

Addictive Disorders

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Disclosures

No stock, options or patents

Research almost 100%NIH supported Occasional consultation fees

None at NIH threshold

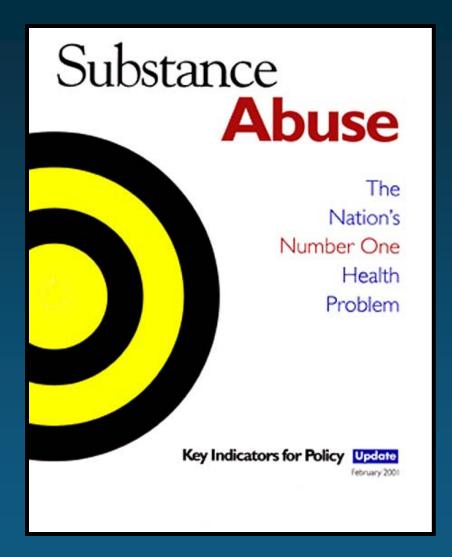
Alkermes

Merck

Purdue

CVT

Embera



The Robert Wood Johnson Foundation has identified **Substance** Abuse as the Nation's **Number One** Health Problem.

Drug Categories

Nicotine

Alcohol

Marijuana

Anabolic Steroids

Inhalants

Club Drugs

Stimulants

Sedatives

Heroin

Use

Use Abuse

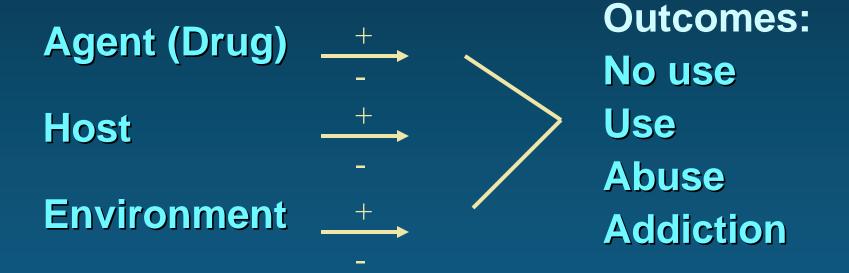
Use

Addiction

Use Abuse

Use

Resultant of interacting variables



Dependence (Addiction)

DSM-IV

- Tolerance
- Withdrawal
- More use than intended
- Unsuccessful efforts to cut down
- Spends excessive time in acquisition
- Activities given up because of use
- Uses despite negative effects

Risk of Addiction

	Ever Used (%)	Dependence (%)	Risk (%)
Tobacco	75.6	24.1	31.9
Cocaine	16.2	2.7	16.7
Heroin	1.5	0.4	23.1
Alcohol	91.5	14.1	15.4
Cannabis	46.3	4.2	9.1

Source: Anthony et al, 1994.

