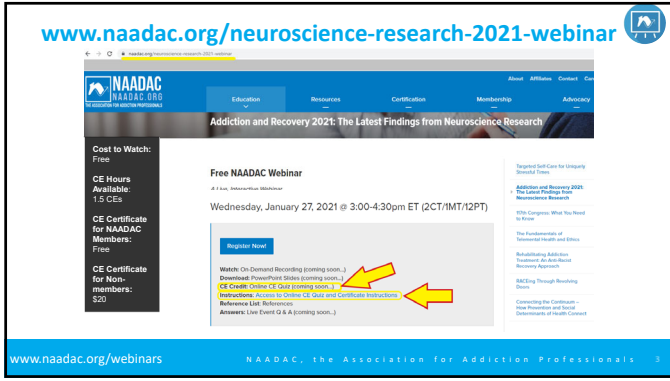


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3

- Kevin McCauley declares no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.
- The interventions mentioned in this program are for educational purposes and should not be interpreted as medical advice. While application of these interventions is discussed, other factors could contribute to the outcomes when applied in clinical practice.

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7

“Disease Model” lecture: things that have to get done

- relapse prevention
- cross-addiction
- unconscious nature of triggers
- “powerlessness” & “unmanageability” and the Frontal Cortex
- AA as a social-spiritual method of stress management
- importance of trauma work (when appropriate)
- genetic determinism problem
- importance of peer support for brain healing and maintenance
- introduction to recovery management concepts

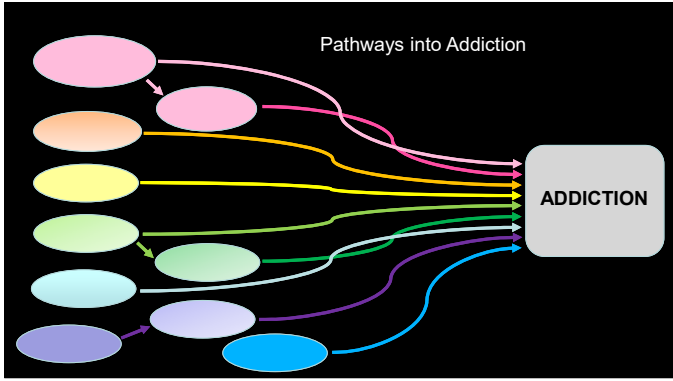
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“Disease Model” lecture: things that have to get done

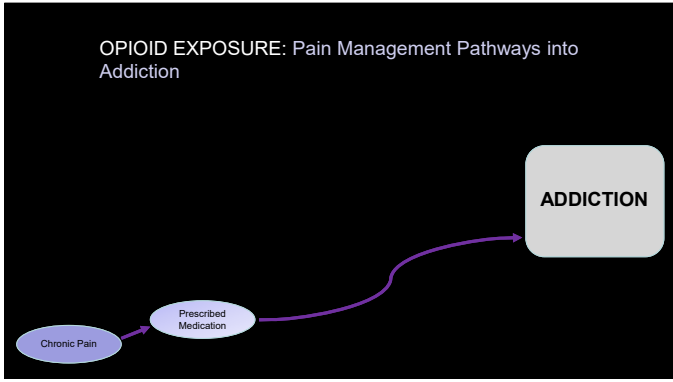
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the therapeutic “turn”
 “I can’t do this alone;
 I’m going to need some
 help”

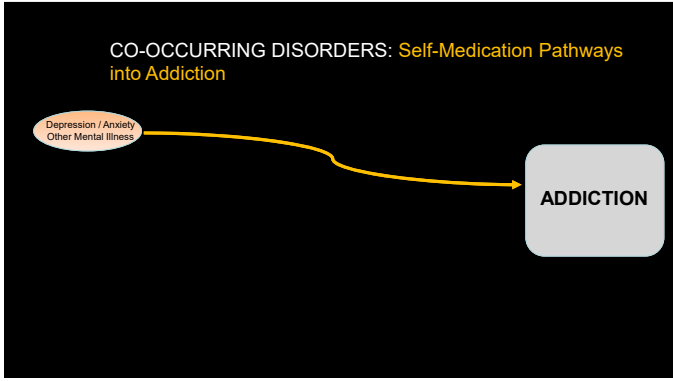
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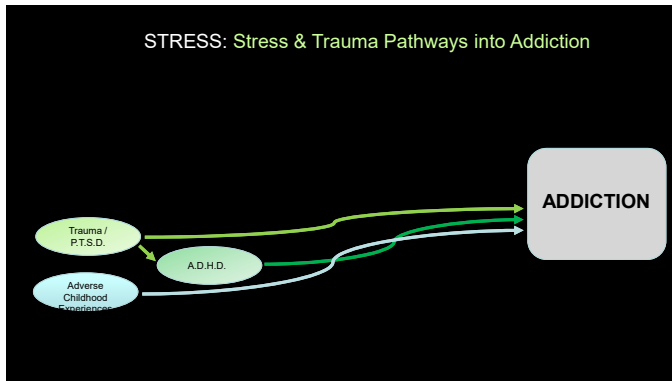
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11



12



13

ASAM Addiction Definition (2011)

Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry characterized by

1. inability to consistently abstain
2. impairment in behavioral control
3. craving
4. diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a
5. dysfunctional emotional response

ASAM Board of Directors, Definition of Addiction (Long Version), Chevy Chase, MD: American Society of Addiction Medicine, April 12, 2011.

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ASAM Addiction Definition Updated (2019)

- Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences.
- People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.
- Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

American Society of Addiction Medicine Definition of Addiction (2019, September 15). <https://www.asam.org/Quality-Science/definition-of-addiction>

15

GENES - not the cause of addiction, but a powerful mediator
genetics / epigenetics

1. Addiction is a disorder of PLEASURE - a hedonic dysfunction / broken "pleasure" DOPAMINE - reward expectancy (value / probability in the future)
2. Addiction is a disorder of CHOICE - a volitional disorder (impaired decision making + loss of insight)
3. Addiction is caused by STRESS - chronic trauma/PTSD

d/o

	severe	ACEs
	repetitive	MDD/GAD/Bipolar
	poorly managed	ADHD
	early in life	
	inherited	

16

Frontal Cortex:
PFC: Prefrontal Cortex
- executive functioning
- behavioral inhibition
ACG: Anterior Cingulate Cortex
- social cognition
- error detection
OFC: Orbitofrontal Cortex
- valuation under shifting conditions of uncertainty
Insular Cortex - interoception

Memory/Learning Areas:
Hipp: Hippocampus
- memory formation
Amyg: Amygdala
- fear conditioning

Reward/Salience Areas:
NAc: Nucleus accumbens (ventral striatum)
VP: Ventral Pallidum
VTA: Ventral Tegmental Area (midbrain)

17

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18

Addiction is a disorder of ...

5. CHOICE (motivation, insight)	OFC, ACC, PFC, IC
4. STRESS (anti-reward system)	HPA axis
3. MEMORY (habits, cues)	glutamate synaptic remodeling
2. REWARD (incentive salience)	dopamine receptors
1. GENES (vulnerability)	polymorphisms epigenetic

19

DSM-5 Criteria for "Substance Use Disorder"
(2 or more in the last year)

VALUATION	FAILURE TO FULFILL major work, school, & home obligations due to drug use
	LARGER AMOUNTS of drug used over LONGER PERIODS than intended
	PHYSICAL & PSYCHOLOGICAL PROBLEMS due to drug does not curtail use
LEARNING	IMPORTANT ACTIVITIES are given up in favor of the drug
	INABILITY to cut down or control drug use
	A LOT OF TIME spent obtaining, using & recovering from drug use
COGNITION / EMOTION / DECISION-MAKING	HAZARDOUS situations occur involving drug use
	SOCIAL & INTERPERSONAL PROBLEMS due to drug does not curtail use
	CRAVING

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: DSM-5.

20

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	CRAVING

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: DSM-5.

21

Is addiction really a “disease?”

22

Common challenges to the Conceptualization of Addiction as a Disease

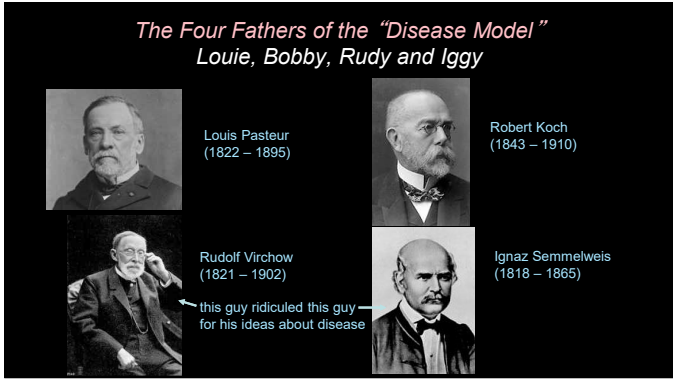
- There's no evidence that addiction is a brain disease ...
- ... and there have been no advances in treatment based on brain research
- Most people mature out of their addictions
- Drug use is situational (Vietnam Vets & heroin study)
- Drugs don't cause addiction (Rat Park study)
- We're all addicted to something
- it doesn't matter ...

23

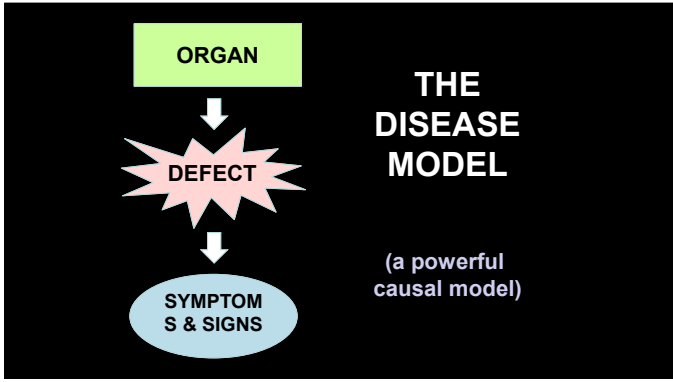
Ways to define “Disease”

- By “fiat” a disease is just that which we call it
- Normative a disease is something that isn't considered “normal”
- Biostatistical a disease is a certain number of standard deviations above/below the mean
- Pathophysiological a disease is a physical defect in an organ or organ system that leads to observable, measurable signs and symptoms (this is the right one)

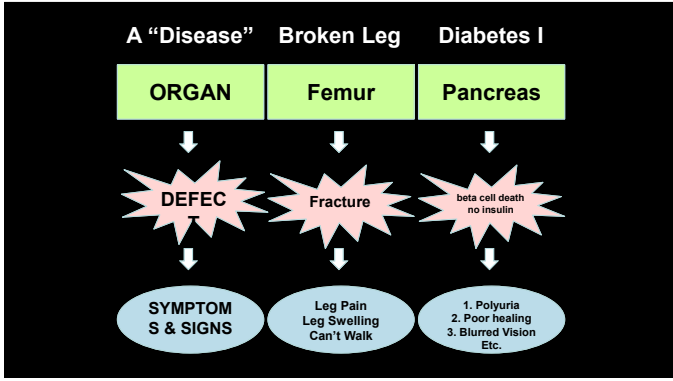
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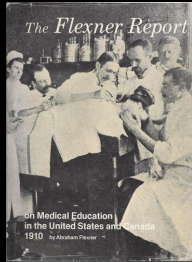


