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UNDERSTANDING THE NEUROBIOLOGY OF AUD

To understand alcohol use disorder (AUD), we must look to the brain.

AUD is a chronic, relapsing brain-based treatable medical condition shaped by a variety of factors that are[1,2]:

BIOLOGICAL **PSYCHOLOGICAL** **SOCIAL**

Yet AUD is often misunderstood as[3]:

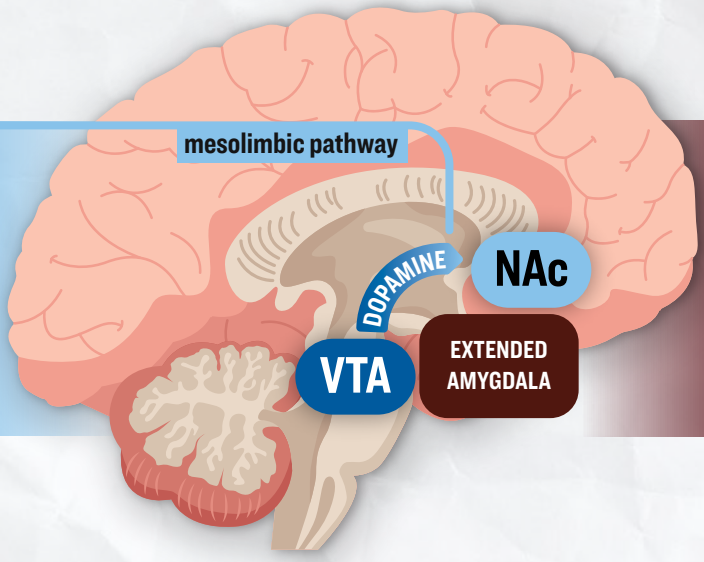
- Not serious enough to require treatment
- A problem that will resolve over time

These perceptions do not reflect the underlying neurobiology of AUD.

AUD is often seen as a personal failing. Bringing neurobiology into your conversations with patients gives you a way to reframe AUD— ***not as a moral failure but as a disorder of brain circuitry.***[4]

Reward and relief are early drivers of the processes that can lead to AUD.[5-7]

↑ Alcohol increases dopamine release in the mesolimbic pathway, producing a reward-associated signal that reinforces drinking.



Alcohol can temporarily relieve distress by modifying GABA and glutamate signaling, dampening activity in stress-related regions such as the extended amygdala. ↓

GABA=gamma-aminobutyric acid.
NAc=nucleus accumbens.
VTA=ventral tegmental area.

Repeated alcohol use disrupts more signaling molecules than just dopamine, a common misconception[2,8-10]

SIGNALING MOLECULE	NEUROBIOLOGICAL PROCESSES AFFECTED
Serotonin	Mood regulation
Dopamine	Motivation and reward
GABA	Tolerance, dependence, and withdrawal
Glutamate	Tolerance and withdrawal
Acetylcholine	Motivation and reward (indirect)
Endogenous opioid peptides	Motivation and reward (indirect)

Chronic alcohol use alters neuronal networks *that regulate reward, motivation, decision-making, and emotion processing.*[11]

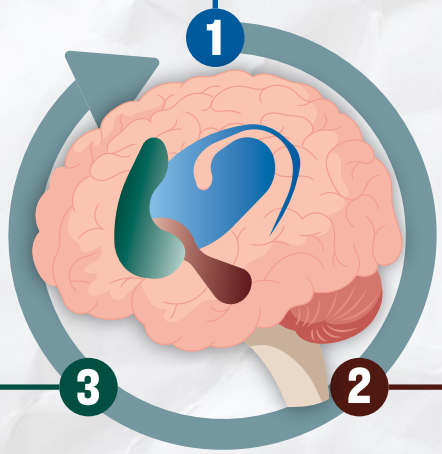
AUD progressively changes the brain in ways that make alcohol use increasingly harder to control.[12]

AUD can be understood as a 3-stage cycle[1,6,11]:

Basal ganglia Binge/intoxication

Intoxication reinforces alcohol use through reward circuitry

Pleasurable cues and positive reinforcement strengthen habitual drinking



Modified from Volkow and Boyle.[11]

Extended amygdala Withdrawal

Withdrawal activates stress circuitry

Over time, reward system activity is reduced, and stress circuitry is activated; this can be experienced as anxiety, irritability, dysphoria, and craving

