Neurobiology of Addiction

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What is an Elephant?
What is Addiction?

• Psychological – Learned behaviors
• Genetic – Driven behaviors
• Spiritual – Seeking behaviors
• Social – Compensatory behaviors
• DSM – set of behaviors – no “why” involved
• The model matters if you want to predict what the elephant is going to do
What is Addiction?

• Addiction is either a disease or it isn’t
• If it isn’t, it doesn’t have a neurobiology, so who cares?
• But what’s a disease?
Disease

• a disorder of structure or function of an organ or system and is not simply a direct result of physical injury
  – Dictionary.com

• Time for a parenthesis
The Brain is Complicated

• There’s a whole bunch of ways I could complicate this
Neurobiology of Alcohol Addiction

Neurobiology of Food Addiction

http://thepaleodiet.com/reality-of-food-addiction/
Neurobiology of Cocaine Addiction

https://en.wikipedia.org/wiki/Addiction
Why are All These So Complicated?

- Each one is a detailed explanation of why a single drug or reward type causes addiction
- An explanation of how each drug damages the normal functioning of the brain
- Each one is an explanation of the injury
- Remember the definition
Disease

• A disorder of structure or function of an organ or system and is not simply a direct result of physical injury

• End of Parenthesis
Why are They All So Complicated?

• These are long drawn out explanations of why each of these drugs causes injury to the brain turning on genetic pathways that cause the symptoms we see in addiction

• But none of them explain why these drugs don’t do this in most people

• They don’t explain what got people started in the first place

• They don’t explain how people get well
The Big Short

• “Mortgage backed securities, subprime loans, tranches...It’s kind of confusing right? Does it make you feel bored or stupid? Well, it’s supposed to. Wall Street loves to use confusing terms to make you think that only they can do what they do or, even better, for you to leave them the _____ alone.”
But I’m Not Here to Impress You

• You don’t want to be impressed
• You want to learn something you can use in your practice or your program
• You want to learn something simple and useful
• You want to learn something so straightforward that it makes sense the first time you hear it
Questions

• And the reason why you want to learn that is because there are things about addiction that don’t make sense.
• Like why do some people get in recovery from one drug and pick up another?
• Why do some people get sober without medications and others can’t?
• Why do some people like cocaine and others don’t?
• Why don’t we all agree if addiction is one disease or not?
• Why do old timers relapse?
• And many others
Promise

• I’ll make you a promise
• If my the end of this talk you can think of a question that I haven’t answered you can call me up and I’ll spend as much time with you as you want to get it answered.
Shorthand and Cartoons

• We can make this really simple
• Will it be exactly right? Probably not, but even if we tried to get every detail right a lot would change with more research in the coming years
• We are aiming for a working and workable model that helps in your daily efforts
Dr Silkworth and the Big Book

• The single best biological description of the illness of addiction and he didn’t know any of what we’ll talk about today

• Two points
  – Can’t stop once started – “Allergy of the body”
  – Can’t stay stopped – “Obsession of the mind” - Restless, Irritable, Discontented
Silkworth - Allergy

• Allergy - “We believe, and so suggested a few years ago, that the action of alcohol on these chronic alcoholics is a manifestation of an allergy; that the phenomenon of craving is limited to this class and never occurs in the average temperate drinker.”

• Alcoholics Anonymous page XXVIII
Silkworth – Base State

• Base State - “They are restless, irritable, and discontented, unless they can again experience the sense of ease and comfort which comes at once by taking a few drinks – drinks which they see others taking with impunity.”

  • Alcoholics Anonymous page XXVIII
What Silkworth Didn’t Know

- Dopamine Spike
- Positive Feedback Loop
- Dopamine Tone
Feedback Loop
The Spike

- Reward Line
- Normal Dopamine Tone
Dopamine Spike

- When dopamine spikes it crashes
- No crash, no craving
- No spike, no crash
- So it is the positive feedback loop and the spike that causes the inability to stop once started – Silkworth’s allergy
What is Dopamine Tone

• NA

Dopamine Tone is produced here

VTA
What is Dopamine Tone

• Product of three things:
  – Amount of dopamine released
  – Function and number of dopamine receptors
  – Length of time the dopamine is at the receptors

• Different from the dopamine level

• Enough dopamine tone and we can pay attention, feel reward, enjoy small rewards, attach to others, remember things

• Decreased dopamine tone has symptoms
Low Dopamine Tone

• Don’t have enough of anything and don’t enjoy things as much as others seem to
• Can’t feel reward or motivation
• Nothing is really fulfilling
• Constantly looking around for something that is
• Frustrated that nothing makes me feel better for long
• Just not happy with what’s going on
• In short:
• Restless
• Irritable
• Discontented
Tone and Spike

• We understand low dopamine tone as Silkworth’s baseline state
• And we understand the spike to be behind the allergy
• But why call it addiction?
Why Call it Addiction?

• You can thank Shakespeare who coined the term in Othello: “... some to dance, some to make bonfires, each man to what sport and revels his addiction leads him.” But where did he get it?

• **Addicere** (Ad = together; dicere = to declare) Roman legal term, a sentence passed on a person who owed someone else money

• It **attached** the debtor to the lender **against his will** – debt slavery
So Addiction is Attachment

- That is important because attachment is not a psychological process but a biological one.
- Oxytocin input to the midbrain dopamine spike is necessary for attachment.
- The resulting dopamine spike is necessary for setting what to attach to.
- Biological beyond our will.