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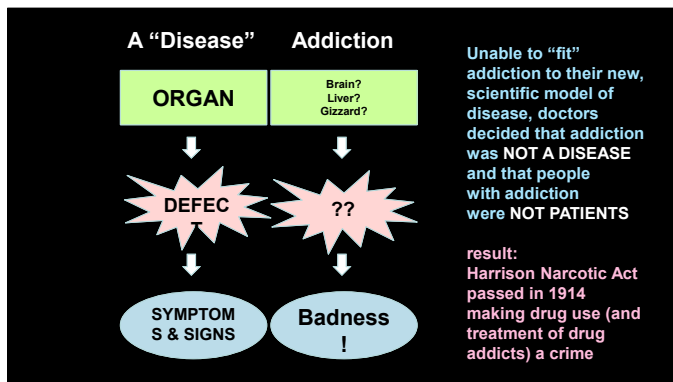
The Flexner Report (1910)



- Medical Schools should be research-oriented, laboratory facilities that adhere to the principles of science
- Lengthened and standardized medical education oriented around biochemistry, physiology and microbiology (embraced "Germ Theory" of disease)
- Called for fewer medical schools with higher standards for admission
- Many medical schools reverted to male-only admissions (except the Women's Medical College of Pennsylvania) and all but two historically black medical schools (Meharry and Howard) were closed

Medical Education in the United States and Canada: A Report to the Carnegie Foundation for the Advancement of Teaching. (2004). In C. Rose (Ed.), American Decades Primary Sources (Vol. 2, pp. 143-147). Gale. https://link-gale.com.ezproxy2.library.arizona.edu/apps/doc/C348/0202259/B/C?u=arizona_main&sd=1&cid=9633a6

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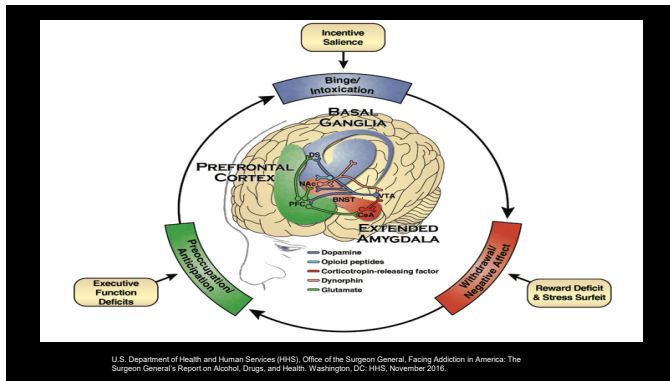
FACING ADDICTION IN AMERICA

The Surgeon General's Report on Alcohol, Drugs, and Health

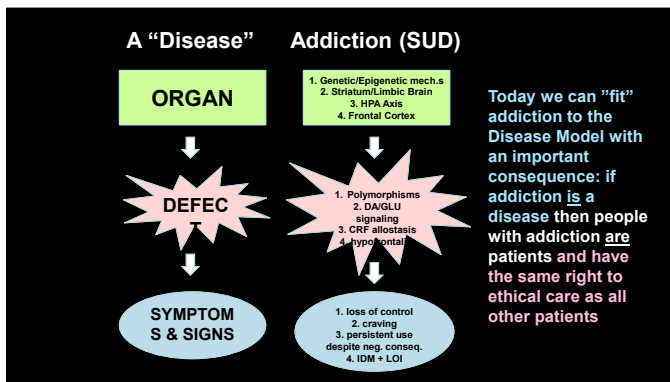
addiction.surgeongeneral.gov

U.S. Department of Health and Human Services (HHS), Office of the Surgeon General. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. Washington, DC: HHS, November 2016.

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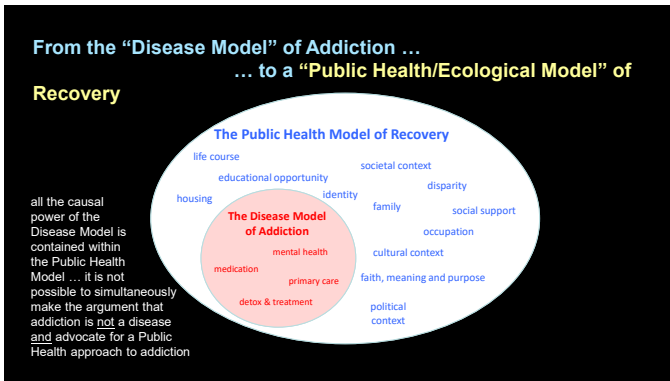


32

one unfortunate consequence of the causal power of the "Disease Model"

<p>We're good at</p> <p>Acute Disease</p> <p>REDUCTIVE: simple causation (traumatic, infectious, toxicologic)</p> <p>EMERGENT: rapid onset, severe symptoms, short duration</p> <p>EPISODIC CARE: Usually cured with a single, intense, time-limited hospitalization involving definitive treatment with ...</p> <p>MATERIALISTIC: primarily surgical or pharmacological interventions</p> <p>TECHONOCRATIC: Expert delivered, expensive, encourages "sick role" dependency, poorly targeted, fragmented care Ex. Heart Attack, Pneumonia, Encephalitis, traumatic injury</p>	<p>Now we need to get better at</p> <p>Chronic Disease</p> <p>CONTEXTUAL: multiple causation (genetic vulnerability, early adverse experiences, poverty, societal disenfranchisement)</p> <p>VARIABLE COURSE: sudden or gradual onset, relapsing, life-course variations</p> <p>LONGITUDINAL CARE: non-urgent, across the life-span, electronic health records, preventive focus</p> <p>PATIENT-CENTERED: care takes personal values, cultural context and spiritual considerations into account</p> <p>COMMUNITY-BASED: mix of professional and lay-treatment, team approach, continuous relationships Ex. Heart Disease, Diabetes, Asthma, Addiction, Depression, etc.</p>
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Discrepant findings for which the Disease Model must account...

- Lee Robins (Vietnam Vets)¹: drug use is situational
- Bruce Alexander (Rat Park)²: it's not the drug that causes addiction, it's the environment
- Marc Lewis³: addiction is a learned habit that can be unlearned; a developmental disorder not a disease
- Gene Heyman⁴: most people with addiction do NOT progress or die – most stop when they get older and start making better choices

1. Robins, L. N. (1993). Vietnam veterans' rapid recovery from heroin addiction: a fluke or normal expectation? *Addiction*, 88(8), 1041-1054. doi: 10.1111/j.1360-0443.1993.tb02123.x
2. Alexander, B. K., Coombs, R. B., & Haddaway, P. F. (1978). The effect of housing and gender on morphine self-administration in rats. *Psychopharmacology*, 56(2), 175-179. doi: 10.1007/bf00428993
3. Lewis, M. D. (2018). *The biology of desire: why addiction is not a disease*. Wellesley, MA: Longmeadow College.
4. Heyman, G. M. (2010). *Addiction: a disorder of choice*. Cambridge, MA: Harvard University Press.

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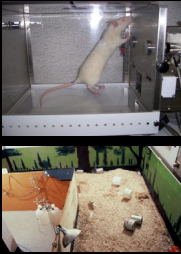
Vietnam Vets Study (Robins, 1975)

- High prevalence of heroin use in US soldiers in Vietnam
- On returning to the US, they did not continue heroin use
- Drug use was situational
- Often used as argument against addiction being a disease, but authors stated later that what surprised them was the idea that any heroin addicts recovered
- Counter-argument: Stress theories of addiction can explain changing vulnerability

Robins, L. N. (1993). The sixth Thomas James Cleary Memorial Lecture. Vietnam veterans' rapid recovery from heroin addiction: a fluke or normal expectation? *Addiction* (Abingdon, England), 88(8), 1041-1054. https://doi.org/10.1111/j.1360-0443.1993.tb02123.x

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Bruce Alexander PhD: "Rat Park" Study

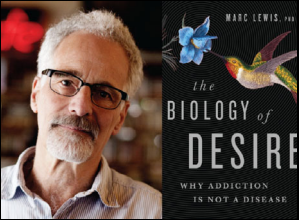


- Morphine consumption by rats housed in isolation vs socially
- Isolated rats drank more morphine ($n = 32$ rats)
- Both groups drank plenty of morphine, and 5 rats died of morphine overdoses (2 in the isolated group and 3 in the socially-housed group)
- Implication: morphine is more reinforcing in isolated environments and less so in enriched environments
- Study has some problems, and subsequent replication studies had mixed results
- Point taken: **Housing matters**
- But: how do you know "cross-addiction" didn't occur?

Alexander BK, Coombs RB, Hadaway PF. The effect of housing and gender of morphine self-administration in rats. *Psychopharmacology* (1978) 61: 170-179.

37

Marc Lewis, PhD: The Biology of Desire




- Brain changes do not necessarily indicate pathology
- Plasticity and synaptic pruning (learning) are normal functions of the brain
- Addiction is a deep form of learning, suboptimal but non-pathologic
- Motivated repetition remodels the brain causing intense desire for drugs (craving) strong cues to repeat over-valuation of drug narrowing of focus
- The very thing that got a person into addiction (plasticity) can get them out (development past addiction into recovery)

Lewis, M. D. (2018). *The biology of desire: why addiction is not a disease*. Counter-argument: Kalivas' work on pathologic

38

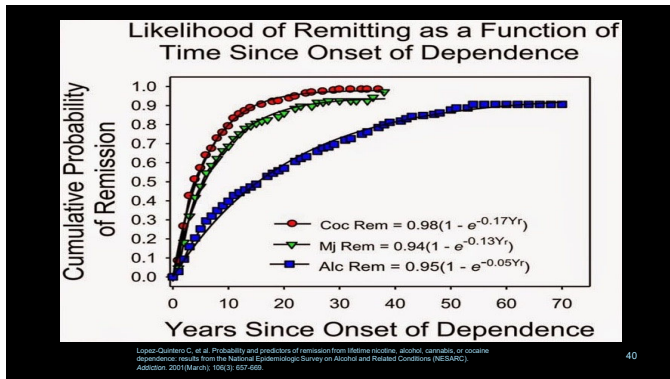
Gene Heyman, PhD: Addiction: A Disorder of Choice



- Self-destructive behaviors such as addiction can be chosen behavior
- Genes affect voluntary behavior (just because a behavior has a genetic cause doesn't make it involuntary)
- Brain changes from drug use do not make it involuntary
- Most addicts do stop on their own, without treatment, and do not display relapse chronicity
- Remission ("maturing out") is the rule, not the exception
- Addicts do not need lifelong treatment
- Remission rates lower for legal drugs than illegal drugs
- Counter-argument: Punishments are unreliable predictors of continued use, and behaviorism alone cannot explain the phenomenological experience of addiction
- Also: see William White response to Heyman – community-based studies often differ from clinical experience

Heyman, G. M. (2010). *Addiction: a disorder of choice*. Cambridge, MA: Harvard University Press.

