Pharmacologic Interventions

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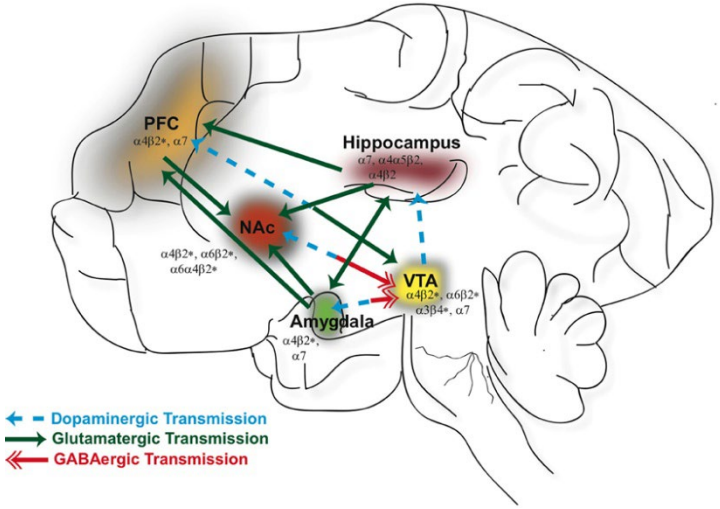
Introduction

- Alcohol and nicotine co-use is common
  - Individuals with Alcohol Use Disorder (AUD) are 3X more likely to use nicotine product
  - Individuals who have Nicotine Use Disorder (NUD) are 3X more likely to develop Alcohol Use Disorder (AUD)
- Co-use increases health risks
  - Cancer (e.g., oral, throat, liver), cardiovascular disease, lung disease
  - Mortality
- Treating AUD without addressing NUD and vice versa often leads to relapse

Falk et al. 2006; Shiffman et al. 1994; Shiffman & Balabanis, 1995

Neurobiological Basis of Co-use of Alcohol and Nicotine

- Cross-reinforcement
  - Both activate the mesolimbic dopamine pathway and enhance dopamine release in the ventral tegmental area (VTA) and nucleus accumbens (NAc)
  - Both substances interact with nicotinic acetylcholine receptors (nAChRs) : Alcohol - α6 subunit; Nicotine - α4β2 subunit
  - Nicotine reduces the sedative effects of alcohol and increases the urge to consume more alcohol
- Cross-tolerance
  - Chronic nicotine exposure reduces the intoxicating effects of alcohol
  - Repeated alcohol exposure creates cross-tolerance to nicotine



Feduccia et al., 2012, Adams, 2017.

Promising Medications for Treating Alcohol and Nicotine Co-use

Varenicline

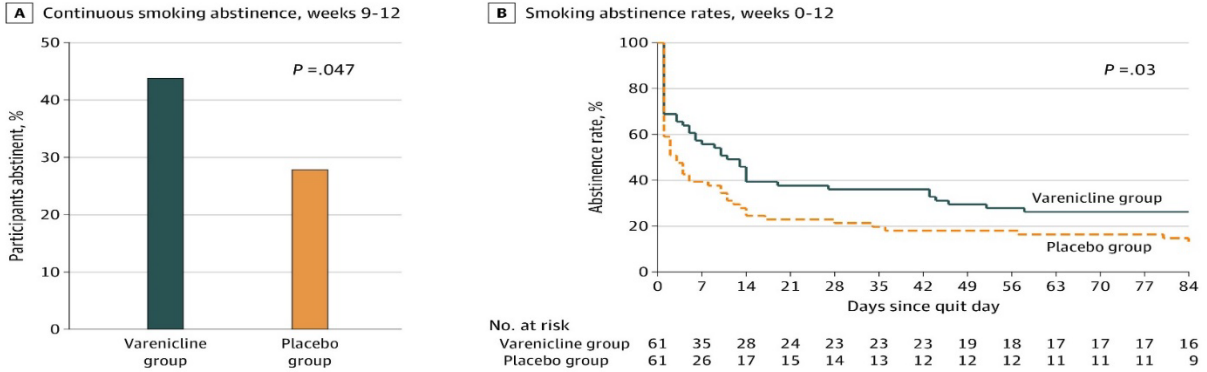
- Mechanism of Action
  - Partial agonist at α4β2 nicotinic acetylcholine receptors
  - Reduces nicotine cravings and withdrawal symptoms
  - Decreases alcohol and nicotine consumption by modulating the mesolimbic dopamine system

- Efficacy: n=33, (Varenicline 16 vs. Placebo 17)
  - 7-day point prevalence smoking abstinence @ 12 weeks - Varenicline 43.8% vs Placebo 5.9%, p=.01. @ 24 weeks - Varenicline 31.3% vs Placebo 0%, p=.02.
  - Reduced alcohol consumption @ 12 weeks – mean [SD] Varenicline 5.7 [3.9] vs. Placebo 9.0 [5.3]

Hurt et al. 2018

Varenicline + Nicotine Patch

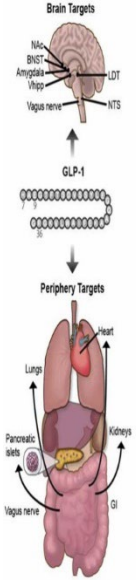
- RCT, N=122, 61 each arm
- Smoking abstinence @ week 9-12 - Varenicline + Nicotine patch 44.3% vs. Placebo + Nicotine patch 27.9%; odds ratio, 2.20; 95% CI, 1.01-4.80; P = .047
- Lower likelihood of relapse in the varenicline group relative to the placebo group (hazard ratio, 0.62; 95% CI, 0.40-0.96; P = .03)



