THE NEUROBIOLOGY OF ADDICTION: ADDICTION 101

Nicole T. Labor, DO
Nicole T. Labor, DO, BCFP, BCABAM

- Associate Medical Director of Addiction Medicine, Summa Physicians Inc., Akron, OH
- Medical Director, Esper Treatment Center, Erie, PA
- Chief Medical Officer, Interval Brotherhood Home, Akron, OH
- Director of Medication Assisted Treatment, STEPs, Wooster, OH
- Associate Clinical Professor of psychiatry and family and community medicine, NEOMED
- Director of Addiction Medicine Fellowship, Summa
ADDITION IS A DISEASE...

BUT HOW DO WE KNOW??

THE DISEASE MODEL
Addiction is a brain disease

- The BRAIN is the organ involved in the disease of addiction
- There are no good tests for brain diseases (at least no inexpensive ones)
- So people with brain diseases start out at a disadvantage
- The symptoms of brain diseases are more likely to be labeled as “badness”
Dorsolateral (dl-PFC)  
- Decision making

Orbitofrontal and ventromedial (vm-PFC)  
- Processing reward

Anterior and ventral cingulate cortex  
- Controls whether a behavior will be performed and to what intensity
“hub” of executive functioning

Confers emotional meaning (semantic content) onto objects in the world

Seat of the Self and Personality

Love, Morality, Decency, Responsibility, Spirituality

Conscious “choice”

• Will power
The limbic system: major route for information transfer between neocortex and hypothalamus

- Limbic lobe
  - Subcallosal area
  - Cingulate
  - Parahippocampal gyri
- Amygdala
- Hippocampus
- Part of basal ganglia
- Anterior thalamic nucleus
- Parts of hypothalamus
- Habenual
- Olfactory cortex

Amygdala, hippocampus and parts of hypothalamus are essential for memory and emotional context as well as affective response to learned associations.
The midbrain is the survival brain

- Not conscious
- Acts immediately, no future planning or assessment of long-term consequences
- A life-or-death processing station for arriving sensory information
The Midbrain (aka Limbic Brain) is the SURVIVAL brain. It handles:

- EAT!!
- KILL!!
- SEX!!!
DRUGS WORK IN THE MIDBRAIN...

- NOT in the Cortex...
- (how do we know?)
  - The Olds Experiments
- Mice preferentially self-administer drugs of abuse like cocaine ONLY to the Reward Centers of the Midbrain

DECISIONS SURROUNDING DRUG SEEKING AND TAKING ARE MORE DRIVEN BY EMOTION AND INSTINCT THAN BY LOGIC
in addiction, the drug hijacks the survival hierarchy and is so close to actual survival that it is indistinguishable from actual survival

- NEW!!! #1 drug!!!
- #2 Eat
- #3 Kill
- #4 Sex
People dying of thirst in the desert will risk losing everything they value for a drink of water → this is the midbrain in action shutting down the frontal cortex in an effort to SURVIVE

(i.e. IN ADDICTION the drug IS survival)
Cortex changes

Cocaine Addict | Nonuser

Most Active | Least Active

NORMAL BRAIN ACTIVITY

COCAINE ABUSER 10 days abstinent

COCAINE ABUSER 100 days abstinent
HOW THE BRAIN WORKS...

- A = presynaptic neuron
- B = synapse
- C = postsynaptic neuron

1. neurotransmitter (NT) in vesicle
2. NT being released/taken back up
3. receptor for NT = effects!!!
Origin and distribution of neurotransmitters

Noradrenaline

Dopamine

Serotonin
fMRI activity increased in VTA and substantia nigra, pons, basal forebrain, caudate and cingulate correlated with self reported “euphoria” after use.

