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Treating Alcohol Use Disorder in Genetically Susceptible Populations: A Case for Combination Medical and Genetic Interventions

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Abstract: Alcohol Use Disorder [AUD] affects millions of Americans every year, directly contributing to their personal suffering. Recent research suggests that the leading treatment for Alcohol Use Disorder, Cognitive Behavioral Therapy [CBT], may lead to increased relapse and self-blame among patients, highlighting the need for new, longer-lasting treatment options. This paper outlines the limitations of current treatments for AUD–including commonly prescribed medications such as naltrexone, acamprosate, and disulfiram–as well as therapeutic options for other addictions like dopamine reuptake inhibitors (DRIs), and seeks to present a combination medical treatment option that takes CBT and a patient's genetic predispositions into account. It argues that potential removal or inhibition of the cannabinoid 1 receptor [CB1] could be an effective strategy to address and prevent the biological causes of addiction–and, therefore, related suffering. Ethical concerns stemming from genetic engineering, such as cost, access to treatment and potential resulting hereditary class disparities, are presented and justified in light of the likelihood that a patient's quality of life would improve through such treatment.

Keywords: Alcohol Use Disorder (AUD), Cognitive Behavioral Therapy (CBT), Cannabinoid 1 Receptor (CB1), Precision Medicine, Genetic Predisposition, Relapse Prevention, Addiction Treatment, Gene Therapy.

DEFINITIONS [MAYO CLINIC, 2022]

Alcohol Use Disorder [AUD]: "a pattern of alcohol use that involves problems controlling your drinking, being preoccupied with alcohol or continuing to use alcohol even when it causes problems."

INTRODUCTION

Happiness has long been the pursuit of humans, driving immigrants to cross dangerous borders, colonists to fight imperial powers, and addicts to consume dangerous substances. In the section "Of What Sort of Proof the Principle of Utility is Susceptible" in his book *Utilitarianism*, philosopher John Stuart Mill from the 1800s proposed that humans consider only what is a "part of happiness or a means of happiness" to be "desirable" [Mill, 1863]. Substance addiction is a particularly intriguing mode of achieving pleasure, since it provides temporary euphoric effects, yet it comes at the cost of reduced well-being and long-term health, which in turn causes unhappiness. Consistently, alcohol consumption creates momentary happiness that does not extend into overall life happiness, while drinking problems notably decrease life wellbeing and happiness [Baumberg Geiger and MacKerron, 2016]. According to Dr. Daniel Falk from the National Institute on Alcohol Abuse and

Alcoholism, 65.4% of Americans drink. According to Mayo Clinic, the risks of alcohol use include impaired decision-making, liver disease, heart problems, neurological complications, birth defects, higher cancer risk, and more. This marks alcohol as a major problem to be targeted to prevent suffering. However, in a study by De Neve et al., a longer and more transcriptionally efficient allele of the 5-HTTLPR gene was linked to higher baseline happiness [2012]. In addition, a meta-analysis of twin and adoption studies estimated that AUD was around 50% heritable [Verhulst et al., 2015]. This debunks the idea that happiness is an emotion solely based on personal choices or environmental influences, thus proving that our genetics play a role. A growing body of research shows that genes influence human behavior and disease vulnerability more than previously thought, including our risk of alcoholism.

Alcoholism, or Alcohol Use Disorder [AUD], is defined by the Mayo Clinic as a pattern of drinking alcohol even when it causes problems, involving having to drink more and more to get the same effect or experiencing withdrawals. According to Evangelia Legaki et al., "Serotonin and dopamine pathways, crucial for regulating mood and processing rewards, have been associated with susceptibility to alcohol use disorder [AUD]" [Legaki et al., 2024]. Traditionally, alcoholism has been thought of as a personal failure or resulting from a lack of morals, and treated as such. This emerging evidence leads to the question: Should medical interventions be used to treat alcoholism in people with genetic predispositions? While current behavioral therapies can be extremely beneficial for certain patients, combination therapies should be considered for alcoholics, especially those with a genetic predisposition.

