Neurology, Immunology, and Microbiology of Addiction/Substance Use Disorders

Heather Zwickey, PhD

Disclosures

Role	Company
Director of Communication and Innovation	Thaena, Inc.
Professor/Faculty	National University of Natural Medicine University of Western States Academy of Integrative Health and Medicine
Scientific Advisory Board	Burt's Bees
Scientific Advisory Board	Clorox
Wellness Advisory Board	GSK
Speaker	Metagenics Institute
Researcher/Principal Investigator	National Center for Complementary and Integrative Health

Goals for this lecture

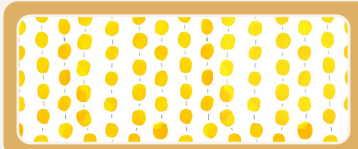
- Compare underlying mechanisms of addictions
- Discuss how the nervous system, immune system, and microbiome interact during addiction
- Recognize brain imaging vs neurotransmitter patterns in addiction
- Discuss the link between emotion and addictive substance use

Why Addictions?

Drug use is at an all time high

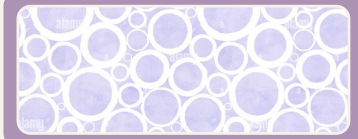
- Drug popularity differs from nation to nation

Genetic, physiological, and environmental influences



Substance Use Disorders

- Opiates, cannabis, cocaine, amphetamines, and other narcotics



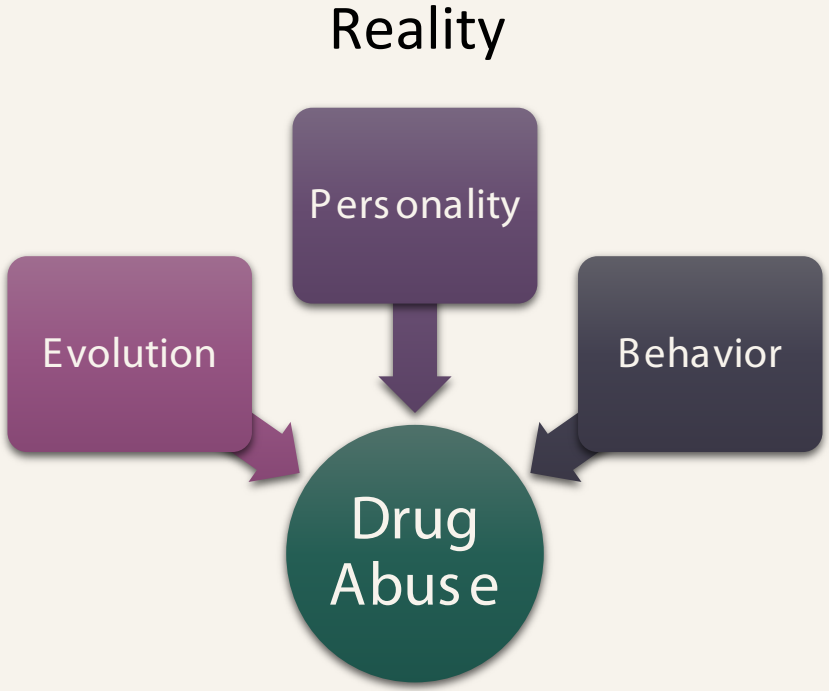
Caffeine, food/sugar, gambling, sex

Have we always had addictions?

Saah, T. The evolutionary origins and significance of drug addiction. Harm Reduct J 2, 8 (2005). https://doi.org/10.1186/1477-7517-2-8

Uncover the underlying causes

"Too often the treatment of addiction simply works to alleviate the symptoms of addiction, dealing with overcoming the physiological dependence and working through withdrawal symptoms as the body readjusts to a non-dependent state of homeostasis."



Saah, T. The evolutionary origins and significance of drug addiction. Harm Reduct J 2, 8 (2005). https://doi.org/10.1186/1477-7517-2-8

Evolution - History

Limited resources – no need for adaptive development or regulatory systems

We relied on limitations in the environment

We have no internal control.

Saah, T. The evolutionary origins and significance of drug addiction. Harm Reduct J 2, 8 (2005). https://doi.org/10.1186/1477-7517-2-8

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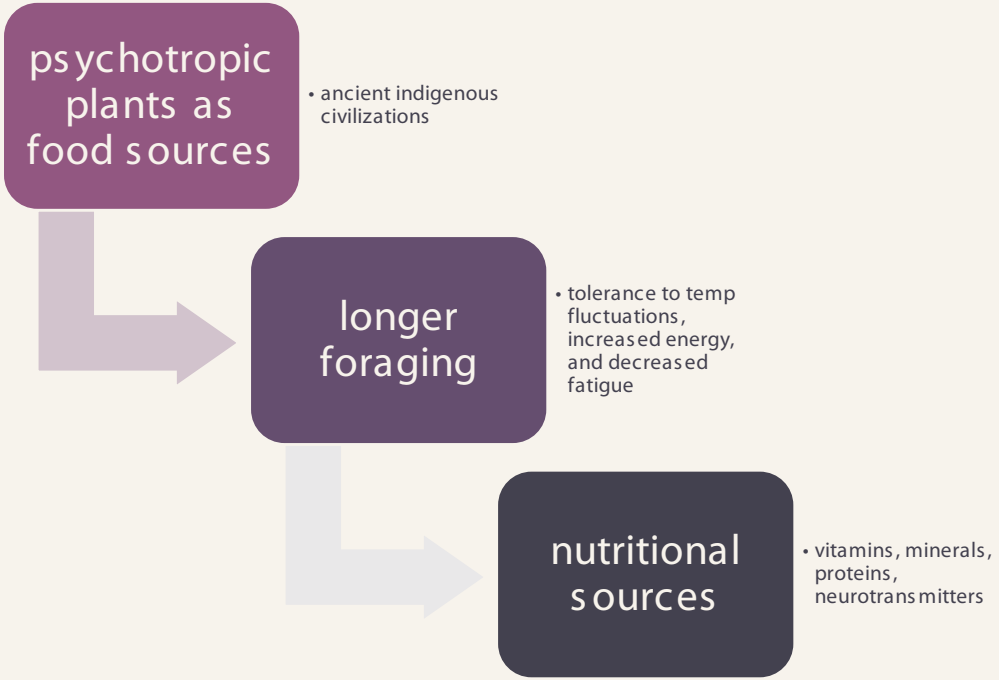
Evolution – History: Psychotropic plants contributed to human fitness



Saah, T. The evolutionary origins and significance of drug addiction. Harm Reduct J 2, 8 (2005). https://doi.org/10.1186/1477-7517-2-8

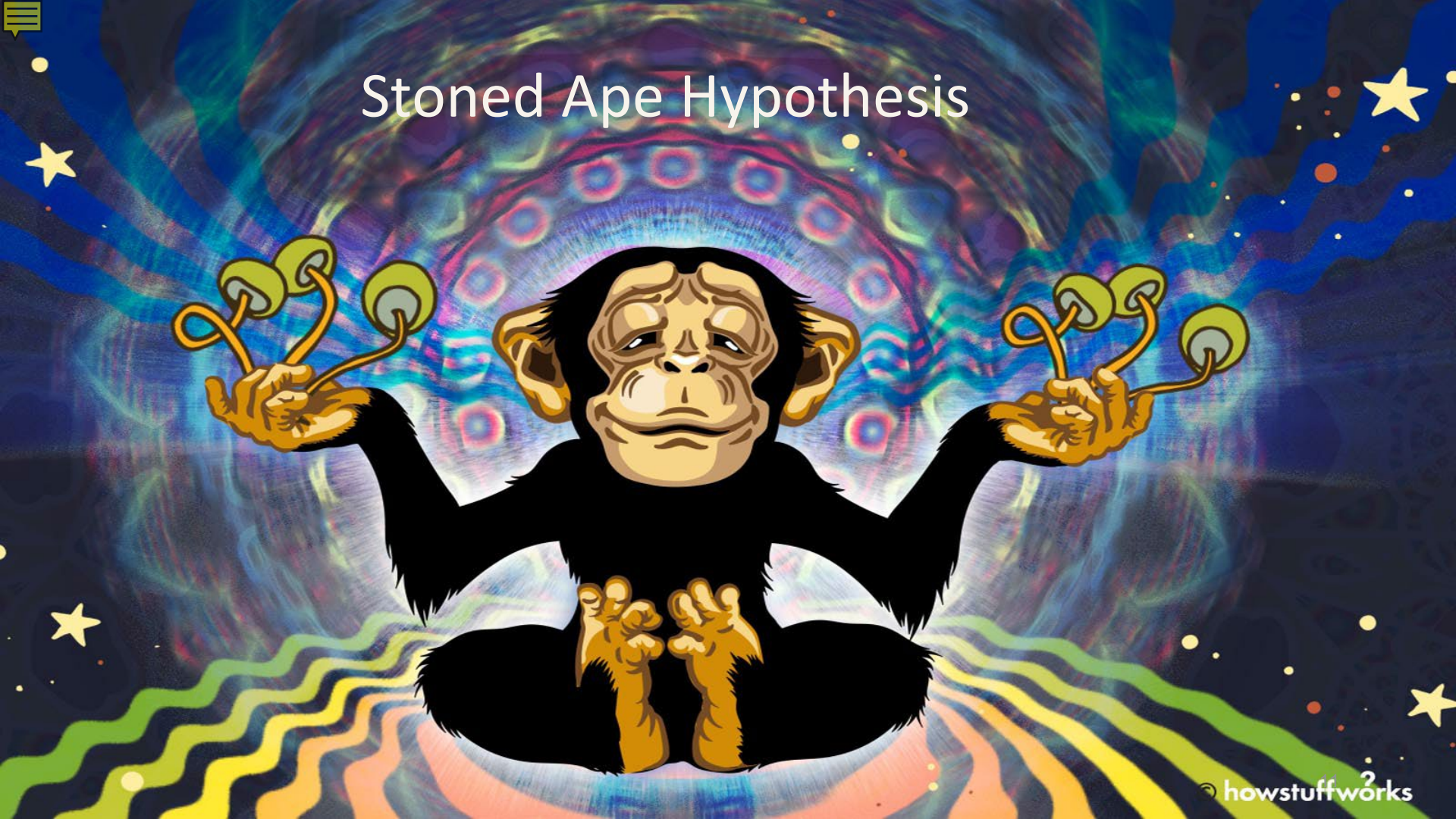
Co-evolution

Mammalian exposure to psychotropics

Series of changes occurred between the mammalian brain and psychotropic plants allowing them affect one another during their processes of evolving

Saah, T. The evolutionary origins and significance of drug addiction. Harm Reduct J 2, 8 (2005). https://doi.org/10.1186/1477-7517-2-8

Stoned Ape Hypothesis



Traditional tea that has a core psychoactive chemical of DMT

Synthetic drug derived from fungus found on grains, also known as acid

Natural substance produced by multiple plants, animals, and even humans

A synthetic drug also known as ecstasy

(PEYOTE) Natural substance that comes from the peyote cactus and can also be synthetically manufactured

Synthetic drug commonly used for anesthesia and procedural sedation

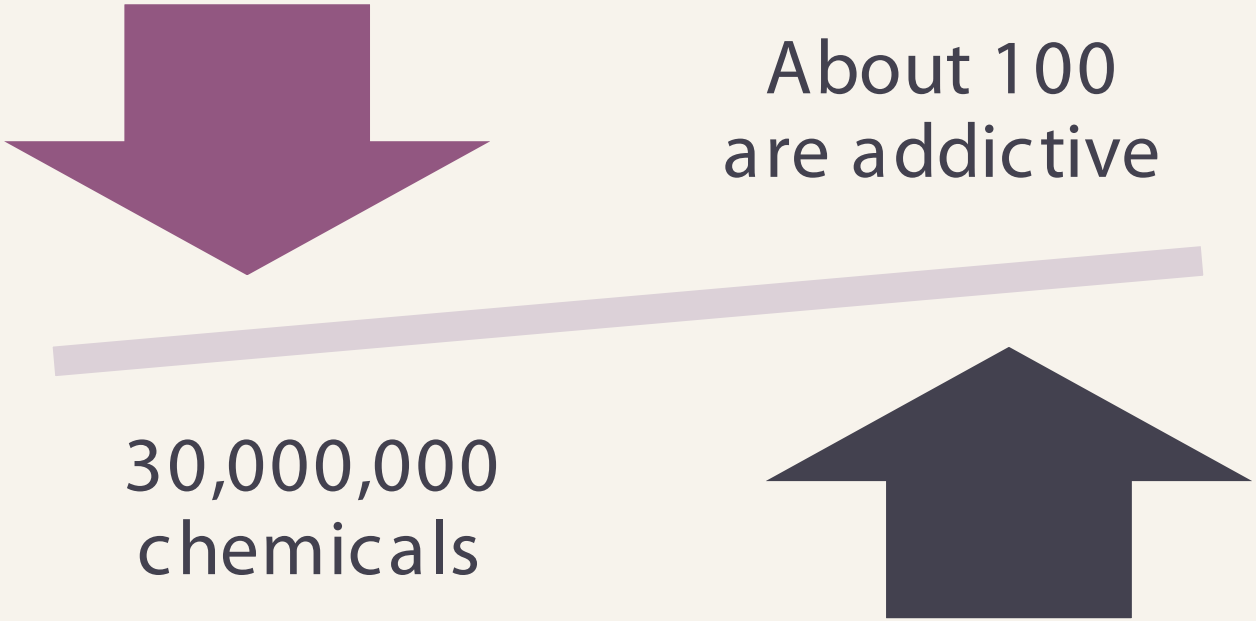
Natural substance derived from the tabernanthe iboga plant

Natural substance produced by more than 100 species of mushrooms

Part 1

Underlying mechanisms of addictions

Relatively few chemicals are addictive



Gardner EL. Addiction and brain reward and antireward pathways. Adv Psychosom Med. 2011;30:22-60. doi: 10.1159/000324065. Epub 2011 Apr 19. PMID: 21508625; PMCID: PMC4549070.

Why are certain chemicals addictive?

Sedatives

- barbiturates, ethanol, opiates, and benzodiazepines

Stimulants

- nicotine, cocaine, and the amphetamines

Anti-nociceptive

- cannabis, opioids

Gardner EL. Addiction and brain reward and antireward pathways. Adv Psychosom Med. 2011;30:22-60. doi: 10.1159/000324065. Epub 2011 Apr 19. PMID: 21508625; PMCID: PMC4549070.