Drug users showed an increase in brain activity in limbic areas and the PFC after presentation of drug associated cues but decreased responsiveness when presented with non-drug reinforcers (e.g. sexually evocative cues) when compared with non-drug users.
Imaging and newer areas of study- the insula

- Essential in detection of interoceptive cues
- Lesions here will disrupt smoking in nicotine dependent people
- Drug associated cues can produce limbic activation in users even when the stimuli are on consciously perceived
Addiction is a disorder in the brain’s Reward (Hedonic) System

It is a broken “pleasure sense” in the brain
Brain Perceptual Systems (all of them):

1. Vision
2. Hearing
3. Touch
4. Smell
5. Taste
6. Linear Acceleration
7. Angular Acceleration
8. Gravity (Proprioception) ← perceptual construct
10. Pleasure ← perceptual construct
Addiction Neurotransmitter #1: Dopamine

• All drugs of abuse and potential compulsive behaviors release Dopamine

• Dopamine is first chemical of a pleasurable experience - at the heart of all reinforcing experiences

• DA is the neurochemical of salience (it signals survival importance)

• DA signals reward prediction error

• Tells the brain this is “better than expected”
The Brain has a Hedonic “Set Point”

- Family vacation, job promotion, winning fantasy sport
- Opiates, cocaine, benzos, alcohol, methamphetamine, etc

Dopamine "pleasure threshold"
Increased drug use reset the brain’s pleasure “set point”

- Family vacation, job promotion, winning fantasy sport
- Opiates, cocaine, benzos, alcohol, methamphetamine, etc

New threshold
Old dopamine "pleasure threshold"
Fewer dopamine receptors means more dopamine needed to feel “normal pleasure”
Midbrain changes

Dopamine D2 Receptors Are Lower in Addiction

- Cocaine
- Meth
- Alcohol
- Heroin

Control vs. Addicted
STRESS: a major player in addiction & relapse

CHRONIC, SEVERE STRESS = ↑ CRF

And ↑ CRF = ↓ DAD2 receptors

And ↓ DAD2 receptors = Anhedonia

Anhedonia: Pleasure “deafness”
(The patient is no longer able to derive normal pleasure from those things that have been pleasurable in the past)
High stress hormone levels ALSO reset the brain’s pleasure “set point”

- family vacation, job promotion, winning fantasy sport
- opiates, cocaine, benzos, alcohol, methamphetamines, etc
Change in Hedonic Set Point: Old pleasures don’t show up

- family vacation, job promotion, winning fantasy sport
- opiates, cocaine, benzos, alcohol, methamphetamine, etc
The patient is no longer able to derive normal pleasure from those things that have been pleasurable in the past.

Addiction is a stress-induced “hedonic dysregulation”
gene present

use of 'activating' substance x activating number of uses

gene activated ("turned on")

use of ANY dopamine releasing substance

midbrain changes occur (down regulation of dopamine receptors→ increased threshold for pleasure)

stress
Addiction Neurotransmitter #2: Glutamate

- The most abundant neurochemical in the brain
- Critical in memory formation & consolidation
- All drugs of abuse and many addicting behaviors effect glutamate which preserves drug memories and creates drug cues (triggers, people, places and things)
- And ... glutamate is the neurochemical of "motivation" (it initiates drug seeking)
Relapse

- Three things that are known to evoke relapse in humans:
  1. Brief exposure to ANY abusable drug OR compulsive behavior (DA release and DA receptor down regulation)
  2. Stress (CRF release and DA receptor down regulation)
  3. Exposure to drug cues (people, places and things!!!) (GLU release)
Now that the midbrain has found what secures survival...

... how does it motivate the individual to repeat that behavior?
Increased stress = increased pleasure threshold = increased need for dopamine= midbrain thinks it is dying= CRAVING

CRAVING is a physiological response to a neurochemical deficiency resulting in symptoms including sweating, stomach cramps, obsession, increased respirations, etc.

fMRI studies have showed increased activity in the NAcc and decrease in the amygdala during cravings

- You don’t actually have to have drug use for the defective physiology of addiction to be active
Once Craving sets in, how does it control behavior???

