Neurobiology of SUD: a context for working with patients with substance use disorders

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April 10, 2019

Outline

- Questions to consider

- Neurobiology of addiction review

- SUD as chronic disease- case examples

- Risk reduction and best practices

- Models of care

A word about language:

- Addiction, SUD, OUD, MAT, Medication for Addiction Treatment, MOUD, addict, dirty, clean, drug overdose, drug toxicity/poisoning

Questions to consider

- What support do our patients need?

- What support do our clinicians need?

- How do you provide reassurance? To timid prescribers? To resistant staff/leadership?

- What is the biggest challenge to our system?

- What clinic and community resources do we have?

- "Low Threshold Buprenorphine"- is it right for our clinic?

- If we don't have the resources- should we give buprenorphine?

- If patient can't follow rules, should they be discharged?

- What if a buprenorphine patient consistently tests positive for methamphetamine?

- When do you switch from buprenorphine to methadone?

- What is our stance on Marijuana?

- Are we reaching all of the patients in our clinic who need buprenorphine?

- What barriers to our patients encounter to getting the services they need?

Neurobiology of SUD review

What is addiction?

- Addiction can be defined as compulsive drug use despite negative consequences

- Physiologic dependence and withdrawal avoidance alone do not explain addiction (this is why detox does not work)

What is neurobiology of SUD?

Neurobiology of SUD attempts to explain the mechanisms by which drug seeking behaviors are consolidated into compulsive use:

- long persistence of relapse risk

- drug-associated cues control behavior

Why focus on neurobiology of SUD?

- Connect with empathy and compassion

- Importance of limits and boundary setting

- Harm reduction vs fostering recovery

# Although drugs of abuse are pharmacologically diverse…

- Stimulants- Cocaine, amphetamines, MDMA

  →act as serotonin-norepinephrine-dopamine reuptake inhibitors

- Opioids- Heroin, morphine, oxycodone, fentanyl

  →agonist action

- Sedatives/Hypnotics- Alcohol, benzodiazepines, barbiturates

  - → GABAergic agonists/modulators

- Cannabis-

  - → binds cannabinoid receptors

…they all lead to a common pathway

All drugs of abuse pharmacologically release
dopamine from ventral tegmental dopamine
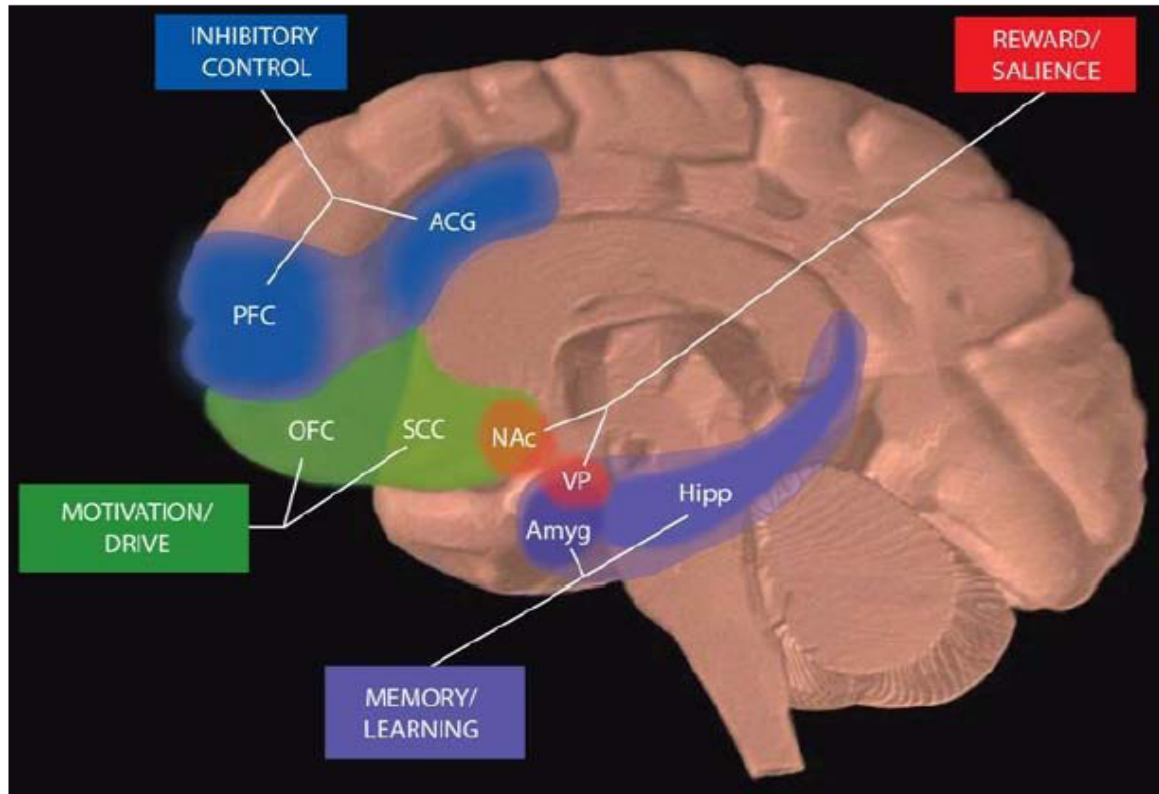neurons to the nucleus accumbens

