

# **Understanding Addiction from the Inside Out**

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## **Financial Disclosures**

- None

## **Learning Objectives**

Upon completion of this session, learners will be able to:

1. Describe the impact of addictive substances on the mesolimbic dopaminergic brain circuitry.
2. Explain the central role of dopamine and dopamine receptors in addictive disease.
3. Discuss the mechanism of action of the pharmacotherapies for treatment of addiction.

## **Hypothetical Patient**

- 32 yo Social Worker at MSBI
- Drinking 1 bottle of wine each evening
- Or
- Consuming 5 Percocets 4X day: no pain
- In stable supportive relationship
- No problems at work so far
- Recognizes that there is a problem, and seeking help and treatment

## ARTICLE

## Why Physicians Are Unprepared to Treat Patients Who Have Alcohol- and Drug-related Disorders

Norman S. Miller, MD, Lorinda M. Sheppard, MA, Christopher C. Colenda, MD, and Jai Magen, DO

## ABSTRACT

Most primary care physicians do not feel competent to treat alcohol- and drug-related disorders. Physicians generally do not like to work with patients with these disorders and do not find treating them rewarding. Despite large numbers of such patients, the diagnosis and treatment of alcohol- and drug-related disorders are generally considered peripheral to or outside medical matters and ultimately outside medical education. There is substantial evidence that physicians fail even to identify a large percentage of patients with these disorders.

Essential role models are lacking for future physicians to develop the attitudes and training they need to adequately approach addiction as a treatable medical illness. Faculty development programs in addictive disorders are needed to overcome the stigma, poor attitudes, and deficient skills among physicians who provide education and leadership for medical students and residents. The lack of parity with other medical disorders gives establishment

and education for addiction disorders low priority. Medical students and physicians can also be consumers and patients with addiction problems. Their attitudes and abilities to learn about alcohol- and drug-related disorders are impaired without interventions. Curricula lack sufficient instruction and experiences in addiction medicine throughout all years of medical education. Programs that have successfully changed students' attitudes and skills for treatment of addicted patients continue to be exceptional and limited in focus rather than the general practice in U.S. medical schools.

The authors review the findings of the literature on these problems, discuss the barriers to educational reform, and propose recommendations for developing an effective medical school curriculum about alcohol- and drug-related disorders.

Acad. Med. 2001;74:410-418.

### **Why Physicians are Unprepared Miller, *Academic Medicine* 2001;7:410-418**

- 12 hours of curricular time in avg.med.sch.
- Do not: 1. feel competent 2.like the patient 3.feel rewarded 4.have role models
- Barriers Identified:
  - 1.Lack of acceptance of medical model
  - 2.Lack of faculty/physician role models
  - 3.Curricular deficits in school/residence
  - 4.Lack of parity and physician advocacy
  - 5.Personal/family hx. of addictive disease

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## Addiction in a Broad Context

- Pulmonary---Tobacco Addiction
- Gastroenterology---Alcohol(Top→Bottom), Hep C, B
- Endo/Diabetes---Food→Obesity→D.M.-2
- Infectious Disease---HIV/AIDS—IDU
- Trauma Team---Alcohol,etc.—MVA
- Psychiatry---Vulnerability/Co-morbidity
- Pediatrics---Abuse, Adolescents
- Geriatrics---Alcohol as a Mimic of other diseases
- Gen. Med.---Insomnia, ↑BP, depression/anxiety weight loss, fatigue, falls, ↑LFT's etc.

## **What Is Addiction?**

**You Never Do What Addicted  
People Do.....Or Do You??**

Continuum

**User**←-----→**Addicted**

Vulnerability  
Understandable  
Logical, Rational, Linear

## **What is Addiction?**

- Chronic Brain Disease
- Generally Progressive
- Not Curable—"Recovering"
- Exacerbations(Relapses) & Remissions
- Treatable---many modalities(evidence base)
- Multidisciplinary Team

## ASAM Definition

- **Short Definition of Addiction:**
- Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.
- Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.

## Substance Use Disorder DSM-V

### Tolerance\*

**More use than intended**

**Unsuccessful efforts to cut down**

**Activities given up because of use**

**Failure to fulfill major role obligations**

**Recurrent use in hazardous situations**

**Severity measured by number of symptoms; 2-3 mild, 4-6 moderate, 7-11 severe**

**\* These do not apply if the medication is prescribed**

### Withdrawal\*

**Craving for the substance**

**Spends excessive time in acquisition**

**Uses despite negative effects**

**Continued use despite consistent social or interpersonal problems**

## What Is Addiction?

- Continued Use of an Activity, Despite Knowledge of Continued Harm to One's Self or Others---"Use Despite Harm"

## ADDICTION—TOWER of BABEL

- |                     |                          |
|---------------------|--------------------------|
| ■ BA/BS             | ■ CASAC, counselors      |
| ■ MPH/MB            | ■ Clergy, Spiritual      |
| ■ Social Work       | ■ Politicians            |
| ■ MDs—various       | ■ Lawyers, Judges        |
| ■ Ph.D—various      | ■ Criminal Justice Court |
| ■ RN/NP/LPN         | ■ Probation/Parole       |
| ■ PA                | ■ Administrators         |
| ■ Comp/Alt          | ■ Regulators             |
| ■ Patient Advocates | ■ Almost Anyone          |

**Staff members in Recovery or Not**

## **What is Addiction? (1) (descriptive)**

- An activity which initially provides pleasure, and is relatively, and usually harmless
- Increases Hedonic Tone
- De gustibus non disputandum
- The vulnerable recognize relief of dysphoric feelings, and often report feeling “normal”

## **What is Addiction? (1) (neuro-biology)**

- An activity which initially stimulates the “limbic” system, which results in changes of neurotransmitter levels, which are perceived as euphoria (↑hedonic tone)





Bungee Cord Jumping





### City Medical Examiner: Cerveny died from "acute cocaine and alcohol intoxication"

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Photo via Facebook  
**Kiersten Cerveny**

Posted: Thursday, October 22, 2015 11:17 am | Updated: 11:20 am, Thu Oct 22, 2015.  
By Joe Nikic  
Dr. Kiersten Cerveny, the Manhasset woman who was found dead on Oct. 4 in the lobby of an apartment building in New York City's Chelsea neighborhood, died from "acute cocaine and alcohol intoxication," according to the New York City Medical Examiner's office.  
The Medical Examiner's office also ruled her death accidental, according to a Daily News report.

?? COCA-ETHYLENE

## Freshman's Drinking Death Stuns a New Jersey University

By RONALD SMOTHERS  
Published: March 31, 2007

LAWRENCEVILLE, N.J., March 30 — An 18-year-old freshman at Rider University died on Friday, a day after he was admitted to a hospital after drinking an excessive amount of alcohol at a fraternity party.



Gary DeVerceley

As word spread about the death of Gary DeVerceley, of Long Beach, Calif., the mood on the 280-acre campus shifted suddenly, with solemn warnings about the need to exercise personal responsibility melting into expressions of shock and sadness.

A spokesman for the Mercer County prosecutor's office, which along with the Lawrence Township police is investigating the death, said that "everything was on the table."



Angelo Onofrio, an assistant prosecutor, said that depending on the outcome of the investigation, there could be charges involving misdemeanor hazing, felony hazing or manslaughter.

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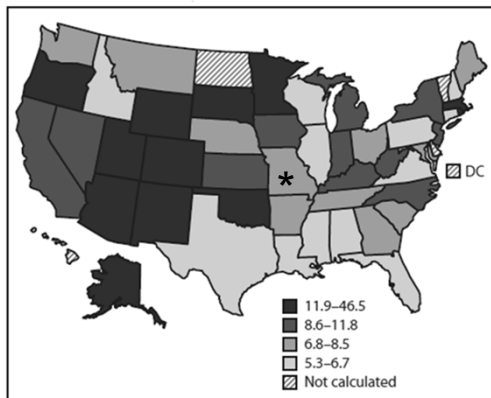
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**BAC=0.432 mg. % (0.08)**


## Vital Signs: Alcohol Poisoning Deaths — United States, 2010–2012

Dafna Kanny, PhD<sup>1</sup>, Robert D. Brewer, MD<sup>1</sup>, Jessica B. Mesnick, MPH<sup>1</sup>, Leonard J. Paulozzi, MD<sup>2</sup>, Timothy S. Naimi, MD<sup>3</sup>, Hua Lu, MS<sup>1</sup>  
(Author affiliations at end of text)

Conclusions: On average, six persons, mostly adult men, die from alcohol poisoning each day in the United States.



The figure above is a map of the United States showing age-adjusted alcohol poisoning death rates, by state, during 2010-2012. States with the highest death rates were located mostly in the Great Plains and western United States, but also included two New England states (Rhode Island and Massachusetts). Rates per 1 million population for persons aged ≥15 years were calculated using U.S. Census bridged-race population for 2010–2012, and were age-adjusted to the 2000 U.S. Census standard population.



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Ecolab Brand Skin Care Supplies, Reorder Code 6032105

Ecolab Quik-Care Aerosol Foam Hand Sanitizer, 500 ml bottle, 12/case

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- 12 per case

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**62.5%= 125 Proof**

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BAC: 312mg/dl: 4X80mg/dl

### Nationwide Alert: Fentanyl a Serious Public Health Threat

Caroline Cassels | March 18, 2015

The US Drug Enforcement Agency (DEA) has issued a nationwide alert about the dangers of the narcotic fentanyl and fentanyl analogues/compounds.

According to the DEA, the drug, which is often used in anesthesia to prevent pain after surgery or other procedures, is commonly laced in heroin, causing significant problems across the country, particularly because heroin abuse has increased.

"Drug incidents and overdoses related to fentanyl are occurring at an alarming rate throughout the United States and represent a significant threat to public health and safety," DEA administrator Michele M. Leonhart said in a statement.

"Often laced in heroin, fentanyl and fentanyl analogues produced in illicit, clandestine labs are up to 100 times more powerful than morphine and 30 to 50 times more powerful than heroin," she added.

The DEA reports that in the last 2 years, the DEA has seen a significant resurgence in fentanyl-related seizures. According to the National Forensic Laboratory Information System, state and local laboratories reported 3344 fentanyl submissions in 2014, up from 942 in 2013. In addition, the DEA has identified 15 other fentanyl-related compounds.

A Schedule II narcotic used fentanyl is the most potent opioid available for use in medical treatment — 50 to 100 times more potent than morphine, and 30 to 50 times more potent than heroin. Fentanyl is potentially lethal, even at very low levels. The DEA notes that ingestion of even small doses — as small as 0.25 mg — can be fatal. Its euphoric effects are indistinguishable from those of morphine or heroin.

## Why People Use Drugs

- To Alter Moods
- To Promote and Enhance Social Interactions
- To Enhance Sensory Experience and Pleasure
- To Aid Religious Practices
- To Explore the Self
- To Stimulate Artistic Creativity
- To Rebel

Weil, *From Chocolate to Morphine*, 1993

### Later On

#### How Steve Jobs was helped by his drug use

with 8 comments

An intriguing column by Glenn Greenwald:

It's fascinating to juxtapose America's reverence for Steve Jobs' accomplishments and its draconian drug policy with this, from the [New York Times' obituary of Jobs](#):

[Jobs] told a reporter that taking LSD was one of the two or three most important things he had done in his life. He said there were things about him that people who had not tried psychedelics — even people who knew him well, including his wife — could never understand.