Two states produced by repeated drug use

"physical" dependence

Compulsive, out of control drugseeking

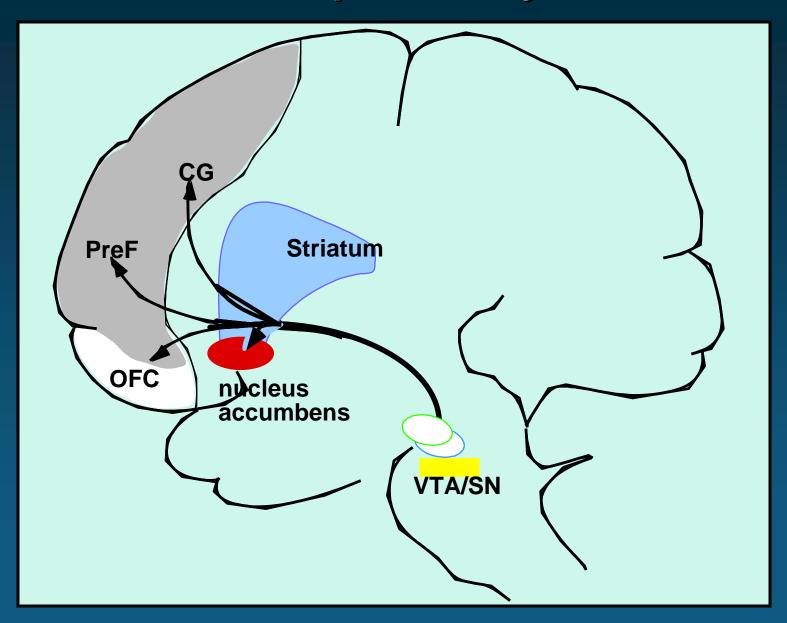
Fundamental basis of addiction

A maladaptive memory, physical changes

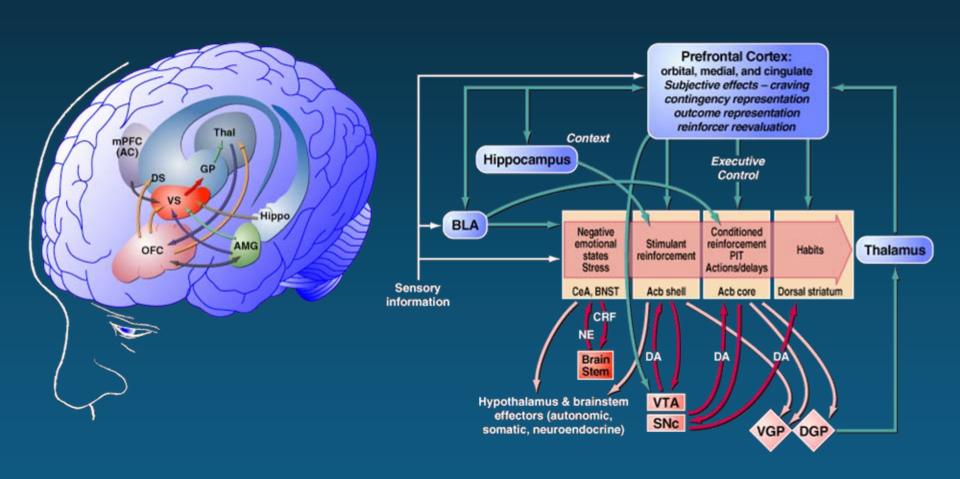
Brain plasticity- over learned behavior

Young brains are efficient at learning good things and bad things

Brain Dopamine System



Key Elements of the Neurocircuitry of Addiction



From: Koob G, Everitt, B and Robbins T, Reward, motivation and addiction. In: <u>Fundamental Neuroscience</u>, in press.

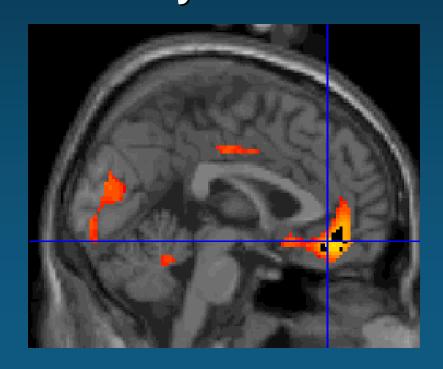
Frontal Inhibitory Systems

- Inability to resist craving
- Unable to "Just say NO!"
- Impulsive behavior
- Poor performance on frontal lobe tests, e.g., gambling
- Possible DSM V spectrum Dx
 OCD, ADHD, ASP, ?