Why are certain chemicals addictive?

All addictive drugs are subjectively rewarding, reinforcing, and pleasurable.

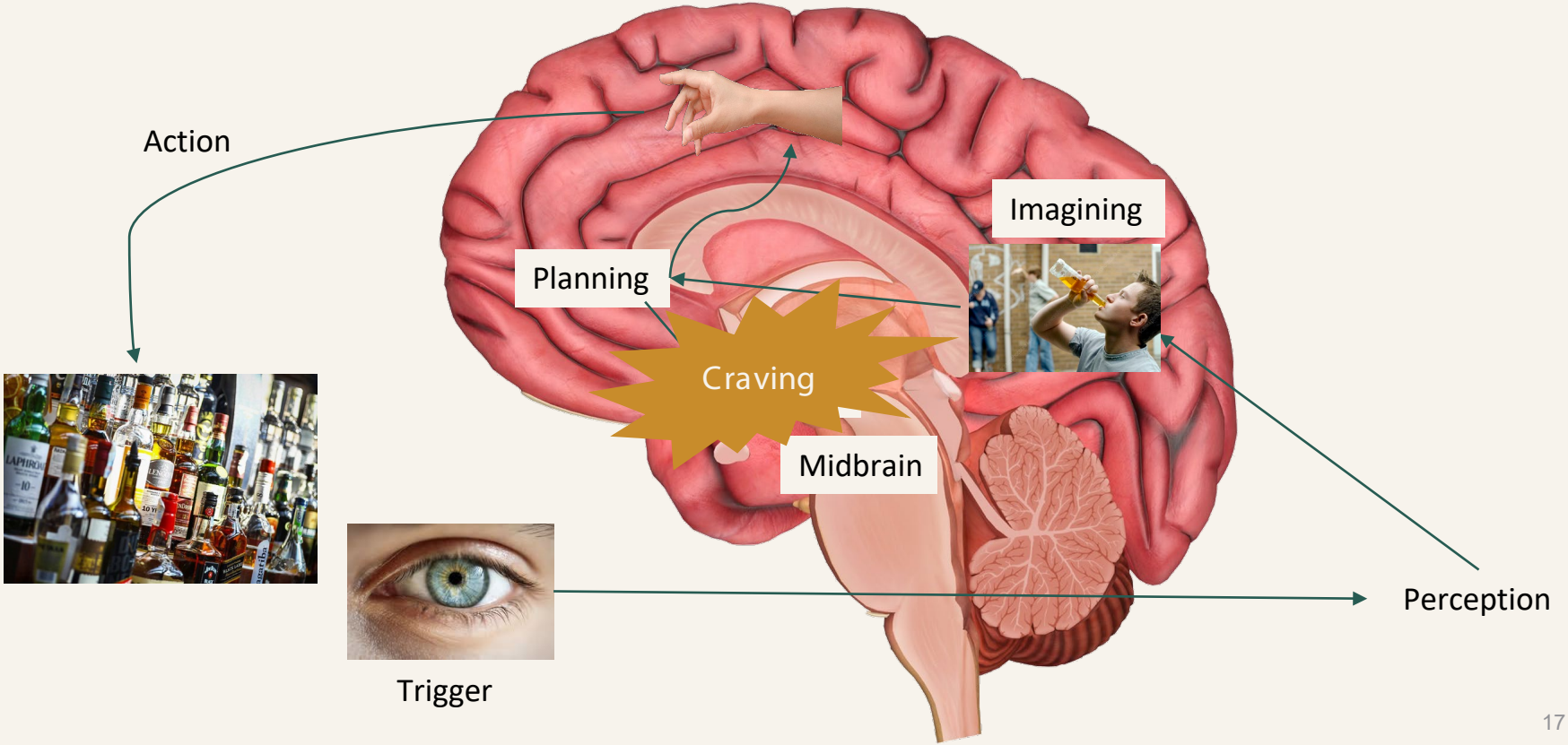
Laboratory animals and humans volitionally self-administer them

- The rank order of appetitiveness in animals parallels the rank order of appetitiveness in humans

All addictive drugs activate the reward circuitry of the brain

- Exceptions: LSD and mescaline

Visual – brain activation in alcohol addiction

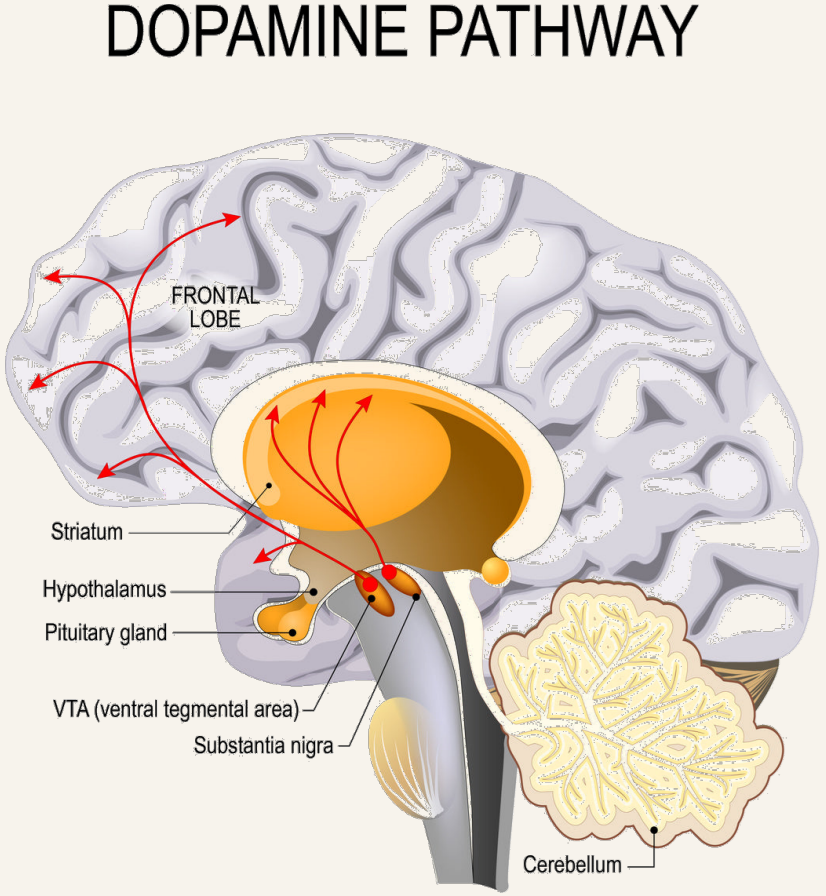


Brain reward circuit

1. The first link is the descending myelinated fiber tract
    Glutamate may play a role in the ventral tegmental area might play a role
2. The second link is the ascending fiber tract from ventral tegmental area to nucleus accumbens, with dopamine as its neurotransmitter
3. The third link is the projection from nucleus accumbens to ventral pallidum, using gamma-aminobutyric acid (GABA), Substance P, and enkephalin as conjoint neurotransmitters

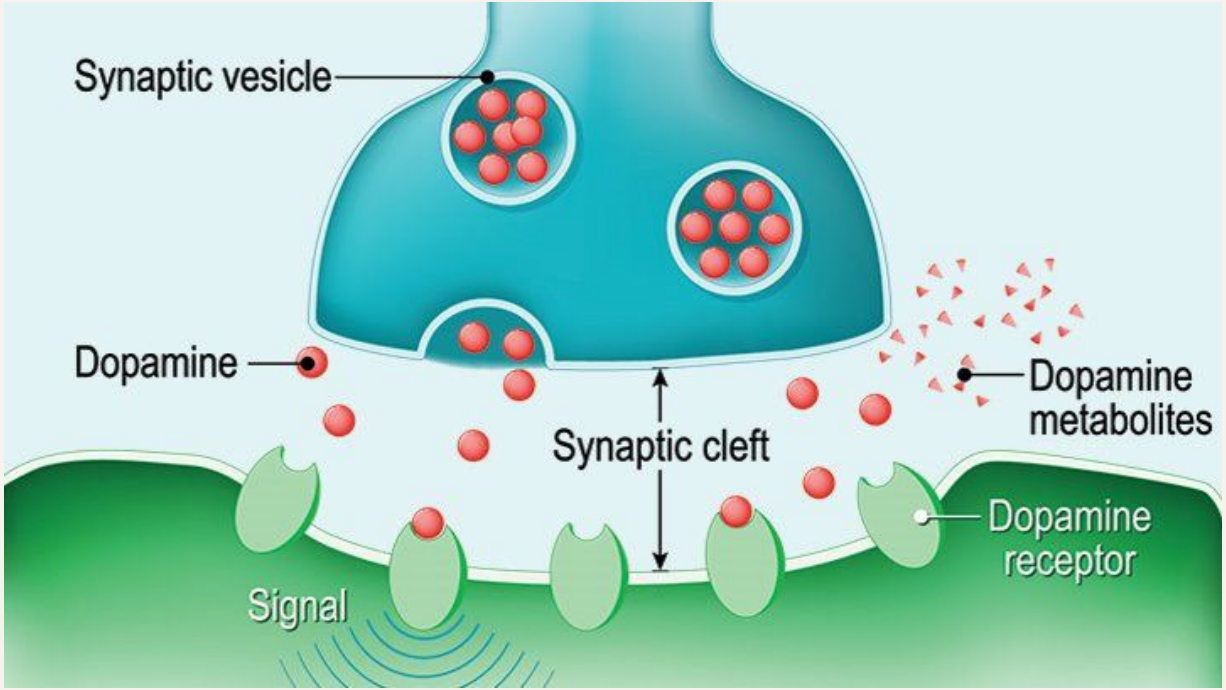
Dopamine

- Reward pathway mediated by dopamine
- Often referred to as “dopamine reward system”
- Nucleus accumbens is the part of the brain is what gives us our sense of reward

