HIGH SCHOOL EDITION
Journal of Student Research
Volume 11 Issue 2 (2022)

Evaluating the United States Minimum Legal Drinking Age: A Medical Review

Sehyun Jung[1] and Chad Doty[#]

[1]Liberty High School, USA
[#]Advisor

ABSTRACT

The Minimum Legal Drinking Age of 21 (MLDA-21) has been a source of contentious debate, enduring over a century of ethical and medical justifications. Critics cite the neurological and behavioral consequences of adolescent alcohol consumption to argue for the maintenance or even an increase from MLDA-21. Advocacy groups even propose mandatory training for adolescents in order to reduce harmful binge-drinking behavior. On the other hand, proponents of lowering the age limit argue that, ethically and politically, MLDA must match the threshold of legal adulthood. They also claim that there are some scientific basis for lowering MLDA. However, this study that analyzed a wide breadth of scientific sources found that medical consensus validates MLDA-21. Studies find that the harms of adolescent alcohol consumption, including mental disorders, behavioral complications, and developmental consequences, outweigh the benefits of making alcohol more legally accessible.

Introduction

Alcohol has long been a source of debate at the intersection between politics and science. When America was still a young republic, the consumption of alcohol stimulated regional economies, with workers everywhere spending their wages at pubs and bars [1]. In response, the Temperance Movement opposed the widespread consumption of alcohol, especially since many of participants' husbands returned home drunk, increasing rates of domestic violence and sexual abuse [2]. Since then, the question of who can drink alcohol has adapted with the times, most notably with the 1984 increase of the federal drinking age from 18 to 21.

The Minimum Drinking Age Act of 1984 encouraged all states to adopt the national drinking age of 21 [3]. Congress justified its decision through the recent rise in traffic accidents, teen pregnancy, and drug abuse among high school seniors who were eligible to drink. Advocacy groups aggressively argued that early adolescent drinking was causing chaos in American society. Still, many teenagers continued to consume and abuse alcohol despite the legal barrier. Research has shown that in 2012, despite the increase in legal drinking age, 42% of high school seniors reported drinking over the 30 days before the survey [3]. In fact, adolescents and young adults have frequent opportunities to binge drink. Studies have found that these activities mostly occurred during unsupervised parties [4]. Thus, it can reasonably be inferred that the risk due to alcohol increases without parental supervision. It is to this reason that proponents of lowering the drinking age argue that with adequate parental control and guidance in consuming alcohol, the inevitability of adolescent drinking can be controlled in a mature, healthy manner [5].

Furthermore, many countries, such as those in Europe and East Asia, already have adopted lower national drinking ages than those of the United States. For example, the Korean national drinking age is around 19, while Germany's national drinking age is 16 [6]. These ages are considerably lower than that of the United States. Combined with the aforementioned possible safeguards, some groups have pushed the United States government to lower the drinking age. However, despite these arguments, the current legislation has not correlated with a reduction in underage drinking with medical and/or political concerns.

The controversy therefore requires a thorough analysis of the available studies to justify and negotiate for the best solution that protects the American adolescents. Specifically, current literature can add a scientific approach to the debate, synthesizing medical studies to consider whether the United States federal drinking age should be lowered, maintained, or raised. The researched answer can guide future legislations to determine next steps to take that can satisfy both sides of the debate.

Methodology

This study analyzes peer-reviewed studies gathered from PubMed, EBSCOhost, and Google Scholar, though some external sources were utilized for elaboration of current research. Inclusion in this study depended on three criteria: (1) its credibility according to currency, authority, accuracy, and purpose; (2) its relevance to the biological effects of alcohol consumption among adolescents; and (3) the article's relationship to other sources. Most studies were completed after 2010, though a few were drawn from earlier if it adds significant validation or refutation. Finally, authors' backgrounds and affiliations were analyzed for potential conflicts of interest. This analysis considers potential bias to evaluate the extent to which it may have influenced the results. During the assessment, four were excluded for reasons such as: (1) insufficient evidence to determine the author(s)' credibility, (2) a lack of relevant scientific research, and; (3) a conflict of interest that created bias within the research.

Sources were then classified according to their theme. One overarching keyword that appeared multiple times was "development." Therefore, this study will first analyze how alcohol influences adolescent development, a topic further subdivided into neurological and psychological development, though there was often overlap between the two. However, the categories were analyzed separately until the final discussion. Altogether, this literature review analyzes 31 sources.

