Drugs, Brain and Behavior
The Neuroscience of Addiction and Trauma
Libby Stuyt, MD
NADA Training
September 2015
Why Do People Try Alcohol, Tobacco, or Drugs in the First Place?

- Parents/family members use
- Peer pressure
- Advertising
Every doctor in private practice was asked:
—family physicians, surgeons, specialists...
doctors in every branch of medicine—
“What cigarette do you smoke?”

According to a recent Nationwide survey:

More Doctors Smoke Camels
than any other cigarette!

The “T-Zone” Test
Will Tell You

Not a guess, not just a trend...but an actual fact
based on the statements of doctors themselves to
nationally known independent research organizations.

Yes, your doctor was asked...along with thousands and
thousands of other doctors from Maine to California.
And they've named their choice—the brand that men
doctors named as their smoke is Camel! Three nationally known
independent research organizations found this to be a fact.

Nothing unusual about it. Doctors smoke for pleasure
just like the rest of us. They appreciate, just as you, a mild
ness that's cool and easy on the throat. They too enjoy the
full, rich flavor of expertly blended0 tobacco. And
they named Camels...more of them named Camels than any
other brand. Next time you buy cigarettes, try Camels.
Back then men gave the wife - at least one day a week - out of the house.

You’ve come a long way, baby.

 VIRGINIA SLIMS

This gener gave me an experience that I never would have thought would work.

Attaching the cover shows the experience that I never would have thought would work.
Smooth character.
Why do they continue to use?

- Numbs pain – physical and emotional
- Helps to cope with the effects of trauma/abuse
- Disinhibits – aids social interactions
- Creates energy
- Provides a temporary sense of well being
- However, the drugs ultimately hijack the learning and memory part of the brain and they develop a life of their own
The Reward Pathway – Why People Continue to Use

prefrontal cortex

nucleus accumbens

VTA
The Reward Pathway

- Dopamine is the primary neurotransmitter of the reward pathway
- All drugs of abuse increase dopamine levels in the brain reward pathway although they often act through separate mechanisms
- Drugs that are not abused do not effect dopamine concentrations in the reward pathway
Natural Rewards Elevate Dopamine Levels

**FOOD**

- Graph showing dopamine concentration (% baseline) over time (min) in the NAc shell.
  - Time: 0, 60, 120, 180 min.
  - Data points indicate changes in dopamine output.

**SEX**

- Graph showing dopamine concentration (% baseline) over time (min) with copulation frequency.
  - Time: 0, 5, 10, 15 min.
  - Data points indicate changes in dopamine output with copulation frequency.

**Source:** Di Chiara et al., Fiorino and Phillips.
Effects of Drugs on Dopamine Levels

**AMPHETAMINE**
- % of Basal Release over time after amphetamine administration.
- Graph shows peak release at 1 hour post-administration.

**COCAINE**
- % of Basal Release over time after cocaine administration.
- Graph shows peak release at 2 hours post-administration.

**NICOTINE**
- % of Basal Release over time after nicotine administration.
- Graph shows peak release at 1 hour post-administration.

**MORPHINE**
- % of Basal Release over time after morphine administration.
- Different doses (0.5, 1.0, 2.5, 10 mg/kg) are shown.

Source: Di Chiara and Imperato

Effects of Drugs on Dopamine Levels
Tolerance

* A state in which an organism no longer responds to a drug
* A higher dose is required to achieve the same effect
Dependence

* A state in which an organism functions normally only in the presence of a drug
* Manifested as a physical disturbance when the drug is removed (withdrawal)
Addiction/Dependence

* A state in which an organism engages in a compulsive behavior
* Behavior is reinforcing (rewarding or pleasurable)
* Loss of Control in limiting intake
Beware: “Iatrogenic Addiction”

* Tolerance causes patient to state this dose is no longer working
* Physician increases dose and/or adds extra narcotic for “break through” pain, which is actually often withdrawal pain
* This becomes a vicious cycle
* The patient does not think they are “addicted” because it was “doctor prescribed”
Percent of those ever using a drug who become addicted

<table>
<thead>
<tr>
<th></th>
<th>Alcohol</th>
<th>Cocaine</th>
<th>Heroin</th>
<th>Tobacco</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent</td>
<td>15.4</td>
<td>16.7</td>
<td>23.1</td>
<td>31.9</td>
</tr>
</tbody>
</table>

Bar chart showing the percentage of those ever using each drug who become addicted.
Why can some people stop using and others can’t seem to?