Unlike many people who have enjoyed success, Jobs is not saying that he was able to succeed **despite** his illegal drug use; he's saying his success is in part — in substantial part — **because** of those illegal drugs (he **added** that Bill Gates would "be a broader guy if he had dropped acid once"). These quotes (first published by a *New York Times* reporter) have been around for some time but have been only rarely discussed in the recent hagiographies of Jobs: a notable omission given that he himself praised those experiences as an integral part of his identity and one of the most important things he ever did. A surprisingly good [Time Magazine article](#) elaborates on this Jobs-LSD connection further:



September 15, 2016

**Eight overdoses in 20 minutes: The night fentanyl-tainted cocaine almost devastated a B.C. town**

By Douglas Guan

*'Don't assume your kids are angels,' one of the victim's parents said. 'Twenty minutes in a small town on a weeknight ... a crisis was averted. It...'*

DELTA, B.C. - Days before he was scheduled to return to military school on the East Coast, 19-year-old Cody wanted one last summer hurrah with his buddies.

To keep the carousing in check, parents Jim and Sheila told their son he could invite his friends over to their Ladies B.C. home.

"You think if you're home and watching, nothing's going to happen," Sheila says from the family kitchen.

But shortly after 1 a.m. on Sept. 1, Jim and Sheila were roused from their sleep by two of Cody's friends.

Something was wrong with Cody, they said. Come quick.

Upstairs in the den, Cody was slumped over in a chair. He was unconscious and blue in the face.

Sheila screamed.

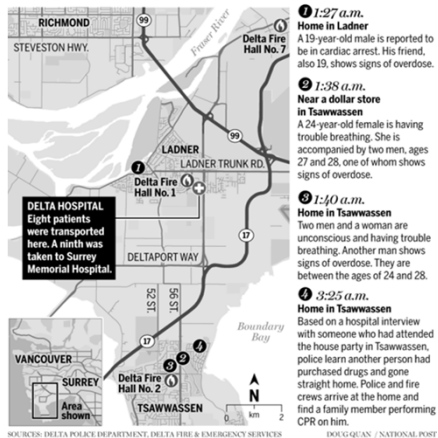
They carried his limp body onto the floor and checked for a pulse or a breath. They detected neither.

With the guidance of a 911 dispatcher, Sheila began pumping her son's chest.

"I was concerned his brain was getting no oxygen," she said. "And his eyes had completely rolled back in his head."

**OVERDOSE EPIDEMIC**

*In the early hours of Sept. 1, police, firefighters and paramedics in Delta, B.C., scrambled to respond to a series of overdoses at four locations within a short time. It is suspected that all nine patients had consumed cocaine tainted with fentanyl.*



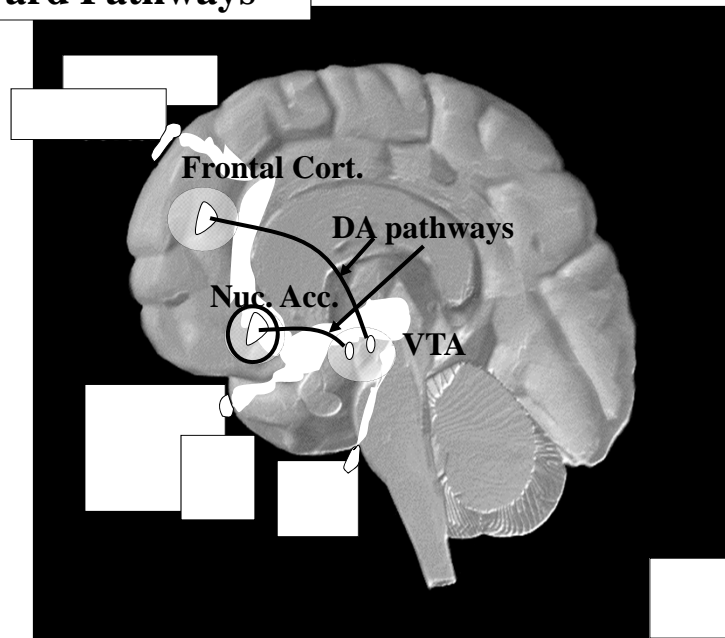
# What is Addiction?

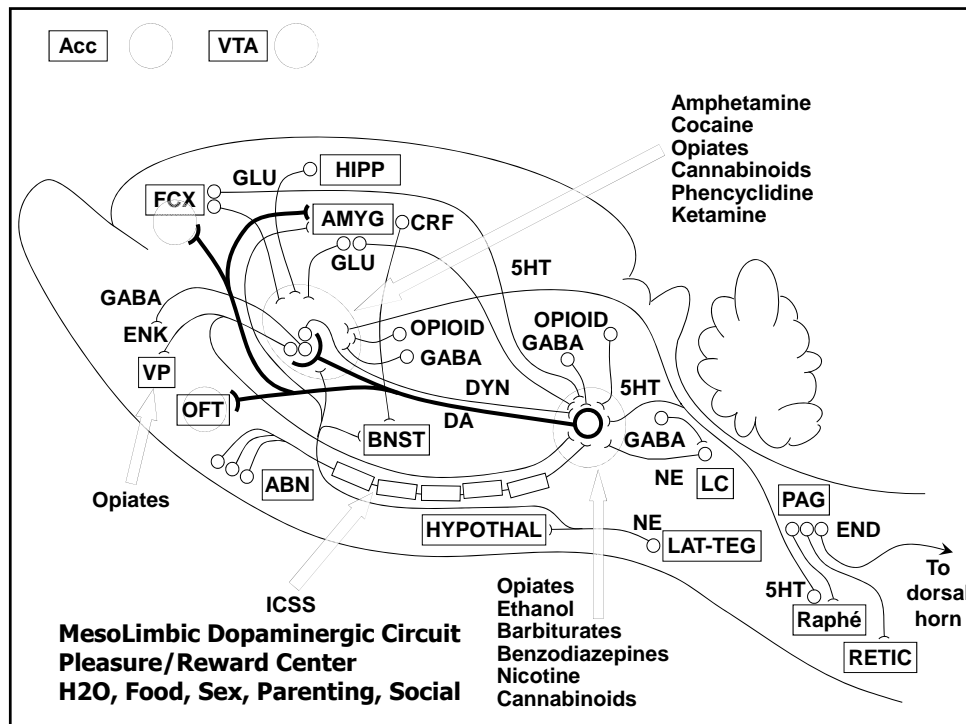
## Agent Usage

1. Abstinent
2. Use – social, religious  
circumstantial (medical)  
experimental  
operational  
recreational
3. Abuse / Misuse
4. Addiction
5. Legal / Illegal



## Reward Pathways





## The NeuroChemical Output of the “Limbic System” sets the organism’s **Hedonic Tone**

Feelings and Emotions are Neurochemical Reactions

Neurochemical Reactions produce Feelings and Emotions



## **HEDONIC TONE**

- Sense of well being, happiness, pleasure, contentment
- "Set" by/in the mesolimbic dopaminergic circuitry(Pleasure/Reward/Survival Center)
- Range: Euphoria ←-→ Dysphoria
- Altered by Psychoactive Activities
- A Delicate Balance
- Human Condition
- (?abnormal tone in the vulnerable, prior to the addictive state)

## **HEDONIC TONE SOURCES**

- SAFE
- DURABLE
- PRODUCTIVE
- DEPENDABLE

e.g. family, work, education, pets

&

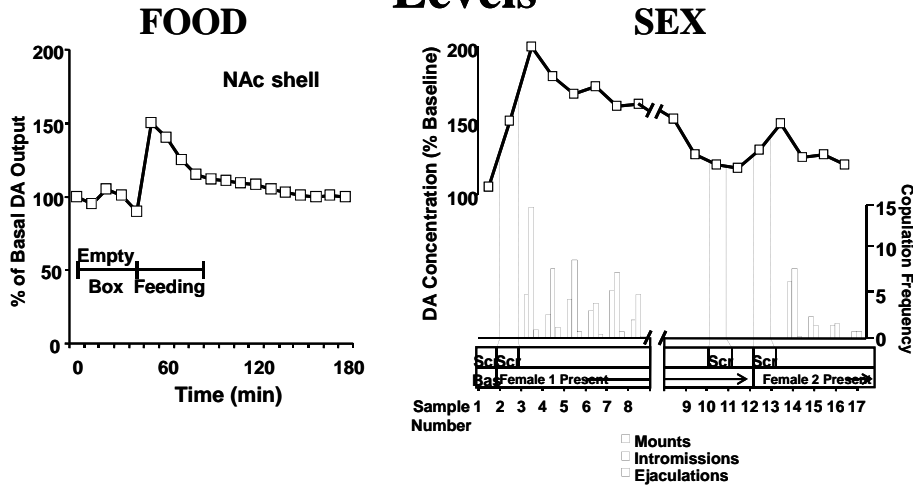
\*Appropriate FUN & EUPHORIA



## **IS X POTENTIALLY ADDICTIVE?**

- Must Activate the Hedonic Tone Circuits
- Water(psychogenic polydipsia)
- Food—Obesity Epidemic
- Sex
- Exercise
- Is Alcohol Addictive??→Only if Vulnerable
- Is Penicillin Addictive??→No
- So, like a Shakespearean tragic flaw, a virtue taken to excess.

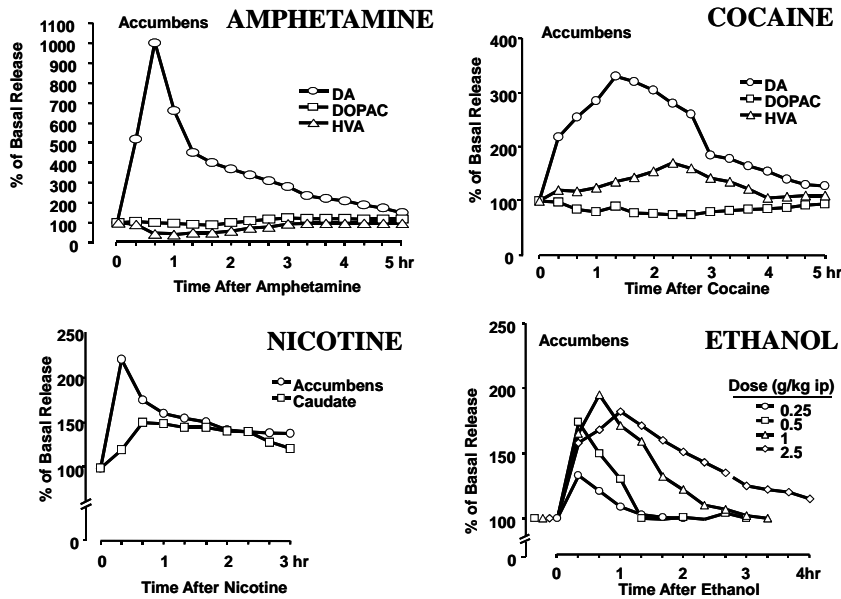
# Natural Rewards Elevate Dopamine Levels