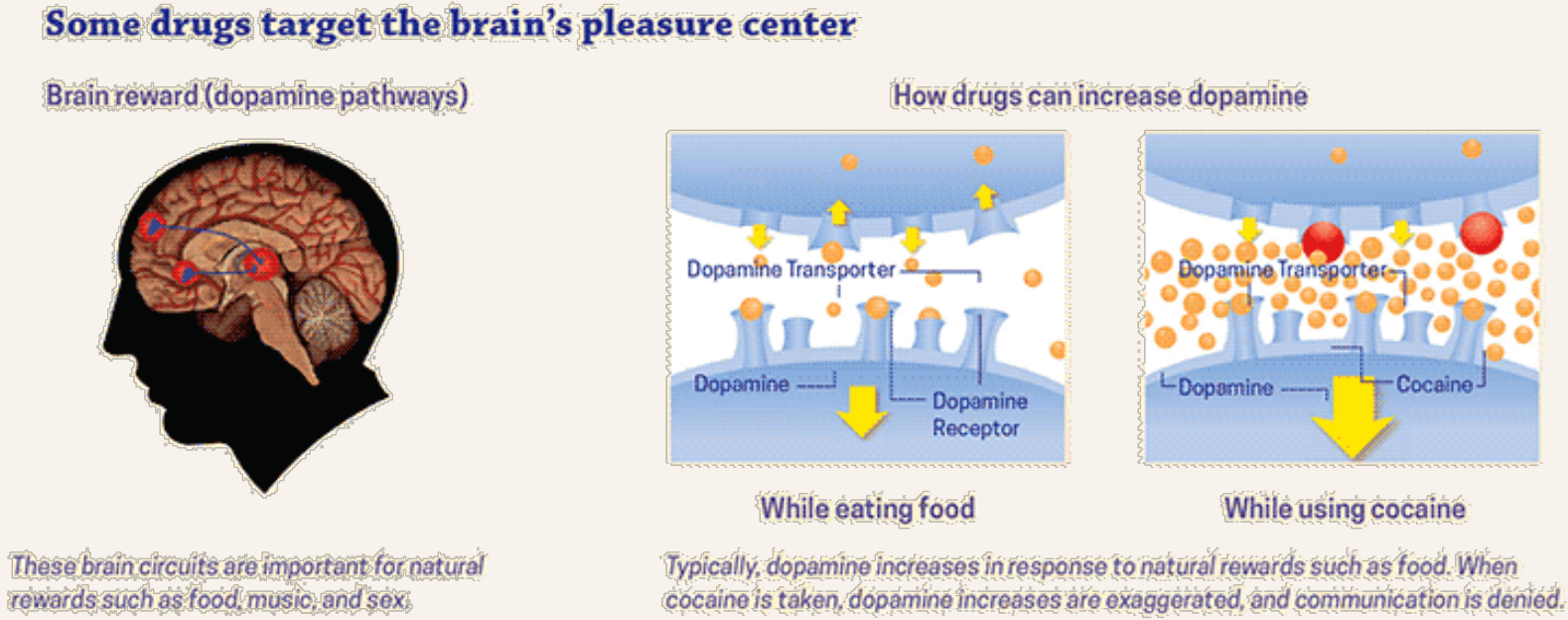


Reward

Dopamine signaling

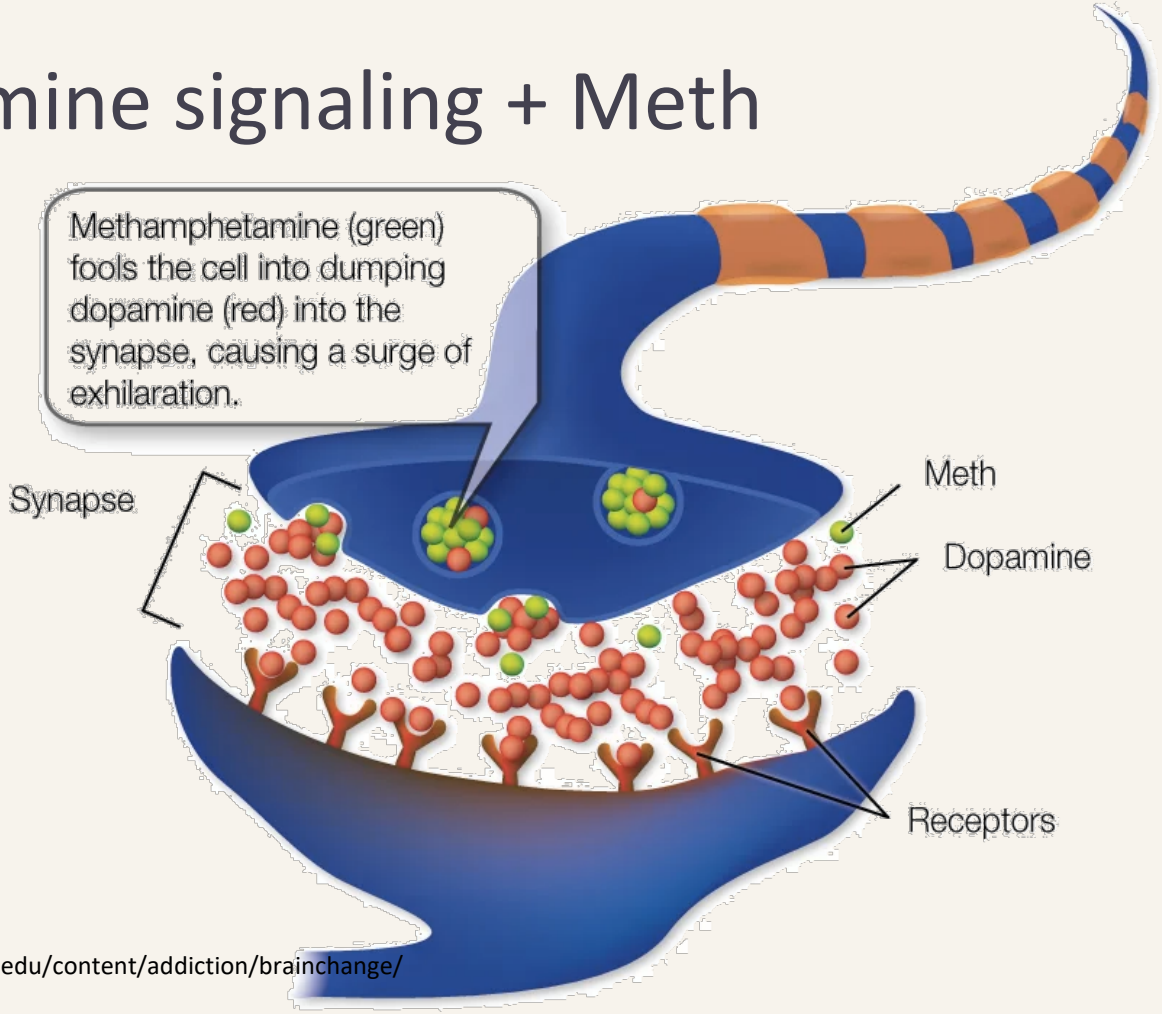


Dopamine signaling + Cocaine



https://nida.nih.gov/publications/drugs-brains-behavior-science-addiction/drugs-brain

Dopamine signaling + Meth



https://learn.genetics.utah.edu/content/addiction/brainchange/

Different substances/different parts of the pathway

Nucleus accumbens

- amphetamine
- cocaine
- opiates
- THC
- phencyclidine
- ketamine
- nicotine

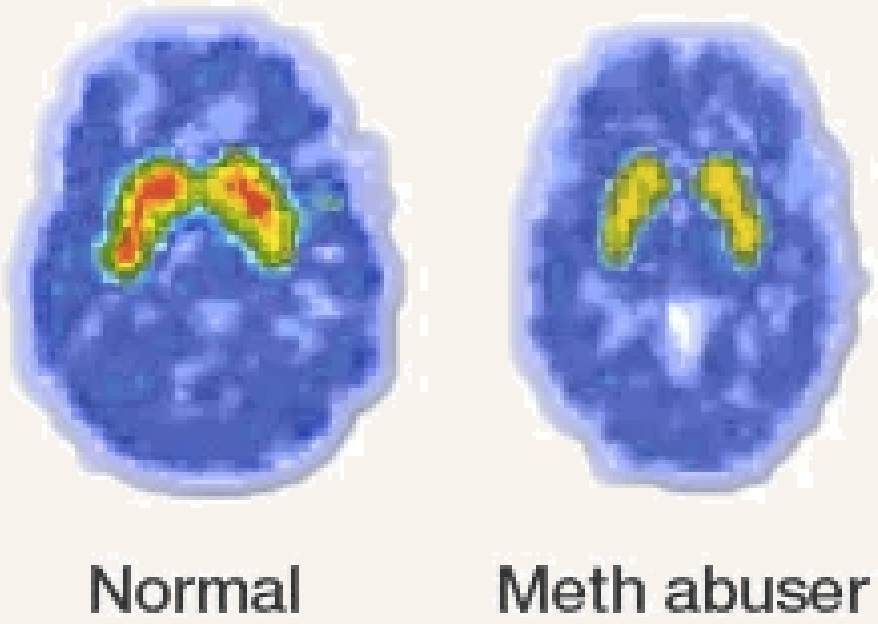
Ventral tegmental area

- opiates
- alcohol
- barbiturates
- benzodiazapines

Dopamine receptors

Dopamine receptors				
D1-like - Gαs coupled		**D2-like** - Gαi/o coupled		
D1	**D5**	**D2**	**D3**	**D4**
Substantia nigra Nucleus accumbens Olfactory bulb Lower levels: Cerebellum Hippocampus Thalamus Kidney	Substantia nigra Hypothalamus Kidney Heart Sympathetic ganglia	Substantia nigra Nucleus accumbens Ventral tegemental area Lower levels: Heart Blood vessels Adrenal glands Sympathetic ganglia	Olfactory bulb Nucleus accumbens	Heart Blood vessels Substantia nigra Hippocampus Amygdala Gastrointestinal tract

