Neurobiology of Addictive Disorders

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Disclosure

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UHS

Objectives:

- To better understand the Neuroscience of addictive disorders.
- To minimize the stigma about addictive disorders
- To appreciate the clinical benefits, as well as limitations of considering addiction as a brain disease.

Outline:

- Is Addiction a brain disease?
- Neuroscience of Addictive Disorders
- Relapse Rate in addictive disorders is similar to other chronic medical illnesses

Is Addiction a Brain Disease?

Disease Vs. Choice

Compulsions Vs. Weakness

Genetics Vs. Moral defect (sinful choice)

The Disease Model:

Cause

Defect of an

Organ resulted in

Symptoms

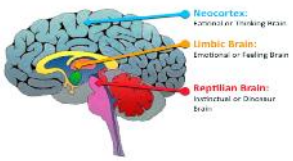
Neurobiology of Addictive Disorders:

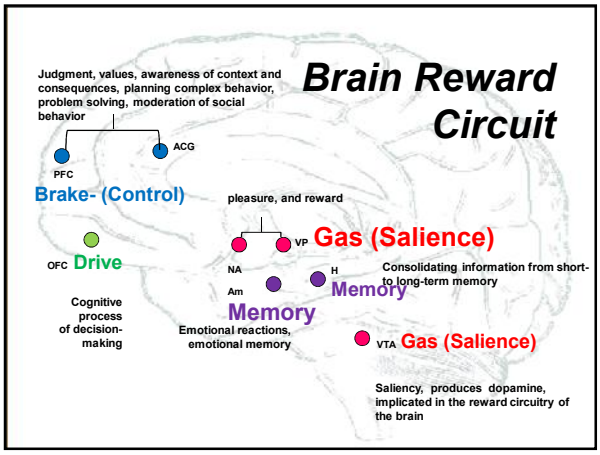
- The brain has many parts each with different functions
  - Midbrain (instinctual Brain): Support Survival including (Reward/ Avoid Harm)
  - Cerebrum (Rational Brain): Decision making
- The parts interact like members of a committee
  - Sometimes the parts cooperate
  - Sometimes they fight each other

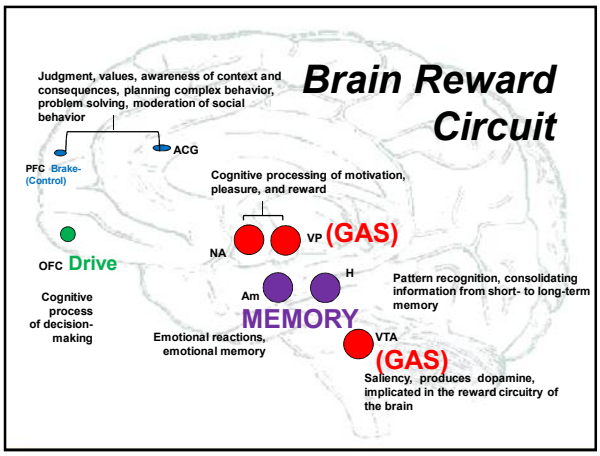
Quick Course on Neurobiology

- The prefrontal cortex handles thinking about risks, judging right from wrong, following or breaking rules
- But the reward circuit starts in lower centers of the midbrain where craving & urges originate
  - This is what leads to impulsive acts
  - Spurred by cues and triggers, emotions, and withdrawal
  - HALTS: Hungry—Angry—Lonely—Tired—Stressed