Cocaine Patients

PET O-15
Hypoactivity

Reduced
Gray Matter



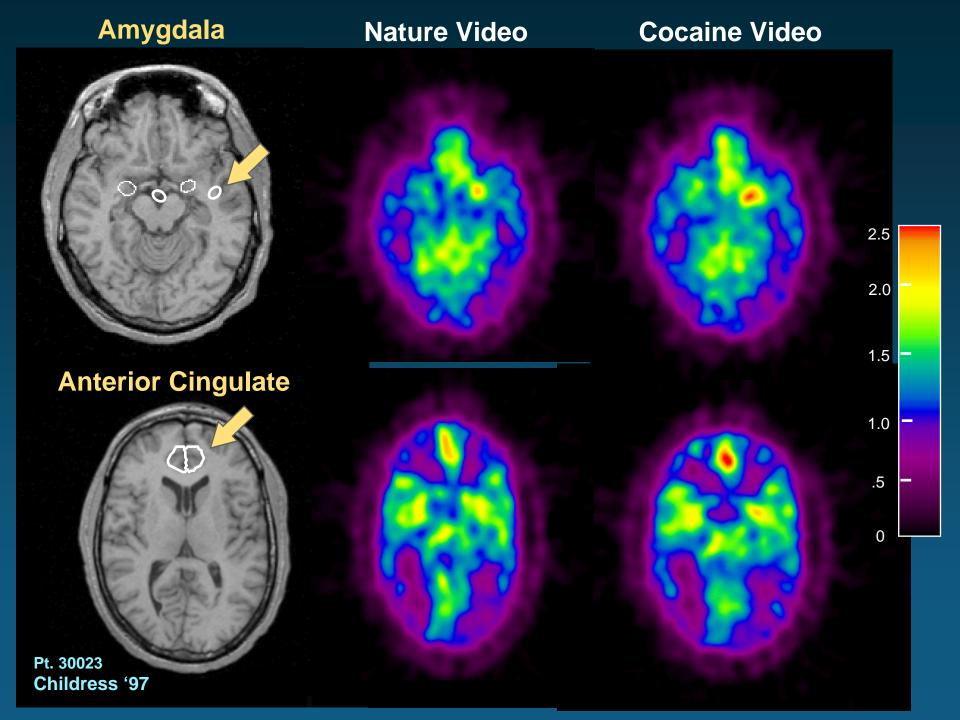
Laboratory Studies of Drug Craving

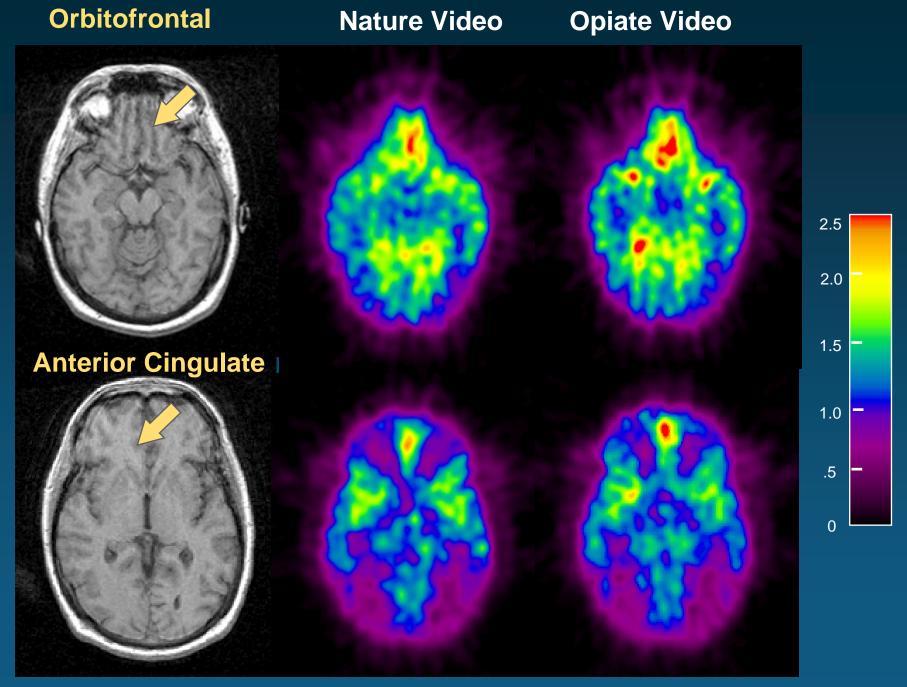
Naturally conditioned responses

- Videos
- Imagery
- Odors

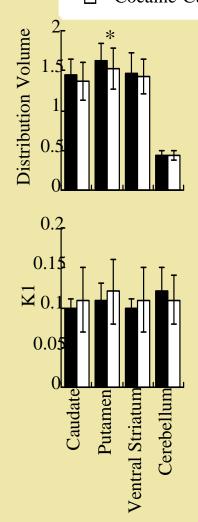


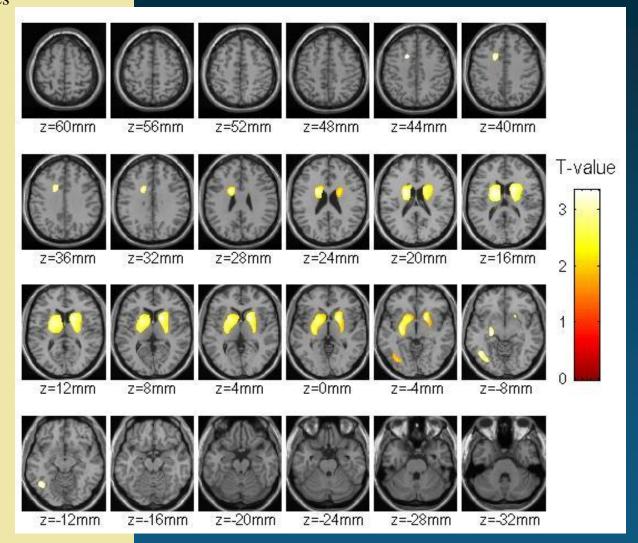


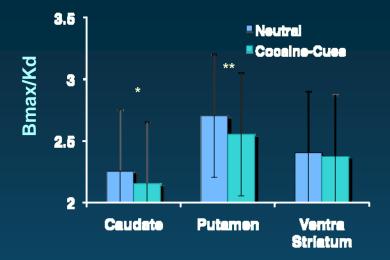


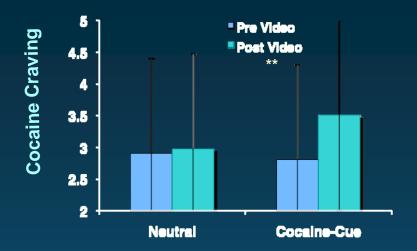


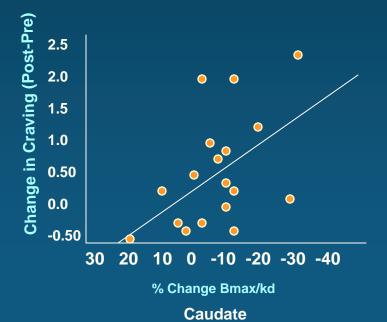
■ Neutral□ Cocaine-Cues

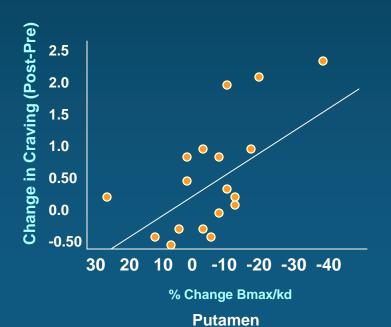












Manual Guided Therapies

Cognitive Behavioral (CBT)

Drug Counseling (DC)

Twelve Step Facilitation (TSF)

Motivation Enhancement Therapy (MET)

BRENDA (Biopsychosocial, Nurse)

Interpersonal Therapy (IPT)

Family Therapy

Group Therapy

Medications

Agonist medications methadone nicotine patch buprenorphine varenicline **Antagonist** Naltrexone for opioid addiction Naltrexone for alcoholism block endorphins Depot meds: Naltrexone, bup 30-40 days blockade Vaccines – cocaine, nicotine

