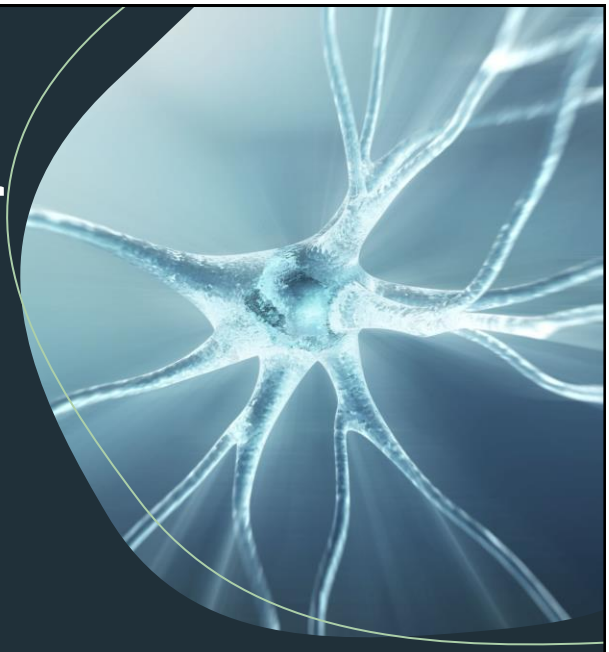
Neurobiology of Substance Use Disorder



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PSACT Symposium 2024

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Disclosure

YS has minimal ownership of FLORA, a Vermont adult-use cannabis retailer. FLORA was not involved in any portion of the studies to be described, their funding, or the decision to submit the planning of this presentation. FLORA was not involved in any content to this session, any presentation, or any participation as an event planner.

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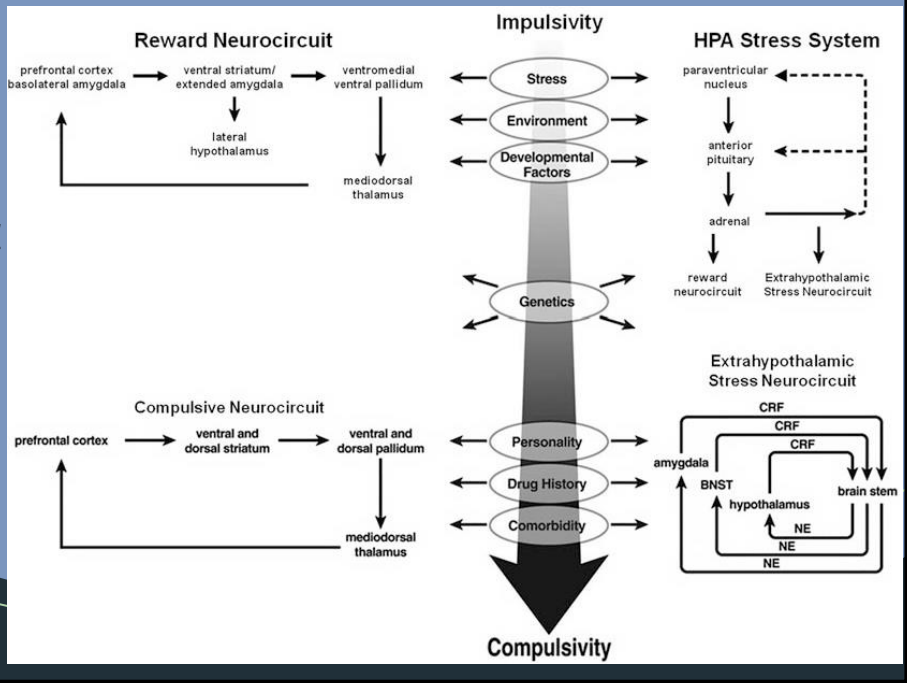
Brain systems regulating development of substance use disorder



Koob, G.F., Kandel, D.B., Baler, R.D., Volkow, N.D. (2023). Neurobiology of Addiction. In: Tasman, A., *et al.* Tasman's Psychiatry. Springer, Cham. https://doi-org.ezaccess.libraries.psu.edu/10.1007/978-3-030-42825-9_29-1

