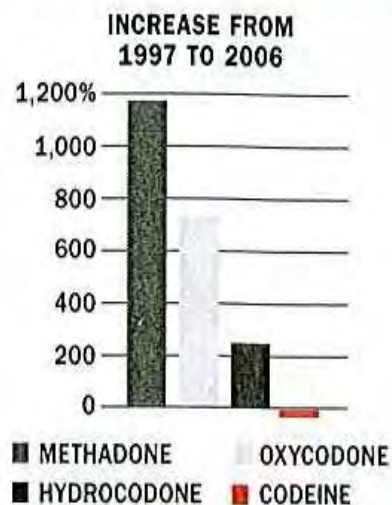


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A Druggy Decade

Sales of most opioids have soared in the U.S.; only codeine is down



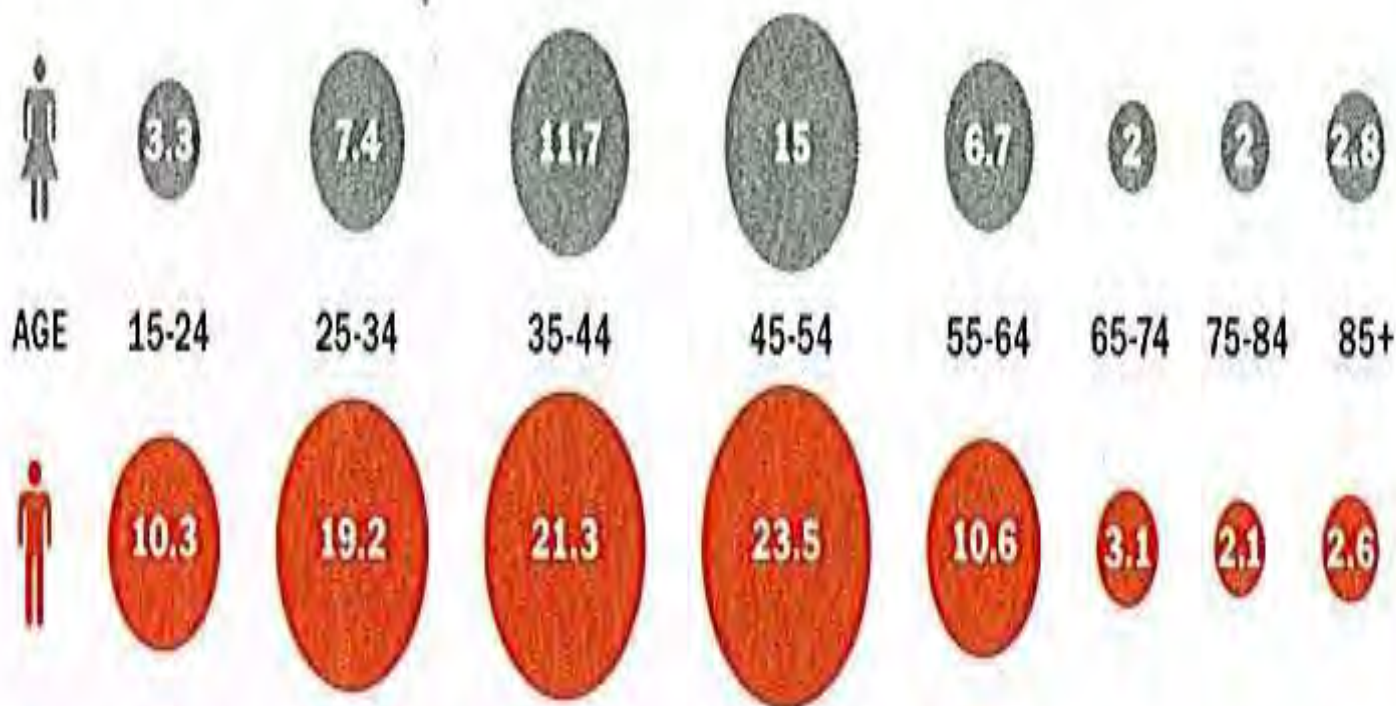
ANNUAL OPIOID CONSUMPTION PER PERSON



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**Overdose
deaths per
100,000
people
in 2007,
by age
and sex**

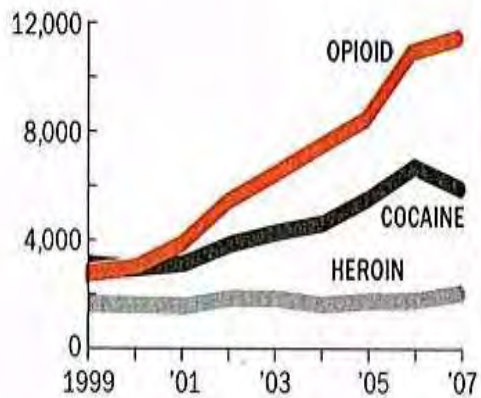




The national toll

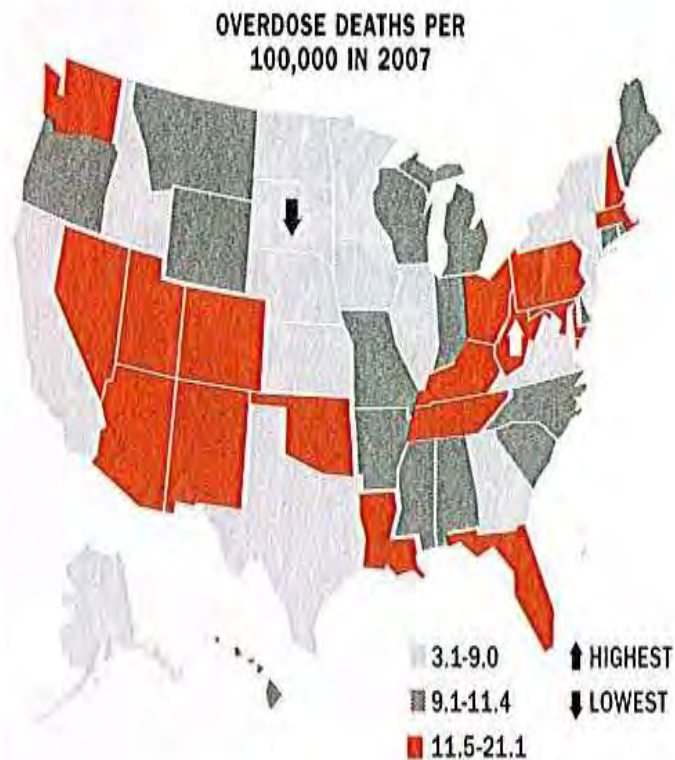
27,658

UNINTENTIONAL DRUG-OVERDOSE DEATHS FROM 1999 TO 2007, INCLUDING THE SUBSTANCES BELOW



Source: CDC/National Vital Statistics System

State by state, the danger differs



RECOVERY
FROM
ADDICTION

Similar Age & Demographics for Child-Bearing Women



Source of Prescription Drugs^a among Those Who Used in Last Year

Grade 12, 2007–2009

(Entries are percentages.)

Where did you get the [insert drug name here] you used without a doctor's orders during the past year? (Mark all that apply.)

	<u>Amphetamines</u>		<u>Tranquilizers</u>		<u>Narcotics other than Heroin</u>	
	<u>2007–2008</u>	<u>2009</u>	<u>2007–2008</u>	<u>2009</u>	<u>2007–2008</u>	<u>2009</u>
Bought on Internet	4.6	3.4	2.4	3.0	2.3	0.0
Took from friend/relative without asking	19.6	10.2	21.1	13.1	24.2	18.6
Took from a friend	—	3.9	—	5.7	—	3.6
Took from a relative	—	7.6	—	8.8	—	17.9
Given for free by friend or relative	58.2	55.1	59.8	64.3	50.5	51.5
Given for free by a friend	—	54.5	—	61.7	—	46.1
Given for free by a relative	—	2.9	—	8.8	—	10.1
Bought from friend or relative	45.0	48.8	44.1	39.3	37.1	33.6
Bought from a friend	—	48.8	—	39.3	—	33.6
Bought from a relative	—	1.8	—	0.6	—	2.9
From a prescription I had	15.1	22.9	18.4	15.3	40.2	30.3
Bought from drug dealer/stranger	26.7	21.8	24.2	18.9	18.6	13.0
Other method	17.8	15.1	7.5	12.3	8.5	10.6
<i>Weighted N =</i>	261	115	226	94	361	153

Source. The Monitoring the Future study, the University of Michigan.

^aIn 2009, the response categories were expanded to differentiate between friends and relatives.

DRUGS OF ABUSE



- Chemical abstracts lists millions of different known chemicals yet only 20 or so are voluntarily self-administered by animals
- Self-administered chemicals differ strikingly from each other in chemical structure and pharmacological class

What Defines A Substance of Abuse



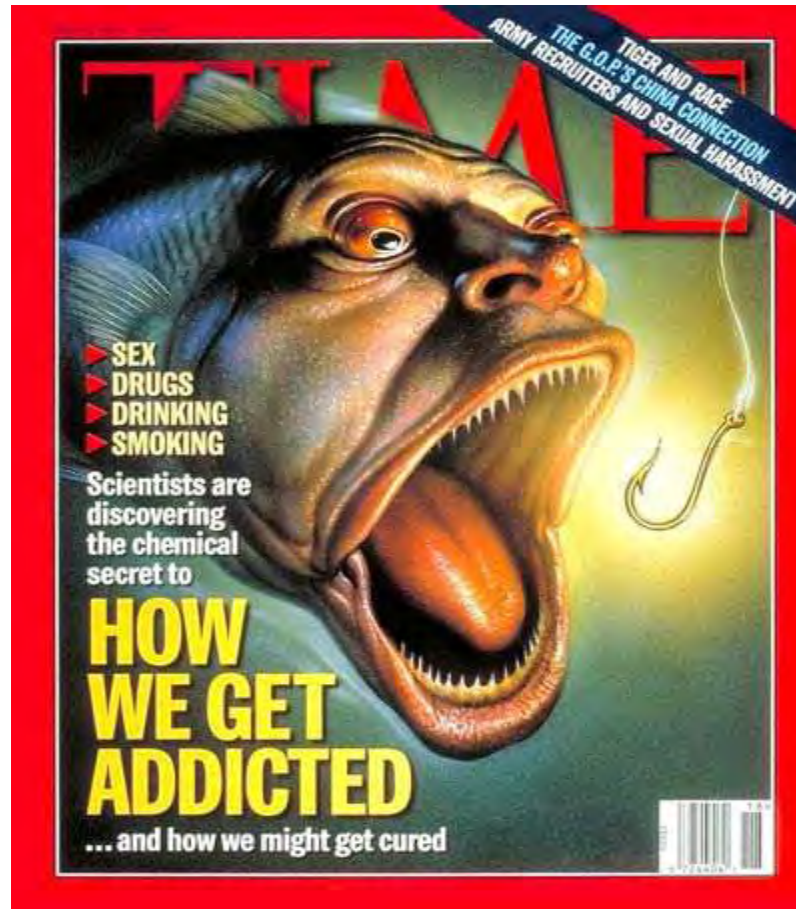
- Animal Models ?
- Chemical Structure?
- Effect on the Brain ?

ADDICTED RATS...



- Self administration is the gold standard for assessing the rewarding properties of drugs of abuse. Hijack normal goal directed behavior
- Cocaine self administration despite pain
- Cocaine self administration despite tremendous work required for a dose
- Continued use even when the drug is unavailable

Animal Models are yielding new CNS-targeted Rx



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ADDICTION

Animal Models & Cocaine Addicted People



- Changed the definition of addiction
- Cocaine became and is the model of an addiction and an addicting drug

Cocaine



RECOVERY
FROM
ADDICTION

Cocaine History - Endorsed by Celebrities



MARIANI WINE

MARIANI WINE Quality Features
**HEALTH, STRENGTH,
ENERGY & VITALITY.**

MARIANI WINE
FORTIFIES, STRENGTHENS,
STIMULATES & REFRESHES
THE BODY & BRAIN

HASTENS
CONVALESCENCE
especially after
INFLUENZA.

His Holiness
THE POPE
writes that he has
fully appreciated the
beneficial effects of
this Tonic Wine and
has forwarded to Mr.
Mariani as a token of
his gratitude a gold
medal bearing his ap-
proual.



MARIANI WINE

is delivered free to all parts of the United Kingdom by WILCOX & CO.,
85, Mark Lane, Street, London, E.C. price 2/- per Single Bottle, 22/6 half-
dozen, 42/- dozen; and is sold by Chemists and Stores.

Celebrity endorsements
were common in the
18th Century. . .

*Even the Pope
recommended
cocaine*

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ADDICTION



RECOVERY
FROM
ADDICTION

Lady Gaga Reveals She Does “Cocaine”



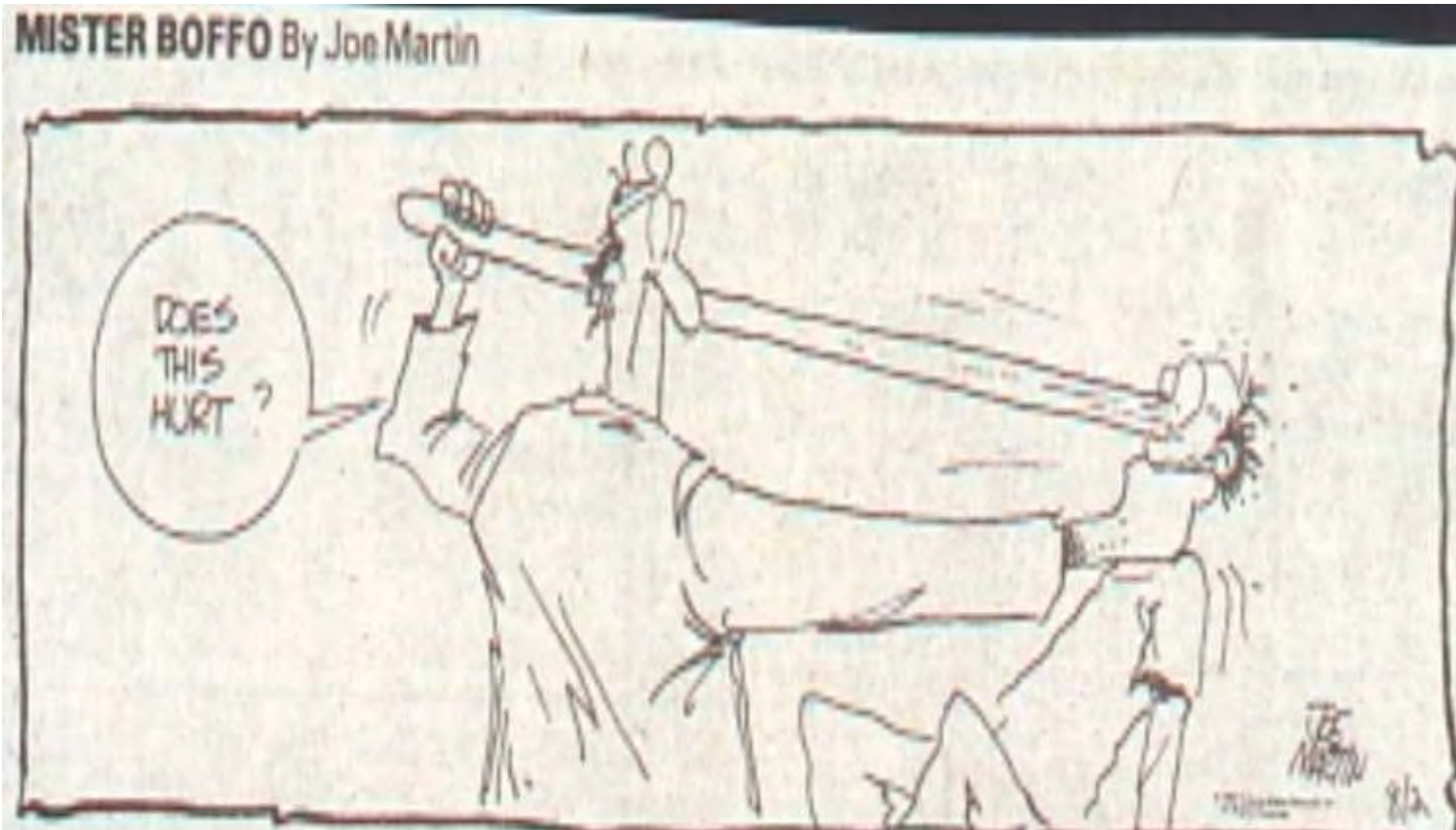
In a new Vanity Fair interview, the 24-year-old singer (real name: Stefani Germanotta) reveals she’s “terrified of heroin”, but still does “mostly cocaine”.

“I won’t lie; it’s occasional,” she says. “and when I say occasional, I mean maybe a couple times a year.”

She told the magazine she doesn’t condone drug use in any way. “I do not want my fans to ever emulate that or be that way,”

RECOVERY
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ADDICTION

Diagnosis of Cocaine Abuse Circa 1980



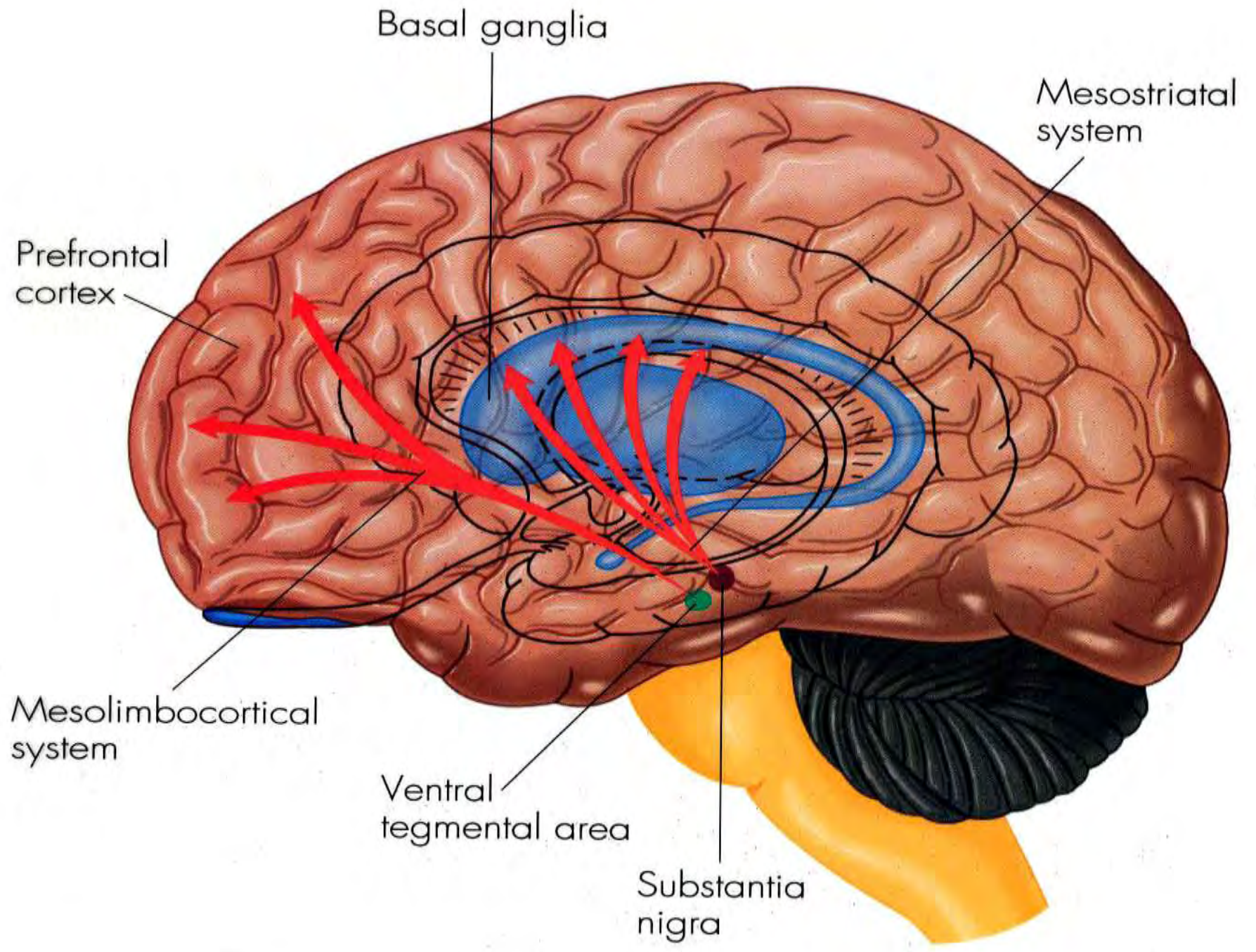
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Common Neurobiology



- Means drugs work and one can be interchanged with another or more than one
- Drug combinations have effects that are more intense, less intense, or considerably different than a single drug used alone
- Tobacco and Sex or Cocaine and Pornography





Brain areas affected by Addiction

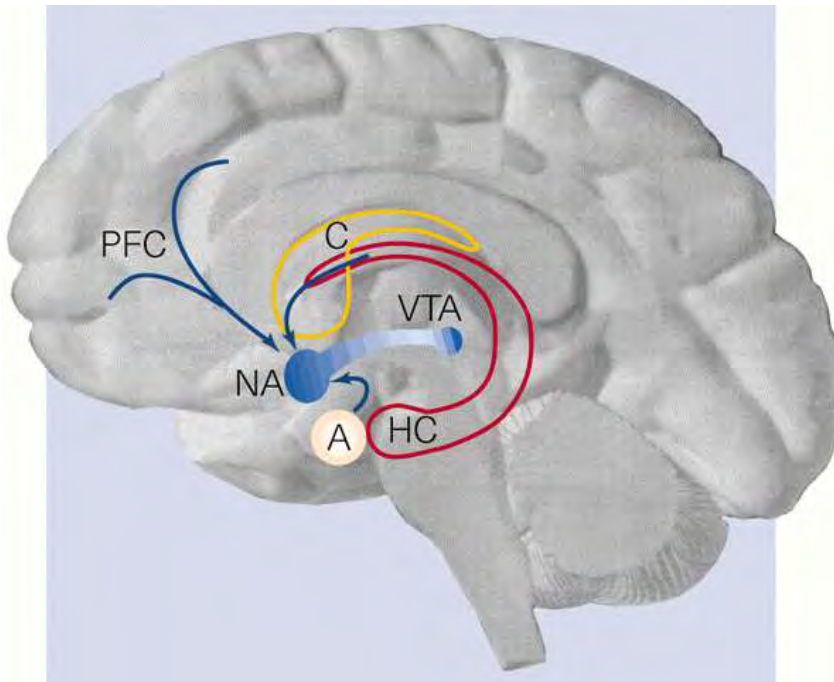
Tobacco, Alcohol, Food, Methamphetamine,
MDMA, Opiates



Prefrontal cortex
Executive function
(e.g. *Planning, higher level behavioural control*)

Orbitofrontal cortex
Evaluation of rewarding or motivational value of stimuli

- Caudate nucleus (cognitive striatum)
- Nucleus Accumbens (limbic striatum)
- VTA (Dopamine neurons)
- *Memory and emotion*
 - Amygdala -
 - Hippocampus



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ADDICTION

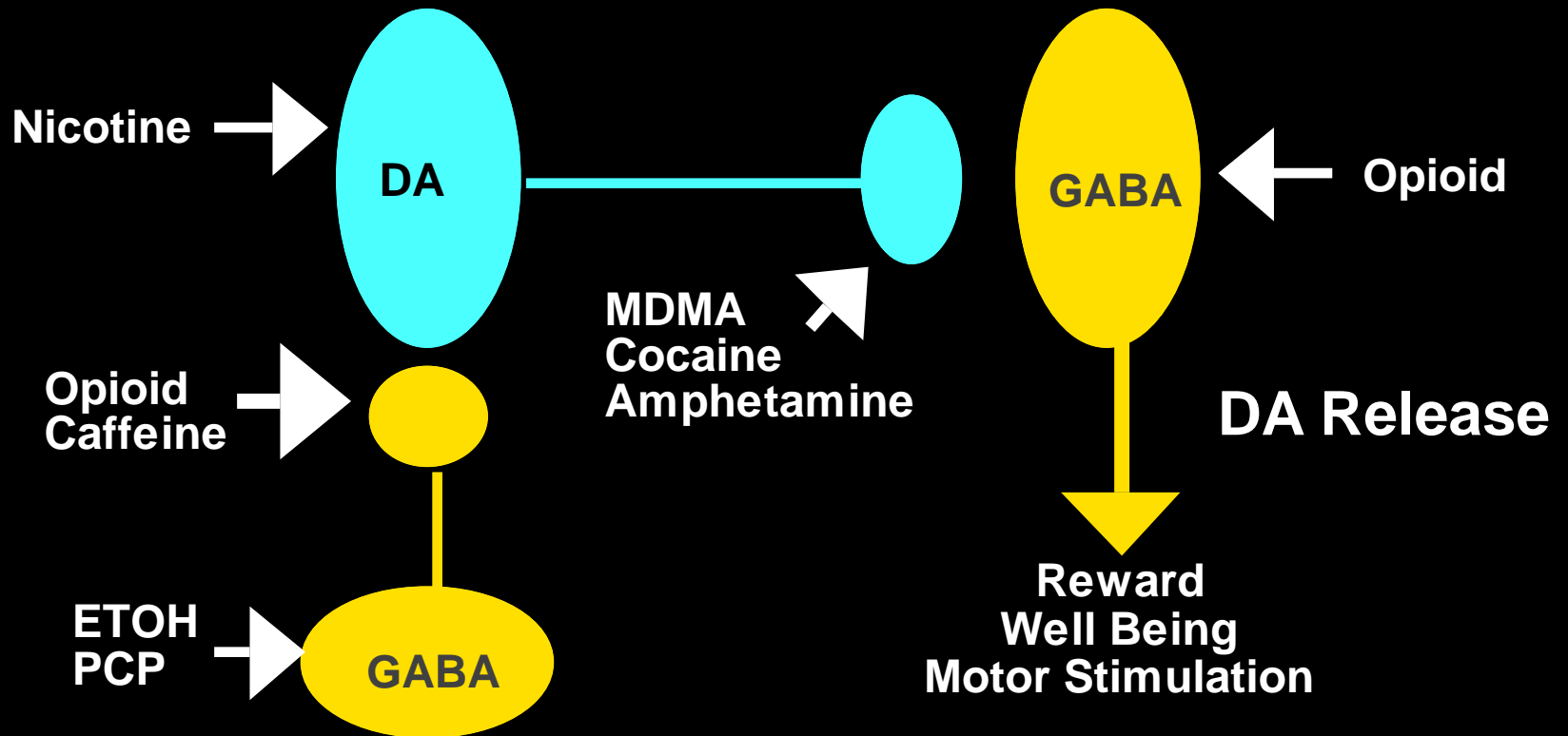
Cocaine & Dopamine



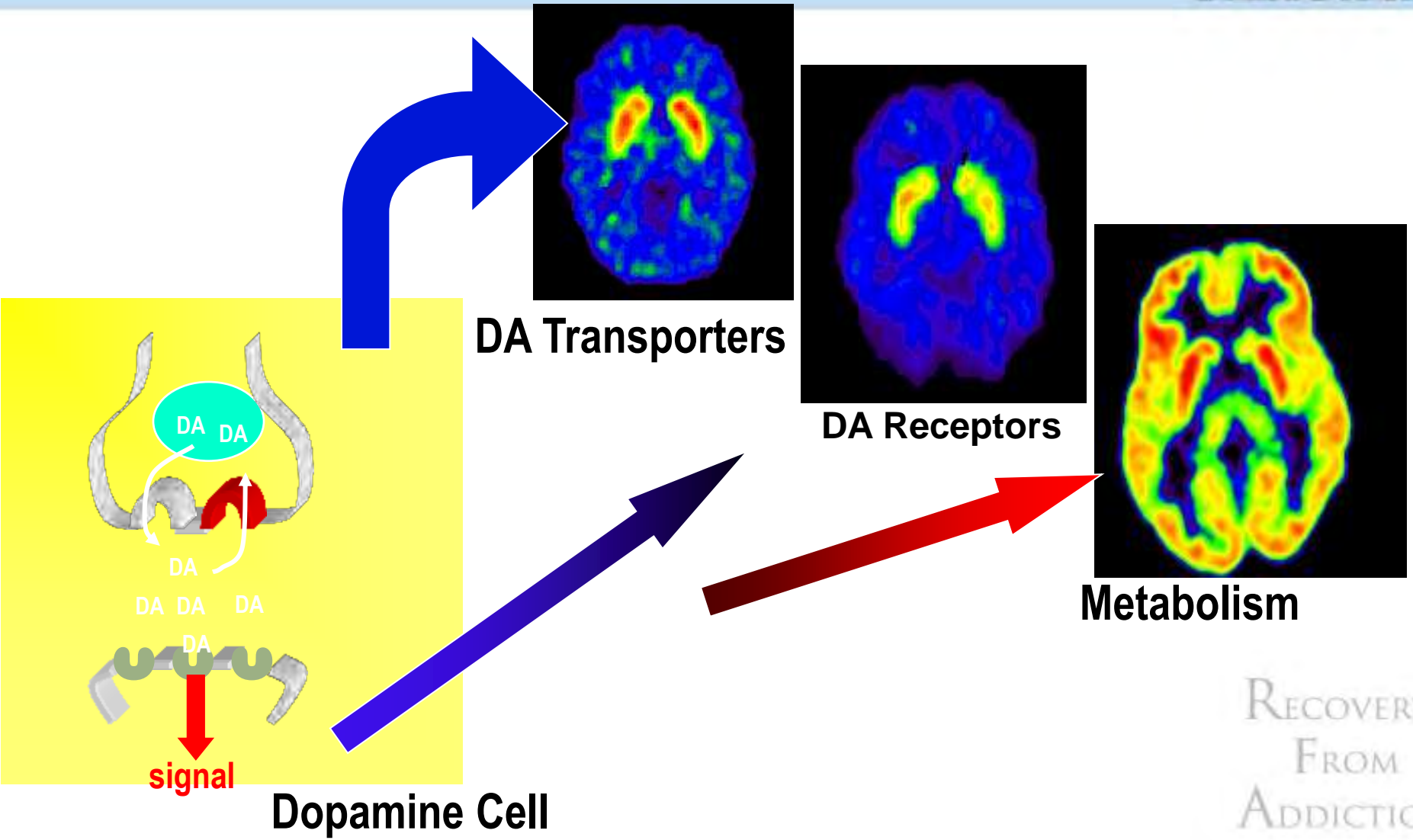
- Cocaine helped scientists learn that reward learning relied on dopaminergic projections from the ventral midbrain (VTA) to the nucleus accumbens, amygdala and prefrontal cortex.
- Cocaine promotes Dopamine release and by binding to DAT prolongs the lifetime of dopamine in the synaptic cleft.

VTA

Accumbens

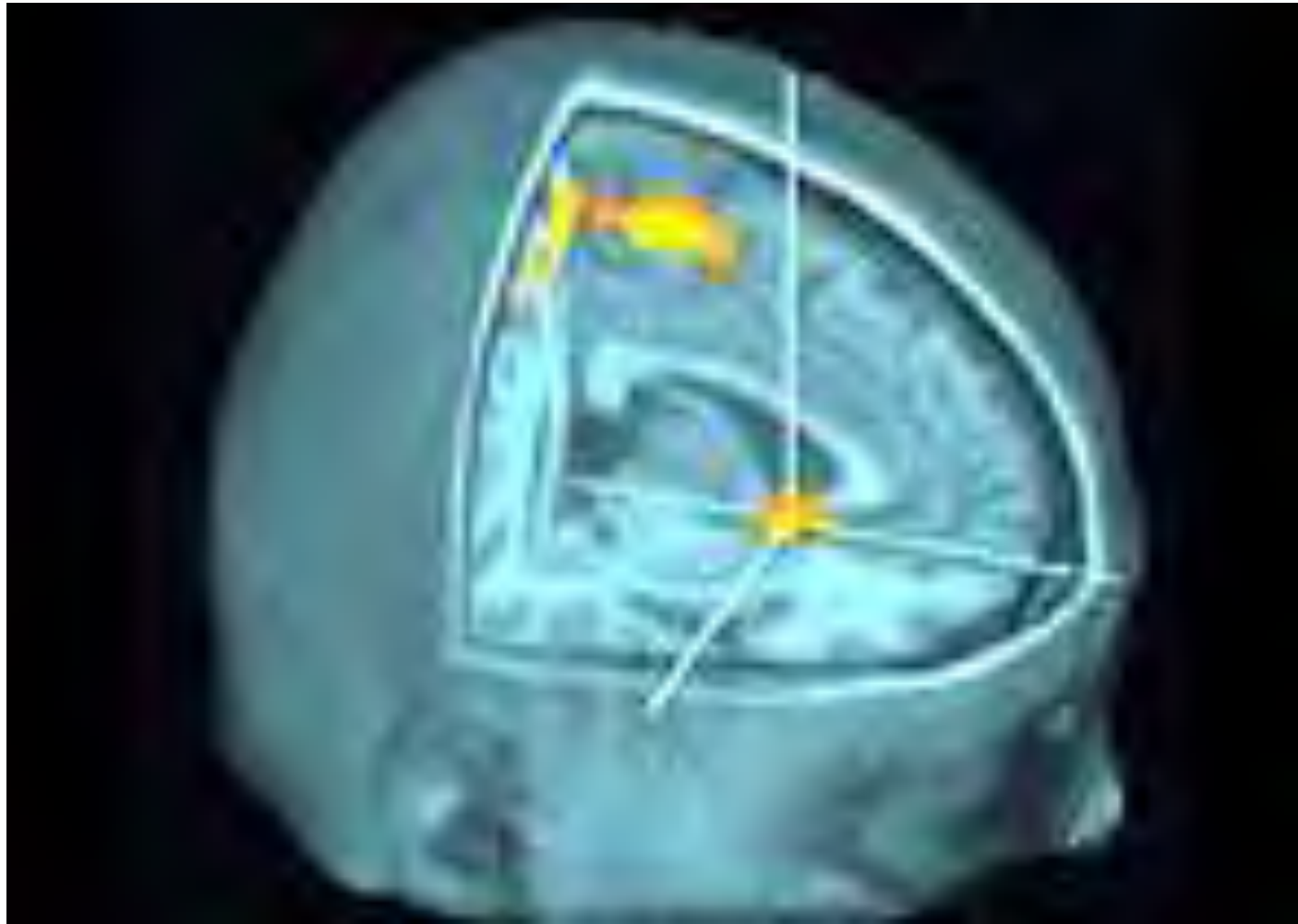


Is Dopamine Involved in Addiction and Obesity?