Neurobiology of Addictive Disorders




Brain Reward Circuit
Judgment, values, awareness of context and consequences, planning complex behavior, problem solving, moderation of social behavior
ACG
PFC
Brake- (Control)
pleasure, and reward
VP
Gas (Salience)
OFC
Drive
NA
H
Consolidating information from short- to long-term memory
Am
Memory
Cognitive process of decision-making
Memory
Emotional reactions, emotional memory
VTA
Gas (Salience)
Saliency, produces dopamine, implicated in the reward circuitry of the brain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Pattern recognition, consolidating information from short- to long-term memory
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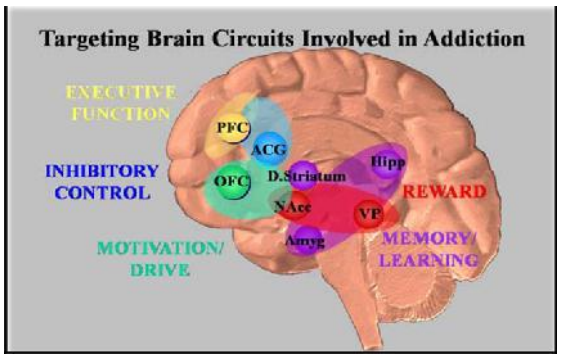

Targeting Brain Circuits Involved in Addiction
EXECUTIVE FUNCTION
PFC
ACG
INHIBITORY CONTROL
OFC
D.Striatum
Hipp
REWARD
NAcc
VP
Amyg
MOTIVATION/ DRIVE
MEMORY/ LEARNING

Neurotransmitters involved in development of Addictive Disorders

- **Dopamine:** Hypo-dopaminergic State and Dopamine surge ↑
- **Glutamate:** Memory formation, drug memory and seeking ↑

The American Psychiatric Publishing Textbook of Substance Abuse Treatment

Neurotransmitters involved in development of Addictive Disorders

- Serotonin ↓
- GABA↓ (Anti-Anxiety)
- DYNORPHINS↑ (Dysphoria)
- NOREPINEPHRINE↑ (Stress)
- CRF ↑ (Stress)
- NPY ↓ (Anti-anxiety)

The American Psychiatric Publishing Textbook of Substance Abuse Treatment

NEUROBIOLOGICAL DEFINITION OF ADDICTION

STRESS induced defect acting on

GENETIC vulnerability in the

REWARD, LEARNING, and MEMORY areas of midbrain and the CHOICE areas of cortex

Advantages of Combined Treatment

- The prefrontal cortex responds to psychosocial treatments
- The midbrain portions are more responsive to many of the medications that have been discovered or invented for addictive disorders.

Advantages of Combined Treatment

- Studies have shown that combined treatments addressing both the primitive, impulsive midbrain (MAT) and the higher centers (psychosocial treatments) have better outcomes than either kind of treatment alone.

Incidence of relapse after Detoxification

JAMA

Drug Dependence, a Chronic Medical Illness: Implications for Treatment, Insurance, and Outcomes Evaluation

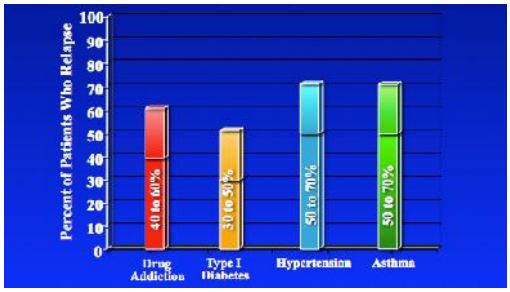
A. Thomas McLellan; David C. Lewis; Charles P. O'Brien; et al.

- **1-year, post-discharge follow-up studies have typically shown that: 40% to 60% of discharged patients are continuously abstinent.**
- Predictors of poor adherence and relapse
  - Low socioeconomic
  - Co morbid psychiatric conditions
  - Lack of family and social supports

Compare relapse with other Chronic Medical Illnesses

- Less than 60% of adult patients with type 1 diabetes mellitus fully adhere to their medication
- 30% to 50% of experience recurrence of symptoms each year to the point they require reestablish symptom remission
- Less than 40% of patients with hypertension or asthma adhere fully to their medication regimens
- About 50% to 70% of experience recurrence of symptoms each year to the point they require reestablish symptom remission

Relapse Rates Are Similar for Drug Addiction & Other Chronic Illnesses



MEDICATION ASSISTED TREATMENT- OPIOID USE DISORDERS

Ahed Zayzafoon , MD .
Board certified in Internal Medicine and Addiction Medicine

Medication Assisted Treatment- Opioid Use Disorders

- Abstinence Oriented Tx. vs. MAT
- Available treatment , settings , side effects
- Treatment selections
- Controversy and obstacles

