Physiology of Addiction

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Physiology of Addiction

Disclaimers

- Consultant, DEA/FBI/DOJ
- Consultant, BCBS
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- Methadone provider, WSU
- Medical Director, Dawn Farm

Review article

What is Addiction?

- Physiologic Dependence?
- Lack of willpower?
- An “amoral” condition?
- A brain disease?

Physiologic Dependence: Tolerance and Withdrawal

- Tolerance: requiring increasing amounts of drug to get the same effect
- Withdrawal: the opposite effect of the drug when it is removed
- NEITHER of these imply chemical dependency (addiction)

Physiologic Dependence: Tolerance and Withdrawal

- 100 people are treated with morphine for two weeks after an accident.
- Their insurance runs out, the morphine is suddenly stopped.
- 95 of them will have “the flu” (physical withdrawal) and will go on with their lives.
- 5 of them will start robbing party stores to get more morphine!!!!
- = ADDICTION

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= ADDICTION
Drug WITHDRAWAL: Gardner 2006

Drug ADDICTION: Gardner 2006

Lack of Willpower?

An “amoral” condition?

Brain disease?

Nucleus Accumbens = the Pleasure Center

- Responds to dopamine (DA)
- Part of the LIZARD BRAIN
- Responds to drugs
- Responds to food
- Responds to sex
- Sends signals to your frontal cortex
- THE PLEASURE CENTER IS ABNORMAL (DAMAGED) IN ADDICTION
Do some people develop addiction because they have “reward deficiency syndrome” (decreased dopamine) OR:

Do people with addiction have low dopamine because they have “burned out” their pleasure centers?

Abnormal response to Ritalin (methylphenidate) is due to abnormal brain chemistry.
Those who “enjoyed” methylphenidate (amphetamine) had LOWER levels of dopamine.
Those who found it “unpleasant” had NORMAL levels of dopamine

Conclusion?
- Addiction is an abnormal response to reward

Women who have an abnormal receptor (brain protein) for dopamine had brain scans
Those who had the abnormal receptor enjoyed a milkshake LESS

Were more likely to gain weight!

Conclusion?
- Addiction is an DECREASED response to NORMAL reward
- If you don’t like something as much, you need to compensate!
“I feel like I don’t belong in my own skin....”

- Decreased Dopamine receptors
  = decreased Dopamine =
- **Decreased Hedonic Tone**

- Salsitz 2006

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**Decreased “hedonic tone”**

- Alcoholics/addicts who finish treatment will often relapse when they re-enter society.
- They will almost ALWAYS relapse if they undergo quick detox and re-enter society.
- But: their withdrawal is gone.
- SO: why do they relapse?????

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**Stimulants & Blood Flow**

- Healthy Control
- Cocaine-dependent

Gottschalk, 2001, Am J Psychiatry

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**Blood Flow Recovery**

- Non users
- Cocaine users, 10 days sober
- Cocaine Users, 100 days sober

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**Can you find the (alleged) future alcoholic?**
Physiology of Addiction

Non users

Cocaine users, 10 days sober

Cocaine Users, 100 days sober

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Tolerance

Withdrawal

Take more/take longer than intended

Can’t cut down or control use

Great deal of time spent in obtaining/using/recovering

Important activities given up 2º to use

Use despite physical/psych problem

A chronic progressive disease characterized by the following physical and psychological symptoms (the four (five) C’s):

Craving

Compulsion

Loss of Control

Continued use despite consequences, and

Chronic use
Chemical Dependence

Behavioral Dependence

Obese subjects have decreased DA: just like methamphetamine addicts!!!

“Hi...I’m Joe. I’m cross addicted”
### Addiction Transfer

- People who recover from alcoholism may:
  - Gain weight
  - Increase their smoking
  - Start gambling
  - Become involved in sexual addiction, internet addiction

- People who undergo **gastric bypass surgery** may:
  - Become alcoholics
  - Develop chronic pain → opiate dependence
  - Gain weight!

### Abuse vs. dependence

- You are worried about your best friend.
- She has a 20 year history of heavy drinking and has just been diagnosed with hypertension and hyperlipidemia (high cholesterol).
- You advise her to quit.

- You went to the Dawn Farm lecture on addiction and you know it is a "disease".
- To your surprise, she does so, without any treatment.
- You vow never to waste your time going to any more Dawn Farm lectures.
- *How did she do it?????*

### Is it abuse...or is it dependence?

- Failure to fulfill work/school/social obligations
- Continued use is risky situations (ie, drunk driving)
- Recurrent legal problems (DUI)*
- Continued use despite social or interpersonal problems (MOR)
- Never fit the criteria for dependence

- The majority of patients you see with drug/alcohol problems do NOT have addiction
- Most people with drug/alcohol problems will be able to stop on their own. (William White)
- The 4Cs helps you to determine which ones have addiction!
Most people who have a problem with alcohol or drugs will stop on their own.
The majority of people who stop do so without treatment.
Even many heroin “addicts” will “quit” and resume normal lives.

“Abuse is a BEHAVIOR....
Addiction is a DISEASE!!”