RECOVERY
FROM
ADDICTION

The nucleus accumbens lighting up



RECOVERY
FROM
ADDICTION

Dopamine D2 Receptors are Lower in Addiction



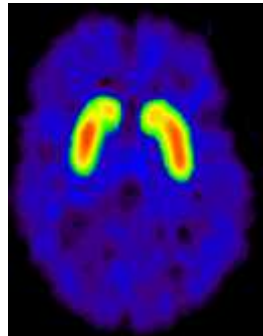
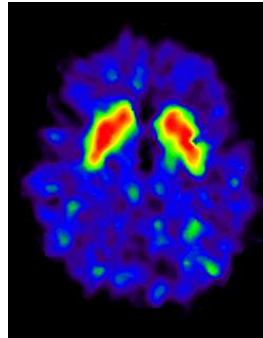
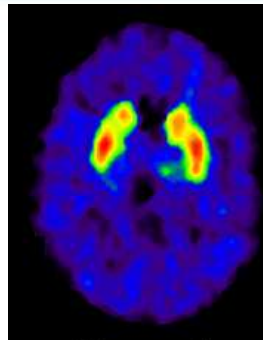
Cocaine



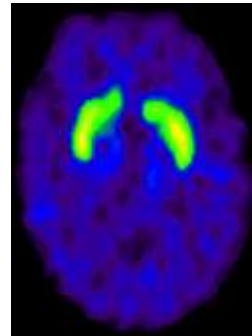
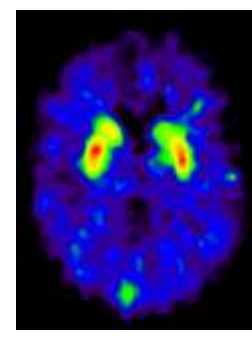
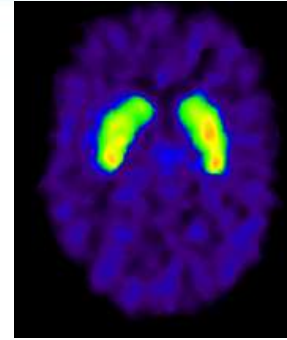
Alcohol



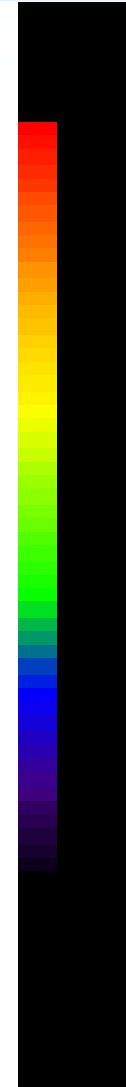
Heroin



control



addicted



DA D2 Receptor Availability \uparrow

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ADDICTION

Parkinson's Disease



- DA Treatments and Increased :
 - Gambling
 - Sex
 - Eating



On Good Morning America Cocaine Epidemic 1983



RECOVERY
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ADDICTION

Routes of Administration



Routes of administration that deliver cocaine rapidly to the brain are the most euphoric and the most addicting

Oral

Intranasal

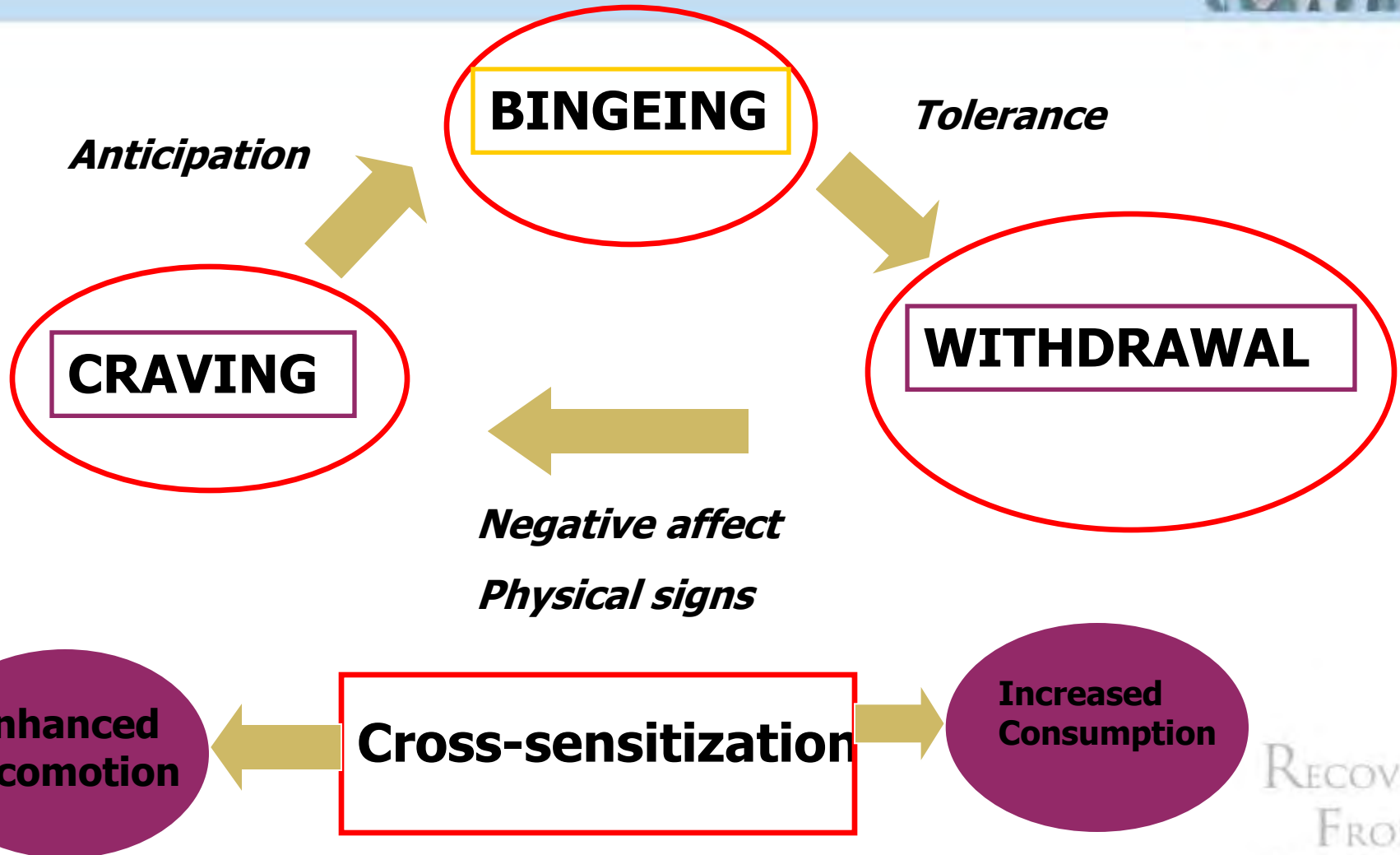
Intravenous

Intrapulmonary

Intrapulmonary
By-passes the
venous system

What is an “addiction”?

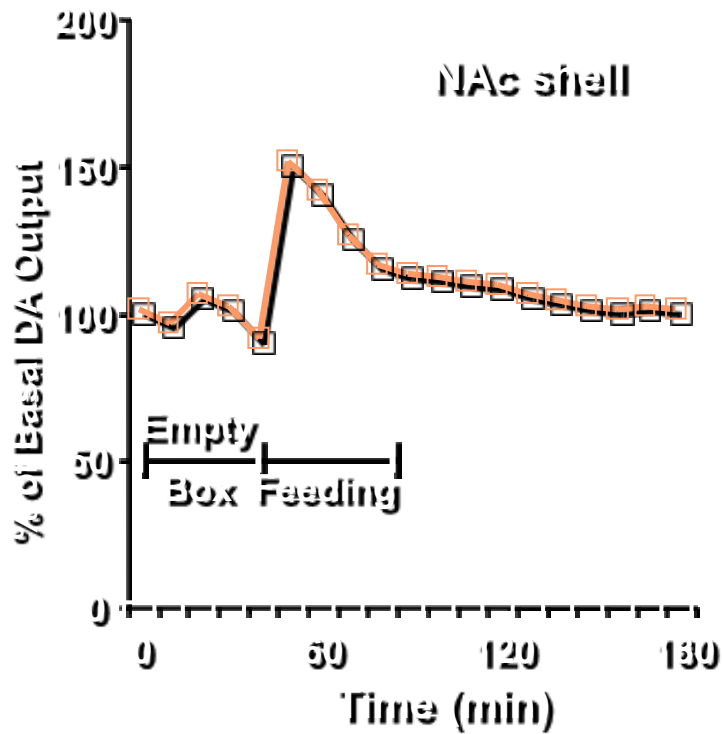
Look at criteria used to study
substance dependence



Natural Rewards Elevate Dopamine Levels

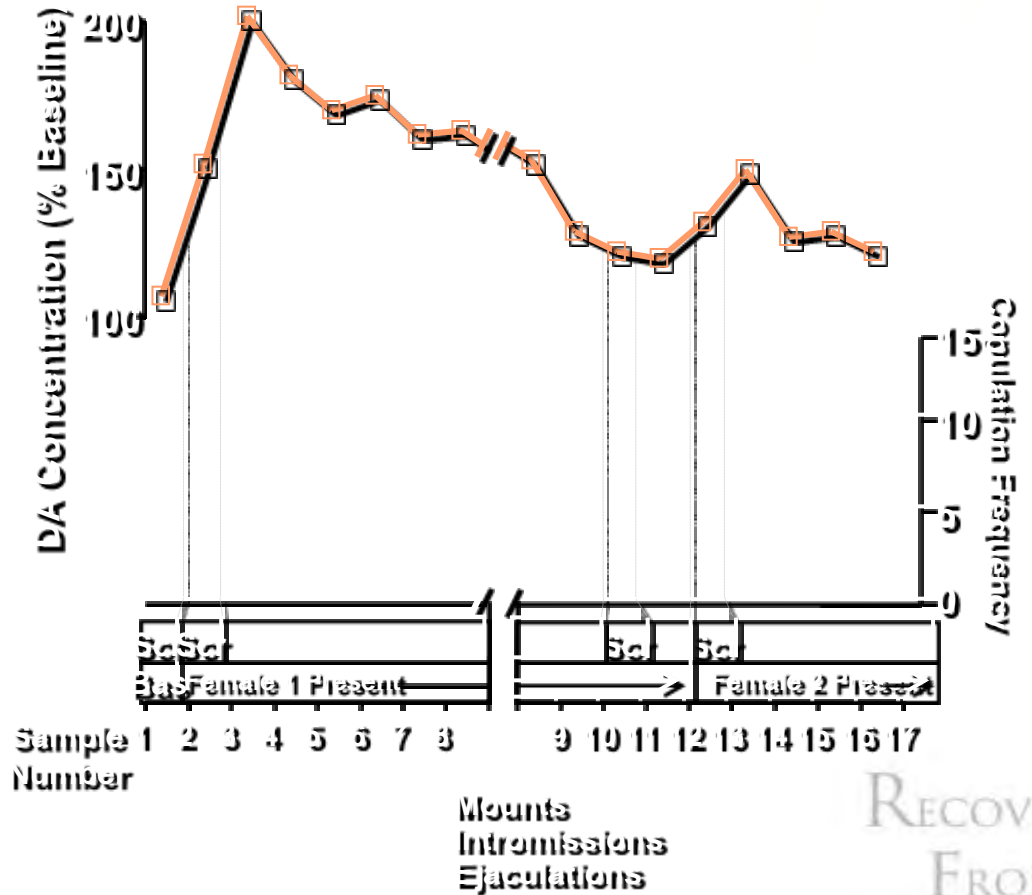


FOOD



Source: Di Ciano et al.

SEX



Source: Fiorino and Phillips

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ADDICTION

Neuroplasticity in the Mesolimbic System Induced by Natural Reward and Subsequent Reward Abstinence



Pitchers KK, Balfour ME,
Lehman MN, Richtand NM, Yu L,
Coolen LM.

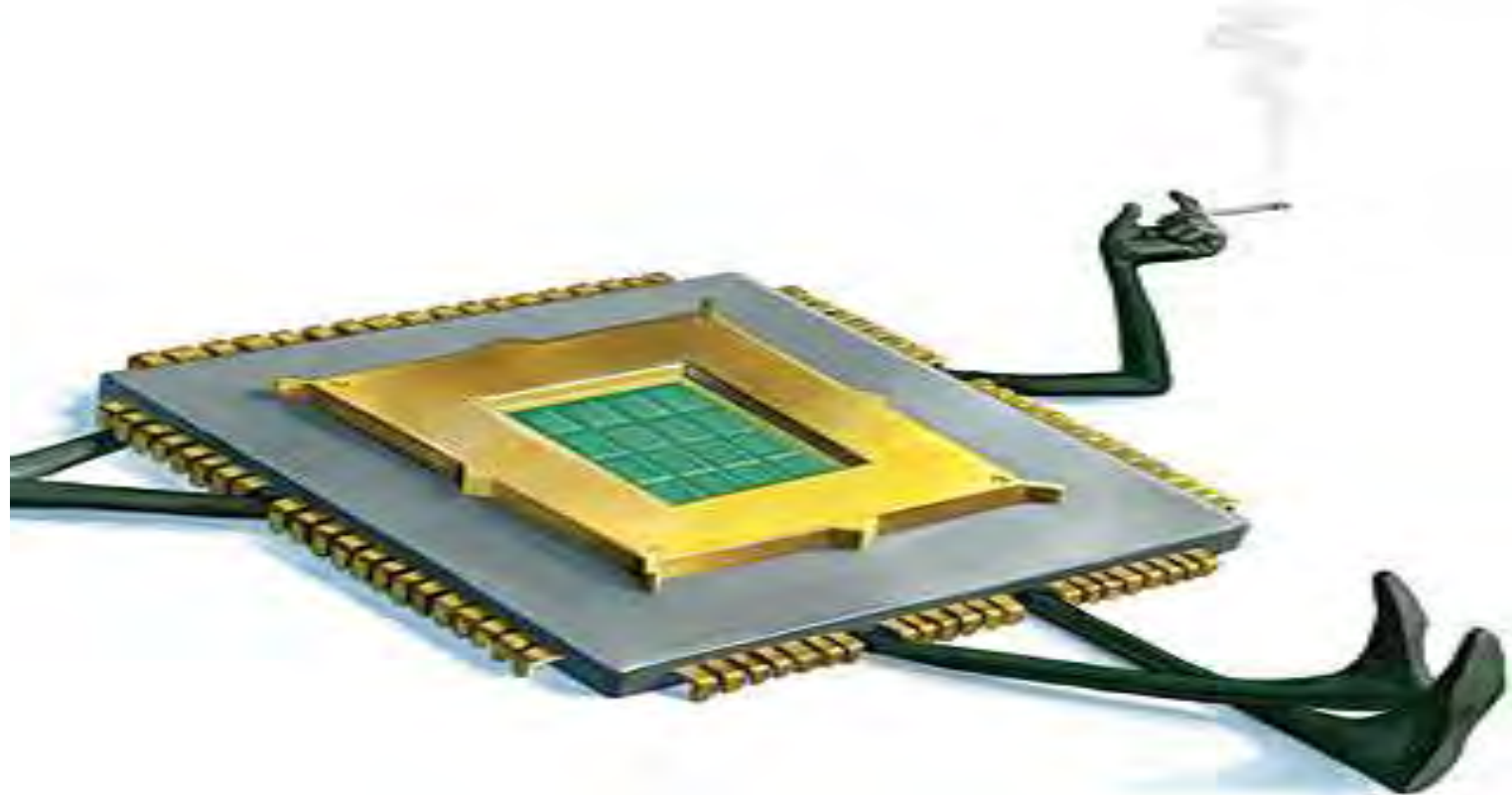


- Male rat brains analyzed; mated vs unmated (sex vs no sex)
- Mated showed changes in reward circuitry similar to those caused by psychostimulant drugs
- Mated rats showed enhanced responses to amphetamine
- Forced abstinence – rats displayed enhanced seeking for drug reward

Biol Psychiatry 2010 May 1;67:872-879.

RECOVERY
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ADDICTION

Sex Chip to stimulate the pleasure centers of the brain?



Matt Collins May, 2009 Scientific American

RECOVERY
FROM
ADDICTION

Lesions of the Medial Prefrontal Cortex Cause Maladaptive Sexual Behavior in Male Rats



Davis JF, Loos M, Di
Sebastiano AR, Brown JL,
Lehman MN, Coolen LM



- When sexual behavior was paired with aversive stimulus (LiCl) healthy male rats abstain from copulating
- mPFC lesioned rats continued copulating under same conditions
- Lesioned rats formed conditioned place preference to sexual reward and place aversion to LiCl
- Conclusion: mPFC regulates the execution of behavioral inhibition toward sexual behavior

Biol Psychiatry 2010, Jun 15;67:1199-1204.

RECOVERY
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ADDICTION




DISCOVER

THE NEWSMAGAZINE OF SCIENCE


MARCH 1993

NEW DISCLOSURES
ABOUT THE
PLOT TO GET
OPPENHEIMER



This amount of cocaine can make you feel that you're brilliant, tireless, masterful, invulnerable, and that you're going to live forever.

It can also kill you.



RECOVERY
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ADDICTION

Neurocircuitry of Addiction

George F Koob & Nora D Volkow



- Addiction cycle composed of three stages , each associated with a specific behavior and mediated by a key brain location as focal point.

1. Binge = Intoxication
2. Withdrawal = Negative affect
3. Preoccupation/anticipation = Craving

- The transition to addiction involves neuroplasticity in all of these structures that may begin with changes in the mesolimbic dopamine system and then a cascade of neuroadaptations.
- The delineation of this neurocircuitry forms a basis for the search for molecular, genetic and pharmacological neuroadaptations that are key to vulnerability for developing and maintaining addiction.

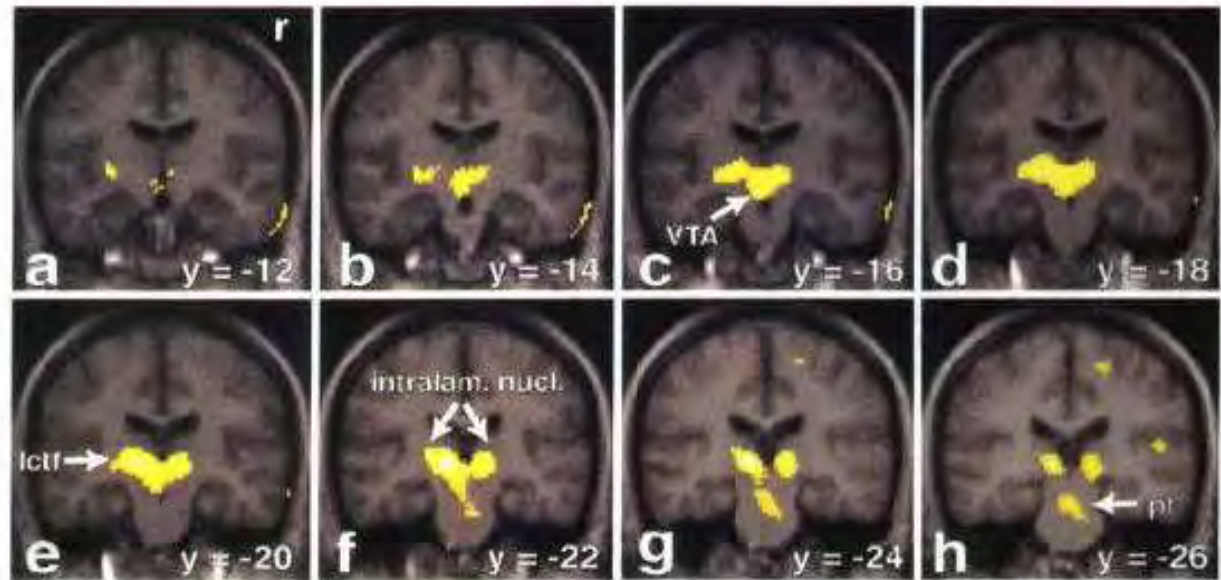
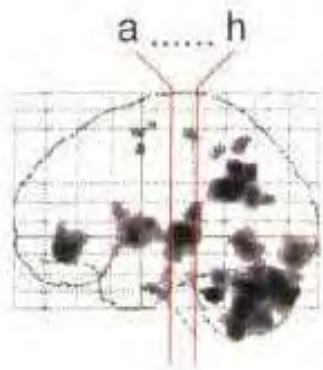
Neuropsychopharmacology (2010) 35, 217 – 238.

Cocaine vs Natural Reinforcers



- Cocaine administrations results in increases in dopamine that is much, much greater in both amplitude and duration than what is physiologically induced by food or sex
- Cocaine by acting at the DAT releases dopamine after each administration as if it was the first or at least novel. Food or sex can not do this for the dopamine systems.
- Cocaine addicts over-learn behaviors associated with cocaine and its acquisition. Cocaine successfully competes with biological rewards.

Brain Activity During Male Ejaculation



RECOVERY
FROM
ADDICTION

Sharon Stone



- Woman might be able to fake orgasms. But man can fake whole relationships.



RECOVERY
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ADDICTION



This beautiful micrograph shows crystals of dopamine - the chemical released when we do naturally rewarding things like eating and procreating.



Photo by Spike Walker; produced by passing polarized light through dopamine crystals. Retrieved from www.newscientist.com on Sept. 13, 2010.

RECOVERY
FROM
ADDICTION

David Duchovny Rehabbing for Sex Addiction



- "I have voluntarily entered a facility for the treatment of sex addiction," Duchovny said in a statement released Thursday by his attorney, Stanton "Larry" Stein. "I ask for respect and privacy for my wife and children as we deal with this situation as a family."
- The 48-year-old *X-Files* star ironically, won a Golden Globe this year for playing an over-sexed struggling writer on Showtime's *Californication*.

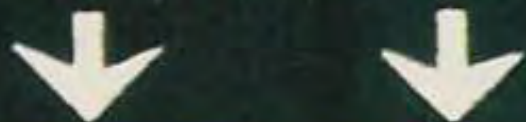
RECOVERY
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ADDICTION

Drug Withdrawal



- Regularly causes anhedonia and **DEPRESSION**
- Resolves in 30+ days but MDs usually treat it with Antidepressants which give the false impression that they were needed in the first place

Depressed For
No Reason



Depressed For
A Good Reason



JUST
DEPRESSED,
DON'T
WANT TO
ANALYZE
IT →

Still Depressed

UN-
DONE
→

A Depressed Rat?



- It is an impossible quest to mimic major depressive disorders completely in rodents
- Instead of anthropomorphizing the human condition, as in the cartoon, investigators have developed paradigms that detect specific behavioral endophenotypic differences (clear-cut behavioral outputs) that are sensitive to the effects of antidepressant treatments (both pharmacological and non-pharmacological)



Nirvana leader Kurt Cobain



- The 27-year-old rock star had a single gunshot wound to the head. A gun and suicide note were found nearby. Kurt had previously been evaluated and treated for drug abuse, addiction, suicide attempts and ideation.
- Ms O'Connor, Kurt's mother, told reporters "I told him not to join that stupid suicide club," she said. Nirvana's Cobain joins a long litany of rock stars - including Jimi Hendrix, Jim Morrison and Janis Joplin - who have died young.
- Four weeks before his death, Cobain attempted suicide in Italy, leaving him in a temporary coma, widely reported in the media at the time.



RECOVERY
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ADDICTION

World's Heaviest Woman



Wed Jun 9, 4:42 PM ET

N.J., USA



- Donna Simpson poses for a portrait at her home in Old Bridge, New Jersey June 8, 2010. Simpson, 42, who weighs more than 600 pounds (272 kg) and aims to reach 1,000 pounds (455 kg), is waging a campaign to become the world's heaviest living woman, admitting that she is as hungry for attention as she is for calorie-rich food.
REUTERS

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FROM
ADDICTION

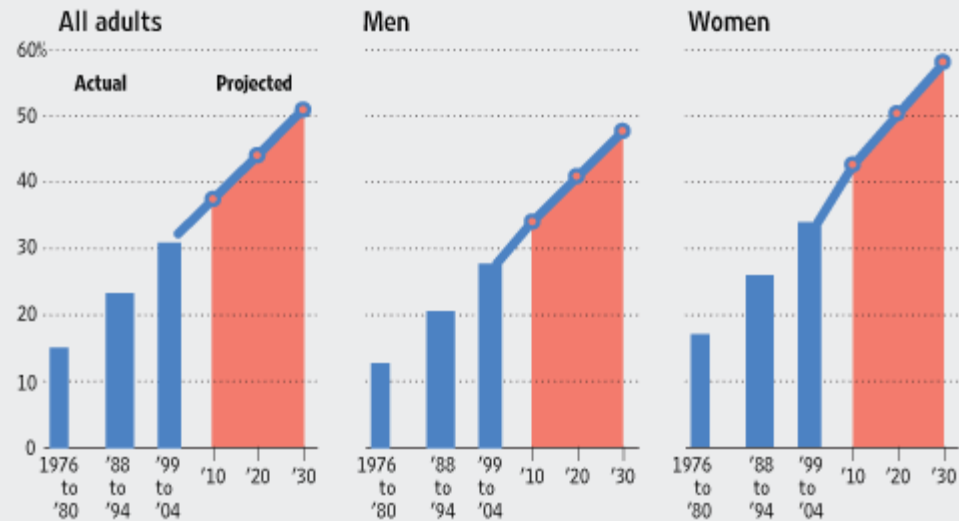
Obesity.....Trends ?



Larding the Numbers

Projections extend recent trends in obesity rates.

Percentage of adults 20 years and older considered to be obese*



*A body mass index (BMI) of 30 or higher

Sources: Epidemiologic Reviews; Obesity

RECOVERY
FROM
ADDICTION


1994-ASAM



Journal of Addictive Diseases™

the official journal of

ASAM
American Society of
Addiction Medicine

 **HMP** Published by The Haworth Medical Press®

Introduction

Obesity is increasingly being recognized as a problem of major public health significance. Overeating and obesity are second only to tobacco in annual associated mortality; almost 300,000 deaths per year. Over 10 years ago, we hypothesized that loss of control over eating, which results in obesity, may be another form of addictive behavior and reported on similarities between overeating and classic descriptions of addictions (*Are They Addictions or Just Other Types of Problems?* ASAM Symposium-1992). Phenomenological and behavioral similarities between substance abuse disorders and food, as a substance of abuse disorder were compelling. At that time, many were critical of including overeating and obesity as an addiction because there were few scientific studies that had directly compared and studied the relationships between these disorders. Researchers only recently have come to a consensus that obesity is a disease, but the debate continues as to whether it is related to depression, personality disorders or addictions. More than a decade after the first ASAM symposium, we were asked again to address this topic (*Are Eating Disorders Addictions?* ASAM Symposium 2003-2004). Today there is a convincing convergence of evidence from the bench in neuroscience, to PET and fMRI neuroimaging, to data from clinical experience that support the hypothesis that there are important similarities between overeating highly palatable and hedonic foods and the classic addictions.

If drugs of abuse hijack the brain, as has been suggested, where does this occur? Certainly not through existing pathways for sex or water. Food reward, however, is a prime target. Tobacco causes weight loss, as do cocaine, amphetamine, MDMA, and long-term opiate abuse. Drugs

[Haworth co-indexing entry note]: "Introduction." Gold, Mark S. Co-published simultaneously in *Journal of Addictive Diseases* (The Haworth Medical Press, an imprint of The Haworth Press, Inc.) Vol. 25, No. 3, 2004, pp. 1-3; and: *Eating Disorders, Overeating, and Pathological Attachment to Food: Independent or Addictive Disorders?* (ed. Mark S. Gold) The Haworth Medical Press, an imprint of The Haworth Press, Inc., 2004, pp. 1-3. Single or multiple copies of this article are available for a fee from The Haworth Document Delivery Service [1-800-HAWORTH, 9:00 a.m. - 5:00 p.m. (EST)]. E-mail address: docdelivery@haworthpress.com.

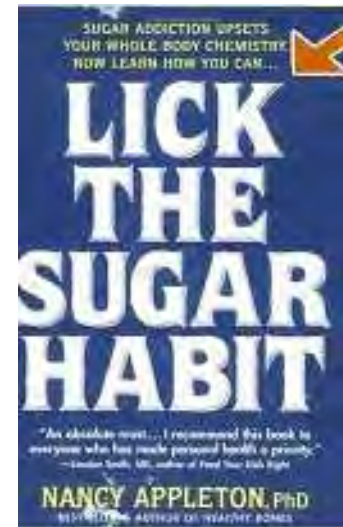
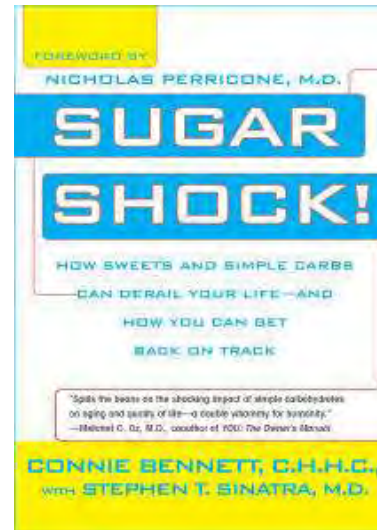
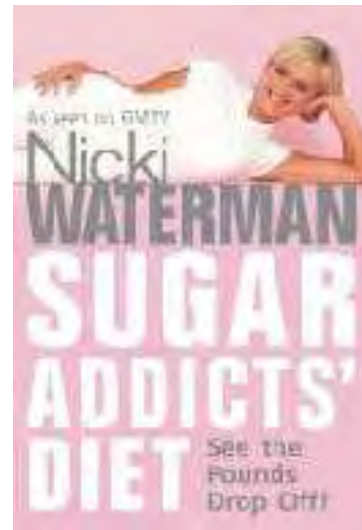
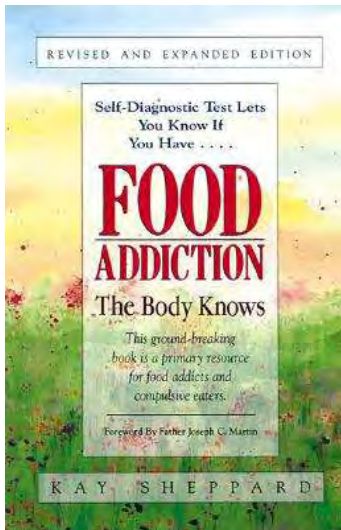
<http://www.haworthpress.com/web/JAD>
© 2004 by The Haworth Press, Inc. All rights reserved.
Digital Object Identifier: 10.1300/J069v23n03_01

RECOVERY
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ADDICTION

Why sugar?



Some people claim they can be addicted to food, particularly sugar.



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A delicious indulgence,
or your next desperate hit?

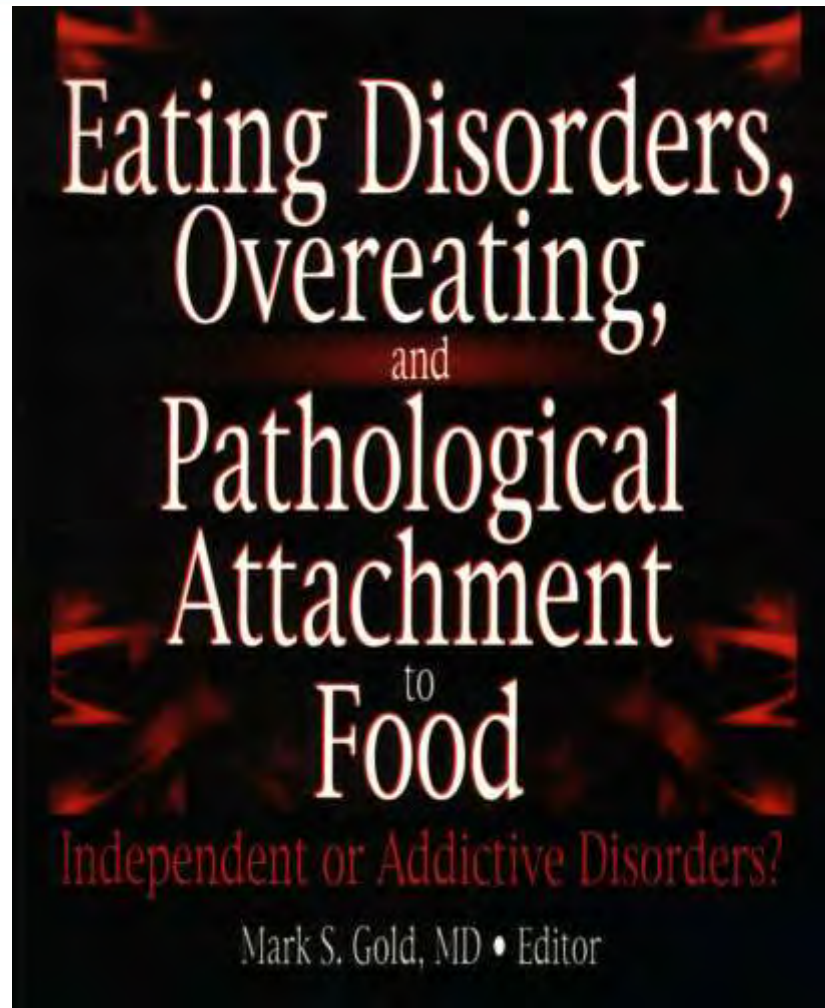


Image: Jonphotography.com Retrieved from www.newscientist.com on 9/13/10.

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ADDICTION



2004



RECOVERY
FROM
ADDICTION



Volume 3, Number 1, March 2009

www.journaladdictionmedicine.com

Journal of

Addiction Medicine

The Official Journal of the American Society of Addiction Medicine

- Food Addiction: An Examination of the Diagnostic Criteria for Dependence
- Imaging of Brain Dopamine Pathways: Implications for Understanding Obesity
- Food Addiction?

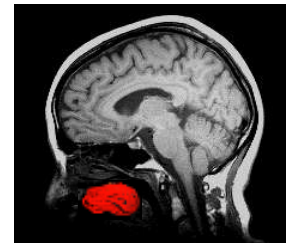


 Wolters Kluwer | Lippincott Williams & Wilkins

ISSN 1532-0623

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ADDICTION

to eat or not to eat ?



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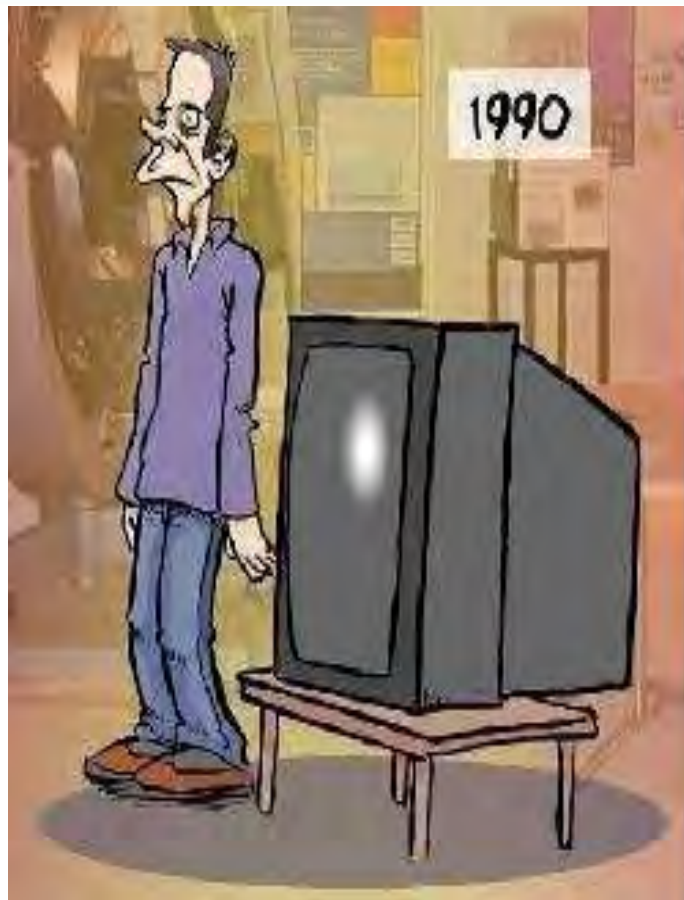
Nation's Number 2 Problem?



Really ?

How did this Happen ?

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ADDICTION



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ADDICTION



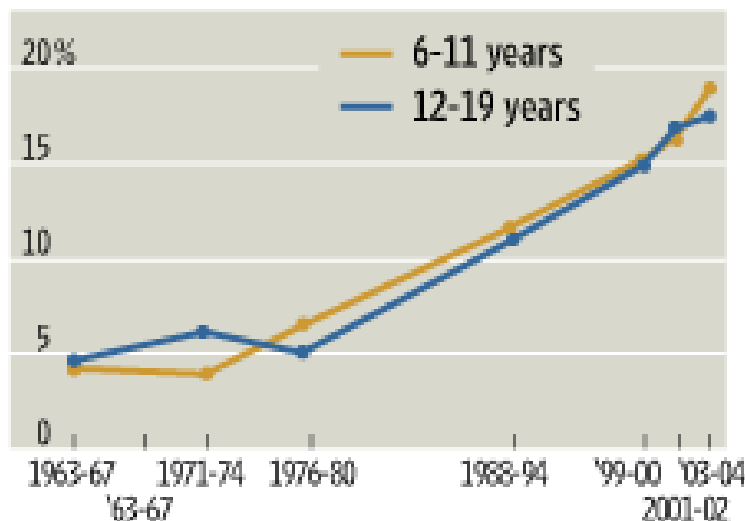
Actual Causes of Death in the United States in 1990 and 2000

Actual Cause	No. (%) in 1990	No. (%) in 2000
Tobacco	400 000 (19)	435 000 (18.1)
Poor diet / inactivity	300 000 (14)	400 000 (16.6)
Alcohol consumption	100 000 (5)	85 000 (3.5)
Microbial agents	90 000 (4)	75 000 (3.1)
Toxic agents	60 000 (3)	55 000 (2.3)
Motor vehicle	25 000 (1)	43 000 (1.8)
Firearms	35 000 (2)	29 000 (1.2)
Sexual behavior	30 000 (1)	20 000 (0.8)
Illicit drug use	20 000 (1)	17 000 (0.7)
Total	1 060 000 (50)	1 159 000 (48.2)



A Growing Problem

Prevalence of overweight among children and adolescents ages 6-19 years, for selected years 1963-65 through 2003-2004, based on results from the National Health and Nutrition Examination Survey (NHANES) for each time period.



Source: Centers for Disease Control and Prevention's National Center for Health Statistics

RECOVERY
FROM
ADDICTION

Childhood & Teen Onset



- Prevention of childhood overeating and obesity



Couch Potato Nation....What's making us so fat? Part of it is genetics; an increasingly popular scientific theory says people are predestined to be a certain weight. Even if you're genetically programmed to get fat, you won't unless you have access to fattening foods. In the last 30 years, the number of fast-food restaurants per capita in the U.S. has doubled, according to the Census Bureau. Between 1980 and 1997, the amount of high-calorie corn syrup consumed per person more than doubled to 87 pounds per year. It's no wonder the population of obese adults in the U.S. has grown 50% since the 1970s.