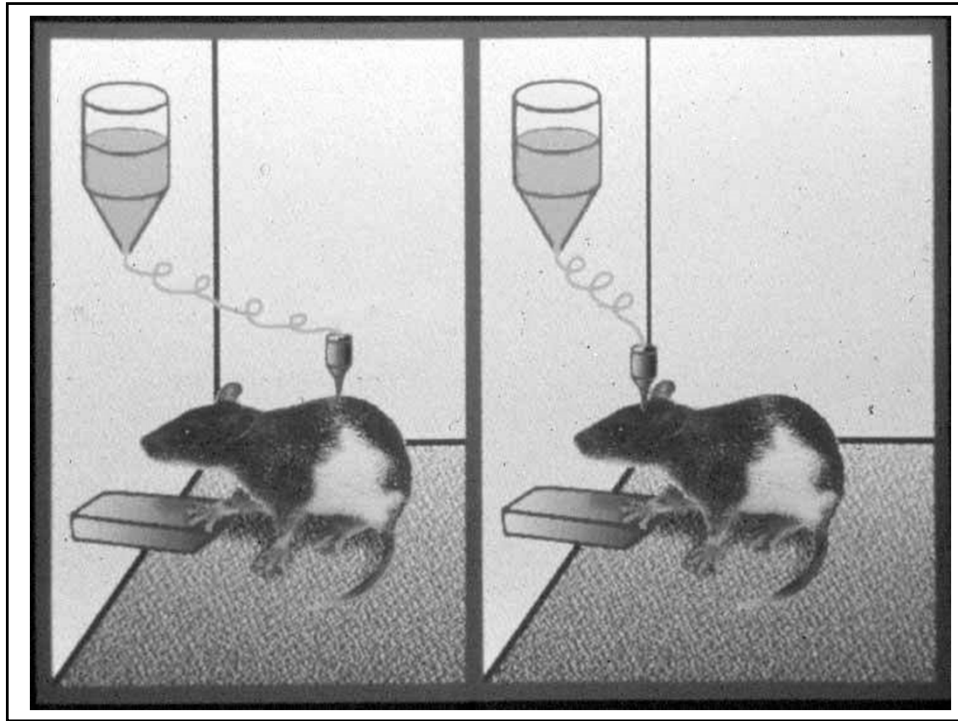
Source: Di Chiara et al.

Source: Fiorino and Phillips

# Effects of Drugs on Dopamine Levels

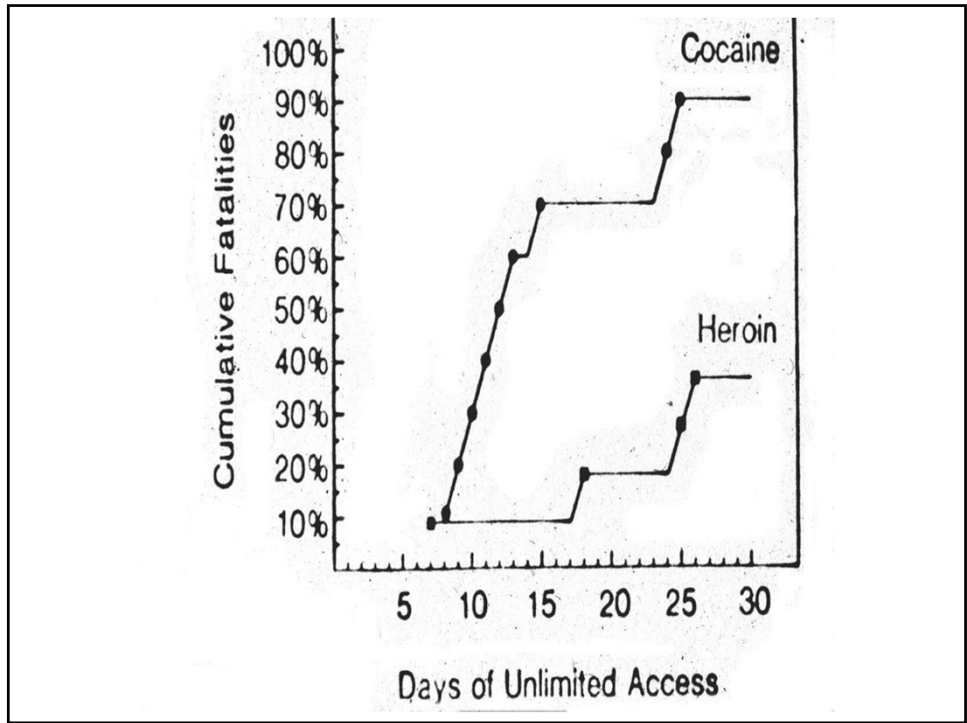


Source: Di Chiara and Imperato



## TOBACCO ADDICTION: 1PPD X 20YEARS

- 8 Puffs/Cigarette
- 160 Puffs/Day
- 1170 Puffs/Week
- 33,600 Puffs/Month
- 403,700 Puffs/Year
- 8,064,000 Puffs/20 Years
- Compare frequency/repetition of administration to any other addiction
- Habitual behavior
- ?Duration of effective pharmacological treatment: 12wks. 24wks. ??

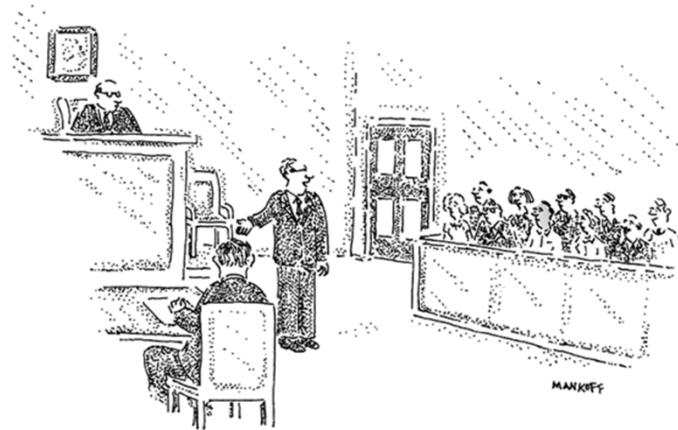


**LIMBIC SYSTEM(pleasure/reward center)**  
Gender Differences





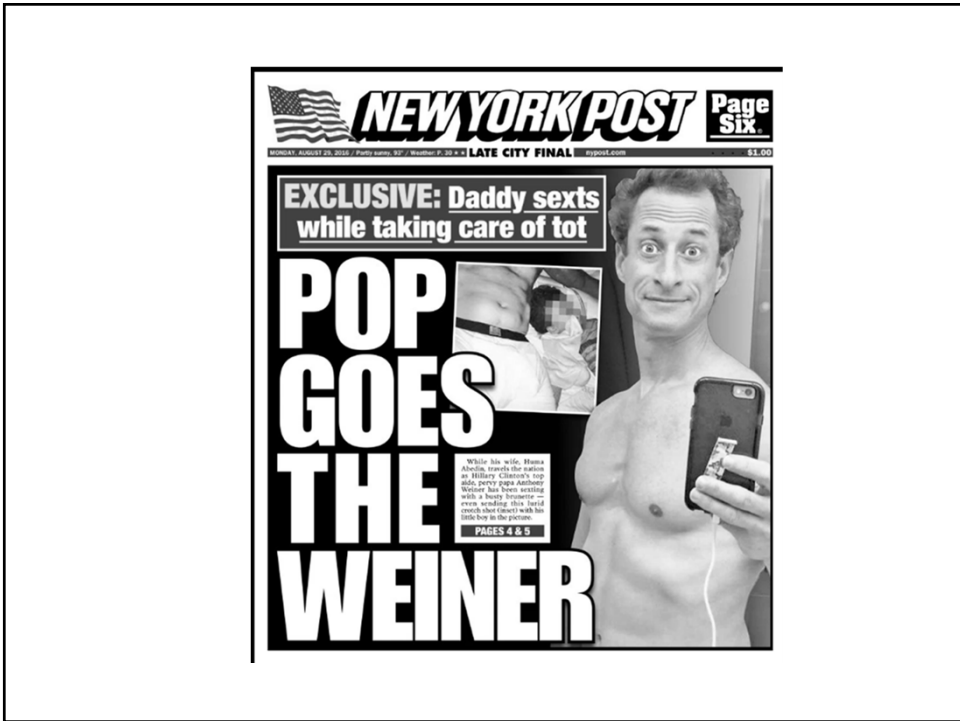
**LIMBIC SYSTEM---MALE/FEMALE**

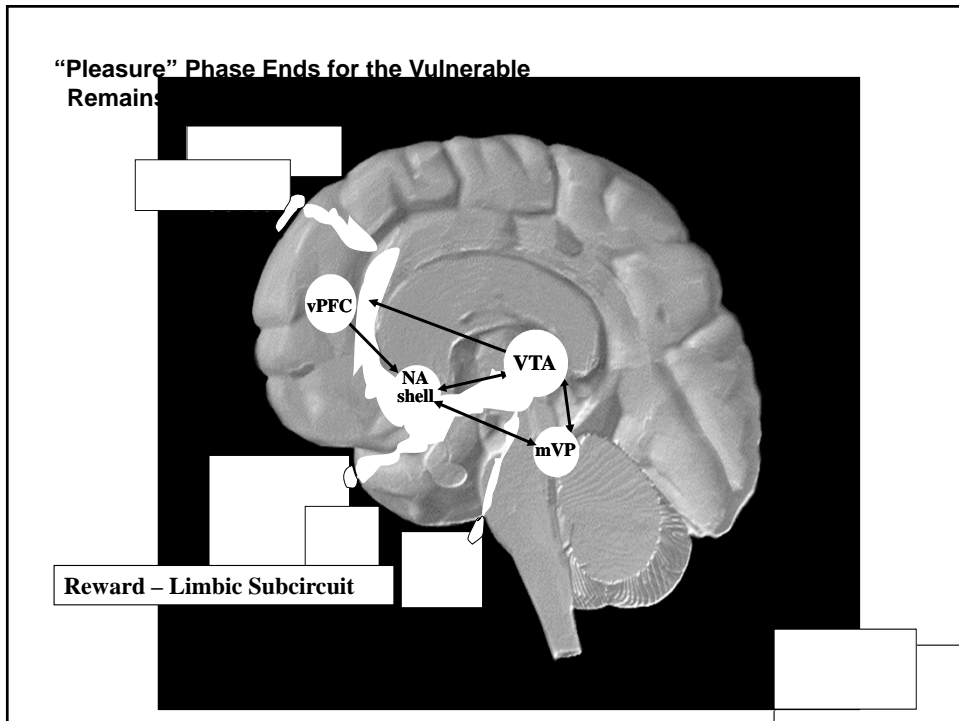


*"So, before passing judgment, please consider that science now shows that the male brain is not fully developed until never."*



March, 2008







## What is Addiction? (2) (descriptive)

- In those who are vulnerable---family history, and "life narrative"/environment--- the frequency, potency, method/route, and salience of the activity increases, the **pleasure/hedonic tone decreases**, and the **harm increases**.

## What is Addiction? (2) (neuro-biology)

- In the vulnerable, as the stimulation to the limbic and other parts of the brain continue, perturbations in brain function result in dysphoria, withdrawal, and impairments.

 **Hedonic Tone**

# Vulnerability to Addiction

- Genetic
- Environmental
- Cultural
- Stress
- Spotlight Euphoria
- Exaggerated Response
- Geriatrics
- Adolescents
- Privileged Upbringing
- Destitution
- Availability

## *Phil Parker, Who Helped Homeless Alcoholics, Dies at 86*

By SAM ROBERTS JUNE 29, 2016



Phil Parker in an undated photo. Mr. Parker had been sober for nearly 48 years when he died. Denis Mc Coy

Phil Parker, the son of a Baptist preacher, said he had never tasted liquor until his Harvard graduate school classmates lured him into a smoky cocktail lounge for the first time.

