Addictions and the Brain

TAAP Conference
September 14, 2012

Acknowledgements

• La Hacienda Treatment Center
• American Society of Addiction Medicine
• National Institute of Drug Abuse
Definition

- A primary, progressive biochemical, psychosocial, genetically transmitted chronic disease of relapse who’s hallmarks are denial, loss of control and unmanageability.

DSM IV Criteria for dependency:
At least 3 of the 7 below

1. Withdrawal
2. Tolerance
3. The substance is taken in larger amounts or over a longer period than was intended.
4. There is a persistent desire or unsuccessful efforts to cut down or control substance use.
5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
6. Important social, occupational, or recreational activities are given up or reduced because of the substance use.
7. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
Dispute between behavior and disease

Present understanding of the Hypothalamus location of the disease hypothesis.
Dispute regarding behavior versus disease
Activation of the reward pathway by addictive drugs

- Alcohol
- Cocaine
- Heroin
- Nicotine
Natural Rewards Elevate Dopamine Levels

Source: Di Chiara et al.

Effects of Drugs on Dopamine Levels

Source: Di Chiara and Imperato

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Striatal FDOPA Activity

Pre-Amphetamine/Control

Post-Chronic Amphetamine (10 days)

4 weeks

6 months

1 year

2 years

Superior → Inferior
Dopamine Transporters in Methamphetamine Abusers

- Methamphetamine abusers have significant reductions in dopamine transporters.

**Normal Control**

**Methamphetamine Abuser**

\[ p < 0.0002 \]
**Dopamine Transporters in Methamphetamine Abusers**

**Motor Task**
Loss of dopamine transporters in the meth abusers may result in slowing of motor reactions.

**Memory Task**
Loss of dopamine transporters in the meth abusers may result in memory impairment.

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**Dopamine D2 Receptors in Addiction**

- **Cocaine**
- **Meth**
- **Alcohol**
- **Food**

Control groups
- Experimental groups

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Challenge:

Normal  Drug Use  Addiction  Treatment
Three Major Relapse Pathways

I. Cross Addicting Drugs
II. People/Place/Things
III. B.H.A.L.T.
Cross Addicting Drugs

a. Chemical of choice
b. Related drugs
c. Tobacco
d. Life long relapse pathway

People/Place/Things

a. History of discovery
b. Three month limit for relapse
B.H.A.L.T.

a. Boredom  
b. Hunger  
c. Anger/emotions  
d. Loneliness  
e. Tiredness

Relapse Prevention Medications

I. Antabuse  
II. Campral  
III. ReVia  
IV. Vivitrol  
V. Off label
Antabuse

a. Mechanism of action
b. Dosing
c. Side Effects
d. Efficacy

Campral

a. Mechanism of action
b. Dosing
c. Side Effects
d. Efficacy
ReVia

a. Mechanism of action
b. Dosing
c. Side Effects
d. Efficacy

Vivitrol

a. Mechanism of action
b. Dosing
c. Side Effects
d. Efficacy
### Phase 3 Clinical Trials
**On A Number of Promising Drugs**

<table>
<thead>
<tr>
<th>Cocaine</th>
<th>Methamphetamine</th>
<th>Opiates</th>
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</thead>
<tbody>
<tr>
<td>Cabergoline</td>
<td>Bupropion</td>
<td>Lofexidine</td>
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<tr>
<td>Disulfiram (Antabuse)</td>
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<td>Reserpine</td>
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<td>Selegiline</td>
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Off label
### Methamphetamine Addiction Pharmacotherapies in Clinical Trials

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
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<tbody>
<tr>
<td>Bupropion</td>
<td>Butorphanol</td>
<td>Buprenorphine</td>
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<tr>
<td>Dextroamphetamine</td>
<td>DAS 431</td>
<td>Buprenorphine/Naloxone</td>
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<td>Metyrapone</td>
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<td>Naltrexone</td>
<td>Methadone</td>
<td>Naloxone</td>
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<td>Nalpropion</td>
<td>Naloxone Depot</td>
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<td>Ondanestron</td>
<td>Nefazodone</td>
<td>Oxazepam</td>
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<td>Pemoline</td>
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### Cocaine Medication Development Projects

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<td>DAS 431</td>
<td>Cocaine Vaccine</td>
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### Dual Diagnosis