The ventral-tegmental dopamine system
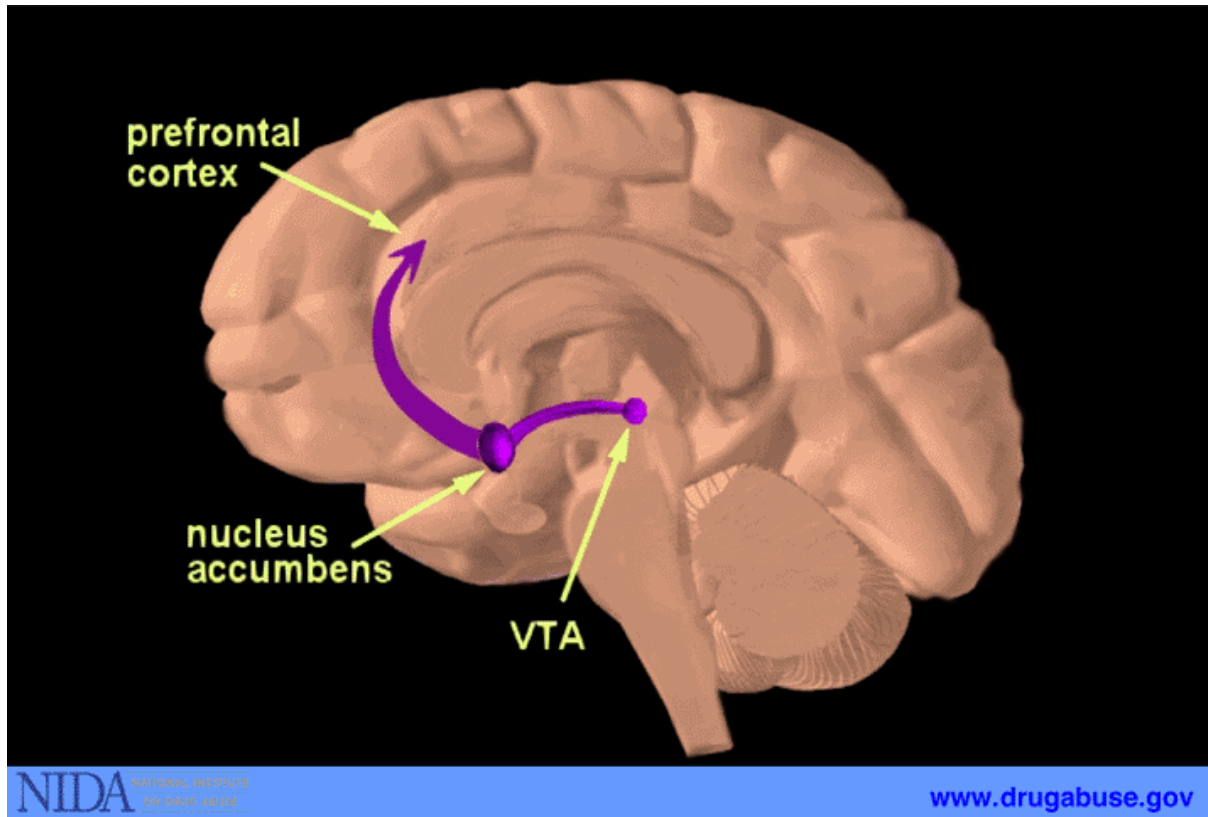
Source: National Institute on Drug Abuse https://www.drugabuse.gov/understanding-drug-abuse-addiction-what-science-says