Review of Scientific Literature

Summarizing Effects of Alcohol on Various Aspects of Development

There is already a broad consensus that early consumption of alcohol correlates to developmental disorders, but the extent to which alcohol causes them remains unclear; there are disagreements on what exactly happens to adolescent drinkers as they mature. Thus, a key question in the debate is how far the effects of alcohol can transfer into adulthood.

Although features of physical development such as brain size and volume remain unimpaired by alcohol, its consumption causes critical changes such as brain cortical volume and refinement of cortical connections that persist into late adolescence and even into the early stages of adulthood [7]. Adolescent drinkers also showed smaller total-brain, frontal-lobe, and temporal-lobe volumes [8]. Thus, alcohol could inhibit vital stages of development, causing various neurological problems that often express themselves as behavioral problems. One such consequence is a disruption in evaluating risk and reward. Because of a heightened sensitivity to alcohol, the developing adolescent brain may recognize alcohol as a reward, making them more prone to initial drinks [9]. They are then more likely to binge-drink than those who are more neurologically and physically mature [10]. Thus, it can be reasonably concluded that early drinking can cause adolescents to seek alcoholic beverages at a greater frequency in the future than those who do not.

Understanding the full effects of alcohol on adolescents also requires an understanding of environmental factors. For example, early pubertal development among adolescents can increase the likelihood of early drinking behaviors, especially among girls [11]. Adolescent girls who begin puberty earlier often engage socially with older students who are more likely to use alcohol frequently [11]. Similarly, a COMPASS Host Study surveyed Canadian high school students and found greater occurrences of binge-drinking among students who engaged in related, risky behavior [12]. Furthermore, the more that students felt connected to their school, especially through involvement in

school sports, the greater the chance of drinking alcohol and binge drinking [12]. It also found that students who had not drunk as lowerclassmen were less likely to drink when they were upperclassmen [12]. Initial exposure has a significant impact on later behavior, emphasizing the need for early alcohol prevention and cessation programs. Habits transfer from adolescence to adulthood, just as those who drank at least once demonstrated a much greater likelihood of chronic drinking habits [12]. These studies agree that alcohol can have different effects based on individuals' environments. From gender to sense of place at school, adolescents have more risk factors associated with drinking; they need policies that consider both health and environmental factors.

However, not all studies seem to agree on the extent of alcohol's influence in teen development. For example, a conducted in London did not find a key correlation between early adolescent drinking and alcohol-related disorders in adulthood [13]. These researchers did concede short-term harms of alcohol consumption, such as the risks associated with malfunction in the central nervous system (CNS) [13]. However, they also emphasized that there is not enough evidence to confirm a connection between teenage alcohol consumption and problems that develop later in adulthood [13]. Despite contradicting most other research, the authors not only reported no competing interests but also were formally approved by the Norwegian Data Protection Authority and the Regional Committees for Medical and Health Research Ethics (REC) in Southeast Norway. Moreover, their study was funded by the Research Council of Norway of Alcohol and Drug Research, so it can be safely concluded that their research is accurate and trustworthy. This then paves the way for another task: there must be more concrete, experimental evidence, especially from cross-sectional studies, to prove that adolescent alcohol consumption actually causes developmental disorders.

Neurological Assessment of the Effects of Alcohol

Unlike for developmental disorders, there is a clear consensus on the immediate neurological effects of alcohol consumption. Casual drinking causes anomalies in the limbic and affective regions of the brain [7]. These asynchronies within the brain can cause a variety of cognitive malfunctions that induce further alcohol usage [7]. Thus, even casual drinking increases the likelihood of binge-drinking, especially for adolescents whose malleable brains perceive alcohol more as a reward than a risk [9]. Several studies have also indicated the possibility of familial influence on alcohol consumption [5, 14]. When parents facilitate drinking habits, it is more likely for adolescents to develop more healthy behaviors than when they drink unsupervised, such as at parties and other social events [5]. However, once these adolescents graduate from high school and leave home, they are no longer under parental supervision. Therefore, there is no guarantee that they will still maintain the same habits without supervision. Moreover, even under parental supervision, adolescents may still binge drink because they are still susceptible to the "reward" their brains perceive alcohol to be [9,14]. This can possibly lead to permanent binge-drinking habits that may take a long period of time to recover from.

