HOPE FOR DEPRESSION
RESEARCH FOUNDATION

- Lecture: *"Depression and Addiction: What's the Connection? What's the Treatment?"*
- Event: HOPE Seminar & Luncheon
  New York - November 16th, 2009
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Depression and Addiction:

What's the Connection?
What's the Treatment?

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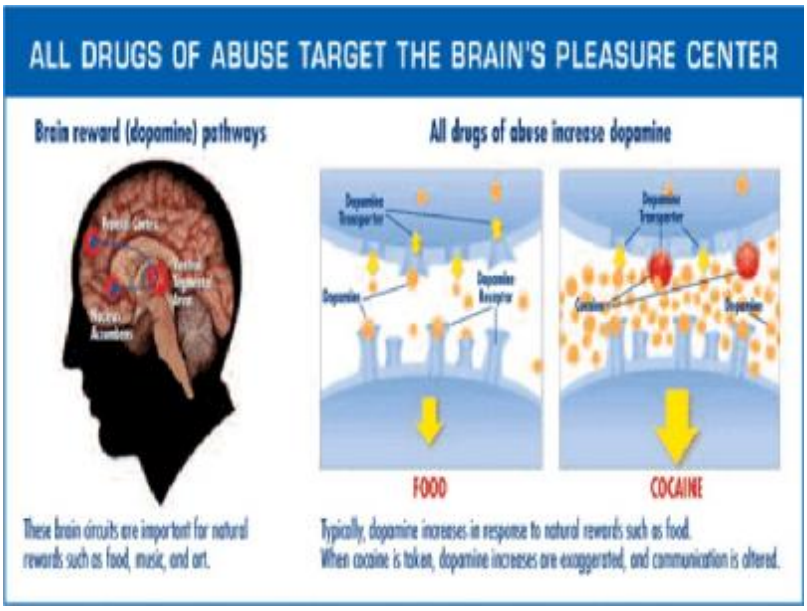
DSM-IV Substance Dependence

- Three domains of symptoms
  - Loss of control (e.g. drinks more than intended, unable to quit, spends a lot of time consuming…)
  - Functional impairment (e.g. physical or psychological health deteriorates, relationships deteriorate, work performance deteriorates…)
  - Tolerance and/or withdrawal

Addiction as a Disorder of the Brain Reward System

- Brain Reward System
  - Phylogenetically ancient system
  - Mesolimbic dopamine fibers
  - Mediates sensations of reward/pleasure and attention to potential rewards in the environment
  - Essential for motivated behavioral and learning
- All addictive substances stimulate the brain reward system
  - Alcohol, caffeine, nicotine, heroin and narcotic painkillers, cocaine, stimulants, sedatives



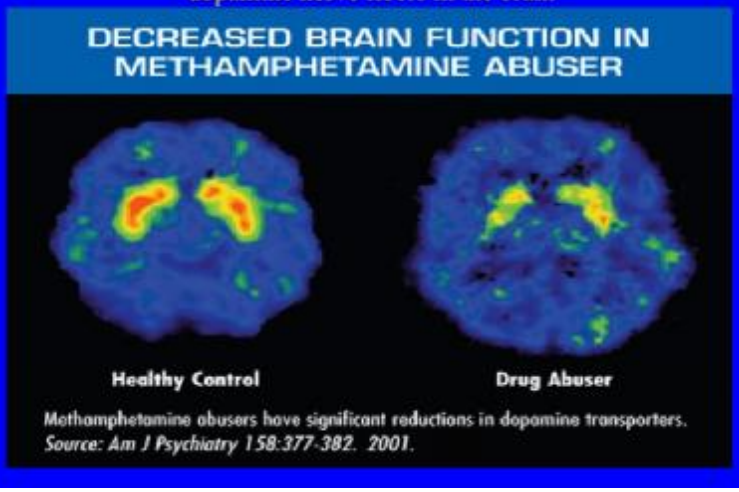
Addiction and the Brain Reward System

- In addiction, brain reward system is:
  - Overly sensitive to the rewarding effect of addictive substance
  - Not sensitive enough to natural rewards (e.g social interaction, food, sex)
- Inherited component
  - People inherit tendency to experience particular drugs as highly rewarding
- Environment and Stress
  - Stress sensitizes the brain reward system to addictive substances

PET scans showing brain activity is reduced in drug addiction, especially in frontal lobes

Reduced Dopamine activity in the Striatum

--Striatrum, along with frontal lobes, are main targets of dopamine nerve fibers in the brain



Addiction is Treatable

- Behavioral Treatments
  - Inpatient and outpatient
- Medication Treatments
  - Alcohol: Naltrexone, antabuse, acamprosate
  - Opioids: Methadone, buprenorphine, naltrexone
  - Nicotine: nicotine patch/gum, bupropion (Zyban), varenicline (Chantix)

Depression and the Brain Reward System

- Anhedonia (loss of interest or pleasure in usual activities) is a typical symptom of depression
- Poor attention is a typical symptom of depression
  - Involves lack of attention to salient rewards in the environment
- Dopamine depletion (reserpine, AMPT), or blockade (neuroleptic medications) can produce anhedonia and dysphoria