Currently, the leading treatment for Alcohol Use Disorder is Cognitive Behavioral Therapy [CBT]. According to Flanagan et al., "Behavioral interventions for AUD include providing psychoeducation on addiction, teaching healthy coping skills, improving interpersonal functioning, bolstering social support, increasing motivation and readiness to change, and fostering treatment compliance" [Flanagan et al., 2018]. Although this treatment may be effective for some patients, the methods used tend to blame the patient, which can result in poor reception and increase stigma, rendering the therapy less effective. In fact, "[r]ecent meta-analysis shows that at most 50% of people with AUD, after a longer follow up period of several years, achieve remission" [qtd. in Sliedrecht et al., 2019]. This means that the majority of people are relapsing under Cognitive Behavioral Therapy, highlighting the need for new treatment approaches. According to researchers Legaki et al., "[AUD's] pathophysiology is complex, involving genetic predisposition, environmental factors, and cumulative effects of alcohol consumption, underscoring the need for effective treatment strategies" [2024]. These new "effective treatment strategies" should take into consideration genetic factors.

LIMITATIONS OF CURRENT TREATMENTS

Naltrexone, Acamprosate, Disulfiram

There are many possible medical interventions to consider, including currently approved medications, dopamine reuptake inhibitors, and genetic engineering. Currently, there are three FDA-approved medicines for AUD: Naltrexone, Acamprosate, and Disulfiram [National Institute on Alcohol Abuse and Alcoholism]. Naltrexone blocks the euphoric effects of

drinking, making it easier to abstain; Acamprosate reduces withdrawal symptoms, aiding addicts in rehab; and Disulfiram prevents the body from breaking down the compounds in alcohol, resulting in highly unpleasant symptoms that discourage alcohol intake [National Institute on Alcohol Abuse and Alcoholism, 2025]. These medicines are all tools to aid people struggling with AUD to reduce or stop their alcohol intake, but they come with some considerable side effects. Naltrexone, in particular, commonly causes headaches and nausea, along with severe and dangerous withdrawals from the drug [SAMHSA, 2025]. Acamproste is known to worsen mental health as a side effect [SAMHSA, 2025]. This is particularly dangerous, considering the AUD population is already vulnerable to unstable mental health. Since Disulfiram prevents the breakdown of toxic compounds, patients who continue drinking while taking this medication experience extremely unpleasant reactions and may even severely harm their bodies. Disulfiram is also very restrictive as it prevents users from comfortably using products containing hidden alcohols in a normal routine, such as those found in cough syrups, mouthwash, tonics, and even sauces or vinegars. Altogether, these limitations introduce new inconveniences alongside reduced treatment compliance as they inhibit the pleasure experienced by the patient.

Dopamine Reuptake Inhibitors

Another possible treatment involves neurotransmitter pathways. A study by researchers Legaki et al. found that “alcohol use disorder's complexity arises from genetic and environmental factors, with [...] neurotransmitter pathways being critical” [2024]. In particular, a key neurotransmitter, dopamine, is involved in these pathways. Dopamine is often known as the “feel-good chemical.” Dopamine plays many roles in the body, including regulating reward, motivation, behavior, cognition, mood, and learning [Cleveland Clinic, 2022]. In a study on rats with a predisposition to alcoholism, researchers found that they had genetic dopamine deficiencies [Quintanilla et al., 2007]. Low dopamine comes with side effects such as tiredness, lack of motivation, unhappiness, mood swings, concentration problems, and, notably, also addiction. According to widely-cited neuroscientist Richard Davidson, four brain circuits influence long-term well-being, the first being “our ability to maintain positive states” and the second being “our ability to recover from negative states” [qtd. in Dalai et al., 2016]. To improve the state of unhappiness as a result of dopamine deficiencies, people would seek some sort of treatment to raise and maintain their dopamine levels so that they do not return to the state of undesirable unhappiness. In the study of low-dopamine rats, researchers found that ethanol stimulated dopamine release in their nucleus accumbens, a region in the brain that plays a key role in addiction, particularly the nucleus accumbens shell [Quintanilla et al., 2007]. This demonstrates that AUD may in part be due to genetic dopamine deficiencies that the patient naturally tries to correct themselves, resulting in self-medicating with ethanol, which increases their dopamine levels and, therefore, happiness. Then, to keep those levels up, they would need to continue drinking regularly without stopping, the major markers of AUD.