Furthermore, binge drinking has detrimental neurological effects. For example, as the adolescents transitioned from moderate to higher levels of drinking, they frequently exhibited unusual cue-elicited brain responses in the dorsal striatum, cerebellum, PNG, and thalamus, a finding which researchers said has "important implications for future intervention strategies" since cue-elicited responses from alcohol could be lowered with at least 28 days of alcoholic abstinence [8]. However, even 18 months were not enough to reduce alcohol dependence for heavy users [8]. Young people are more susceptible to alcohol dependence; they have lower engagement of the frontoparietal network and greater engagement of the premotor cortex after the onset of binge drinking [8,14]. Thus, adolescents were more likely to fail to successfully respond to external stimuli than peers who did not drink.

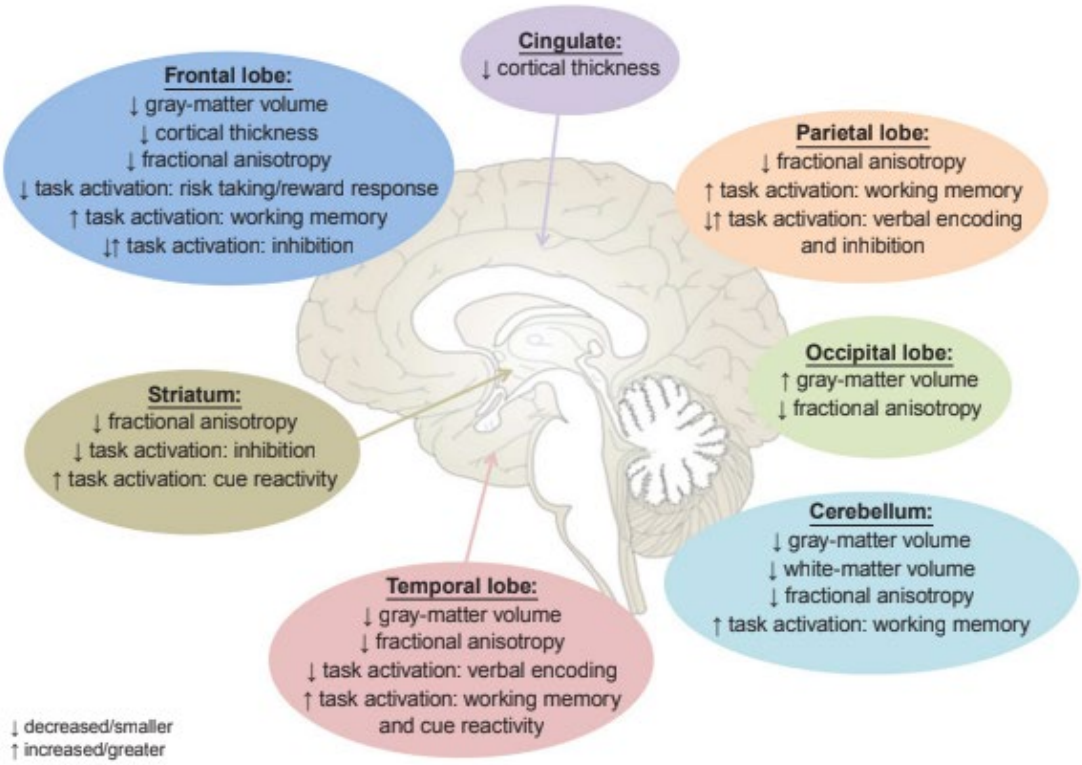

Figure 1. Replicated image that summarizes the impacts of alcohol in the developing adolescent brain [8].

As exemplified in Figure 1, researchers found many other complications associated with adolescent alcohol consumption, such as reduced cholinergic neuron makers and reduction of hippocampal neurogenesis [8, 14]. They emphasized neurobiological consequences could more quickly lead to an Alcohol Use Disorder (AUD) diagnosis [8]. Another study on the effect of different drug substances on rodents also agreed, finding that alcohol inhibits conditional discrimination and object recognition [15]. Furthermore, rodents injected with ethanol had a higher prevalence of depressive symptoms [15]. Alcohol can create a neurological imbalance that increases the likelihood of psychological problems such as anxiety and depression. Because the adolescent brain is so vulnerable to external damage, interruptions in neurological processing can lead to various behavioral, psychological, and physiological problems [7, 8, 15].