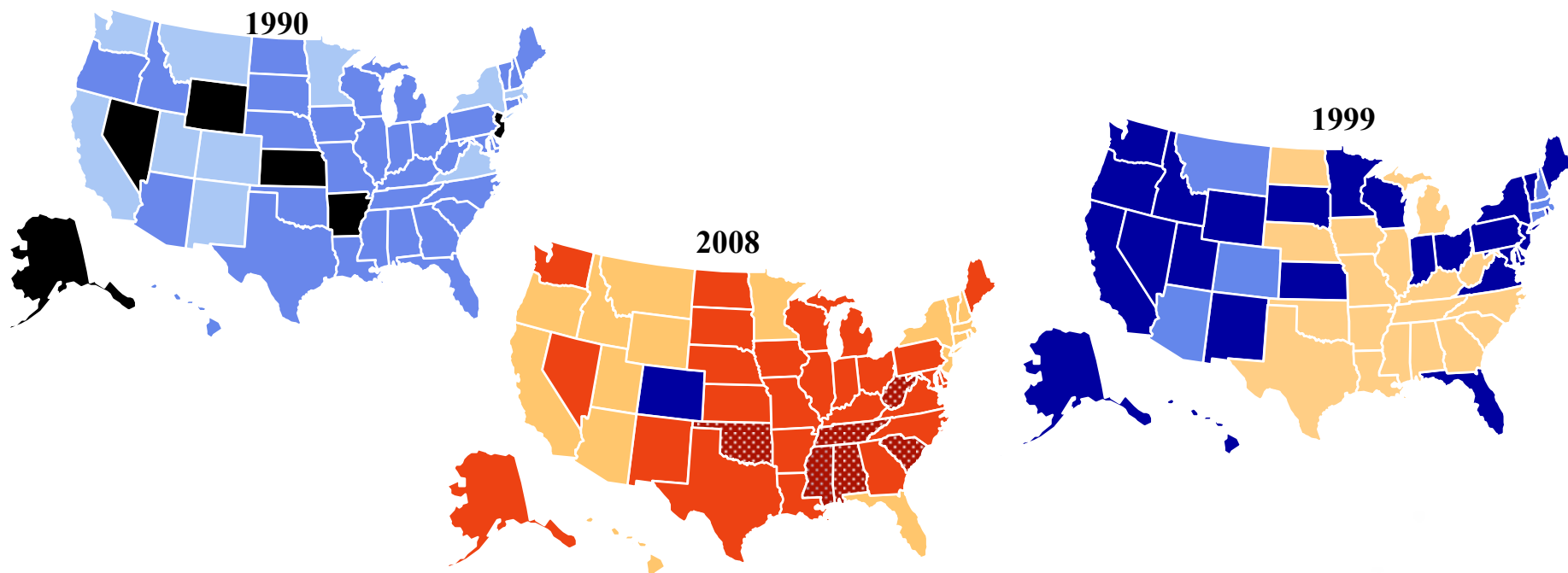


RECOVERY
FROM
ADDICTION

Obesity Trends* Among U.S. Adults BRFSS, 1990, 1999, 2008



(*BMI ≥ 30 , or about 30 lbs. overweight for 5'4" person)



No Data
 <10%
 10%–14
 15%–19%
 20%–24%
 25%–29%
 $\geq 30\%$

Some Factors Contributing to Obesity



- **Pre-Natal Environment**
- **Child-Rearing & Culture**
- **Genetics**
- **Diet=High energy intake**
- **Couch Potatoes**
- **No Exercise**
- **Abnormal eating behavior**

Critical Periods



- Languages
- Music
- Cigarettes-Smoking
- Drugs
- Pediatric Onset

BARBIE: from Malibu to 50!



1970



2009

RECOVERY
FROM
ADDICTION

Is Soda the new Tobacco

by Mark Bittman

Published February 12, 2010



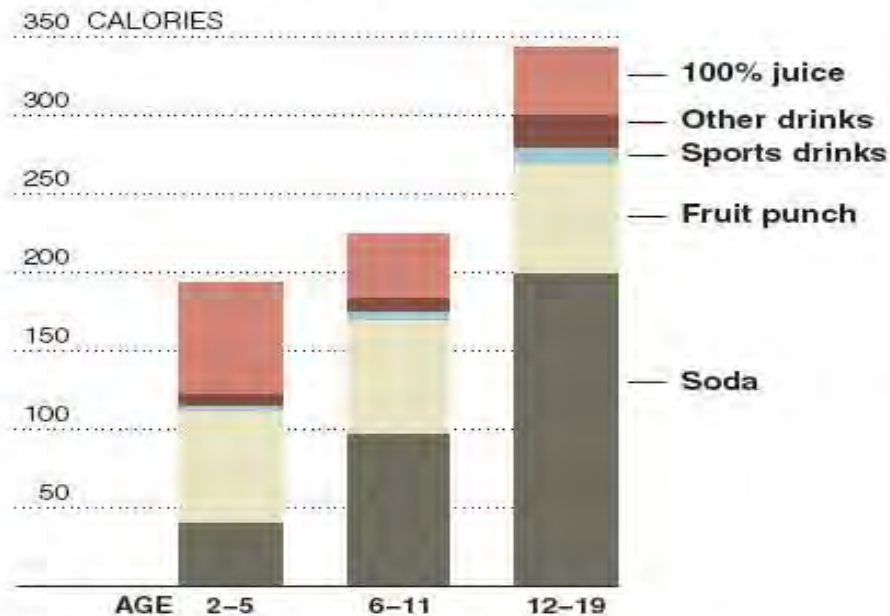
The New York Times



Sugar It's not addictive the way nicotine is, but we drink too much of it.

Drinking Sugar

Per capita daily caloric intake of sugar-sweetened beverages by younger Americans:



Sources: Pediatrics (data from 1999-2004); Robert Wood Johnson Foundation

RECOVERY
FROM
ADDICTION

Current — Treatment — Strategies



- Blame the Patient
- Diet
- Tapes, Books, Classes
- Exercise
- Detoxification & Abstinence
- Take Drugs of Abuse or Related Prescribed Medications
- Surgery
- All the above...and again

No Medications ?



- [A recent study](#) conducted partly by the federal [Centers for Disease Control and Prevention](#) estimated that treating obesity and diseases caused by it cost as much as \$147 billion in 2006, or 9 percent of all health care spending.
- Americans spent an estimated \$59 billion last year fighting fat — on weight-loss programs, special foods, low-calorie soft drinks, appetite suppressants, gym memberships, [diet](#) books, exercise videos, even stomach-clamping surgery.
- Diet and Exercise , relapse, and more diet and exercise and overall failures are typical as Americans have become more and more obese and diabetic.
- Less than 1 percent of the nearly \$60 b spent, as estimated by the research firm Marketdata Enterprises, was spent on prescription drugs.
- Despite years of research effort — and haunted by diet drugs that proved dangerous, like fen-phen in the 1990s — the pharmaceutical industry has not made meaningful progress in combating [obesity](#), one of the nation's biggest and costliest health problems.
- The still-investigational drug is lorcaserin -- a combination of benzazepine and hydrochloride, two neurological agents. **Lorcaserin is a selective 5-HT_{2C} receptor agonist, working through the serotonin system, which regulates appetite, mood, and motor behavior.**
- **Two other investigational obesity drugs target the dopamine reward system -- Contrave, which is a combination of bupropion and naltrexone, and Qnexa, which combines phentermine and topiramate.**
- **In 2010 Gene Jack Wang called the new medications "a bright light for the treatment of obesity."**
- [Arena Pharmaceuticals](#), [Orexigen Therapeutics](#) and [Vivus](#) — plan to apply in the coming months for regulatory approval of anti-obesity drugs that could reach the market in late 2010 or in 2011.

RECOVERY
FROM
ADDICTION



PORTION CONTROL



OXYMORON

RECOVERY
FROM
ADDICTION

1900
Hershey's



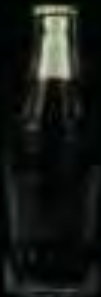
2 oz
297 calories



7 oz
1,000 calories

...AND THE REAL

1916
Coca-Cola



6.5 fluid oz
79 calories



16 fluid oz
194 calories

1954
Burger King



2.8 oz
202 calories

2004



4.3 oz
310 calories

1980s
Movie popcorn



3 cups
174 calories



21 cups (buttered)
1,700 calories

1955
McDonald's



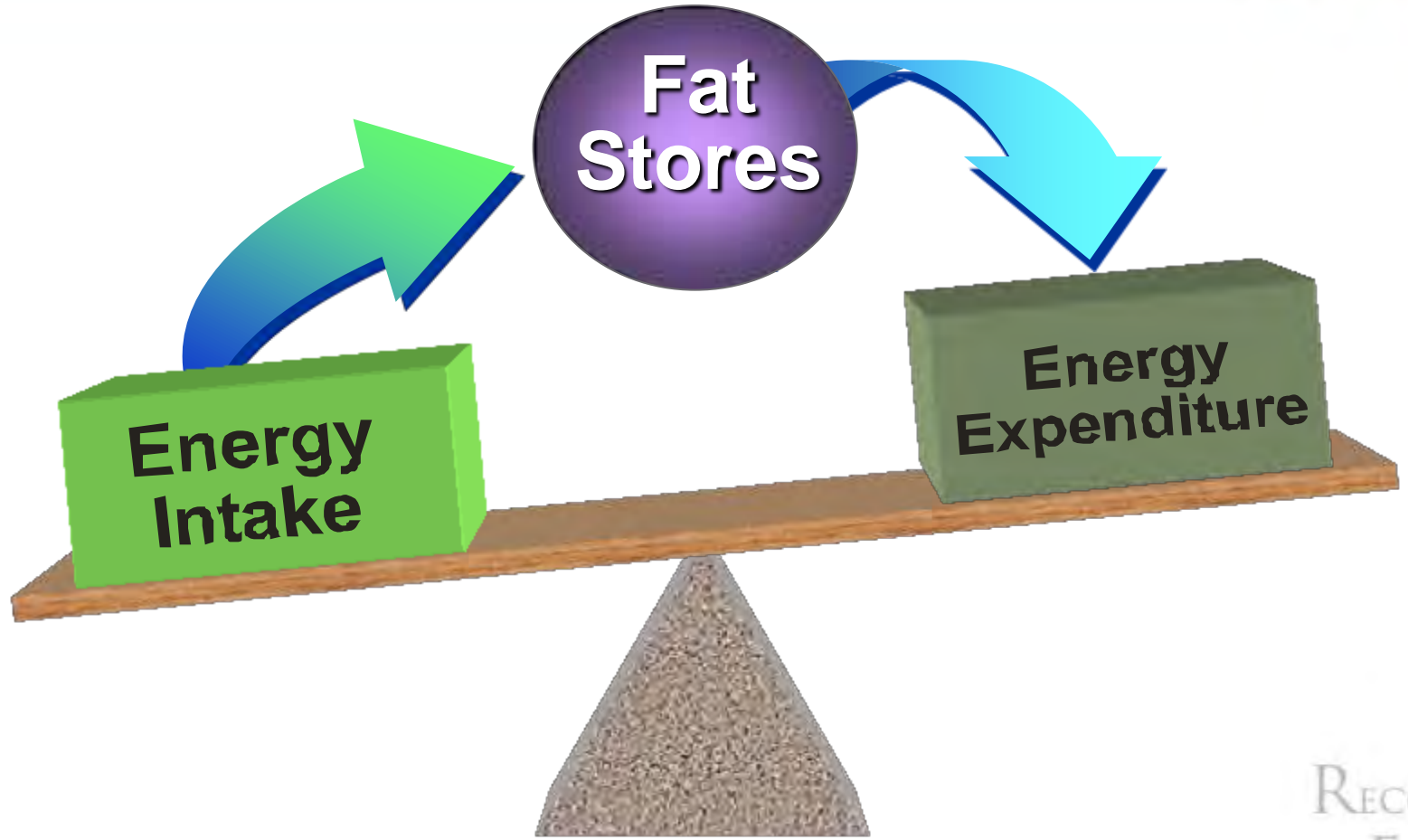
2.4 oz
210 calories



7 oz
610 calories



Obesity Is Caused by Long-Term Positive Energy Balance



Work on Portions



- Plate Size
- Food Labels
- Bariatric Surgery
- And So On...



"I shouldn't, but I'm going to have the garbage."

No Energy Expended



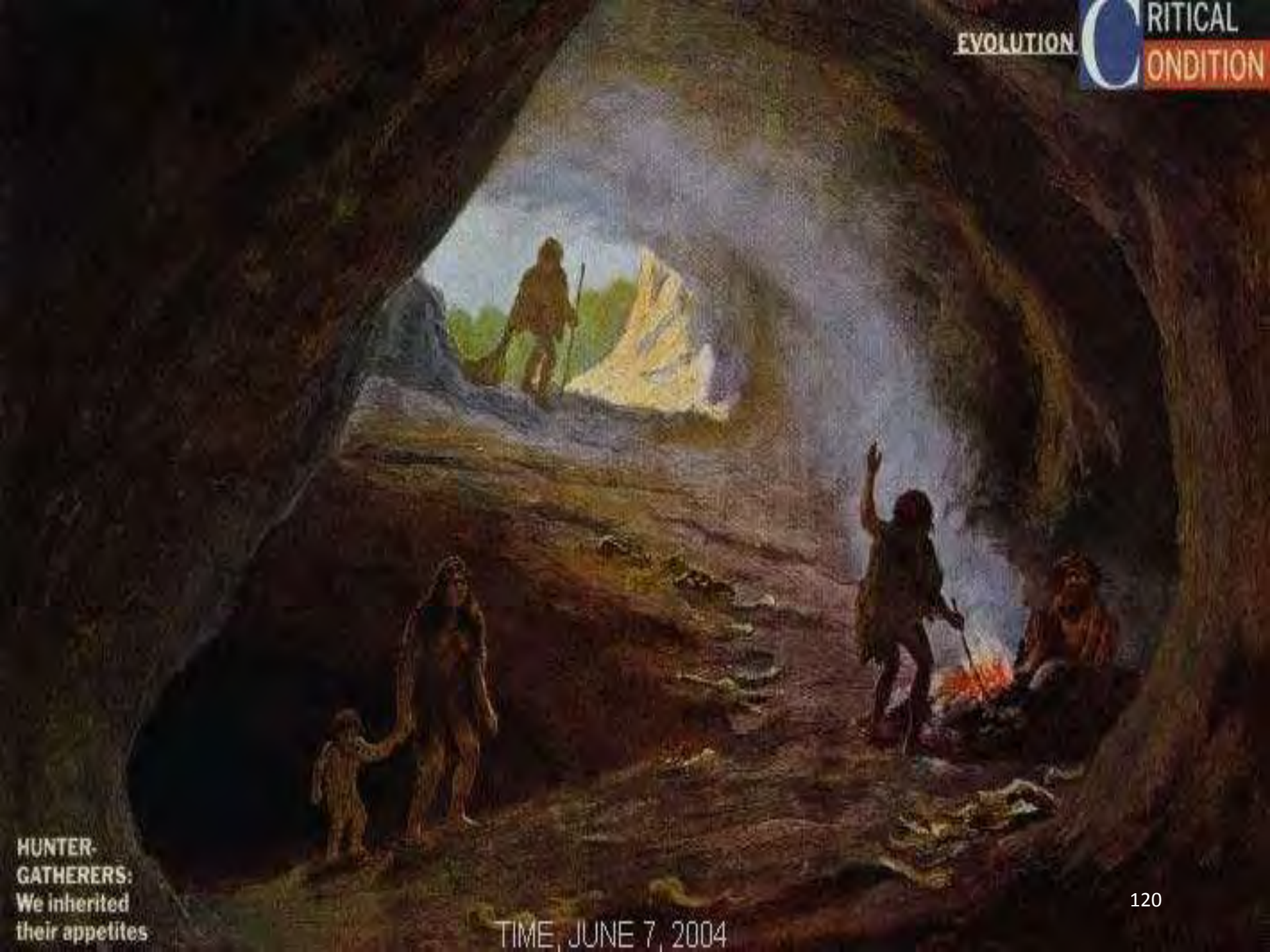
No Exercise

RECOVERY
FROM
ADDICTION

Change Our Lives To Make Exercise Fit Better Into Them



RECOVERY
FROM
ADDICTION



HUNTER-GATHERERS:
We inherited
their appetites

TIME, JUNE 7, 2004

HUNTING CIRCA 2010



RECOVERY
FROM
ADDICTION

Moderate Exercise Yields Big Benefits



Moderately strenuous exercise, about 30 minutes a day, can lead to enormous benefits in terms of your mood, health, weight and the ability to live an independent and fulfilling life. The exercise doesn't need to be athletic or difficult. Studies have shown that simply walking at a brisk pace for 30 minutes or more on most days can lead to significant health improvements. Add simple strengthening exercises two or three times a week and the benefits are even greater.

Lower blood pressure: A reduction of 5 to 10 millimeters of mercury (mm Hg) is possible. In some cases, that's enough to prevent or reduce the need for blood pressure medications.

Improve cholesterol: Exercise often increases the concentration of high-density lipoprotein (HDL or "good" cholesterol in the blood), especially when accompanied by weight loss. Exercise also helps reduce triglyceride levels.

Prevent or manage type 2 diabetes: Exercise helps insulin work better, lowering blood sugar.

Manage weight: Coupling exercise with a healthy diet is the best way to shed fat and maintain a healthier body composition.

Prevent osteoporosis: Exercise may increase bone density and protect against bone mass decline, especially if weight-bearing activities are involved.

Prevent cancer: Exercise has been shown to strengthen the immune system, improve circulation, reduce body fat and speed digestion. Each has a role in preventing cancer, particularly cancers of the colon, prostate, uterine lining and breast.

Maintain mental well being: Exercise may help reduce stress, improve mild-to-moderate depression and anxiety, improve sleep and boost moods.

Increase energy and stamina: A lack of energy often results from inactivity, not age.

Mayo Clinic
200 First St. SW
Rochester, MN 55902
United States
<http://www.mayoclinic.com>

RECOVERY
FROM
ADDICTION

EXERCISE



It is an employee perk to have a parking spot next to the Office

Prescribe Exercise



RECOVERY
FROM
ADDICTION

EXERCISE in Greenwich



• CANINE CONSTITUTIONAL



The Herald-Examiner

A brisk walk in the park keeps Marty II in shape between dog shows. His owner, Columbus resident Cathy Stumbo, got up early to give her 3-year-old Doberman his regular workout. They typically log 20 miles in Berliners Park.

RECOVERY
FROM
ADDICTION

Tell Patients to go to the GYM !



RECOVERY
FROM
ADDICTION



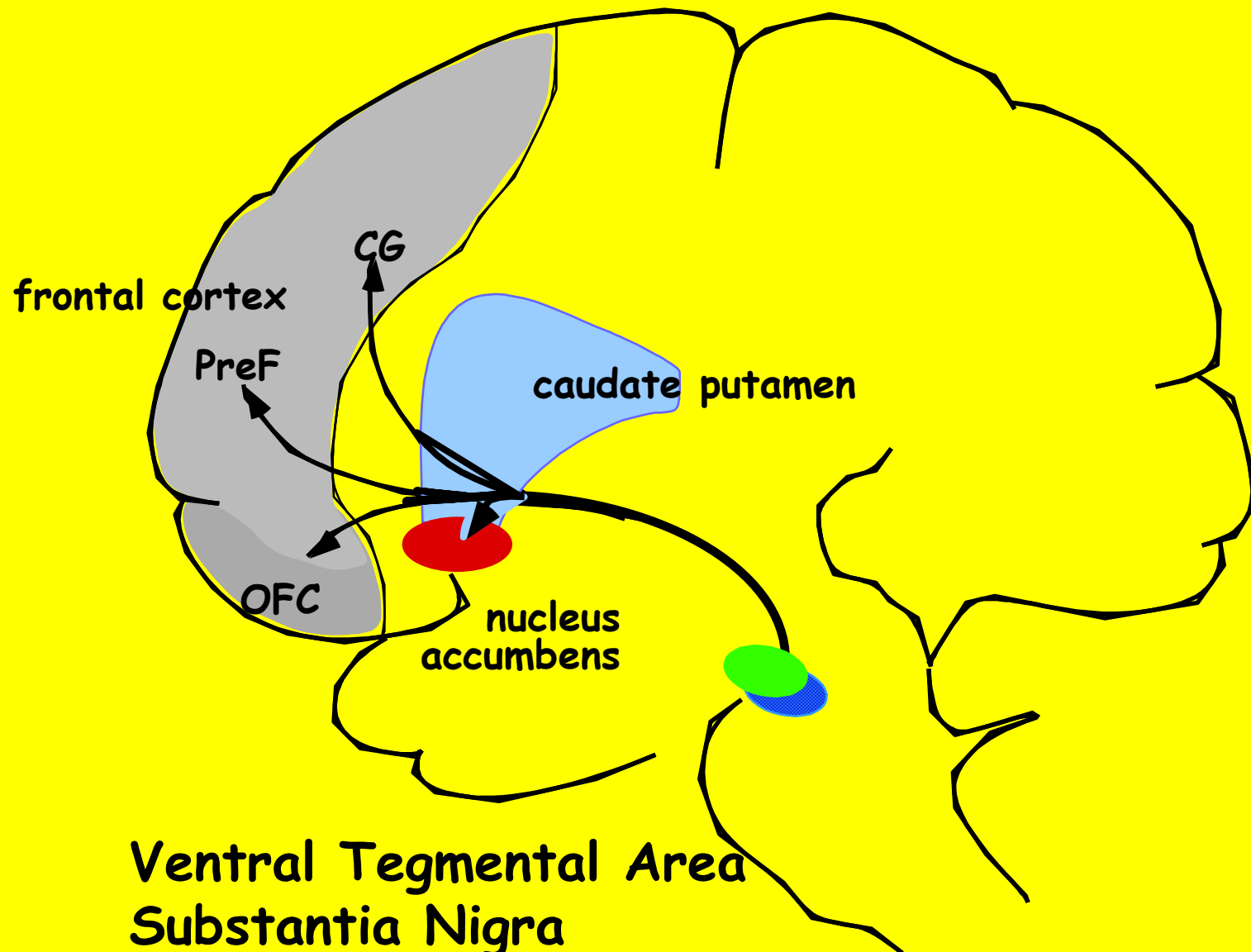
RECOVERY
FROM
ADDICTION

Develop New Treatments and Theories Based on Attachment & Addictions

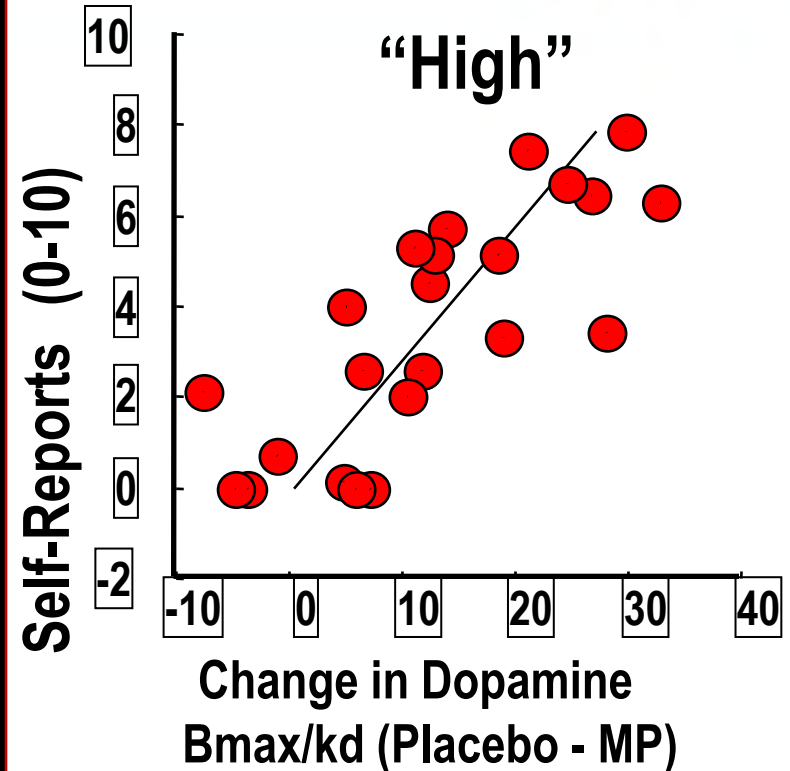
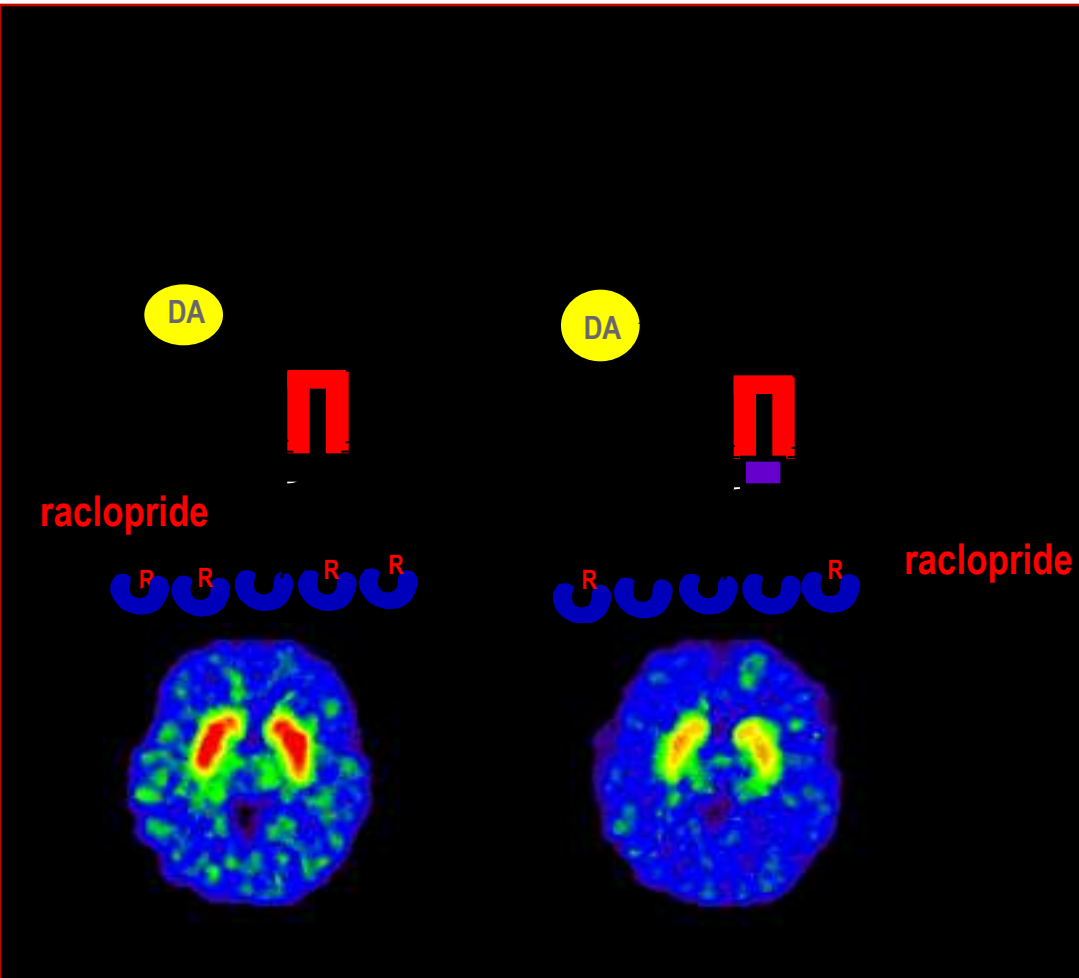


RECOVERY
FROM
ADDICTION

BRAIN DOPAMINE SYSTEM



DA and Drug Reinforcement



DA initiates and maintains responses to salient stimuli such as drugs

RECOVERY FROM ADDICTION

Most drugs of abuse can increase extracellular dopamine in the nucleus accumbens



Ethanol

Nicotine

Amphetamine (speed)

Cocaine (crack)

Phencyclidine (angel dust)

Heroin

Morphine

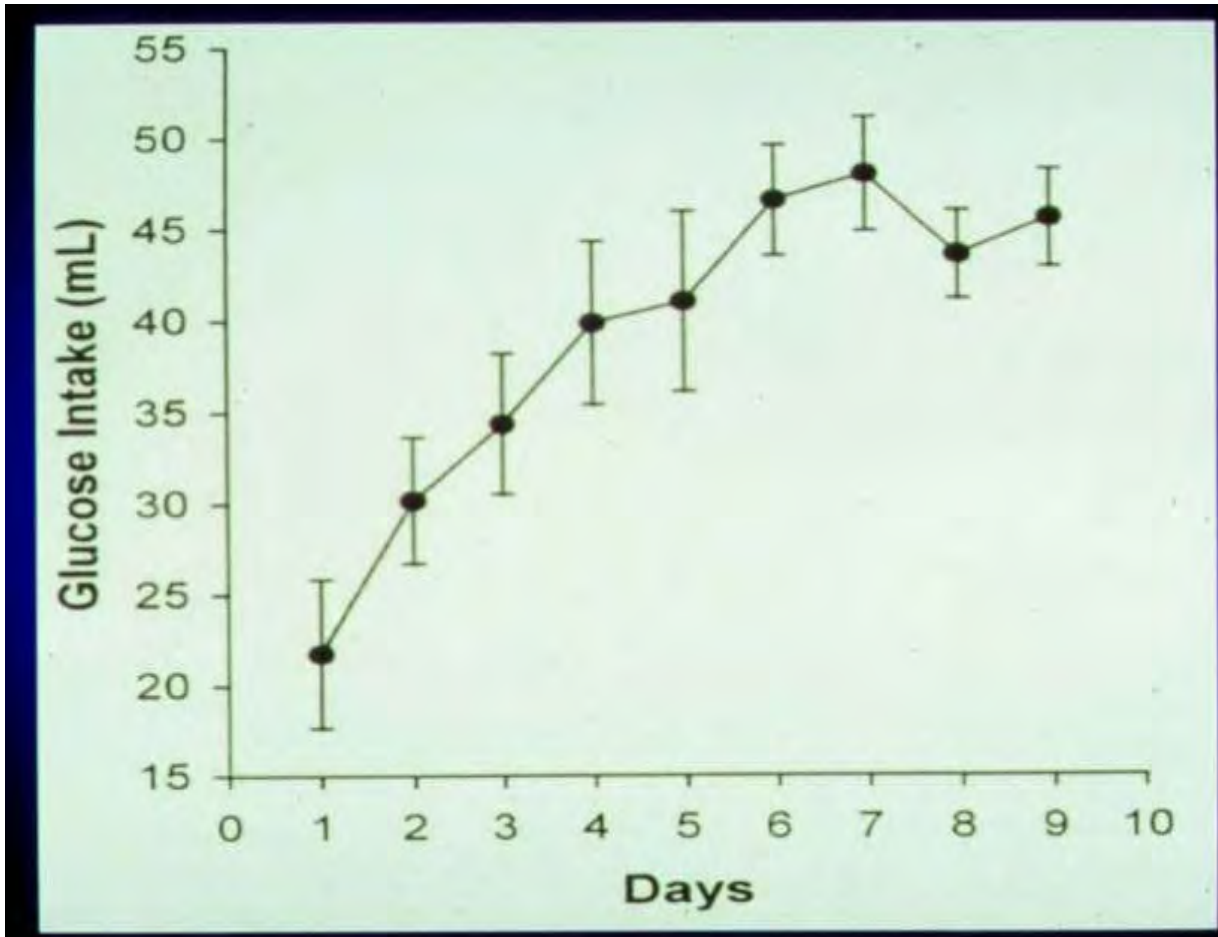
Not Valium (an exception to the DA rule)

Can food be like a drug of abuse?



RECOVERY
FROM
ADDICTION

Access to sugar (25% glucose) leads to escalating intake



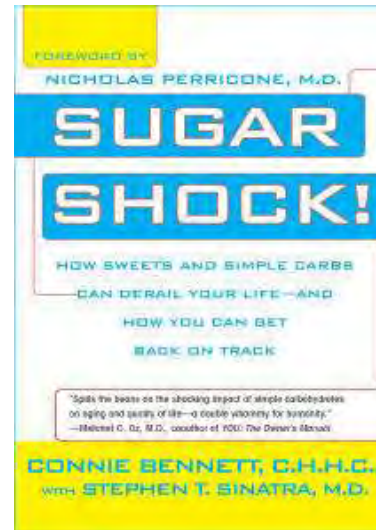
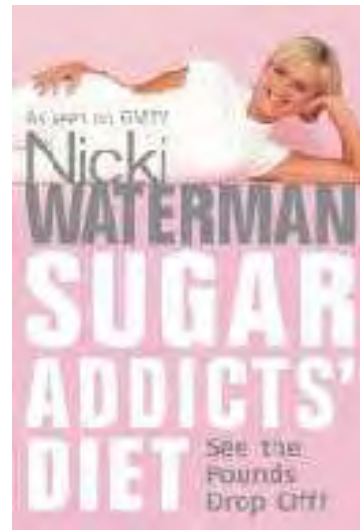
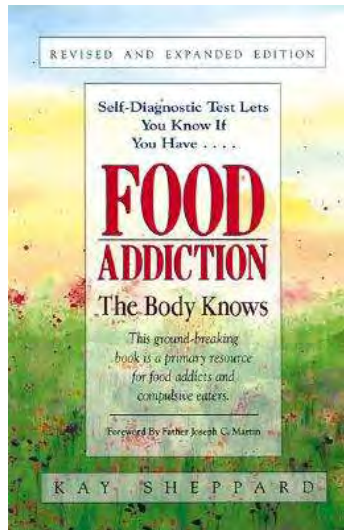
Avena and Hoebel, 2009

RECOVERY
FROM
ADDICTION

Why sugar?



Some people claim they can be addicted to food, particularly sugar.



RECOVERY
FROM
ADDICTION

Evidence of sugar dependence so far.....

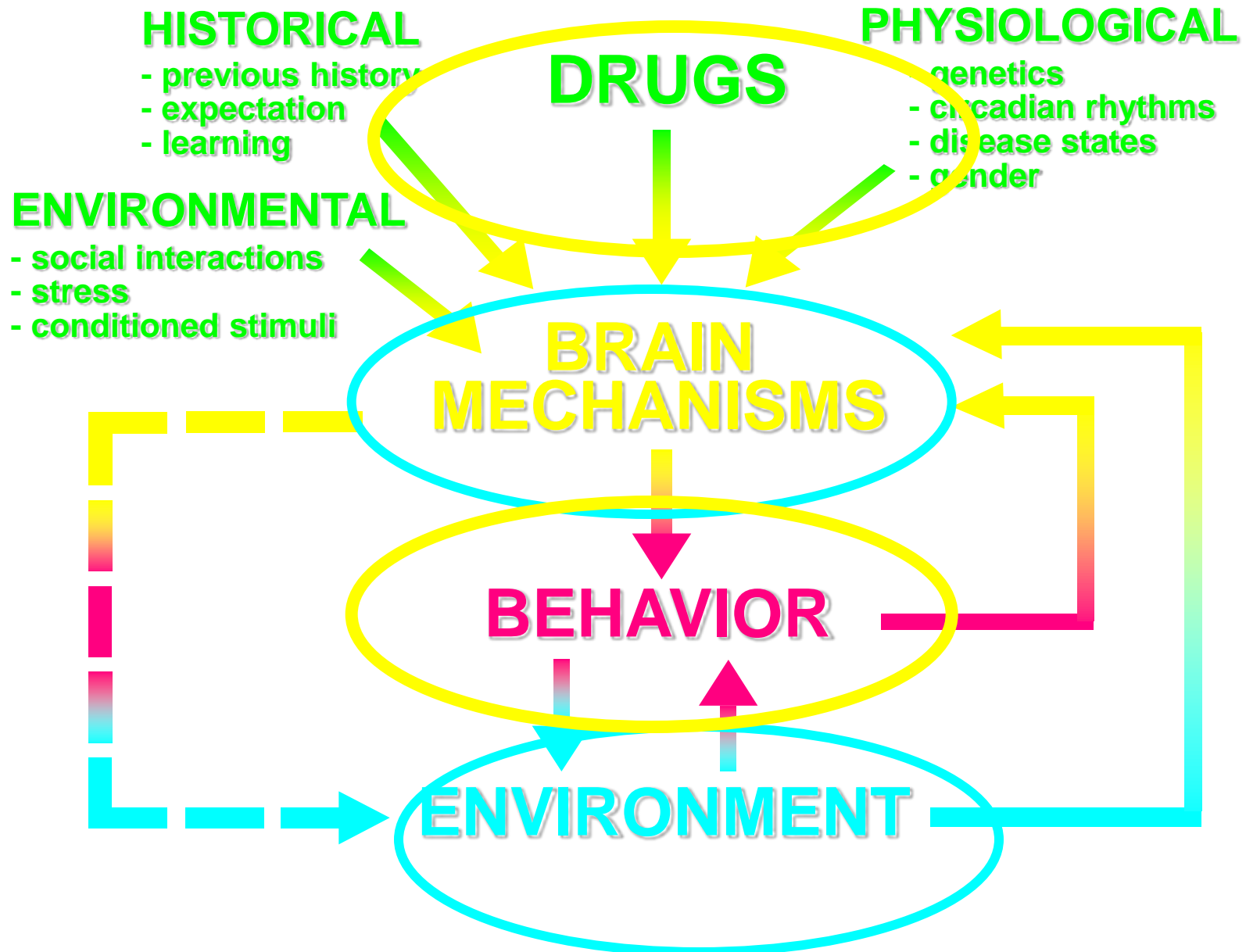


- ***Bingeing*** on sugar during the first hour of access, with ***escalation*** of daily intake (Colantuoni et al., 2001)
- ***Brain changes***: increased mu and D₁ receptor binding, increased D₃ receptor mRNA in the NAc and decreased D₂ binding in the striatum (Colantuoni et al., 2001, Spangler et al., 2004)
- ***Withdrawal***: both behavioral and neurochemical signs such as anxiety, depression and ACh release with low DA (Colantuoni et al., 2002)
- ***Cross-sensitization*** with amphetamine (Avena and Hoebel, 2003), and augmented ethanol intake (Avena et al., 2003)
- ***“Craving”*** during abstinence that could lead to relapse: the ***“deprivation effect”*** (Avena et al, 2005) and ***“incubation effect”*** (Grimm et al. 2005).

Shall we call this “sugar addiction”?

RECOVERY
FROM
ADDICTION

Drug Addiction: A Complex Behavioral and Neurobiological Disorder



Neurocircuitry of Addiction

George F Koob & Nora D Volkow



- Addiction cycle composed of three stages , each associated with a specific behavior and mediated by a key brain location as focal point.