The ventral-tegmental dopamine system

The Dopamine Reward Pathway:
How Dopamine leads to behavior change

- Dopamine required for natural stimuli (food, opportunity for mating, etc) to be rewarding and drive behavior

- Natural rewards and addictive drugs both cause dopamine release in the Nucleus Acumbens

- Drugs of abuse mimic effects of natural rewards and thus *shape behavior*

The Dopamine Reward Pathway:
How Dopamine leads to behavior change

- Survival demands that organisms find and obtain needed resources (food, shelter) and opportunity for mating despite risks -survival relevant goals

- These goals have natural "rewards" (eating, safety, sex)

- Behaviors with rewarding goals persist to a conclusion and increase over time as they are positively reinforcing

The Dopamine Reward Pathway:
How Dopamine leads to behavior change

- Internal states (hunger) increase value of goal-related cues and increase pleasure of consumption

- Likelihood that complex behavioral sequence (hunting) will be brought to successful conclusion

The Dopamine Reward Pathway:
How Dopamine leads to behavior change

- Behavioral sequences involved in obtaining reward (steps required to hunt) become overlearned/automatized

- Automatized behavioral repertoires can be activated by cues predictive of reward

Prediction Error Hypothesis

▶Exposure to an unexpected reward causes transient firing of dopamine neurons which signals brain to learn a cue.

▶Once cue is learned, burst of firing occurs at cue, *not at reward.*

▶If the reward does not arrive, dopamine firing will decrease below baseline levels → serves as an error signal about reward predictions

▶If reward comes at unexpected time, dopamine firing will increase → positive predictive error signal:

"better than expected!"

Dopamine Gating Hypothesis

- Because drugs cause dopamine release (due to pharmacological actions), dopamine firing upon use does not decay over time → brain repeatedly gets positive predictive error signal: "better than expected!"

- Drug cues become ubiquitous (drug cues difficult to extinguish)

- Cues that predict drug availability take on enormous incentive salience (consolidates drug seeking behavior)

- Drug cues will become powerfully overweighted compared to other choices (contributes to loss of control over drug use)

Cue Learning

- Glutamate is another excitatory neurotransmitter involved in cue learning:

  - Specific information about cues

  - Evaluation of cue significance

  - Learned motor responses

- Enhances dopamine dependent learning

Source: Am J Psychiatry 2005;162:1414-1422

Clinical Implications

- "Addictive" behaviors are a important and normal part of human behavior

- Drugs of abuse pharmacologically modify functioning of reward circuits to overvalue drug rewards and reduce the comparative value of other rewards

- **Intention to stop use is not enough to stably quit substance use.**

SUD is a Chronic Disease

Chronic Disease Case #1

- 76-year-old male with uncontrolled hypertension, cardiovascular disease with myocardial infarction, hypertension, elevated cholesterol levels, diabetes, gastroesophageal reflux disease, stent procedures and a variety of behavioral issues associated with the patient, including noncompliance with treatment plans, appointment cancellations and "no shows," and rude and demeaning behavior toward office staff.

Chronic Disease Case #2

- 59 year-old female with HIV, paranoid schizophrenia, obesity, hypertension, and hyperlipidemia. She is refusing to take any medications for medical or mental health conditions. When she speaks she rambles and complains of being monitored by microphones implanted in her walls. She lives in a group home and her basic needs are met but is often disheveled and slightly malodorous. Her CD4+ count is 130 and her viral load is 500,000

Chronic Disease Case #3

- 69-year-old man with type 2 diabetes presents with recent weight gain, and foot pain. He had been started on glyburide (Diabeta), 2.5 mg daily, but stopped taking it because of dizziness. He does not test his blood glucose levels at home and expresses doubt that this procedure would help him improve his diabetes control.