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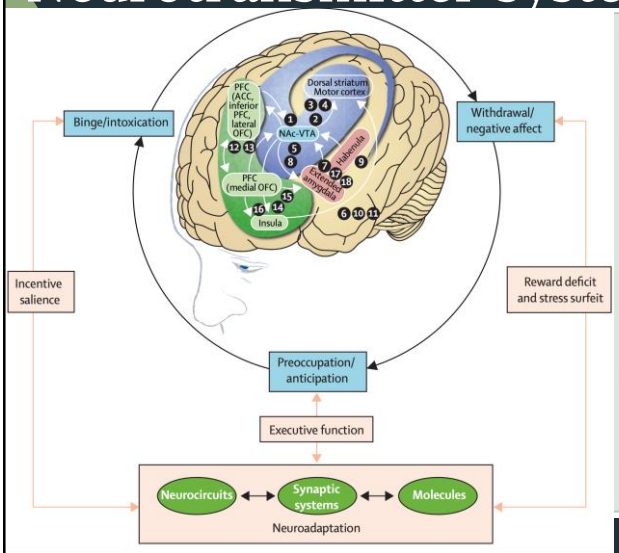
Neurotransmitter systems in SUD



Koob and Volkow, *Lancet Psychiatry* 2016

	Response
Binge/intoxication	
Dopamine[15]	Increase
Opioid peptides[16]	Increase
Serotonin[17]	Increase
γ-aminobutyric acid[18]	Increase
Acetylcholine[19]	Increase
Withdrawal/negative affect	
Corticotropin-releasing factor[20]	Increase
Dynorphin[21]	Increase
Norepinephrine[22]	Increase
Hypocretin (orexin)[23]	Increase
Substance P[24]	Increase
Dopamine[25]	Decrease
Serotonin[17]	Decrease
Opioid peptide receptors[26]	Decrease
Neuropeptide Y[27]	Decrease
Nociceptin[28]	Decrease
Endocannabinoids[29]	Decrease
Oxytocin[30]	Decrease
Preoccupation/anticipation	
Dopamine[25]	Increase
Glutamate[32]	Increase
Hypocretin (orexin)[23]	Increase
Serotonin[17]	Increase
Corticotropin-releasing factor[33]	Increase

Table 1: Neurotransmitter systems involved in the neurocircuitry of addiction stages and functional domains

	Neurotransmitter
Binge/intoxication	
Ventral tegmental area (circuit 1)[43]	Glutamate
Ventral tegmental area (circuit 2)[44]	γ-aminobutyric acid
Dorsal striatum (circuit 3)[45]	Dopamine
Dorsal striatum (circuit 4)[46]	Glutamate
Withdrawal/negative affect	
Ventral tegmental area (circuit 5)[47]	Corticotropin-releasing factor
Central nucleus of amygdala (circuit 6)[48]	Corticotropin-releasing factor
BNST (circuit 7)[12]	Norepinephrine
Nucleus accumbens shell (circuit 8)[13]	Dynorphin
Habenula (circuit 9)[49]	Acetylcholine
Central nucleus of amygdala (circuit 10)[49]	Neuropeptide Y
Central nucleus of amygdala (circuit 11)[29]	Endocannabinoids
Preoccupation/anticipation	
Prefrontal cortex (circuit 12)[50]	Glutamate
Prefrontal cortex (circuit 13)[50]	γ-aminobutyric acid
Hippocampus (circuit 14)[51]	Glutamate
Basolateral amygdala (circuit 15)[52]	Glutamate
BNST (circuit 16)[53]	Corticotropin-releasing factor
BNST (circuit 17)[53]	Norepinephrine
Insula (circuit 18)[54]	Corticotropin-releasing factor

BNST=bed nucleus of the stria terminalis.

