Neurobiology of Substance Use Disorders: Understanding the Addicted Brain

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Disclosures

- Dr. Liepman occasionally serves Reckitt Benckiser Ltd. and Alkermes Inc. as a paid speaker informing clinician audiences about their respective products: Suboxone™ or Vivitrol™, but he is not engaged in that activity today.
- Drs. Lagos & Gross have no conflicts of interest to disclose.
Objectives

1. Describe the brain reward circuit in normal brain and how it changes in the addicted brain

2. Explain how different parts of the brain reward circuit respond to cues/triggers for relapse

3. Explain the effect of medications and psychosocial interventions in the dysfunctional reward circuit of the brain.

Addiction: chronic relapsing disorder

- Preoccupation
- Anticipation (obsessiveness)

- Negative Emotional/Physical Distress (when access is denied)

- Bingeing
- Intoxication (loss of control)
Progression of the condition

- Drugs/substances of abuse activate same reward system as natural reinforcers
- Natural reinforcers become less important and the substance of abuse becomes a priority despite catastrophic consequences

Impulsive use  Compulsive use
Dopamine: the versatile neurotransmitter

- Motor activity
- Cognitive functioning
- Attention
- Regulation of reward and motivation
- Salience attribution
- BUT….
- GABA, Glutamate, opioid peptides, are also important neurotransmitters
Basic Reward Circuit

- **Amygdala**: memory and emotional reactions
- **Hippocampus**: pattern recognition, consolidating information from short- to long-term memory
- **Ventral Tegmental Area**: saliency, produces dopamine, implicated in the drug and natural reward circuitry of the brain
- **Nucleus Accumbens & Ventral Pallidum**: cognitive processing of motivation, pleasure, and reward.
- **Orbitofrontal cortex**: cognitive process of decision-making
- **Prefrontal cortex & Anterior Cingulate Gyrus**: judgment, values, awareness of context and consequences, planning complex behavior, problem solving, and moderation of social behavior
Part II

- Exercises
www.hdwallpapers.in/cute_baby_boy_2-wallpapers.html

www.lostateminor.com/2013/03/05/now-you-can-smell-like-dog-poop-or-your-grans-dentures/
halloftheblackdragon.com/reel/the-curse-of-being-a-beautiful-woman/

loeken.deviantart.com/art/Beer-in-Mug-257497224
Part III
Circuits Involved In Drug Abuse and Addiction

All of these brain regions must be considered in developing strategies to effectively treat addiction

Part IV

- Developmental differences in the reward circuit
**Brain Development**

- Newborns have well developed instinctual brains
- But the frontal cortex, as well as other cortical structures, develop gradually up until about age 26
- During this interval, we see gradual acquisition of more “adult” knowledge and skills, including:
  - Organizational, planning skills (executive function)
  - Understanding of context (rules, social mores)
  - Abilities to delay gratification (control basic drives)
  - Skill in balancing different influences when making decisions
  - Time sense, future orientation, consequences.
The instinctual brain (midbrain)

- Very primitive
- Manages bodily functions:
  - Breathing
  - Heart rate, blood pressure
  - Body temperature, shivering, sweating
  - Sneezing, coughing, vomiting,
  - Itching, scratching, blinking, yawning
  - Appetite, digestion, nutrition
  - Falling asleep, waking up
  - Sexual arousal
  - Craving, desire
- Does not know or care about context
- Cannot talk to this part of the brain.

The emotional brain (Amygdala)

- Very primitive
- Manages feelings:
  - Sadness, disappointment
  - Fear, anxiety, stress
  - Anger
  - Happiness, excitement
### Pattern recognition (Hippocampus)

- Remembers objects, places, circumstances
- Identifies associations to these memories
- Children learn about the environment as they learn language
  - Naming
  - Implications, properties, uses

### Decisions (Frontal cortex)

- Prefrontal cortex/Anterior cingulate cortex
  - Understands rules, consequences, context
  - Planning, organizing, executive function
  - Weighing pros and cons of actions
  - Considers input from instinctual midbrain
  - Takes the guilt from amygdala when bad things result from decisions
- Orbitofrontal cortex promotes compulsive, repetitive behavior
Latency age children

- Prefrontal cortex/Anterior cingulate cortex not well developed
- Instinctual midbrain promotes impulsive actions
- Orbitofrontal cortex promotes compulsive, repetitive behavior
- Children who can delay gratification tend to have better outcomes in life than those who cannot, consistent with better executive function
- Harm avoidant and social reward dependent (type I) have better outcomes than thrill seeking and risk taking (type II) children.

Adolescents

- Prefrontal cortex/Anterior cingulate cortex not well developed
- Instinctual midbrain promotes impulsive actions
- Orbitofrontal cortex promotes compulsive, repetitive behavior
- Peer pressure and rebelliousness against authorities can promote unwise decisions
**Adults**

- Prefrontal cortex/Anterior cingulate cortex better developed
  - Role is to “put the brakes” on the impulsive unwise behaviors being considered
- Instinctual midbrain promotes impulsive actions
- Orbitofrontal cortex promotes compulsive, repetitive behavior
- Counseling and 12-step support fellowship participation strengthen the PFC/ACC.