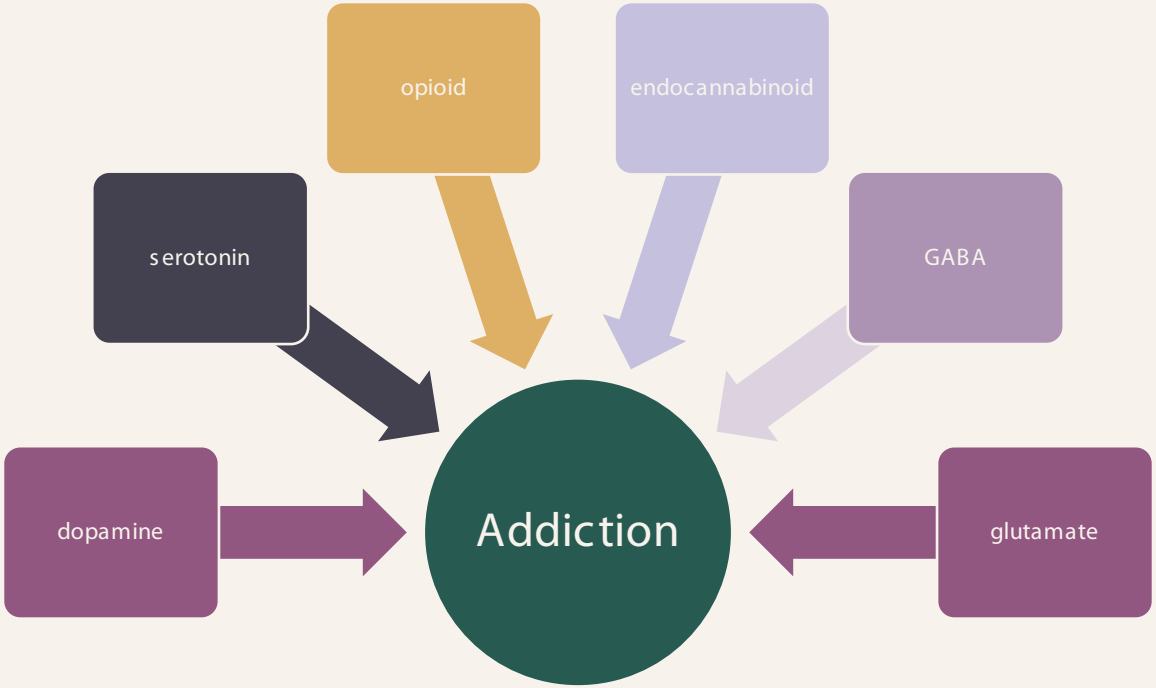
Dopamine receptors in addiction



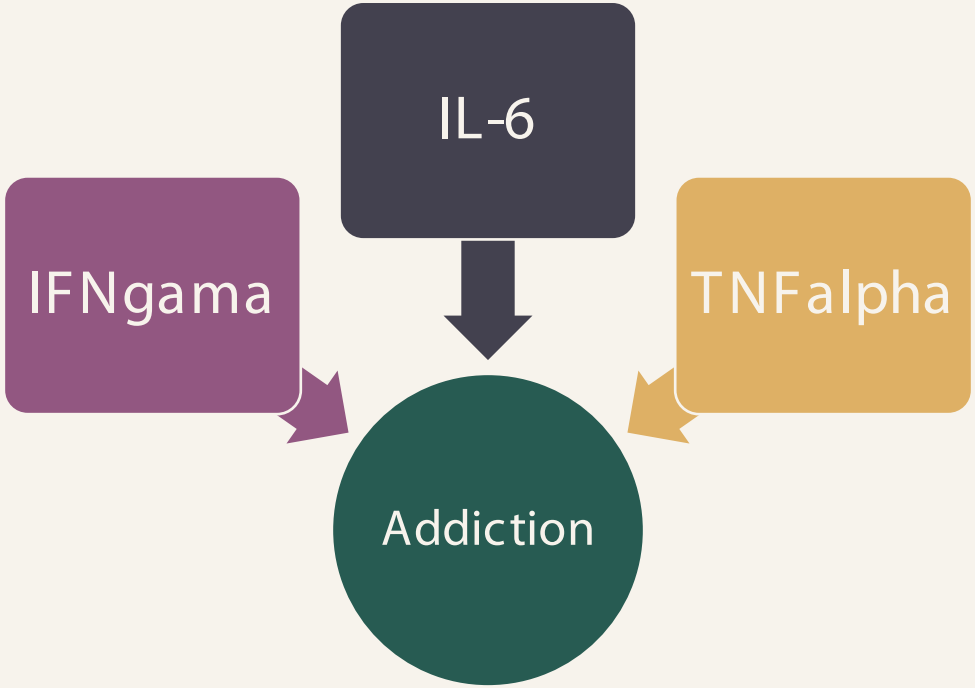
Part 2

How the nervous system, immune system, and microbiome interact during addiction

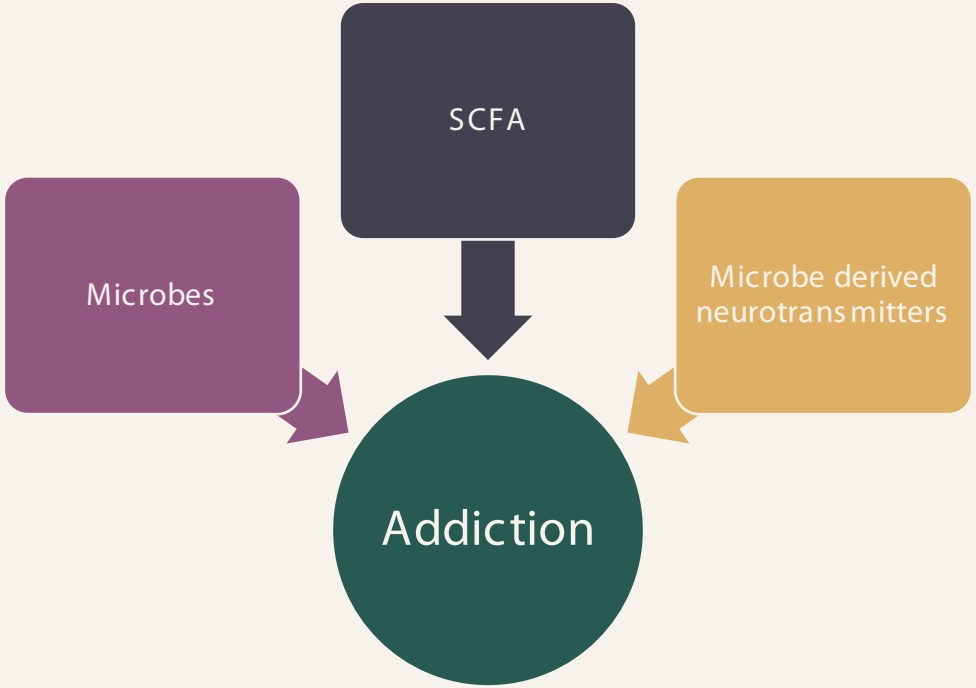
Dopamine plus…

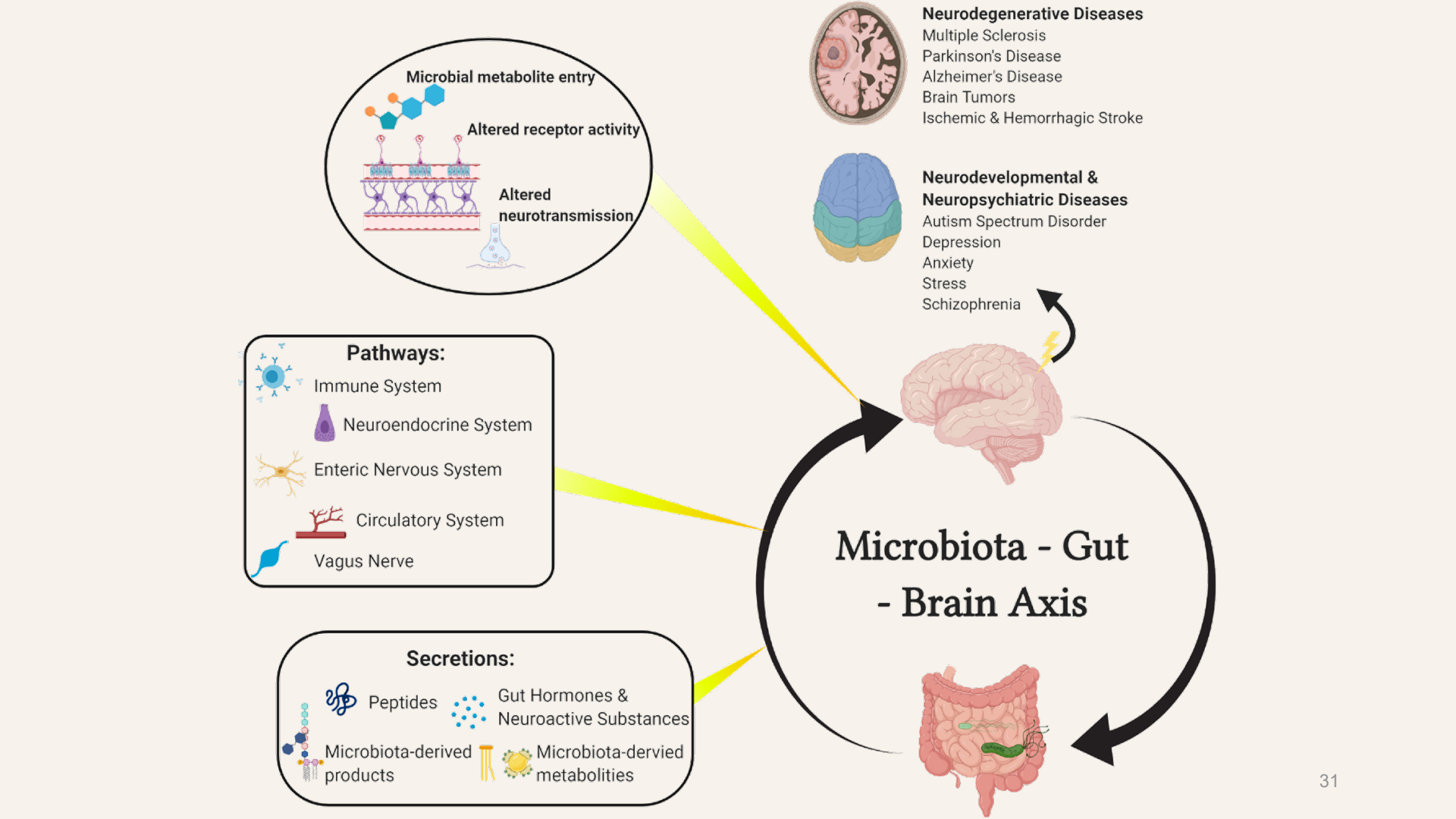


Dopamine plus…

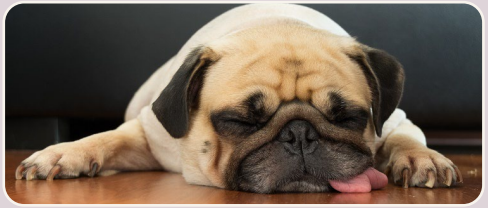


Dopamine plus…




Microbial metabolite entry
Altered receptor activity
Altered neurotransmission
Neurodegenerative Diseases
Multiple Sclerosis
Parkinson's Disease
Alzheimer's Disease
Brain Tumors
Ischemic & Hemorrhagic Stroke
Neurodevelopmental & Neuropsychiatric Diseases
Autism Spectrum Disorder
Depression
Anxiety
Stress
Schizophrenia
Pathways:
Immune System
Neuroendocrine System
Enteric Nervous System
Circulatory System
Vagus Nerve
Microbiota - Gut - Brain Axis
Secretions:
Peptides
Gut Hormones & Neuroactive Substances
Microbiota-derived products
Microbiota-dervied metabolities

Behavioral Symptoms of Inflammatory Cytokines



IL-1

Malaise, fatigue, depression

IL-6

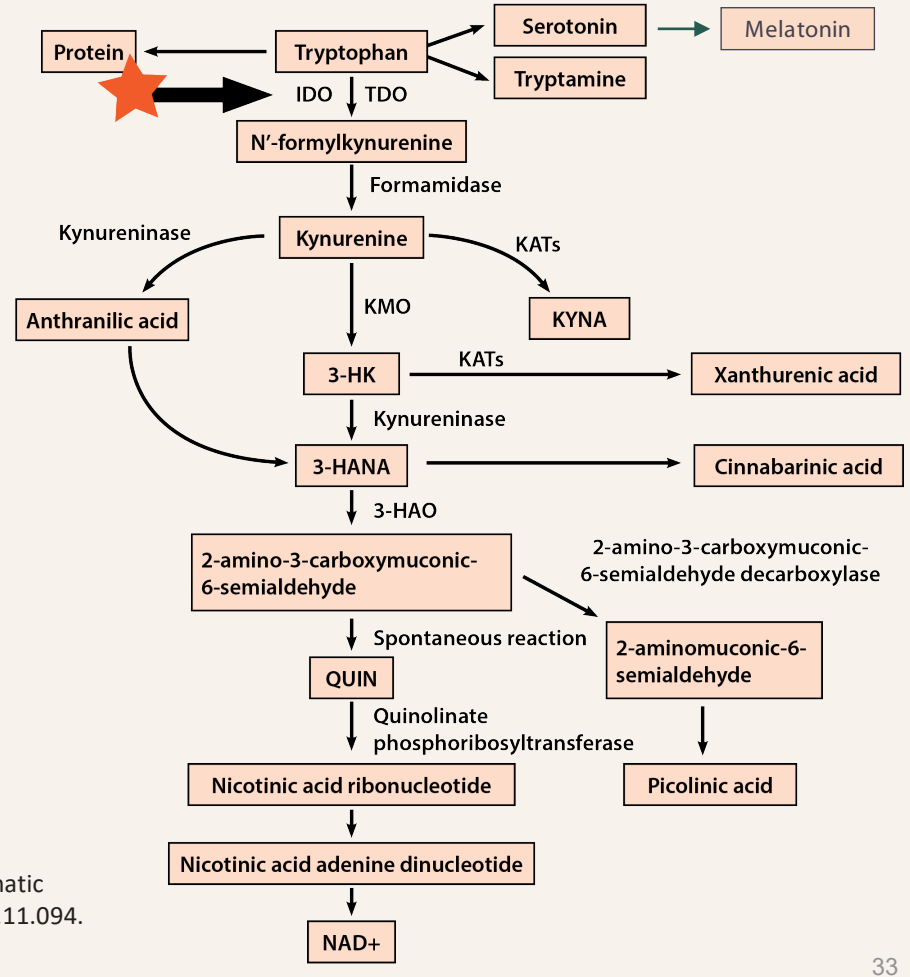
Anxiety, fatigue, pain

TNF

Hostility, pain

The Biochemistry

IL-6 increases expression of IDO, which shuttles tryptophan away from serotonin and toward QUIN



Quagliato LA, Nardi AE. Cytokine alterations in panic disorder: A systematic review. J Affect Disord. 2018 Mar 1;228:91-96. doi: 10.1016/j.jad.2017.11.094. Epub 2017 Dec 7. PMID: 29241050.

Behavioral Symptoms of IFNgamma

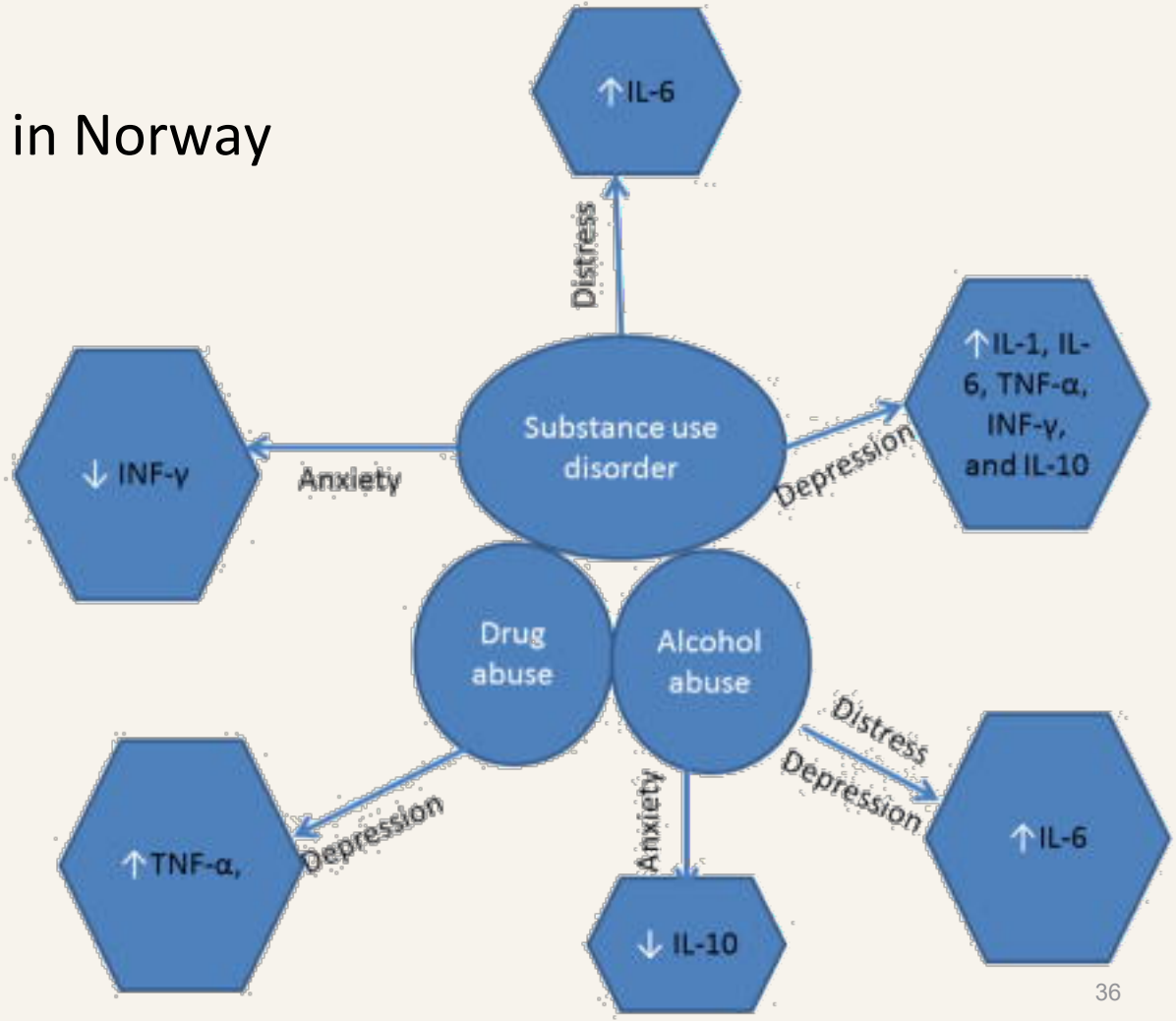
IFNgamma

Filiano AJ, Xu Y, Tustison NJ, Marsh RL, Baker W, Smirnov I, Overall CC, Gadani SP, Turner SD, Weng Z, Peerzade SN, Chen H, Lee KS, Scott MM, Beenhakker MP, Litvak V, Kipnis J. Unexpected role of interferon-γ in regulating neuronal connectivity and social behaviour. Nature. 2016 Jul 21;535(7612):425-9. doi: 10.1038/nature18626. Epub 2016 Jul 13. PMID: 27409813; PMCID: PMC4961620.

Behavioral Symptoms of TGFbeta

Zhang K, Yang C, Chang L, et al. Essential role of microglial transforming growth factor-β1 in antidepressant actions of (R)-ketamine and the novel antidepressant TGF-β1. *Transl Psychiatry*. 2020;10(1):32. Published 2020 Jan 27. doi:10.1038/s41398-020-0733-x

80 people with SUD in Norway



Martinez P, Lien L, Zemore S, Bramness JG, Neupane SP. Circulating cytokine levels are associated with symptoms of depression and anxiety among people with alcohol and drug use disorders. J Neuroimmunol. 2018 May 15;318:80-86. doi: 10.1016/j.jneuroim.2018.02.011. Epub 2018 Feb 22. PMID: 29500107; PMCID: PMC5880738.

Neurotransmitters and Mood/Behavior

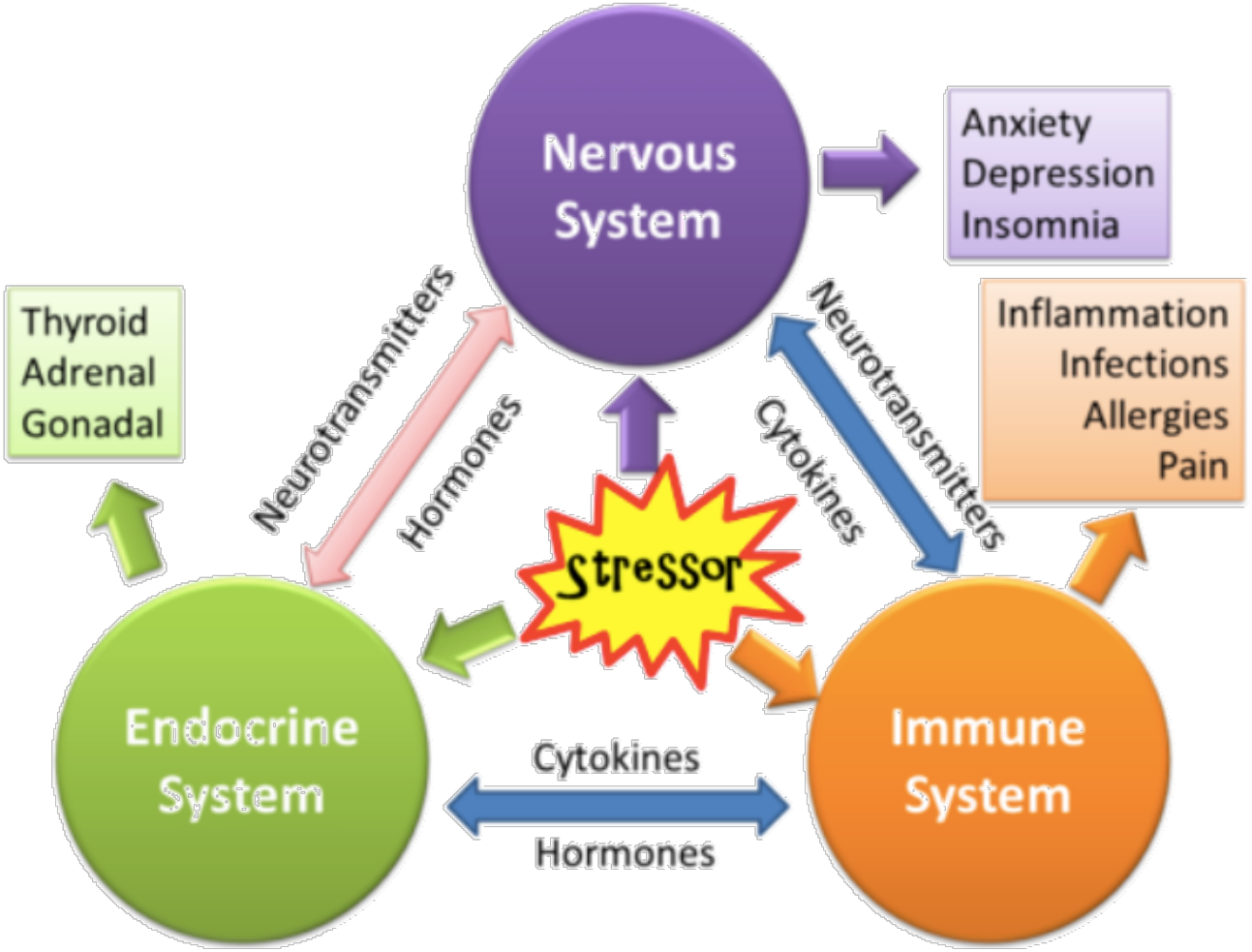
Dopamine	Serotonin	GABA	Acetylcholine
• Reward • Positive effect • Extraversion	• Happiness • Motivation • Calm	• Relaxation • Focus • Sleep	• Calm • Anxiety regulation

Dfarhud D, Malmir M, Khanahmadi M. Happiness & Health: The Biological Factors- Systematic Review Article. Iran J Public Health. 2014;43(11):1468-1477.