"This night in the bar was like no other time in my life," he wrote years later. "Not only was I completely at ease, but I actually loved all the strangers around me and they loved me in return, I thought, all because of this magic potion, alcohol."

After that, he wrote, he lived only to drink. He graduated, but was fired from one teaching job after another, wound up in an asylum and finally landed homeless on the then-squalid Bowery in Manhattan in the mid-1960s. There, he met a social worker, a member of the Bowery Mission.

Anonymous, who told him how she had sobered up.

"I had been preached to, analyzed, cursed, and counseled," Mr. Parker wrote, "but no one had ever said, 'I identify with what's going on with you. It happened to me, and this is what I did about it.' She got me to my first A.A. meeting that same evening."

In 1974, just a few years after he stopped drinking, Mr. Parker founded a supported work program that over the next several decades would help countless other homeless alcoholics. And as the derelict population became disproportionately young and black, Mr. Parker, who was black, became a social worker himself, supervising the program at the city's Third Street

## “Exaggerated Response”

What Did It Feel Like The First Few Times?

- “All My Problems Disappeared”
- “Felt Like I Was Under a Warm Blanket”
- “Thought This is How Normal People Feel”
- “Forgot About All the Abuse”
- “Felt Like the World Was at Peace”
- “Totally Relaxed” “Not Shy”
- “Looking at a Beautiful Sunset”
- “I Was Energized!!”
- *This is a Vulnerability (Liking Opioids)*

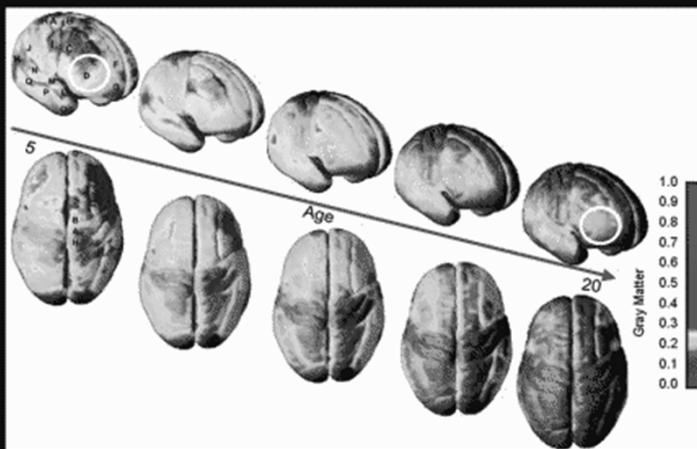
## “Exaggerated Reponse”

- “Best Dream You Ever Had, But You Are Awake”
- “Put A Bubble Around Me”
- “Exact Medication I Needed”
- “Felt Like The Best Massage, From The Inside Out”



*"The great thing about self-medicating is there is a low co-pay."*

### *MRI Scans of Healthy Children and Teens Over Time*



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Gogtay, Giedd, et al. Proc. Natl. Acad. Sci., 2004

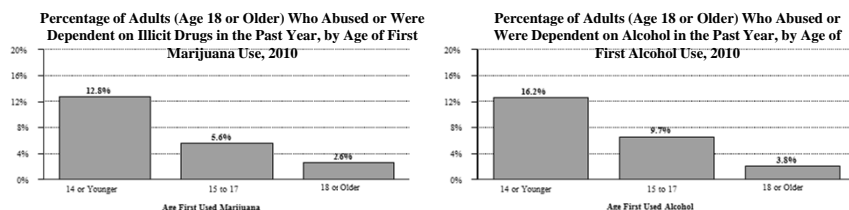
# CESAR FAX

December 12, 2011  
Vol. 20, Issue 47

A Weekly FAX from the Center for Substance Abuse Research  
University of Maryland, College Park

## Early Marijuana or Alcohol Use Related to Later Substance Use Disorders

Early marijuana or alcohol use is related to later substance use disorders, according to data from the National Survey on Drug Use and Health (NSDUH). Adults who first used marijuana at age 14 or younger were more than twice as likely to meet the criteria for past year illicit drug abuse or dependence than those who first used marijuana between the ages of 15 and 17 (12.8% vs. 5.6%) and nearly five times more likely than those who started when they were 18 or older (12.8% vs. 2.6%). Similar results were found for early alcohol use; those who first used alcohol at or before the age of 14 were nearly twice as likely to meet the criteria for past year alcohol abuse or dependence than those who started using alcohol between the ages of 15 and 17 (16.2% vs. 9.7%) and more than four times more likely than those who started using alcohol at the age of 18 or older (16.2% vs. 3.8%). While these findings illustrate the need for early alcohol and drug prevention efforts, it is likely that early substance use is an indicator of a disposition to engage in a variety of high-risk behaviors, suggesting that prevention efforts that encompass the whole person may be more effective.

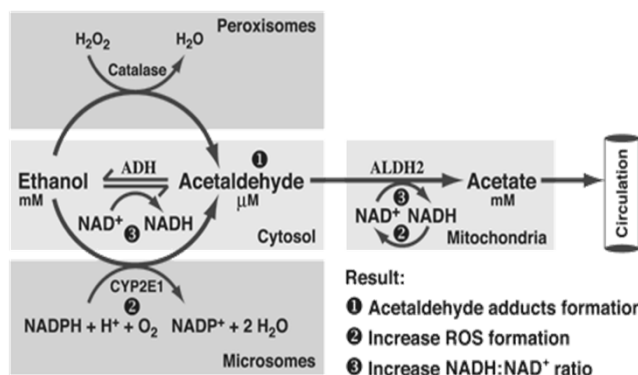


NOTE: Abuse or dependence are defined using DSM-IV criteria.

SOURCE: Adapted by CESAR from Substance Abuse and Mental Health Services Administration, *Results from the 2009 National Survey on Drug Use and Health: Detailed Tables*, 2010. Available online at <http://www.samhsa.gov/data/NSDUH/2K10ResultsTables/Web/PDEW/Sec6peTab3Sto40.pdf>

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## Genetic Protection



**ALDH.** Several isozymes of ALDH have been identified, but only the cytosolic ALDH1 and the mitochondrial ALDH2 metabolize acetaldehyde. There is one significant genetic polymorphism of the *ALDH2* gene, resulting in allelic variants *ALDH2\*1* and *ALDH2\*2*, which is virtually inactive. *ALDH2\*2* is present in about 50 percent of the Taiwanese, Han Chinese, and Japanese populations (Shen et al. 1997) and shows virtually no acetaldehyde metabolizing activity in vitro. People who have one (i.e., heterozygous) or especially two (i.e., homozygous) copies of the *ALDH2\*2* allele show increased acetaldehyde levels after alcohol consumption (Luu et al. 1995; Wall et al. 1997) and therefore experience negative physiological responses to alcohol.



Facial flushing in a 22-year-old ALDH2 heterozygote before (left) and after (right) drinking alcohol. The individual pictured in this figure has given written consent for publication of his picture using the PLoS consent form.

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### Scientists Discover Gene Responsible For Eating Whole Goddamn Bag Of Chips

TITLACA, NY--In an announcement with major implications for future generations of big fat hogs, Cornell University geneticists announced Monday that they have isolated the specific DNA series that makes an individual susceptible to eating a whole god-damn bag of chips.

"We have long known that the tendency to sit down and eat the whole god-damn bag runs in certain families," said team leader Dr. Edward Alvaro. "However, until we completed our work, we weren't sure whether the disposition to cram chips down your greasy gullet was genetic or whether it was a behavioral trait learned from one or both fat-suck parents. With the discovery of gene series CHP-48/OZ-379, we have proof positive that single-case serial chip-eating is indeed hereditary."

For years, scientists have been aware of the numerous health complications linked to a person's pre-disposition to plop down and mow through a whole bag of chips, but it wasn't until now that they were able to isolate the gene that carries the trait.

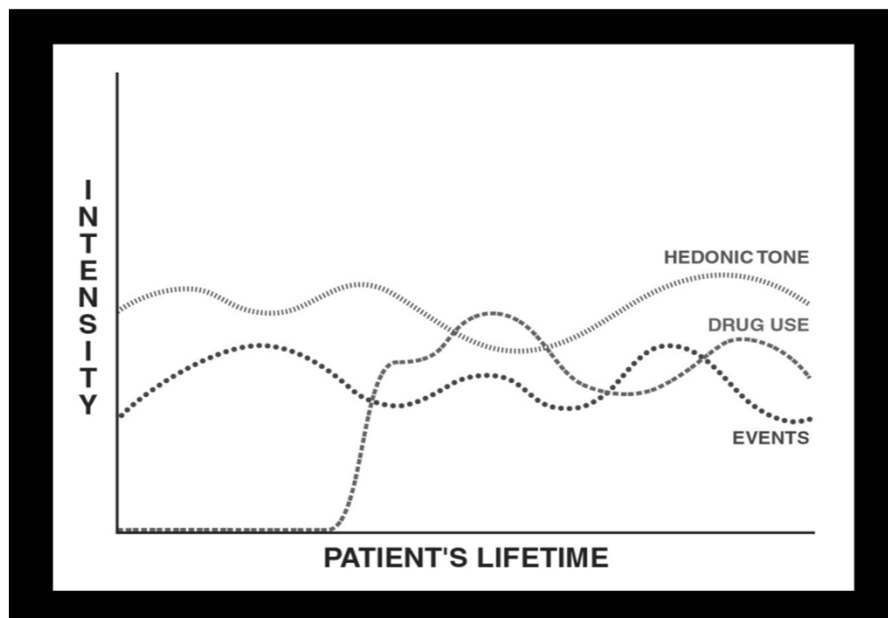
According to the Cornell team, series CHP-48/OZ-379 is a set of "alleles," or collections of genetic material, that cause chip-eaters to develop a markedly larger number of chip-responsive nerve endings in their cerebral material.

"People with this gene have up to four times the amount of interoceptors normally found in a human," Alvaro said. "This increases their pleasure response to mannamine-2, the human body's principal chip-eating hormone, which is released in response to giant handfuls of chips being shoveled into the mouth. This tends to promote entire-goddamn-bag-eating behavior in those individuals who possess the series."

## Addiction History

- Which drugs are you using?
- Age of onset for each drug.
- Route of administration for each drug.
- Previous treatment history.
- Medical/Psych problems.
- Other consequences.
- Almost nothing about events prior to addiction hx.
- "As if addiction fell from the sky."

## Understanding Addiction



The New York Times

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October 16, 1998  
FIGURE SKATING

### FIGURE SKATING; Striving for Recovery From Grip of Alcohol

By JERE LONGMAN

NEWARK, Del., Oct. 15— Seeking discipline and direction after four dizzying years of gold-medal heights and alcoholic depths, Oksana Baiul of Ukraine has begun training seriously again with a goal of competing in the 2002 Winter Olympic Games in Salt Lake City.



**In retrospect, Baiul said in an interview, her drinking problems began because she achieved too much too fast and did not have parental guidance when she moved to the United States after the 1994 Winter Games. Several years earlier, she had slept alone in an ice rink. Now she was suddenly able to earn \$2 million a year and live in a \$450,000 house in Simsbury, Conn. She said she felt "a lot of pain inside" and "pressure" and she turned to alcohol for consolation. In January 1997, she crashed her Mercedes into a tree and was charged with driving under the influence of alcohol.**

Oksana Baiul—1994 Gold Metal

### Michael Phelps to enter six-week treatment program after DUI arrest

October 05, 2014 | By Alison Knezevich | The Baltimore Sun

Olympic swimming champion Michael Phelps plans to enter a six-week in-patient treatment program after his recent drunken-driving arrest, he and his agent said Sunday. The move should help his legal case and boost his public image as he seeks to keep a swimming comeback alive, legal and sports experts said.