Depression and Addiction Occur Together

- If a person has unipolar major depression, it increases the chances that the person will have an alcohol or drug use disorder by a factor of 2
- If a person has bipolar disorder, it increases the chances of an alcohol or drug use disorder by a factor of at least 4
- Among patients presenting for treatment for alcohol or drug use disorders, 20% to 50% will also have a major depression
- When mood and substance use occur together the prognosis tends to be worse, and treatment outcome is worse

Clinical Presentation

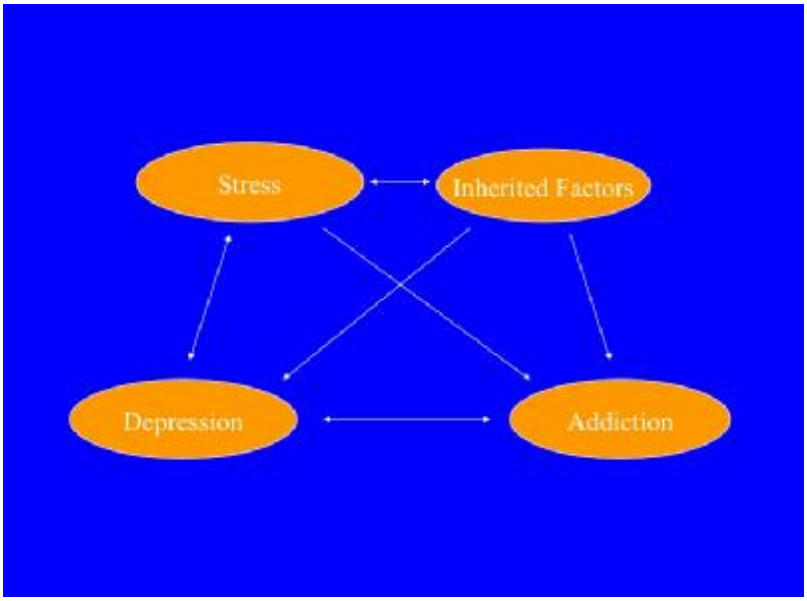
- A patient presents with symptoms of depression and symptoms of an addiction:What to do?
  - Treat the addiction first?
  - Wait for abstinence before treating the depression?
  - Treat the depression first?
  - Treat both simultaneously?

What's the Relationship?

- Self-medication?
  - Drugs or alcohol are taken to relieve the symptoms of depression or anxiety
  - Implications: Treat the depression
- Toxic effects of alcohol/drugs?
  - Chronic exposure to alcohol or drugs causes symptoms that look like depression or anxiety (low mood, low energy, insomnia, anxiety, etc)
  - Implications: Treat the addiction and the depression will resolve

It's More Complicated

- Stress
  - Stress predisposes to both mood/anxiety disorders and to substance use disorders
  - Job, marital stress, loss/bereavement, combat
- Moods become conditioned cues triggering substance use
- Avoid simplistic thinking



Abstinence Improves Depression

- Multiple studies show this
- Patients with alcohol or cocaine dependence admitted to inpatient detoxification or rehabilitation programs
- Opioid addicts admitted to methadone maintenance treatment
- Some cases of depression persist despite abstinence

The Combination of Depression and Addiction Results in Worse Outcome

- Multiple studies show this, among alcohol, cocaine, or opioid dependent patients
- Depends on a good history and careful diagnosis of major depression or dysthymia

Major depression observed during active substance use persists after the patient becomes abstinent (Nunes, Hasin et al., J Clin Psychiatry 2006)

- N = 100 patients admitted to an inpatient addiction program, who also had major depression at the time of admission
- Followed as outpatients for one year
- Most depressions persisted, even when patients were abstinent during the follow-up
- Depends on detailed clinical history and careful diagnosis of depression

Mild to Moderate Alcohol Dependence Does not Interfere with Medication Treatment of Depression (McGrath, Nunes et al., in preparation)

- STAR*D study: N = 2,000 outpatients with depression, at community clinics, treated with citalopram (Celexa), a standard antidepressant medication. – 50% had a good response.
- Alcohol dependence was allowed, as long as alcoholism was not so severe as to need inpatient detoxification
- Among N = XX with alcohol dependence, response to antidepressant medication was just as good as among those without alcohol problems

Antidepressant Medication is Effective for Patients with Both Addiction and Depression (Nunes and Levin, JAMA 2004)

- Meta-analysis of 14 placebo-controlled antidepressant trials, among patients (N > 800 total) in drug/alcohol treatment settings with co-occurring major depression or dysthymia
- Effect of antidepressant medication was similar to that seen among outpatients with depression and no addiction
- Effect depended upon careful clinical history and diagnosis to identify mood disorders (as opposed to toxic effects of substances)
- When antidepressant medication improved mood, it also improved substance use outcome (levels of substance use went down)

Depression and Cigarette Smoking (Glassman, Covey, others)

- A history of major depression is common among smokers
  - Associated with difficulty quitting
- The antidepressant medication bupropion ("Zyban") is one of the best treatments for nicotine dependence
- Quitting smoking is sometimes followed by relapse of depression (Glassman, Covey, others)

Conclusions

- Addiction is common among patients with mood and anxiety disorders
- Diagnose and treat both disorders, both mood/anxiety disorder and addiction, avoid simplistic thinking
  - If one or another disorder goes untreated, outcome is worse
- We are learning more about the complex relationships and the underlying neurobiology
  - Epidemiology, clinical trials, brain imaging
- This should lead to more and better treatments in the future