Another study analyzed the effects of binge-drinking on transgenic, modified mice and wild-type mice [16]. They evaluated hippocampal-dependent learning and the memory functions of both types of mice, exposing them to saline (SAL) and ethanol (EtOH). To maintain the integrity of the research, all of the test mice were housed under identical conditions, including housing space, temperature, a reversed light schedule (white lights from 19:30 to 07:30), and food and water provided when necessary. Researchers evaluated the mice's spatial learning and the extent of memory disturbances caused by ethanol accumulation by counting the number of errors and measuring the time each mouse took to complete a Hebb-Williams maze under different difficulty levels. They evaluated the data with two-way ANOVA studies, a technique in line with other neurological studies [16].

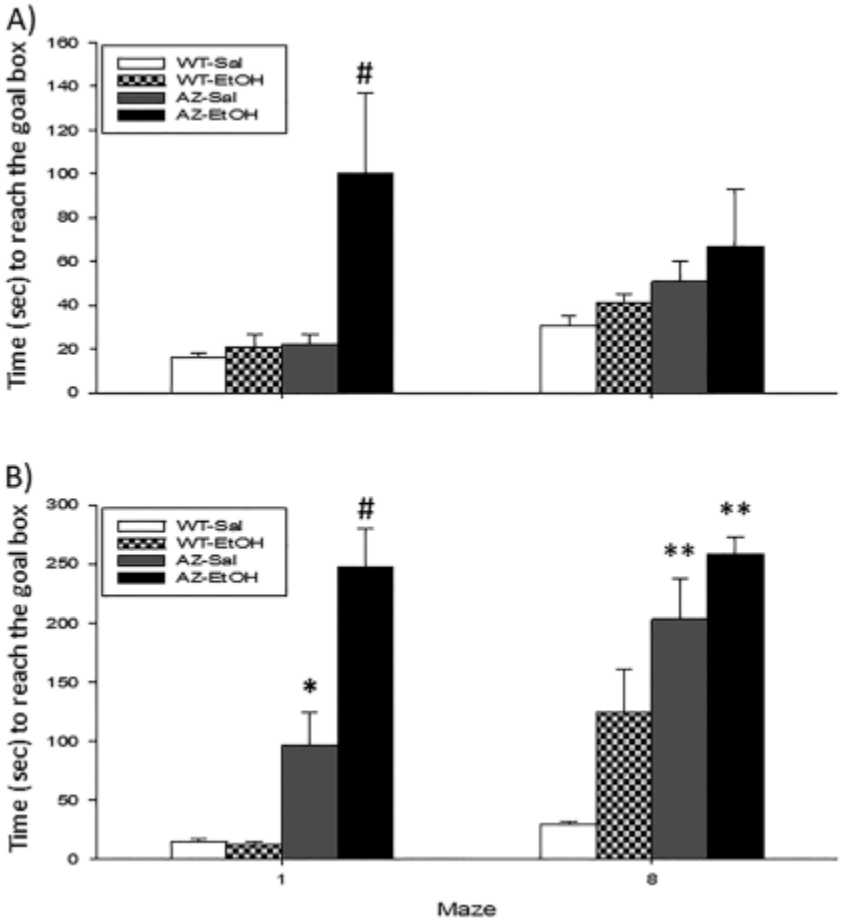

Figure 2. The chart above depicts the results of the described experiment [16].

Charts A and B demonstrate the time that the wild-type (WT) and transgenic Alzheimer's type (AZ) mice took to solve an easy maze (labeled as 1) and a difficult maze (labeled as 8). Graph A visualizes the data for mice at 6-months of age, and graph B visualizes the data for the mice at 12-months of age. A (#) mark identifies that alpha level $P < 0.05$ was significantly different from all other collected data, while (*) and (**) identified that $P < 0.05$ and 0.01, respectively, were significantly different from their corresponding WT-Sal counterparts.

The data show that ethanol exposure accelerates the appearance of AZ-like symptoms and a corresponding cognitive decline [16]. Ethanol consumption worsened cognitive impairment, significantly increasing the time it took for AZ-EtOH much to navigate the maze, especially at 12 months of age. Even mice without the AZ gene took much longer to complete the maze after EtOH was administered, especially for twelve-month-old mice at the most difficult maze [16]. The research supports the conclusion that adolescent binge drinking exacerbates the progression of dementia and cognitive impairment [16, 17]. The EtOH mice also experienced discrepancies in hippocampal function; they were unable to make precise actions in response to given stimuli. Further research will be needed to identify the exact mechanism through which EtOH activates inflammatory processes and exacerbates the onset of AZ [16].