In statements on social media Sunday morning, Phelps told his fans that he plans to take time off to "attend a program" and focus on his personal life.

Recommend 2

0

18

Tweet Submit +1





## Addiction Medicine Office Supplies



**Requires Privacy, Time, and Interest**



## Addiction and Culture

- Stroke of Midnight—20th→21st Birthday
- POWER HOUR—"21 for 21"-Bar Closes 2AM
- "After 30 minutes and the 13<sup>th</sup> shot-a Prairie Fire, or Tequila with Tabasco- he vomits into a metal bucket, provided by the bar, the birthday souvenir taken home. Then he resumes drinking."
- "It's the best time of his life," a friend slurs to the camera."
- Deaths in CA. MI. NM. ND. RI. TX. NYT—2/05-ND



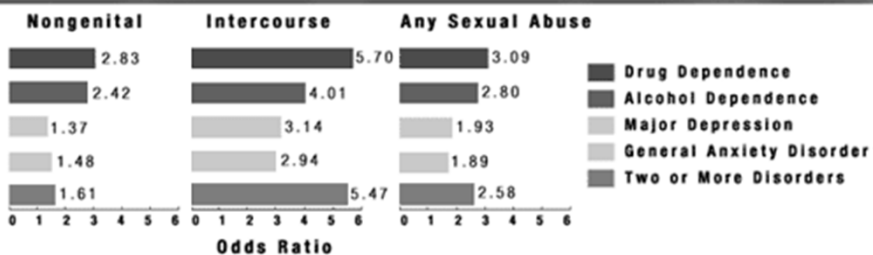
Research in rhesus monkeys suggests that good mothering may buffer the deleterious effects of a genetic variant in offspring that has been linked to behavioral problems. *JAMA. 2006;295:1756-1760*

## Addiction Vulnerability Gene/Environment Interaction

- Monkeys with short 5-HTT variant who were peer-reared had deficits in serotonin met.
- Monkeys with long 5-HTT variant who were peer-reared had elevated serotonin met.
- Mother-reared monkeys all had normal serotonin met. whether short/long 5-HTT
- Aggression in P-R, but not M-R short
- Low aggression in long, P-R or M-R

Suomi, JAMA, 2006, 295:1759

### Association of Childhood Sex Abuse With Drug Dependence And Psychiatric Disorders in Adult Women



Kendler, et. Arch Gen Psychiatry. 2000;57(10):953-959.

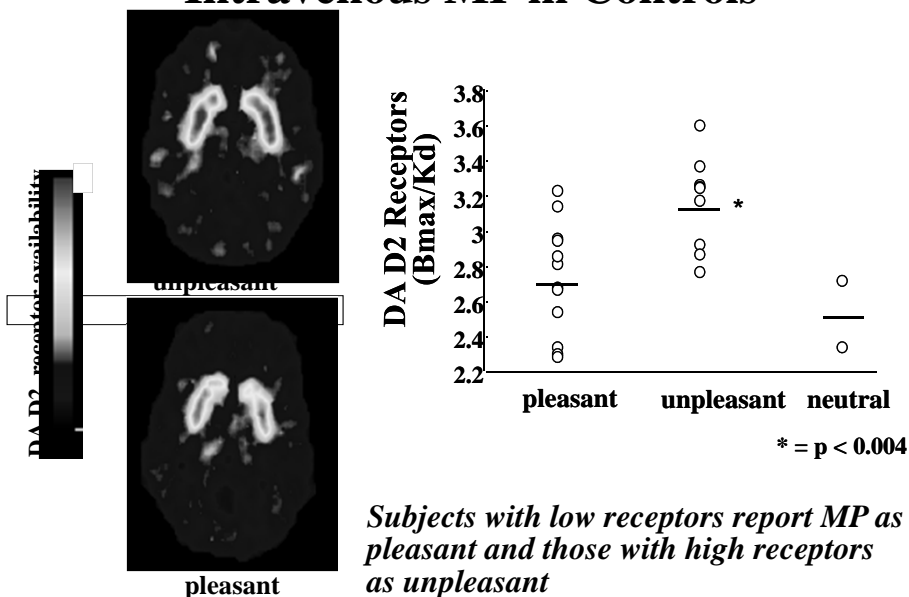
Brief Reports

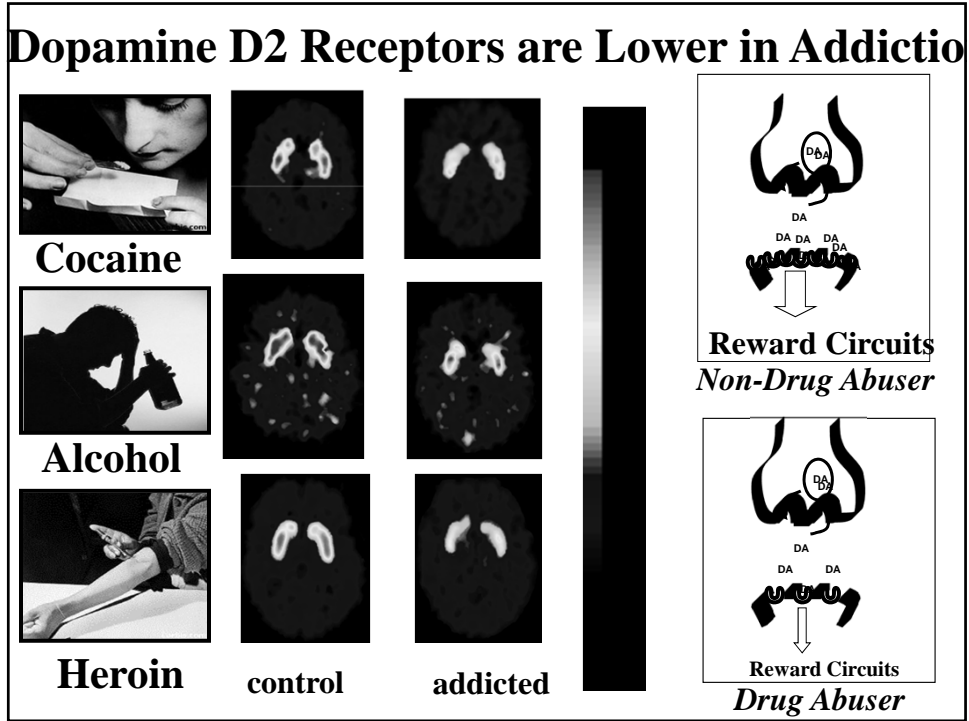
**Prediction of Reinforcing Responses to Psychostimulants in Humans by Brain Dopamine D<sub>2</sub> Receptor Levels**

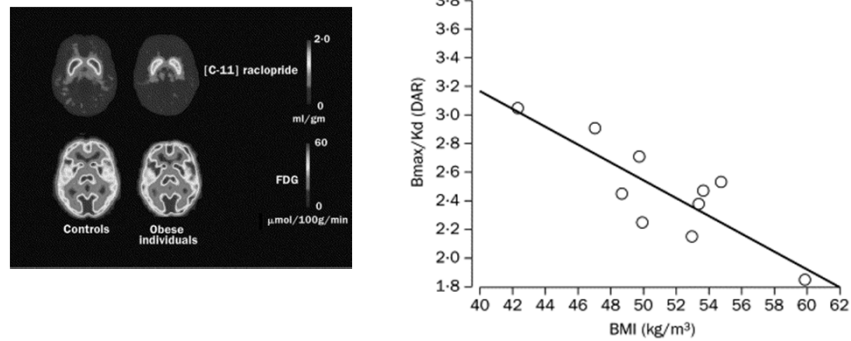
Nora D. Volkow, M.D., Gene-Jack Wang, M.D., Joanna S. Fowler, Ph.D., Jean Logan, Ph.D., Samuel J. Gatley, Ph.D., Andrew Gifford, Ph.D., Robert Hitzemann, Ph.D., Yu-Shin Ding, Ph.D., and Naomi Pappas, M.S.

**Objective:** This study assessed whether brain dopamine D<sub>2</sub> receptor levels, which show significant intersubject variability, predict reinforcing responses to psychostimulants in humans. **Method:** [<sup>11</sup>C]Raclopride and positron emission tomography were used to measure D<sub>2</sub> receptor levels in 23 healthy men (mean age=34 years, SD=7) who had no drug abuse histories in order to assess if there were differences between the subjects who liked and those who disliked the effects of intravenous methylphenidate (0.5 mg/kg). **Results:** Subjects who liked the effects of methylphenidate had significantly lower D<sub>2</sub> receptor levels (mean=2.72 B<sub>max</sub>/Kd, SD=0.3) than subjects who disliked its effects (mean=3.16, SD=0.3). Moreover, the higher the D<sub>2</sub> levels found, the more intense were methylphenidate's unpleasant effects. **Conclusions:** These results provide preliminary evidence that D<sub>2</sub> receptor levels predict response to psychostimulants in humans and that low D<sub>2</sub> receptors may contribute to psychostimulant abuse by favoring pleasant response. (Am J Psychiatry 159: 1440-1443)

**DA D2 Receptors and Response to Intravenous MP in Controls**







Drugs which block D2 receptors are orexigenic, e.g. antipsychotics  
 Drugs which increase dopamine are anorexigenic, e.g. cocaine

## “FOOD ADDICTION”

- A VERY USEFUL PARADIGM FOR UNDERSTANDING AND IDENTIFYING WITH PATIENTS/PEOPLE WHO SUFFER FROM ADDICTION TO ALCOHOL, OTHER DRUGS, GAMBLING, etc.

## Social dominance in monkeys: dopamine D<sub>2</sub> receptors and cocaine self-administration

Drake Morgan<sup>1</sup>, Kathleen A. Grant<sup>1</sup>, H. Donald Gage<sup>2</sup>, Robert H. Mach<sup>1,2</sup>, Jay R. Kaplan<sup>3</sup>, Osrice Prioleau<sup>1</sup>, Susan H. Nader<sup>1</sup>, Nancy Buchheimer<sup>2</sup>, Richard L. Ehrenkaufer<sup>2</sup> and Michael A. Nader<sup>1,2</sup>

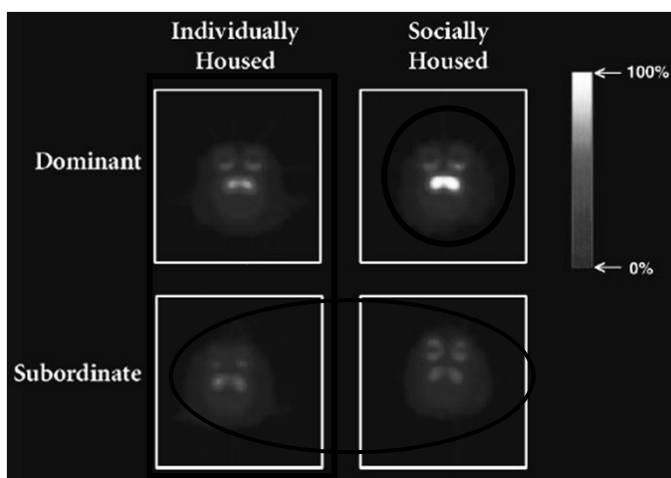
<sup>1</sup>Department of Physiology and Pharmacology, <sup>2</sup>Department of Radiology, <sup>3</sup>Departments of Pathology (Comparative Medicine) and Anthropology, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, North Carolina 27157, USA  
Correspondence should be addressed to M.A.N. (mnader@wfsjc.edu)

Published online: 22 January 2002, DOI: 10.1038/nn798

Disruption of the dopaminergic system has been implicated in the etiology of many pathological conditions, including drug addiction. Here we used positron emission tomography (PET) imaging to study brain dopaminergic function in individually housed and in socially housed cynomolgus macaques ( $n = 20$ ). Whereas the monkeys did not differ during individual housing, social housing increased the amount or availability of dopamine D<sub>2</sub> receptors in dominant monkeys and produced no change in subordinate monkeys. These neurobiological changes had an important behavioral influence as demonstrated by the finding that cocaine functioned as a reinforcer in subordinate but not dominant monkeys. These data demonstrate that alterations in an organism's environment can produce profound biological changes that have important behavioral associations, including vulnerability to cocaine addiction.