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40

A "Disease" of Volition

- Could such a thing exist? (I'm making an ontologic argument that it can)
- What would happen if such a thing existed? (most advocates for addiction being a disease who run treatment centers are making this teleologic argument)
- What is the nature of volition/free will/choice?
- Is there something special (non-material) about "choice"?
- If so, what is it?
- If not, then how is "choice" realized in the brain, and how is addiction fundamentally different from any other brain disease process?
- It is very hard for Americans especially to accept addiction as a disease because we print words like "Liberty" on our money

41

What would it be like if there could be a such thing as a "broken leg?"

Broken Leg

- Hurts
- Deformity / Trauma
- Disability
- Want to get up and run (can't)
- Confusion when can't
- Tx: fixation / immobilization
- Healing / Physical therapy
- +/- Lifelong vulnerability

42

How does Addiction (SUD) run in families?
 What is the genetic component of Addiction (SUD)?

46

Addiction is a disorder of ...

5. CHOICE (motivation, insight)	OFC, ACC, PFC, IC
4. STRESS (anti-reward system)	HPA axis
3. MEMORY (habits, cues)	glutamate synaptic remodeling
2. REWARD (incentive salience)	dopamine receptors
1. GENES (vulnerability)	polymorphisms, epigenetic

47

Heritability of Addiction (from twin studies)

Alcohol: 48 – 66%	<ul style="list-style-type: none"> Heritability: an aggregate measure of the variability of a characteristic due to genetics vs environment (the risk due to genes – “risk genes”) First-order family members of a person with SUD have a 4 – 8 x increased risk of developing SUD Applies to <u>populations</u>, not individuals (that would be <i>inheritance</i>) Probabilistic, not deterministic
Cannabis: 51 – 59%	
Cocaine: 42 – 79%	
Opioids: 23 – 49%	
Nicotine: 33 – 71%	
shifts from adolescence (environment) to young adulthood (genetics) Gambling: 49%	

Agrawal, A., et al. (2016). Heritability of addiction: A translational perspective. *Translational Psychiatry*, 2(7), e140. <https://doi.org/10.1038/tp.2016.54>

48

Heritability of Addiction

(from twin studies)

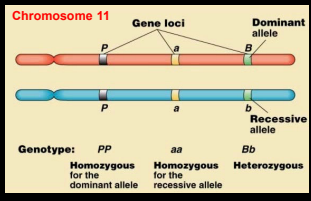
<p>Alcohol: 48 – 66%</p> <p>Cannabis: 51 – 59%</p> <p>Cocaine: 42 – 79%</p> <p>Opioids: 23 – 49%</p> <p>Nicotine: 33 – 71%</p> <p style="font-size: small;">shifts from adolescence (environment) to young adulthood (genetics)</p> <p>Gambling: 49%</p>	<ul style="list-style-type: none"> • Heritability: an aggregate measure of the variability of a characteristic due to genetics vs environment (the risk due to genes – “risk genes”) • First-order family members of a person with SUD have a 4 – 8 x increased risk of developing SUD • Applies to <u>populations</u>, not individuals (that would be <i>inheritance</i>) • Probabilistic, not deterministic
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Agrawal, A., et al. Heritability of addiction: a translational perspective. *Translational psychiatry*, 2(7), e140. <https://doi.org/10.1038/tp.2012.54>

49

Taq1 A1 allele of the DRD2 gene

(Blum & Noble, 1990)



Chromosome 11

Gene loci: P, a, B

Dominant allele: a

Recessive allele: b

Genotype: PP (Homozygous for the dominant allele), aa (Homozygous for the recessive allele), Bb (Heterozygous)

A single nucleotide polymorphism the carriers of which have 30-40% fewer DAD2 receptors and are at high risk for:


- Alcoholism and Addiction
- Repeated addiction treatment failures
- Increased mortality from alcoholism
- Lower striatal DAD2 receptor availability and lower striatal DA

Blum, K, Noble EP, Sheridan PJ, et al. Allelic association of human dopamine D2 receptor gene in alcoholism. *Journal of Molecular Psychiatry*, 1(1), 1990

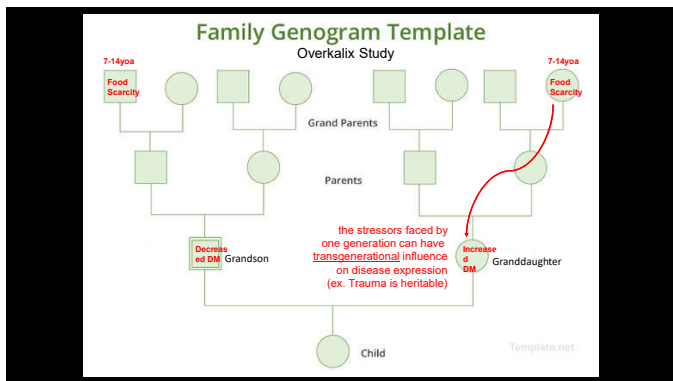
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Epigenetics

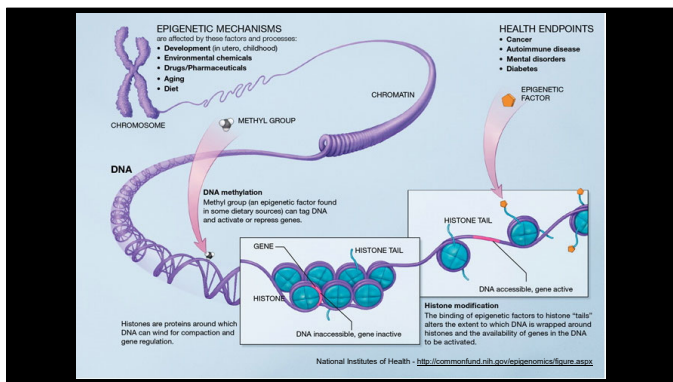
- Overkalix study: Starvation during adolescence increased the prevalence of diabetes in *grandchildren*
- Holocaust survivors with PTSD: their children also had PTSD without having been exposed to trauma
- A mechanism exists to transmit environmental exposure information from one generation to the next



51



52



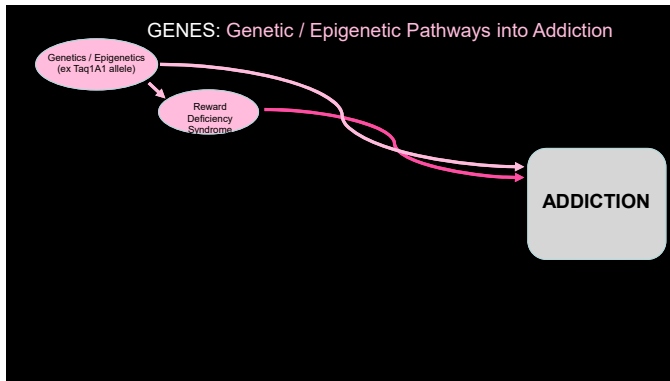
53

Nicotine primes cocaine use (Kandel & Kandel)

- Nicotine acts as a "Gateway Drug" for cocaine
- Nicotine for 7 days enhanced rewarding properties of cocaine
- Effect is unidirectional: did not see cocaine prime nicotine
- Nicotine inhibits histone deacetylase causing widespread acetylation in the striatum

Kandel, E. R., & Koob, G. F. (2014). *Statistical Lectures: A molecular basis for nicotine as a gateway drug. The New England Journal of Medicine, 371*(10), 932-943. <https://doi.org/10.1056/NEJMs1405000>

54



55

How does what we know about genetics help me get sober?

- Genes are a powerful influence on our behavior (voluntary and involuntary) and our choices
- Epigenetics, too, deepens our understanding of how we make choices
- But genetics and epigenetics do not determine our behaviors and choices
- We can “acquire” resiliency in recovery to offset our genetic vulnerability
- Epigenetics provides a mechanism by which recovery can be heritable too

56

Two Areas of Brain Research that reinforce the idea that volition can be part of a disease process

1. Epigenetics
2. Psychoneuroimmunology
The interaction between the physical and psychological functioning of the CNS and the immune system (ex. the immune system is the brain's sensory organ for stress).

57

Two Areas of Brain Research that reinforce the idea that volition can be part of a disease process

1. Epigenetics

2. Psychoneuroimmunology
The interaction between the physical and psychological functioning of the CNS and the immune system (ex. the immune system is the brain's sensory organ for stress).

58

Psycho-neuro-immunology

- A way to understand how stress and trauma cause mental illness through the immune system (the immune system is the stress)
- Adler & Cohen (1975): conditioned rats to drink saccharin water & Cytoxan (an immunosuppressant drug that tastes bad); later when they drank saccharin water the rats died of infection (immunosuppression in the absence of Cytoxan)
- Visintainer (1983): inescapable tail shock associated with decreased lymphocyte proliferation and decreased tumor rejection
- Also: lower antibody response to psychotic individuals given pertussis vaccination
- The Immune-Brain(-Gut) Loop: immune system is in constant communication with the brain (and the digestive system)
- CNS neurons terminate in thymus and spleen near clusters of lymphocytes

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Inflammation ("itis")

- a physiologic (normal) response of the body to pathogens (infection), irritants (intoxication) or tissue damage (injury) (... that too much of kills u)
- protective response: immune cells, blood vessels, & chemical mediators
- also to repair tissue damage & clear out necrotic cells
- acute inflammation: movement of white blood cells into the area
maturation of those white blood cells
amplification of their response
- chronic inflammation: simultaneous destruction and healing of tissue
shift of the type of cells in the area

60

Microglia

The diagram illustrates the origin of microglia from the yolk sac and their migration to the CNS. It shows that microglia are derived from the yolk sac and migrate to the CNS. In the CNS, they perform various functions: they appear as IBA1+ cells, secrete BDNF, assist in neuronal circuit development, and perform synaptic pruning. The term 'Synaptic pruning' is circled in red in the original image.

- Predominant immune cells of the CNS
- Cover a specific territory
- Usually in resting (ramified) state
- Secrete Brain-Derived Neurotrophic Factor (BDNF)
- Assist neuronal circuit remodeling across development (synaptic pruning)
- Responsible for CNS

61

Reactive Microgliosis: response to pathogen/injury

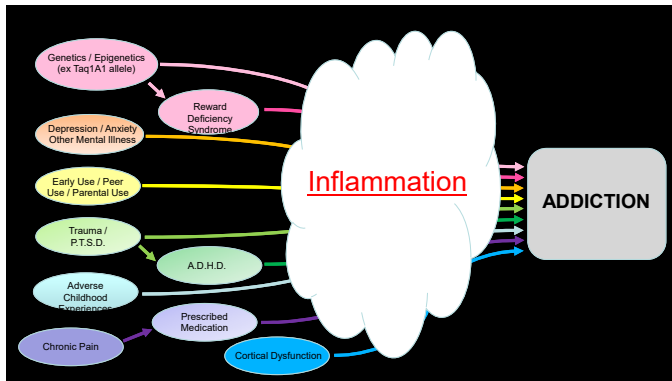
The diagram compares the 'Healthy State' and 'Disease State' of microglia. In the healthy state, microglia are resting and homeostatic. In the disease state, they become reactive (amoeboid) in response to injury, pathogens, or stress. This leads to increased phagocytosis of debris, synaptic pruning, and the release of pro-inflammatory cytokines.