- The midbrain hijacks the abilities of the frontal cortex...
  - The brain will utilize the most likely reasoning to get the addict to feel like they have to use
    - Pain (won’t cause death)
    - Anxiety (won’t cause death)
    - Stress (won’t cause death)
    - Specific people or events/reservations (ALWAYS a choice)

Striatum (caudate-putamen)
  - dorsal → basal ganglia
  - ventral → accumbens

Mogensson stated that the accumbens is the “place where motivation is translated into action”

The striatum is the link between the limbic system and the motor system
Once there is a “reason”, suddenly behaviors become “justified”

- Lying
- Manipulating/stealing
- Reasoning/making excuses
- Rationalization
- Justification
Once the behaviors become habits, the behaviors themselves become the disease

- The need for instant gratification
  - And subsequent inability to wait or practice
- Needing a pill or chemical for EVERYTHING
  - while OTC sleep medications have few addictive properties, the BEHAVIOR of needing something to make the body do what it should naturally learn to do, IS addictive
- Looking for reasons to avoid recovery related behaviors and activities
  - Seeking reasons to use
• Nothing’s higher than survival
• No threat matches loss of survival
• The addict must first secure survival before attending to anything else
• And the survival imperative exists at the level of the unconscious in the limbic system
DEFINITION OF ADDICTION

- Addiction is a dysregulation of the midbrain dopamine (pleasure) system due to unmanaged stress resulting in symptoms of decreased functioning, Specifically:
  - 1. Loss of control
  - 2. Craving
  - 3. Persistent drug use despite negative consequences
Addiction is a disease...

But how do we know??

The Disease Model

midbrain

hedonic dysregulation of the dopamine reward system

drug use genetics stress

1. loss of control
2. craving
3. P.U.D.N.C
We MUST treat the most acute problem first

- MOST OF THE TIME ADDICTION IS THE MOST ACUTE PROBLEM. THE EXCEPTIONS ARE...
  - ACUTE PAIN FROM A TRAUMATIC INJURY/SURGERY
  - ANY EMERGENT ILLNESS

- Addicts have pain and often need higher than normal doses to treat that pain, they should be treated the same as any other patient with the given condition
  - This includes cessation of pain medication when it would normally be stopped for the same condition in a non-addict (detox may be required at this point)
The hierarchy of treatment

- DETOX - medical stabilization/removal of substance and its immediate effects
- Post detoxification - intensive development of coping skills, restructuring of self, accountability
  - Residential, partial hospitalization, Intensive Outpatient (IOP)
  - MAT
- Lifelong maintenance
  - 12-step
  - Service organizations and spiritual engagement
• We have to change the misperception of the hedonic aspects of the drug (thinking the drug gives us pleasure)

• We must change the attribution of survival salience to the drug on the level of the unconscious

1. Midbrain (unconscious) DRUG=SURVIVAL
The Two Tasks of Addiction Treatment:

- To give the addict workable, credible tools to proactively manage stress and decrease craving
  1. COPING SKILLS
  2. STRESS RELIEF
  3. SOCIAL SUPPORTS
  4. SAFE ENVIRONMENT

- For each individual addict, find the thing which is more emotionally meaningful than the drug- and displace the drug with it
  1. SPIRITUAL GROWTH
  2. PERSONAL DEVELOPMENT
THE DIVISION OF LABOR...

AA/BEHAVIORAL THERAPY WORK HERE

- Frontal cortex = emotional meaning

DRUGS/MEDICATIONS WORK HERE

- Midbrain = survival/craving
With the installation of coping mechanisms (A.A.), the Cortex comes back “on-line” and Free Will returns... even during periods of craving (midbrain activity)
new threshold
returns to the
old dopamine "pleasure threshold"

family vacation, job promotion, winning fantasy sport

opiates, cocaine, benzos, alcohol, methamphetamine, etc
Role of Medication in Addiction treatment practices
COMBINATION THERAPY (THE ULTIMATE TOOLBOX)

- ALLOWING THE MIDBRAIN TO ‘REST’ BUT SIMULTANEOUSLY STRENGTHENING THE FRONTAL CORTEX
- ALLOWING THE BEHAVIORAL AND EMOTICOMENTAL TOOLS TO DEVELOP AND BE PRACTICED IN A “LESS STRESSFUL” ENVIRONMENT (THE BRAIN)

- APPROPRIATE USE:
  - Recovery setting where the medication is on the bottom of the priorities
  - Using the medication as a “carrot” to get addict to participate in activities that would otherwise be the antithesis of the addicted mind

- INAPPROPRIATE USE:
  - As the ONLY tool
  - As the most important tool
  - Allowing the individual to prioritize the drug over recovery practices
Questions
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