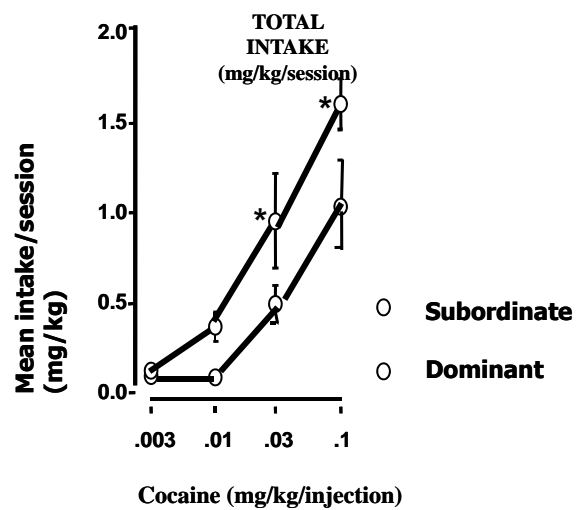
*Nature Neuroscience* 5, 169 - 174 (2002)

## PET Images: Dopamine Receptor Density



Social Dominance in Monkeys: Dopamine Receptors and Cocaine Self-Administration  
Morgan et al, *Nature Neuroscience* 2002

## Effect of Social Dominance on Cocaine Self-Administration



It's Good to Be the King!





# Watch Your Back

## Music/Neurobio/Hedonic Tone

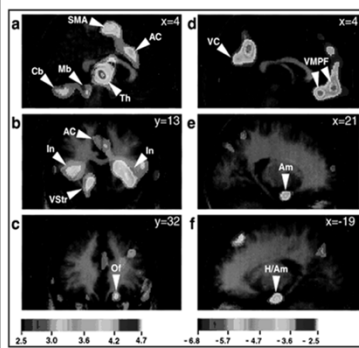
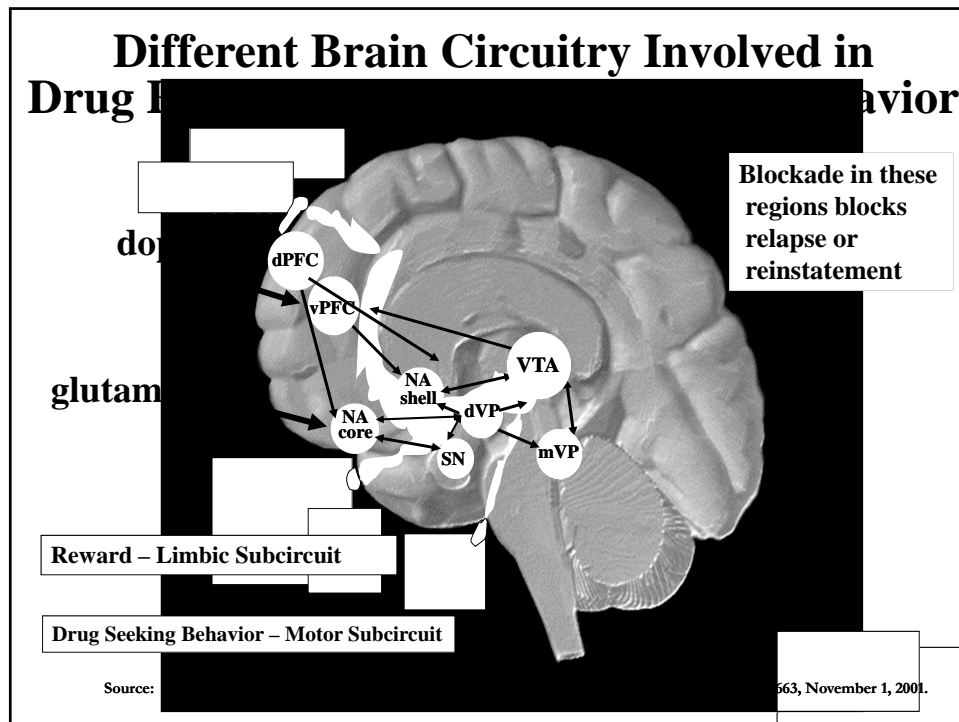


Fig. 2. Neuroanatomical regions demonstrating significant rCBF correlations with chills intensity ratings. Regression analyses were used to correlate rCBF from averaged PET data for combined subject-selected and control music scans with ratings of chills intensity (0 to 10). Correlations are shown as *t*-statistic images superimposed on corresponding average MRI scans (see Table 1, all music). The *t*-statistic ranges for each set of images are coded by color scales below each column, corresponding to *a-c* (positive correlations with increasing chills intensity), and *d-f* (negative correlations). *a* (sagittal section, *x* = 4 mm) shows positive rCBF correlations in left dorsomedial midbrain (Mb), right thalamus (Th), AC, SMA, and bilateral cerebellum (Cb). *b* (coronal section, *y* = 13 mm) shows left ventral striatum (VStr) and bilateral insula (In, also AC). *c* (coronal section, *y* = 32 mm) shows right orbitofrontal cortex (Of). *d* (sagittal section, *x* = 4 mm) shows negative rCBF correlations in VMPP and visual cortex (VC). *e* (sagittal section, *x* = 21 mm) shows right amygdala (Am). *f* (sagittal section, *x* = -19 mm) shows left hippocampus/amygdala (H/Am).

Blood, Zatorre, *PNAS*, 98, 20, 2001 11818-11823

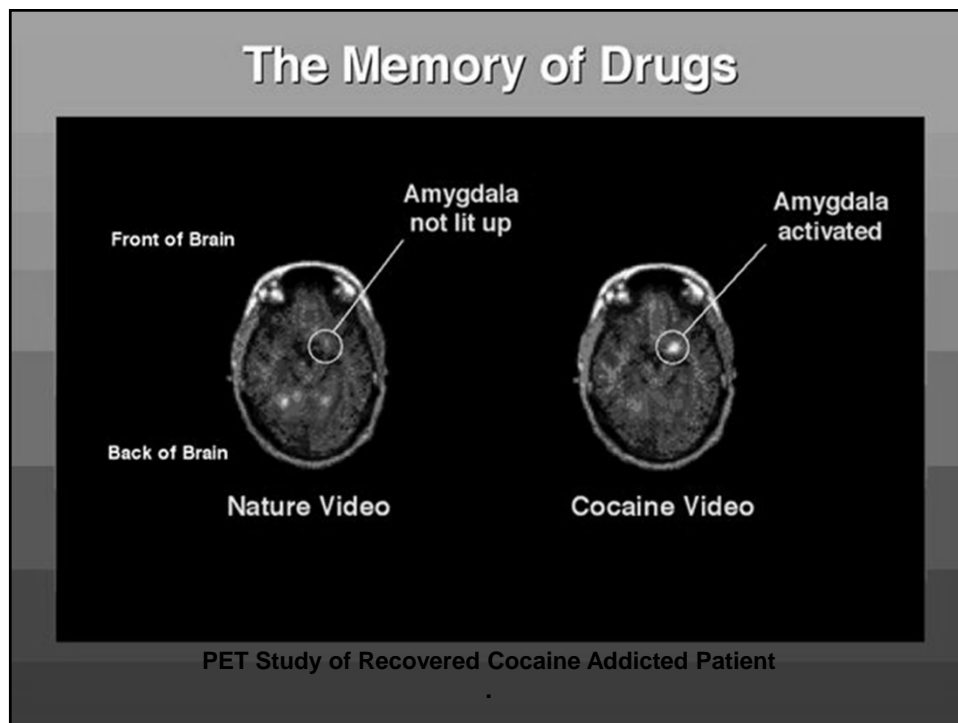


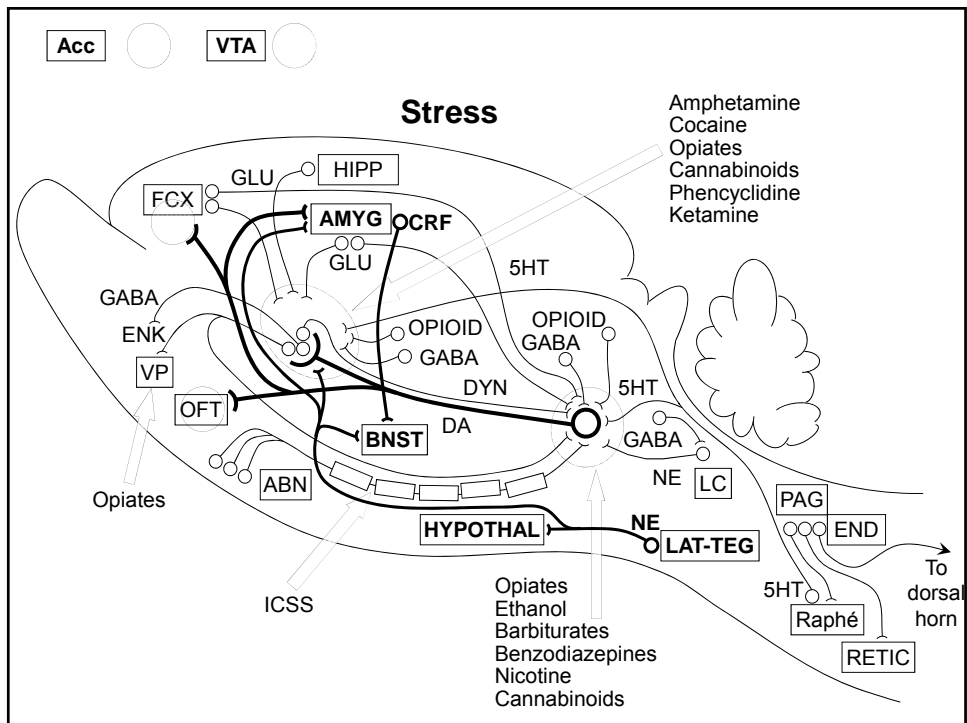
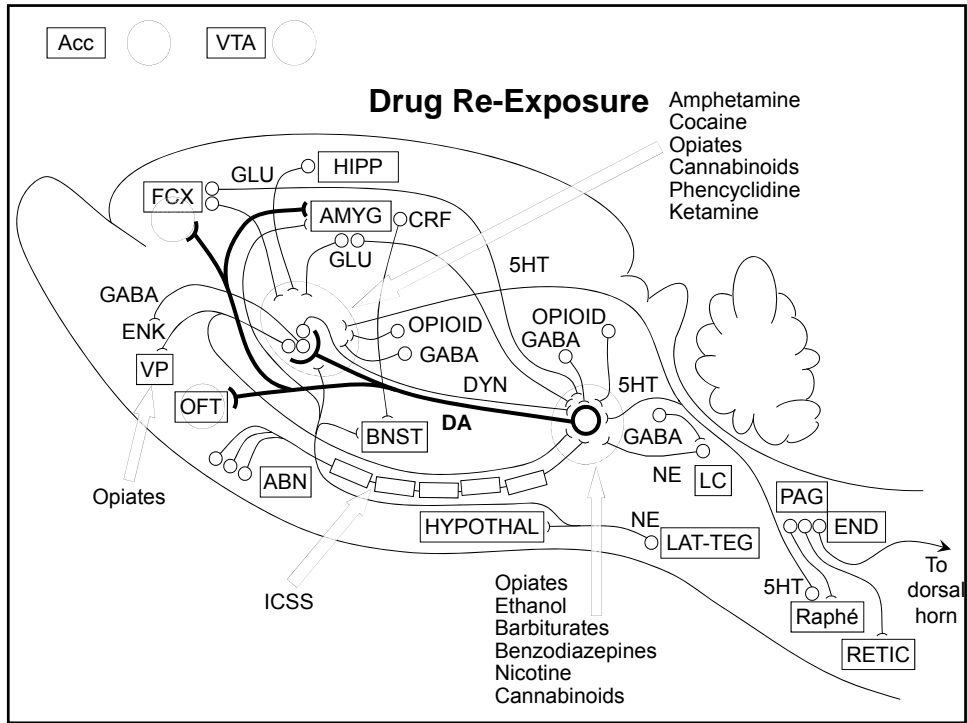
## What is Addiction? (3) (descriptive)