- Diet history reveals excessive carbohydrate intake in the form of bread and pasta. His wife has offered to make him plain grilled meats, but he finds them "tasteless." He drinks 8 oz. of red wine with dinner each evening.

- He stopped smoking more than 10 years ago. His hemoglobin A1c (A1C) has never been <8%. His blood pressure has been measured at 150/70, 148/92, and 166/88 mmHg on separate occasions during the past year. He does not practice any preventive foot care.

Chronic Disease Case #4

- 38-year-old female in an abusive relationship with alcoholism, depression, pelvic inflammatory disease. Frequently misses scheduled appointments or shows up an hour or more late. Sometimes presents to clinic smelling of alcohol or appearing intoxicated. Often has bruises and or cuts on her face, neck, arms and legs.

How might we engage this patient, what actions might we take?

- 4 minutes: Individually read through the two cases and write down your ideas, one idea per sticky

- 6 minutes: Discuss at your table

- What engagement strategies and actions did you come up with?

Opportunity for MAT

Models in Primary Care

- MD/MA/Patient Coordinator

- Nurse Care Manager or Clinical Pharmacist model

- Group Visits model

- Buprenorphine Induction Clinic model

- Hub and Spoke model

- Most of the above models include behavioral staff – social workers, SUD counselors, Psychologists

Risk Reduction and Best Practices

- Two major factors to consider:

    - Patient Goals of Care

    - Treatment Capacity

Treatment Goals

Range of treatment goals

Minimization of harms from ongoing use ⟵⟶ Sustained recovery with abstinence from all substances

Treatment Capacities

- "Street Clinic"
  - Multiple x-waivered providers
  - No counselors
  - Limited durations of medication prescribed, with frequent visits

- Large well resourced primary care clinic MOUD Program
  - Abstinence based
  - Weekly group required
  - Random urine call backs
  - Robust medication management
  - Robust counseling

What Does Not Work

- Confrontation
- Kicking people out of treatment

What Does Work

- Motivational incentives/Contingency management

- Motivational Interviewing

- Team Based Care Models

- Protocols that RN's, MAs, CADACs can execute

- Treat co-occurring MH and SUD disorders

- Provide resources- transportation, assist with access to insurance, benefits, etc

Risk reduction

- Limited supplies of buprenorphine

- More frequent visits

- Team based care, multidisciplinary if feasible

- Checking CURES

- Ensuring naloxone is dispensed to patients

- Operating or linking to needle exchange, if appropriate

Key Question to Consider

- Are our challenging patients using in a way that is less dangerous?

Developing and Strengthening Models of Care

- Are our challenging patients using in a way that is less dangerous?

→Then you have valid model

- More frequent visits/limited supply of buprenorphine allows:

→closer monitoring of high risk conditions

→establishing and developing relationships and therapeutic alliance

→getting ready for next step in recovery

References/Resources/Recommended Reading

- Addiction: A Disease of Learning and Memory. Am J Psychiatry 2005;162:1414-1422

- Confrontation in Addiction Treatment, William R. Miller, PhD and William White, MA (http://www.cafety.org/miscellaneous/755-confrontation-in-addiction-treatment

- VA/DoD Clinical Practice Guideline: Management of Substance Use Disorders (www.healthquality.va.gov/sud/sud_full_601f.pdf)

- Treating Addiction in the Primary Care Safety Net: https://tapcprogram.com

- ATSH for Primary Care: https://www.careinnovations.org/addiction-primary-care-2019

- Provider Clinical Support System: https://pcssnow.org

- ASAM National Practice Guideline: https://www.asam.org/npg

- CSAM: https://cme.csam-asam.org

- National Survey on Drug Use and Health (NSDUH) https://nsduhweb.rti.org/

- Substance Abuse & Mental Health Services Administration http://www.samhsa.gov/

Questions?

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