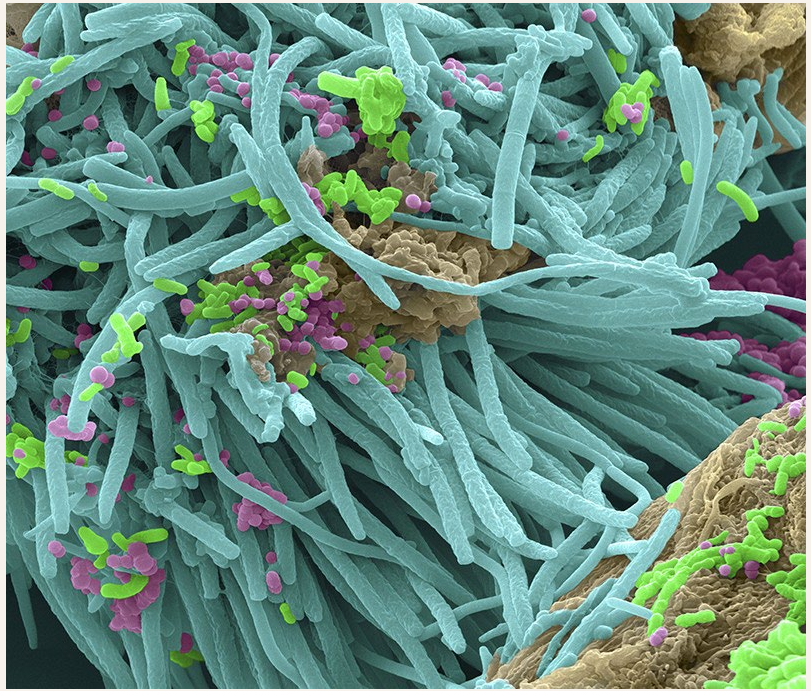
Neurotransmitters, Cytokines and Mood/Behavior

Putting the pieces together – No studies demonstrating this yet

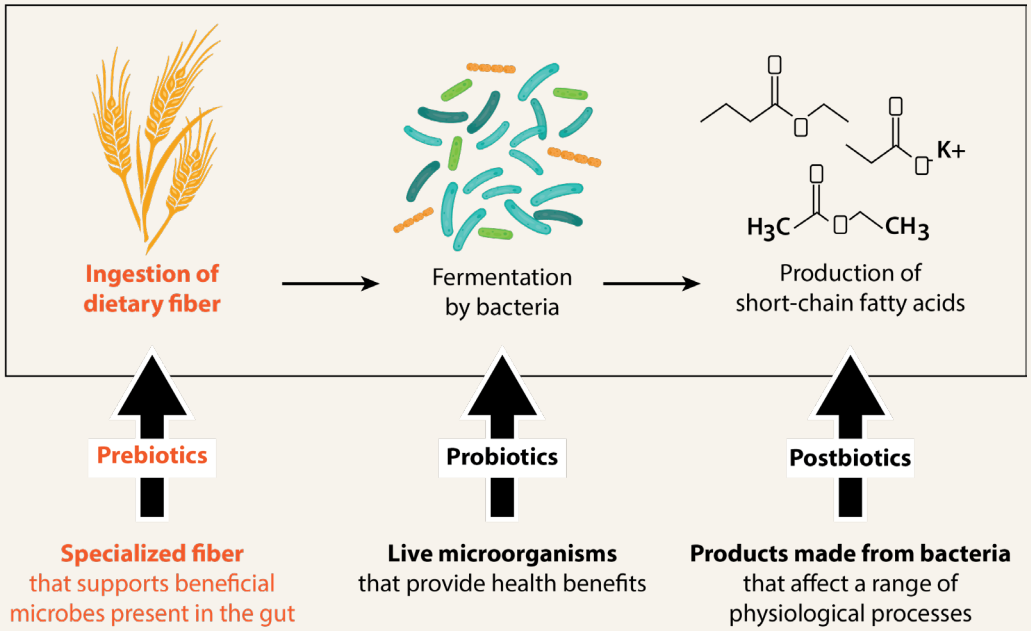
Extraversion	Happiness	Relaxation	Calm
• Dopamine	• Serotonin	• GABA	• Acetylcholine
Higher IFNgamma	Low IL-1, IL-6	Higher TGFbeta	Unknown


Nervous System
Anxiety
Depression
Insomnia
Thyroid
Adrenal
Gonadal
Neurotransmitters
Hormones
Cytokines
Neurotransmitters
Inflammation
Infections
Allergies
Pain
Stressor
Endocrine System
Cytokines
Hormones
Immune System

Bringing in the microbes



Fermentation of non-digestible fibers → SCFA



What are some of the metabolites/ postbiotics produced by the gut microbiome?

Examples of products of gut microbial fermentation of carbohydrates, protein, and dietary polyphenols

Acetate	Propionate	Butyrate
Short-chain fatty acids and branched-chain fatty acids	Kyneurenines	Indoles
Indole derivatives	Tryptamine	Serotonin
Histamine	Dopamine	p Cresol
Phenylacetyl glutamine	Imidazole propionate	Succinate

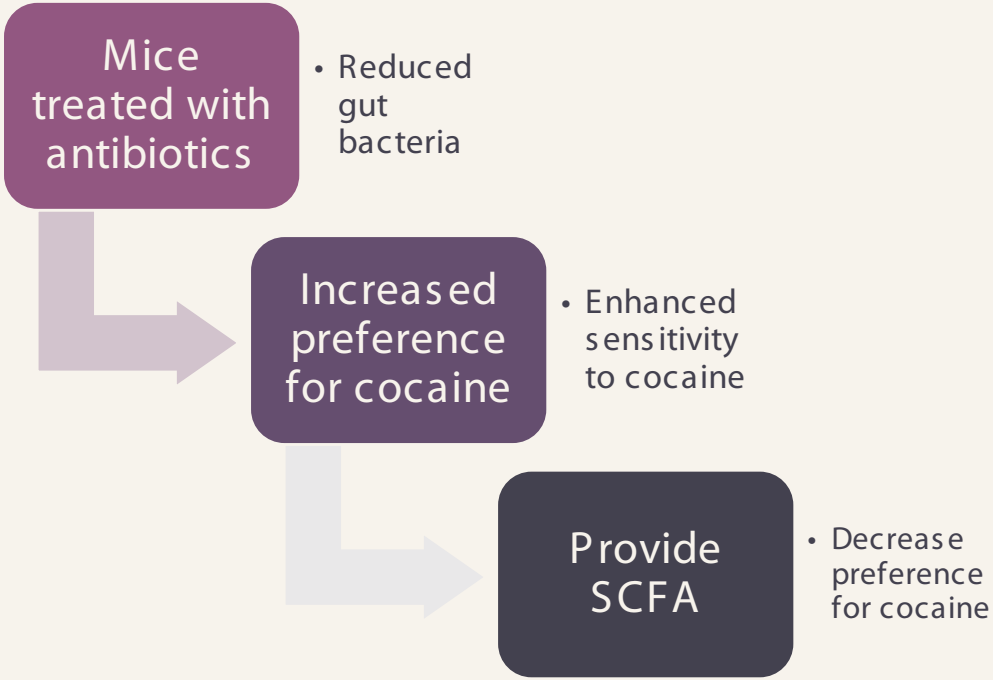
Krautkramer KA, Fan J, Bäckhed F. Gut microbial metabolites as multi-kingdom intermediates. Nat Rev Microbiol. 2021 Feb;19(2):77-94. doi: 10.1038/s41579-020-0438-4. Epub 2020 Sep 23. PMID: 32968241.

Microbes produce neurotransmitters

Neurotransmitter	Microbial Species
GABA	Lactobacillus & Bifidobacterium
Noradrenalin	Escherichia, Bacillus, and Saccharomyces
Serotonin	Candida, Streptococcus, and Escherichia, and Enterococcus
Dopamine	Bacillus
Acetylcholine	Lactobacillus

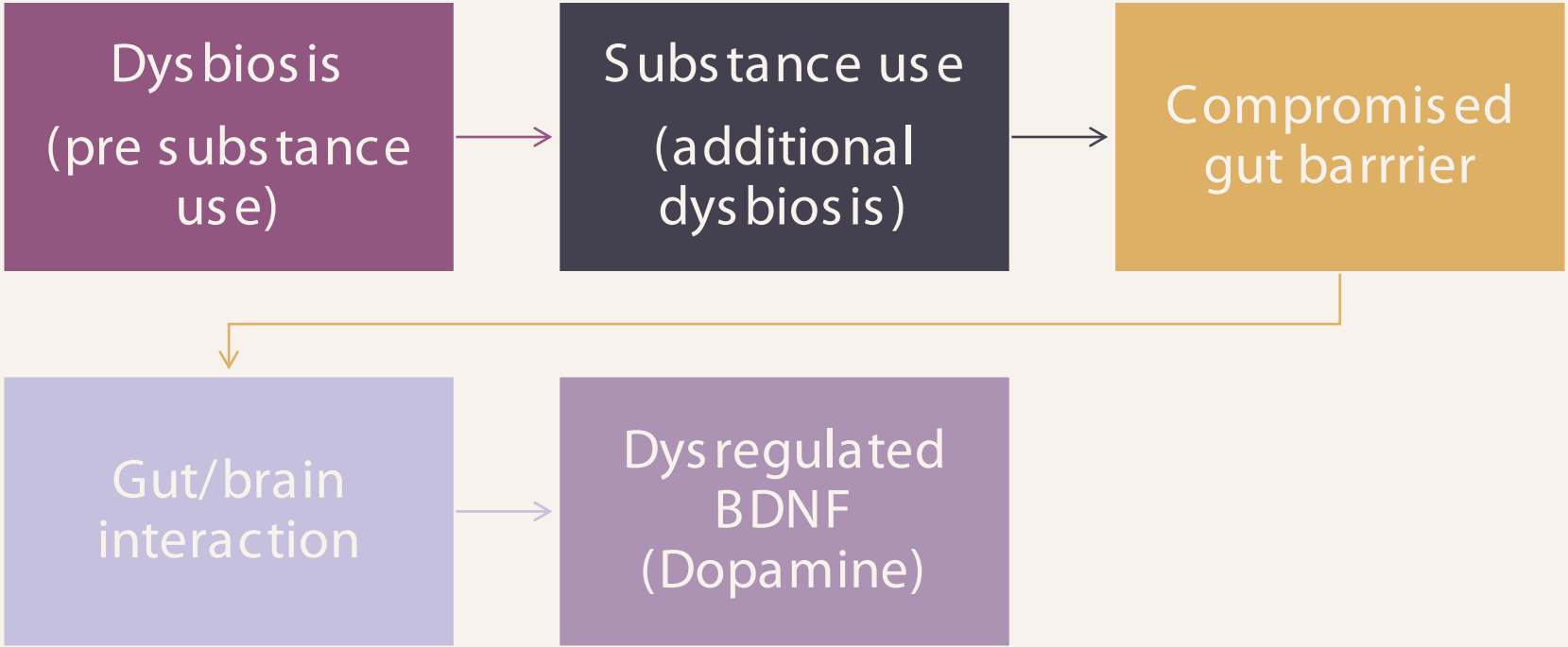
Cenit MC, Sanz Y, Codoñer-Franch P. Influence of gut microbiota on neuropsychiatric disorders. World J Gastroenterol. 2017 Aug 14;23(30):5486-5498. doi: 10.3748/wjg.v23.i30.5486. PMID: 28852308; PMCID: PMC5558112.