- Resting microglia: injury to brain > Reactive Microgliosis
- Microglia respond rapidly to stress and trauma
- Shift from ramified (resting) state to amoeboid (activated) state
- Microglia are very fast moving cells (fastest in the brain: entire brain parenchyma scanned by microglia every few hours)
- Become macrophages > phagocytize pathogens and debris
- Antigen-presenting cell to T lymphocytes

62

A flowchart showing various factors that lead to addiction. The factors include: Genetics / Epigenetics (ex Taq1A1 allele), Depression / Anxiety / Other Mental Illness, Early Use / Peer Use / Parental Use, Trauma / P.T.S.D., Adverse Childhood Experiences, Chronic Pain, Reward Deficiency Syndrome, A.D.H.D., Prescribed Medication, and Cortical Dysfunction. All these pathways converge on a central point labeled 'All of these pathways pass through and are affected by ...' which then leads to a box labeled 'ADDICTION'.

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64

1. Addiction is a disorder of PLEASURE

2. Addiction is a disorder of CHOICE

3. Addiction is caused by STRESS

Symptoms of Addiction (S.U.D.):

1. Loss of Control
2. Persistent Drug Use Despite Negative Consequences
3. Relapse
4. Craving
5. Impaired Decision-making + Loss of Insight

65

What causes the Persistent Use Despite Negative Consequences symptom of Addiction (SUD)?


66

Addiction is a disorder of ...

5. CHOICE (motivation, insight)	OFC, ACC, PFC, IC
4. STRESS(anti-reward system)	HPA axis
3. MEMORY (habits, cues)	glutamate synaptic remodeling
2. REWARD (incentive salience)	dopamine receptors
1. GENES (vulnerability)	polymorphisms epigenetic

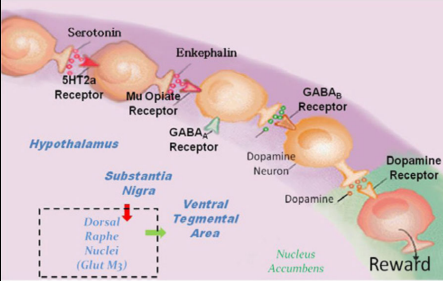
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Addiction is a disorder in the brain's hedonic system (pleasure sense)



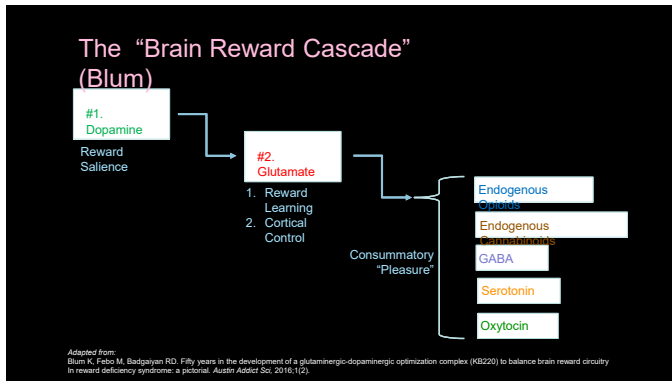
68

The "Brain Reward Cascade"



Blum K, Febo M, Badgley RD. Fifty years in the development of a glutamatergic-dopaminergic optimization complex (KB220) to balance brain reward circuitry in reward deficiency syndrome: a personal history. *Addict Sci*. 2016;1(2).

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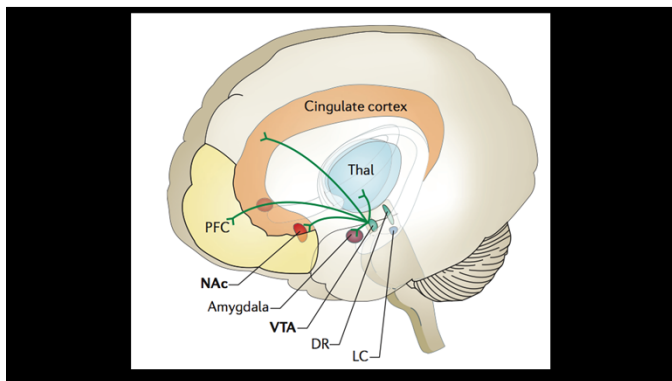


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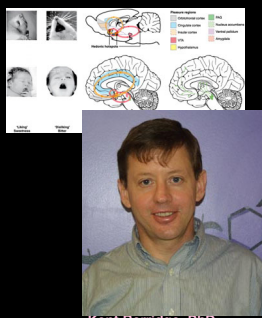
Addiction Neurochemical #1: Dopamine

- All drugs of abuse and potential compulsive behaviors release Dopamine
- Dopamine is the first chemical in the cascade of chemicals that generate a rewarding experience
- DA is the chemical of salience (survival importance)
- DA is more about "wanting" than "liking"
- DA is more about expectation than consumption
- DA signals reward prediction error - it tells the brain when something is "better than expected"

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Incentive-Sensitization (Berridge & Robinson)

- Distinguished between a “liking” and a “wanting” role for Dopamine (it’s more about “wanting”)
- Created hyper-dopaminergic Dopamine Transporter “knock-down” mice (mice with increased synaptic Dopamine)
- Observed increased intake of reinforcing substances in these mice and greater thwarting of obstacles to get them (i.e. more “wanting”)
- But did not observe greater “liking” of these substances by these mice

Kent Berridge, PhD
University of Michigan

Berridge, K. C., & Robinson, T. E. (2003). Parsing reward. *Trends in Neurosciences*, 26(9), 507-513. doi:10.1016/s0166-2236(03)00233-9

73


DA NAc neurons do more than encode receipt of reward

- Expectancy of reward
- Amount of reward
- Delay of reward
- Errors in reward prediction
- Motivation for drug seeking
- Contribute to synaptic neuroplasticity that underlies the acquisition of addictive behaviors

Gardner EL. Addiction and brain reward and antireward pathways. In: Clark, MR, Treisman GJ (eds). Chronic pain and addiction.

74

Dopamine, Dopamine Receptors and Addiction

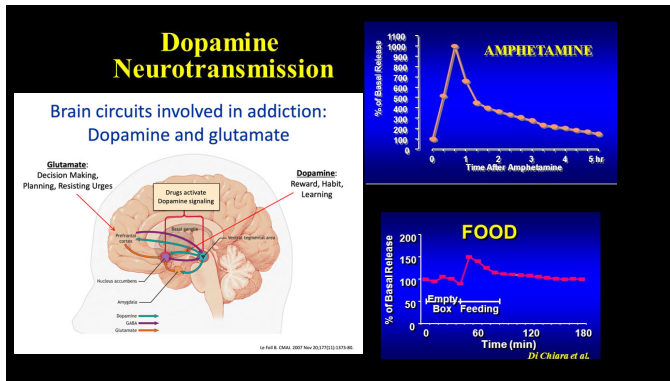


- Drugs of abuse cause supraphysiologic increases in extracellular dopamine in the striatum that correlate with subjective feelings of being “high”
- PET scan studies: impaired striatal dopamine signaling due to decreased DAD2 receptors
- fMRI scan studies: brain activation abnormalities in striato-cortical pathways that regulate reward, self-control, and affect
- Overlap in brain circuitry underlying addiction and disorders such as binge eating and pathological gambling
- Other brain chemicals matter, too (glutamate, GABA, endogenous opioid and cannabinoids)

Nora D. Volkow, MD
Director, National Institute on Drug Abuse

Volkow, N. D., & Morales, M. (2013). The Brain on Drugs: From Reward to Addiction. *Cell*, 162(4), 712-725. https://doi.org/10.1016/j.cell.2015.07.046

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- ### Dopamine-Releasing Chemicals
- Alcohol & Sedative/Hypnotics
 - Opiates/Opioids
 - Cocaine
 - Amphetamines
 - Entactogens (MDMA)
 - Entheogens/Hallucinogens
 - Dissociants (PCP, Ketamine)
 - Cannabinoids
 - Inhalants
 - Nicotine
 - Caffeine
 - Anabolic-Androgenic Steroids

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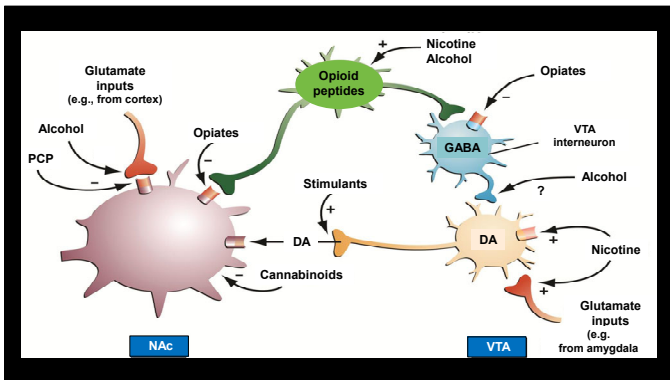
- ### Dopamine-Releasing Behaviors
- Food (Bulimia & Binge Eating)
 - Sex
 - Relationships
 - Other People ("Codependency," Control)
 - Gambling
 - Cults
 - Performance ("Work-aholism")
 - Collection/Accumulation ("Shop-aholism")
 - Rage/Violence
 - Media/Entertainment

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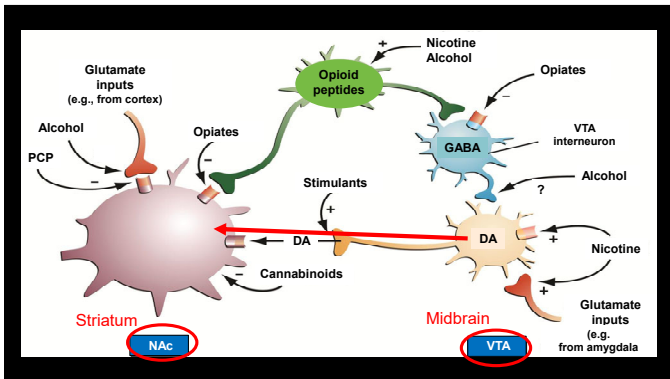
The Full Spectrum of Addiction

- Alcohol & Sedative/Hypnotics
- Opiates/Opioids
- Cocaine
- Amphetamines
- Entactogens (MDMA)
- Entheogens/Hallucinogens
- Dissociants (PCP, Ketamine)
- Cannabinoids
- Inhalants
- Nicotine
- Caffeine
- Anabolic-Androgenic Steroids
- Food (Bulimia & Binge Eating)
- Sex
- Relationships
- Other People ("Codependency," Control)
- Gambling
- Cults
- Performance ("Work-aholism")
- Collection/Accumulation ("Shop-aholism")
- Rage/Violence
- Media/Entertainment