Why not use modern treatment for drug law offenders?

- Meds developed almost entirely with NIH funds
- High research standards
- FDA approval
- Meds rarely used in US system
 revolving door

2.1 Million Americans in prison

Philadelphia prison system

18 % of parolees have history of opiate addiction

Relapse should/could result in re-incarceration

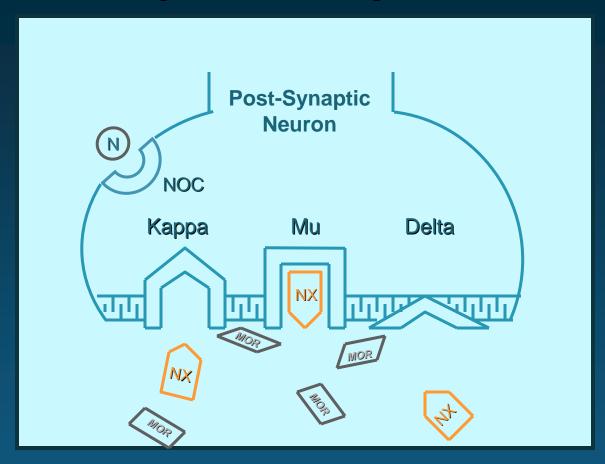
Approximately 1 Million opiate addicts in US Most support habit by crime

Major source of HIV and hepatitis C in population at large

Federal Parolees: Opioid Addiction

- Random assignment
 - Treatment as usual
 - Oral naltrexone
- Blocks effects of opioids
- No opioid "high"

Opiate Receptors



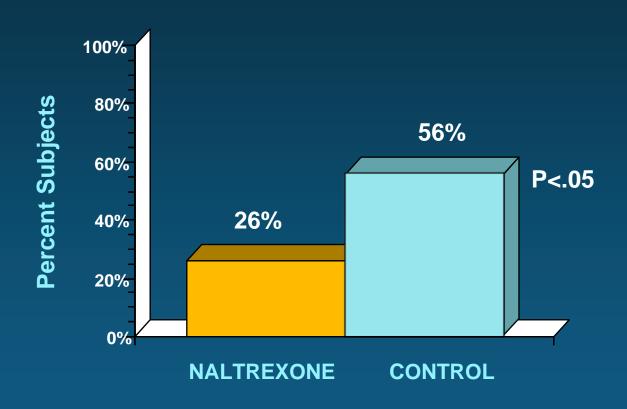
Affinity for Receptor

	<u>Kappa</u>	<u>Mu</u>	<u>Delta</u>
Naltrexone	406	108	54
Morphine	1	1	1

Mean Percent Positive Urines

Substance	Oral Nitx (N = 34)	Control (N = 17)	Sign
Opiate	8%	30%	P<.05
Cocaine	33%	49%	NS
Amphetamine	0%	1%	NS
Benzodiazepine	2%	6%	NS
Marijuana	13%	19%	NS
Alcohol	2%	4%	NS