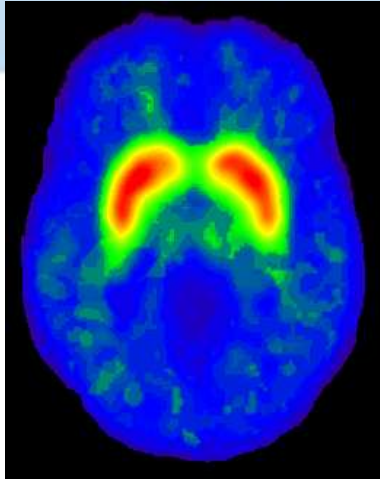
1. Binge = Intoxication
2. Withdrawal = Negative affect
3. Preoccupation/anticipation = Craving

- The transition to addiction involves neuroplasticity in all of these structures that may begin with changes in the mesolimbic dopamine system and then a cascade of neuroadaptations.
- The delineation of this neurocircuitry forms a basis for the search for molecular, genetic and pharmacological neuroadaptations that are key to vulnerability for developing and maintaining addiction.

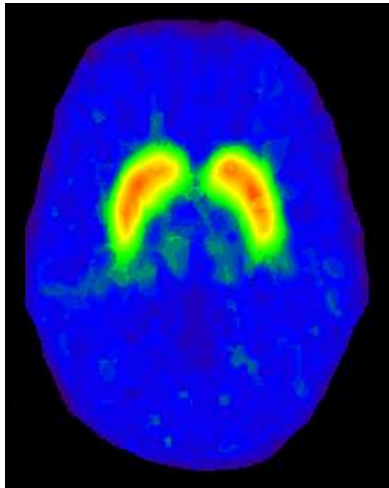
Neuropsychopharmacology (2010) 35, 217 – 238.

Lower dopamine receptors in obese than in control subjects

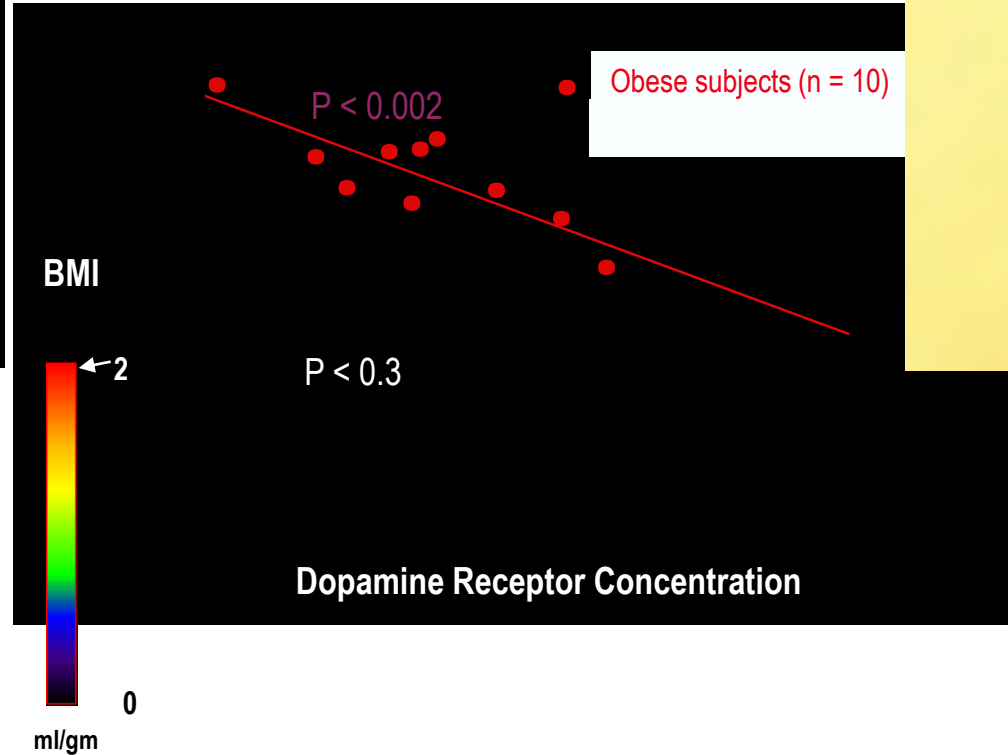
[¹¹C]raclopride



10 Control Subjects
(BMI: 25±3 kg/m²)



10 Obese Subjects
(BMI: 51±5 kg/m²)

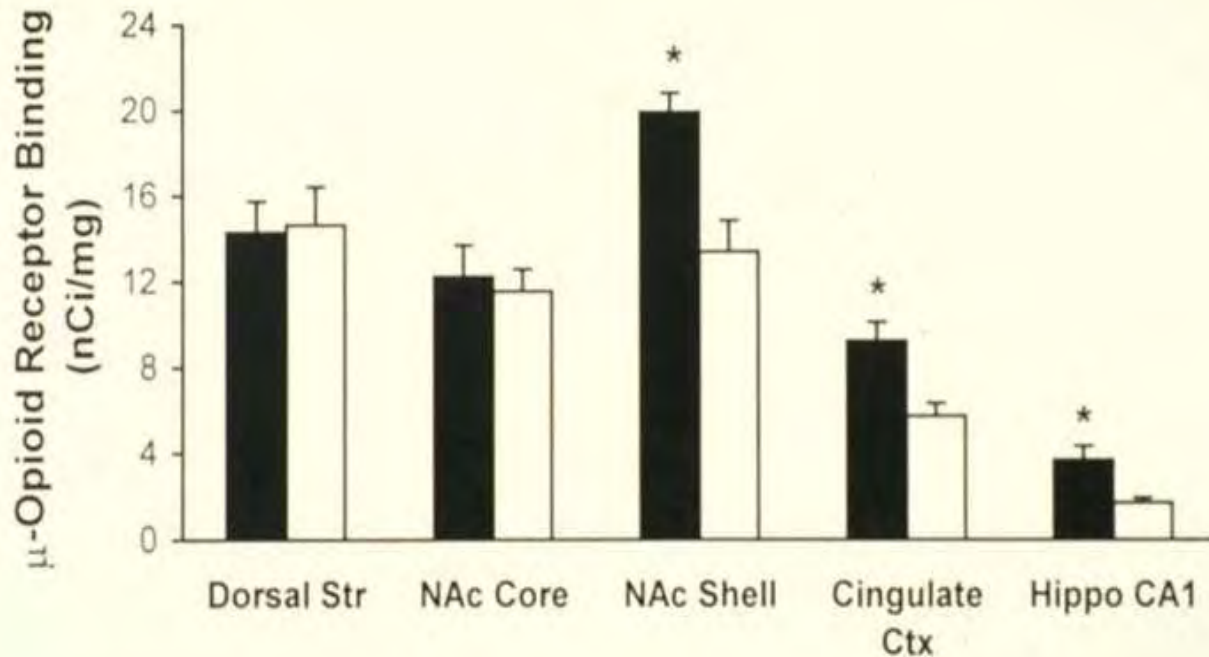


Dopamine modulates motivation and reward circuits and hence dopamine deficiency in obese subjects may perpetuate pathologic eating as a means to compensate for the decrease activation of reward circuits.

Wang et al, Lancet 2001

RECOVERY
FROM
ADDICTION

Increased mu-opioid receptor binding in the accumbens shell



Avena and Hoebel, 2009



What is an addiction?



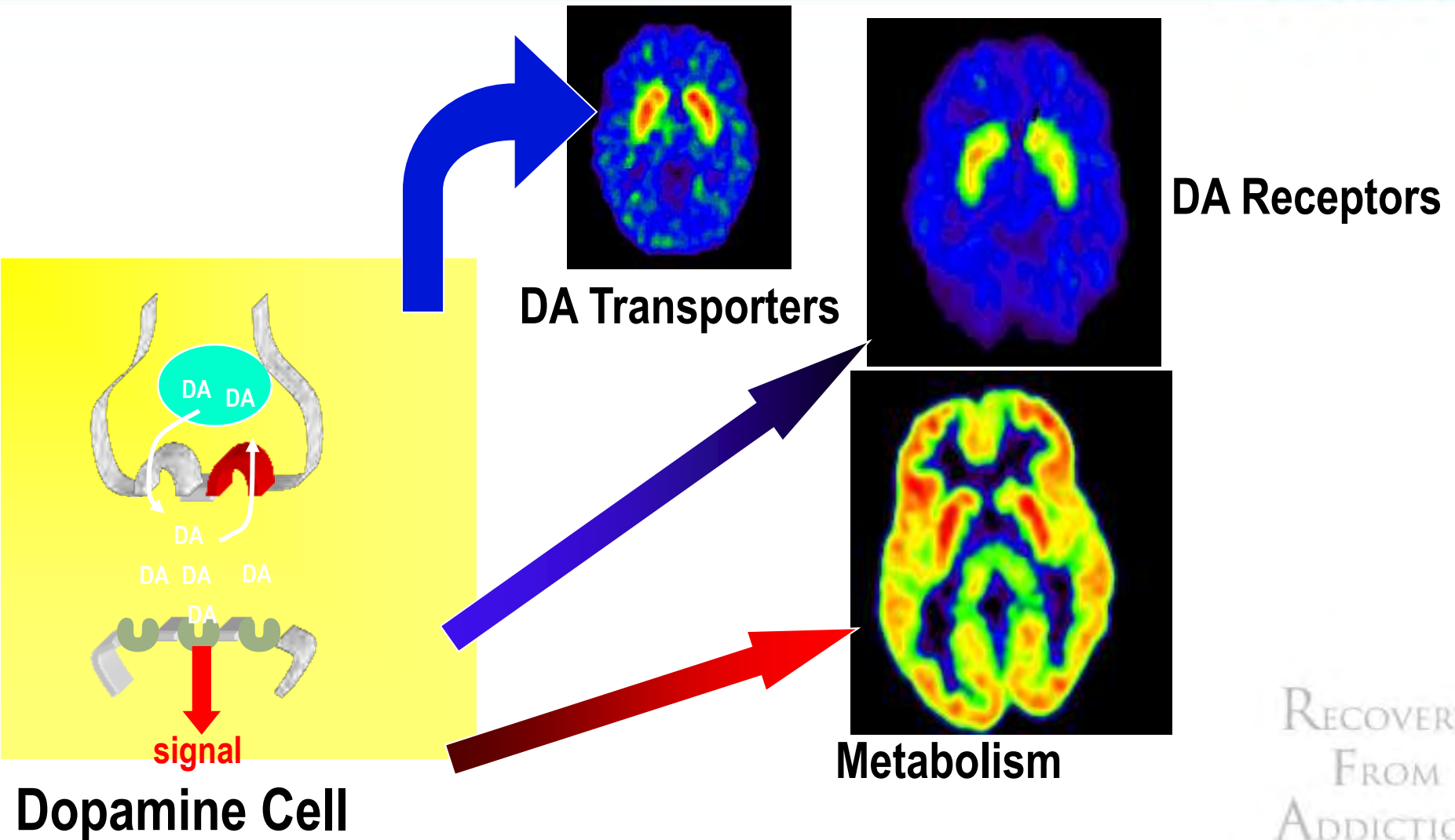
The DSM IV uses behavioral criteria to classify a substance as addictive.

- **Tolerance (escalation)**
- **More use than intended (bingeing)**
- **Withdrawal (aversive aftereffects)**
- **Spends excessive time in acquisition (locomotor sensitization)**
- **Unsuccessful efforts to cut down (incubation during abstinence)**
- **Activities given up because of use and use despite negative effects (gateway to drugs)**

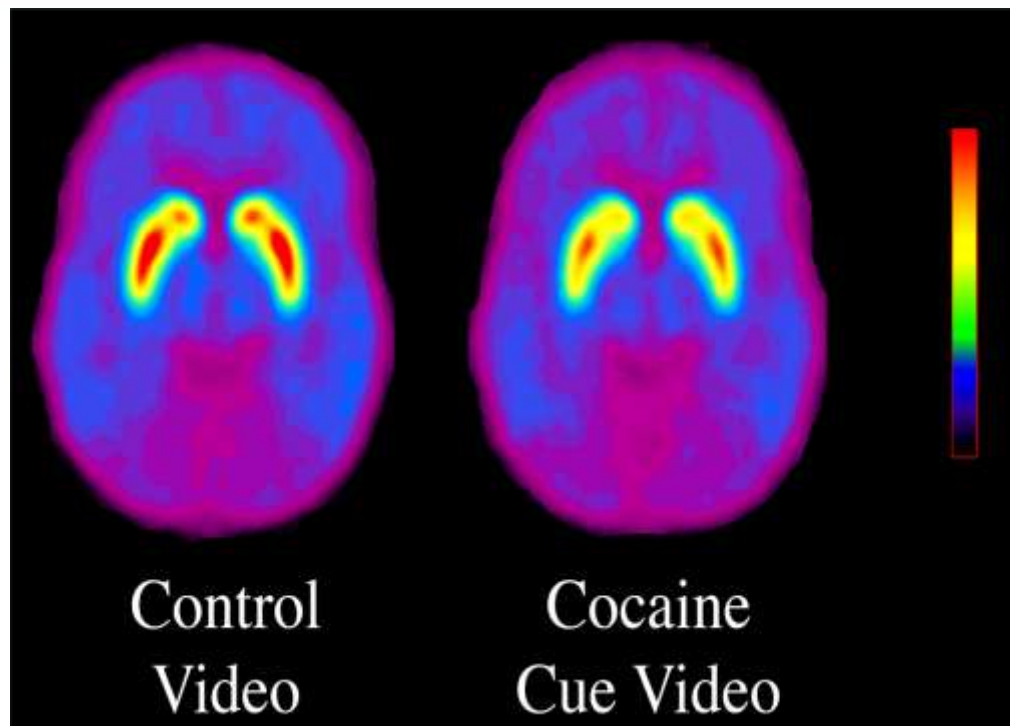
Neuroscientists can add more.

RECOVERY
FROM
ADDICTION

Is Dopamine Involved in Addiction and Obesity?



[¹¹C]Raclopride Binding In Cocaine Abusers (n=18) Viewing a Neutral and a Cocaine-Cue Video



Viewing a video of cocaine scenes decreased specific binding of [¹¹C]raclopride presumably from DA increases

Gambling, Sex, Food...



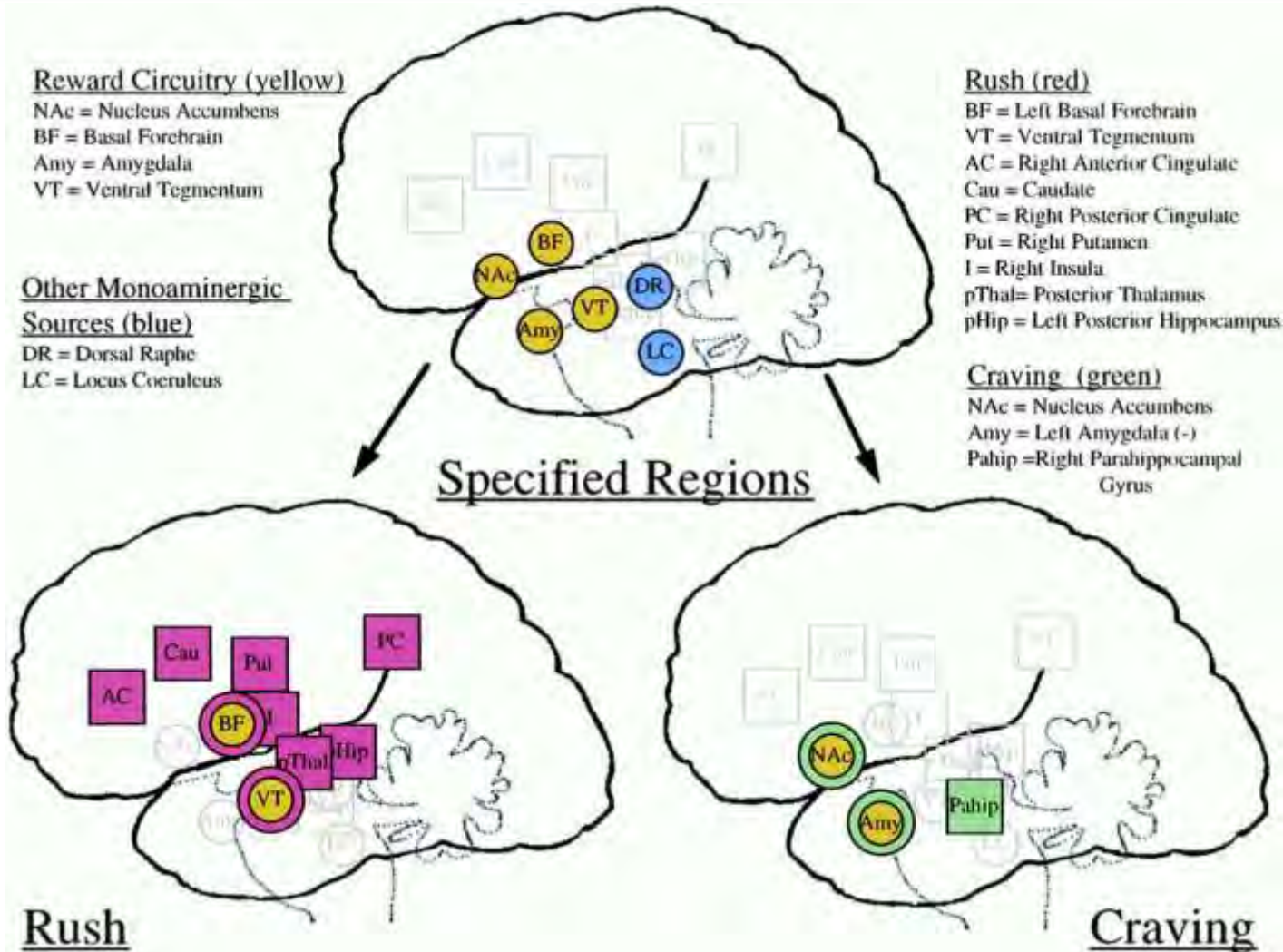
- Behavioral studies show similarities among certain patterns of overeating and other excessive behaviors such as drinking too much alcohol and compulsive gambling. These behaviors activate brain circuitry that involved reward, motivation, decision-making, learning, and memory.
- Some ingredients in palatable food (i.e. sugar, corn oil) can be a substance of abuse and lead to a natural form of addiction.
- Ingestion of sugar induces brain release of opioids and dopamine. In rats, certain conditions (i.e. intermittent, excessive sugar intake) rats can display behavioral and neurochemical changes that resemble those observed in animal models of drug dependence.
- From an evolutionary perspective, animals would benefit from a neural mechanism (circuitry) that supports an animal's ability to pursue natural rewards (food, water, sex), these circuits however sometimes are dysfunctional leading to various types of disorders.

Parkinson's Disease



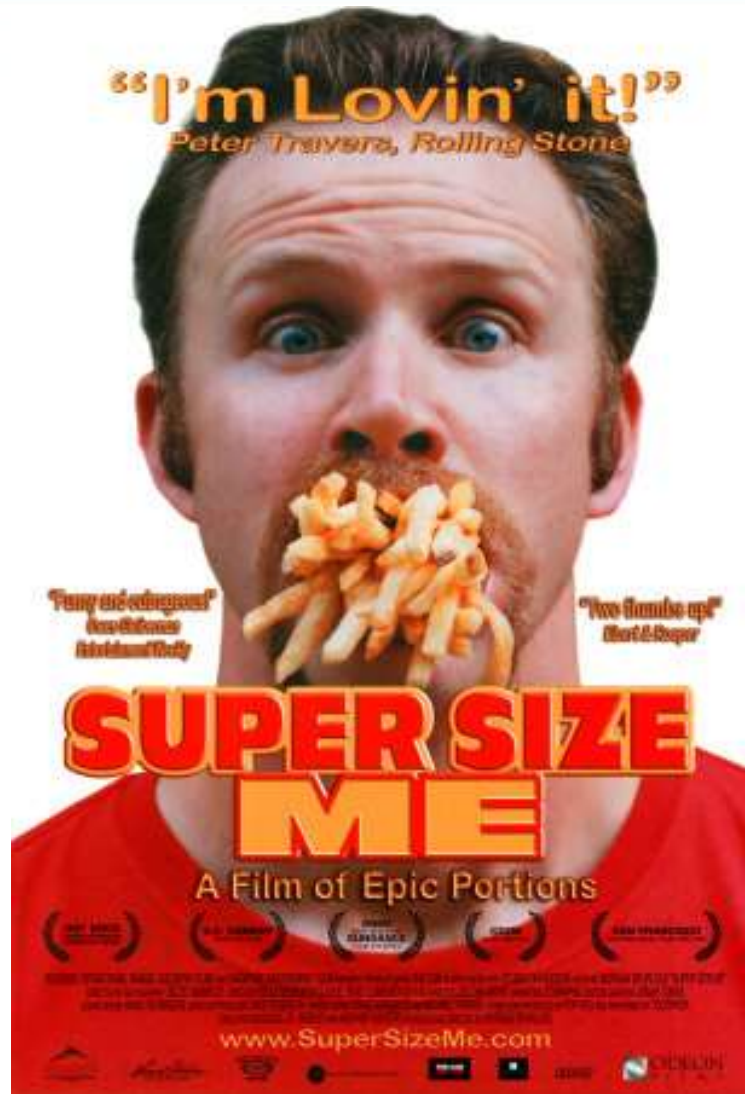
- DA Treatments and Increased :
 - Gambling
 - Sex
 - Eating

Chocolate & Cocaine : fMRI



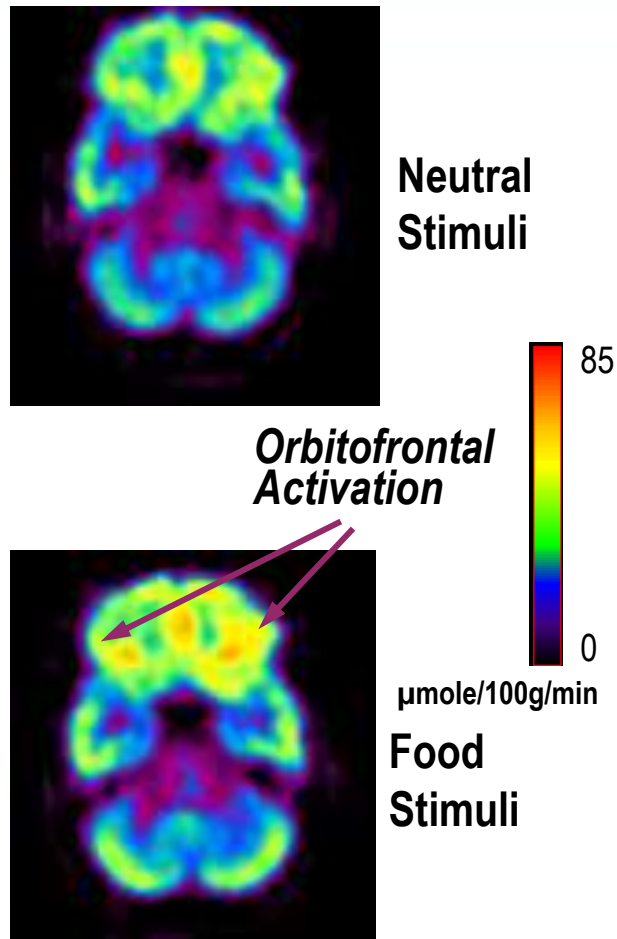
RECOVERY
 FROM
 ADDICTION

Food Addiction and Sugar Addiction: A Brain Disease?

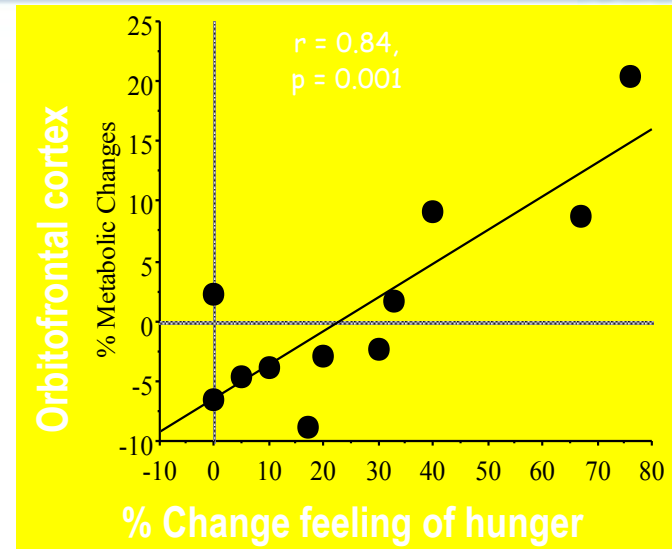


RECOVERY
FROM
ADDICTION

Brain Activation with Food Stimuli



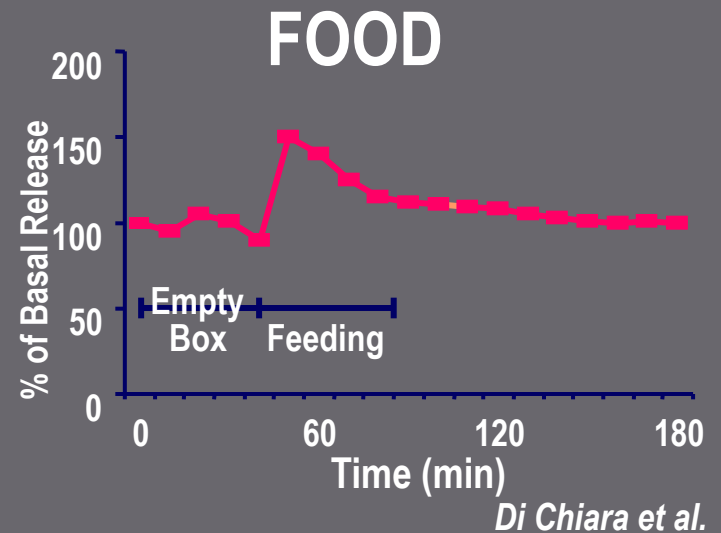
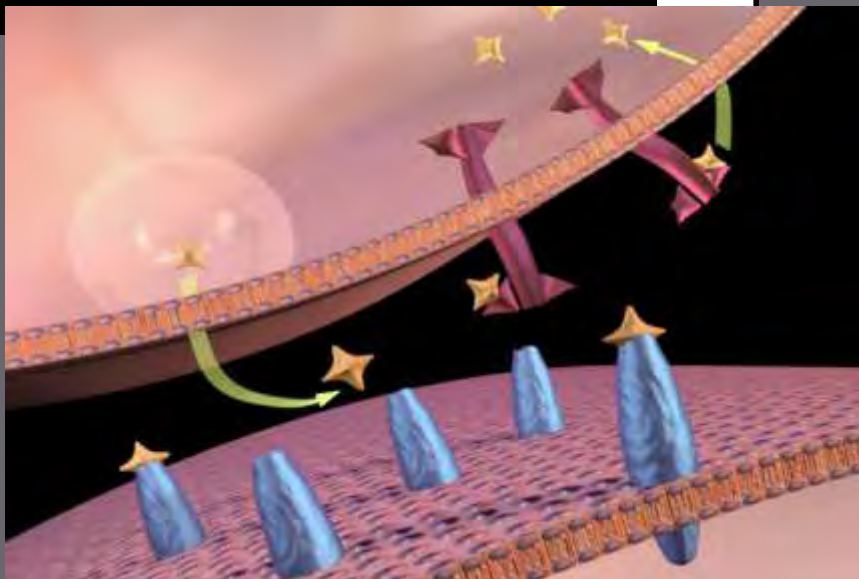
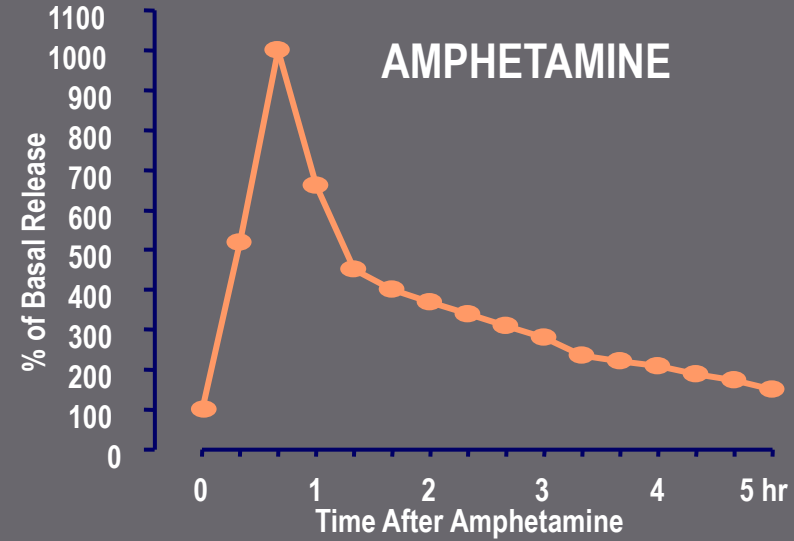
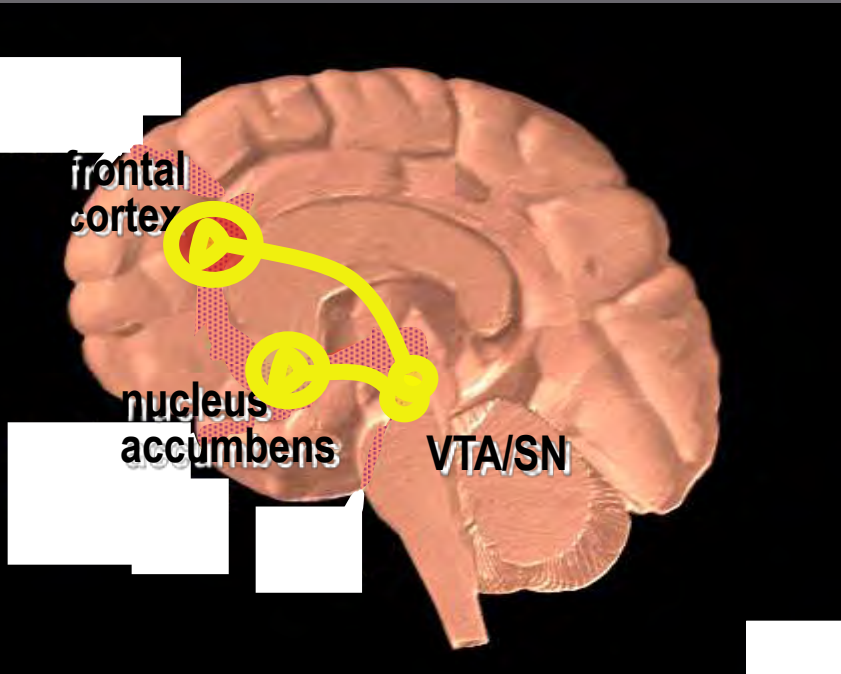
Wang et al, Neuroimage 2004



- The orbitofrontal cortex (OFC), which is in part regulated by DA activity, is a key brain region for controlling and planning behaviours. It also determines the pleasantness and palatability of food.
- The enhanced OFC activation by the food stimulation are likely to reflect downstream DAergic effects and are likely to participate in DA's involvement in the drive for food consumption.

RECOVERY
FROM
ADDICTION

Dopamine Neurotransmission



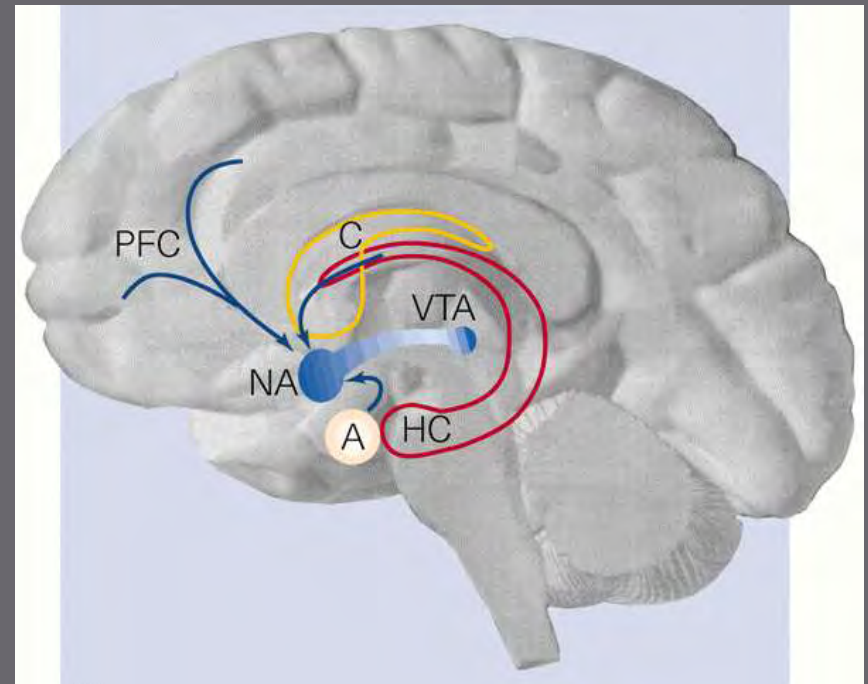
Di Chiara et al.

Brain areas affected by addiction

Prefrontal cortex
Executive function
(e.g. Planning, higher level behavioural control)

- Caudate nucleus (cognitive striatum)
- Nucleus Accumbens (limbic striatum)
- VTA (Dopamine neurons)
- *Memory and emotion*
 - Amygdala -
 - Hippocampus

Orbitofrontal cortex
Evaluation of rewarding or motivational value of stimuli



Banff 2010 Summary



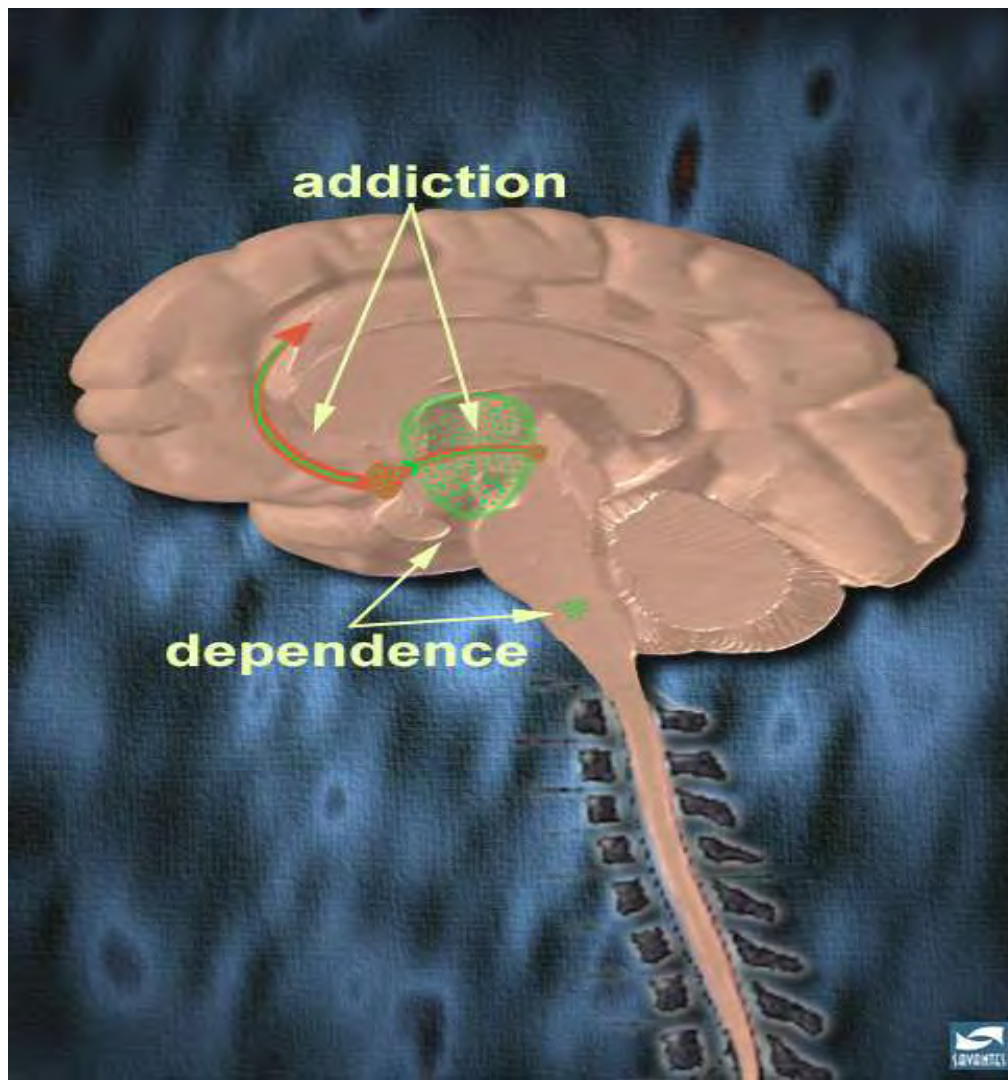
RECOVERY
FROM
ADDICTION

Lesson 1 : Addiction Is Not Withdrawal



- Addiction is pathological attachment
- Desire and motivation to take a drug
- **Self Administration**
- Continued Compulsive Use Despite Extreme Consequences
- Continuous Thinking or Seeking of Drugs Even When They Are Unavailable

Withdrawal Syndromes Do Not Define Drugs of Abuse or Addiction



RECOVERY
FROM
ADDICTION



Diet Switching Can Activate Brain's Stress System & Lead to 'Withdrawal' Symptoms



DHHS says 2/3 of U.S. adults are overweight or obese, costing an estimated \$117 billion in medical expenses and lost productivity. Researchers from The Scripps Research Institute have shown in animal models that cycling between periods of eating sweets and regular food can activate the brain's stress system and generate overeating, anxiety, and withdrawal-like symptoms.

ScienceDaily (Nov. 10, 2009)

RECOVERY
FROM
ADDICTION

Lesson 2: Routes of Administration



- How fast a drug gets to the brain plays a key role in whether it is reinforcing.
- Smoking and iv injection are the most rapid ways to get drugs to the brain.
- Abuse liability is an important issue in the development of therapeutic drugs.