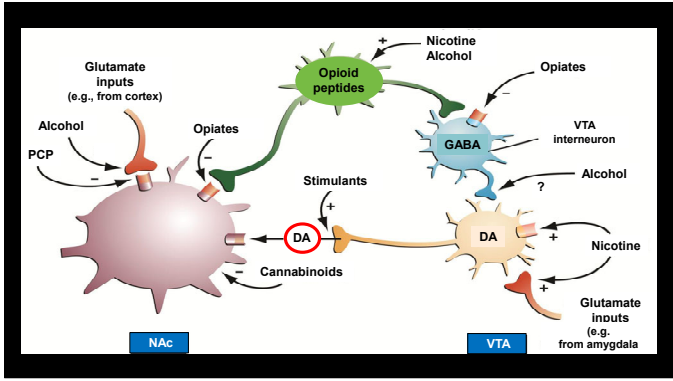
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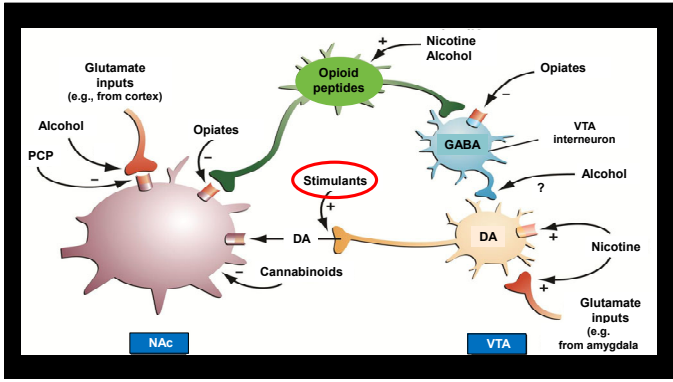
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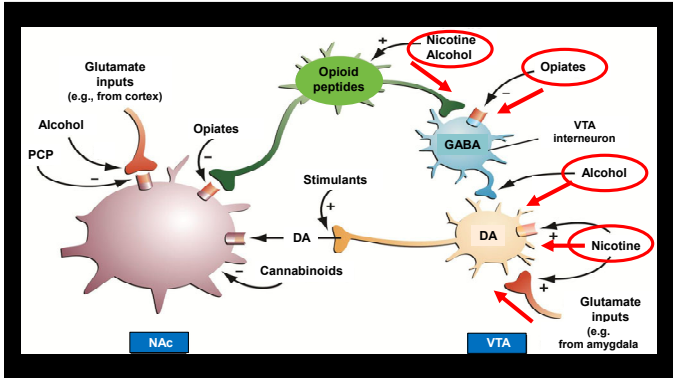
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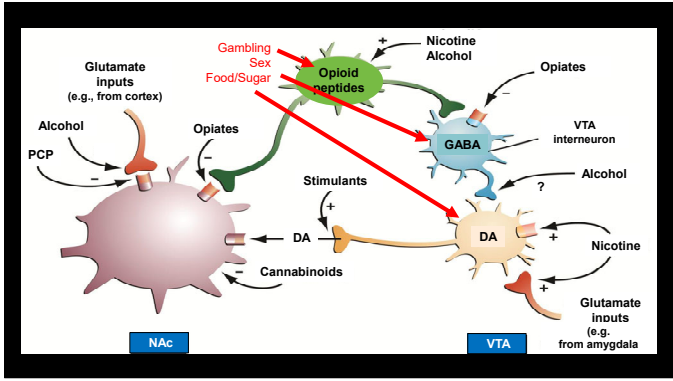
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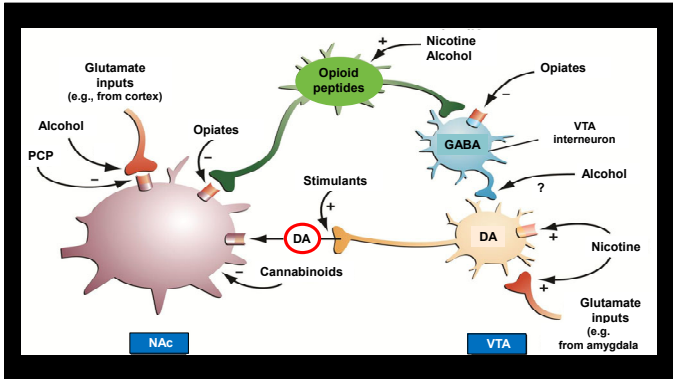
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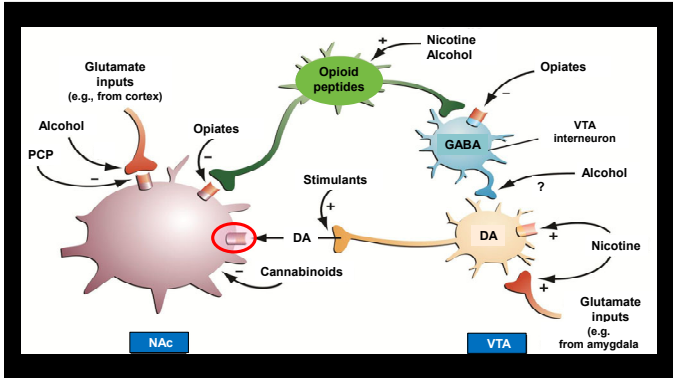
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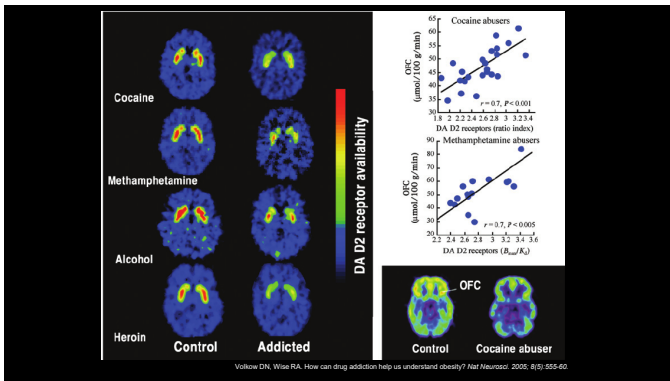
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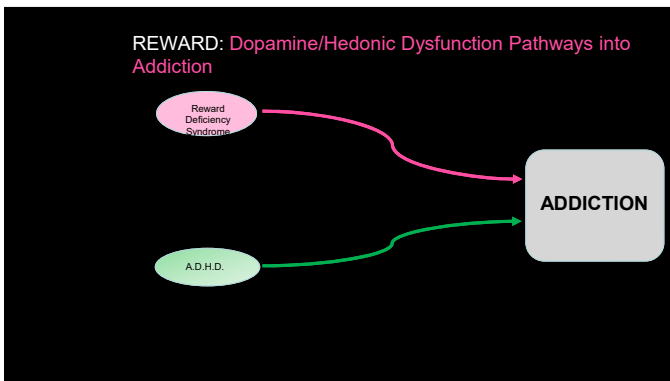
DA release and euphoria: more complex?

Prof. David Nutt, FMedSci
Safra Chair in Neuropsychopharmacology
Imperial College London, UK

- Stimulants increase striatal dopamine levels, yes, but alcohol less so
- Little evidence that cannabis and opioids increase striatal dopamine levels
- Striatal dopamine receptor availability decreased in Stimulant UD and Alcohol UD, but not in Opioid UD, Nicotine UD or Cannabis UD
- Daghlas: 50mg of IV heroin had no effect on striatal dopamine levels despite producing euphoria
- Dopamine Hypothesis has not led to new treatments

Nutt DJ, King LA, Phillips LJ. Drug harms in the UK: a multicriteria decision analysis. Lancet. 2010;376(9752):1568-65.

89



90

How does what we know about reward help me get sober?

- All intoxicants (chemicals and behaviors) cause large and fast dopamine releases in brain reward structures which is toxic to dopamine receptors
- I may have had a dysfunctional dopamine system prior to using drugs
- By avoiding intoxication I can restore the number and function of my dopamine receptors
- This may mean avoiding cross-addicting chemicals and behaviors like nicotine and sugar
- Practicing normal pleasurable activities restores my brain's ability to respond to normal pleasures normally (hedonic rehabilitation)

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What causes the Relapse symptom of Addiction (SUD)?

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ASAM Definition: Relapse

- Persistent relapse / and risk thereof
- Even after periods of abstinence
- Triggered by:
 1. Re-exposure to drug itself (DA release in NAc)
drug-induced reinstatement DOPAMINE
 - 2.
 - 3.

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Dopamine begins reward but quickly fades to support cues

- Drug-induced fast DA increases in the striatum (incl NAc) mediate their rewarding effects
- In addiction: drug-induced DA increases (as well as subjective rewarding effects) are markedly blunted (pharmacologic effects fade)
- In addiction: but CUE-induced DA increases in the striatum are still significant and are associated with self-reports of craving (conditioned responses strengthened)
- In addiction: lower levels of striatal DAD2Rs

Volkow ND et al. Addiction: beyond dopamine reward circuitry. PNAS 108(37): 15037-15042 (2011)

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ASAM Definition: Relapse

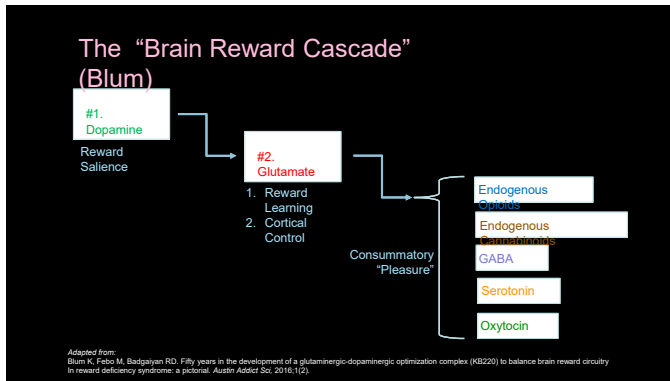
- Persistent relapse / and risk thereof
- Even after periods of abstinence
- Triggered by:
 1. Re-exposure to drug itself (DA release in NAc)
drug-induced reinstatement DOPAMINE
 2. Exposure to drug cues (GLU release in Amygdala/Hipp)
cue-induced reinstatement GLUTAMATE
 - 3.

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Addiction is a disorder of ...

