SMMH ROUNDS, JUNE 12, 2025

DEVON TILBROOK MD CCFP (EM) FCFP

THIRSTY FOR CHANGE: ANTI-CRAVING MEDICATIONS FOR ALCOHOL USE DISORDER

CONFLICT OF INTEREST

- None

MY EXPERIENCE

- Doctor for Minden RAAM, in association with PRHC. About 70% of patients attending are for AUD.
- Family doctor in Haliburton
- ED doctor in Haliburton and SMMH
- Previously worked in First Nations communities in Sioux Lookout Zone

OBJECTIVES

By the end of the session, participants will be able to

- Initiate naltrexone and acamprosate for anti-craving for AUD in the office or the ED
- Understand which off label options are available for AUD
- Counsel patients on pros and cons of different anti-craving options for AUD

(Not talking specifically about treatment of withdrawal today)

A FEW CASES

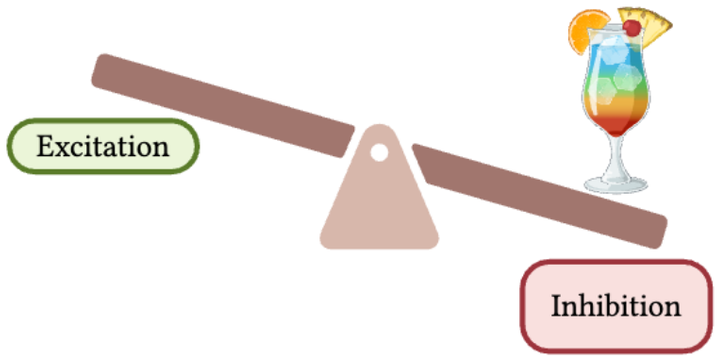
1. 65 yo male. Drinks 13 oz vodka daily. No alcohol for 24 hours. Presents in active withdrawal. PHMx alcoholic hepatitis (2022). On no meds.
2. 65 yo male. Drinks 13 oz vodka daily. Been sober for 1 week. PMHx hepatitis C (treated 2022), osteoarthritis. Takes Percocet daily.
3. 64 yo male. Drinks 13 oz vodka daily. Not in withdrawal. PMHx hepatitis C (treated 2022).

ALCOHOL USE NEUROADAPTATION

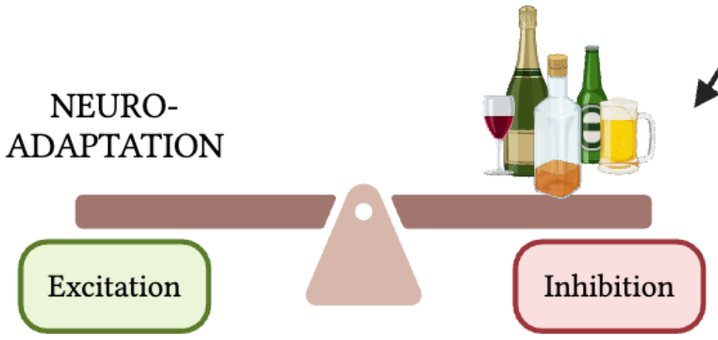
- Alcohol affects many neurotransmitters including **GABA, glutamate** and **dopamine**.
- Chronic alcohol consumption drives a chemical imbalance that forces a homeostatic response →creates an equilibrium in which ethanol becomes integral in neuronal function →tolerance, withdrawal