Abstinence Oriented Tx. vs. MAT

- Relapse rate after opioid detoxification ranges from 72 to 88% after 12–36 months, despite multidisciplinary endeavors
- Early relapse after inpatient detoxification has been found to be significantly predicted by younger age, greater heroin use prior to treatment, history of injecting, and failure to enter aftercare
- Abstinence has also been found to be significantly associated with completion of the 6-week inpatient treatment program and attendance at outpatient aftercare and negatively associated with a family history of substance misuse[5]

- Dose-response effects of methadone in the treatment of opioid dependence. (56.4% versus 67.6% and 73.6% for the 20-mg and 0-mg groups, respectively; $P<0.05$)
- Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. The proportion of urine samples that were negative for opiates was greater in the combined-treatment and buprenorphine groups (17.8 percent and 20.7 percent, respectively) than in the placebo group (5.8 percent, $P<0.001$ for both comparisons)

Abstinence Oriented Treatment

- Best Candidates:
  - Short duration of addiction
  - Early in treatment history, not a lot of failed attempts
  - Lower level of severity
  - Lack of significant medical or psychiatric co-morbidities

Medication Assisted Treatment

- Full Agonist
- Partial Agonist
- Full Antagonist

Full Agonist

Methadone

- licensed opioid treatment programs or licensed inpatient hospital units in the United States are permitted to order and dispense methadone for withdrawal or long-term treatment of an opioid use disorder

To be eligible for methadone maintenance in the United States

- Documentation of the presence of an opioid use disorder for at least one year of continuous use
- An age of 18 years or older. Younger individuals are eligible for treatment, with the consent of a parent, guardian, or designated responsible adult, if they have current opioid physical dependence and have at least two previous attempts at detoxification or psychosocial substance abuse treatment.

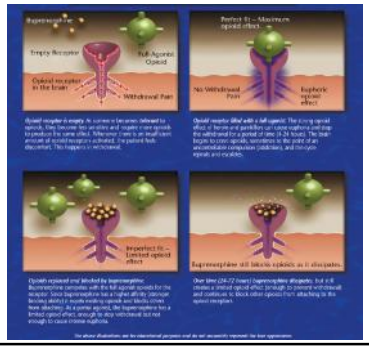
Side Effects

- Cardiac arrhythmias
- Hyperalgesia
- Overdose

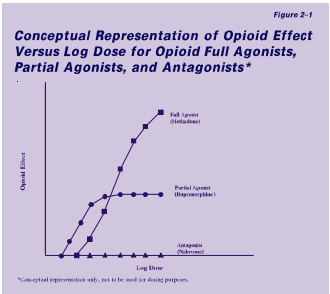
Partial agonist: Buprenorphine

- **Oral formulation**
- **Long-acting subdermal implant**

Partial Agonist: Buprenorphine



Because buprenorphine is a partial mu-opioid agonist with high affinity for the mu-opioid receptor, it can displace full agonist opioids from the receptor and precipitate opioid withdrawal



Supply

Buprenorphine-Naloxone films
Suboxone – Zubsolve – Bunavail

Buprenorphine
Subtex

Dosing

- film, sublingual (Suboxone): Schedule III
  - 2mg/0.5mg
  - 4mg/1mg
  - 8mg/2mg
  - 12mg/3mg
- Film, buccal (Bunavail): Schedule III
  - 2.1mg/0.3mg
  - 4.2mg/0.7mg
  - 6.3mg/1mg
- tablet, sublingual (Zubsolv): Schedule III
- 1.4mg/0.36mg
- 2.9mg/0.71mg
- 5.7mg/1.4mg
- 8.6mg/2.1mg
- 11.4mg/2.9mg
- tablet, sublingual (generic): Schedule III
  - 2mg/0.5mg
  - 8mg/2mg

Proper Handling

Long-acting subdermal implant

- The implant is intended for use only in patients who have first achieved clinical stability with sublingual or buccal buprenorphine at a daily dose of 8 mg or less.
- (96.4 versus 87.6 percent)

Pregnancy

- Sixty-seven percent of women receiving buprenorphine and 82 percent of women receiving methadone continued treatment through the end of the pregnancy.
- The neonates born to women in the buprenorphine-treated group required less Morphine (mean dose, 1.1 mg versus 10.4 mg), experienced shorter hospital stays (10 versus 17.5 days), and had a shorter duration of treatment for neonatal abstinence syndrome (4.1 versus 9.9 days) compared with neonates born to women in the methadone-treated group.