5. CHOICE (motivation, insight)	OFC, ACC, PFC, IC
4. STRESS(anti-reward system)	HPA axis
3. MEMORY (habits, cues)	glutamate synaptic remodeling
2. REWARD (incentive salience)	dopamine receptors
1. GENES (vulnerability)	polymorphisms epigenetic

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Addiction Neurochemical #2: Glutamate

- The most abundant neurochemical in the brain
- Critical in memory formation & consolidation
- All drugs of abuse and many addicting behaviors effect Glutamate which preserves drug memories and creates drug cues
- And ... glutamate is the neurochemical of "motivation" (it initiates drug seeking)

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Glutamate "spillover"

- Enduring vulnerability to relapse due to recruitment of "cortico-fugal" GLU projections to striatum
- Excess GLU "spills" out of the synapse to bind to extra-synaptic GLU receptors
- Changes in synaptic plasticity leads to pathologic learning and memory
- Result: impairment of inhibition of drug seeking

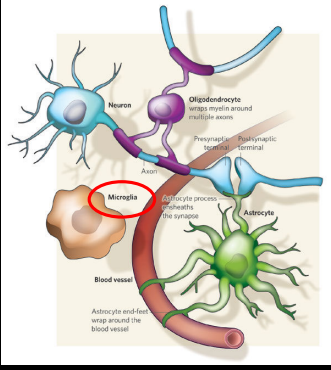


Peter W. Kalivas, PhD
Department of Neurosciences
Medical University of South Carolina

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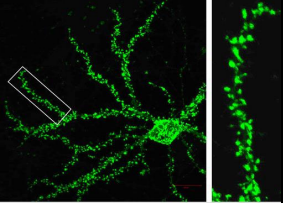
Glial Cells

- Caretaker cells of the CNS & PNS
- Half the total volume of the brain
- Equal number as neurons (in Cortex: 4 glial cells to each neuron)
- Can divide as adult cells



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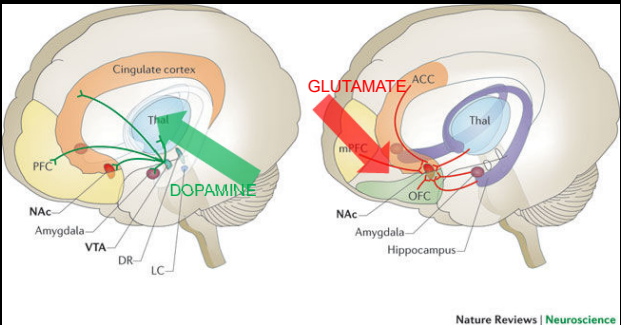
Transcription Factor: delta-FosB



- Mediates the structural plasticity induced in the NAc by cocaine
- Changes in number, shape and size of dendritic spines of NAc DAD1R-expressing MSNs
- Larger changes in spine density with self-admin over experimenter-admin of cocaine
- Also induced by chronic consumption of natural rewards (sucrose, high fat foods, sex, wheel running)
- "ΔFosB is both necessary and sufficient for many of the changes in the brain after chronic drug exposure"

Robison AJ, Nestler EJ. Transcriptional and epigenetic mechanisms of addiction. *Nature Neuroscience Reviews*, 12: 623-637 (2011).

101



Nature Reviews | Neuroscience

102

The hypofrontal/craving brain state represent an imbalance between 2 brain drives

<p>Amygdalar-Cortical Circuit</p> <ul style="list-style-type: none"> • "GO!" • Impulsive • Non-reflective • Poorly conceived • Socially inappropriate <p>THERE'S TOO MUCH OF THIS (Behavioral Impulsivity)</p>	<p>Cortico-Striatal Circuit</p> <ul style="list-style-type: none"> • "STOP!" • Organized, Attentive • Sensitive to consequences • Well-planned • Socially appropriate <p>THERE'S TOO LITTLE OF THIS (Failure of Behavioral Inhibition)</p>
---	---

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Reward: overvaluation
drug = survival

Learning: drug hyper-memories
drug cues > relapse

Reward Salience
Memory/Learning
Habit Formation

Reinforcement
Attention

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What is Alcoholism?

A.A. Concept of "powerlessness"

Alcoholics Anonymous

"The idea that somehow, someday he will control and enjoy his drinking is the great obsession for every abnormal drinker." (AA BB pg. 30)

"The delusion that we are like other people, or presently may be, has to be smashed." (AA BB pg. 30)

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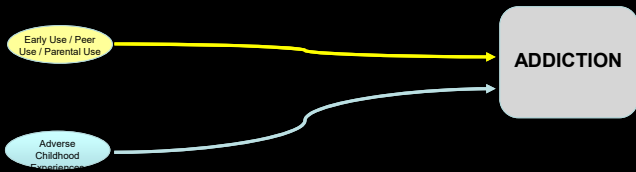
The paradox of powerlessness

- Admitting powerlessness means admitting that no amount of trying or practicing or self-control is going to change the way that drugs or alcohol affect your brain.
- Powerless does not mean helpless. The First Step does not say that you are powerless over your actions, your decisions, or your relationships; it says that you are powerless over alcohol/drugs. This is not an excuse for continuing down the same destructive path. It is not about laying down and giving up. It is about complete and wholehearted surrender.

<https://www.marinc.org/powerlessness-is-not-weakness/>

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MEMORY: Socio-behavioral/Conditioned Pathways into Addiction

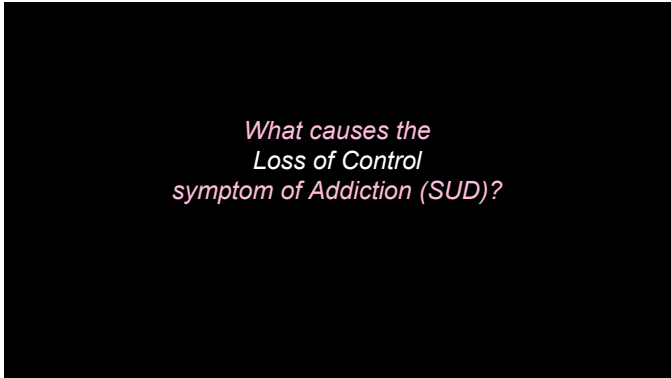


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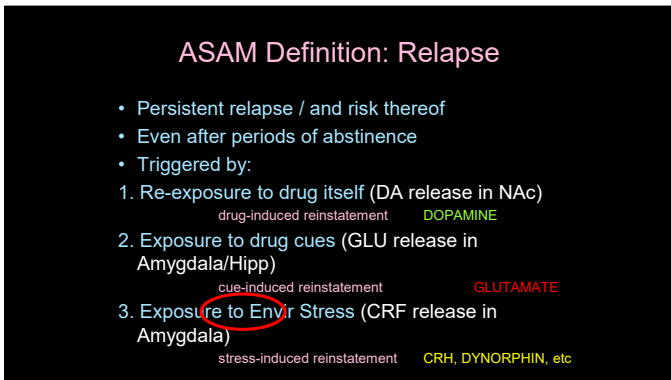
How does what we know about memory help me get sober?

- Sensory and Environmental Cues are powerful relapse triggers of which we are not always conscious
- Relapse Prevention Strategy:
 - caution with people, places and activities previously associated with drug use
 - self-talk of Cognitive-Behavioral Therapy can strengthen commitment to sobriety (improve cortical inhibition)
 - Medications that stabilize glutamate (Acamprosate – Campral ©) or provide opioid receptor blockade (Extended-release Naltrexone – Vivitrol ©) can provide a margin of safety to avoid or minimize relapse

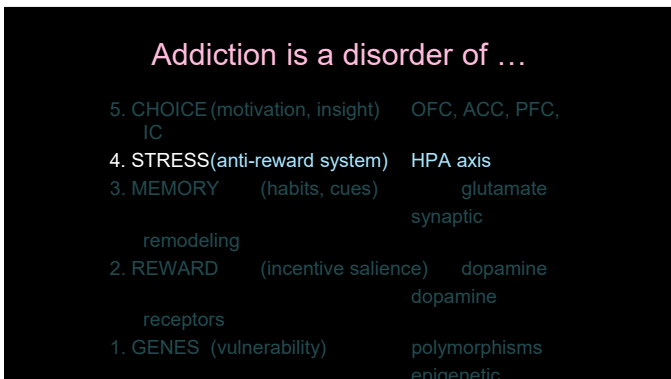
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Hedonic Allostasis Theory
(Koob & LeMoal)

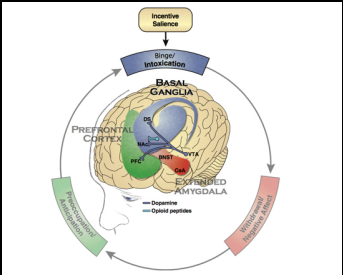


George Koob, PhD
Chair, Neurobiology of Addictive Disorders
Scripps Neurosciences Institute

- With continued drug use and withdrawal, the “anti-reward” system is recruited to *counter-balance* excess Dopamine using the stress hormone CRF
- Brain is unable to maintain normal “homeostasis”
- So the brain reverts to “allostasis” - change of the hedonic “set point” under stress in an attempt to maintain stability
- The result is anhedonia – an inability to find pleasure in normally pleasurable activities

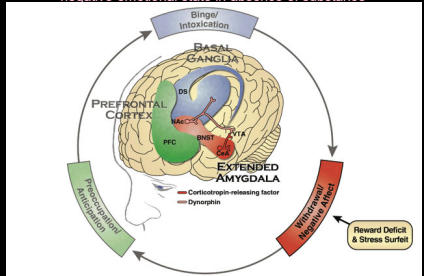
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Stage 1: Binge/Intoxication
consumption of intoxicating substance/experience of pleasurable effects

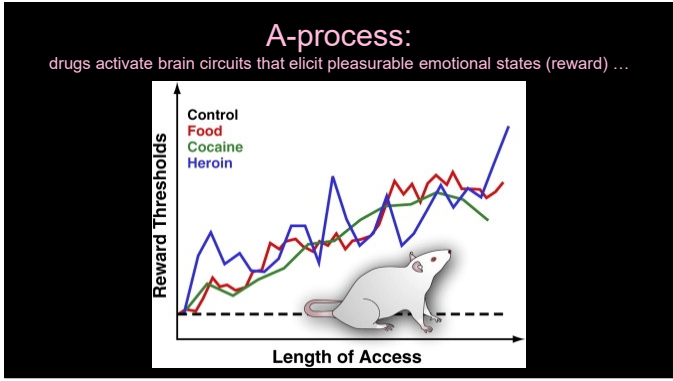


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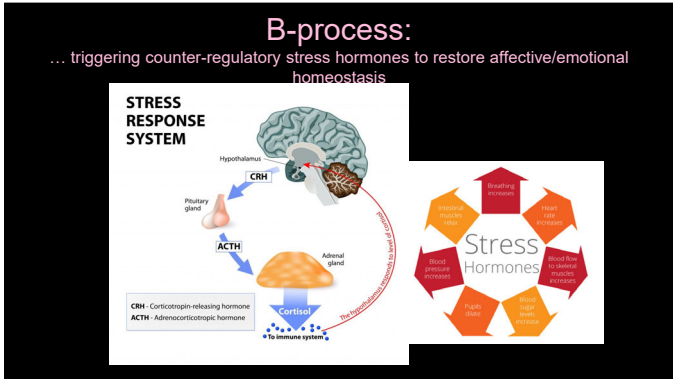
Stage 2: Withdrawal/Negative Affect
negative emotional state in absence of substance