Re-Incarceration at 6 months



Recent Oral Naltrexone Study

- 111 subjects randomized
- Data and follow-ups in progress
- Prior small study not going to be replicated
- Try with depot version monthly injection

Multi-site study

Six sites: Penn, MUSC, VCU, NYU,
 Columbia, Brown

Pilot phase funded by Dana Foundation

Collaborative RO 1, starting now

Penn Pilot Data

- N = 44
- 6 months treatment
- 12 months follow up
- Several patients request continuation beyond 6 months, in progress
- Well accepted by patients and parole officers

Depot product

- Vivitrol for randomized study
 - \$520 per dose
 - 30-40 days protection
 - Oral naltrexone approved in 1985 for heroin addiction
- Potential FDA approval of depot for opiate addiction

NIH large clinical trial

- Naltrexone N= 200
- Control N= 200
- Type of psychosocial intervention
 - CBT
 - Motivational Enhancement
- Duration: 6 months & 12 month follow up
- No Placebo injection

Coerced Treatment is Effective!

- Physicians face loss of license-long term results are excellent
- Consider using naltrexone in plea bargaining for non violent crimes
- Consider shortened sentences if offender agrees to long-term treatment

Physician Addicts: Required Treatment Irony: No ethical questions

- 904 physicians in 16 state PHPs
 - Intent to treat no exclusions
 - Consecutive admissions, from Sept 2001
- Results During Treatment Contract
 - Medical license held hostage
 - Official records and medical charts
 - Laboratory Results
- Results at 5 7 Year Follow Up
 - Official Board records

Results During Contract

904 Physicians
Consecutively Enrolled into
16 state Physician Health Programs

Completed

448 - No Longer being monitored

67 - Completed but monitored voluntarily

515 (57%)

Continuers

132 - Still being monitored

132 (15%)

Non-Completers

85 - Voluntarily stopped / retired

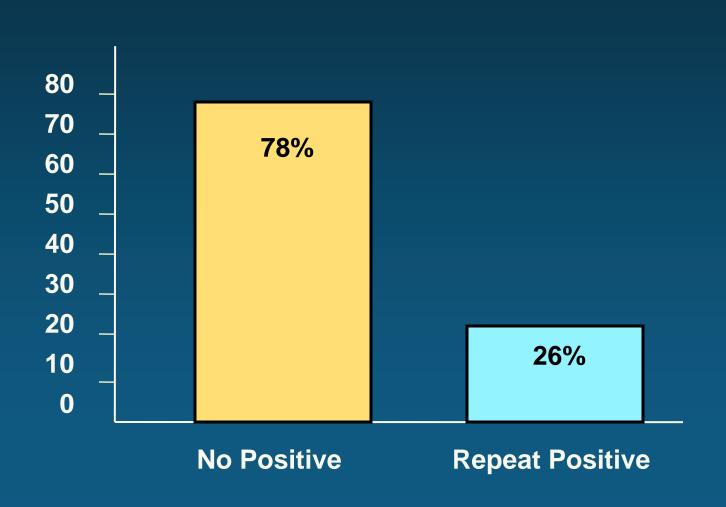
48 - Failed, license revoked

22 - Died (6 suicides)

102 - Transferred/Moved

257 (28%)

Urine Testing over 4 years



Results at 5-7 Years

Practicing Medicine

 Completers 	92%
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 Continuers 	73%
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Non-Completers 28%

Results at 5-7 Years

Revoked License

 Completers 	2%
	4 / U

 Continuers 	11%
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Non-Completers 32%

Conclusions

Why not use medications to prevent relapse in criminal justice population?

- Far cheaper than incarceration
- Make effective medical treatment an alternative to prison
- Ethically acceptable because offender is given a choice
- California DWI experience is positive;
 meds more effective with opioids

FOR MORE INFORMATION

http://www.med.upenn.edu/csa/o r obrien@mail.trc.upenn.edu