So Consider…

• A person with low midbrain dopamine tone
• Nothing much is causing attachment because nothing is causing dopamine to get up to the reward line
• Along comes (fill in the blank) and it works
• Nothing much else does, so you can see how life constricts to the “important” things
• What sort of things can quickly raise DA tone?
Attachment From the Spike

- Dangerous or risky behavior
- Staying up late or sleeping in
- Being the center of attention
- Being liked
- Making someone smile
- Completion of a hard task
- Sexual climax
- Taking in food

Cue Induced Craving

- This brings us to another phenomenon we have to explain
- Cue induced craving, otherwise known as euphoric recall
Cue Induced Craving
You Don’t Even Have to Notice

- 22 people with addiction involving cocaine
- Given different types of visual stimuli, some neutral, some drug related, some aversive
- Some drug related were shown for 33 msec
- Showed up on fMRI scanning and predicted craving from the “unseen” stimuli

So This Isn’t Euphoric Recall

• It’s euphoria
• It’s a real spike and a real crash and, as before, the crash leads to craving
• There’s also a smaller version of this called the anticipatory spike
Anticipatory Spike

- Smaller spike caused, not by seeing the drug itself, but by being otherwise reminded
- Get’s dopamine going so that we’ll get up and go
- Less chance that the crash will cross the line to cause irresistible craving but it’s still a chance
- An Example
Experience the Spike
And Yet Another Phenomenon

• Reward Overvaluation
Reward Overvaluation

- Groceries across the street
- Caused by low DA tone and the memory of a reward that raises DA
- The salience of pre-recorded rewards increases
- Gain vs risk
- The more exposed we are the greater the sensitivity of the system so we can react faster
Now Let’s Look at Types

• Cloninger’s system for types of alcoholism
Type I and Type II “Alcoholism”

- **Cloninger** – Interests in psychiatry and genetics – has done a lot more than this, but this is why his name is known in our field
- **Type I** – not linked to family history, don’t like stimulants, follow rules, start late
- **Type II** – strong family history, likes stimulants, don’t follow rules, starts early
- Believed type I is more common.
Not What I See

• Of the people I’ve met who came to addiction treatment:
  – 80% were type II
• While all of them had decreased dopamine tone, not all had decreased dopamine levels
• We have to look at the receptors as well
Stress and Dopamine Receptors

Socially Housed

Housed in Isolation

Socially Housed

Coincidentally, what do you get from an AA meeting?

Social Dominance in Monkeys: Dopamine Receptors and Cocaine Self-Administration Morgan et al, Nature Neuroscience 2002
So Far

- Decreased Dopamine Tone = Restless, Irritable, Discontented
- Dopamine Spike leads to crash and craving
- The spike makes us attach to the source of the spike and limit our world
- Cue Induced Craving
- Reward Overvaluation
- Type I and Type II addiction
- The stress of being isolated or less than
Implications for Treatment

• Dopamine Tone
  – What drives most AMA discharges?
  – “He’s not ready”
  – “He doesn’t want sobriety bad enough”
• We’d love this to be a cortical thinking disease so we could talk people out of it, but it’s not.
• Who gets better without meds?
What’s Treatment - Medical

The medical goal is to normalize hedonic function and suppress symptoms enough so that the patient can hear the message of the non-pharmacologic part of treatment.
Getting Better Without Meds

• Find another “non-drug” to raise dopamine release
• Increase dopamine receptors
“Non-Drugs”

• “One of the many doctors who had the opportunity of reading this book in manuscript form told us that the use of sweets was often helpful, of course depending upon a doctor’s advice. He thought all alcoholics should constantly have chocolate available for the quick energy value at times of fatigue.”

• Alcoholics Anonymous page 133-134
What Does It Profit?

• The average adolescent entering addiction treatment gains 11 pounds in just the first 60 days
• There are different health effects but health effects none the less
• But really, this switching of drugs to lower risk drugs with smaller health effects is good harm reduction isn’t it?

And it Gets Worse

• Continuing to smoke after treatment for addiction increases the likelihood of return to use of the substance addressed in treatment
• Makes sense when you realize that you’re spiking dopamine and causing crashes multiple times a day

But, The Disease Progresses

- The man of thirty from the Big Book
- Did he really start off from where he stopped?
- Was he really 4 years from death at 30?
Losing Dopamine Production

Dopamine Transporters, a proxy for VTA cells

Losing Dopamine Reception

Volkow, et al. Decreased dopamine D2 receptor availability is associated with reduced frontal metabolism in cocaine abusers. Synapse 14:169-177, 1993
Addiction Risk Goes Up as We Age

• Why do old-timers go back out?
• Do they have permission to ask for help from an addiction medicine specialist?
Summary I

• Decreased Dopamine Tone = Restless, Irritable, Discontented
• Dopamine Spike leads to crash and craving
• The spike makes us attach and limit our world
• Cue Induced Craving
• Reward Overvaluation
• Type I and Type II addiction
• The stress of being isolated or less than
Summary II

• Low DA tone can be treated medically to aid in the patient’s ability to profit from psychosocial treatment
• Addiction is a single illness regardless of drug or behavior and must be addressed as such
• It’s chronic and progressive, so short solutions don’t do much for survival
End With the Why

• Why do I do this?
• Why do you?
The Point

• 10-20% of Americans have addiction
• Less than 16% ever get treatment
• Of those who try but don’t finish treatment, only 50% ever try again – the bottom is a myth
• The biggest losses in treatment is in the first 2 weeks
• What are you willing to do to deal with a 50% death rate?