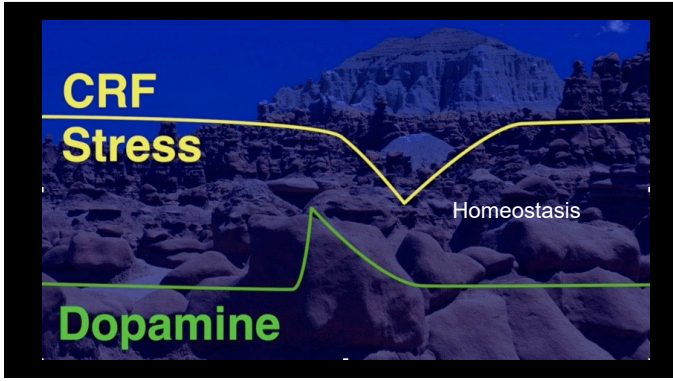
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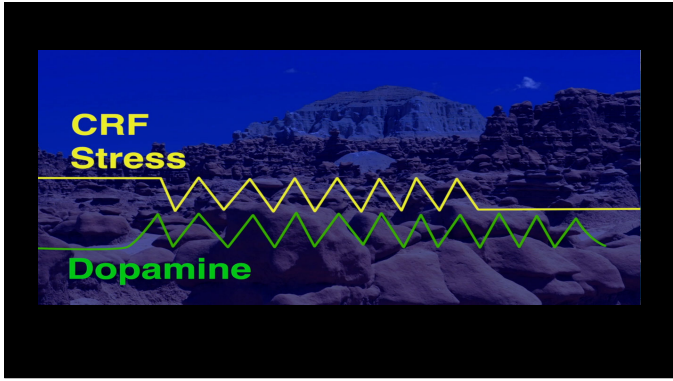
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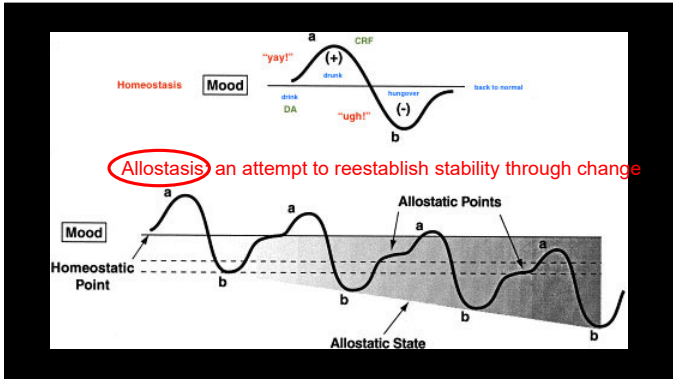
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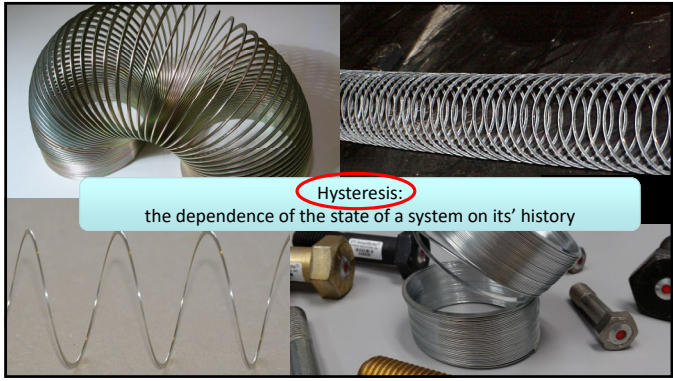
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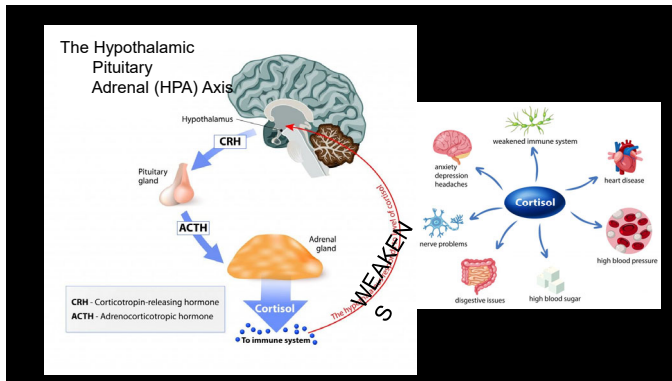
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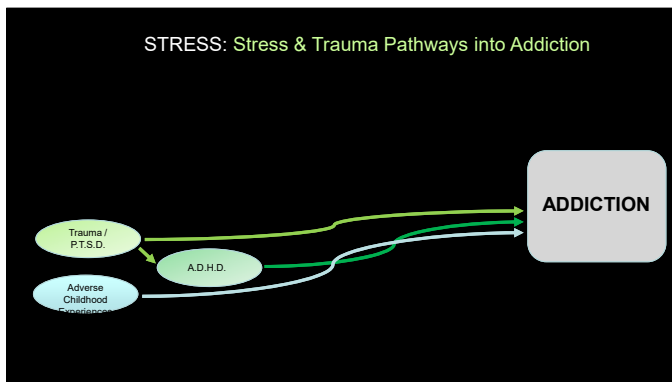
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- How does what we know about stress help me get sober?
- Proactive Stress Management
 - Peer-based coping
 - Contingency Management
 - Building social capital, recovery capital and resilience
 - Safe Housing
 - Trauma-informed Therapy
 - Immune system support
 - Medications: ex. to decrease sympathetic discharge (Clonidine)

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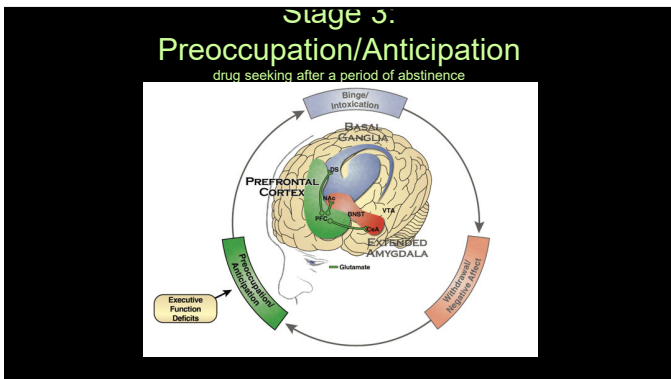
*What causes
Craving,
Impaired decision-making,
Loss of insight,
and
Emotional dys-regulation
symptoms of Addiction (SUD)?*

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Addiction is a disorder of ...

5. CHOICE (motivation, insight)	OFC, ACC, PFC, IC
4. STRESS (anti-reward system)	HPA axis
3. MEMORY (habits, cues)	glutamate synaptic remodeling
2. REWARD (incentive salience)	dopamine receptors
1. GENES (vulnerability)	polymorphisms epigenetic

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Anterior Cingulate Cortex (ACC)

Figure 1. Corticolimbic system

Motivation and executive function (DLPFC)

Reward anticipation, decision making, empathy, emotion, and impulse control (ACC)

Learning and memory (Hippocampus)

Processing of emotions (Amygdala)

DLPFC, dorsolateral prefrontal cortex; ACC, anterior cingulate cortex; AMY, amygdala; HPC, Hippocampus.

- Conflict monitor, discrepancy “alarm”
- Self-monitoring
- Inhibition of goal-directed behavior
- Appreciation and valuation of social cues
- rostral ACC: emotional processes, expected pain/social rejection
- dorsal ACC: cognitive processes, unexpected pain/social rejection
- fMRI: active in tasks requiring empathy and trust, engaged in cognitive tasks requiring attention

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damage to Anterior Cingulate Cortex (ACC)

Figure 1. Corticolimbic system

Motivation and executive function (DLPFC)

Reward anticipation, decision making, empathy, emotion, and impulse control (ACC)

Learning and memory (Hippocampus)

Processing of emotions (Amygdala)

DLPFC, dorsolateral prefrontal cortex; ACC, anterior cingulate cortex; AMY, amygdala; HPC, Hippocampus.

- Causes a loss of a crucial behavioral guidance system
- Inflexibility/Inability to respond to errors in the past with regard to rewards/punishments
- Deficits in social responding due to decreased awareness of social cues
- Impulsivity and perseverance increases

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Insular Cortex (IC)

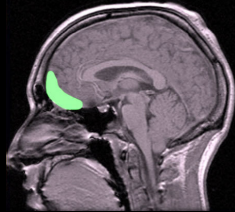
- Abrupt cigarette smoking cessation with IC lesions (Naqvi et al)
- Important in emotional awareness, empathy, interoception
- Insular cortex impairment is one part of craving
- Alexithymia: the inability to put words to emotions or describe them to others
- Yoga, mindfulness meditation, deep breathing exercises all helpful in repairing the Insular

Interoception

Heart, Kidneys, Bladder, Skin, Hormones, Lungs, Stomach, Intestines, Bone, Immune cells

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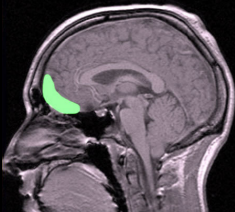
Orbitofrontal Cortex (OFC)



- Decision-making guided by rewards
- Integrates sensory and emotional information from lower limbic structures
- Flexible assignment of value to environmental stimuli to motivate or inhibit choices & actions
- Self-monitoring and social responding

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damage to Orbitofrontal Cortex (OFC)



- Causes a loss of a crucial behavioral guidance system
- Responses are impulsive and inappropriate
- Deficits of self-regulation
- Inability to properly assign value to rewards (such as money vs. drugs)
- Tendency to choose small & immediate rewards over larger but


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In addition,
the brain's ability to correctly calculate
1. value
and
2. probability
becomes severely biased
This means that people in early recovery
have a hard time assessing
likelihood of future harm
... or **RISK**

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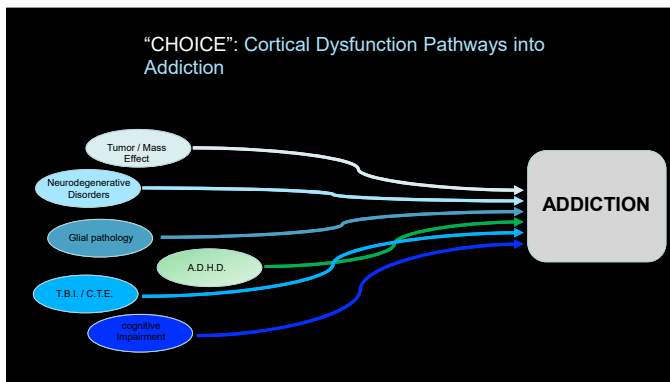
What is Alcoholism?

A.A. Concept of "unmanageability"



"We were having trouble with personal relationships, we couldn't control our emotional natures, we were a prey to misery and depression, we couldn't make a living, we had a feeling of uselessness, we were full of fear, we were unhappy, we couldn't seem to be of real help to other people." (AA BB pg. 52)

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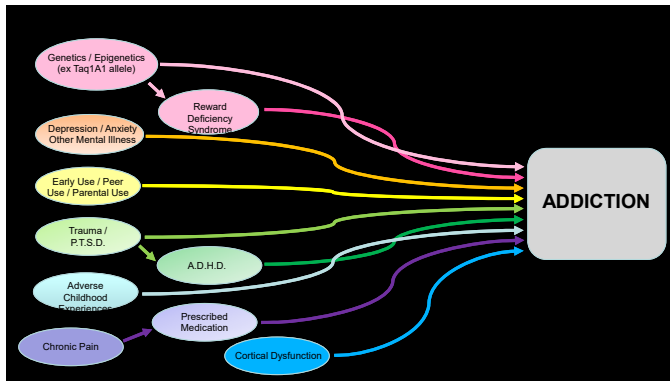


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How does what we know about choice help me get sober?