DEA Administrator Jack Lawn Gold awarded for 1st report on crack-1985



RECOVERY
FROM
ADDICTION

Lesson 3: Critical Periods: Age of Initiation and Onset

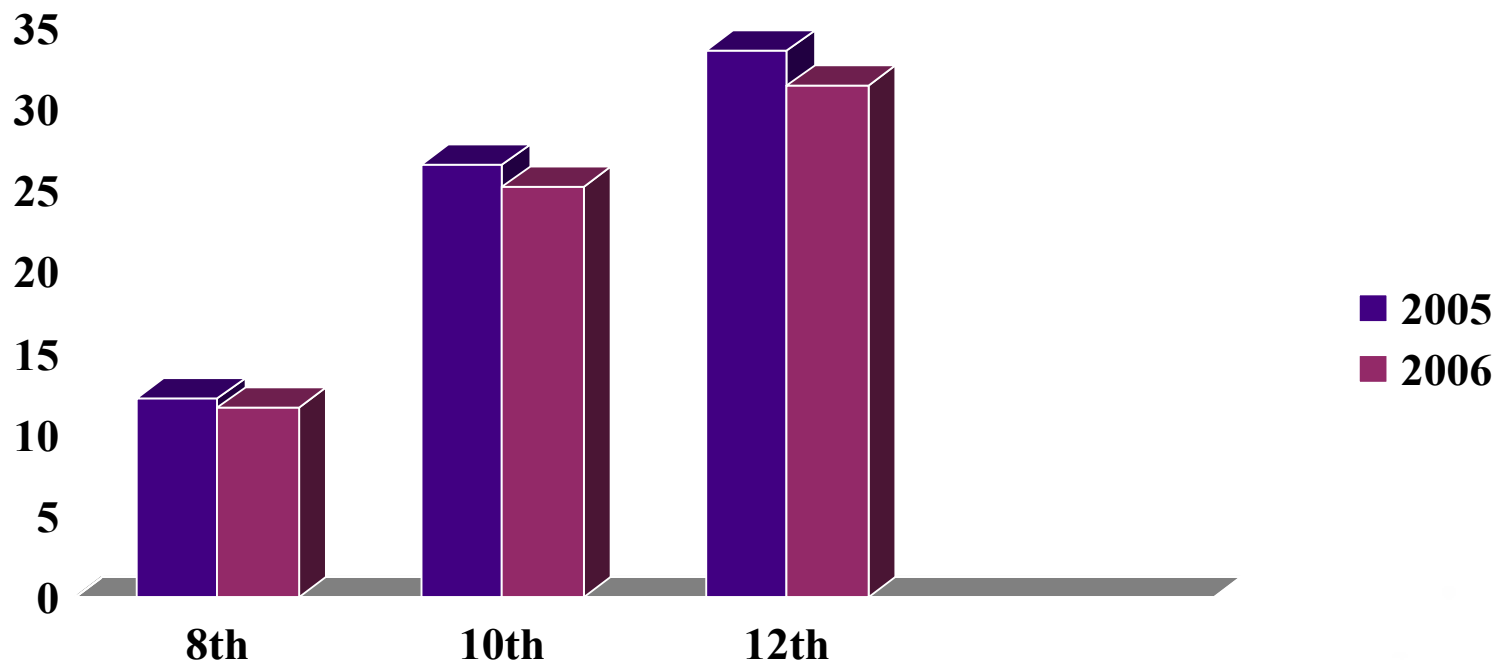


- Languages
 - Music
 - Cigarettes-Smoking
 - Drugs
-
- Age of initiation and onset matters a great deal !

High School Survey



Marijuana Use



Teen Onset of Addiciton(s)



- **Inhaling From Just One Cigarette Can Lead To Nicotine Addiction: Kids Show Signs Of Addiction Almost Immediately**

Science Daily

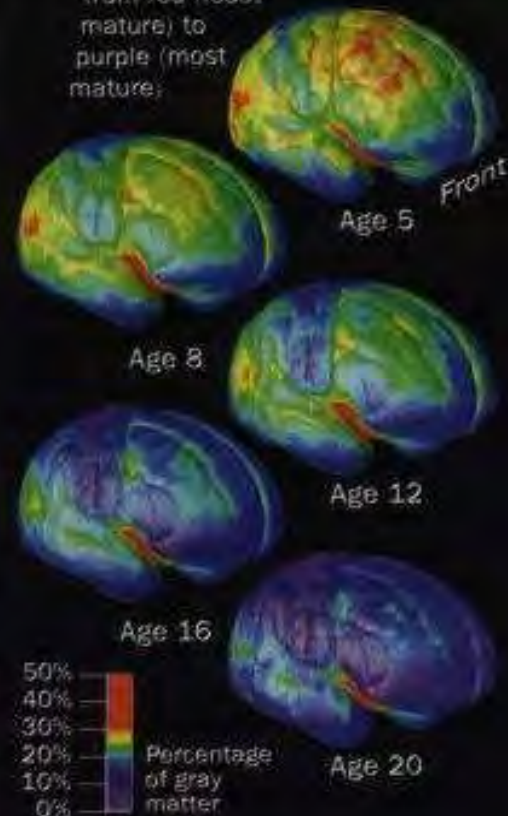
July 6, 2007

A new study published in the Archives of Pediatric and Adolescent Medicine shows that 10 percent of youth who become hooked on cigarettes are addicted within two days of first inhaling from a cigarette, and 25 percent are addicted within a month. The study found that adolescents who smoke even just a few cigarettes per month suffer withdrawal symptoms when deprived of nicotine, a startling finding that is contrary to long-held beliefs that only people with established smoking habits of at least five cigarettes per day experience such symptoms.



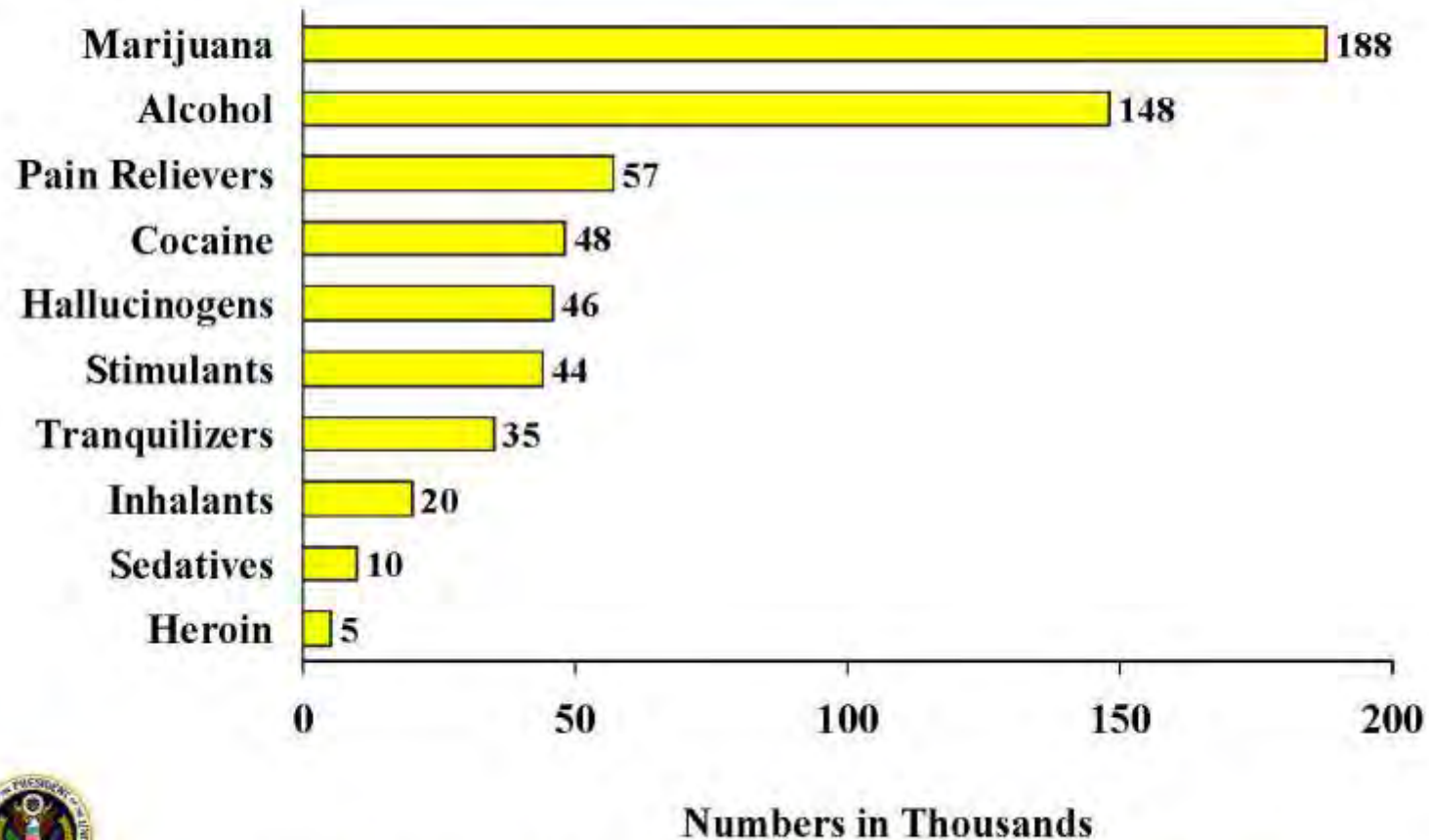
Time-Lapse Brain

Gray matter wanes as the brain matures. Here, 15 years of brain development are compressed into five images showing a shift from red (least mature) to purple (most mature):



RECOVERY
FROM
ADDICTION

Challenge: High Numbers of Youth (12-17 yrs) Treated for abuse/addiction in the Past Year



Source: SAMHSA, 2006 *National Survey on Drug Use and Health* (September 2007).

Drugged Driving, Walking Biking...



RECOVERY
FROM
ADDICTION

Kids, Teenagers and Soft Drinks



Soft Drinks: Sugar Content

Number of Teaspoons of Sugar

	12-oz. Can	20-oz. Bottle	64-oz. Big Cup
Orange Slice	11.9	19.8	63.5
Minute Maid Orange Soda	11.2	18.7	59.7
Mountain Dew	11.0	18.3	58.7
Barq's Root Beer	10.7	17.8	57.1
Pepsi	9.8	16.3	52.3
Squirt	9.5	15.8	50.7
Dr. Pepper	9.5	15.8	50.7
7-Up	9.3	15.5	49.6
Coke Classic	9.3	15.5	49.6
Sprite	9.0	15.0	48.0

Lesson 4: Self Administration Defines Addiction



- Acquired new drive
- Use despite pain and suffering
- Bad or pathological learning
- Intrusive thoughts about the drug called preoccupation



ADDICTED RATS...



- Self administration is the gold standard for assessing the rewarding properties of drugs of abuse. Hijack normal goal directed behavior
- Cocaine self administration despite pain
- Cocaine self administration despite tremendous work required for a dose
- Continued use even when the drug is unavailable
- THC, Alcohol, and Other Drugs Self administered

What are the limitations of animal models for addiction?



Rat or Human Models

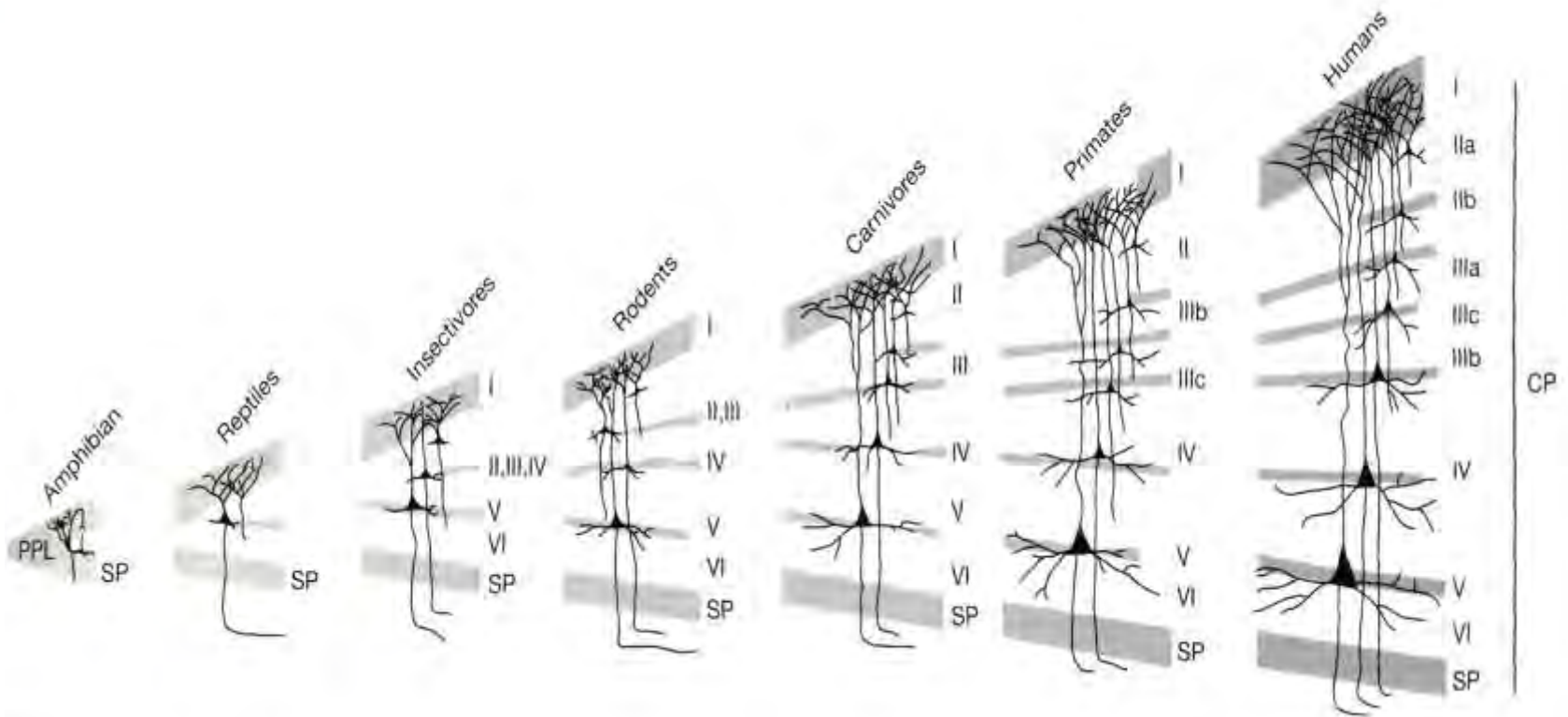


- The National Institutes of Health have announced that they will no longer be using rats for medical experimentation. In their place, they will use attorneys. They have given three reasons for this decision:
 1. There are now more attorneys than there are rats.
 2. The medical researchers don't become as emotionally attached to the attorneys as they did to the rats.
 3. No matter how hard you try, there are some things that even rats won't do.

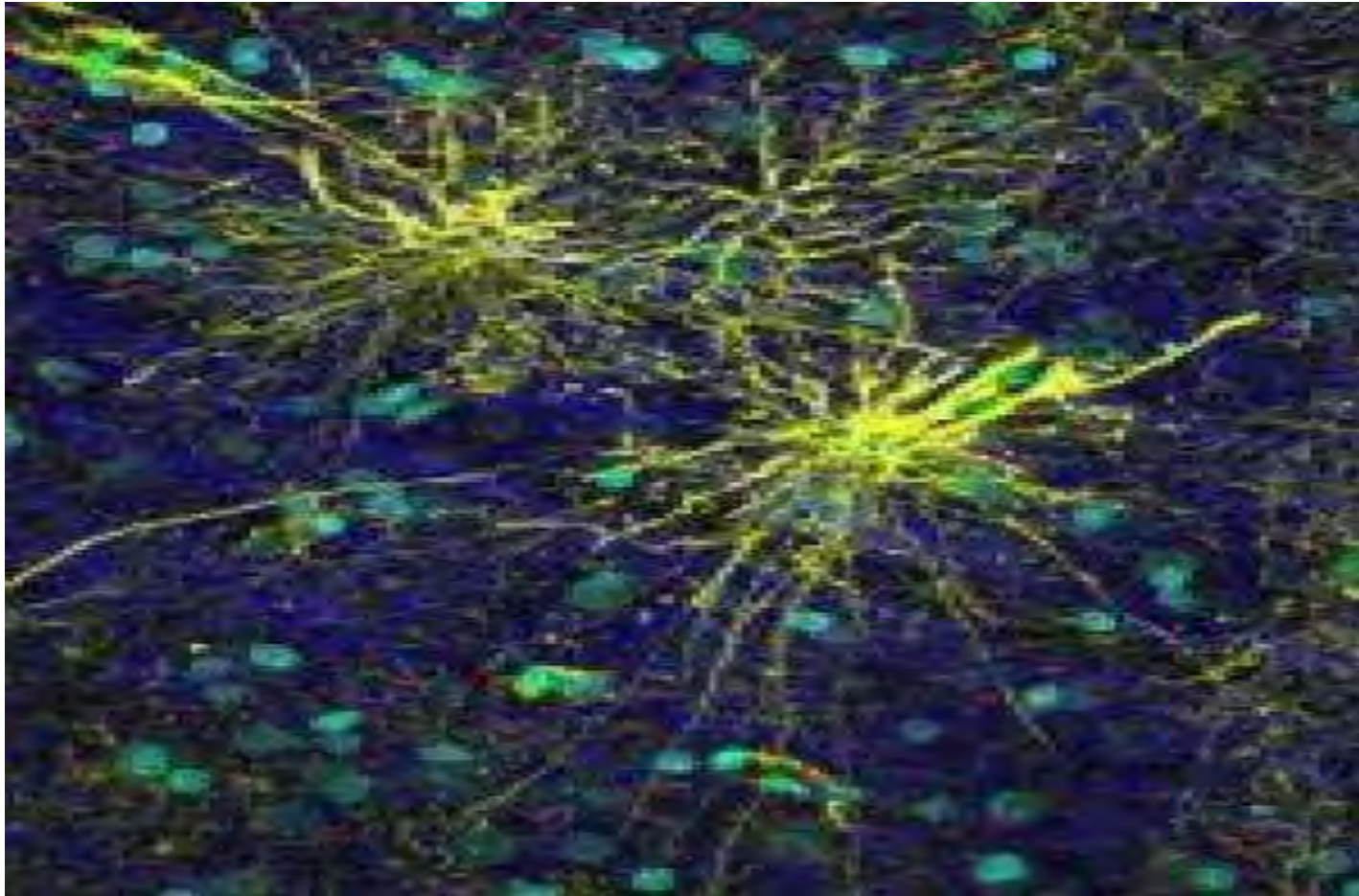


RECOVERY
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ADDICTION

Brain Cell Morphology



What Separates Humans From Mice? Bigger, Faster Astrocytes In Brain



RECOVERY
FROM
ADDICTION

RODENT BRAIN IS MINIMAL



Mouse



Chimpanzee



Human



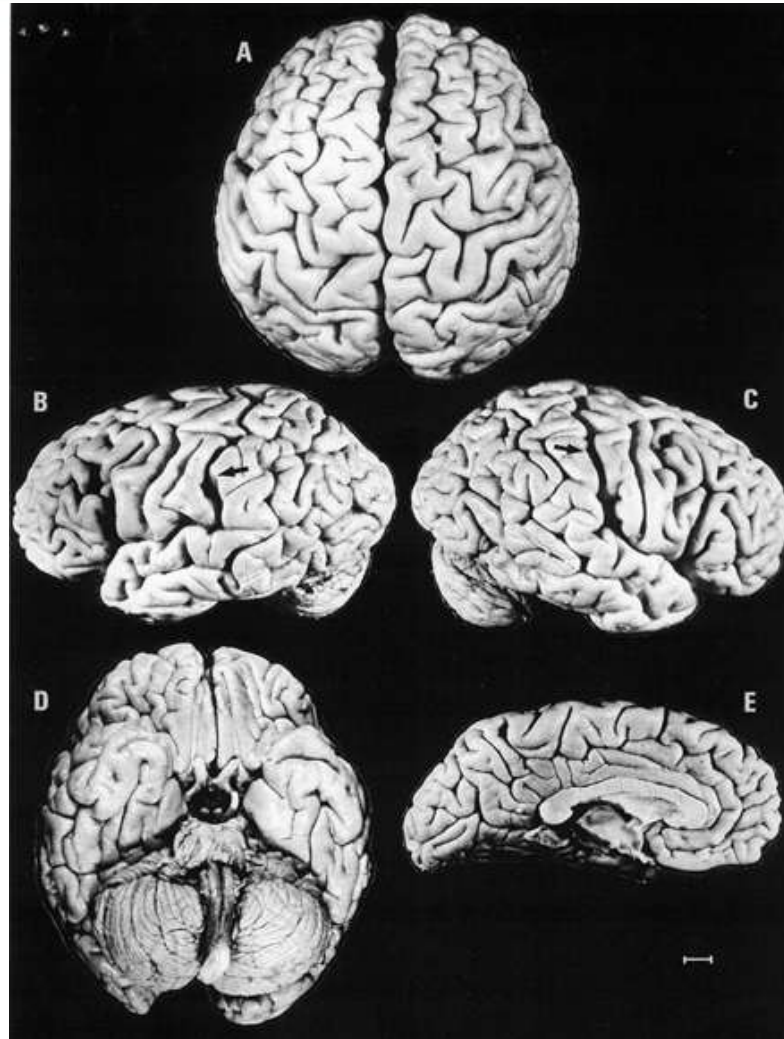
1 cm



RECOVERY
FROM
ADDICTION



**Einstein's brain,
photographed in 1955,
is almost perfectly
round**



RECOVERY
FROM
ADDICTION

Lesson 5: Drugs “Hijack” & Change The Brain



- How ?
- Where ?
- New, —Bad Learning ?



Motivational Toxicity



- Intense motivation is critical in the disease of addiction
- Hierarchy of work-reward disrupted
- Pathological attachment or Fatal Attraction
- Brain is unprepared by evaluation for reward in demand or cocaine
- Drug effects persist — forever: in coded — bad learning” and with brain cell damage and loss too!

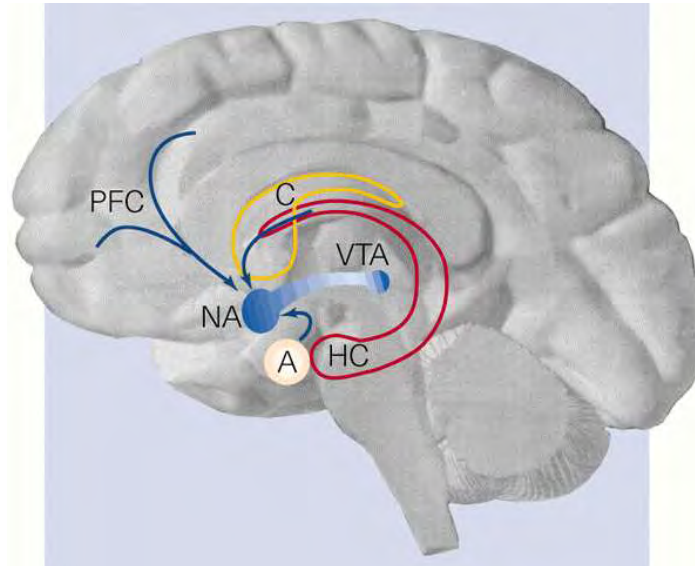
Brain areas affected by addiction



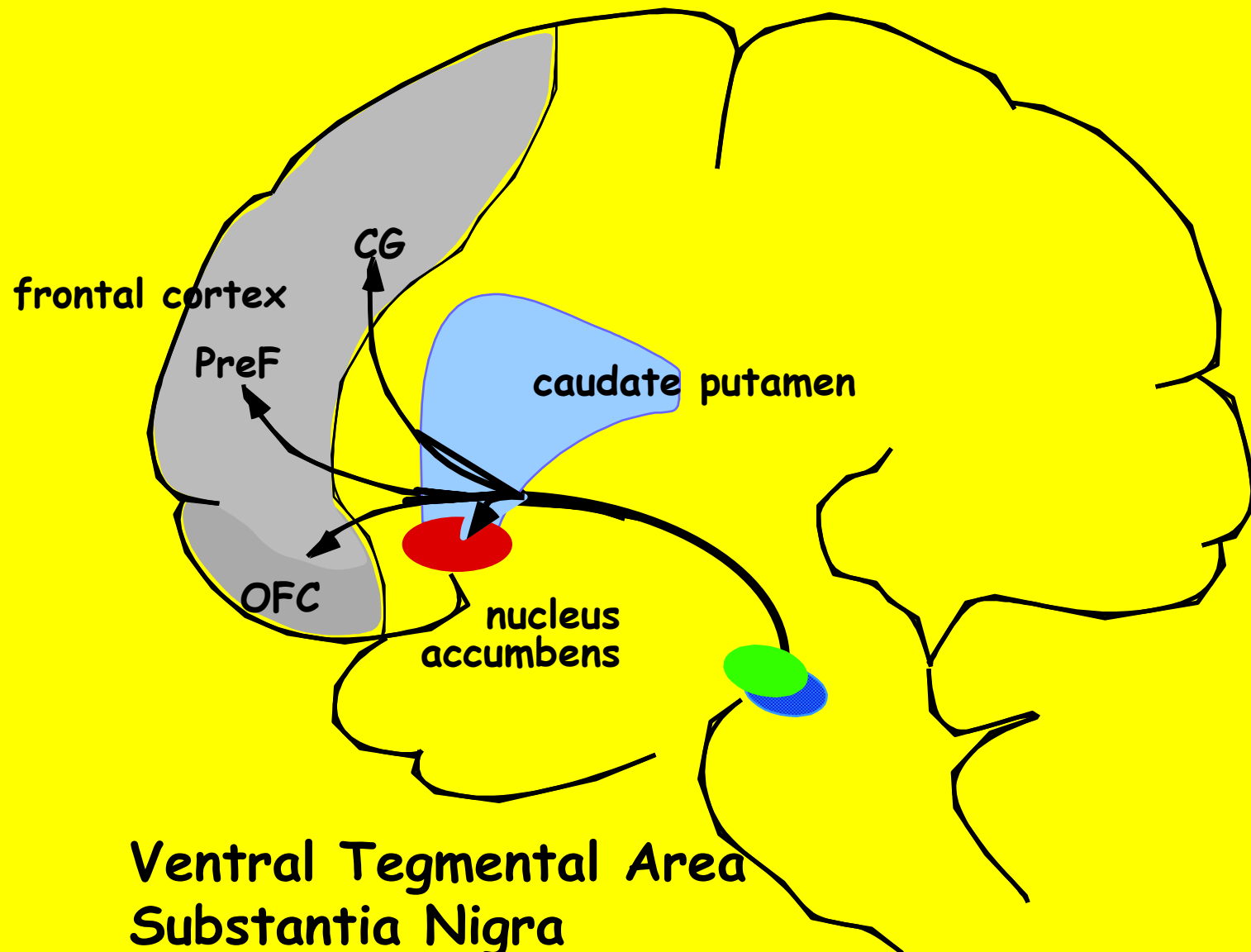
Prefrontal cortex
Executive function
(e.g. Planning, higher level behavioural control)

- Caudate nucleus (cognitive striatum)
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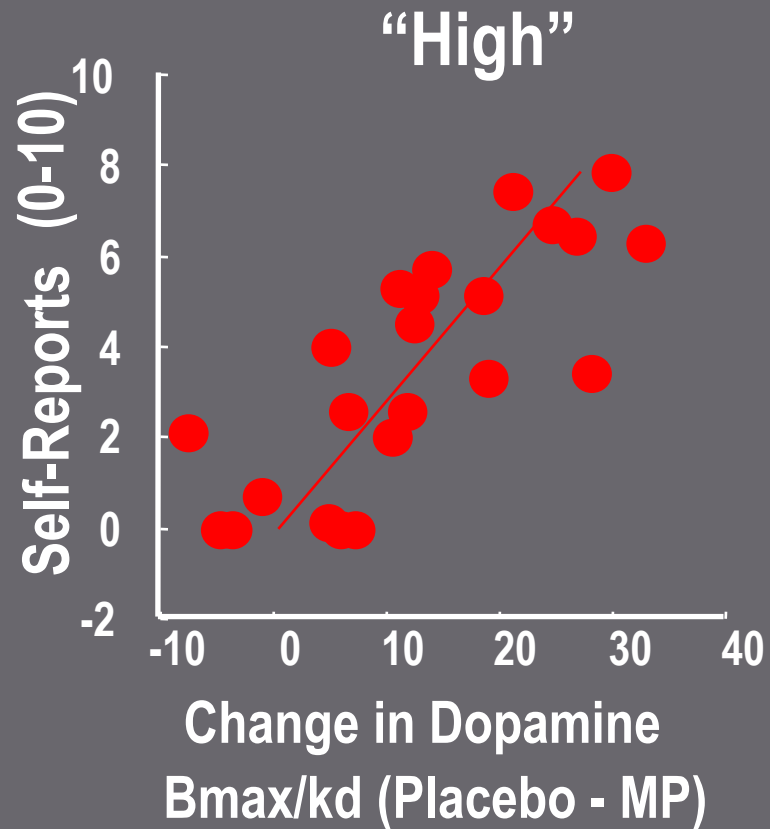
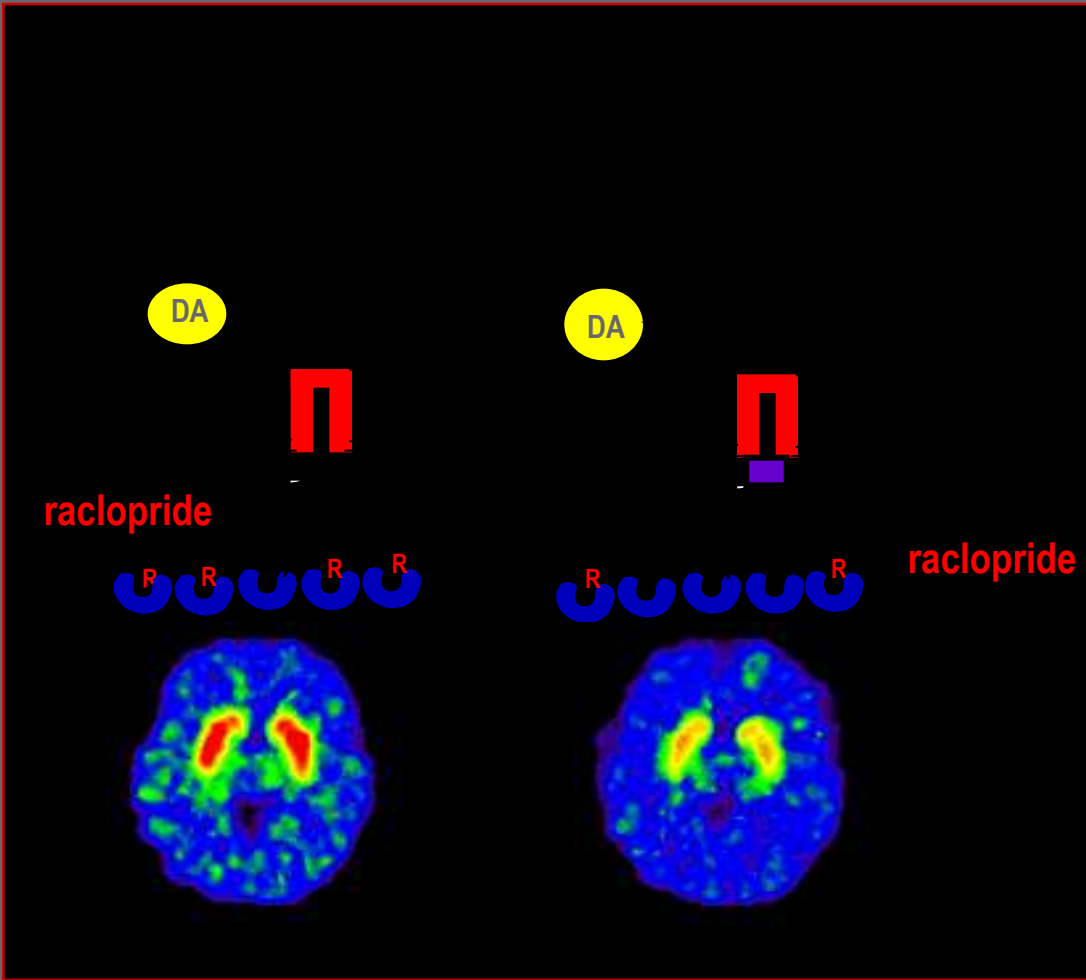
Orbitofrontal cortex
Evaluation of rewarding or motivational value of stimuli



BRAIN DOPAMINE SYSTEM



DA and Drug Reinforcement



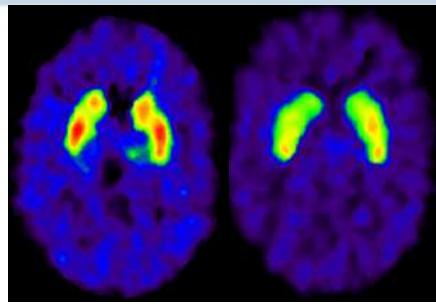
DA initiates and maintains responses to salient stimuli such as drugs



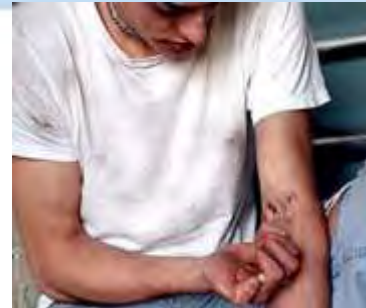
Dopamine D2 images of Drug Addiction



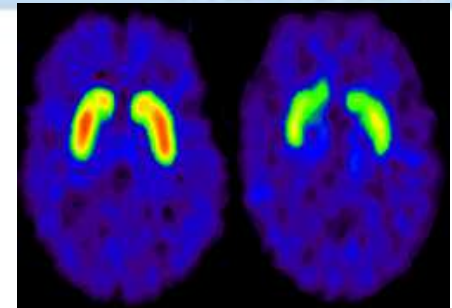
Cocaine



Control Abuser



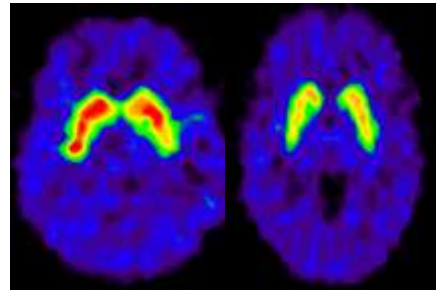
Heroin



Control Abuser



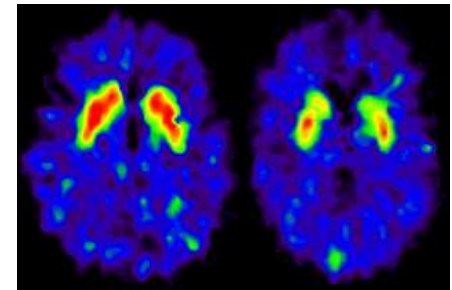
METH



Control Abuser



Alcohol



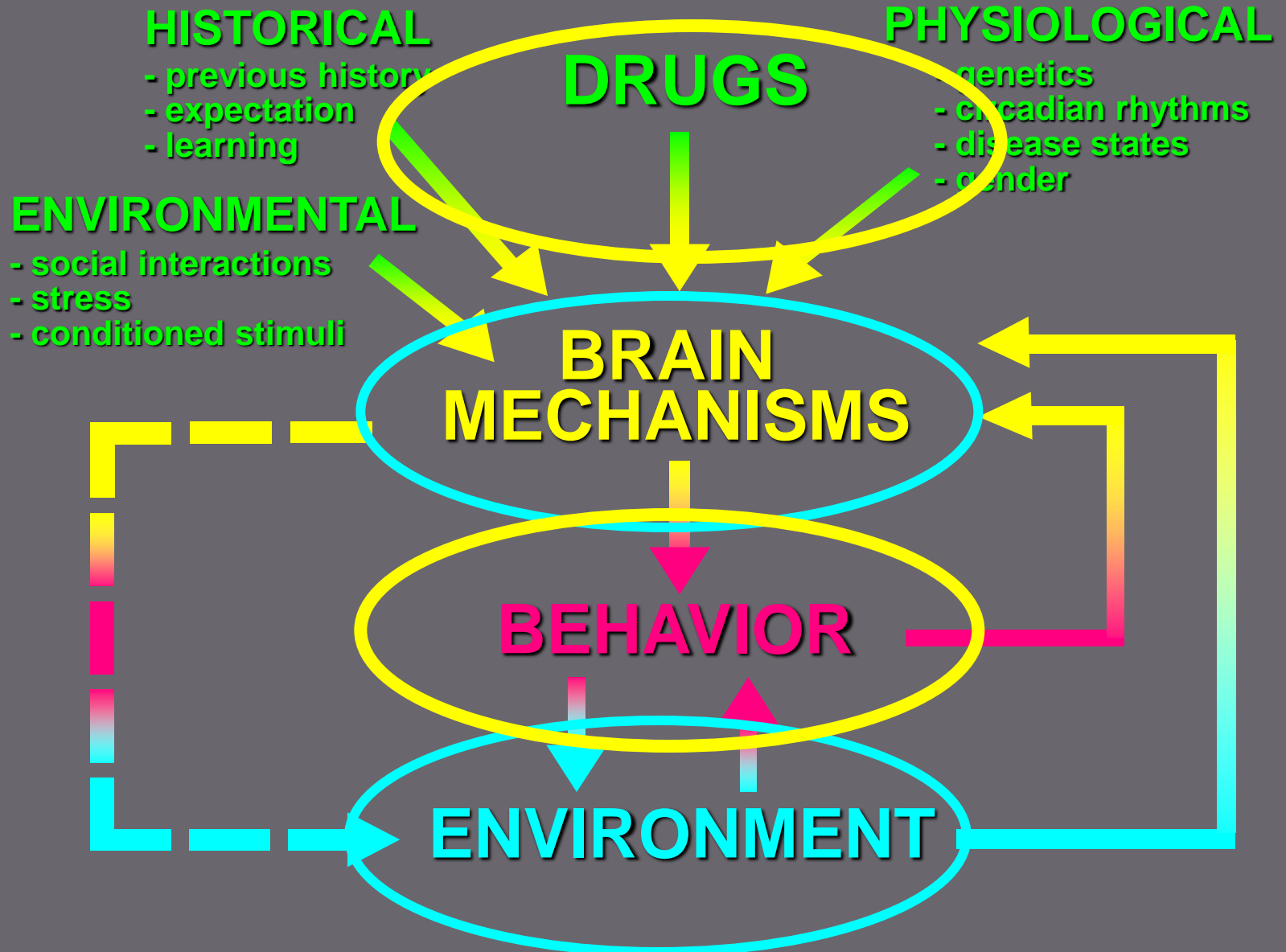
Control Abuser

Drug abusers have low brain dopamine activity indicating an under-stimulated reward system.