Mark Minestrina, MD
Brighton Hospital

“anyone can quit drinking......”

“Just walk up and hit a cop!”

Herb Malinoff, MD
RELAPSE: the problem with addiction

- **Drug** triggered: “I thought I could (eat/smoke/drink) just one...”
- **Stress** triggered: “I’m going through too much right now. Gimme that!”
- **Cue** triggered: “Wet faces and wet places”

**Drug Triggered Relapse: Gardner 2006**

**Stress Triggered Relapse: Gardner 2006**

**Cue Triggered Relapse: Gardner 2006**

Which of these cues do you respond to?
Hypertension: the most common cause of “essential” (unexplained) hypertension is alcohol.
Diabetes: damage to the pancreas (temporary or permanent)
Cholesterol: LDL (bad cholesterol) goes up, triglycerides (fat) goes up.

Fatty liver: from drinking; body uses alcohol rather than fat. Fat accumulates.
Alcoholic Hepatitis: inflammation of the liver; fever, jaundice, pain, nausea and vomiting.
Viral Hepatitis: usually hepatitis C, from sharing needles, straws (cocaine), sex.
Cirrhosis: scarring of the liver

Your friend is an alcoholic. His family left him. When you see him today, he denies that he has a problem, but says that he needs to “take a break”. His wife left him, he says, because of his mother in law.
As you discuss his situation, you are amazed by his ability to:
- Minimalize
- Rationalize
- Deny
- Deflect

Recovering addicts make bad decisions
Ex: 3 weeks into recovery, a man decides to make a trip to Amsterdam?
Q: what does an alcoholic bring on a 2nd date?
A: a U haul.
**Cognition and Addiction**

**Reward pathway in alcoholism & more....**

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**Consequences: brain**
- You are asked to see him in the hospital several years later.
- He says he knows you, but cannot remember your name. You become alarmed.
- You ask him who the president is, he replies “Who cares? They’re all crooks.”
- He walks with a shuffling broad-based gait and has to hold his hand on the wall to keep his balance.

**Wernike-Korsakoff Syndrome**
- Immediately after stopping drinking: 
  - Wernike’s encephalopathy (brain disease)
- Caused by thiamine (B1) deficiency
  - Eye muscles are paralyzed
  - Ataxia (can’t walk straight)
  - Encephalopathy: confusion, agitation, restlessness

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**Korsakoff’s psychosis**
- Confabulation: make things up
- Retrograde amnesia: can’t remember what happened in the past
- Antegrade amnesia: can’t remember info you are given (remember these 3 objects...)
- Polyneuropathy: peripheral nerve damage

**Consequences: liver**
- You see him one more time, several years later. He has been readmitted for vomiting blood, jaundice, and encephalopathy.
  - He is given multiple transfusions. He has esophageal varices from his cirrhosis.
  - He is jaundiced. He says that he is asking his sister to pay for a liver transplant. She died 5 years ago....
  - When he is speaking to him, his hands will occasionally flap.
Alcoholic Cirrhosis

- Hardening of the liver (scar tissue)
- Causes blood to back up in the veins feeding the liver:
  - Esophageal varices: vomit blood
  - Hemorrhoids: rectal bleeding
- Can’t metabolize toxins: encephalopathy
- Can’t make proteins:
  - bleeding (coagulopathy)
  - Can’t hold fluids: ascites

Cirrhosis

- He dies several weeks later of liver failure.
- “Jails, institutions, and death”
  - Narcotics Anonymous

Ascites/Jaundice

“Caput Medusae”
“We have driven miles in the dead of night to satisfy a craving for food. We have eaten food that was frozen, burnt, stale, or even dangerously spoiled. We have eaten food off of other people’s plates, off the floor, off the ground. We have dug food out of the garbage and eaten it.”
THE SOLUTION?

TREATMENT OF ADDICTION

- Medical
- Behavioral
- Spiritual
- Surgical

TREATMENT OF ADDICTION: Medical

- Agonists: similar to the “drug”
  - Suboxone for opiate dependence
  - Methadone for opiate dependence
  - Nicotine patches for tobacco dependence
  - THC for marijuana dependence
  - Dilaudid for heroin dependence! (Canada)

- Antagonists: opposite effect of the drug
  - Naltrexone for opiate dependence
    - Oral: Rivea
    - Injectable: Vivitrol
  - Naltrexone for alcohol dependence: Vivitrol
  - Disulfiram (Antabuse) for alcohol dependence
  - Rimonabant for obesity

BOTTOM LINE:

- In both controlled and retrospective studies, the success rate for most medications is between 40 and 60% (one to two years).
- When patients come off the medication, they relapse.
- Relapse may be associated with an increased chance of overdose and death.

- Why would you expect otherwise?
Doc, when can I get off this sh*t (medication)?

Detoxing During Pregnancy? Luty 2003
- 101 women underwent detox during pregnancy
- 40 successfully detoxed.
- No adverse fetal effects documented
  - Luty et al, J Sub Abuse Treat 24 (2003); 363 - 367

Detoxing During Pregnancy? Luty 2003
- "Nevertheless, very few women who successfully completed detoxification remained abstinent through to delivery"
  - Luty et al, J Sub Abuse Treat 24 (2003); 363 - 367

Maintenance vs. Detox?
- 40 heroin addicts were started on Suboxone.
- 20 were "detoxed" off and offered counseling.
- 20 were kept on Suboxone and offered counseling.
- A year later.

