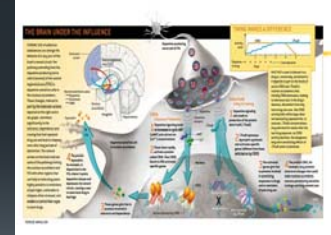


## Adolescent Opioid Addiction: Awareness, Understanding & How to Respond

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## You don't need to remember...

- Increases neuronal dendritic branching and spine density in the NAc and prefrontal cortex—an adaptation that is thought to participate in the enhanced incentive motivational value
- Compulsive behavior (OFC) and disinhibition (25) (cingulate gyrus).
- Nigrostriatal circuit (including the dorsal striatum)



## ASAM Definition of Addiction

- A primary chronic bio-behavioral disease of
  - Brain reward
  - Motivation
  - Memory
  - Related Circuitry

## ASAM Definition

- 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 the individual pursuing reward and/or relief by substance use and other behaviors.

## ASAM Definition

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- Addiction is characterized by impairment in behavioral control, craving, inability to consistently abstain, and diminished recognition of significant problems with one's behaviors and interpersonal relationships.

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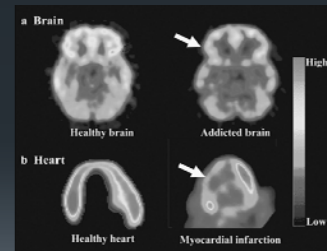
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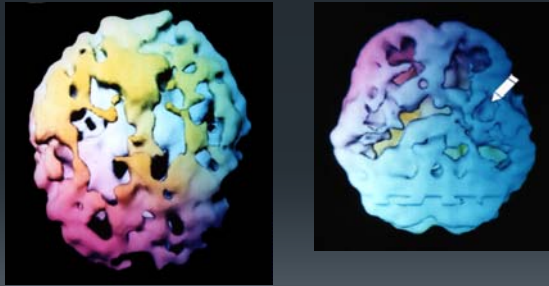
- Like other chronic diseases, addiction involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death

## Addiction as a disease of the brain

- Imaging studies consistently show specific abnormalities in the brain function of addicted individuals



## Heroin and Cannabis SPECT Scans



## Addiction is defined by

- Compulsion
- Inability to resist the compulsion: loss of control
- Use despite escalating harm
- Use at the expense of natural rewards
- Development of a negative affect state leading to escalating compulsion

## Addiction: Volkow

- Repeated drug use leads to long-lasting changes in the brain that undermine voluntary control
- Underlying disruption to brain regions that are important for the normal processes of motivation, reward, and inhibitory control in addicted individuals

## Volkow: Dopamine

- Increases in dopamine are not directly related to reward per se, as was previously believed, but rather to the prediction of reward and for salience
- Salience refers to stimuli or environmental changes that are arousing or that elicit an attentional-behavioral switch

## Dopamine: Salience (importance)

- Increases are not directly related to reward per se, as was previously believed, but rather to the ***prediction of reward***
- Salience, which, in addition to reward, applies to aversive, new, and unexpected stimuli, affects the motivation to seek the anticipated reward and facilitates conditioned learning

## Salience

- Adaptation that is thought to participate in the enhanced incentive motivational value of the drug (a process that results in increased “wanting” in contrast to just “liking” the drug) in the addicted person

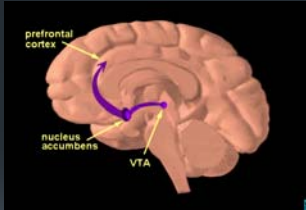
## Disease of Maladaptive Learning

- “Addiction represents a pathological usurpation of the neural mechanisms of learning and memory that under normal circumstances serve to shape survival behaviors related to the pursuit of rewards and the cues that predict them.”
  - Steven Hyman

## Cognitive effects: Executive function

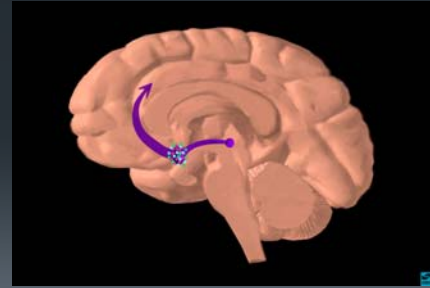
- Inhibition: Situations that require the overcoming of a strong habitual response or resisting temptation and strong impulse
- Error checking
- Flexibility of thinking
- Problem solving, planning
- Concept formation
- Abstract thinking