SCFA and addiction

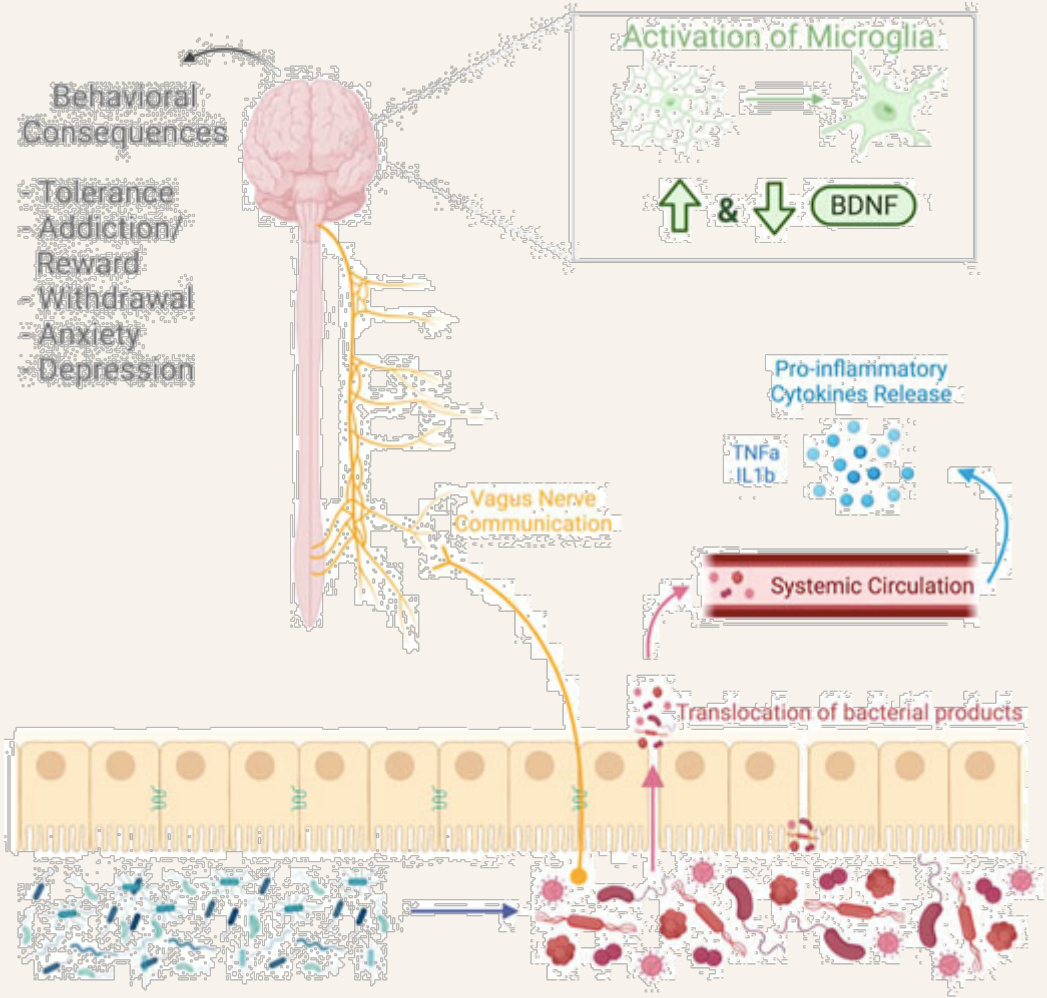


Kiraly DD, Walker DM, Calipari ES, Labonte B, Issler O, Pena CJ, Ribeiro EA, Russo SJ, Nestler EJ. Alterations of the Host Microbiome Affect Behavioral Responses to Cocaine. Sci Rep. 2016 Oct 18;6:35455. doi: 10.1038/srep35455. PMID: 27752130; PMCID: PMC5067576.

Microbiome and Substance Use



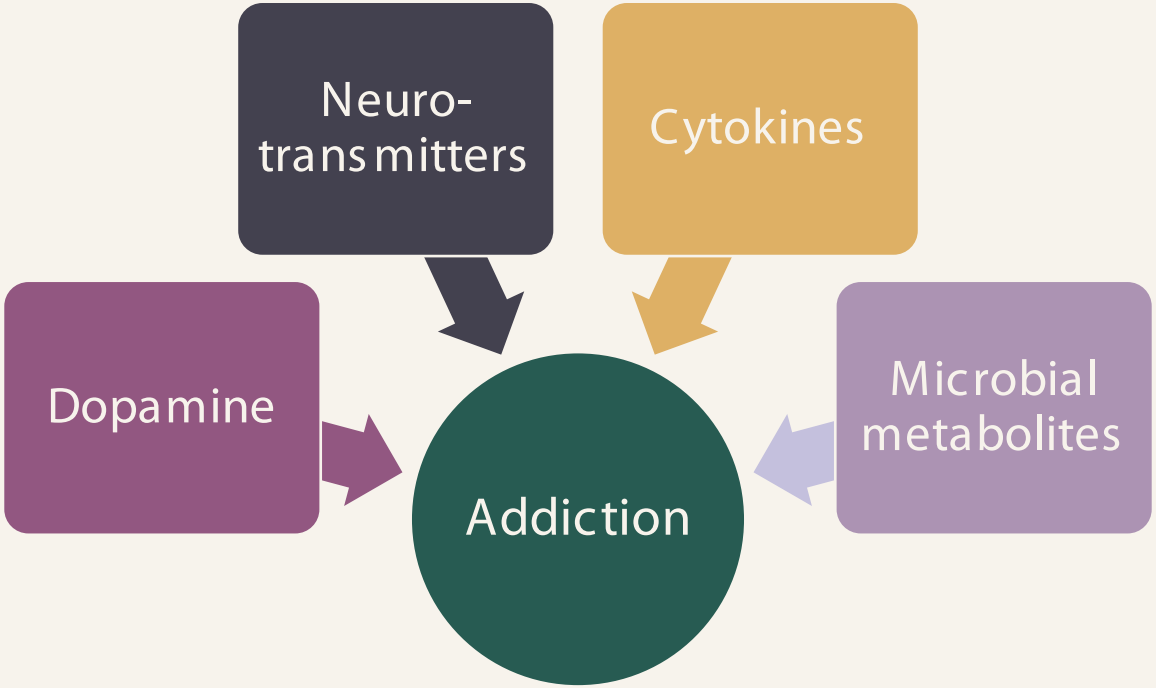
Herlihy B and Roy S (2022) Gut-Microbiome Implications in Opioid Use Disorder and Related Behaviors. *Adv. Drug. Alco. Res.* 2:10311. doi: 10.3389/adar.2022.10311



Dysbiosis of Microbiome

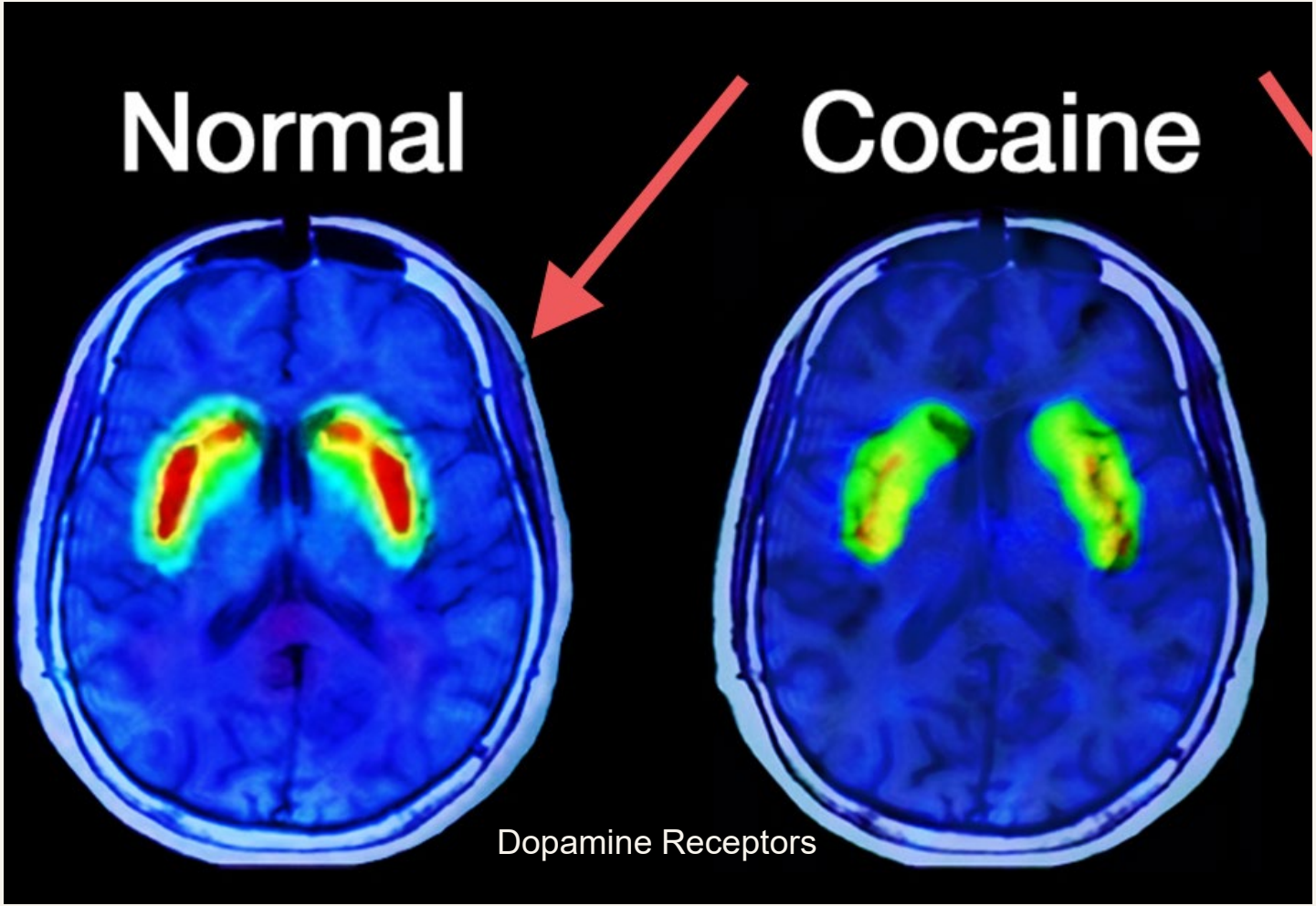
Herlihy B and Roy S (2022) Gut-Microbiome Implications in Opioid Use Disorder and Related Behaviors. *Adv. Drug. Alco. Res.* 2:10311. doi: 10.3389/adar.2022.10311