- Abstinence from intoxication
- Peer-based coping; social connection and reflection
- Agency-building exercises;
- AA: service work, working with newcomers, taking commitments
- Purposeful, meaningful goals
- Once safe, returning to work; practicing occupational/vocational skills

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How does the Neuroscience of Addiction fit with the "spiritual program" of AA?

- Powerlessness: pathological salience
hyper-learning of intoxicant
- Unmanageability: failure of ACC & social cognition
failure of OFC & risk calculation
- Surrender: volitional baseline
- Character defects: frontal hypofunction (acquired narcissism)
- God and Sponsor: volitional buffering
- Making Amends: catastrophizing
- Spiritual Awakening: mindfulness, narrative, purpose, meaning,
focused on others

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Cochrane Meta-analysis: Twelve-Step Facilitation for Alcohol Use Disorder
(Kelly, Abry, Ferri & Humphreys, 2020)

- Follow-up to Previous Cochrane publication
- AA/TSF was better than CBT and MET in facilitating continuous abstinence and AUD remission
- AA/TSF was at least as effective as CBT and MET in reducing intensity of drinking, alcohol-related consequences and severity of Alcohol Use Disorder
- AA/TSF reduced healthcare costs more than CBT, MET or IOP alone (by \$10,000 per patient over two years)

John P. Kelly, Alexandra Abry, Marica Ferri, Keith Humphreys, Alcoholics Anonymous and 12-Step Facilitation Treatments for Alcohol Use Disorder: A Distillation of a 2020 Cochrane Review for Clinicians and Policy Makers, Alcohol and Alcoholism, Volume 55, Issue 6, November 2020, Pages 641-651. <https://doi.org/10.1093/alz/kzaa020>

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The Problem:
 How can I protect myself
 from relapse (decision-making)
 when my ability to assess relapse
 risk
 is itself impaired (loss of insight)?

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Recovery Management
 (a form of "Risk Management")

Recovery management is a philosophy of integrating addiction treatment and recovery support services to:

1. *increase pre-recovery engagement*
2. *facilitate recovery initiation*
3. *promote long-term recovery maintenance*
4. *improve quality of personal/family life in long-term recovery*

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Aviation Safety Practices

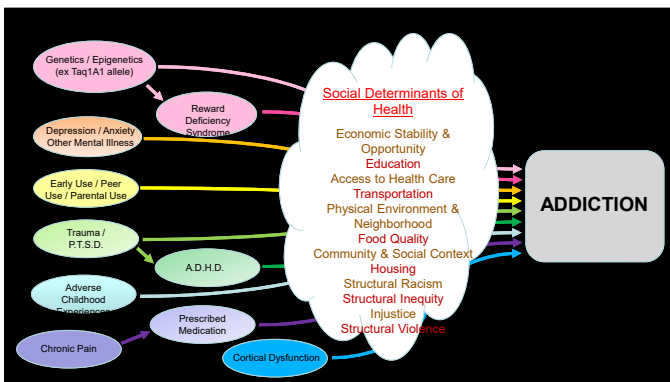
1. Checklists
2. Sterile Cockpit (distraction avoidance)
3. Briefings, Standardized Comm, Read-backs
4. Crew Resource Management
5. Protective Devices (TCAS, voice enunciators: "Nagging Nora" & "Barking Bob," G-suit)
6. Shared-value safety slogans
 ("Aviate, Navigate, Communicate")
 ("Confess, Climb, Conserve, Communicate, Comply")

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... applied to Recovery

1. Checklists: 12-Steps & 12-Traditions, Relapse Safety Plan
2. Sterile Cockpit: support during critical moments of sobriety - first hours after discharge, surgeries, court appearances
3. Standardized Comm: recovery vocabulary
4. Read-backs: calling my sponsor
5. CRM: Network Therapy
6. Non-hierarchical social structure: "the most important person at any meeting ..."
7. Protective devices: Extended-release NTX
8. Shared-value Slogans: "Keep coming back," "Take the next indicated step," "When we were wrong ..." etc.

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Social Determinants of Health:
 conditions in the environment in which people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning and quality of life outcomes and risks

Health Disparities:
 systemic, avoidable health differences adversely affecting socially disadvantaged groups; different from health differences

Health Equity:
 a commitment to reduce/eliminate health disparities; social justice with respect to health; equal opportunity to be healthy

Healthy People 2020 Approach to SDHs
<https://www.healthypeople.gov/2020/topics-objectives/topic/social-determinants-of-health>

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Social Determinants of Health

Social Determinant of Health	Health Disparity	Health Inequity
1. Safety	early life adversity (ACEs)	chronic disease, shorter lifespan
2. Healthy Food	low availability, food deserts	higher diabetes, obesity
3. Income Security	poverty, lack of social safety net	chronic disease, shorter lifespan
4. Housing	housing insecurity / rent as % of income	higher asthma, lead exposure
5. Education, Job Training	lower HS graduation rates	unhealthy behaviors (smoking)
6. Social / Family Support	isolation, intimate partner violence (IPV)	greater depression & suicide
7. Community	stigma, racism, discrimination	inaccessible services > chron dis.
8. Employment	unemployment, lack of opportunity	chronic disease, suicide, SUD
9. Access to Health Care	ineligibility / work requirements	ex. less cancer screening
10. Justice	disprop. policing / mass incarceration	chronic disease, shorter lifespan

<http://thenationshealth.aphapublications.org/content/infographics-social-determinants-health>

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An Effective Recovery Management Plan

1. Treatment (Residential or IOP)	evidence-based treatment, enculturation
2. Therapist/Counselor/Coach linkage	on-going f/u, advocacy, ROSC
3. Recovery Residence	housing security, peer support
4. Mutual Support Groups	social connectedness, social narrative
5. Relapse Plan	contingency management
6. Testing	chronic disease monitoring, parity
7. Job/School/Future	educational / vocational opportunity
8. Addiction Medicine Specialist	access to longitudinal primary care

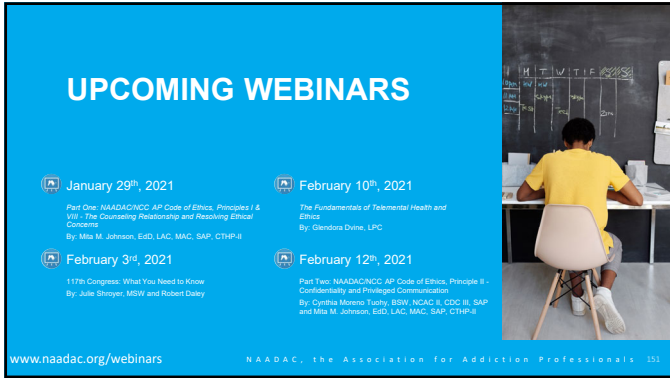
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 Meadows Behavioral Healthcare
www.protectingsobriety.com

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UPCOMING WEBINARS

January 29th, 2021
 Part One: NAADAC/NCC AP Code of Ethics, Principles I & VIII - The Counseling Relationship and Resolving Ethical Conflicts
 By: Mita M. Johnson, EdD, LAC, MAC, SAP, CTHP-II

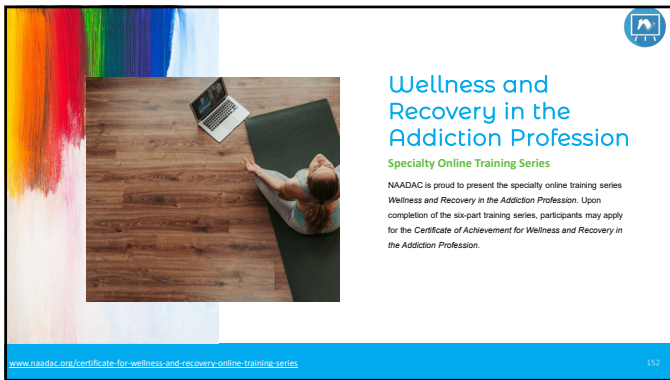
February 10th, 2021
 The Fundamentals of Telemental Health and Ethics
 By: Genndora Dvire, LPC

February 3rd, 2021
 117th Congress: What You Need to Know
 By: Julie Shroyer, MSW and Robert Daley

February 12th, 2021
 Part Two: NAADAC/NCC AP Code of Ethics, Principle II - Confidentiality and Privileged Communication
 By: Cynthia Moreno Tuohy, BSW, NCAC II, CDC III, SAP and Mita M. Johnson, EdD, LAC, MAC, SAP, CTHP-II

www.naadac.org/webinars NAADAC, the Association for Addiction Professionals 151

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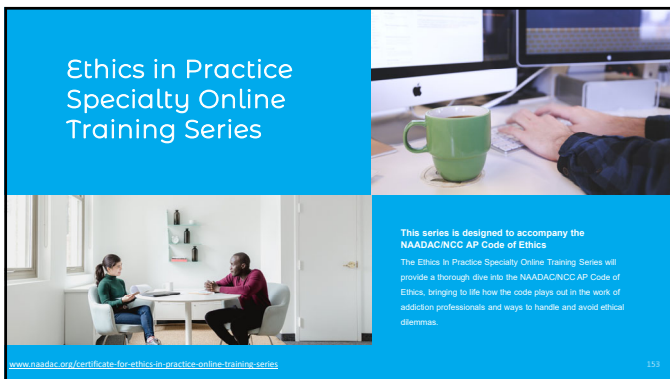


Wellness and Recovery in the Addiction Profession
 Specialty Online Training Series

NAADAC is proud to present the specialty online training series *Wellness and Recovery in the Addiction Profession*. Upon completion of the six-part training series, participants may apply for the *Certificate of Achievement for Wellness and Recovery in the Addiction Profession*.

www.naadac.org/certificate-for-wellness-and-recovery-online-training-series 152

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Ethics in Practice Specialty Online Training Series

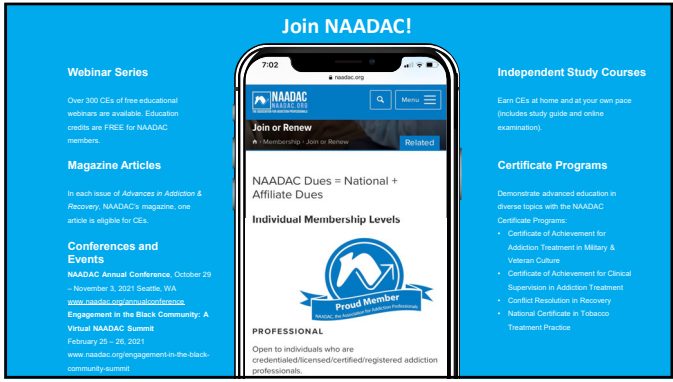
This series is designed to accompany the NAADAC/NCC AP Code of Ethics. The Ethics In Practice Specialty Online Training Series will provide a thorough dive into the NAADAC/NCC AP Code of Ethics, bringing to life how the code plays out in the work of addiction professionals and ways to handle and avoid ethical dilemmas.

www.naadac.org/certificate-for-ethics-in-practice-online-training-series 153

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