**Genetics**

**Culture**

**Experience**

**Trauma**

**Other Illness**
Part V: Case

Tony is a 12 year old Italian American boy whose father and uncles have alcoholism. He helps them make homemade wine and samples the product. He likes how it makes him feel and he enjoys the camaraderie of working with his family.

Now 13, Tony finds popularity among peers when he brings them bottles of wine pilfered from his home to share with them. They experience intoxication during their drinking binges.

Their immature frontal lobes combined with the disinhibiting (anxiety reducing) effect of alcohol make it easy for them to misbehave and occasionally get caught.
Part V: Case

- Now 16, Tony has a juvenile delinquency record, as do several of his peers. He has been held back at school, despite a prior promising academic performance in elementary and middle school.
- He got a DUI, with open container, and minor in possession, and has been sent to driver education classes by the court.
- His drinking is more regular and his attitude is denial.

Part V: Case

- Now 20, Tony has lost his driver’s license. He is no longer welcome at his parent’s home due to violence. He drinks daily. He has added cannabis and alprazolam.
- He has had 2 detox & rehabs but has not been compliant with aftercare plans.
- He relapses easily on cues.
Part V: Case

Now 24, Tony has been living in a long-term residential program. He takes naltrexone to manage his craving and prevent relapse. He is a daily participant in Alcoholics Anonymous meetings, and has 8 months sobriety. He is working with his sponsor on his inventory (4th step).

Part V: Case

Now 26, Tony has been living in the community, working and going to Community College.

He is a daily participant in Alcoholics Anonymous meetings, and has 22 months of sobriety.

His girlfriend was murdered by a burglar. He is struggling with craving.
Part VI: Treatment

- Decrease the reward value of the drug of choice
- Increase the salience value of natural reinforcers

Strengthen frontal inhibitory & executive, cognitive control

Weaken conditioned memories to the drug and related stimuli

Circuits Involved In Drug Abuse and Addiction

All of these brain regions must be considered in developing strategies to effectively treat addiction
Multimodal Treatment

- **Glutamate modulation:** acamprosate
- **GABA modulation:** topiramate, gabapentin
- **Dopamine blocker:** antipsychotics
- **Opioid antagonist:** naltrexone

**Signaling Systems/NT**

- **Decreasing the Reward value**
  - Methadone, buprenorphine
  - Nicotine replacement, varenicline

**Decreasing the Reward value**

- **Memory modifiers?**
  - Associates nausea with alcohol: Disulfiram

- **Rehabilitation**
  - Self-help groups
  - Sponsorship
  - CBT
  - Family therapy

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Treatment

- Naltrexone: blocks the actions of endorphins.
- Topiramate: augments GABA activity
- Methadone: binds to opioid receptors (long acting)
- Buprenorphine: binds to opioid receptors → partial agonist (delta and mu receptors)
- Nicotine patch: binds to nicotine receptors (partial agonist) and blocks nicotine effects while preventing craving
- Disulfiram causes unpleasant symptoms if alcohol is taken, countering pleasant dopamine induced pleasurable experiences.
40 y/o married male with alcohol dependence in early full remission (sober for 4 months)

- Relapsed on alcohol after stressful event at work
- Multiple previous relapses, each after 4-6 months sobriety
- Inpatient rehab x 2 weeks at age 18.
- Does not attend AA meetings or individual counseling.
- Never tried meds for relapse prevention
- Otherwise healthy
- Uneventful detoxification for 5 days

How would you approach treatment planning for this patient? What areas of the brain are targeted with each recommendation?

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35 y/o (28 weeks) pregnant woman with opioid dependence in early full remission

- Relapsed on heroin, in context of marital strife
- She attends NA meetings 3x/week
- Regular contact with sponsor, except this last time
- Previous inpatient rehab x 2
- Worked the 12 steps once

Treatment approach
What areas of the brain can be targeted?
45 y/o, divorced mother of two with alcohol dependence

- History of depression and anxiety.
- Has made serious suicide attempts during episodes of intoxication
- Admitted to psychiatric unit after another attempt, following a 1-week drinking binge
- Has a sponsor, working the 12 steps, attends AA meetings regularly, until a new stressor (work, relationships, daughters) leads to relapse
- No prior use of meds for relapse prevention

How would you approach treatment planning for this patient?
What areas of the brain are targeted with each recommendation?

38 y/o male w/ cocaine dependence

- Admitted to the hospital with an acute heart attack after cocaine binging
- No history of treatment (rehab, meetings, etc.)
- Short periods of abstinence on his own.
- Pt concerned about his current medical condition and is considering rehab, but he has reservations.
- Stage of change
- Treatment approaches
- Target brain areas
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That's all folks!

- Thank you
- Questions?
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