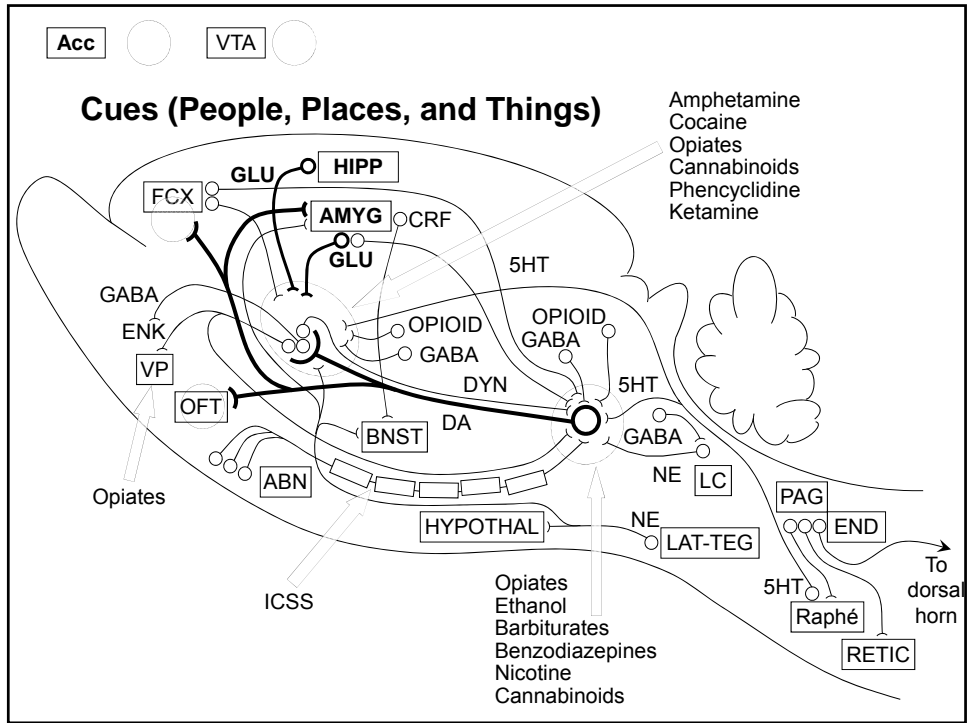
- Attempts to abstain from the activity are thwarted by cravings and “prolonged” withdrawal syndromes.
- Relapse is common, and often related to drug cues, stress, or drug exposure.

## What is Addiction? (3) (neuro-biology)

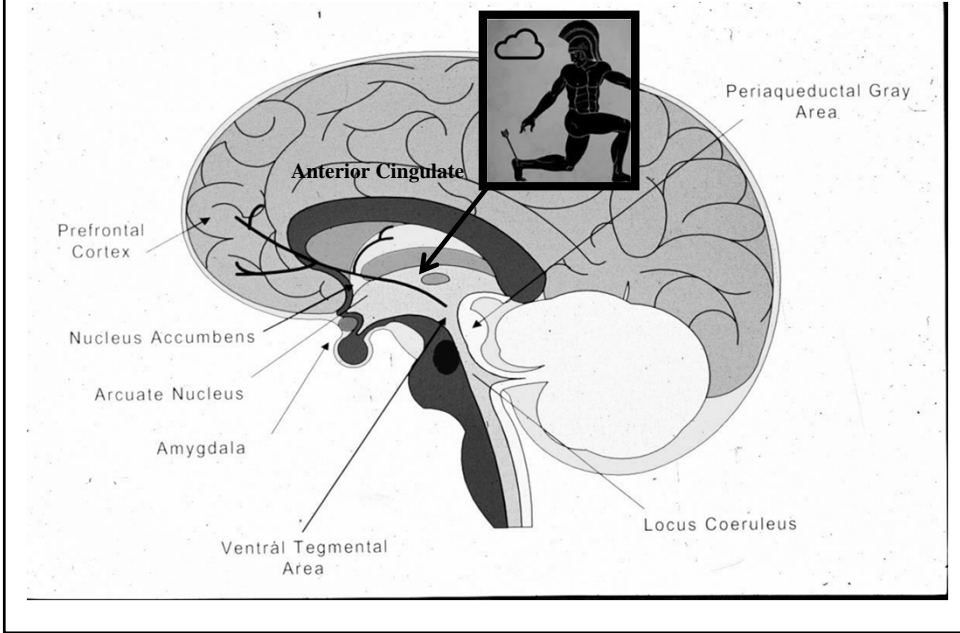
- Attempts to be abstinent are thwarted by the as yet ill-defined concepts of craving and prolonged withdrawal syndromes. The vulnerability, which is not "curable," may also play a role.
- Evidence suggests that relapse may be mediated via glutamatergic, dopaminergic, HPA axis, amygdala, and hippocampal mechanisms.







### Cortex/Limbic System "Equilibrium"



# HEDONIC TONE



**"Life is Short; Eat Dessert First"** Margie's Candies, Lincoln Park IL.



## **What Is Addiction? (4) (descriptive)**

- Treatment is directed at improving, and maximizing function in the personal, vocational, educational, psychological, and spiritual aspects of the patient's life.

## **What is Addiction? (4) (neuro-biology)**

- Treatment is directed at stabilizing, improving, and hopefully reversing the neurobiological perturbations secondary to the addictive agent, and the underlying vulnerability(?psychiatric co-morbidity).



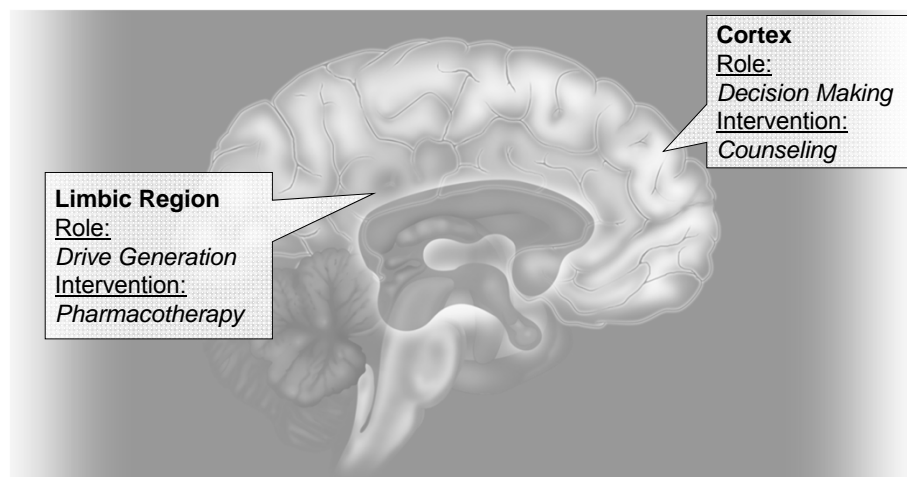
# MEDICATION ASSISTED ADDICTION TREATMENT

“**All** Treatments Work For **Some**  
People/Patients”

“**No One** Treatment Works for **All**  
People/Patients”

**Alan I. Leshner, Ph.D**  
Former Director NIDA

## Comprehensive Addiction Treatment



## **TOBACCO ADDICTION**

- Tobacco vs. Nicotine (Coffee vs. Caffeine)
- Nicotine Replacement Therapy (NRT)  
patches, gum, lozenges, inhaler, nasal spray
- Bupropion (Zyban, Wellbutrin)
- Varenicline (Chantix)
- Electronic Cigarette
- (Rimonabant—cannabinoid antagonist)

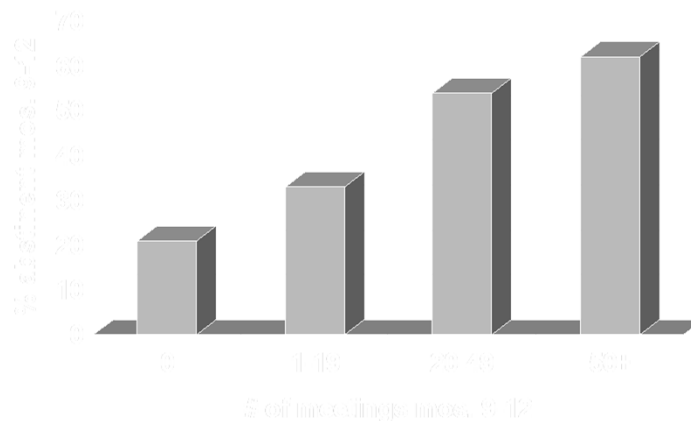
## **OPIOID ADDICTION**

- Opioid Agonist Therapy:  
Methadone Maintenance, MMTP, OTP  
Buprenorphine Maintenance, OBOT,  
OTP
- Opioid Antagonist Therapy:  
Naltrexone tablets and IM Injection

## ALCOHOL ADDICTION

- Disulfiram (Antabuse)
  - Naltrexone tablets
  - Naltrexone injectable (Vivitrol)
  - Acamprosate (Campral)
  - Gabapentin\* Mono or with NTX
  - Topiramate\* (Topamax)
  - Varenicline\* (Chantix)
- \*not FDA approved