Equilibrium

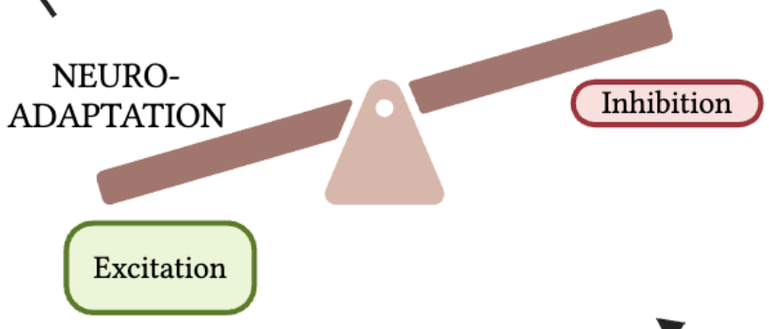
Acute alcohol



Chronic alcohol



Alcohol
withdrawal



ALCOHOL USE NEUROADAPTATION

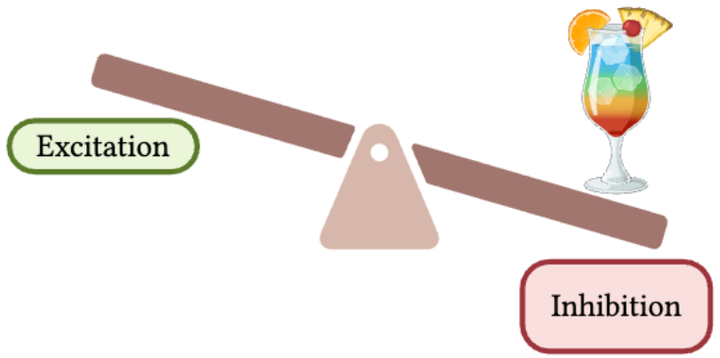
- Alcohol affects many neurotransmitters including **GABA, glutamate** and **dopamine**.
  - Acute effects of alcohol
    - Inhibition through activation of GABA receptors and inhibition of glutamate receptors (eg NMDA, AMPA)
    - indirect downstream increase in dopamine release and acetylcholine activity involved in reward and motivation
    - Increases serotonin release, contributing to reward aspect
    - Increases levels of endogenous opioids, which are drastically reduced during withdrawal (increasing risk of opioid seeking)

ALCOHOL USE NEUROADAPTATION

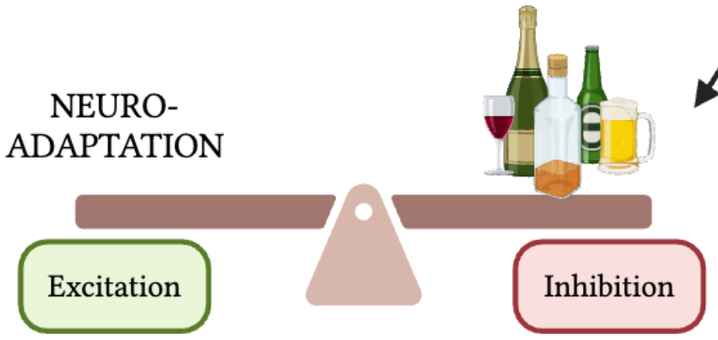
- Alcohol affects many neurotransmitters including GABA, glutamate and dopamine.
  - Chronic alcohol exposure
    - downregulates GABA receptors, and upregulate glutamate receptors
    - Loss of alcohol → unopposed sympathetic activation eg tachycardia, hypertension, tremulousness and hyperreflexia. Seizures when severe. Anxiety, craving and insomnia can persist with subacute withdrawal.
    - Loss of alcohol →decrease in dopamine and serotonin levels →dysphoria, depression, anxiety

