Addictions and the Brain
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

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Natural Rewards Elevate Dopamine

FOOD

Levels

SEX

Source: Di Chiara et al.

Source: Fiorino and Phillips

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Effects of Drugs on Dopamine Levels

**AMPHETAMINE**

- DA
- DOPAC
- HVA

Accumbens

Time After Amphetamine

% of Basal Release

0 100 200 300 400 500 600 700 800 900 1000 1100

0 1 2 3 4 5 hr

**COCAINE**

- DA
- DOPAC
- HVA

Accumbens

Time After Cocaine

% of Basal Release

0 100 200 300 400

0 1 2 3 4 5 hr

**NICOTINE**

- Accumbens
- Caudate

Accumbens

Time After Nicotine

% of Basal Release

0 100 150 200 250

0 1 2 3 hr

**MORPHINE**

- Dose (mg/kg)
  - 0.5
  - 1.0
  - 2.5
  - 10

Accumbens

Time After Morphine

% of Basal Release

0 100 150 200 250

0 1 2 3 4 5 hr

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
Methamphetamine abusers have significant reductions in dopamine transporters.
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.
Dopamine D2 Receptors in Addiction

Control groups

Experimental groups

Cocaine

Meth

Alcohol

Food

DA D2 Receptor Availability

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on cocaine
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
Off label
# 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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<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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### Methamphetamine Addiction Pharmacotherapies in Clinical Trials

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<th>Phase II</th>
<th>Phase III</th>
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<tr>
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### Opiate Medication Development Projects

<table>
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Dual Diagnosis

1. Prevalence
2. Testing
3. Treatment
Spiritual Component of Recovery
Dr. Daniel Boone
La Hacienda Treatment Center
800-749-6160
dboone@lahacienda.com
www.lahacienda.com