Table 2: Molecular neurocircuits as focal points for neuroplasticity in addiction

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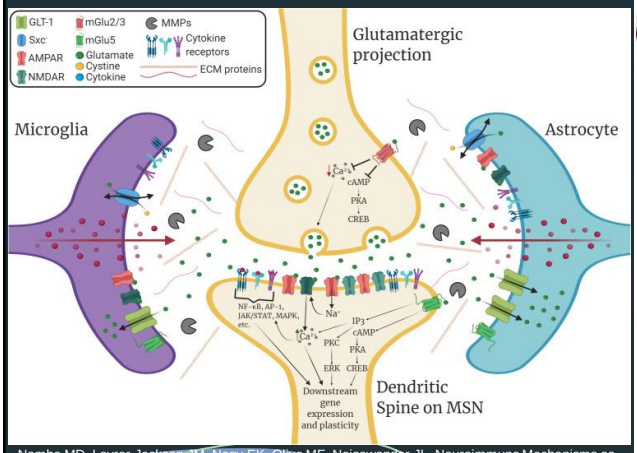
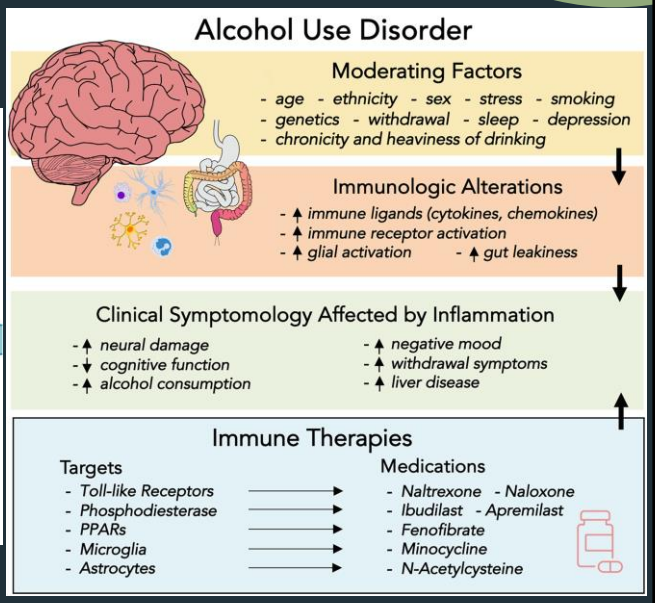
Neuroimmune system in SUD



Namba MD, Leyrer-Jackson JM, Nagy EK, Olive MF, Neisewander JL. Neuroimmune Mechanisms as Novel Treatment Targets for Substance Use Disorders and Associated Comorbidities. Front Neurosci. 2021 Apr 15;15:650785.



Meredith LR, Burnette EM, Grodin EN, Irwin MR, Ray LA. Immune treatments for alcohol use disorder: A translational framework. Brain Behav Immun. 2021

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Speakers

Faculty

- Megan Fox- Fentanyl causes molecular and functional adaptations to ventral tegmental area neurons depending on downstream projection target
- Patrick Randall- Deciphering Neuroimmune Interactions in Substance Use: Alcohol and Nicotine

Trainees

- Sunderland Baker- White matter connectivity differences in early-stage alcohol use disorder: Diffusion tensor and neurite orientation dispersion and density measures of microstructural integrity
- Quinn Wade- Neuronal adaptations in the anterior cingulate cortex and their association with symptoms of opioid use disorder