A solution to low dopamine is Dopamine Reuptake Inhibitors [DRIs]. DRIs work by preventing nerve cells from reabsorbing the dopamine that they release [Cleveland Clinic, 2022]. This increases the actual amounts of dopamine in the brain, helping offset the side effects of low dopamine. In fact, DRIs are already in use for the treatment of many addictions, such as smoking, binge eating, and street drug addictions [Cleveland Clinic,

2022]. Unfortunately, DRIs are not approved for AUD, so doctors and researchers would need to evaluate this medication to determine if AUD patients might benefit from it. However, if approved, DRIs still carry unique limitations. According to Dan Wagener from American Addiction Centers, patients may develop addictions to the DRIs themselves. Though this risk is much lower than it is for non-therapeutic substances, and medical professionals can further minimize the risk by selecting the most suitable DRI and prescribing the correct dose [Wagener, 2019], this still presents inherent risk because many AUD patients have a history of substance abuse, so prescribing addictive substances as a treatment for addiction may trigger adverse effects. This strongly necessitates treatments for AUD that do not carry risk of further substance addiction–like genetic engineering.

GENETIC ENGINEERING AS AN EFFECTIVE TREATMENT FOR AUD

Since AUD is caused in part by genetic factors, patients may benefit from genetic engineering– in particular, the removal or inhibition of the cannabinoid 1 receptor [CB1]. In a study by Hungund et al., researchers found that mice without cannabinoid 1 receptors [CB1] had reduced alcohol consumption because they did not experience a dopamine rush after consuming ethanol. If applied to humans with comparable effect, this method of treatment would completely circumvent the potential of further addiction since it does not involve any medications at all. It relies instead on the indication that patients would be repelled from ethanol use to supplement their dopamine, removing the reliance and euphoric effects from alcohol altogether. This treatment has many benefits. Firstly, by interrupting the general addiction pathway, patients would likely no longer develop addictions to substances. Unlike treatments such as Disulfiram or Naltrexone, patients would not end up switching to another, possibly even more dangerous, substance to get their dopamine fix. In other words, the patient would no longer have substance abuse. Next, there would be no need for medications. The FDA-approved treatments and DRIs require frequent administration, often through daily pills or injections. This inconvenience is an obstacle to patient treatment and can create issues if there is low compliance. Genome editing would solve this issue of inconvenience and patient compliance, making it a more straightforward treatment plan.

Also, according to bioethicists Giovanni Rubeis and Florian Steger, genetic engineering on germ-line cells would be inherited [2018]. This means that the offspring of the patient would receive the benefit of the procedures without needing to undergo treatment themselves, solving the issue of AUD within that hereditary line through a single procedure. Gene editing raises ethical dilemmas, however. This treatment would likely be prohibitively expensive since gene editing is extremely modern and considered high-technology. Any research or funding diverted into research may not be immediately accessible to low-income candidates. In addition, this treatment could create genetic disparities between those socioeconomic classes. In fact, many consider gene editing to be a “societal risk because it could lead to the creation of two classes of humans, the enhanced and the non-enhanced,” “[challenging] the very ideas of justice and equality which are crucial to modern society” [Rubeis and Steger, 2018]. However, gene editing could be ethically justified in this case because it is treating a medical condition to improve the quality of life for patients.

CONCLUSION

With three main medical interventions that could be administered with behavioral therapies– FDA-approved medications, DRIs, and gene editing–the exact treatment plan would be determined by a medical professional, taking into account the patient's circumstances. For example, someone with mild addiction may benefit from the FDA-approved medications if they just need a small reduction of obstacles in their journey to sobriety. People with low dopamine and a cleaner history of substance abuse may benefit the most from DRIs. Wealthier clients with genetic predispositions to AUD may choose for their child to receive gene editing to proactively prevent substance addictions. Some overall implications of these compounded treatments may include higher remission rates, improved health, increased awareness of genetic factors in healthcare, decreased stigma around AUD, more patients seeking treatment, and better patient experiences. In summary, while current behavioral therapies can be extremely beneficial for certain patients, combination medical interventions should be considered for alcoholics, especially those with a genetic predisposition.

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