## Neural circuitry of reward

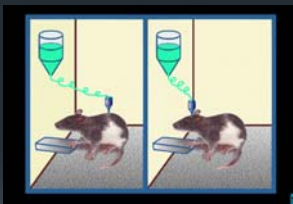
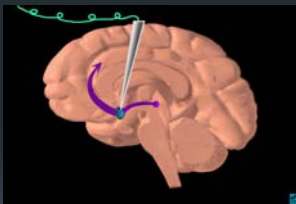


- Present in all animals
- Produces pleasure for behaviors needed for survival:
  - Eating
  - Drinking
  - Sex
  - Nurturing

## All drugs of abuse bind to the neural circuitry of reward



## Self-stimulation studies



## George Koob

- “Addiction is a cycle of spiraling dysregulation of brain reward systems that progressively increases, resulting in compulsive drug use and a loss of control over drug taking”
- Counteradaptive hedonic dysregulation

## Neuroadaptation

- Drugs change the brain's reward and mood balance
- The brain has mechanisms to oppose this change
- The balancing action overshoots
- The stronger the drug, the higher the dosage, the longer the use the more the opposing change

## Allostasis

- Change to a new, vulnerable state
- Activation of stress circuitry
- Deficit state: inhibition of brain reward system
- Increased reward threshold
- Altered hedonic tone
- Drugs create the stress that require that they be used to create the very problem that they have created

## Stress reinstatement paradigm

- Foot shock, foot shock, foot shock



## Adolescent opiate addiction

- New England has the highest per capita rate of opiate addiction in the nation
- Opiate addiction in New England is a pediatric epidemic
- No area, rural, suburban or urban is spared
- All socioeconomic groups are affected
- These facts remain a surprise to most

## Adolescent opiate addiction

- Prescription opioids increasingly the gateway drug for young teens
- Increasing progression to intravenous abuse
- Quantities used often very great
- Concurrent abuse of cocaine, benzodiazepines and increasingly methamphetamine and bath salts
- High overdose rates

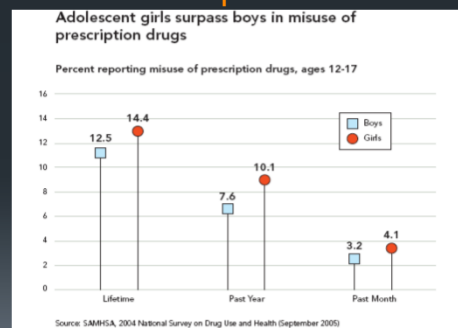
## Importance of age of first use

- 2006 DASIS REPORT: average age of first use has decreased
- The earlier the exposure, the greater the risk of life-time diagnosis of dependence
- The earlier the use, the greater the exposure to other risky behaviors

## New patient: Diana M

- 35 years old
- Mother crack and heroin addicted and began Diana using at 12
- Diana was sexually abused from age 6
- Heroin initially helped numb her emotional trauma
- By 20 she was using 3 grams of heroin intravenously daily
- She supported herself with sex work, filling her with tremendous shame
- Shame and guilt and lack of access to treatment kept her in her addiction until today

## Adolescent opiate abuse



## Why the increased female risk?

- High rates of physical and sexual abuse
- High rates of depression, risky sexual activity (especially with older partners)
- Subculture acceptability and increased susceptibility to peer pressure than boys
- Studies show correlation between low self-esteem and body image and drug abuse

## Why the increased female risk?

- PTSD: Harvard meta-analysis: 59% of women in treatment
  - Three times greater incidence than male patients
- Trauma independent of PTSD:
  - 55-99% female patients report physical or sexual trauma before age 18
  - Women victims of both types of abuse twice as likely to abuse drugs as those with one type

## Epidemiology

- Largely a rural disease although all areas of the State are affected
- Onset early with rapid progression
- MYDAUS study demonstrates easy access to opiates and other drugs and permissive/supportive attitudes towards drug use

## Screening - CRAFFT

1. Have you ever ridden in a CAR driven by someone (including yourself) who was "high" or had been using alcohol or drugs?
2. Do you ever use alcohol or drugs to RELAX, feel better about yourself, or fit in?
3. Do you ever use alcohol or drugs while you are by yourself, or ALONE?
4. Do you ever FORGET things you did while using alcohol or drugs?
5. Do your FAMILY or FRIENDS ever tell you that you should cut down on your drinking or drug use?
6. Have you ever gotten into TROUBLE while you were using alcohol or drugs?