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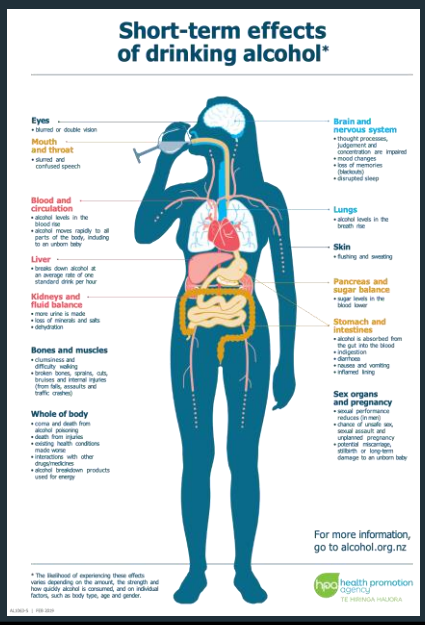
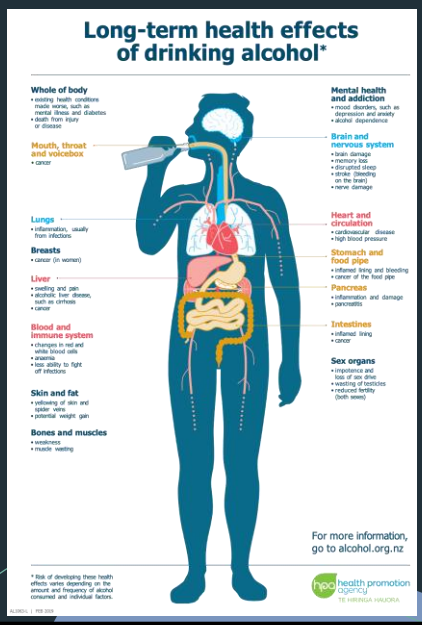
Interaction of central and peripheral systems in SUD

drugs impacts all parts of the body





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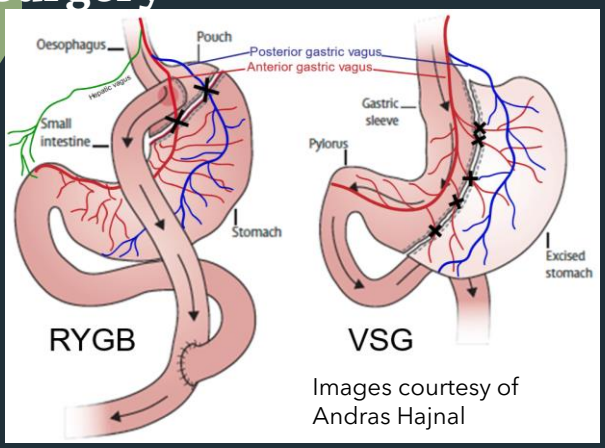
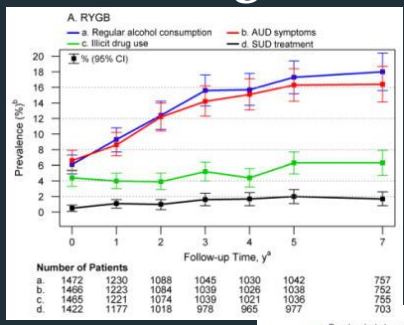
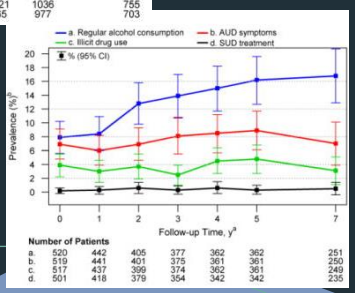
Disruption of vagus nerve function may lead to increased alcohol intake; lessons from gastric bypass surgery



Images courtesy of Andras Hajnal





RYGB= increased seeking and intake of alcohol and other rewards
VSG= variable risk for seeking and intake of alcohol and other rewards