Furthermore, the accumulation of ethanol in the central nervous system caused other symptoms throughout the body. In the muscular system, when the blood alcohol concentration was elevated, the rate of protein synthesis decreased by 25% in the first hour after alcohol consumption[18]. Moreover, intragastric alcohol reduced both sarcoplasmic and myofibrillar protein synthesis rates, although muscle protein synthesis remained unaffected after an adequate two-hour recovery period followed by twenty-four hours of admission of alcohol [18]. The immunological effects of ethanol remain largely unexplored, opening areas of possible investigation in the future. However, the accumulation of ethanol prevented cells from storing Vitamin C and E, impairing the ability of T-cells to respond quickly and precisely to pathogens [19, 20]. Chronic consumption of alcohol also caused disturbed body osmolality and thyroid interruptions, signaling a deleterious effect on endocrine homeostasis [21]. Alcohol's damage beyond the nervous system adds weight to the argument that maintaining or even raising the drinking age will reduce health complications associated with binge drinking, especially among adolescents. Research all agreed that physical and mental maturation before consuming alcohol was critical for safe consumption.

Correlation between Alcohol Consumption, Age, and Behavior

Illogical decision-making due to alcohol consumption is often dangerous enough to harm others. The United States saw an initial decrease in crime rates when the drinking age was first raised to 21 from 18 [3]. However, during Prohibition (1919 to 1933), crime rates dramatically increased. Legal sales of alcohol were banned, but many were still drinking illegally, increasing the number of violent mafia organizations who profited from these illegal sales [22]. Furthermore, traffic accidents and teen pregnancy rates remained at similar rates [22]. Banning alcohol today may not bear as sever consequences today, but people will continue to drink, even illegally [22]. Thus, it may be illogical to raise the drinking age just to avoid neurological problems.

Despite the controversy that surrounds the relationship between drinking age and behavior, neurological problems do lead to behavioral consequences. Alcohol causes damage in the visuospatial function, worsening verbal memory and mechanical learning [23]. These psychological effects transferred into adulthood and positively correlated to binge-drinking rates among young adults [23, 24]. Frequent binge-drinking also led to the development of criminal behavior and teenage pregnancy [25]. To support these findings, a five-year longitudinal study surveyed eighty-nine young adolescents with moderate to heavy drinking behavior found a higher prevalence of unprotected sex, which explains the rise in teen pregnancy rates when the drinking age was initially set to 18 [23]. Adolescent drinkers also experienced anxiety-like, impulsive behavior [24]. The strong positive correlation between underage drinking and behavioral issues makes underage drinking inadvisable. Early initial drinking encourages further drinking and causes cognitive impairment. Binge drinking then creates proven, tangible neurological and physical consequences that harm the wider community [24].

Differences due to sex and gender still remains unclear [23]. There are some studies on differences in consumption by sex, but not across the age spectrum [11]. More research on how sex affects the extent of cognitive impairment and behavioral damage attributed to alcohol would allow for more personalized AUD treatment based on social and demographic factors.

An important case study in Toronto, Canada from 1970 to 1972 shows what could occur if the United States were to lower the federal drinking age. Researchers asked twelve questions on how the new minimum drinking age of 18 impacted student behavior within the respondents' schools and communities, answering with either "yes," "no," or "uncertain," based on the recent decrease in drinking age to 18. 170 responses were collected as part of the case study [26].

Behavior	Yes	No	Uncertain	No Reply
More drinking of alcohol on school property	31	52	16	1
More drinking by students during lunch hours	40	40	19	1
More disciplinary problems involving drinking	34	60	6	0
More absenteeism related to drinking	22	60	17	1
More signs of hangovers among students	23	57	19	1
More discussion of drinking among students	43	29	26	2
More students arriving at school functions (i.e. dances, football games) with alcohol on their breath	56	28	14	2
More drinking at school functions	58	30	10	2
More students appearing "high" at school dances	43	39	16	2
Less smoking of cigarettes	1	70	28	1
Less smoking of marihuana	11	37	51	1
Less use of drugs such as LSD, speed, etc.	19	26	52	3

Figure 3. The reproduced chart above illustrates the responses collected. All numbers are calculated as percentages.