## Abstinence & AA meeting amount



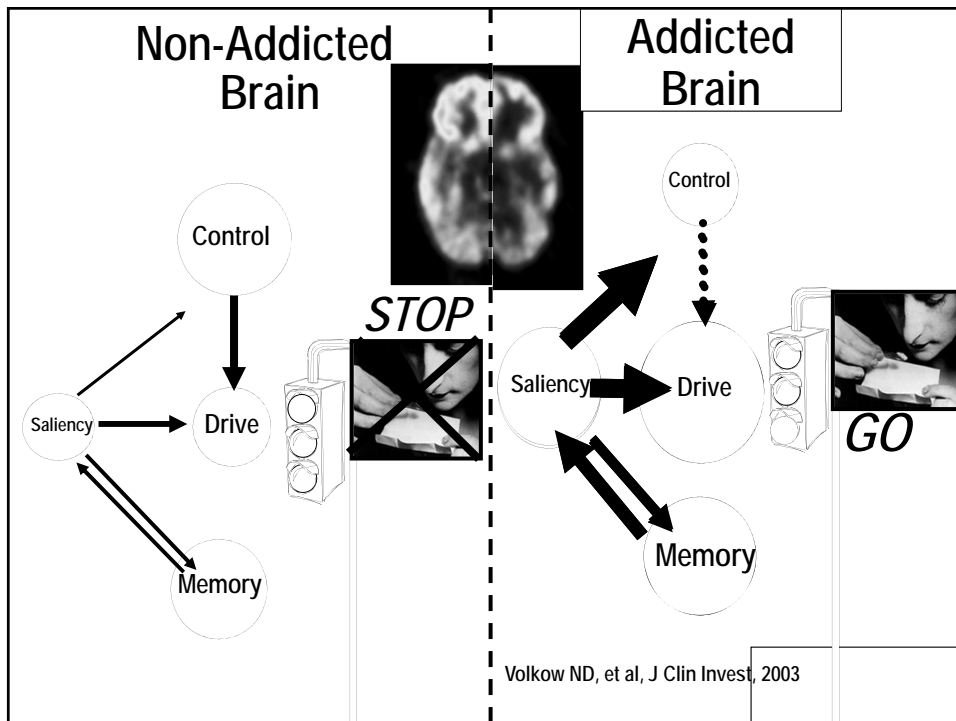
Male VA residential patients  
n = 2376

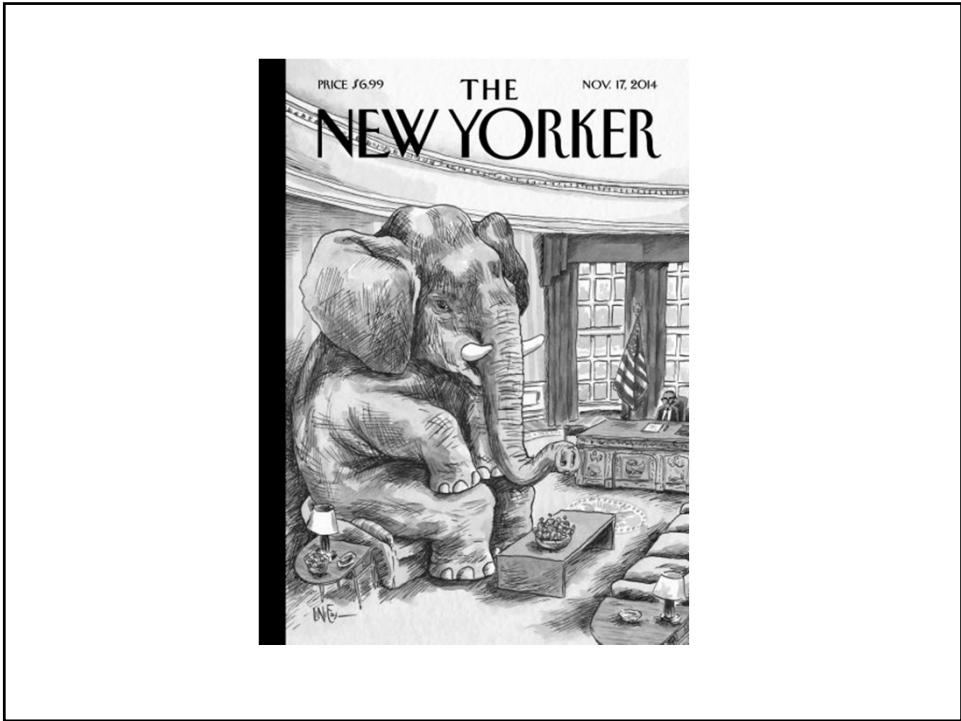
Moos et al., *J Clin Psychol* 2001

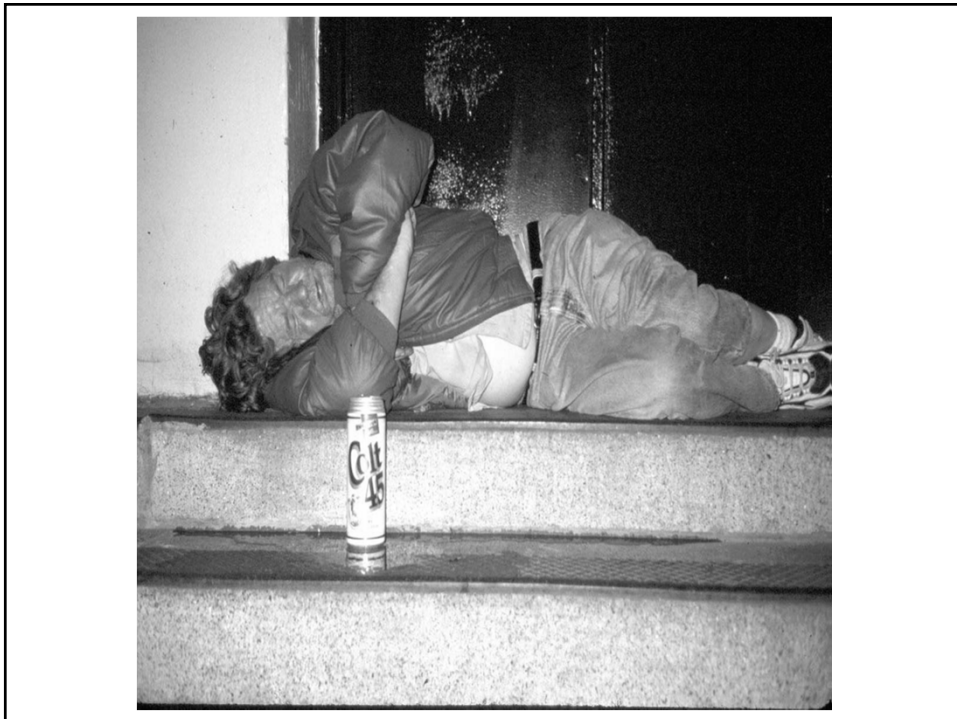
# Psychotherapy/Non-Pharmacologic Treatments



"We get in, we get help, and we get out."















## Destitution

- Lacking something needed
- Lacking possessions and resources
- Suffering extreme want
- Such extreme want as threatens life unless relieved
- Disconnected from society
- "Chaotic"

## DESTITUTION & ADDICTION

- |                     |                              |
|---------------------|------------------------------|
| ■ Housing-Homeless  | ■ Medical Co-morbidity       |
| ■ Family & Friends  | ■ Psychiatric Disorders      |
| ■ Education         | ■ HIV/AIDS                   |
| ■ Literacy          | ■ Criminal Justice           |
| ■ Vocational Skills | ■ Racial Issues              |
| ■ Employment        | ■ Societal Attitudes         |
| ■ Finances          | ■ Despair, Hopeless          |
| ■ Welfare           | ■ Civility, Anger, Gratitude |
| ■ Abuse ←→          | ■ Societal Institutions      |
| ■ Spirituality      | ■ <b>Addictions</b>          |

**The Whole is Greater than the Sum of its Parts**

## DESTITUTION & ADDICTION

- Often interrelated→ synergistic effects
- Addiction ≠ Destitution
- Which is the bigger problem?
- Which is easier to treat?
- Can Addiction (or DM, BP, asthma) be treated in the context of destitution?
- With appropriate resources, Addiction (or DM, BP, asthma) be treated in the context of destitution.
- Evidence-based harm reduction modalities useful.
- Is destitution masquerading as addiction?
- How “Painful” is destitution?
- Politically sensitive issues



**Girl Before a Mirror, Picasso**

# ENTERTAINMENT

ENTERTAINMENT HOME

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- POP TARTS
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HOT TOPICS

- VIDEO: FOX NEWS FLASH

FOXNEWS.COM HOME > ENTERTAINMENT

## Report: Lindsay Lohan Back in Rehab

Tuesday, May 29, 2007

FOX NEWS

E-MAIL STORY | RESPOND TO EDITOR | PRINTER FRIENDLY VERSION



Lindsay Lohan

AP

Lindsay Lohan is back in rehab, according to a report, after she crashed her car, got arrested on suspicion of DUI, was caught with alleged cocaine and passed out in front of paparazzi — all in one crazy Memorial Day weekend.

Lohan's lawyer drove her to the Promises Malibu Treatment Center in California, the same rehab facility attended by Britney Spears, TMZ.com reported. The site said Lohan will be in rehab possibly for 30 days, but will also be in an outpatient treatment program for much longer.

Less than 48 hours after she was arrested on suspicion of driving under the influence and

investigators found what they believed to be cocaine at the scene, Lohan, 20, was at it again Monday, partying with friends until she collapsed, according to photos and reports.

7th Edition [DailyNews.com](http://www.DailyNews.com) SPORTS FINAL Recalling media stars 4/20 Monday, February 13, 2012

# DAILY NEWS

NEW YORK'S HOMETOWN NEWSPAPER

## RX FOR DEATH

Whitney found in tub with Valium & Xanax near her PAGES 2 & 3

THE GRAMMYS PAY TRIBUTE TO HOUSTON SEE PAGES 4, 5 & 6

2/13/12



HIP MOM: A bikini-clad Britney Spears chats with dancers at One Little West 12th after she tried on one of their costumes.

'BLONDE' HAVING MORE FUN: Britney Spears plays tress-up at The Roxy Club in Hollywood yesterday. She stormed out 45 minutes later.

FAME, FORTUNE AND MISFORTUNE

Anna Nicole Smith

Born Vickie Lynn Hogan on Nov. 28, 1967, in Houston, Anna Nicole Smith dropped out of high school after 11th grade and went on to become a mother, model and celebrity.

1985: Marries at 17; son, Daniel Smith VIII, born  
Sept. 1991: Lands Playboy cover  
Feb. 1992: Files for divorce from Billy Wayne Smith  
March: Playboy cover debuts; later signs contract with Guess? Jeans  
April 1993: Film debut in "The Hud-sucker Proxy"  
Feb. 1994: Hospitalized after mixing prescription drugs and alcohol  
June: Marries J. Howard Marshall III at age 26  
Aug. 1995: Marshall dies of pneumonia at age 90

Feb. 1996: Files bankruptcy in California  
Feb. 1998: Smith arrested for battery for allegedly assaulting a hotel employee  
Sept. 2000: Anna Nicole awarded \$474 million judgment  
May 2001: Former stepson E. Pierce Marshall appeals, judge dismisses \$474 million ruling  
March 2002: Smith awarded \$88 million of J. Howard Marshall's oil fortune  
Aug.: "The Anna Nicole Show" premieres.

Oct. 2003: Becomes spokeswoman for TrimSpa, a diet pill company  
Dec. 2004: Court overturns \$88 million inheritance  
Sept. 2005: Supreme Court agrees to review Smith's appeal over the Marshall fortune  
2006: Attends Supreme Court hearing, avoids making statement  
Sept.: Anna Nicole gives birth to a girl, son Daniel Smith dies in the Bahamas days later  
Feb. 8, 2007: Anna Nicole collapses and is pronounced dead in Hollywood, Fla.



AP

## WHAT IS ADDICTION?

- Addiction is a Failed and Doomed Attempt to Elevate and Maintain Adequate HEDONIC TONE.