King et al Surg Obes Relat Dis. 2017

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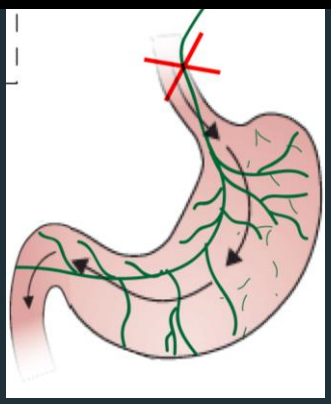
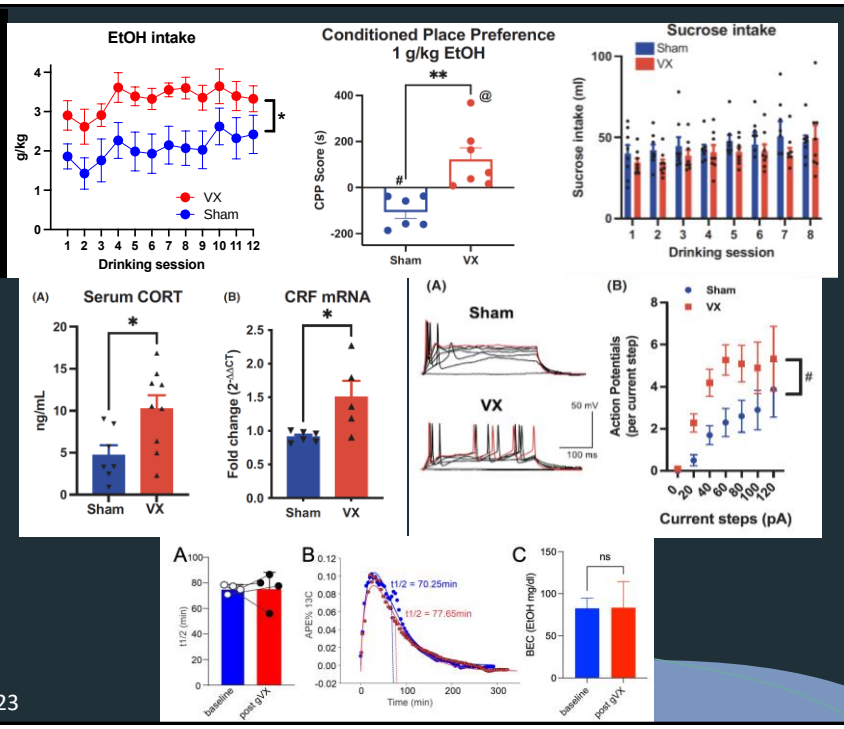
Anterior Gastric branch vagotomy (VX) increases alcohol intake and preference

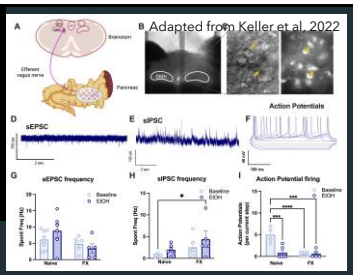


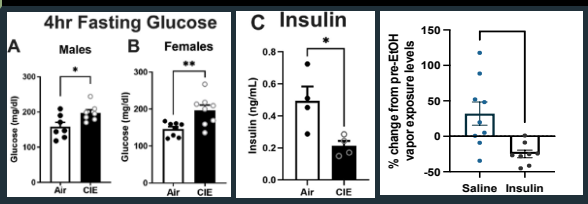


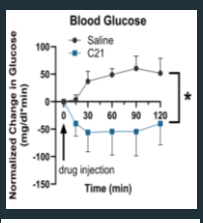
Hajnal and Silberman labs, ACER 2023

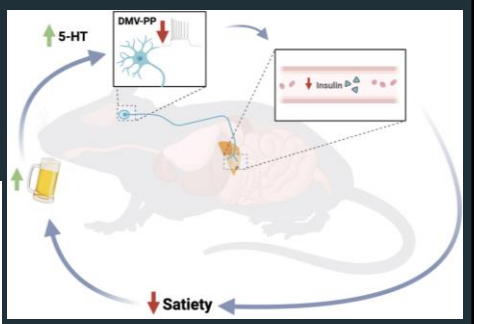
9

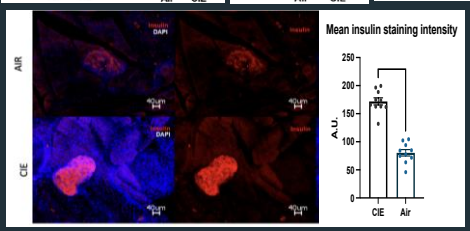
Insulin can regulate alcohol intake and central control over insulin function is disrupted by alcohol

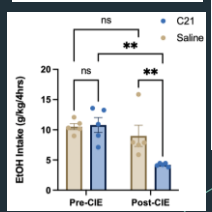












Evans, in preparation

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11

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