RECOVERY
FROM
ADDICTION

Drug Addiction:

A Complex Behavioral and Neurobiological Disorder

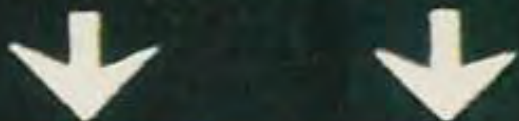


Lesson 6:

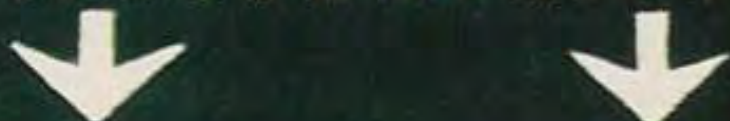


- Add drugs of abuse target the pleasure system and initially produce euphoria
 - It would be logical to assume that this system is compromised over time and that all withdrawal states have the opposite symptoms to those produced by the drug state

Depressed For
No Reason



Depressed For
A Good Reason



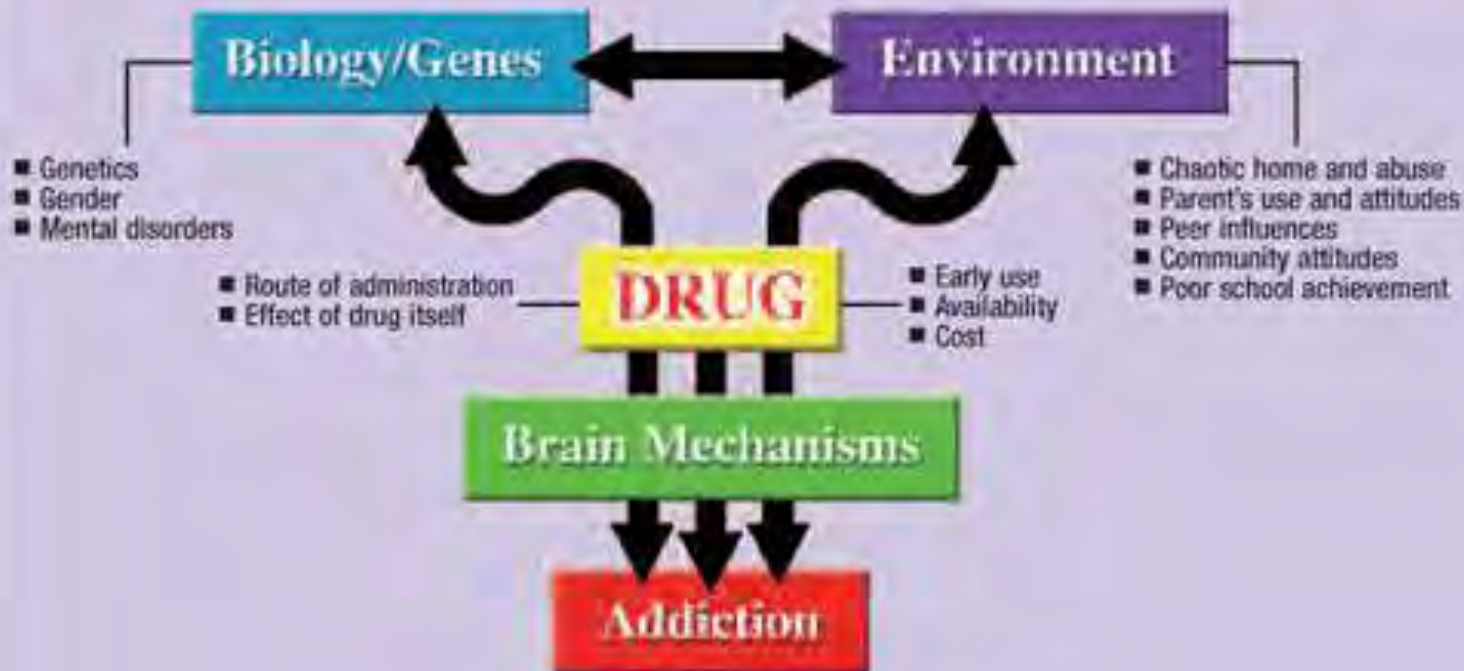
JUST
DEPRESSED,
DON'T
WANT TO
ANALYZE
IT →

Still Depressed

UN-
DONE
→



RISK FACTORS



RECOVERY
FROM
ADDICTION

Lesson 7



M.D.s Rarely Make A Diagnosis

Only 3% of patients in treatment for addiction came because of a M.D. referral

Huge Public Health Problem MDs Are Out of the Loop Penn Addiction Referral Sources



Source of Addiction Referrals

	1990	2004
Criminal Justice	38%	59%
Employers/EAP	10%	6%
Welfare/CPS	8%	16%
Hosp/Phys	4%	3%

Lesson 8



Start with the Basics



Many more Users/Misusers/Abusers

The Alcohol Pyramid



In Spec Treatment – 1,000,000

Abuse/Dependent – 18,000,000

“Harmful Users” – ??,000,000

RECOVERY
FROM
ADDICTION

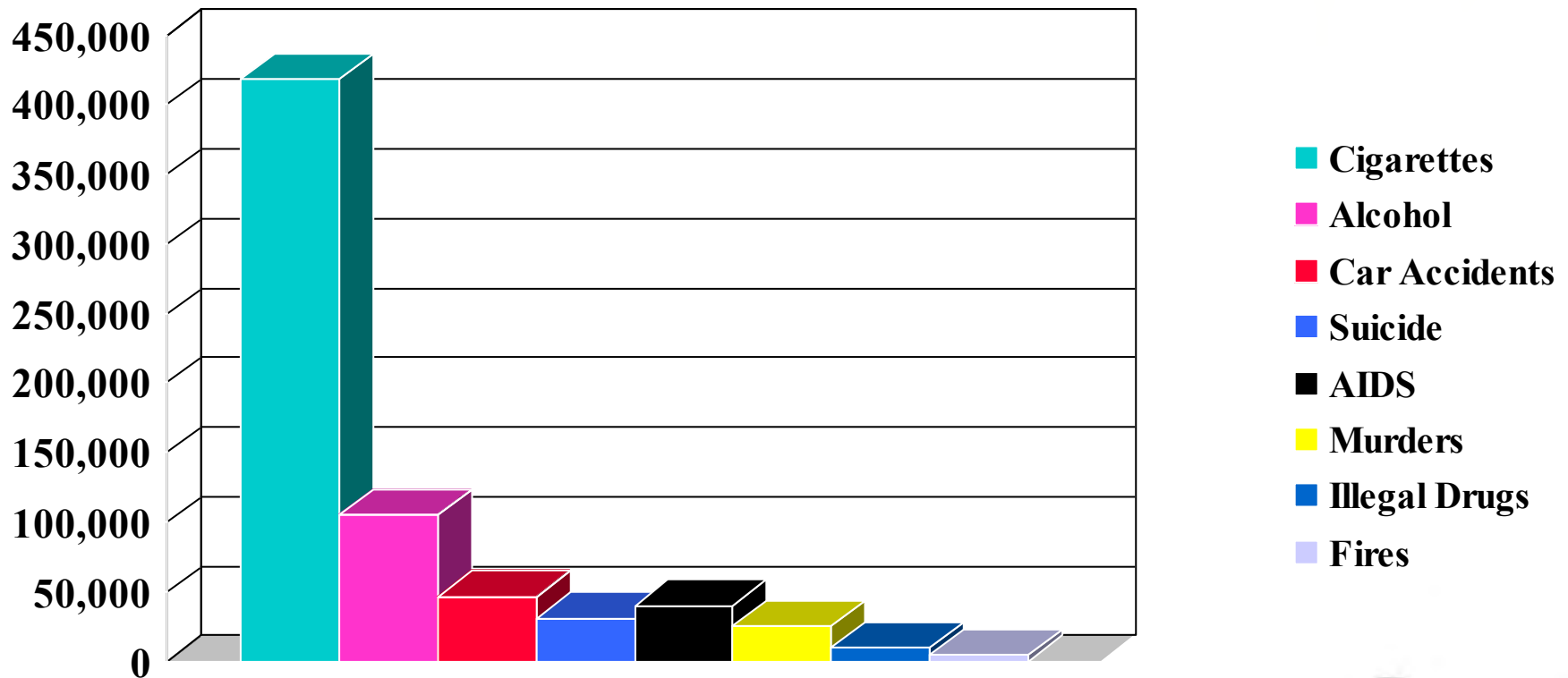
Buckfast ---2010



15 percent alcohol by volume, a bit stronger than most wines.
Each bottle has as much caffeine as eight cans of Coke
(<http://www.nytimes.com/2010/02/04/world/europe/04scotland.html>).

RECOVERY
FROM
ADDICTION

Cigarettes Kill More Americans than AIDS, Alcohol, Car Accidents, Fires, Illegal Drugs, Murders and Suicides Combined



Actual Causes of Death in the United States in 1990 and 2000



Actual Cause	No. (%) in 1990	No. (%) in 2000
Tobacco	400 000 (19)	435 000 (18.1)
Poor diet / inactivity	300 000 (14)	400 000 (16.6)
Alcohol consumption	100 000 (5)	85 000 (3.5)
Microbial agents	90 000 (4)	75 000 (3.1)
Toxic agents	60 000 (3)	55 000 (2.3)
Motor vehicle	25 000 (1)	43 000 (1.8)
Firearms	35 000 (2)	29 000 (1.2)
Sexual behavior	30 000 (1)	20 000 (0.8)
Illicit drug use	20 000 (1)	17 000 (0.7)
Total	1 060 000 (50)	1 159 000 (48.2)

Mokdad et al., JAMA 2004

MSG

RECOVERY
FROM
ADDICTION

Lesson 9



Get The Message Out Drug Free Pregnancy

Treatment and the Obstetrician-Gynecologist.

From: Substance Use and Women by Gold MS as part of the *American College of Obstetricians and Gynecologists (ACOG)* guidelines.



- Role of ob-gyn includes prevention, screening, early intervention, diagnosis, referral with consultation and pretreatment for substance abuse.
- Also to provide counseling on the risks and dangers of substance abuse and to treat the patient respectfully even when she continues to decline specific drug rehabilitation.
- Pretreatment is the major contribution of the ob-gyn or primary health care provider as often encouragement and support may lead the patient to reduce or eliminate use.
- As the most significant health care practitioner for many women, the obstetrician–gynecologist may be influential in a patient’s decision to accept treatment or referral.

RECOVERY
FROM
ADDICTION

Pregnancy and Substance Use.

From: Substance Use and Women by Gold MS as part of the *American College of Obstetricians and Gynecologists (ACOG)* guidelines.



- Substance abuse has serious implications for the health of women, including adverse effects on reproductive function and pregnancy.
- No difference in the prevalence of recent substance abuse among pregnant women when those with private insurance were compared with medically indigent patients.
- Pregnancy complications appear more frequently among heavy smokers (pre-term birth, intrauterine growth restriction, small head circumference, low Apgar score at 5 min., stillbirths and neonatal deaths).
- Alcohol is the most common teratogen to which a fetus is exposed, and alcohol consumption during pregnancy is a leading preventable cause of mental retardation, developmental delay, and birth defects in the fetus.
- Birth defects associated with prenatal alcohol exposure can occur in the first 3 to 8 weeks of pregnancy before a woman even knows she is pregnant.

RECOVERY
FROM
ADDICTION

Pregnancy and Substance Use.

From: Substance Use and Women by Gold MS as part of the *American College of Obstetricians and Gynecologists (ACOG)* guidelines.



- **ALCOHOL USE DURING PREGNANCY CAN CAUSE:**
 - Fetal Alcohol Syndrome (FAS) characterized by growth restriction, facial abnormalities, and CNS dysfunction.
 - Skeletal abnormalities
 - Structural cardiac defects
 - Neurodevelopmental abnormalities such as problems with:
 - intelligence
 - communication skills
 - attention
 - memory
 - learning ability
 - visual/spatial skills
 - motor development.

RECOVERY
FROM
ADDICTION

The health effects of parental problem drinking on adult children.



Balsa AI, Homer JF, French MT.
J Ment Health Policy Econ. 2009
Jun; 12(2): 55-66.

- NLSY79 dataset used. Cohort of individuals who were between 14 and 22 when first surveyed in 1979. Surveys redone each year through 1994, then biennially.
- Purpose: to assess the long-term impacts of parental problem drinking on late adolescence and young adulthood.
- Respondents with a problem-drinking mother more likely to have ever been diagnosed with a mental health problem.
- Outcomes were worse for daughters of problem drinkers than for sons.

Pregnancy and Substance Use.

From: Substance Use and Women by Gold MS as part of the *American College of Obstetricians and Gynecologists (ACOG)* guidelines.



- USING COCAINE/CRACK DURING PREGNANCY CAN:
 - Cause microcephaly in infant
- Difficult to separate role played by cocaine in adverse pregnancy outcomes from other factors associated with cocaine use, such as:
 - Smoking
 - Malnutrition
 - Lack of prenatal care
 - Older maternal age
 - Presence of infectious disease in the mother
- Cocaine definitely crosses the placenta and also passes into breast milk.

RECOVERY
FROM
ADDICTION

Pregnancy and Substance Use.

From: Substance Use and Women by Gold MS as part of the *American College of Obstetricians and Gynecologists (ACOG)* guidelines.



- USING HEROIN DURING PREGNANCY CAN CAUSE:
 - Stillbirth
 - Fetal growth restriction
 - Prematurity
 - Neonatal mortality
 - All of above 3-7 times higher than general population
- Neonatal Abstinence Syndrome – as many as 2/3 of offspring
- Children of heroin users have higher rates of :
 - Inattention
 - Behavior problems
 - ADHD

RECOVERY
FROM
ADDICTION

Pregnancy and Substance Use.

From: Substance Use and Women by Gold MS as part of the *American College of Obstetricians and Gynecologists (ACOG)* guidelines.



- NEONATAL ABSTINENCE SYNDROME (NAS)
 - Severe, potentially fatal narcotic withdrawal syndrome
 - Signs usually appear 24-72 hours after birth
 - Can occur 1-2 days later (if mother taking methadone)
 - Occasionally appear after 10 days (after infant discharged)
 - Characterized by: high-pitched cry, poor feeding, hypertonicity, tremors, irritability, sneezing, sweating, vomiting, diarrhea, and sometimes seizures

Lesson 10



- Nation's Number 1 Problem?
But Evidence Is Clear Treatment Works---
McLellan, Dupont, Gold

GENES



Change your GENES

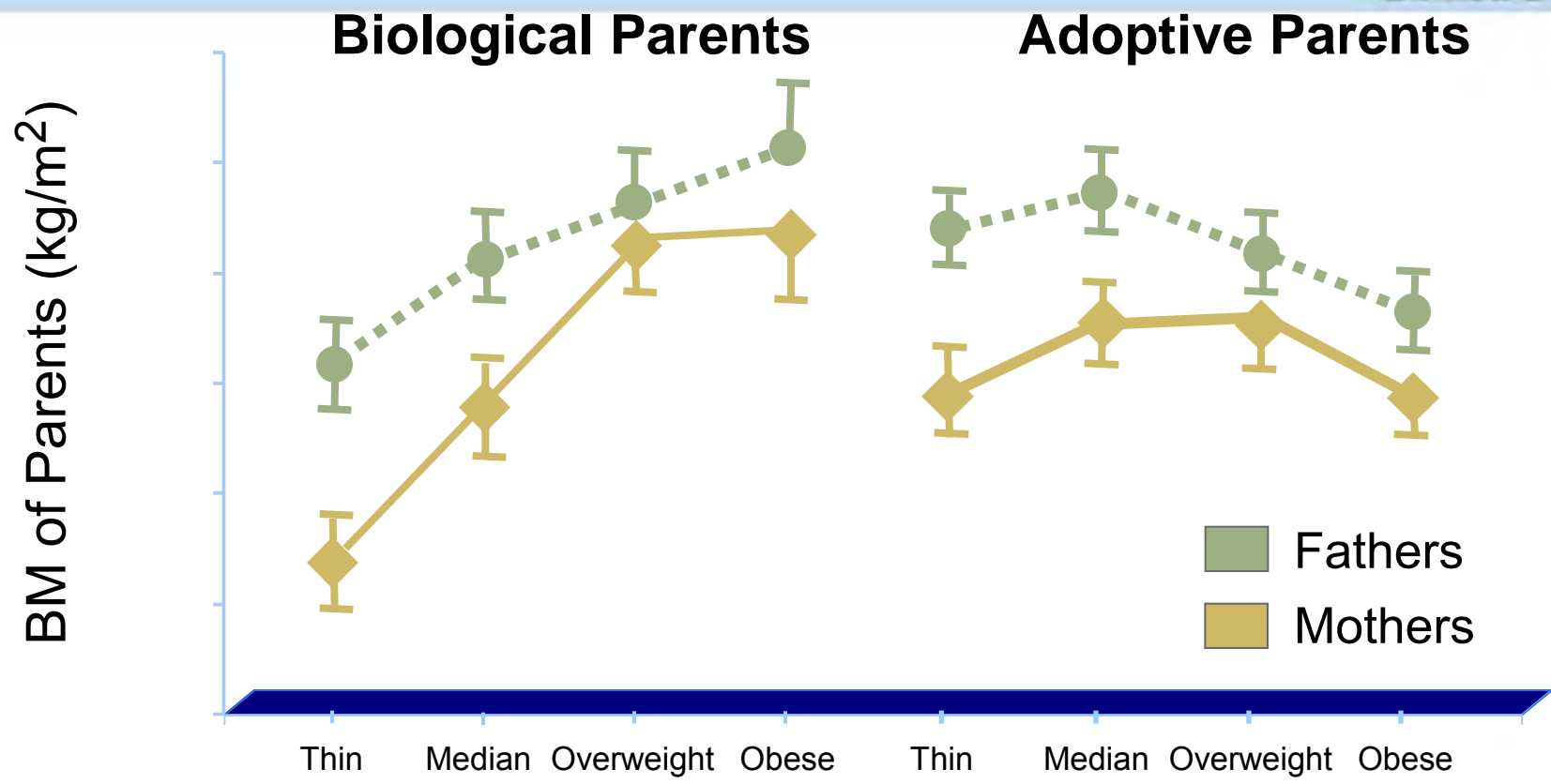
RECOVERY
FROM
ADDICTION



A person with an excess of abdominal fat (apple shape) is at greater risk for cardiovascular disease than a person with fat deposits in the lower body (pear shape). A new study suggests waist-to-hip ratio is a better indicator than body mass index of cardiovascular risk.

RECOVERY
FROM
ADDICTION

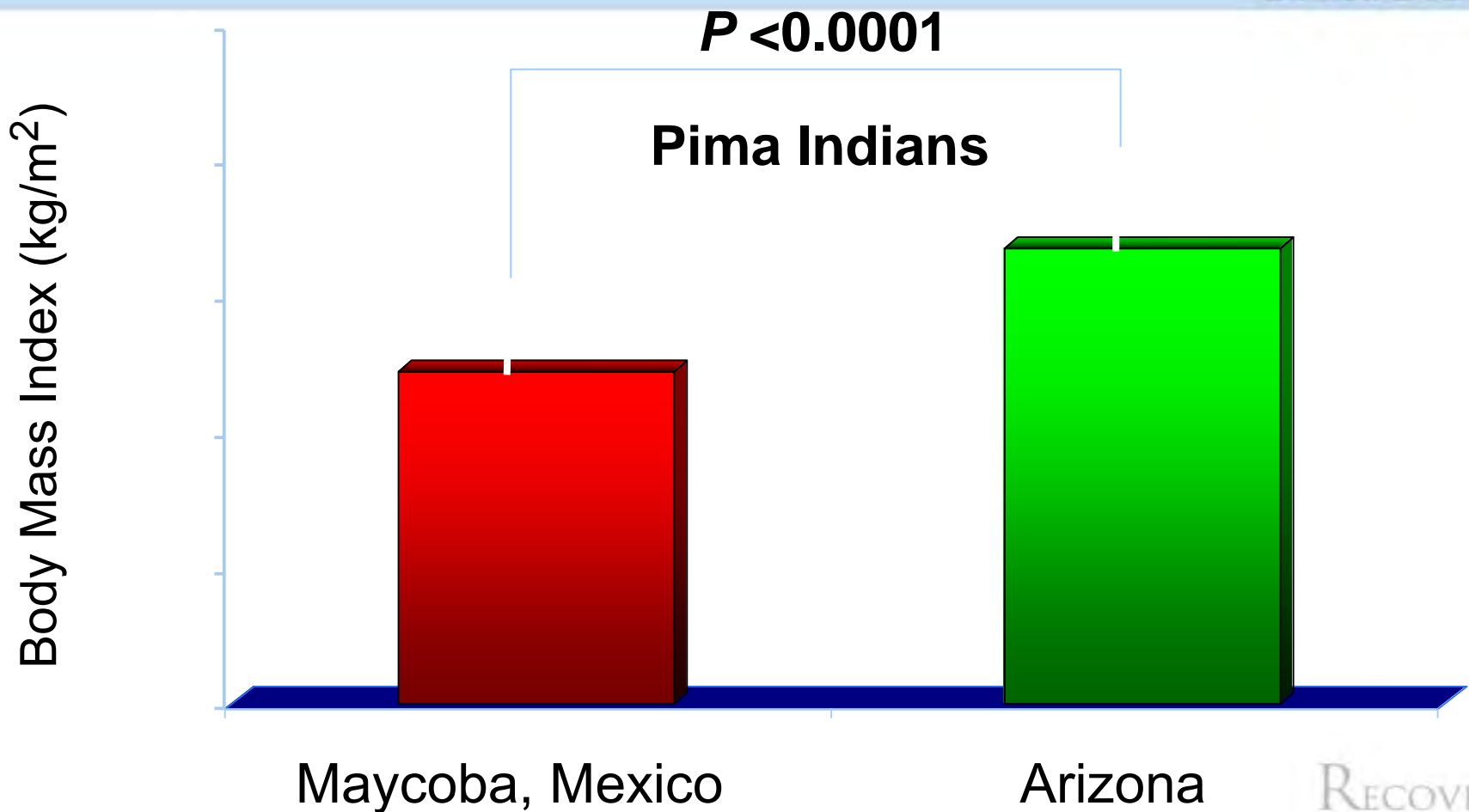
Relationship Between Adoptee Weight and Weight of Biological or Adoptive Parents



Weight Classification of Adoptees

Stunkard et al. *N Engl J Med* 1986;314:193.
 Copyright © 1986 Massachusetts Medical Society. All rights reserved.

Gene-Environment Interaction in the Pathogenesis of Obesity



Ravussin E et al. *Diabetes Care* 1994;17:1067-1074.

Obesity-Genetics



- Obesity represents the upper end of a bodyweight continuum, rather than a qualitatively different state. Obesity can derive from a variety of causes (i.e. genetic, culture, nutrition intake, physical activity).¹
- Most notably, obesity is more prevalent (ten times more likely) in persons whose parents, brothers, or sisters are obese. Studies in identical twins have clearly demonstrated that genetics plays a major role.² Nonidentical twins raised together were less similar in weight than identical twins raised apart. However despite the importance of genetics it is likely that the changes in the environment are the main contributors to the rapid escalation and magnitude of the obesity epidemic in recent decades.
- The nature and nurture interactions associated with obesity are thought to occur after conception but before birth. Maternal nutritional imbalance and metabolic disturbances during pregnancy could affect gene expression and contribute to the development of obesity and diabetes mellitus of offspring in later life.³ Recent experiments have shown nutritional exposures, stress or disease state after birth may also result in lifelong remodeling of gene expression.⁴

- 1-Bessesen DH. Update on obesity. *J Clin Endocrinol Metab.* Jun 2008;93(6):2027-2034.
- 2-Segal NL, Allison DB. Twins and virtual twins: bases of relative body weight revisited. *Int J Obes Relat Metab Disord.* Apr 2002;26(4):437-441.
- 3-Catalano PM, Ehrenberg HM. The short- and long-term implications of maternal obesity on the mother and her offspring. *Bjog.* Oct 2006;113(10):1126-1133.
- 4-Gallou-Kabani C, Junien C. Nutritional epigenomics of metabolic syndrome: new perspective against the epidemic. *Diabetes.* Jul 2005;54(7):1899-1906.

Current USA Diet is Diabetes-Inducing Diet



RECOVERY
FROM
ADDICTION

Prescriptions of Type 2 diabetes drugs for children doubled from 2002 to 2005



- [WebMD](#) (11/8, DeNoon) reports, "Driven by huge increases among tween and teen girls, pediatric prescriptions for type 2 diabetes drugs doubled from 2002 through 2005," according to findings presented at this week's annual meeting of the American Public Health Association in Washington, D.C. The study used "data on prescription drug use among insured children served by St. Louis-based Express Scripts." Researchers found that "from the beginning of 2002 to the end of 2005, the percentage of U.S. kids on diabetes drugs doubled from about 0.3 per 1,000 children to about 0.6 per 1,000 children." This trend was fueled by "a 166 percent increase among girls aged 10-14, and a 135 percent increase among girls aged 15-19." No similar trend was found among young boys, and the researchers could not explain why the increase occurred.

USA

Overweight
of men
37% of women

32% of men

Obese

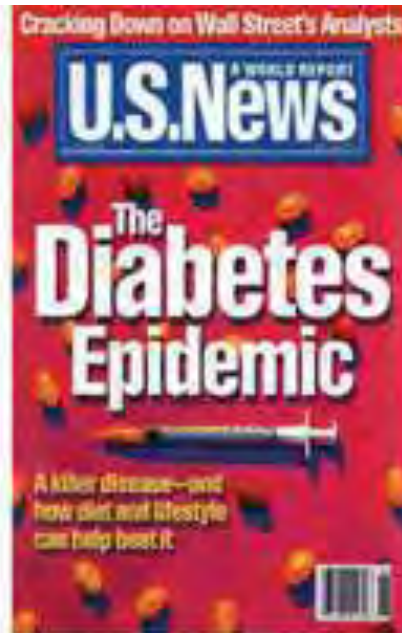
70% of women

72%



D'Aluisio M. HUNGRY PLANET: What The World Eats. Napa: Material World Books, 2005.

Type 2 Diabetes Epidemic



Japan

of men
2% of women

Overweight
2% of men

Obese

19% of women










23%



D'Aluisio M. *HUNGRY PLANET: What The World Eats*. Napa: Material World Books, 2005.



Impact of Weight Loss on Risk Factors

	~5% Weight Loss	5%-10% Weight Loss
HbA1c	 1	 1
Blood Pressure	 2	 2
Total Cholesterol	 3	 3
HDL Cholesterol	 3	 3
Triglycerides		 4

1. Wing RR et al. *Arch Intern Med.* 1987;147:1749-1753.
2. Mertens IL, Van Gaal LF. *Obes Res.* 2000;8:270-278.
3. Blackburn G. *Obes Res.* 1995;3 (Suppl 2):211S-216S.
4. Ditschuneit HH et al. *Eur J Clin Nutr.* 2002;56:264-270.

Obese Pet Theories



- Energy imbalance
- Environment
- Culture
- Hormonal disorders
- Genetics



Hunger, Craving, Addictions



- DO Hebb (1949)
 - – Attributes the idea of hunger as an addiction to AJ Carlson (1916).
 - – —“Sated peanuts” paradox.
 - – Hunger and learning:
 - • Initial effect of hunger is disruptive.
 - • Infant learns that eating relieves unpleasant effects (e.g. stomach contractions).
 - • Eventually hunger becomes an organized behaviour
- • RA Wise (1978)
 - – Dopamine blockade reduces the reinforcing and rewarding effects of food.
 - – Dopamine codes the —“yumminess” of food.
 - – Addictive drugs act on brain circuitry that originally developed to serve feeding behaviour.

Preliminary investigation of the impulsive and neuroanatomical characteristics of compulsive sexual behavior (CSB).



Miner MH, Raymond N, Mueller BA, Lloyd M, Lim KO.



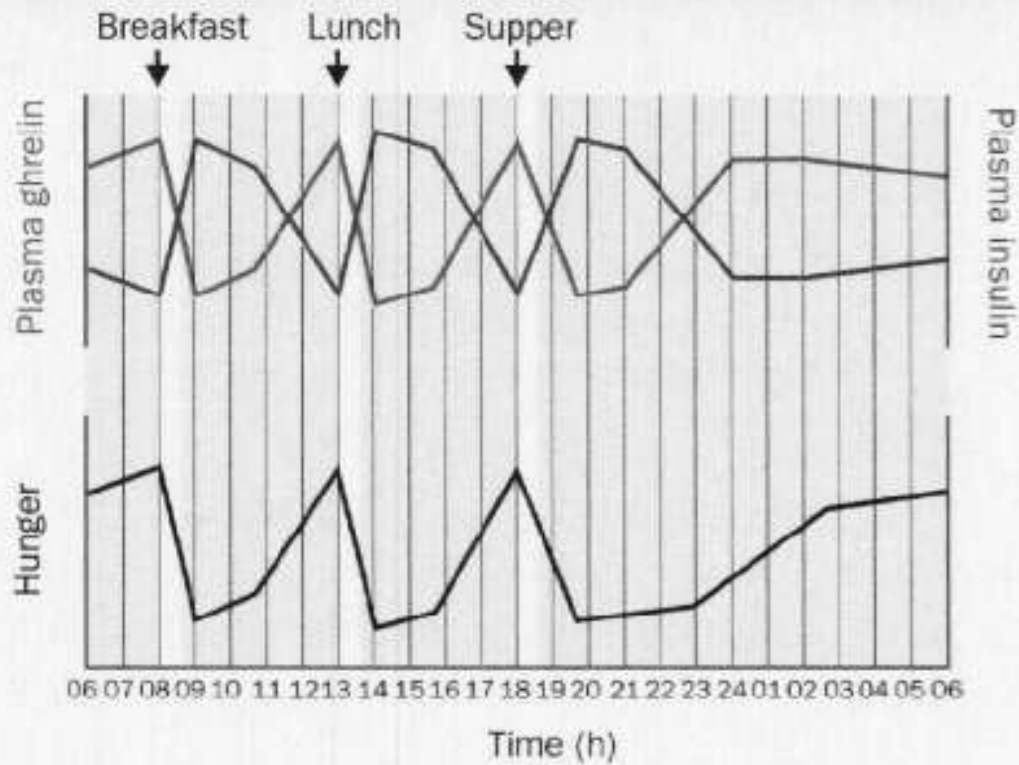
Psychiatry Research: Neuroimaging,
174 (2009) 146-151.

- CSB (n=8) vs normal controls (n=8)
- Completed psychometric measures, performed Go/NoGo task, underwent diffusion tensor imaging (DTI)
- CSB group significantly more impulsive than controls, DTI results not consistent with Impulse Control Disorders

RECOVERY
FROM
ADDICTION

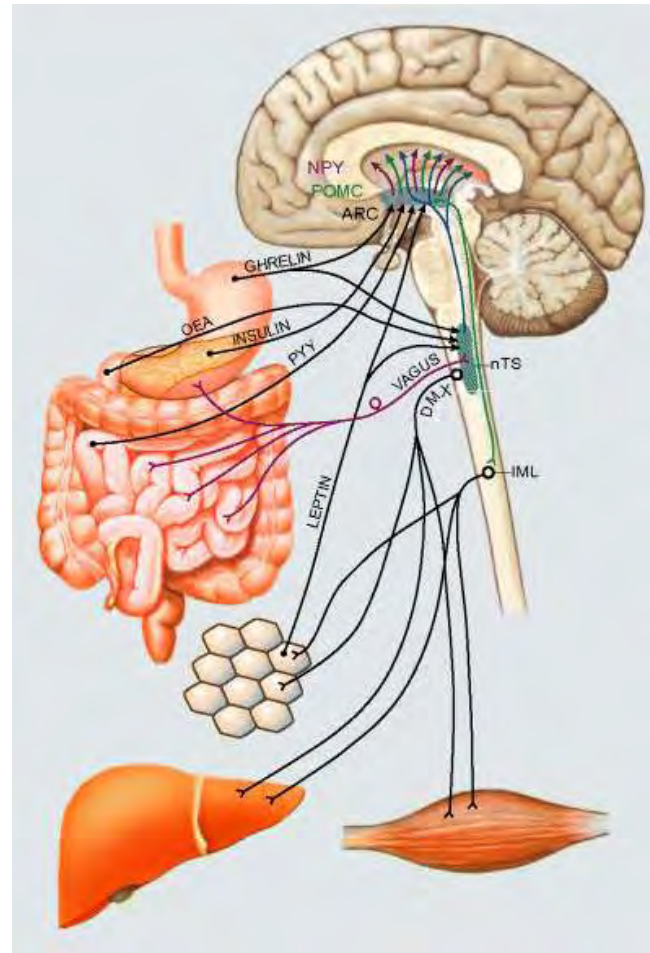


Plasma ghrelin and hunger

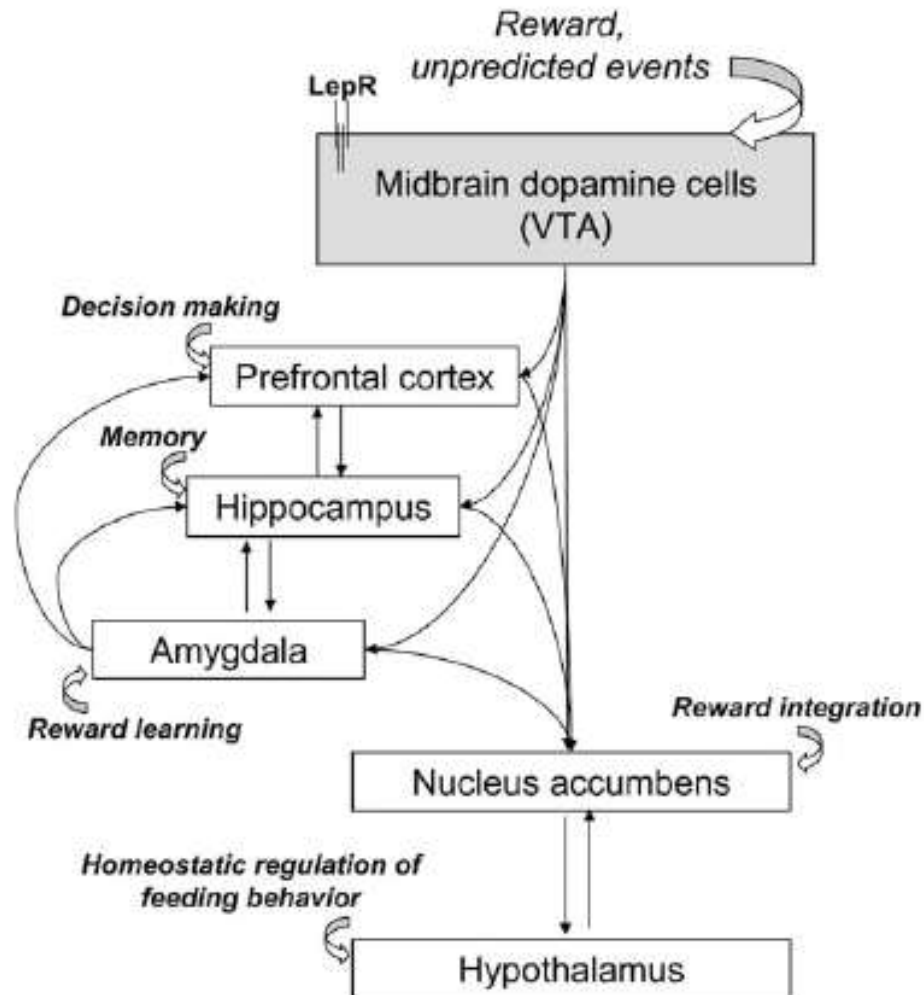


RECOVERY
FROM
ADDICTION

Gut-Brain Interactions

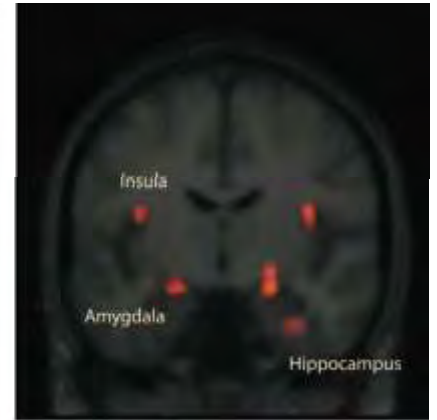
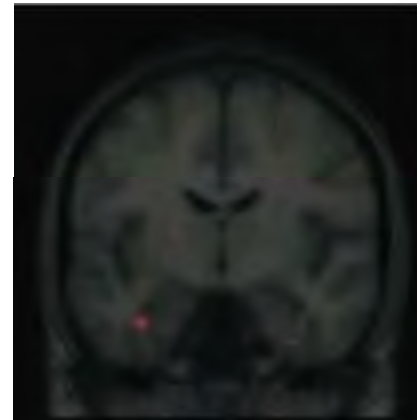
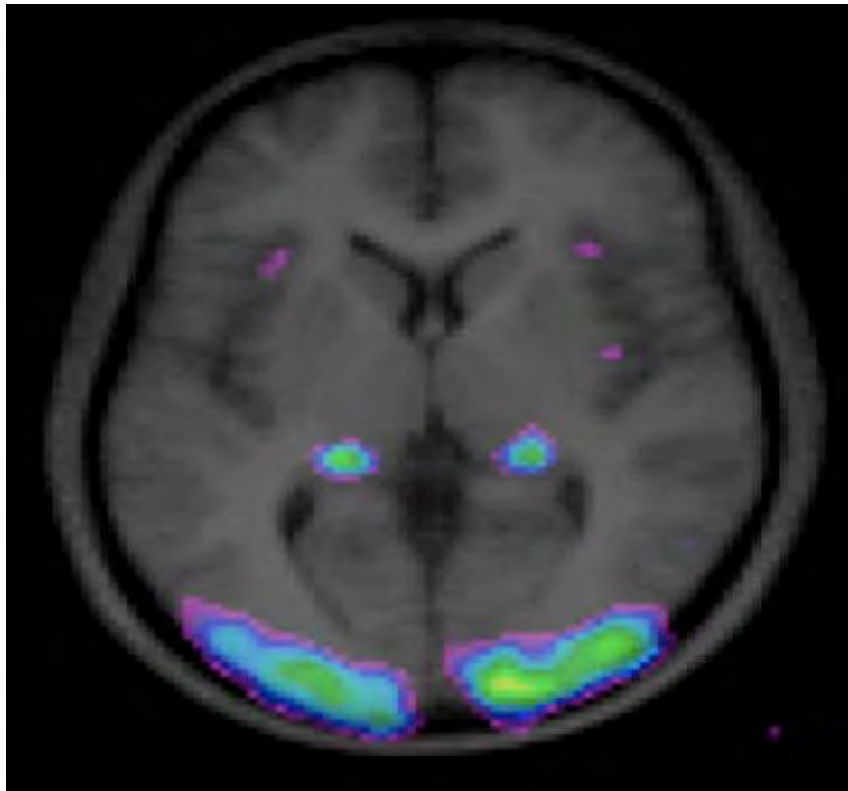