Surprisingly, the study shows that the majority of respondents answered that alcohol did not cause more dangerous behavioral consequences within the school, as 60% answered that they did not see more disciplinary problems or absences involving drinking [26]. However, the majority reported that they did see more students participating in school-related activities and social gatherings after drinking, though the questions did not ask how much students were drinking [26]. Some answered that more students appeared "high" during school dances [26], but despite the fact that alcohol did not cause a reduction in the consumption of other drugs such as nicotine, research demonstrates that the aftermath of the reduction in drinking age was not as detrimental as many feared.

Even so, the survey was based only on students' opinions, and there was no quantitative evidence on the consumption of alcohol or its effects. For example, the study did not measure students' blood alcohol content, nor could it determine how many absences were due to alcohol consumption outside of school. Moreover, the world has rapidly transformed since the 1970s, especially with the mass proliferation of the internet and mobile devices. The geographical, political, and ideological landscape has also transformed; students have a different understanding and knowledge of alcohol than students would have had in the 1970s. Thus the case study cannot apply directly across the United States today.; it requires careful assessment to determine its true meaning.

Even so, the case study warns that lowering the drinking age may lead to more students attending school after consuming alcohol and more students drinking during school-facilitated activities or parties. These activities can potentially lower academic success rates among students [26]. Before lowering the drinking age, lawmakers must consider the behavioral and social consequences just as carefully as they do the consequences to health.

Results

All studies in this review agree that early drinking facilitates the onset of neurological and behavioral complications that may cause developmental disorders. However, the extent of these developmental disorders remains in dispute, which contributes to the controversy surrounding the current federal drinking age.

Discussion

Many agree that lowering the drinking age can be dangerous. The overwhelming majority of the studies analyzed reported harmful effects that occur when alcohol is consumed at an early age. Only a consider the effects negligible,

but even these generally agree that binge drinking causes problems among young adults [13]. Furthermore, research proves a link between early drinking and chronic drinking in adulthood. Lowering the drinking age may create more severe health problems in the future [16].

Raising the drinking age does not seem to be a viable option either. The adolescent brain continues to mature well into the 20s; in fact, the complete development of the prefrontal cortex of the brain occurs around the age of twenty-five [27]. Excessive alcohol consumption between the minimum drinking age of 21 and the full maturation of the prefrontal cortex impairs critical functions such as cognitive thought process and moderation of social behavior [28]. However, adolescents continue to drink illegally even with the current minimum age of 21 [29]. Thus, raising the drinking age may not have the intended effect of reducing the amount of underage drinking.

Instead, mandatory education regarding alcohol consumption behavior may be more effective. Regardless of the drinking age, adolescents will still find both legal and illegal methods of binge drinking. Thus, the question is not a matter of "when" but a matter of "how" – how can legislators keep adolescents safe as they consume alcohol? Current studies show that current high school students often consume alcohol through dangerous methods such as combining alcoholic beverages with non-alcoholic beverages to increase their consumption [12]. Such methods of drinking lead to a higher prevalence of binge drinking among adolescents in unregulated settings such as parties [4]. Education can help students monitor their own consumption and drink more safely.

Maintaining the current drinking age appears to be the best option. Drinking after the age of 21 allows individuals to complete most critical maturation processes and avoid the complications of binge drinking during adolescence [30]. Moreover, adults are more likely to self-regulate and make safer choices [30]. With individuals more matured to consume alcohol, they can stand more firmly against aggressive peer pressure to make better decisions that protect their physical and mental health from inappropriate drinking.

Comparing alcohol education and intervention options to determine which is most effective requires further cross-sectional study. Current research has gaps where subjective surveys leave room for bias and misrepresentation. Furthermore, current cross-sectional studies have large disagreements, necessitating an urgent requirement for much wider variety of data to support either one case or the another. [13, 31]. These gaps must be filled in order to strengthen the scientific perspective on the drinking age controversy by providing a common data that the public and lawmakers can rely on.