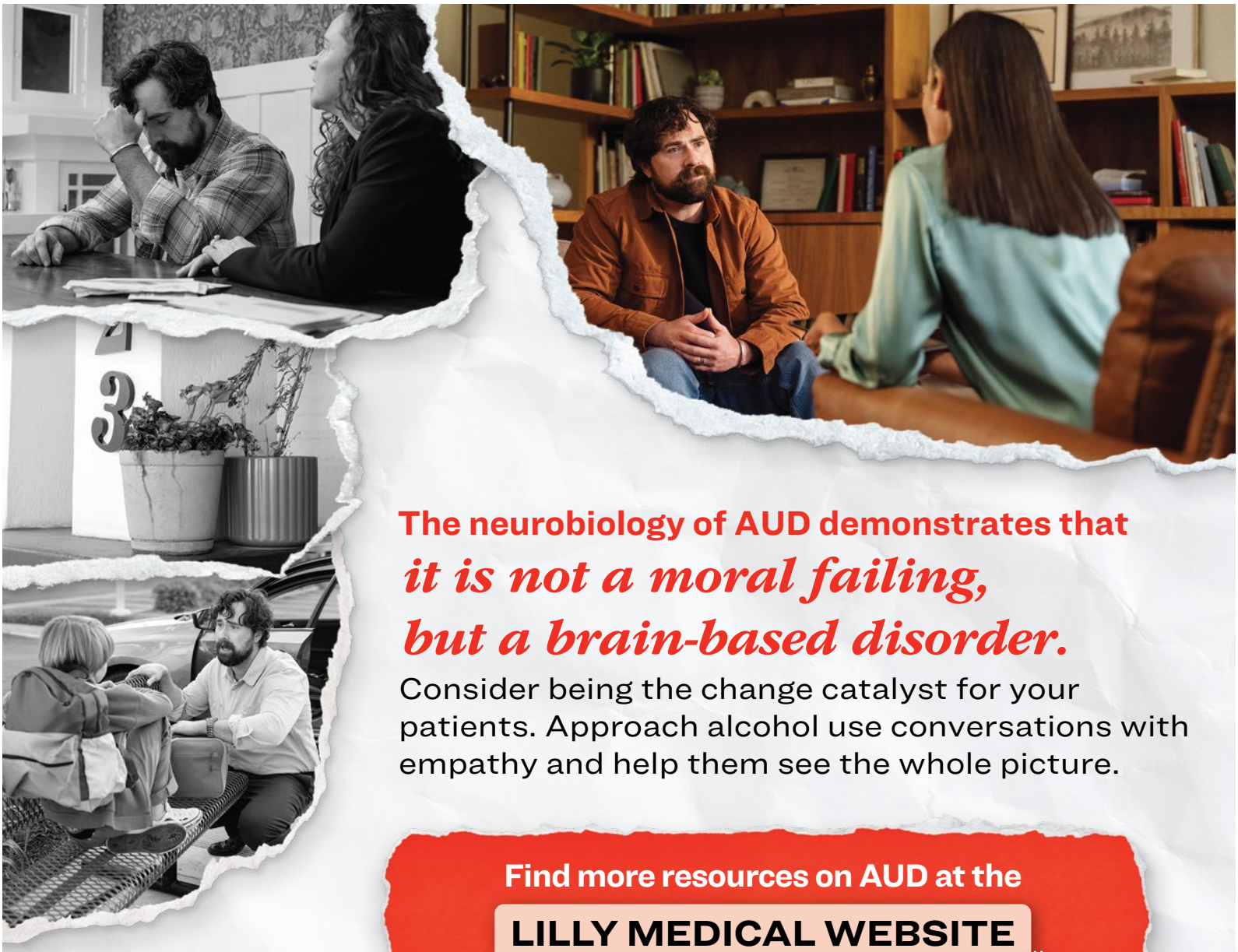
At this stage, drinking may shift from seeking pleasure to temporarily relieving this distress, perpetuating the cycle

Prefrontal cortex
Preoccupation/anticipation

Dysregulation of prefrontal cortex function makes it harder to resist drinking

Reduced executive function weakens the ability to ignore alcohol-related cues

AUD changes the brain in ways that perpetuate alcohol use and *increase susceptibility to relapse despite negative consequences.*[1]



The neurobiology of AUD demonstrates that

it is not a moral failing, but a brain-based disorder.

Consider being the change catalyst for your patients. Approach alcohol use conversations with empathy and help them see the whole picture.

Find more resources on AUD at the

LILLY MEDICAL WEBSITE

References

1. National Institute on Alcohol Abuse and Alcoholism. The cycle of alcohol addiction. Published 2021. Accessed June 23, 2026. https://www.niaaa.nih.gov/publications/cycle-alcohol-addiction **2.** MacKillop J, et al. *Nat Rev Dis Primers.* 2022;8(1):80. **3.** Hammarlund R, et al. *Subst Abuse Rehabil.* 2018;9:115-136. **4.** Heilig M, et al. *Neuropsychopharmacology.* 2021;46:1715-1723. **5.** Ferrer-Pérez C, et al. *Psychoactives.* 2024;3(1):35-47. **6.** National Institutes of Alcohol Abuse and Alcoholism. Neuroscience: the brain in addiction and recovery. Accessed June 23, 2026. https://www.niaaa.nih.gov/health-professionals-communities/core-resource-on-alcohol/neuroscience-brain-addiction-and-recovery **7.** Roberto M, et al. *Cold Spring Harb Perspect Med.* 2012;2:a012195. **8.** Banerjee N. *Indian J Hum Genet.* 2014;20(1):20-31. **9.** Yang W, et al. *Biomedicines.* 2022;10(5):1192. **10.** Volkow ND, et al. *Physiol Rev.* 2019;99:2115–2140. **11.** Volkow ND, Boyle M. *Am J Psychiatry.* 2018;175(8):729-740. **12.** National Institute on Alcohol Abuse and Alcoholism. Alcohol use disorder: from risk to diagnosis to recovery. Published May 8, 2024. Accessed June 23, 2026. https://www.niaaa.nih.gov/health-professionals-communities/core-resource-on-alcohol/alcohol-use-disorder-risk-diagnosis-recovery

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