Equilibrium

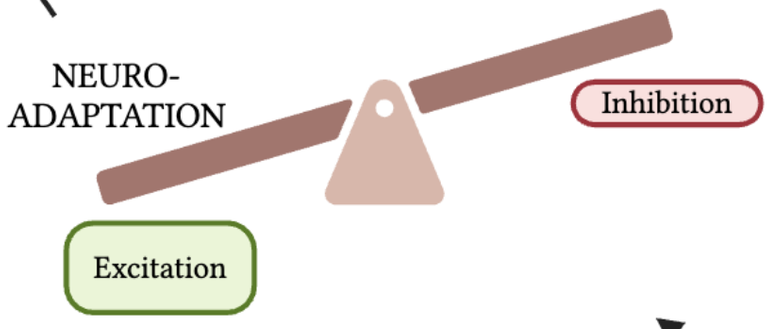
Acute alcohol



Chronic alcohol



Alcohol
withdrawal



NALTREXONE

- “Revia”
- Opioid mu receptor antagonist
- 1st line agent, approved by health Canada
  - NNT 20 for return to any drinking, 13 for return to heavy drinking
- Reduces **opioidergic-dependent dopamine** activity
  - Decreases cravings by reducing rewarding and euphoric effect
  - “Wine doesn’t taste as good.” “Allows me to think twice”
- Covered by ODB (LU 532) and all private plans
- 50mg daily = 118$ per month

NALTREXONE

- Limitations: side effect of nausea, interaction with opioids
- Listed side effects: depression, suicidality, somnolence, anorexia, GI discomfort
- Benefits: can be effective in patients still drinking, can be used prn (Sinclair method)
- What about hepatotoxicity?
  - A historical concern which has prevented many patients from benefiting from therapy

Short communication

JHEP|Reports

Safety of naltrexone in patients with cirrhosis

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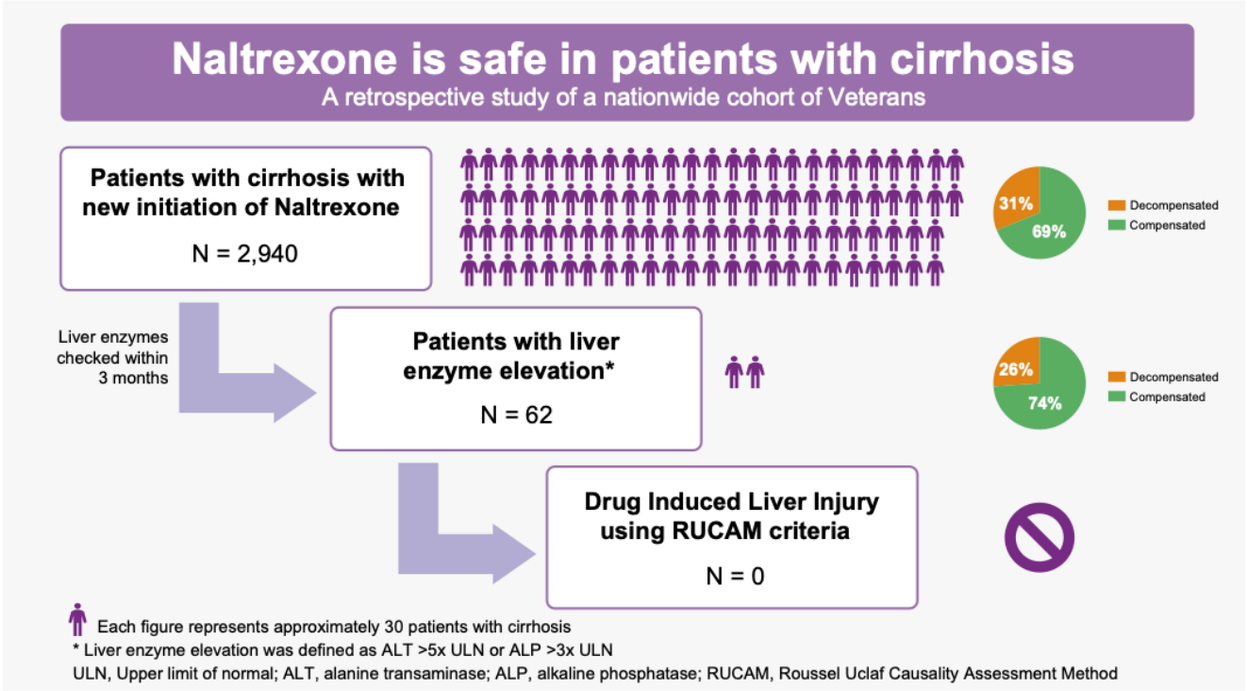
Graphical abstract



Highlights:

- Naltrexone is an effective medication for alcohol use disorder but is underutilized owing to fears of hepatotoxicity.
- Naltrexone in patients with cirrhosis was not associated with development of DILI using RUCAM scoring.
- Naltrexone appears to be safe in patients with compensated and decompensated cirrhosis.
- This study may encourage use of naltrexone in patients with existing liver disease and ongoing alcohol use disorder.

