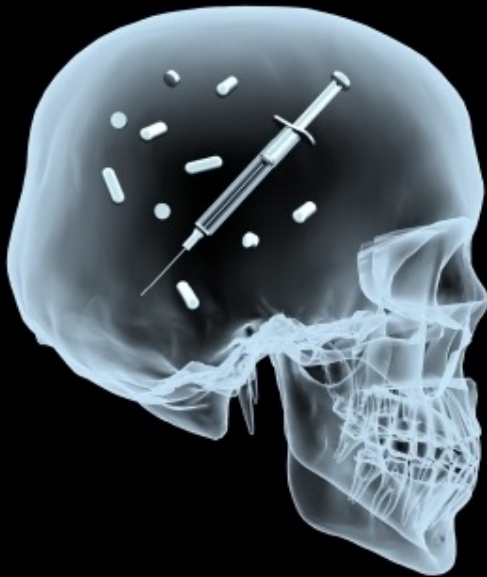


ADDICTION

PHENOMENOLOGY

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FINANCIAL DISCLOSURES

- None

ASAM

- American Society of Addiction Medicine

HEART DISEASE? DIABETES?

- Real diseases?
- Do they have weak willpower?
- Does anyone choose to have heart disease or diabetes?



WHAT CAUSES HEART DISEASE AND DIABETES?

- Genetics
- Diet
- Exercise
- Smoking
- Pathologic physiological changes



HOW WOULD YOU TREAT CAD OR DM?

WHAT CAUSES ADDICTION?

- Genetics 50%
- Exposure to substances
- Environment
- Pathologic physiological changes



DO PEOPLE HAVE THE ABILITY TO CHOOSE FREELY OR WISELY?

- At first usually yes, after pathology has set in and progresses, not as likely



WHY DO PEOPLE MAKE THESE CHOICES?

- Diet – pleasure, stress, socioeconomic status, environment
 - Exercise ?
 - Smoking?
 - Exposure to substances?
-

ADDICTION VS. PSYCHOSES

- Paranoia, AVTH, and choice?
- Addiction and choice?

WILLPOWER

- Do people who suffer from mental illness have weak willpower?
- Why do psychotic, depressed, or anxious people make different choices than non-afflicted individuals?
- Does severity of neurobiological changes correlate with ability to make choices freely or wisely?



ARE PEOPLE BORN ADDICTS OR BECOME
ADDICTS?

DID NEURAL CIRCUIT CHANGES AFFECT HIS ABILITY TO MAKE CHOICES?



STEPS OF HEART DISEASE, DIABETES, AND ADDICTION

- CAD – arterial plaque – thrombus - death
- DM – impaired insulin sensitivity – end organ damage - death
- Addiction – neural circuit changes – cognitive impairment – relapse - death

ADDICTION & RISKY SUBSTANCE USE

- Largest and most costly preventable health problem in US
- Cause and contribute to more than 70 medical conditions
- Account for nearly 1/3 hospital inpatient costs
- Account for 20% of deaths in US
- Nearly 1/3 US engages in risky use of addictive substances
- 16% US meet criteria for addiction (less than heart disease, diabetes, or cancer)

DESPITE THESE FACTS

- “Addiction remains the only disease for which available and effective preventative interventions are not routinely provided within the health care system.”

ORIGINS OF ADDICTION

- 9 out of 10 with addiction smoked, drank, or used other drugs before they turned 18
- The earlier substance use starts the greater the risk for developing addiction
- Average high school age to use addictive substances is 13-14 years old
- Critical period physiologically and socially to develop addiction is adolescence
- $\frac{3}{4}$ high school students have used
- $\frac{1}{2}$ high school students current users
- $\frac{1}{8}$ high school students meet criteria for addiction

IS ADDICTION A DISEASE?



ADDICTION HISTORICALLY

- Addressed at late stage
- Patient health and well being already severely impacted
- Perceived as a moral or social problem (by public and medical community)
- Not seen as a treatable and preventable health condition

ADDICTION VS. RISKY SUBSTANCE USE

- Both cause and contribute to numerous health problems
- Different conditions
- Require different approaches to be effectively addressed
- Not varying intensities of the same condition
- Addiction is a disease
- Risky use of substances is a public health problem

ADDICTION VS. RISKY SUBSTANCE USE

- Risky substance use has potential to progress to addiction
- Most engaging in risky addictive substance use do not develop addiction
- Combining and confusing the two has impaired appropriate treatment interventions

WHAT IS ADDICTION?