* Some have genetic loading – perhaps 10% - but this doesn’t predict addiction
* Exposure to substances in the environment as a fetus/baby/child/adolescent – can prime the brain
* Substance use initiated during adolescence is highly problematic – making it much more difficult to put on the brakes, realize there is a problem and to quit
Use vs. Abuse vs. Dependence

* Use
  * 90% of the general population have consumed alcohol at some point in their life
* Abuse
  * 30% of the general population abuse alcohol on occasion
* Dependence
  * 14% of the general population have the disease alcohol dependence
Epidemiology

* 14% alcohol dependence in the general population
* 56% of persons with bipolar disorder have a life-time diagnosis of some type of substance abuse/dependence
* 92% of prisoners with schizophrenia have a comorbid addictive disorder
Hallmarks for Addiction

* compulsive use of the substance
  * what, when, how much
* continued use in spite of adverse consequences
  * medical, legal, work, school, family, friends
* loss of control of use
  * this differentiates substance abuse from dependence, loss of free will
3-Pronged Dependence

* Physical – can explain continued use while the drug is driving the use
  * tolerance
  * withdrawal
* Psychological
  * “self-medicating” underlying psychiatric disorder (dual disorder) versus
  * substance induced psychiatric disorder
* Behavioral – learned behavior
There is no cure but this is a very treatable disease

- the solution is simple - eliminate the agent
- However, the person has to become willing to change his/her behavior
  - simple and easy are not the same thing
- It is up to the health care provider to provide an environment in which the person can relearn or retrain the brain with new thinking/behavior
So How Does the Brain Work?

* The Mind can be thought of as a process that regulates the flow of energy and information in the Brain (drugs can shift the direction of energy)

* The Mind emerges from the interaction of neurobiological processes in the brain and interactions with the environment (situations, interpersonal relationships, etc.)

* The Mind shapes the brain – the flow of information can actually change the function and structure of the brain
100 billion neurons, each neuron has 10 thousand connections
Memory

* The way an experience at one time alters the way you function in the future.

* Association – “neurons that fire together are wired together” – become linked together in a neural net
Biology/Genes and Environment Play Key Roles in Vulnerability

Biology/Genes

Biology/Environment Interaction

Environment

DRUG

Addiction
Dopamine D2 Receptors are Lower in Addiction

Cocaine

Alcohol

Heroin

Volkow et al

control

addicted

Reward Circuits

Non-Drug Abuser

Drug Abuser
Subjects with low receptors report MP as pleasant and those with high receptors as unpleasant. Volkow et al.
Addiction becomes a Brain Dysfunction

* Addiction – A problem with the learning and memory part of the brain
* Neural systems related to the pursuit of rewards are hijacked
* Neural adaptations occur to reinforce the behavior
* The behavior becomes hard-wired into the system
* The process is basically the same for all drugs of addiction
Brain Development

- Human brains continue to develop after birth and are not fully developed until late adolescence/early adulthood
- Amygdala is on-line at birth
- Hippocampus is on-line about 18 months old
- Prefrontal cortex (judgment) not fully developed until late adolescence/early adulthood
- Use of drugs/alcohol/tobacco can impede development
Functions

- Reward pathway – Nucleus Acumbens – ‘GO’ system
- Middle Prefrontal Cortex – ‘STOP’ system
- Amygdala – warning system
- Hippocampus – episodic new memory and learning, salience
- Neurons that are wired together – fire together
Rats exposed to nicotine as adolescents self-administer more nicotine than rats exposed as adults Levin ED et al. Psychopharm 2000;169:141-149
Rats First Exposed to Nicotine in Adolescence Show Greater Sensitization to Cocaine Than Rats First Exposed as Adults

*Activity level after cocaine administration was measured by counting the number of times in 10 minutes each rat crossed light beams projected in a grid across its cage.

Sources: Collins *et al.*, 2004, Levin *et al.*, 2003, NIDA Notes v19.2
Adult rats exposed to Ritalin during adolescence self-administered more cocaine.
Brain Structure
(use of hand model from Dan Siegel, MD)

* Spinal cord (wrist)
* Brain Stem (palm) – fundamental processes – alertness, hunger, thirst, survival (fight/flight)
* Limbic System (thumb) – Amygdala – regulation of fear, hippocampus, hypothalamus, nucleus acumbens
* Cortex - back of hand = perception of body, front = motor action, motor planning, thinking
* Prefrontal cortex (fingers) – executive functioning
The amygdala, hippocampus and prefrontal cortex talk to the reward pathway via glutamate.

Changes in sensitivity to glutamate enhance the release of DA from VTA to NA, promoting CREB and delta fos B.