Opioid Antagonist: Mechanism of Action

- Opiate receptor antagonists such as naltrexone block opioid triggered midbrain dopamine release within the ventral tegmental area and the nucleus accumbens in the reward center
- Thus, opiate receptor blockade attenuates rewarding properties, resulting in decreased opioid intake over time.

- **Oral naltrexone**

- **Long-acting injectable naltrexone**

- Highly motivated patients with a mild opioid use disorder.
- Situations in which medication use can be supervised.
- For patients in occupations that do not permit opioid agonist treatment. In areas such as public safety, transport of hazardous materials, licensed drivers, and healthcare, some employees are not allowed to use methadone and, in some cases, buprenorphine.

Medication to aid with withdrawal Symptoms

- Symptomatic treatment
- Ondansetron
- Clonidine
- Neurontin
- Loperamide
- Ibuprofen / Tylenol
- Mirtazapine / Trazadone / Melatonin

Naloxone for Opioid Agonist Overdose

- Can save a life by reversing overdose
- Can be given by friend or family member
- Can be prescribed by any physician for the patient, or for the friend or family member, to have and administer as needed
- Must be carried by all first responders
- Should be in the home of all persons taking prescribed opioids, as well as abusers of opioids

Controversy and Obstacles

- Stigma
- Diversion
- Availability

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Pine Rest Addiction Services

Motivational Interviewing

...or How To Talk To Potentially Difficult Patients.....

.....and on opiates or other stuff.

AMBIVALENCE

RESISTANCE DENIAL

CHANGING BEHAVIOR

- Everyone possess the capability for meaningful and healthy change.
- Accept the patients ambivalence.
- Avoid confrontation.
- Recovering women and men deal with their personal ambivalence all the time.

Motivational Interviewing

1. Express empathy: reflective listening.
2. Develop discrepancy: compare patients goals and their present behavior
3. Avoid arguments and confrontation
4. Roll with resistance
5. Support self-efficacy and optimism.

Express Empathy

- "It sounds like you're very afraid to consider life without Oxycontin."
- "I don't expect you to change these medications without a lot of support from other modalities."
- "I realize that this is difficult and confusing because we are talking about how you see the quality of your life."

AVOID ARGUMENTS

- If you argue for change the ambivalent patient will argue against it.
- Labeling the patient as "an addict" isn't necessary to move in a positive direction.
- Avoid becoming defensive in approaching the patient.
- Meet the patient wherever they are at that moment.

Roll With Resistance

- The patient probably has a different perspective on this.
- Try to understand the patients viewpoint and go from there.
- Listen carefully and use reflective listening.

Practice Reflective Listening

- Not always easy.
- Listen carefully
- Repeat back to the patient what you think they just said or how it appears they are feeling.

Resistance

- *Simple Reflection*
- "I don't plan on giving up Xanax at this time."
- "So you don't think that going through your day without it is going to work for you."

Resistance

- *Amplified Reflection*
- "My family is really blowing this out of proportion."
- "I'm a bit confused. They were really frightened when you fell asleep at the dinner table."

Resistance

- *Double Sided Reflection*
- "I'm not going to stop taking Vicodin!"
- "You could see that it was a big problem running out 10 days early, but you are not willing to talk about a safe program to taper Vicodin."

Resistance

- *Shifting focus*
- "I really need my Oxycontin for my shoulder pain."
- "We are way ahead of ourselves here. I want to talk about this concern with your cleanliness."

Resistance

- *Agreement With a Twist*
- "Why is it you, my husband and the pharmacist are so bent out of shape over these Ativan prescriptions."

Resistance

- *Agreement With a Twist*
- "You're making an important point. Situations like this involve all kinds of people. I agree we shouldn't single anyone out for blame. Medication problems like this do involve the whole family."