Summary so far…

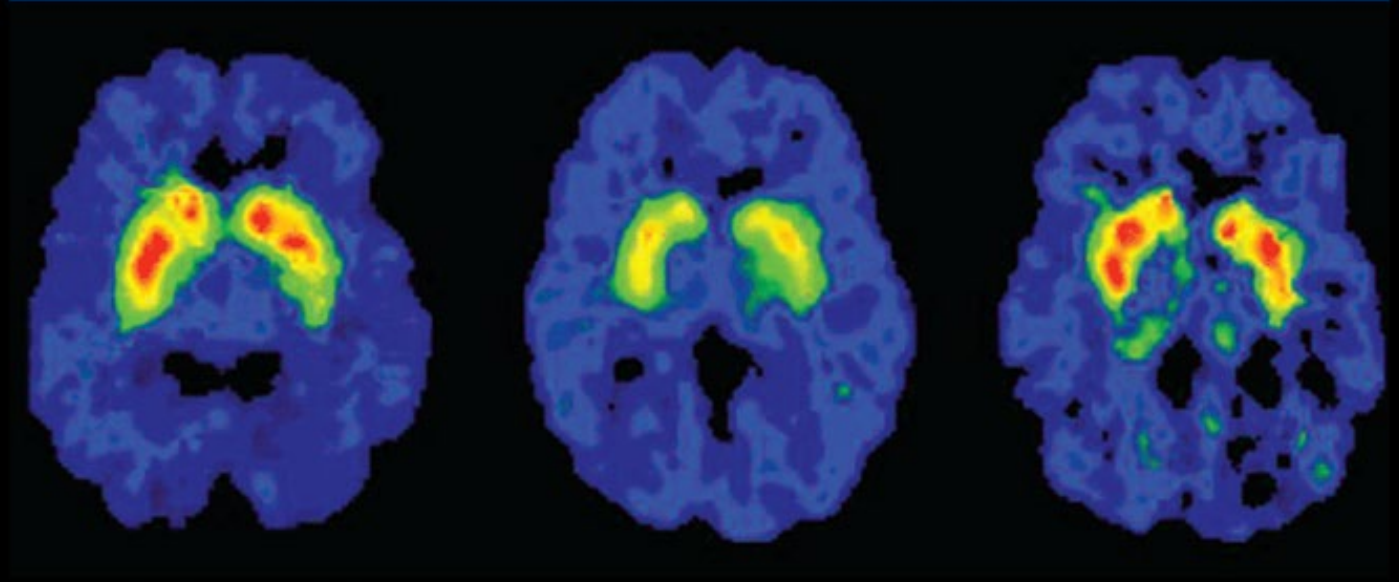


Part 3

Brain imaging vs neurotransmitter patterns in addiction


Normal
Cocaine
Dopamine Receptors

BRAIN RECOVERY WITH PROLONGED ABSTINENCE

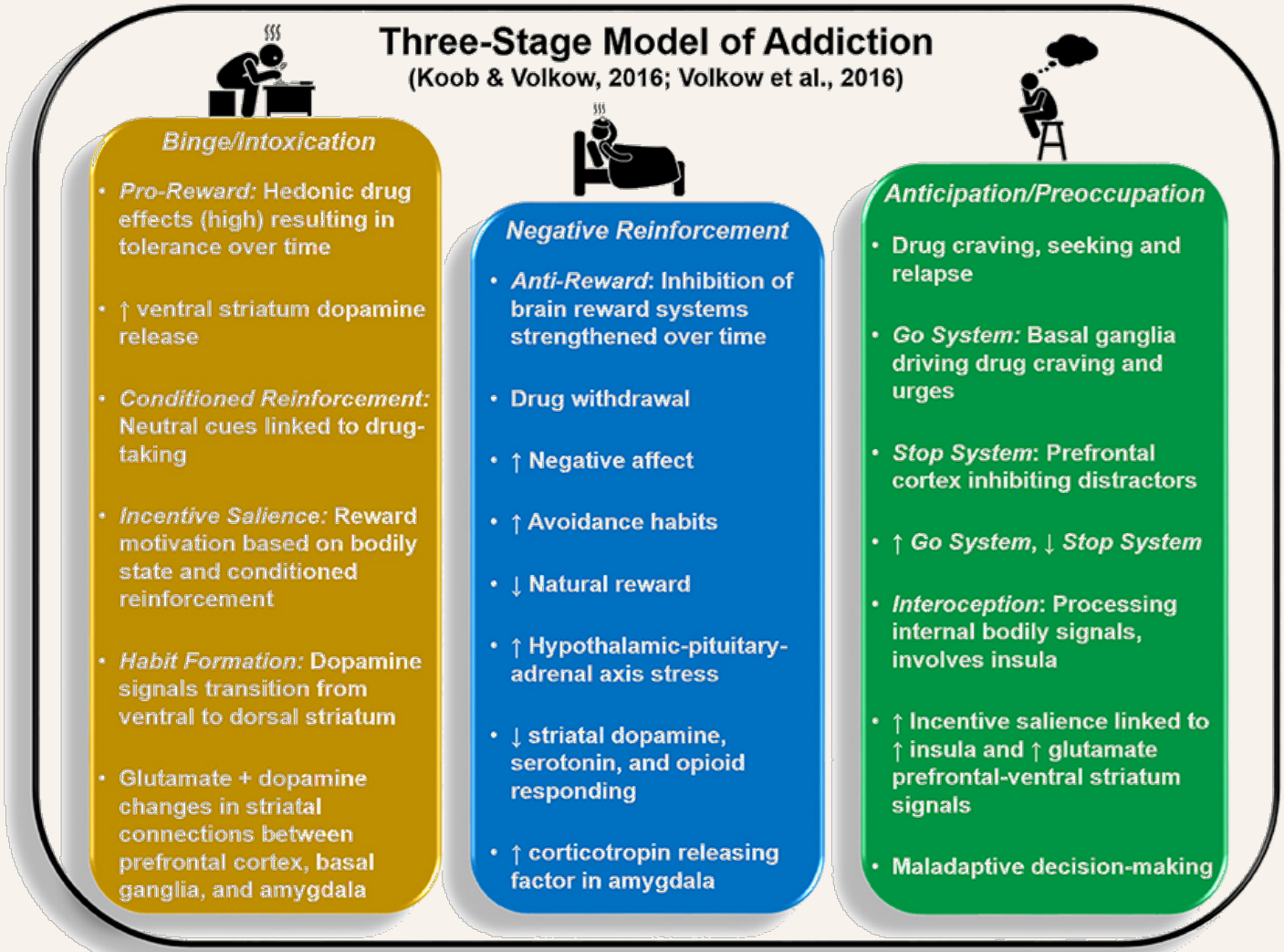


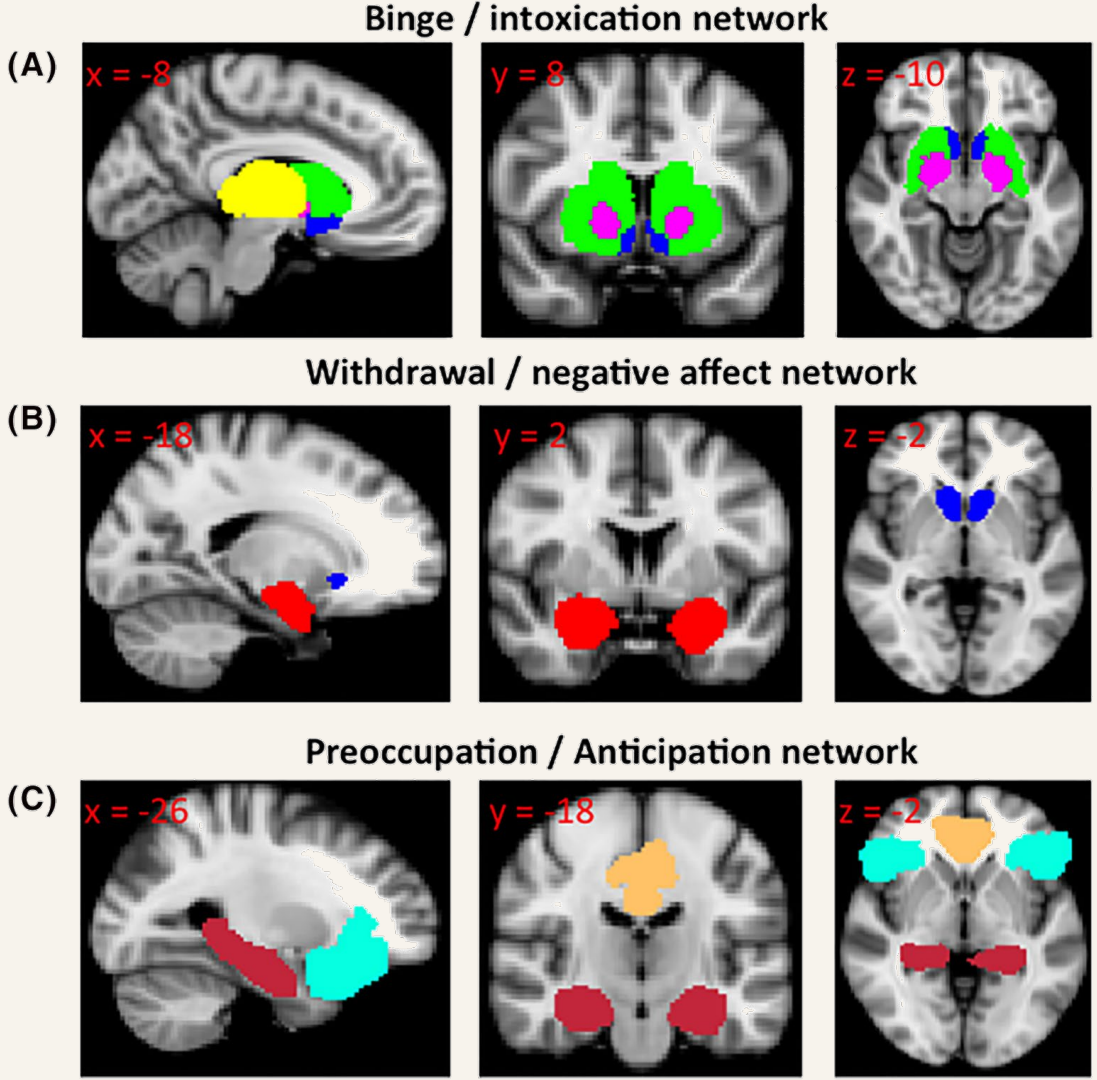
HEALTHY CONTROL

PATIENT WITH METHAMPHETAMINE USE DISORDER

1 MONTH OF ABSTINENCE

14 MONTHS OF ABSTINENCE


Three-Stage Model of Addiction
(Koob & Volkow, 2016; Volkow et al., 2016)
Binge/Intoxication
• Pro-Reward: Hedonic drug effects (high) resulting in tolerance over time
• ↑ ventral striatum dopamine release
• Conditioned Reinforcement: Neutral cues linked to drug-taking
• Incentive Salience: Reward motivation based on bodily state and conditioned reinforcement
• Habit Formation: Dopamine signals transition from ventral to dorsal striatum
• Glutamate + dopamine changes in striatal connections between prefrontal cortex, basal ganglia, and amygdala
Negative Reinforcement
• Anti-Reward: Inhibition of brain reward systems strengthened over time
• Drug withdrawal
• ↑ Negative affect
• ↑ Avoidance habits
• ↓ Natural reward
• ↑ Hypothalamic-pituitary-adrenal axis stress
• ↓ striatal dopamine, serotonin, and opioid responding
• ↑ corticotropin releasing factor in amygdala
Anticipation/Preoccupation
• Drug craving, seeking and relapse
• Go System: Basal ganglia driving drug craving and urges
• Stop System: Prefrontal cortex inhibiting distractors
• ↑ Go System, ↓ Stop System
• Interoception: Processing internal bodily signals, involves insula
• ↑ Incentive salience linked to ↑ insula and ↑ glutamate prefrontal-ventral striatum signals
• Maladaptive decision-making



Schmidt A, Vogel M, Baumgartner S, Wiesbeck GA, Lang U, Borgwardt S, Walter M. Brain volume changes after long-term injectable opioid treatment: A longitudinal voxel-based morphometry study. Addict Biol. 2021 Jul;26(4):e12970. doi: 10.1111/adb.12970. Epub 2020 Oct 1. PMID: 33000891.

Summary so far

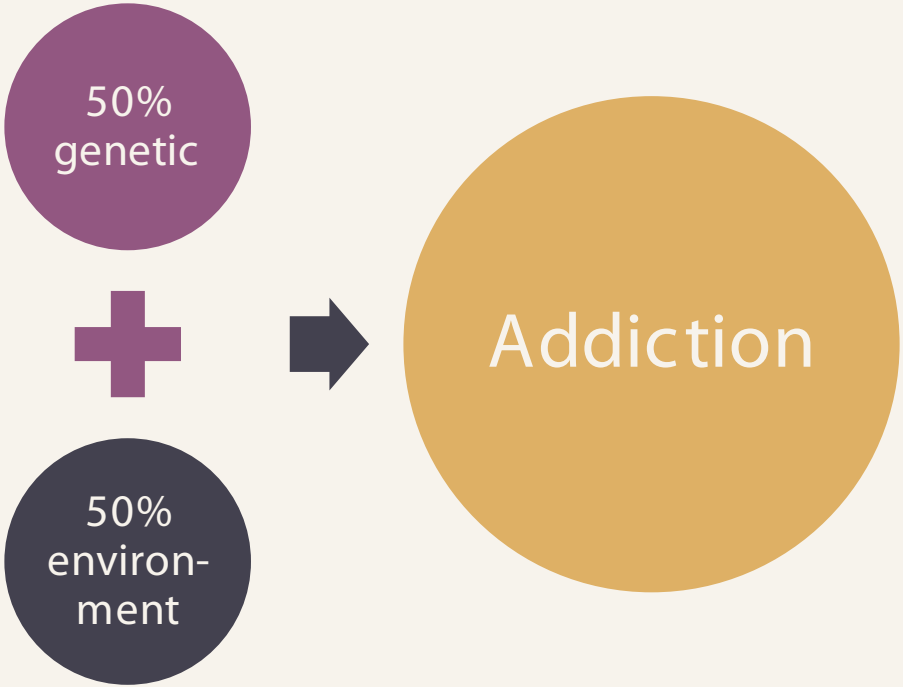
MRI can demonstrate substance use disorder – all stages

Abstinence leads to repair of dopamine reward pathway

Part 4

Emotion and Substance Use Disorder

Why are some people more prone to addiction?



NIDA. 2019, August 5. Genetics and Epigenetics of Addiction DrugFacts. Retrieved from https://nida.nih.gov/publications/drugfacts/genetics-epigenetics-addiction on 2022, August 1

Genetic testing

Genome-wide association studies (GWAS)

Single Nucleotide Polymorphisms (SNPs)

NIDA. 2019, August 5. Genetics and Epigenetics of Addiction DrugFacts. Retrieved from https://nida.nih.gov/publications/drugfacts/genetics-epigenetics-addiction on 2022, August 1

Genetic example: Cannabis addiction

GWAS

- 2,387 cases
- 48,985 controls

Chromosome 8

- Controls the levels of the gene CHRNA2 expressed in the brain

Low levels of expression of the gene CHRNA2 in the cerebellum associated with cannabis use disorder

NIDA. 2019, August 5. Genetics and Epigenetics of Addiction DrugFacts. Retrieved from https://nida.nih.gov/publications/drugfacts/genetics-epigenetics-addiction on 2022, August 1

Genetic example: Alcohol use

GWAS – UK Biobank

- self-reported alcohol consumption in 112 117

Genetic associations

- 14 loci

Clarke TK, Adams MJ, Davies G, Howard DM, Hall LS, Padmanabhan S, Murray AD, Smith BH, Campbell A, Hayward C, Porteous DJ, Deary IJ, McIntosh AM. Genome-wide association study of alcohol consumption and genetic overlap with other health-related traits in UK Biobank (N=112 117). Mol Psychiatry. 2017 Oct;22(10):1376-1384. doi: 10.1038/mp.2017.153. Epub 2017 Jul 25. PMID: 28937693; PMCID: PMC5622124.

Genetic example: Alcohol use

Alcohol metabolizing genes

- ADH1B/ADH1C/ADH5
- KLB
- GCKR, CADM2 and FAM69C

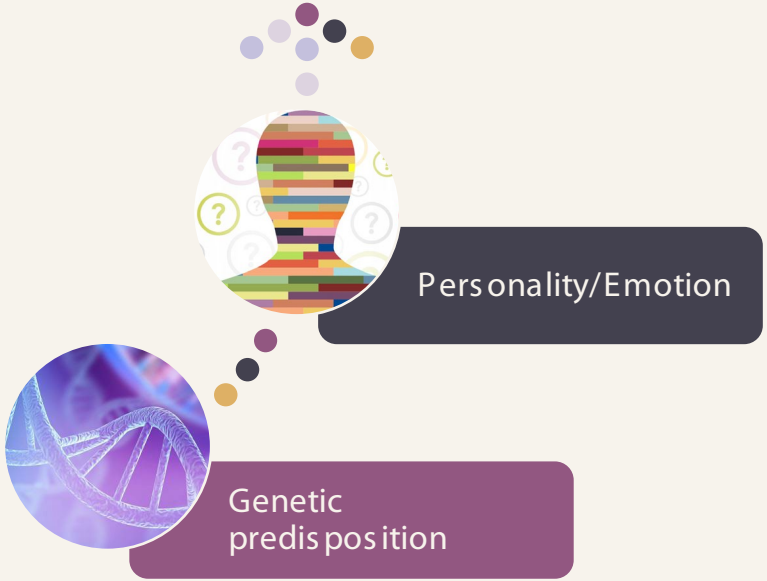
Neurobiology of substance use

- DRD2, PDE4B
- shared with tobacco, caffeine and cannabis use

KLB, a gene recently associated with alcohol consumption

Clarke TK, Adams MJ, Davies G, Howard DM, Hall LS, Padmanabhan S, Murray AD, Smith BH, Campbell A, Hayward C, Porteous DJ, Deary IJ, McIntosh AM. Genome-wide association study of alcohol consumption and genetic overlap with other health-related traits in UK Biobank (N=112 117). Mol Psychiatry. 2017 Oct;22(10):1376-1384. doi: 10.1038/mp.2017.153. Epub 2017 Jul 25. PMID: 28937693; PMCID: PMC5622124.

Why are some people more prone to addiction?