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FROM
ADDICTION



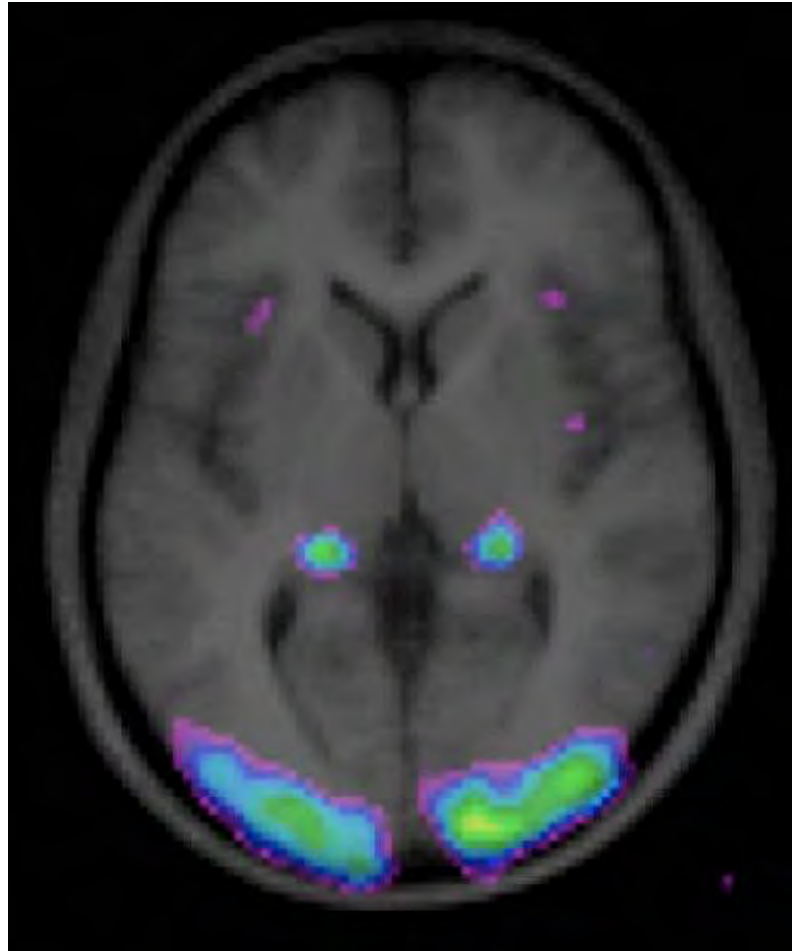
RECOVERY
FROM
ADDICTION

Effect of ghrelin on response to food pictures



RECOVERY
FROM
ADDICTION

Ghrelin effects on visual areas



RECOVERY
FROM
ADDICTION



Mayan vessel (600 BC - 200 AD)



CHOCOLATE

- Chocolate is a psychostimulant (caffeine + theobromine).
- Chocolate use by Aztecs and
- Europeans (initially) more akin to drug than food.
- —More than a food, less than a drug”
- – Ryan J Huxtable

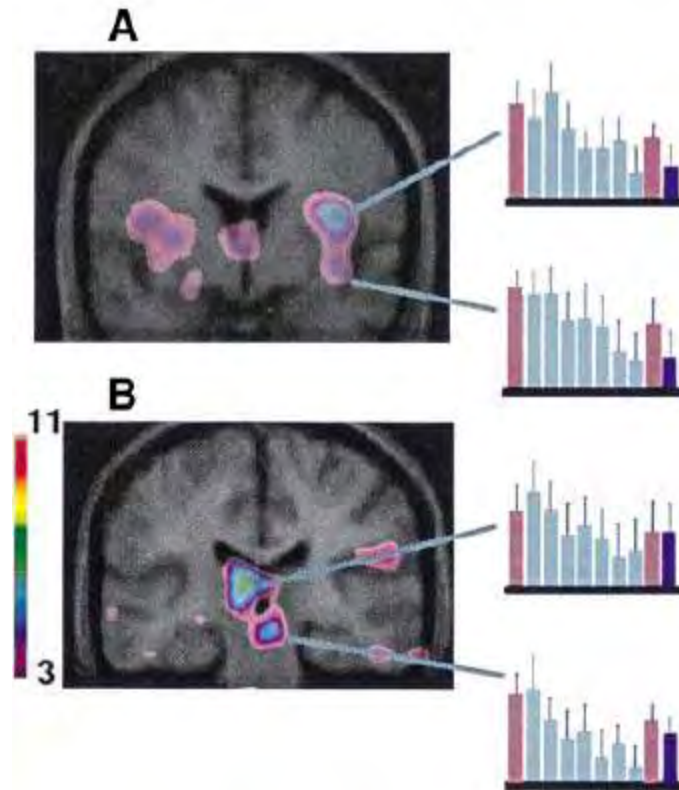
Chocolate : Is it a food or drug?



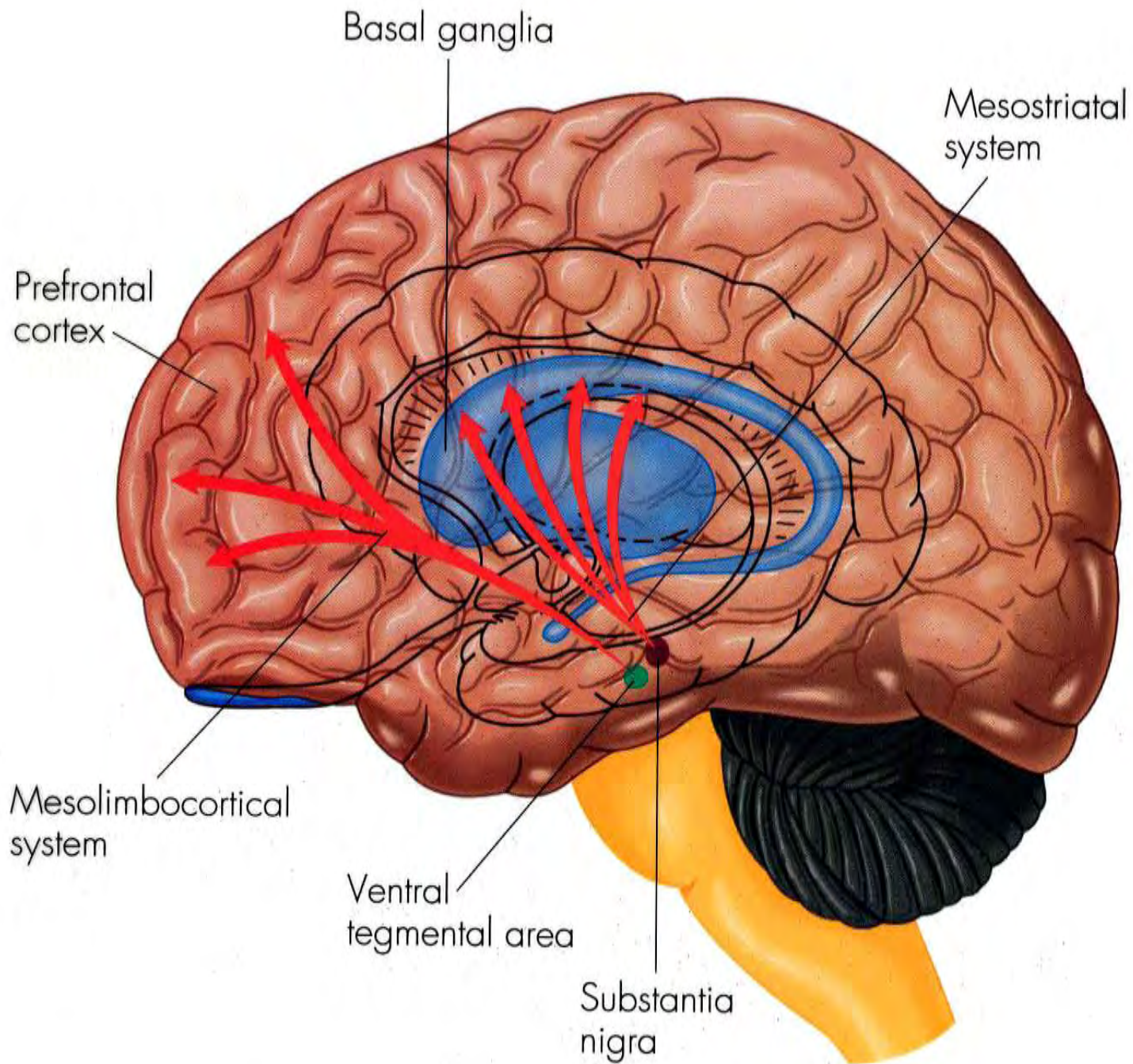
Neuronal Response to Eating Chocolate

- CBF while eating chocolate
- proportional to motivation to eat
- and pleasantness:
- Dorsal caudate putamen
- Midbrain and thalamus
- Medial OFC
- Insula (taste cortex)

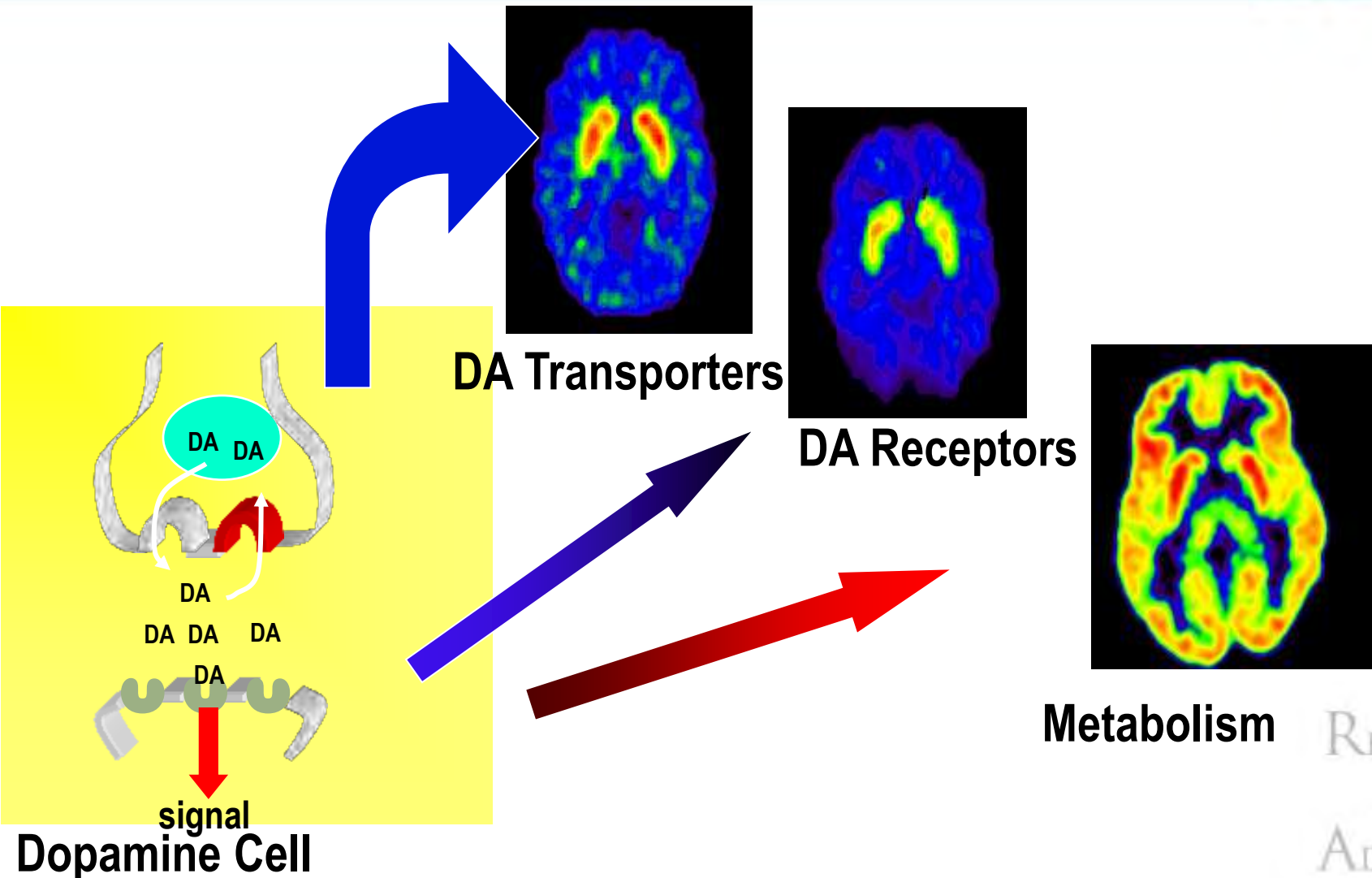
Dana Small, Ph.D. *vale*



RECOVERY
FROM
ADDICTION



PET tracers for obesity research



RECOVERY
FROM
ADDICTION

Parkinson's Disease



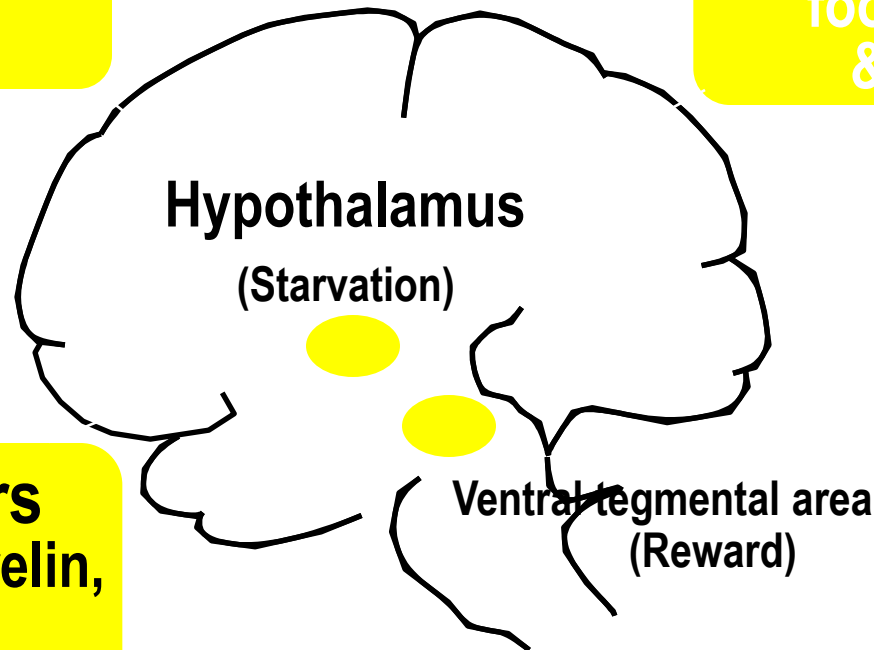
- DA Treatments and Increased :
 - Gambling
 - Sex
 - Eating

Signals that Control Food Intake



**Emotional Factors
(Stress)**

**Extrinsic factors
food-related cue
& availability**



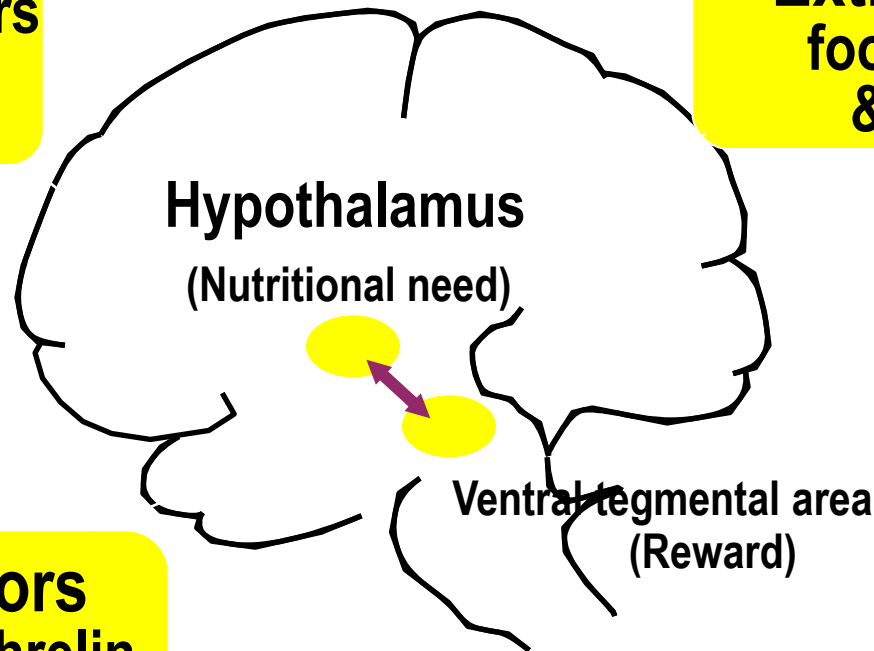
**Intrinsic factors
Leptin, Insulin, Ghrelin,
PYY**

Signals that Control Food Intake



**Emotional Factors
(Stress)**

**Extrinsic factors
food-related cue
& availability**



**Intrinsic factors
Leptin, Insulin, Ghrelin,
PYY**

Phentermine & Fenfluramine



RECOVERY
FROM
ADDICTION

Medications for Obesity



- Rimonabant, a [Sanofi-Aventis](#) drug once viewed a surefire blockbuster, failed to win F.D.A. approval in 2007 because of links to [depression](#) and [suicidal](#) thoughts. The drug, also known as Acomplia, was then taken off the market in Europe. And [Merck](#) and [Pfizer](#) abandoned their efforts to develop drugs with a similar mode of action.
- Even drugs that have made it to market have not done well. [IMS Health](#), which tracks prescriptions, estimates combined sales of obesity drugs last year at only \$173 million in the United States. According to IMS, about 75 percent of the 6.8 million diet prescriptions last year were for phentermine, a 50-year-old generic stimulant that was an element in the fen-phen combination but was not taken off the market.
- Experts say the two name-brand diet drugs now on the market have suffered from limited effectiveness — a weight loss of about 5 percent, typically — and potentially significant side effects. Meridia, sold by [Abbott Laboratories](#), can increase [blood pressure](#) and [heart rate](#), while Xenical, from [Roche](#), can cause [flatulence](#) and embarrassing [loss of bowel control](#). A lower-dose version of Xenical, called Alli, is available without a prescription from [GlaxoSmithKline](#).

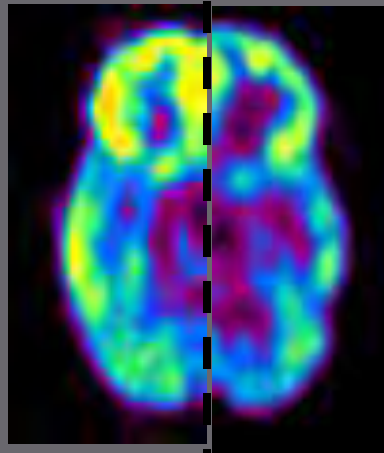
Meg Evans of California lost 55 pounds in a year in a trial for Qnexa, a diet drug by Vivus (NY Times 2009)



RECOVERY
FROM
ADDICTION

Non-Addicted Brain

Addicted Brain



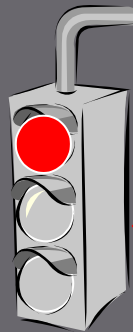
Control



Saliency

Drive

Memory



STOP



Control



Saliency

Drive

Memory



GO

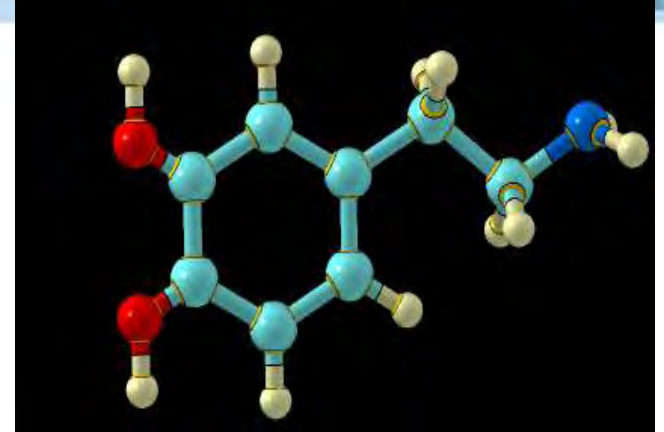
Dopamine is important in



Movement

Motivation

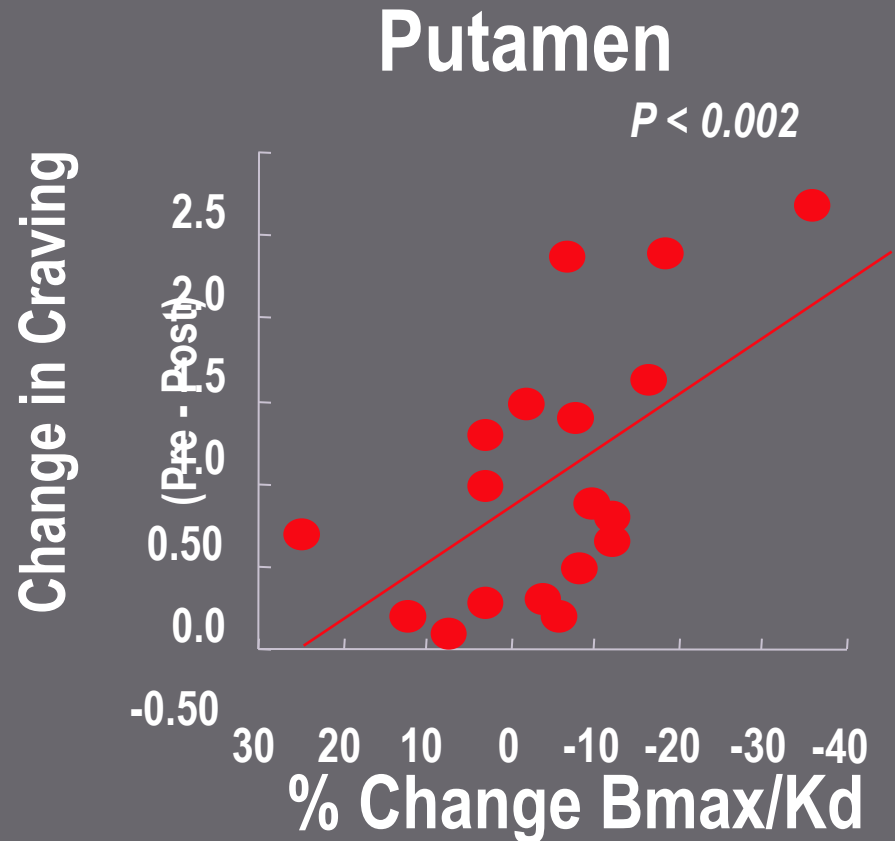
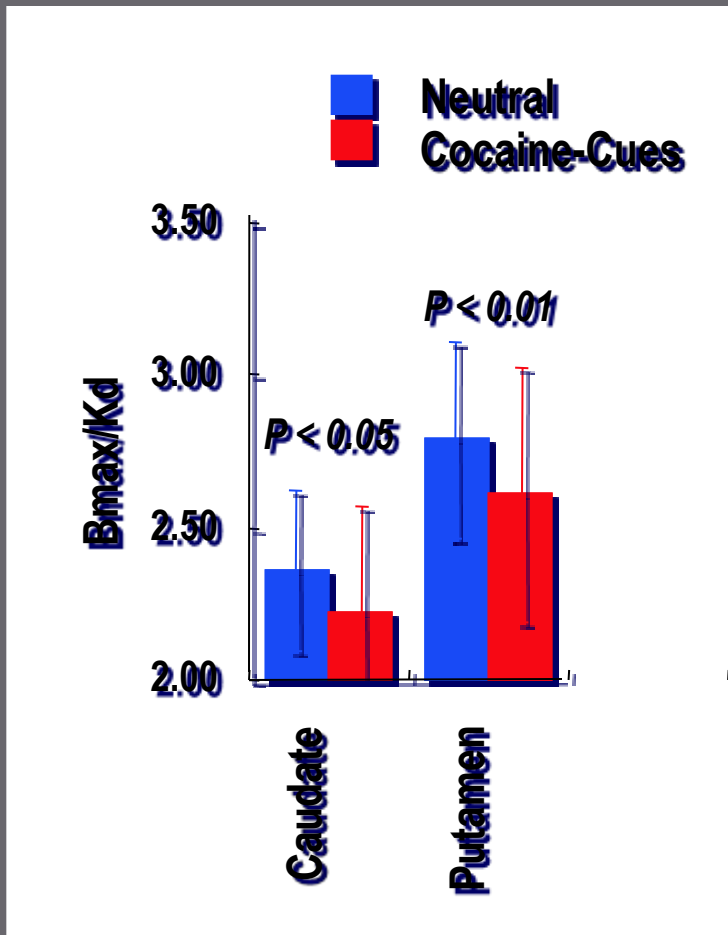
Reward & well-being



Dopamine is also the major brain chemical involved in addiction

RECOVERY
FROM
ADDICTION

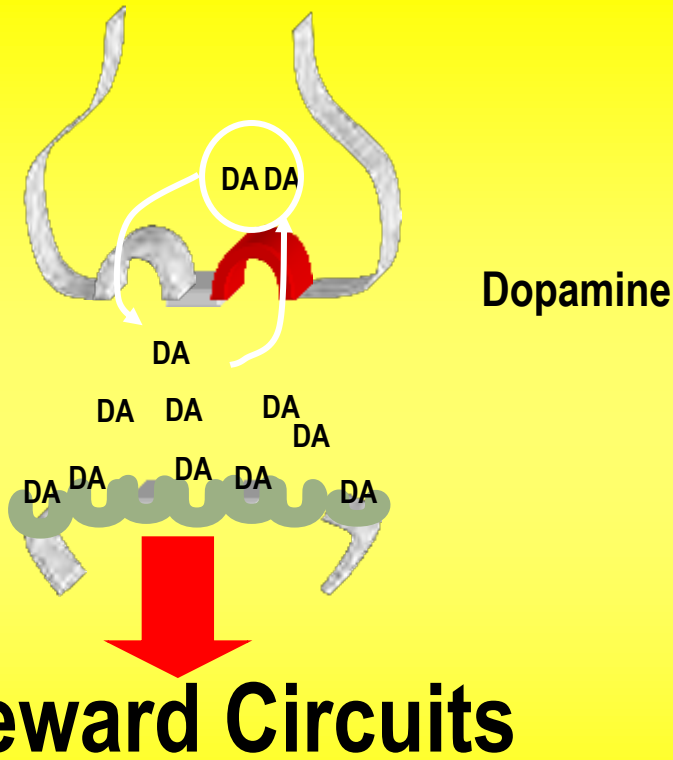
Relationship between Cue-Induced Decreases in [¹¹C]raclopride Binding and Cocaine Craving



Volkow et al J Neuroscience 2006

Cue-induced increases in DA were associated with craving

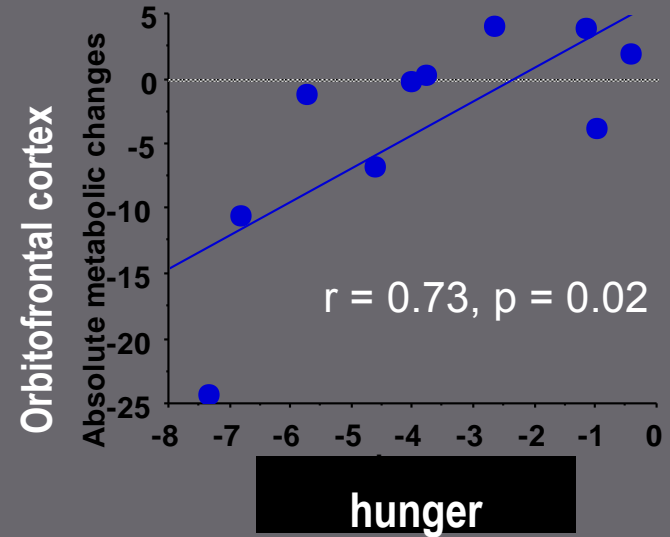
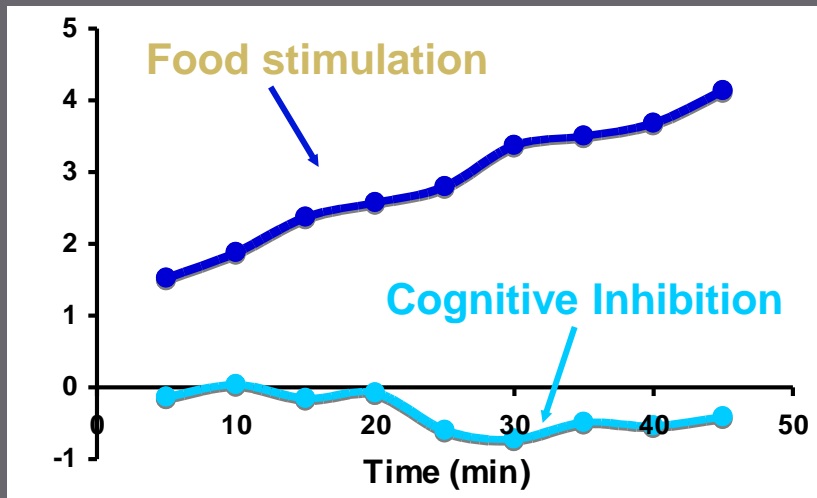
Low Dopamine (DA) State in Addiction



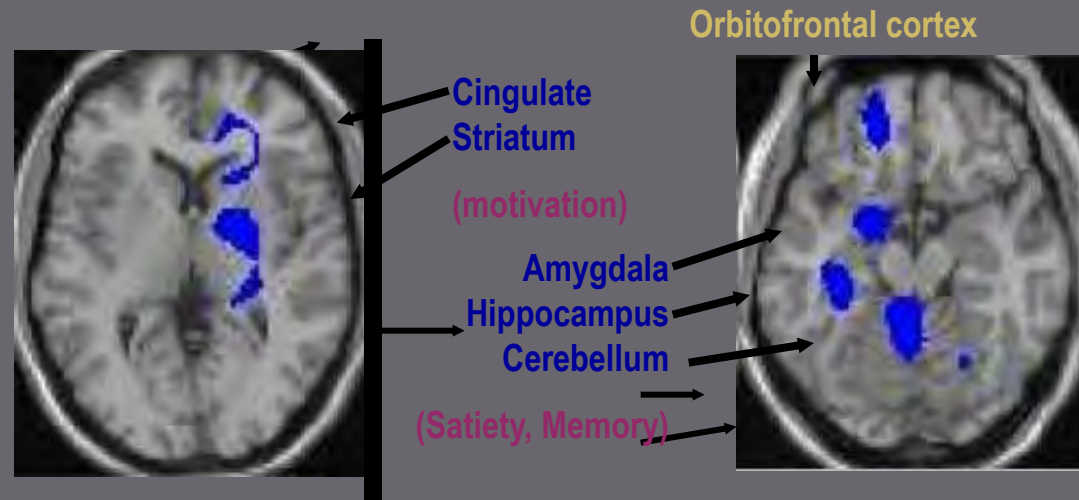
Non addicted subjects

RECOVERY
FROM
ADDICTION

Decreased brain activation during cognitive inhibition of hunger

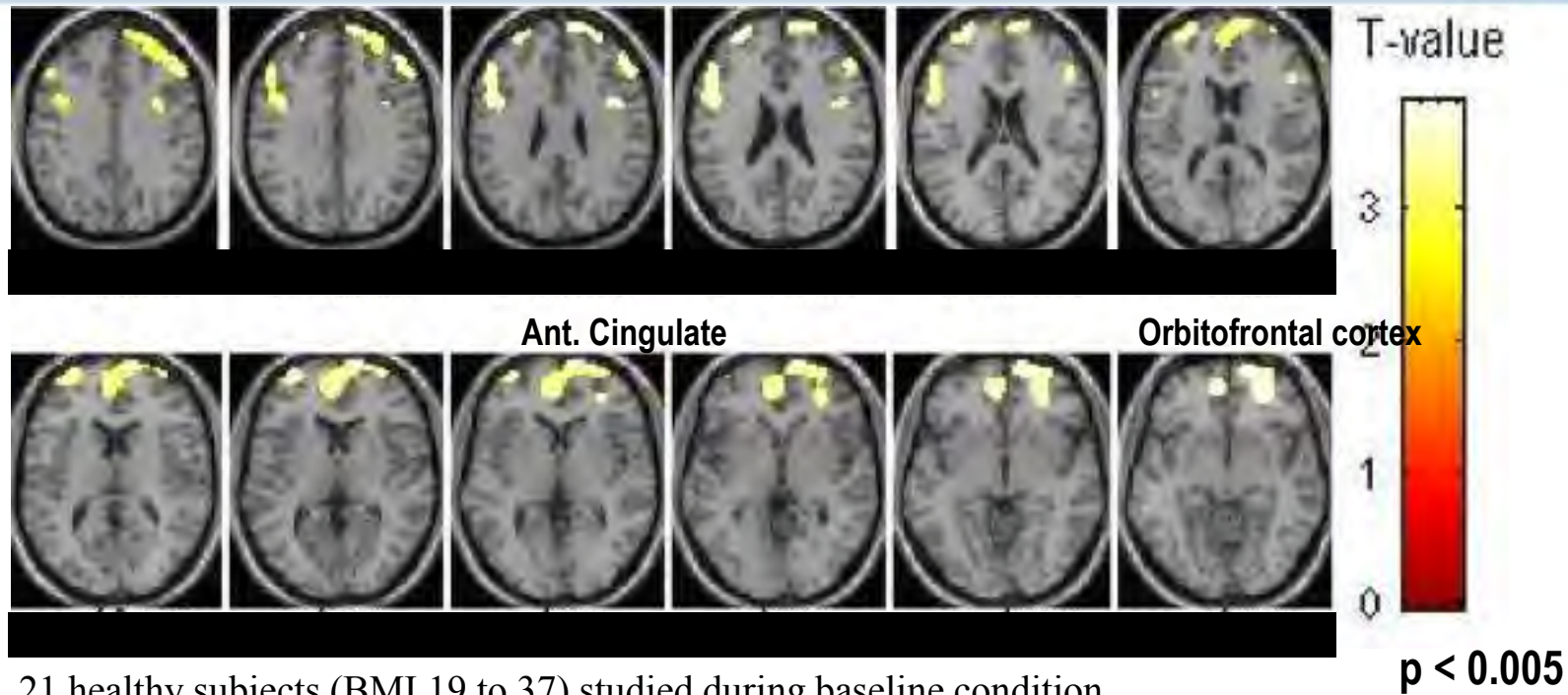


- n PET - FDG
- n 10 male subjects (BMI \leq 30).
- n Fasting for 14-16 hours.
- n Suppression of activation in regions involved in the regulation of satiety and motivation to eat suggests this is the mechanism by which cognitive inhibition decreases the desire for food.