Resistance

- *Reframing*
- "I'm sick of the ER doctors calling me an addict."

Resistance

- *Reframing*
- "I understand that doesn't feel good. When faced with situations like this docs and nurses get really frustrated because they're seeing a problem they can't help solve in the ER."

Resistance

- *Siding With the Negative*
- "I really have trouble with my nerves. I can't cut down on this Klonopin."

Resistance

- *Siding with the negative*
- "It sounds like what you are saying here is that these changes are just too difficult for you."

Resistance

- *Emphasizing Personal Choice*
- "Changing your relationship with these pain medications is really up to you. At the same time other people such as *your husband, your kids, me and even the pharmacist* might have to make important choices around this situation."

Ask Open Questions

- "Tell me what is happening with your family, (the police, the pharmacist,), *you* and your pain medication?"

Pros and Cons

- "Tell me about the good things that Xanax does for you."

Ask Evocative Questions

- "What is the down side of taking Dilaudid pills?"

Ask for Elaboration

- "We've talked about the constipation problems, having to go to the ER, the terrible withdrawal when you run out and having to count pills. **How is this affecting your life?"**

Imagining Extremes

- "What is the worst thing that could happen if things kind of keep going like this?"

Looking Back

- "What was life like before you had to start taking these pain pills?"

Looking Forward

- "What are your goals for your pain treatment?"
- What are some things that ***you*** can do to help meet those goals?"

Create Discrepancy

- "How are the troubles with the (pain medication, opiates, nerve pills, police, your family, your boyfriend, your doctor, the pharmacist, your boss, etc.) going to help you meet your goals?"

Affirming

- "Nobody ever plans or volunteers or signs up for trouble with these medications. This isn't anybody's fault certainly not yours. This is about the brain chemistry in ***all human beings.***!"

Affirming

- " I know it is tough to come here and talk about this. You are doing great and it really feels like you are being honest and thinking about everything that's going on."

Elicit Self-Motivating Statements

- *Showing Concern*: "It sounds like you and your family are really hurting."
- "I'm worried that you could lose your kids over this."
- "I've lost patients to overdose on these medications."
- "You don't deserve the consequences that these pills hold for people who have lost control."

Self Motivational Statements

- "I am sick of my life being run by these pills."
- "I don't want my children to be harmed by all this."
- "Something in all this has to change."
- "I really need to stop behaving this way."
- "I think with some help I can do this."
- "Tell me about getting off this stuff."

Don'ts

- Ordering and directing
- Warning and threatening
- Giving advice, forcing solutions, making strong suggestions
- Arguing, lecturing
- Moralizing, preaching
- Judging, criticizing, blaming

Don'ts

- Approving or praising bad choices
- Shaming, labeling, name calling
- Interpreting, analyzing
- Reassuring and consoling
- Probing, questioning
- Withdrawing, distracting, humoring, changing the subject

Clearly Spell Out Solutions

- Opiate withdrawal:
  - Clonidine; oral or transdermal
  - Bentyl for cramping, diarrhea
  - NSAIDs for muscle joint and "bone pain."
  - Hydroxyzine for anxiety, sleep, nausea
  - Trazodone for sleep
- Opiate withdrawal:
  - Suboxone (buprenorphine/naltrexone)

Clearly Spell Out Solutions

- Opiates staying off:
  - Suboxone
  - Naltrexone
  - Vivitrol (IM sustained release naltrexone)

Clearly Spell Out Solutions

- Benzodiazepine withdrawal:
  - Slow taper over several months
  - Gabapentin (Neurontin)
  - Valproic acid (Depakote)

Clearly Spell Out Solutions

- Treatment Centers:
  - www.findtreatment/samhsa.gov
- Finding local treatment centers for detoxification and treatment of addiction.
- Keep lists of 12 step meetings; aa.org, na.org.
- Keep lists of other docs to call for help.
- Don't do this alone.

PRACTICE !

- Use Motivational Interviewing with your patients with DM, HTN, compliance issues.

Thanks

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Thanks!

- Questions?