Impact and Implications:

Naltrexone is an effective medication for treating alcohol use disorder but is underutilized in patients with underlying liver disease due to historical concerns regarding hepatotoxicity. This retrospective study shows no drug-induced liver injury in a large cohort of patients with cirrhosis with new initiation of naltrexone. This study may encourage providers to prescribe naltrexone to patients with existing liver disease with ongoing alcohol use disorder.

https://doi.org/10.1016/j.jhepr.2024.101095

 JHEP Reports, 2024, 6, 1–5

NALTREXONE

- 25mg (1/2 tab) for 3-4 days, then 50mg od
- 100mg listed as max dose, if tolerated up to 150 off label
- Peaks a few hours after taking
- PRN use possible
- Can be combined with other AUD meds
- Depot injection (“vivitrol”) available in USA but not Canada (yet)

ACAMPROSATE

- “Acampral”
- 1st line agent, approved by Health Canada
  - NNT 12 for return to any drinking
- exact mechanisms not known
- decreases **glutamate**, indirectly potentiates **GABA**
- I describe it to patients as the medication “rebalances” their brain chemistry → less craving

ACAMPROSATE

- limitations: ineffective while drinking, tid dosing, renal dosing, contraindicated in severe renal disease
- Initial 333 tid x 1 week, then 666mg tid
- Benefits: well tolerated
- Covered by ODB (LU 531) and private plans, $241/month
- Listed side effects: suicidality, amnesia, anxiety, depression, somnolence, n/v, abdo pain, pruritis, rashes

OFF LABEL ANTI-CRAVING MEDS

- Gabapentin
  - Titrate up to 900 tid
  - Cheap, can be combined with other AUD meds
  - Helps with withdrawal as well
  - ↑ GABA in the brain
- Pregabalin
- Baclofen
  - GABA agonist, ↓ dopamine release
- Topiramate
  - ↑GABA receptor activity, ↓glutamate release, ↓dopamine release
- Herbal GABA

ANTI-CRAVING MEDS — WHAT'S NEXT

- Can use virtually any combination of anti craving meds
  - Naltrexone + gabapentin
  - Acamprosate + gabapentin
  - Acamprosate + naltrexone
  - Any of the above with baclofen, or topiramate
  - Pregabalin instead of gabapentin if gabapentin not tolerated
- Average 9 months to a year
  - Patient directed taper or discontinuation
  - Consider prn use of naltrexone

A FEW CASES

1. 65 yo male. Drinks 13 oz vodka daily. No alcohol for 24 hours. Presents in active withdrawal. PHMx alcoholic hepatitis (2022). No seizures. On no meds.

    - diazepam taper (home or ED), followed by naltrexone

2. 65 yo male. Drinks 13 oz vodka daily. Been sober for 1 week. PMHx hepatitis C (treated 2022), osteoarthritis. Takes Percocet daily.

    - acamprosate

3. 64 yo male. Drinks 13 oz vodka daily. Not in withdrawal. PMHx hepatitis C (treated 2022).

    - naltrexone or acamprosate if pt willing to pay
    - consider gabapentin

RESOURCES USED

Dharavath, R.N. et al. (20 Oct 2023). GABAergic signaling in alcohol use disorder and withdrawal: pathological involvement and therapeutic potential. *Frontiers in Neural Circuits*. 17:1218737.

Finley, C.R. et all (August 2020). *Pharmacologic treatment of alcohol use disorder. Canadian Family Physician*. 66 (8), 583.

Thompson, R. Et al. (2024). Safety of naltrexone in patients with cirrhosis. *JHEP Reports.* 2024(6), 1-6.