Medical Withdrawal vs. Maintenance
- N=20
- Both groups received counseling
- High mortality rate in detox group (20%, n=4)

Lakkie et al., Lancer; 361:662-665, Feb 22 2003
Medical Withdrawal vs Maintenance

- N=20
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ORT: yes or no???

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Short term and long term treatment with buprenorphine in prescription opioid dependent patients

**Online First**

Adjunctive Counseling During Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence

A 2-Phase Randomized Controlled Trial

- Roger D. Nelson, MD, Jennifer Sharp Peters, PhD, David A. Conover, MD, Marilyn Byrne, MSc
- Milan S. Grombeck, MD, MPH (Chair), L. Hall, MD, M. H. Smith, MD, D. N. Chang, MD, J. M. Jacobs, MD
- Jeffrey S. Sturmer, PhD, Robert Corwin, MD, MPH, Halpern C. Fein, MD, Scott D. Provenzano, MPH
- Jeffrey W. Stein, MD, Eugene S. Sommerville, MD, P. J. B. Standen, MD, F. M. Devries, MD, P. F. McGonigle, MD

ORT: yes or no???

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**Phase 1**

- 654 pts → 2 weeks BUP → Taper 3 to 4 weeks → f/u 5 to 12 weeks

ORT: yes or no???

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**Outcome Phase 1**

- Only 43 of 653 patients remained abstinent (6.6%)
- All other relapsed!!
- Next step: Phase 2

ORT: yes or no???

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**Phase 2**

- 360 pts → 12 weeks BUP → Taper 3 to 2 weeks → f/u 5 to 12 weeks

ORT: yes or no???

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**Outcomes Phase 2**

- 49% stayed abstinent when they went back on buprenorphine!
- But when they were taken off buprenorphine again, only 8.6% remained abstinent!
Ball 1988: reduction in IVDU

Ultra Rapid Detox?

Vivitrol® (injectable naltrexone) for opioid dependence

Vivitrol: abstinence

Vivitrol: craving
As with methadone and buprenorphine, when the medication is stopped, relapse may lead to death due to lack of tolerance. It is difficult to treat acute pain while on Vivitrol.

Do You HAVE to Use Meds?
- Docs, Nurses & Pharmacists: HPRP
- Lawyers & Judges: LJAP
- Pilots: HIMS

Continuous monitoring
Treatment / 12 step
Rapid consequences
Graded response

CBT Iceberg Model
- Behavior (drinking) is due to false beliefs (I can’t stop)
- Change the false beliefs, change the behavior.
- Apologies to therapists everywhere......
**Physiology of Addiction**

**Twelve Step Programs**

- **AA involvement in Veterans 1987, 1988**

  Alcohol abstinence & AA/12-step group exposure

  - AA
  - 12-step
  - no AA

  % abstinent

  - at 1 yr.
  - at 18 mos.

**Abstinence by treatment group: Project MATCH**

- **“Dose Response Curve”**

  Alcohol and drug abstinence & number of 12-step meetings

  - % abstinent, % relapse

  - # of meetings mos. 5-12

**Treatment of Addiction: Surgical**

- Gastric Bypass for eating disorders
- Liver transplant for cirrhosis
  - ETOH and Hepatitis C: most common indication
- Brain surgery for addiction?
  - Destroy the nucleus accumbens (China, Russia)
  - Accidental injury to the insula: quit smoking!

**Why Bother to Treat Addiction?**

- May 19, 2015
**Why Treat Addiction?**

**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.  

- Only about 40% of patients will be abstinent at one year after treatment.  
- Failure rates may be due to lack of aftercare, often due to insurance difficulties  
- Low economic status, psych comorbidity and lack of family/social supports also predict relapse.  
- Relapse is often viewed as “inevitable” and drug dependence as “hopeless”*

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**Addiction: a chronic illness**

- If you were to stop taking your insulin, and you wound up in a coma in the ICU, your doctor would say:  
  - “you need to go back on insulin! You could have died!”  
- If you were to stop your Suboxone/methadone/12 step treatment, and wind up in the ICU, your doctor would say:  
  - “You’re an addict. You’re hopeless!!!!!!!”

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**Benefits of Opioid Maintenance Therapy (OMT)**

- Decreased HIV infection rates  
- Decreased incarceration  
- Decreased drug use  
- Decreased mortality

- McLellan, 2000

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**Drug Dependence, a Chronic Medical Illness: McLellan 2000**

- Decreased HIV infection rates  
- Decreased incarceration  
- Decreased drug use  
- Decreased mortality

- “There is little evidence of effectiveness from detoxification or short-term stabilization alone without maintenance or monitoring such as in (opioid) maintenance or AA.”
Chronic, Treatable but Incurable Diseases

- Obesity
- Hypertension
- Diabetes
- Asthma
- Addiction

Which one is an addict?

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