$p < 0.01$

Inverse Association between BMI and Prefrontal Metabolic Activity in Healthy Adults

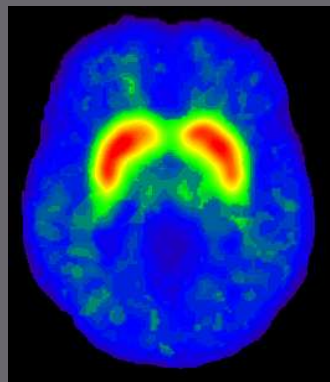


- n 21 healthy subjects (BMI 19 to 37) studied during baseline condition.
- n Negative correlation between BMI and metabolic activity in prefrontal regions.
- n Metabolism in these prefrontal regions was positively associated with performance in tests of memory (California verbal learning tests) and executive function (Stoop interference and Symbol digit modality tests).
- n Deleterious effects of excessive weight on cognitive function in healthy individuals may be mediated in part via its association with decreased activity of prefrontal regions.

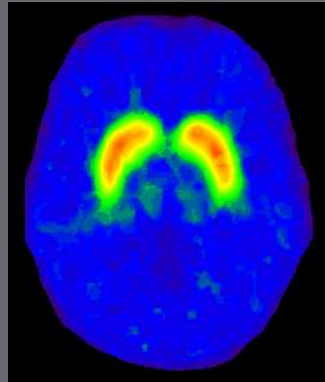
Volkow, Wang et al, Obesity 2008

RECOVERY
FROM
ADDICTION

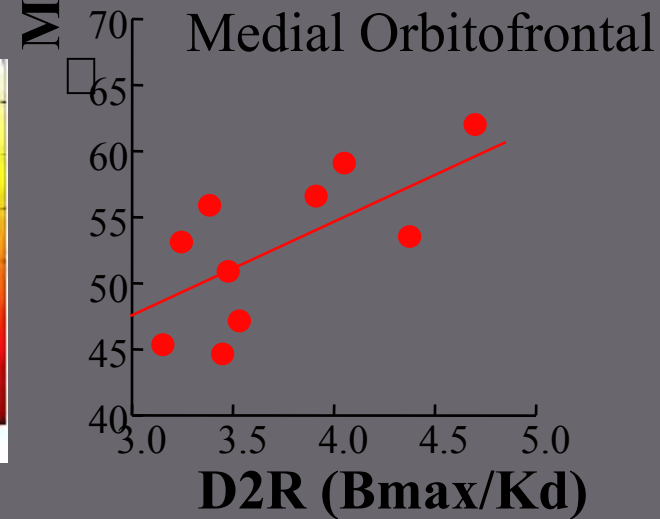
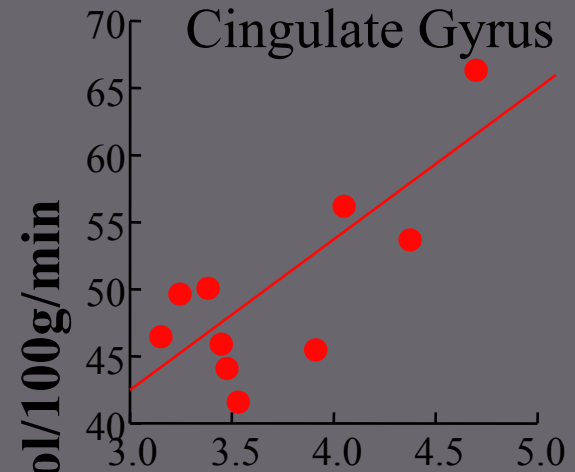
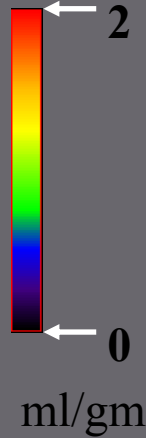
Relationship Between DA D2 Receptors and Brain Metabolism in Obese Subjects



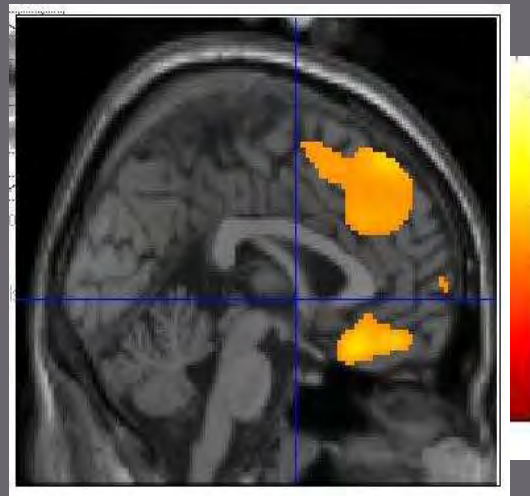
Control Subjects



Obese Subjects



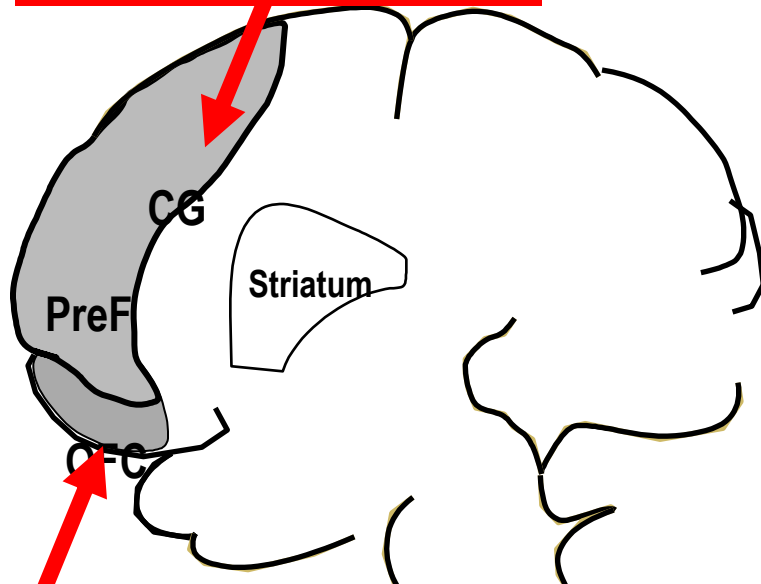
The association between DA D2 receptors and metabolism in orbitofrontal cortices and cingulate gyrus suggests that D2 receptor-mediated dysregulation of regions implicated in inhibitory control may underlie the inability to control their food intake despite their conscious attempts to do so.



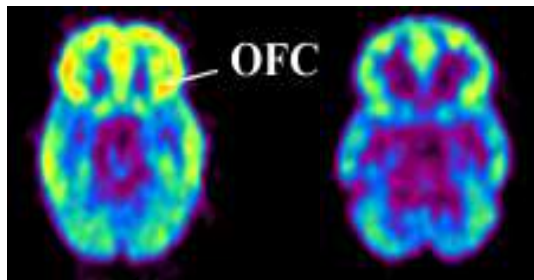
$p < 0.005$

Correlations Between D2 Receptors in Striatum and Brain Glucose Metabolism in Drug Addicts

Inhibitory Control

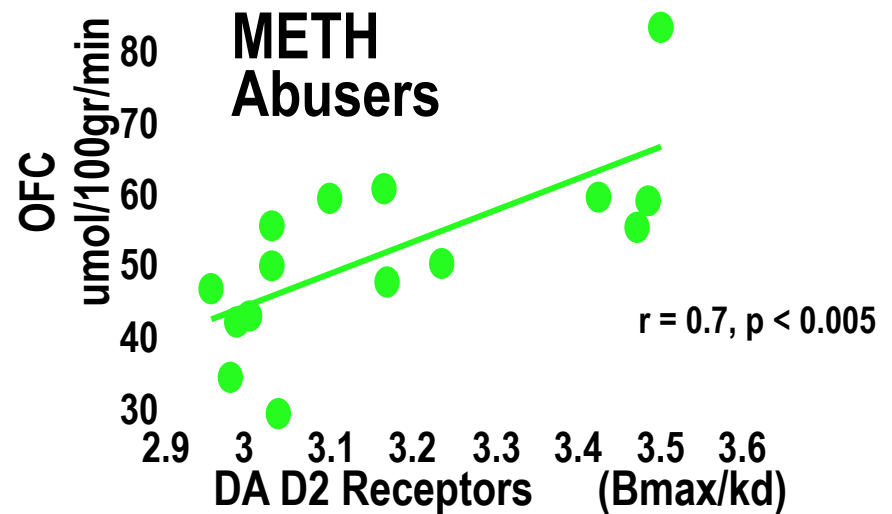
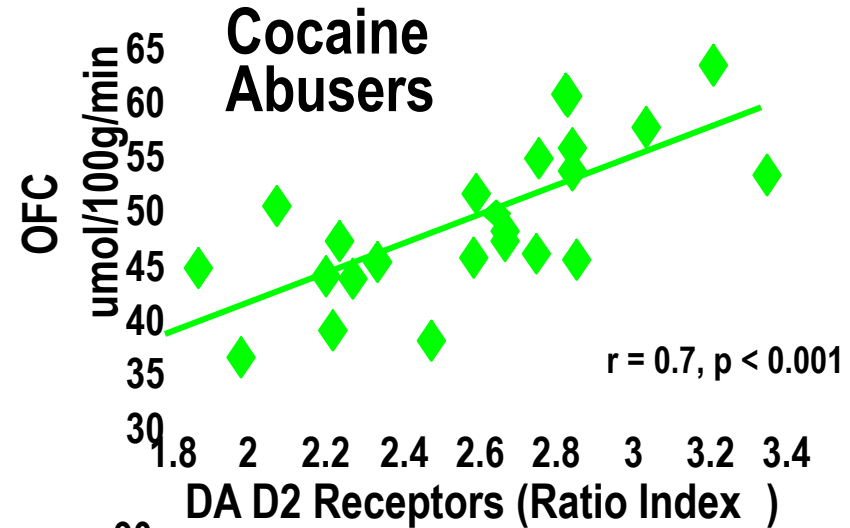


Salience Attribution



control

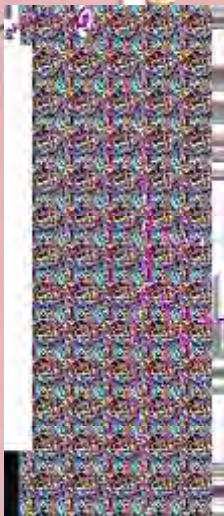
cocaine abuser



Signals from the gastrointestinal system to CNS



Nucleus Solitarius

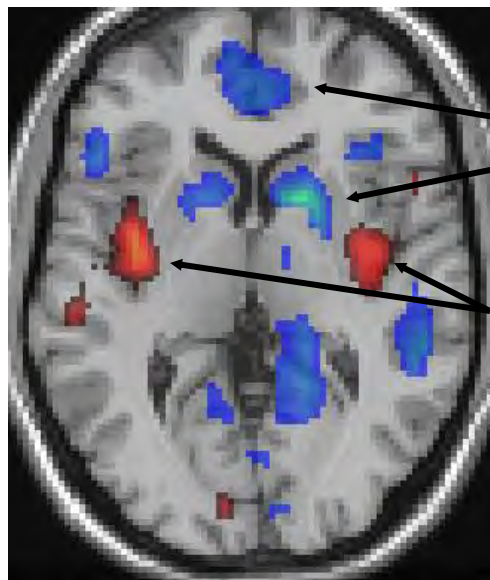
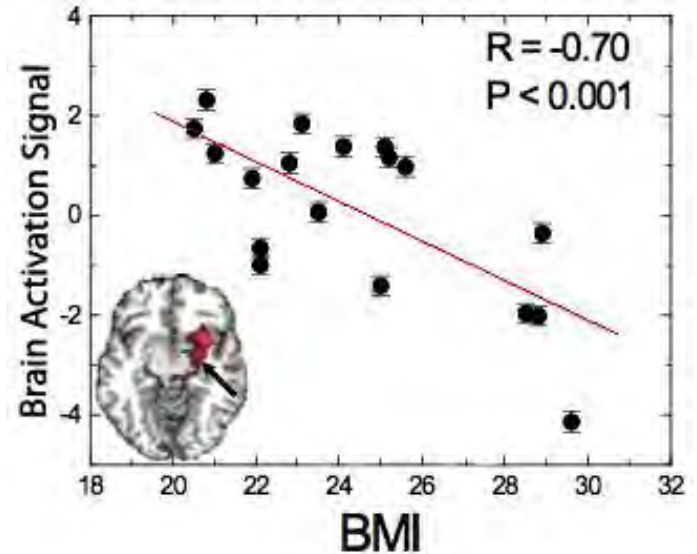
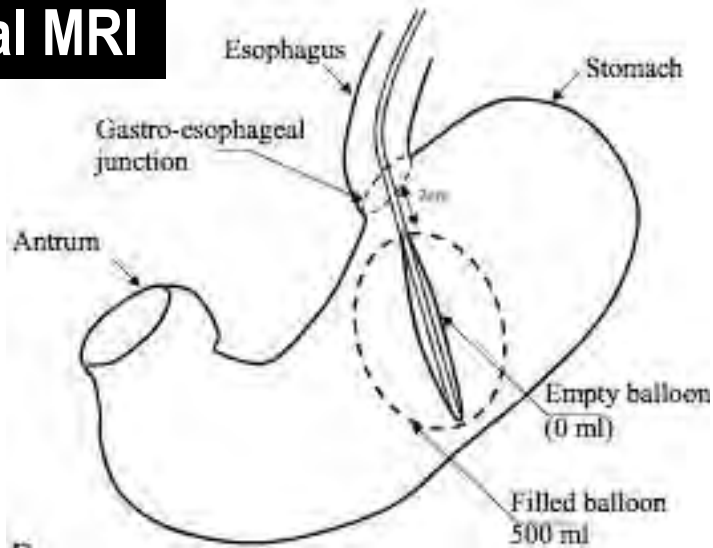


Spinal Cord

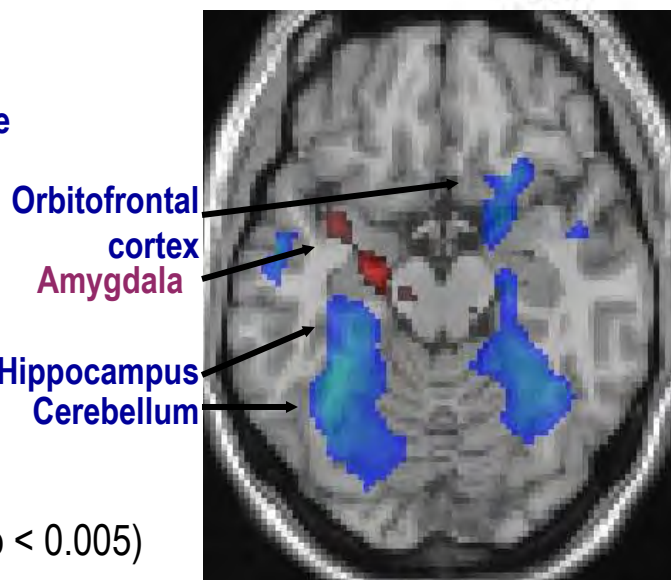
- The inhibitory processes arise from satiety signals (i.e. electrical and chemical) after food consumption.
- The vagus nerve is one of the ways by which satiety signals are conveyed to the brainstem.
- Gastric vagal afferents increase their firing in response to the mechanical pressure from the ingested nutrients and in response to food-induced release of a variety of brain gut peptides (i.e. CCK, ghrelin).

Brain activation during dynamic gastric distention

Functional MRI



Cingulate
Striatum
Insula



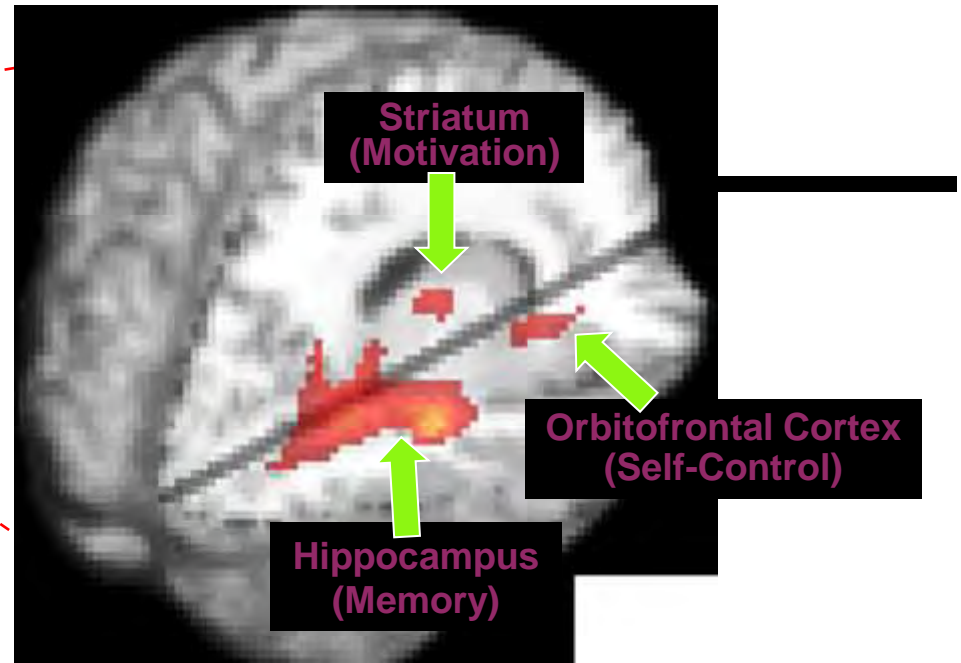
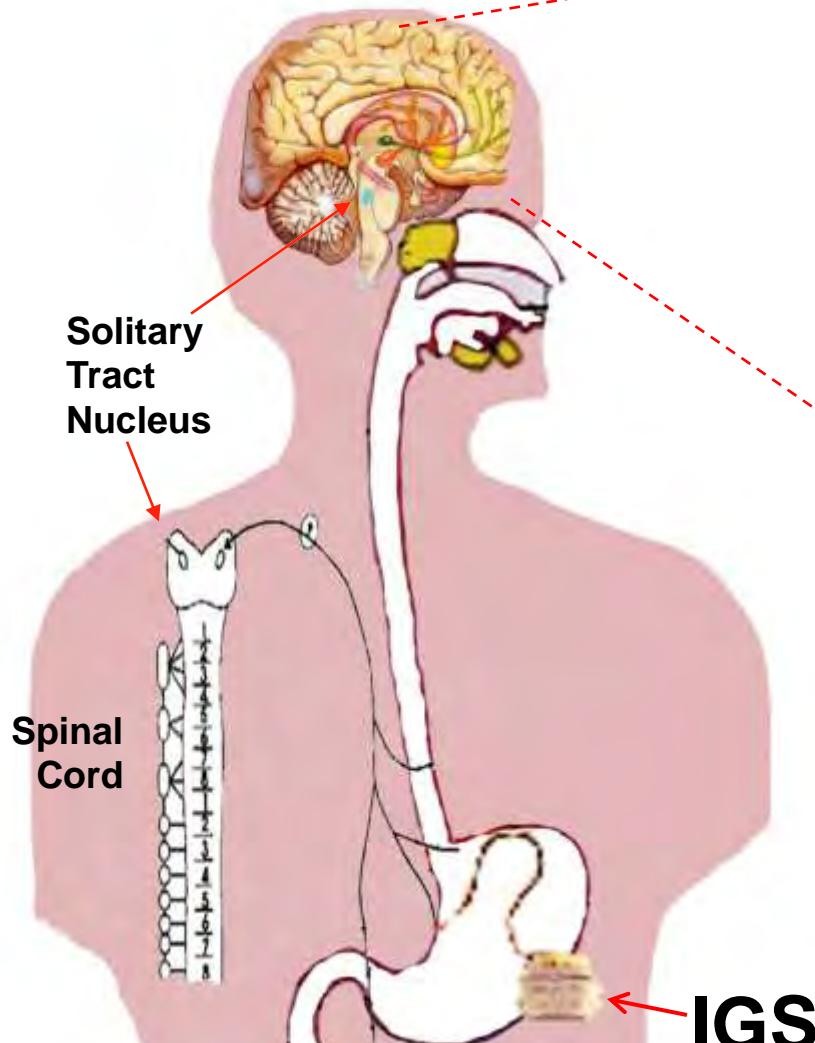
($p < 0.005$)

Red: Activation, Blue: Deactivation

Wang et al, NeuroImage

Why do some people continue to eat when the stomach is full?

^{18}F FDG-PET (IGS "on" vs IGS "off" in obese subjects)



Brain scans in obese subjects reveal higher metabolism in brain reward pathways when a "stomach stimulator" is turned on to simulate fullness vs. off. These same areas are also activated during drug craving in addicted subjects, supporting similarities between compulsive overeating and drug addiction

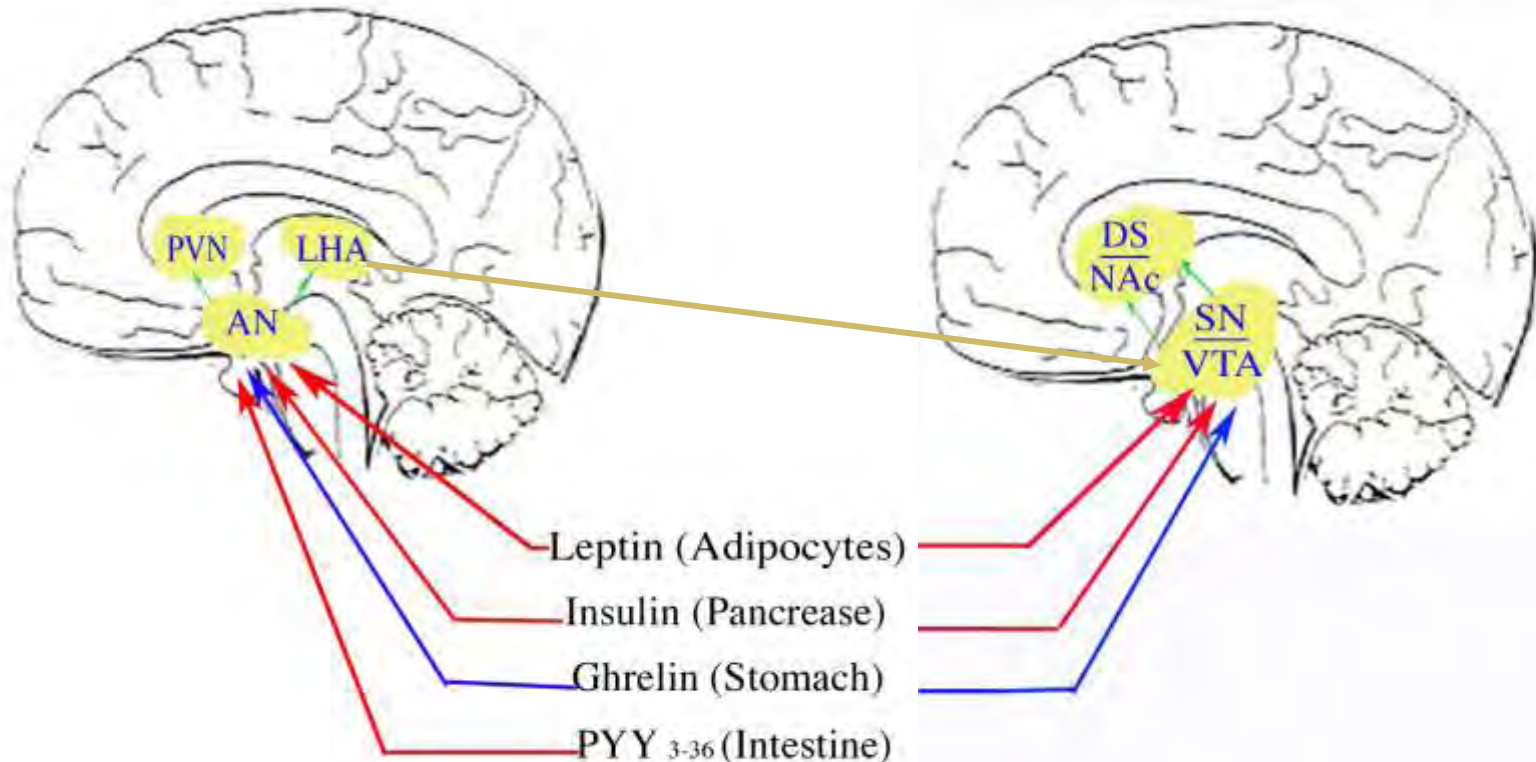
Wang et al, PNAS USA 2006

IGS: Implantable gastric stimulator

Factors regulate eating behaviors

Homeostatic Pathways

Reward Pathways



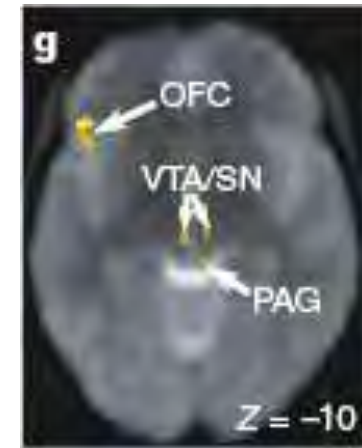
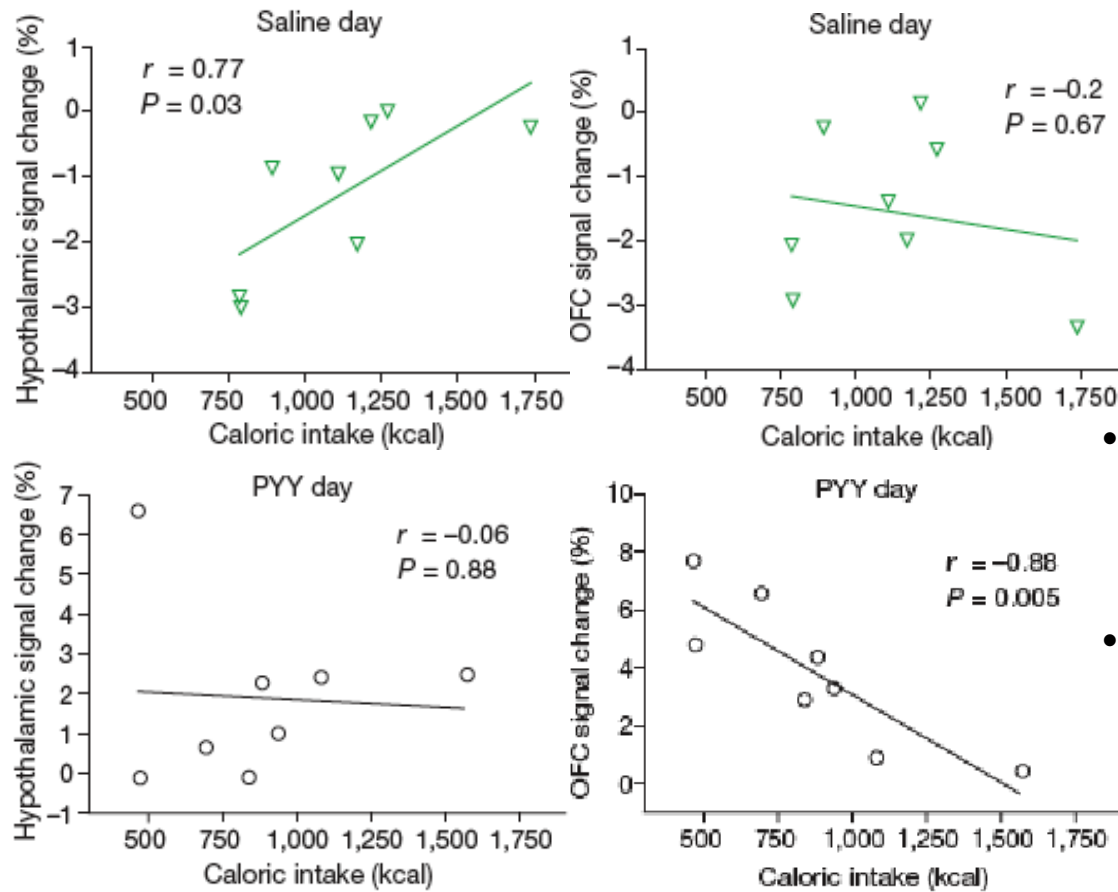
Blue: Excitatory input

Red: Inhibitory input

Wang GJ, et al, J Addiction Medicine, 2009

Why some people still have room for dessert after a big meal?

Functional MRI



- During fasting state, changes in the hypothalamus correlated with subsequent caloric intake.
- In the presence of high plasma PYY concentration that mimicking the fed state, changes in OFC predict caloric intake independently of meal-related sensory experience.

Hypothalamus

Orbitofrontal cortex

Switching food intake regulation from a homeostatic to a hedonic area in the presence of a postprandial satiety factor

Princeton Collaborators Reference

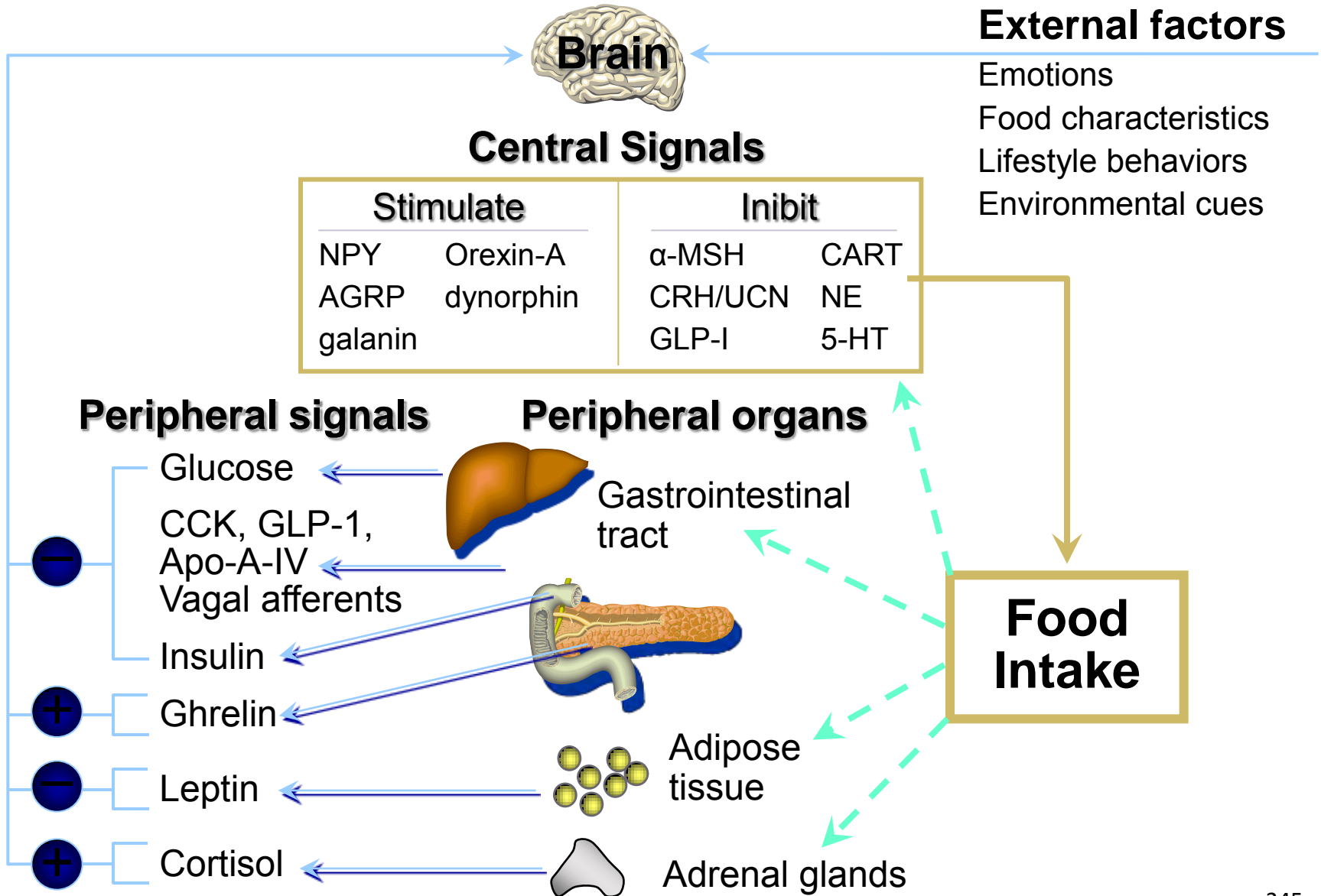


Avena, Rada, Hoebel.

Evidence for sugar addiction: ...

Neuroscience & Biobehavioral Reviews 32:20-
39, 2008

Regulation of Food Intake



Relying on Crash Diets



Determined to lose 10 pounds fast, you turn to a crash diet. Perhaps your plan calls for nothing but grapefruit or cabbage soup each day. You slash your daily calories to fewer than 1,000 -- and sure enough, the pounds melt away. But when you eat so few calories, you train your metabolism to slow down. Once the diet is over, you have a body that burns calories more slowly -- and gains weight more quickly -- than ever before.



RECOVERY
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ADDICTION

Skipping Breakfast



Skipping breakfast seems like a simple way to cut calories, but the result can be insatiable hunger the rest of the day. This may lead to unplanned snacking at the office and eating a super-size portion at lunch, making calorie counts soars. But breakfasts that are high in protein and fiber can reduce hunger throughout the day. In fact, studies show people who eat breakfast every morning are more likely to maintain a healthy weight.



RECOVERY
FROM
ADDICTION

Not Snacking at All



While mindless snacking can pad your waistline, *thoughtful* snacking may do just the opposite. People who eat several small meals and snacks a day are more likely to control hunger and lose weight. Snacking helps keep your metabolism in high gear, especially if the snacks are protein-rich. Nuts are a good, high-protein choice, and research suggests people who snack on nuts tend to be slimmer than those who don't.



RECOVERY
FROM
ADDICTION

Sipping Too Many Calories



When counting calories, many of us tend to overlook what's in our drinks. This is a big mistake when you consider that some fancy coffees and alcoholic beverages have more than 500 calories. Even the calories in fruit juice and soda can add up quickly. What's worse is that liquid calories don't curb hunger. You're not going to eat any less after a high-calorie drink.



RECOVERY
FROM
ADDICTION

STRESS



RECOVERY
FROM
ADDICTION

Too Little Sleep



RECOVERY
FROM
ADDICTION



Multicenter, Placebo-Controlled Trial of Lorcaserin for Weight Management

N Engl J Med 2010; 363(3): 245-56



- Lorcaserin is a small-molecule agonist of the serotonin 2C (5-HT_{2C}) receptor
- 2 year study; 3182 adults with BMI of ≥ 36.2
- With behavior modification, lorcaserin was associated with significant weight loss (5.8 ± 0.2 kg) and improved maintenance of weight loss (67.9%), compared with placebo (2.2 ± 0.1 kg; 50.3%)
- Lorcaserin caused no significant increase in FDA-defined valvulopathy

THE NEW ENGLAND
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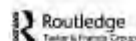
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REVIEW ARTICLE 109

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Addiction to Food and Brain Reward Systems

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Overeating is emerging as one of the most pressing health issues affecting developed countries. While it is known that overeating leads to overweight and obesity and a number of associated health risks, the etiology of overeating remains unclear. Overeating shares many characteristics with substance use disorders. Furthermore, overeating has been characterized as an addiction and most likely arises from a combination of abnormal cognitive and neuroendocrine processes. Although emotional states have been shown to modulate reward processing, the implications for hunger-mediated reward have not been fully elucidated. In this paper, we discuss the relationship between overeating and obesity with other substance addictions and the neural circuitry they share. Additionally, we discuss genetic and environmental influences on eating behaviors and the implications that these influences have on treatment.

Obesity is reaching pandemic proportions. Recent surveys indicate that 40 million Americans (approximately one-seventh of the American population) weigh 20% more than their ideal weight (McKesson Health Solutions, 2011). Among adults aged 20 to 74, obesity (body mass index [BMI] greater than 30) rates have soared from approximately 15% to 27% over the past two decades. Health problems linked to obesity are numerous and include stroke, heart disease, non-insulin dependent diabetes mellitus, osteoarthritis, and increased risk for developing cancer (Ps-Sanyal, 2002; Raman, 2002). According to a report by the American Medical Association (Allison, Fontaine, Manson, Stovens, & Vulvalic, 1999) every year, more than 280,000 deaths are associated with overeating and obesity. Obesity-related deaths rival the deaths attributed to alcohol and tobacco smoke, including secondhand smoke. Researchers generally agree that obesity is a disease (James, Gold, & Liu, 2001) but often debate its relationship to depression, personality disorders,

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How did I start Thinking About Obesity as an Addiction



- Woodstock
- Tobacco Cases
- Drug Addiction Treatment
 - HALT
 - Drug Craving...Eat...Chocolate/Cake/ Cookies



Bench to Bedside, Research Update from the McKnight Brain Institute 2010

RESEARCHERS

RECOVERY
FROM
ADDICTION

Adriaan Bruijnzeel, PhD
Associate Professor



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Firas H. Kobaissy, PhD

Research Assistant Professor



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Nicole M. Avena, PhD
Research Assistant
Professor



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Drake Morgan, MD
Assistant Professor



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Sara Jo Nixon, PhD
Professor



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Yijun Liu, PhD
Associate Professor



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Lisa J. Merlo, PhD
Assistant Professor



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C. Shawn Dotson, PhD
Assistant Professor

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Gary M. Reisfield, MD

**Associate Professor
Director of Pain
Management**



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Herbert E. Ward, MD
Associate Professor
Psychiatry Vice Chair
Division Chief of Adult
Outpatient Services



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Mark H. Lewis, PhD
Professor & Asst Chair



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Mark S. Gold, MD
Distinguished Professor, Eminent Scholar, Chairman



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