## Treatments

- Residential
- Outpatient
- Individual counseling
- Co-occurring therapy
- Medication:
  - Vivitrol
  - Buprenorphine
  - Methadone

\*\* Note that virtually none of these are available to adolescents\*\*

## Adolescent treatment literature

- Adult literature, including the 1997 NIH Consensus Conference, confirms the dramatic improvement in outcomes for patients who receive maintenance medication, including methadone and buprenorphine
- Little adolescent literature

## Adolescent treatment literature

- Highest retention in treatment of methadone-maintained youths
- As good or better outcomes for long-term therapeutic community participants but much lower retention rates
- Challenges of providing care to rural youth with limited treatment access

## Buprenorphine

- Newer treatment for opioid dependence
- Alternative to methadone maintenance therapy
- Can be prescribed by office-based physicians
- Increases access to effective treatment
- Safety
- Mainstreams treatment of addictive disorders
- Very little access for adolescents

## Buprenorphine

- Novel type of opioid medication with documented clinical and cost effectiveness
- Can be prescribed by physicians in mainstream practice
- Safety
- Limited access for adolescents

## Buprenorphine and adolescents

- Safety
- Less physical dependence
- In theory, easier access to care for teens
- No requirement for year-long dependence as with methadone
- Patients can and should participate in abstinence-based treatment and 12 step recovery

## Buprenorphine: therapeutic effects

- Blocks opiate withdrawal
- Blocks opiate craving
- Blocks all opiate effects
- Suboxone: formulation of buprenorphine plus naloxone
- DATA 2000 limits

## Adolescent treatment research

- Lisa A. Marsch, University of Vermont
  - Archives Gen Psychiatry, 10/05
- Outcomes 36 adolescents treated either with buprenorphine or clonidine plus 3x/week counseling
- 72% buprenorphine vs 39% stayed in treatment
- Double the negative UDS rate

## NIDA's Clinical Trial Network

- 17 Nodes: academic centers nationwide
- Northern New England Node: Harvard/McClean plus CTP's in five states

## CTN 0010: George Woody, PI

- Buprenorphine/Naloxone-Facilitated Rehabilitation for Opioid-Addicted Adolescents/Young Adults
- Compares two three-month treatment protocols:
  - 14-day Suboxone stabilization/detoxification
  - 3-month Suboxone

## CTN 0010

- 30 patient/site trial
- Ages 14-21
- 'Real world' population with few exclusions (repeat UDS positive for methadone and/or benzodiazepines)
- Patients received extensive evaluations before, during and after the trial

## CTN 0010

- Dispensing trial: Monday-Saturday with Sunday take-home
- Both groups received weekly manualized individual and group therapy plus family psychoeducational workshops
  - Delinda Mercer, Dennis Daley and George Woody

## CTN 0010

- Human subjects training
- Extensive IRB review
  - Penn, Harvard, Mercy Hospital
- Site investigator quality assurance function plus FDA, Harvard and NIDA oversight
- Parental consent for minors (plus patient assent)

## CTN 0010

- Six sites with enrollment since 2002
  - Two sites unable to enroll adequate numbers
  - Mercy began enrollment February, 2005 and completed randomization and primary treatment within 10 months
  - 100% retention in both primary treatment and at all follow up research appointments

## CTN 0010

- Mercy enrollment
  - Youngest: 16 years old
  - Median age: 19 year old
  - 16/14 F/M
  - Average duration of opioid dependence:
    - Five years (vs 6 months to 1 year at other sites)

## What we found...

- The kids were better citizens than most of our adult patients
- We loved the kids
- The model of frequent, one-on-one contacts seemed to work better than our more intensive program models for the patients who had experience with both

### What we found...

- Everyone did better after reaching a stable, effective dose
- Everyone relapsed when Suboxone was withdrawn, whether after a week or two months

### What we found...

- Three pregnancies (two during the trial)
- One incidental diagnosis of thyroid cancer
- High rates of HCV at trial entry

### What we found...

- Excitement of participation in research
- The Caribou experience
- Pervasive risk of the drug subculture
- The value of parental involvement
- The value of community involvement
- Suboxone important but not sufficient
- Need for sober housing, age-specific therapy, fundamental changes in peer network and 12 step involvement

### Conclusions

- The epidemic continues to grow
- Treatment availability, including medication, is very limited
- HCV is highly prevalent
- Federal funds for research and treatment are shrinking
- The time for wishful thinking is long past
- Treatment works and the kids want it
- It's not available