- Addiction to substances can be conceptualized as a reward deficit disorder
- Characterized by a transition from controlled to impulsive and compulsive drug intake
- Negative reinforcement (behavioral mechanism recruited to alleviate negative emotional state in absence of drug) becomes main driver after compulsive drug use begins
- Compulsive drug intake despite adverse consequences appear to rely on neuroadaptations in brain reward and stress systems

WHY ADDICTION IS A DISEASE

- Chronic drug abuse affects the brain leading to behavioral disruptions that characterize addicted individuals
- Addictive substances induce long lasting changes in many neuronal circuits affecting:
 - ✓ Processing response to rewarding/aversive stimuli
 - ✓ Interoception
 - ✓ Emotions
 - ✓ Decision making
 - ✓ Cognitive control
- Drug use turns into automatic compulsive behavior
- Addiction is a chronic and relapsing disease of the brain

NEUROBIOLOGY OF ADDICTION

- Many neurotransmitters have been implicated
- Dopamine has consistently been associated with reinforcing effects
- Addictive substances increase extracellular dopamine in limbic brain areas including the nucleus accumbens
- Drugs of abuse surpass dopamine release initiated by natural reinforcers such as food or sex

NEUROBIOLOGY OF ADDICTION

- Abnormally high or protracted elevation of dopamine mediated activity in cortical and subcortical brain structures are translated into corrupted messages involving:
 - ✓ Reward prediction
 - ✓ Stimulus response
 - ✓ Approach behavior
 - ✓ Learning
 - ✓ Decision making

NEUROBIOLOGY OF ADDICTION

- Supraphysiologic dopamine stimulation effects become more pronounced, widespread, and long lasting as substance use becomes chronic
- Addicted individuals shows lower levels of D2 receptors in striatum (including NAc)
- This results in lower baseline activity in frontal brain regions implicated in salience attribution (OFC) and inhibitory control (ACG)
- These disruptions lead to compulsivity and impulsivity

NEUROADAPTATIONS OF ADDICTION

- Decreases in dopamine and GABA in the ventral striatum
- Enhancement of corticotropin releasing factor in extended amygdala
- Blunting of hypothalamic pituitary adrenal axis
- Evidence of antireward system in habenula activated by aversive stimuli or when expected rewards do not materialize inhibiting DA cell firing
- Habenula activity increases with repeated drug exposures that may underlie negative mood linked with drug withdrawal
- Upregulation of dynorphin signaling through kappa receptors implicated in increased sensitivity to stress associated with chronic drug exposures

PFC

- Compulsive drug consumption involves poor inhibitory control and executive functioning mediated by prefrontal cortical brain regions
- Alcohol selectively damages PFC regions resulting in poor decision making perpetuating the addiction cycle
- Damaged PFC result in perturbed regulation of limbic reward regions and impairment of its involvement in higher order executive function
- Abnormalities in these frontal regions could underlie both the compulsive nature of drug administration of addicts and their inability to control urges to take the drug when exposed to it
- PFC damage also is likely to contribute to impaired judgment and cognitive deficits seen in addicts

WHAT IS THE MECHANISM OF ADDICTIVE DISEASE?

- Drugs alter expression of specific transcription factors and wide variety of proteins involved in neurotransmission in several key brain regions
- Epigenetic mechanisms mediate drug induced changes in pattern of gene expression leading to long lasting changes in structural, synaptic, and behavioral plasticity in the brain
- Addiction related adaptations for dopamine, glutamate, GABA, opiates, cannabinoids, serotonin, and various neuropeptides reported to contribute to abnormal function of brain circuits
- Imaging studies show how cocaine addiction reduces striatal D2 receptors causing reduced OFC and anterior cingulate gyrus baseline activity impairing salience attribution and inhibitory control

VULNERABILITY

- 40% to 60% of vulnerability to addiction attributable to genetic factors
- Genetic variants that metabolize substances leading to higher levels of aversive metabolites can serve as a negative stimulus for continued drug consumption
- Environments increasing addiction risk include low socioeconomic status, poor parental support, within-peer group deviancy, physical/psychological abuse, drug availability

VULNERABILITY

- Stress is a common feature in wide variety of environments increasing drug abuse risk
- Social isolation during critical adolescent period (increasing anxiety) increases risk
- Animal studies show environments that increase D2 receptors in nucleus accumbens decrease drug consumption

COMORBIDITY WITH MENTAL ILLNESS

- Significantly higher risk of substance use and mental illness due than general population due to overlapping environmental, genetic, neurobiologic factors
- 30% of people with psychiatric disorders exhibit substance abuse
 - 25% alcohol
 - 40% nicotine
 - 15% other drugs

ARE WE BEING SMART ABOUT OUR POLICIES?
...SANE?