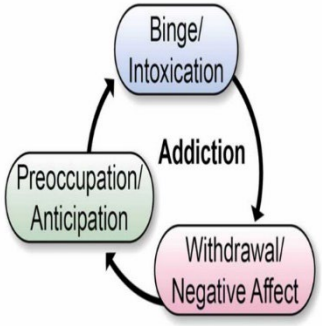
King et.al 2022

Glucagon-like Peptide-1 (GLP-1) Receptor Agonists

- Mechanism of Action
  - Primarily used for type 2 diabetes and weight management
  - May reduce alcohol and nicotine cravings by modulating the mesolimbic dopamine system
  - GLP-1RAs affect dopamine's synaptic availability and dopamine reuptake transporter (DAT) expression, which is known to mediate motivation and reward behaviors



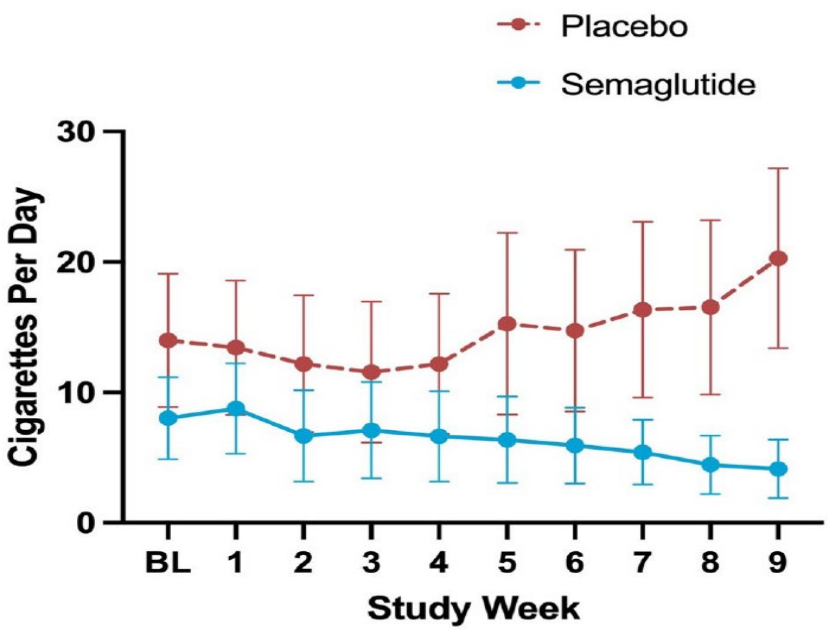
- GLP-1R agonists have shown to reduce alcohol, psychostimulants, opioids, and nicotine use and other addiction-related outcomes in preclinical models.
- Initial clinical studies support the safety and potential efficacy of GLP-1R agonists in addiction treatment. Several randomized controlled trials are underway.



Herman et al. 2024; Lee et al. 2024; Klausen et al. 2025

AUD Treatment with Semaglutide

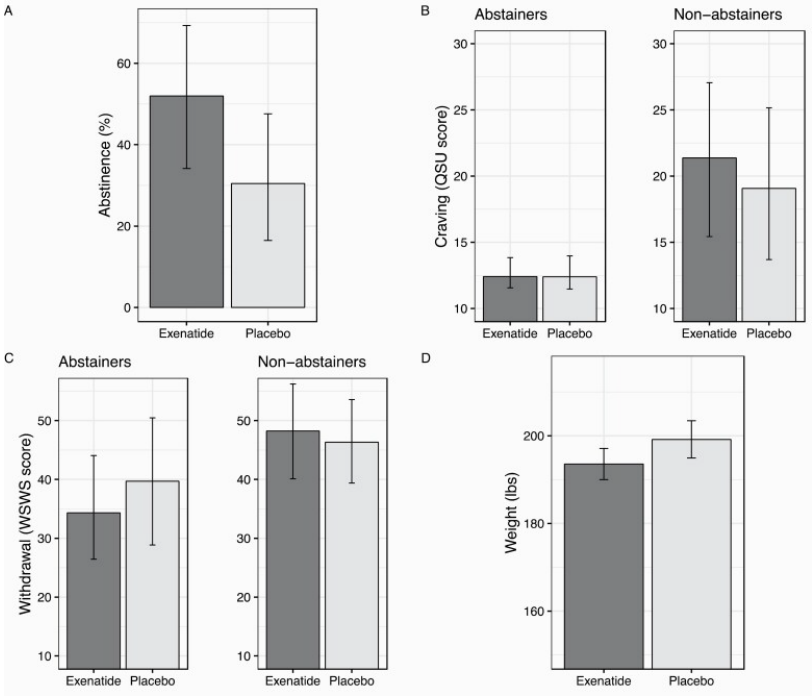
- RCT - n =48
- A significant reduction in alcohol craving and 41% reduction in alcohol intake among participants
- Decreased cigarette use in those who use cigarettes



Hendershot et al. 2024

NUD Treatment with Exenatide

- RCT n=84
- Exenatide (2mg s.c. once weekly for 6 weeks) + NRT improved smoking abstinence, reduced craving and withdrawal symptoms, and decreased weight gain among those who were able to abstain from smoking



Yammine et al. 2021,

Conclusion

- Alcohol and nicotine co-use is common
- FDA-approved medications for NUD show promise
- There is need for large-scale clinical trials to evaluate GLP-1 Receptor Agonists for alcohol and nicotine co-use

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Thank you ☺!