Strengthens pathways that link memories of drug taking with reward - LTP.
Long Term Potentiation

* Primes cells to react more strongly, releasing DA more abundantly in response to future exposure
* A single exposure to cocaine can establish LTP in mice
* All drug of abuse trigger the same change
* Medications that are active in the brain but not addictive, do not have this effect
LTP – Increase in AMPA to NMDA ratio
Stress and LTP

* In mice, stress alone can induce increased AMPA:NMDA ratios in VTA cells within 24 hours
* These changes are similar to those induced by drugs of abuse
* This suggests a priming mechanism – that someone who has experienced stress may be more vulnerable to addiction
Addictive Drugs and Stress Increase Sensitivity of DA Cells in Mice (Saal et al. Neuron 2003;37:577-582)
Effects of Drug Use on the Hippocampus

- Drugs of abuse are potent negative regulators of adult neurogenesis in the hippocampus
- Chronic administration of opiates, THC, nicotine or ethanol decrease hippocampal function, decreasing ability of adult brain to adapt to new information
Effects of Stress on the Hippocampus

- Stress is associated with hippocampal neuronal damage, hippocampal volume reduction on MRI and memory deficits in human subjects with stress/PTSD
- Stress results in reduced hippocampal neurogenesis and ability to adapt to new information and new environments
Which means that as long as the alcohol/drug/tobacco is still being used:

* The drug drives the use and the neural circuitry that has been “hard wired” is continually engaged and the same behavior occurs over and over

* The person has difficulty with new learning and memory due to decreased hippocampal volume/function and disrupted sleep patterns

* The person has difficulty making different (healthier) decisions as the prefrontal cortex is impaired
Biochemical Explanation for Denial?

* Does the effect of addictive drugs and stress/trauma - decreasing neurogenesis in the hippocampus - give us a biochemical explanation for denial?

* Why someone continues to use in spite of consequences

* Why someone stays in an abusive relationship in spite of consequences
Given the neurobiology of all drugs of abuse, how can treatment help?

* By providing the brain an opportunity to heal and the hippocampus to regenerate – improving the patients’ ability to adapt to new information they are receiving in treatment

* By providing a safe environment – removing patient from chronic stress/abuse/trauma

* By providing an environment free of all addictive drugs, including tobacco
Nature and Nurture

* Both genetics and experiences can change development of the brain.
* Neuroplasticity = how the neurons change in the brain in response to experience.
  * Altered synaptic connections – 100 billion neurons, each neuron has 10 thousand connections.
  * Neurogenesis – growing new neurons from uncommitted neural stem cells – takes about one month to get inspired and two additional months to grow
Treatments that Promote Neurogenesis

- Enriched environment that promotes physical activity and learning (Gage, Science 2000;287:1433-1438)
- SSRI medication, Lithium, ECT, Transcranial magnetic stimulation (normalization of serotonin and glucocorticoid dysfunction, activation of growth factor and cAMP pathways)
Use of Medications

- Psychotropic Medications often helpful in stabilizing psychiatric symptoms
  - Antidepressants
  - Anticonvulsants
  - Antipsychotics
  - Anti anxiety agents (avoid benzodiazepines)
- Medications approved for treating chemical dependence – often useful as an aid
  - Acamprosate (Campral)
  - Naltrexone (Revia, Vivitrol)
  - Disulfiram (Antabuse)
  - Varenicline (Chantix)
Medications used in addiction, an aid – not a stand alone treatment

- **Naltrexone** – reduces alcohol cravings and consumption by blocking opiate receptors that modulate release of dopamine in the nucleus acumbens – blocks cue induced relapse but less effective with stress induced relapse

- **Acamprosate** – reduces alcohol cravings and consumption by decreased glutamate release, decreased NMDA receptor excitability, decrease Ca influx, increased taurine (inhibitory neurotransmitter)

- **Varenicline** – reduces tobacco cravings and decreases pleasurable effects of tobacco – nicotinic receptor partial agonist – produces modest levels of dopamine and prevents binding of nicotine

- **Disulfiram** – blocks metabolism of alcohol - producing increased sensitivity, also inhibits dopamine-beta-hydroxylase preventing breakdown of dopamine, reduces alcohol and cocaine consumption
Complementary Treatment Modalities to Help Re-Wire the Brain

- Recovery Education
- Relapse Prevention
- Cognitive/Behavioral Therapy
  - Dialectic Behavioral Therapy (DBT)
  - Strategies for Self Improvement and Change (SSIC)
- Trauma Work
  - EMDR
  - Brain Synchronization Therapy
- Stress Management Techniques
  - Acudetox – 5 point auricular acupuncture (NADA)
  - Other meridian therapies – TAT, EFT, TFT
  - Mindful Meditation
  - Biofeedback – Cardiac Coherence
  - Yoga, Tai Chi
Restorative Yoga

Asanas with Props
The ancient yogis used logs of wood, stones, and ropes to help them practice asanas effectively. Extending this principle, Yogacharya Iyengar invented props which allow asanas to be held easily and for a longer duration, without strain.

YOGACHARYA IYENGAR IN SETUBandHA SARVANGASANA
This version of the posture requires considerable strength in the neck, shoulders, and back, requiring years of practice to achieve. It should not be attempted without supervision.
Not so restorative Yoga