ABSTINENCE?

- Strang et al. (2003) study with 137 patients following 28 day inpatient detox/rehab that those “who “successfully” completed detoxification were more likely than other patients to have died within a year. No patients who failed to complete detoxification died.”
- Binswanger et al. (2007) found inmates after first two weeks from prison were 129 times more likely to die from drug poisoning than the general public.

ABSTINENCE?

- Abstinence programs for opioid addiction can be more harmful and more likely lead to death of the patient
- Isn't this common sense?
- What can we do in the meantime until treatment progresses?
- EVZIO

EVZIO



WHAT DID FRANCE DO?

- Treatment with buprenorphine has shown to be effective and safe for opioid dependent addictive disease.
- In France general practitioners prescribe suboxone as this country has tried to curtail their population's use of heroin. From 1994 to 2002 they were able to reduce the number of heroin overdoses by four fifths.
- Due to the addition of naloxone in the suboxone product IV use is not as likely. France was able to reduce the incidence of HIV in IV drug users from 25% in the mid 90's to 6% by 2010 (Bourkaib).
- Despite that this treatment has been proven effective and safe some people (including physicians), see buprenorphine treatment in a bad light with the most common argument being "you are just replacing one addiction or drug with another"

WHAT CAN WE DO TO TREAT ADDICTION?



MAT?

TREATMENT

- Chronic exposure to substances induces long lasting brain adaptations
- Addiction must be viewed as a chronic disease
- Long term treatment required for addiction in most cases just like HTN, CAD, DM
- Chronic management model necessary to help prevent likelihood of relapse
- Multiple brain area involvement associated with behavioral disruptions indicate need for multimodal approach
- Inhibiting rewarding effects of a drug alone not sufficient
- Enhance saliency of natural rein forcers such as social support

TREATMENT

- Strengthen executive function improving inhibitory control and decision making
- Decrease drug related conditioned responses
- Improve mood disruptions
- Decrease stress sensitivity
- Incorporation of pharmacologic and behavioral interventions thought to work through different mechanisms producing additive or synergistic effects
- Treat comorbid conditions (medical conditions can contribute to substance use and vice versa)

TREATMENT

- Addiction isolates people from family and community
- Family and community integral to effective treatment
- Stigma reduction necessary
- Reconsideration of social policy
- Impact of criminal justice system
 - Unemployment
 - Poverty
 - Family/social dysfunction
 - Chronic adverse circumstances

TREATMENT

- Recognition of addiction as a disease of the brain
- Involvement of medical community
 - Screening
 - Early detection
 - Pediatricians
 - Family physicians
 - Teaching addiction in medical school
 - Physician training on addiction management
- Pharmaceutical industry involvement
- Research

CRITICS OF MEDICAL MODEL OF ADDICTION

- Argue medical model removes responsibility of addicted individual from their behavior
- Value of medical model not in misguided use as public policy to excuse maladaptive behavior
- Rather it should be used to better understand and more effectively treat addiction

STIGMA

- Pregnant patient makes her first appointment with OB
- Patient in serious MVA breaks several bones, dislocates hip
- Patient goes to ER with kidney stones crying due to pain
- Patient goes to pharmacy to pick up their medications gets interrogated about their disease
- Patient gets multiple rejections looking for a Psychiatrist, he has been looking for over 6 months now
- Patient goes to ER with specific complaint, proper workup not done believing they are med seeking when patient reveals they take suboxone.
- Pharmacy requests patient to be on a taper schedule for suboxone interfering with treatment and increasing risk for relapse if patient follows a pre-planned taper

STIGMA

- Stigma will only stop with better education, starting with the medical community.
- Can you imagine being humiliated, mistreated, marginalized, or refused to be treated at all while having a deadly disease?



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THANK YOU