DISEASE MODEL OF ADDICTION

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Director, Aerospace Medicine Center
University of Texas Medical Branch
Dopamine transporter blocked by cocaine

Transmitting neuron

Cocaine

Receiving neuron

Dopamine

Dopamine receptor

Intensity of effect

From NIDA
### 2014 Substance Use, Past Year Initiation of Substance Use, and Met Diagnostic Criteria for a Substance Use Disorder in the Past Year Among Persons Aged 12 Years or Older (in Millions)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Past Year Use or Misuse</th>
<th>Past Year Initiation Among Total Population</th>
<th>Met Diagnostic Criteria for a Substance Use Disorder</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>#</td>
<td>%</td>
<td>#</td>
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<tr>
<td>Alcohol</td>
<td>175.8</td>
<td>65.7</td>
<td>4.8</td>
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<tr>
<td><strong>Drinking Pattern</strong></td>
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<tr>
<td>Binge Drinking</td>
<td>66.7</td>
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<td>Heavy Drinking</td>
<td>17.3</td>
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<tr>
<td><strong>Any Illicit Drug</strong></td>
<td>47.7</td>
<td>17.8</td>
<td>nr</td>
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<td>Cocaine/Crack</td>
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<td>1.8</td>
<td>1.0</td>
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<tr>
<td>Heroin</td>
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<td>0.1</td>
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<td>1.2</td>
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<td>Marijuana</td>
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<td>2.6</td>
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<tr>
<td>Inhalants</td>
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<td>Misuse of Psychotherapeutics</td>
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<td>Pain Relievers</td>
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PAST MONTH RATES OF SUBSTANCE USE AMONG PEOPLE AGED 12 OR OLDER: PERCENTAGES, 2002-2014, 2014
NATIONAL SURVEY ON DRUG USE AND HEALTH (NSDUH)
**Type 1 Diabetes**

Muscle unable to use glucose due to low insulin

Glycogen and protein breakdown, causing keto-acidosis

**Type 1 Diabetes**

Pancreas

Increased glucose due to low insulin

**Type 2 Diabetes**

Muscle unable to use glucose due to insulin resistance

Obesity, inheritance & other factors leading to insulin resistance

**Type 2 Diabetes**

Pancreas

Increased glucose in the blood steam

Sufficient insulin secreted in the blood stream

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**Nigrostriatal Pathway**
Substantia Nigra to Striatum
- Motor Control
- Death of neurons in this pathway can result in Parkinson's Disease

**Tuberoinfundibular Pathway**
Hypothalamus to Pituitary Gland
- Hormonal regulation
- Maternal Behaviour (nurturing)
- Pregnancy
- Sensory Processes

**Mesolimbic and mesocortical Pathways**
Ventral Tegmental Area to Nucleus Accumbens, Amygdala & Hippocampus, and Prefrontal Cortex
- Memory
- Motivation & emotional response
- Reward and desire
- Addiction
- Can cause hallucinations and schizophrenia if not functioning properly
Dopamine Pathways

Frontal Cortex

Nucleus Accumbens

VTA

Hippocampus

Serotonin Pathways

Striatum

Substantia Nigra

Raphe Nuclei

Functions

Reward (motivation)
Pleasure, Euphoria
Motor Function (fine tuning)
Compulsion
Perserveration

Functions

Mood
Memory
Sleep
Cognition
Dopamine Pathways in the Brain

- Frontal cortex
- Nucleus accumbens
- VTA
- Striatum
- Substantia nigra
- Hippocampus
Volkow ND, Wise RA. How can drug addiction help us understand obesity? Nat Neurosci 8: 555-560
Well-supported scientific evidence shows that disruptions in three areas of the brain are particularly important in the onset, development, and maintenance of substance use disorders: the basal ganglia, the extended amygdala, and the prefrontal cortex. “
These disruptions (are):

(1) enable substance-associated cues to trigger substance seeking (i.e., they increase incentive salience); Cunning

(2) reduce sensitivity of brain systems involved in the experience of pleasure or reward, and heighten activation of brain stress systems; Baffling

and

(3) reduce functioning of brain executive control systems, which are involved in the ability to make decisions and regulate one’s actions, emotions, and impulses. Powerful
CHARACTERISTICS OF ADDICTION (2016)

- Impulsivity
- Positive Reinforcement
- Negative Reinforcement
- Compulsivity

HENCE, STEP 1 – POWERLESSNESS AND NEED FOR HIGHER POWER
A modified version of the \textit{BChE} gene is attached to a virus.

Mouse is injected with the virus-gene combination.

The gene directs the cells to produce a highly active version of BChE, which rapidly breaks down cocaine.

The virus enters the mouse cells and inserts the gene into the cell nucleus.
IN THE MEANTIME...

- **Cognitive-behavioral therapy** seeks to help patients recognize, avoid, and cope with the situations in which they're most likely to use drugs.

- **Contingency management** uses positive reinforcement such as providing rewards or privileges for remaining drugfree, for attending and participating in counseling sessions, or for taking treatment medications as prescribed.

- **Motivational enhancement therapy** uses strategies to make the most of people's readiness to change their behavior and enter treatment.

- **Family therapy** helps people (especially young people) with drug use problems, as well as their families, address influences on drug use patterns and improve overall family functioning.

CHANGING NEURAL PATHWAYS

- Recently heard quote from Austin TX:
  
  ” The more I miss meetings, the more I miss drinking”
TIME-RELATED DECREASE IN DOPAMINE RELEASED IN THE BRAIN OF A COCAINE USER

Low dopamine D2 receptors may contribute to the loss of control in cocaine users.
TIME-RELATED INCREASE IN DOPAMINE TRANSPORTERS
## CNS Vital Signs Clinical Report

**Test Date:** March 31, 2012 08:49:04  
**Test Date GMT:** March 31, 2012 13:49:08

**Administrator:** William Lambos  
**Age:** 13  
**Total Test Time:** 48:12 (min:secs)

### Patient Profile

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<th>Standard Score Range</th>
<th>Percentile</th>
<th>Valid Score**</th>
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DOPAMINE AGONISTS (STIMULATORS)

- LEVODOPA – TREATS PARKINSON’S MOVEMENT DISORDER
- METHYLPHENIDATE and others – ADHD
- PRAMIPEXOLE – TREATS RESTLESS LEG SYNDROME
- PROMAZINE – TREATS AGITATION/RESTLESSNESS
DOPAMINE ANTAGONISTS (INHIBITORS)

- RESPIRIDINE, THIORIDAZINE, FLUPHENAZINE – TREAT PSYCHOSIS
- PIMOZIDE – TREATS TICS IN TOURETTE’S SYNDROME
- ZIPRASIDONE – TREATS BIPOLAR I
- PROMAZINE – TREATS AGITATION/RESTLESSNESS
MEDICATIONS TO TREAT ADDICTION

- Naltrexone (Vivitrol).
- Buprenorphine (Probuphine, Suboxone).
- Disulfiram (Antabuse).
- Acamprosate (Campral)
- Modafinil (Provigil).
- Mirtazapine (Remeron).
- Bupropion (Wellbutrin, Zyban).
- Gabapentin (Neurontin).
- Vigabatrin (Sabril).
- Baclofen (Lioresal).
- Topiramate (Topamax).
MEDICATIONS TO TREAT ADDICTION

• Opioid
  • Methadone
  • Buprenorphine
  • Extended-release naltrexone
  • Lofexidine

• Nicotine
  • Nicotine replacement therapies (available as a patch, inhaler, or gum)
  • Bupropion
  • Varenicline

• Alcohol
  • Naltrexone
  • Disulfiram
  • Acamprosate