1. Prevalence
2. Testing
3. Treatment
Co-Occurring Disorders

37% of alcohol dependent → another disorder
53% of drug dependent → another disorder

Etiology

Mental Illness → Substance Use

- ↓ Symptoms
- ↑ Social skills
- ↓ Medication side effects
Etiology

Substance Use → Mental Illness

- Dependence → ↑ psychosis, depression, anxiety
- Withdrawal → ↑ depression and anxiety
- ? Shared genetics

Anxiety

- **Generalized**
  - Pervasive
- **Panic**
  - Sudden onset and resolution
- **Social** *(9% same as general population)*
  - Associated with social situations
- **PTSD**
  - Hypervigilence resulting from trauma
- **OCD**
  - Germs, organizing, checking and re-checking
Withdrawal from alcohol, benzodiazepines, opiates, and other sedatives mimics anxious state

Treatment – Anxiety

• Behavioral
  – Therapy as good as medications in most research trials
  – Hypnosis, Biofeedback, Exercise
  – *The Anxiety Cure* – Author Dupont

• Medications
  – SSRIs (Prozac, Paxil, Lexapro, Celexa, Zoloft)
  – SNRIs (Cymbalta, Effexor, Pristiq)
  – Buspar
  – Short-term: Inderal, Vistaril, Neurontin
  – Trazodone
Mood

• Depression
  – Major Depression
  – Dysthymia

• Mania
  – Mania
  – Hypomania

• Bipolar
  – I – Manic Episode(s) with or without Depressive Episode(s)
  – II – Depressive Episodes(s) with Hypomania
  – Cyclothymia – Hypomania and dysthymic episodes

Withdrawal can mimic mania or depression
Treatment - Mood

- Medications
  - SSRIs, SNRIs
  - Wellbutrin (Bupropion)
  - Mood Stabilizers/Augmenters – Lithium, Depakote, Risperidone, Seroquel, Topamax, Lamictal, Trileptal, Abilify, Geodon, Zyprexa

- Behavioral
  - Therapy = medications for depression
  - Exercise, diet, sunlight useful

ADD/ADHD

- 25 fold ↑ in Adderall use last decade
- USA = 80 % of Ritalin used worldwide
- No study shown long term use stimulants in adults is good
Symptoms

- Not listening
- Fails to finish tasks
- Difficulty organizing
- Loses things
- Easily distracted

Other Causes

- Anxiety
- Mania
- Withdrawal
- Learning Disorders

Treating for ADD first can lead to worsening of above
Treatment - ADD

• Therapy and treatment of any underlying learning disability
• Exercise
• Atypical stimulants – Strattera (amoxetine)
• Guanfacine (Tenex, Intuniv)
• SNRIs – Effexor, Prestiq
• Wellbutrin (Bupropion)

Personality Disorders

• Disorders?
• Phases?
• Artifacts of Addiction?

“so you are anti-social, histrionic, borderline, and narcissistic but otherwise well.”
PERSONALITY DISORDERS

- Totality of Emotional + Behavioral Traits
- Onset Teens
- Enduring, Inflexible, Consistent, Maladaptive

Causes Significant Impairment and/or Distress

Personality Characteristics

**Cluster A – Eccentric or Odd**
- Paranoid: Suspicious, Jealous, but not Psychotic or Unlawful
- Schizoid: Unemotional, Cold, Indifferent
- Schizotypal: Odd /Magical, not Paranoid

**Cluster B – Dramatic, Emotional, or Erratic**
- ASPD: Aggressive, Unlawful, Impulsive
- Borderline: Unstable, Chaotic, Impulsive
- Histrionic: Dramatic, Seductive but not Unlawful
- Narcissistic: Self-Centered, Entitled, Lacks Empathy, but not Unlawful

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Personality Characteristics

Cluster C – Anxious or Fearful

**Avoidant**
- Needs people but Fears Relationships

**Dependent**
- Needs Relationships, Indecisive, Abandonment

**Obsessive-Compulsive**
- Rigid, Perfectionist + Inefficient

**Passive**
- Negative Attitudes with Passive Aggressive Resistance to Demands

Summary

- Very common to have both a substance use disorder and another disorder
- Even more common to feel like you have one when using or withdrawing
- The six month challenge
- The twelve month reward
Spiritual Component of Recovery
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