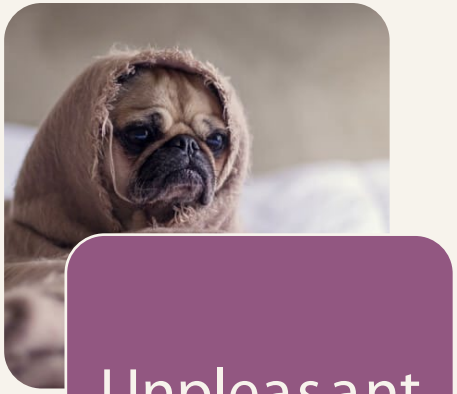
Emotion and Addiction

Emotion regulation predicts intensity of emotion state

Well-established influence on substance use

Individuals who exhibit emotion regulation difficulties more likely to engage in substance to alleviate or distract themselves from emotional states

Weiss, N. H., Kiefer, R., Goncharenko, S., Raudales, A. M., Forkus, S. R., Schick, M. R., & Contractor, A. A. (2022). Emotion regulation and substance use: A meta-analysis. *Drug and alcohol dependence*, *230*, 109131. https://doi-org.liboff.ohsu.edu/10.1016/j.drugalcdep.2021.109131



Unpleasant emotion

Substance use

Distraction

- Immediate and short-term gratification

Weiss, N. H., Kiefer, R., Goncharenko, S., Raudales, A. M., Forkus, S. R., Schick, M. R., & Contractor, A. A. (2022). Emotion regulation and substance use: A meta-analysis. *Drug and alcohol dependence*, *230*, 109131. https://doi-org.liboff.ohsu.edu/10.1016/j.drugalcdep.2021.109131

The down-regulation of emotions is an effortful, and not necessarily immediately rewarding, process. As the need for regulation persists, individuals experience a shift in motivation from the regulation of emotion toward the acquisition of rewarding experiences.

In turn, there is increased allocation of attention toward cues that signal immediate reward, thereby increasing substance use.

Weiss, N. H., Kiefer, R., Goncharenko, S., Raudales, A. M., Forkus, S. R., Schick, M. R., & Contractor, A. A. (2022). Emotion regulation and substance use: A meta-analysis. *Drug and alcohol dependence*, *230*, 109131. https://doi-org.liboff.ohsu.edu/10.1016/j.drugalcdep.2021.109131

Evidence for Emotional Regulation

Individuals with alcohol and drug use disorders have been shown to exhibit greater deficits in emotion regulation

Cross-sectional correlational studies have found that greater deficits in emotion regulation relate to worse substance use

Clinical research provides evidence for impacts of emotion regulation on substance use treatment outcome

Weiss, N. H., Kiefer, R., Goncharenko, S., Raudales, A. M., Forkus, S. R., Schick, M. R., & Contractor, A. A. (2022). Emotion regulation and substance use: A meta-analysis. *Drug and alcohol dependence*, *230*, 109131. https://doi-org.liboff.ohsu.edu/10.1016/j.drugalcdep.2021.109131

Alcohol
Drug
Tobacco
Multiple
Substances

ER Construct	*K*	*B*	95% CI	*Q (df)*	*p*
Clinical Adults vs. College Students					
All	303	0.13	0.09 to 0.17	44.96(1)	< 0.001
Negative Overall	96	0.17	0.11 to 0.24	26.76(1)	< 0.001
Negative Non-Accept	30	0.15	0.06 to 0.23	12.26(1)	< 0.001
Negative Goals	28	0.16	0.07 to 0.24	11.84(1)	< 0.001
Negative Impulse	29	0.15	0.05 to 0.25	8.15(1)	0.004
Negative Strategies	27	0.21	0.08 to 0.34	9.58(1)	0.002
Clarity	29	0.05	-0.08 to 0.17	0.57(1)	0.45
Awareness	27	0.01	-0.03 to 0.05	0.28(1)	0.60
Adaptive Strategies	15	-0.11	-0.24 to 0.03	2.33(1)	0.13
Maladaptive Strategies	14	0.28	0.14 to 0.42	15.70(1)	< 0.001
Reappraisal	11	-0.03	-0.23 to 0.17	0.10(1)	0.75
Suppression	10	0.13	-0.06 to 0.32	1.74(1)	0.19

Weiss, N. H., Kiefer, R., Goncharenko, S., Raudales, A. M., Forkus, S. R., Schick, M. R., & Contractor, A. A. (2022). Emotion regulation and substance use: A meta-analysis. *Drug and alcohol dependence*, *230*, 109131. https://doi-org.liboff.ohsu.edu/10.1016/j.drugalcdep.2021.109131

Younger generations

Participants

- 472 students aged 13-21

Outcomes

- Emotional regulation and attachment
- Substance use (alcohol and drug abuse)
- Non-substance-related addictions (gambling disorder, video game addiction, and problematic Internet use)

Estévez A, Jáuregui P, Sánchez-Marcos I, López-González H, Griffiths MD. Attachment and emotion regulation in substance addictions and behavioral addictions. J Behav Addict. 2017 Dec 1;6(4):534-544. doi: 10.1556/2006.6.2017.086. PMID: 29280395; PMCID: PMC6034944.

Results

Emotion regulation was a predictor for all addictive behaviors assessed (both substance and non-substance related)

Emotional control was the most powerful predictor of addictive behavior

Poor attachment predicted gambling disorder, problematic Internet use, and video game addiction.

Results indicated that females scored significantly higher in maternal attachment and peer attachment

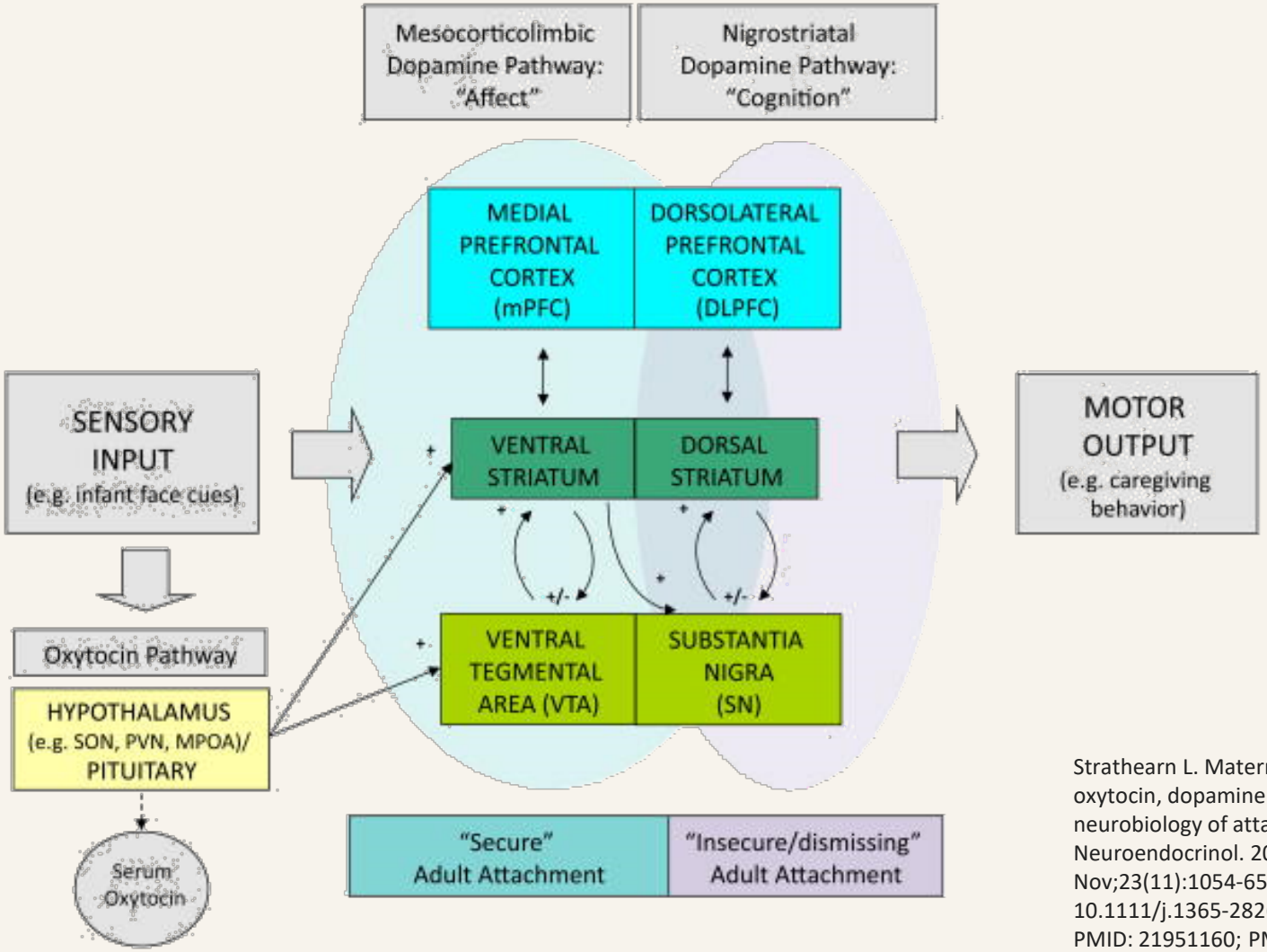
Males scored significantly higher in relation to gambling disorder and video game addiction

Estévez A, Jáuregui P, Sánchez-Marcos I, López-González H, Griffiths MD. Attachment and emotion regulation in substance addictions and behavioral addictions. J Behav Addict. 2017 Dec 1;6(4):534-544. doi: 10.1556/2006.6.2017.086. PMID: 29280395; PMCID: PMC6034944.

Attachment

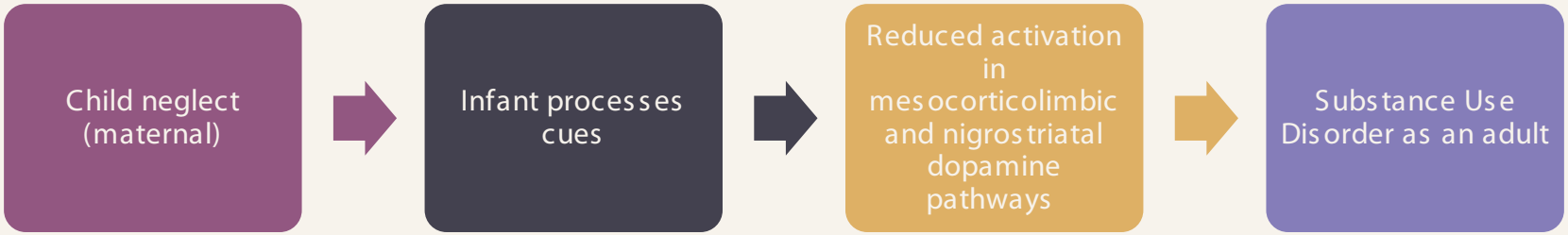
Secure attachment prevents addiction?	Individuals with secure attachment are characterized by the self-acceptance of their own emotional needs
	individuals with non-secure attachments (e.g., anxious-avoidant) pay little attention to their emotional needs and do not feel they can rely on somebody else's support
	Disturbed parent–child interactions cause difficulties in affect regulation, difficulties in separation/individuation, and interpersonal difficulties. Furthermore, they are viewed as antecedent variables in the development of addiction
	If an individual feels unlovable and neglected and has developed a negative self-concept because of negative relationships during childhood, the individual can try to avoid this by engaging in a potentially addictive behavior

Estévez A, Jáuregui P, Sánchez-Marcos I, López-González H, Griffiths MD. Attachment and emotion regulation in substance addictions and behavioral addictions. J Behav Addict. 2017 Dec 1;6(4):534-544. doi: 10.1556/2006.6.2017.086. PMID: 29280395; PMCID: PMC6034944.



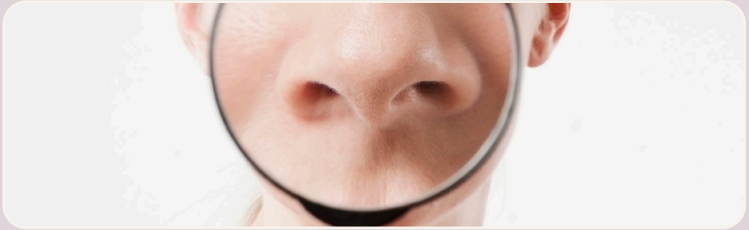
Strathearn L. Maternal neglect: oxytocin, dopamine and the neurobiology of attachment. J Neuroendocrinol. 2011 Nov;23(11):1054-65. doi: 10.1111/j.1365-2826.2011.02228.x. PMID: 21951160; PMCID: PMC3319675.

Relationship between attachment, emotional regulation, and dopamine



Strathearn L. Maternal neglect: oxytocin, dopamine and the neurobiology of attachment. J Neuroendocrinol. 2011 Nov;23(11):1054-65. doi: 10.1111/j.1365-2826.2011.02228.x. PMID: 21951160; PMCID: PMC3319675.

“Fix” maternal child neglect



Intra-nasal oxytocin

Address mother’s own attachment history

Strathearn L. Maternal neglect: oxytocin, dopamine and the neurobiology of attachment. J Neuroendocrinol. 2011 Nov;23(11):1054-65. doi: 10.1111/j.1365-2826.2011.02228.x. PMID: 21951160; PMCID: PMC3319675.

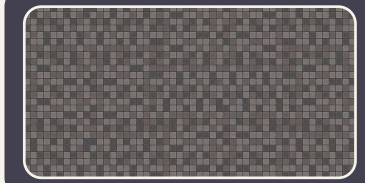
People stop taking drugs

Time frame	
	Cocaine – 4 years
	Marijuana – 6 years
	Alcohol – 15 years
	Nicotine - 25 years

Neuroscience of Addiction – with Marc Lewis: https://www.youtube.com/watch?v=aOSD9rTVuWc

Summary

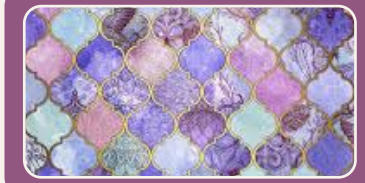
Dopamine mediates the reward experienced from substances and addictive behaviors



Cytokines, neurotransmitters, and microbial metabolites contribute to addiction

Brain scans of addiction highlight the absence of dopamine receptors

Summary



Addiction is 50% Genetic and 50% Environment

Ability to regulate emotion related to addiction

Maternal attachment related to emotional regulation and healthy dopamine reward pathway

Thank you!

Instagram: @hzwickey. @Thaena.inc