Conclusion

Evidence suggests that rather than raising or lowering the current drinking age, maintaining the current United States minimum drinking age is the safest, most feasible option. Researchers have also highlighted the importance of intervention and education programs in preventing the development of physical, neurological, behavioral, and social complications through adolescent binge drinking. Further study is needed to compare possible strategies as soon as possible in order to reduce binge drinking across demographics.

Limitations

There are hundreds of already published alcohol-related research, many of which were not included in this review. Thus, this study is not a complete, systematic review of currently available research. The conversation in the medical community is ongoing, especially in regard to behavior – through what mechanisms does cognitive impairment lead to a rise in crime rates and risky behavior? The how and the why of the behavioral consequences of alcohol remains unknown. It will be critical to identify these processes in upcoming research in order to guide the development of more advanced treatment options for AUD.

Finally, though this study carefully evaluated each source for credibility, there always is the possibility of bias even without stated conflicts of interest. Thus, it becomes increasingly critical to adopt a holistic approach in

evaluating another available research to ensure that one source does not detract from understanding scientific consensus.

Acknowledgements

I would like to thank Mr. Chad Doty of Liberty High School (Frisco, Texas, United States) for a total support in completing the project successfully. He has provided me the guidelines and resources necessary to complete the research as an extension of the course curriculum in AP Seminar. I would also like to thank Mr. Daniel Koh and Dr. John Abt for their advice and guidance on academic writing.

References

1. Klugewicz, S. M. (2020, May 31). *The Glory of Mankind: Alcohol and the Early Republic. The Imaginative Conservative.* https://theimaginativeconservative.org/2013/03/glory-mankind-alcohol-early-republic-stephen-klugewicz.html
2. Britannica, T. Editors of Encyclopaedia (2021, November 9). *temperance movement.* Encyclopedia Britannica. https://www.britannica.com/topic/temperance-movement
3. "21 Is the Legal Drinking Age." *Consumer Information*, Federal Trade Commission, 13 Mar. 2018, www.consumer.ftc.gov/articles/0386-21-legal-drinking-age.
4. Mair, C., Lipperman-Kreda, S., Gruenewald, P. J., Bersamin, M., & Grube, J. W. (2015). Adolescent Drinking Risks Associated with Specific Drinking Contexts. *Alcoholism, clinical and experimental research,* 39(9), 1705–1711. https://doi.org/10.1111/acer.12806
5. Choose Responsibility (2012) *FAQs.* chooseresponsibility.org
6. ProCon. (2016, March 10). *Minimum legal drinking age in other countries - drinking age - procon.org*. Drinking Age. https://drinkingage.procon.org/minimum-legal-drinking-age-in-other-countries/
7. Windle M. (2016). Drinking Over the Lifespan: Focus on Early Adolescents and Youth. Alcohol research : currentreviews, 38(1), 95–101.
8. Jones, S. A., Lueras, J. M., & Nagel, B. J. (2018). Effects of Binge Drinking on the Developing Brain. *Alcohol research : current reviews*, 39(1), 87–96.
9. Spear, L. P., & Swartzwelder, H. S. (2014). Adolescent alcohol exposure and persistence of adolescent-typical phenotypes into adulthood: a mini-review. Neuroscience and biobehavioral reviews, 45, 1–8. https://doi.org/10.1016/j.neubiorev.2014.04.012
10. Krieger, H., Young, C. M., Anthenien, A. M., & Neighbors, C. (2018). The Epidemiology of Binge Drinking Among College-Age Individuals in the United States. *Alcohol research : current reviews,* 39(1), 23–30.
11. Lanza, S. T., & Collins, L. M. (2002). Pubertal timing and the onset of substance use in females during early adolescence. *Prevention science : the official journal of the Society for Prevention Research*, 3(1), 69–82. https://doi.org/10.1023/a:1014675410947
12. Holligan, S. D., Battista, K., de Groh, M., Jiang, Y., & Leatherdale, S. T. (2019). Age at first alcohol use predicts current alcohol use, binge drinking and mixing of alcohol with energy drinks among Ontario Grade 12 students in the COMPASS study. Utiliser l'âge de la première consommation d'alcool pour prédire la consommation d'alcool, la consommation excessive d'alcool et le mélange d'alcool et de boissons énergisantes chez les élèves de 12e année en Ontario dans le cadre du projet COMPASS. *Health promotion and chronic disease prevention in Canada : research, policy and practice*, 39(11), 298–305. https://doi.org/10.24095/hpcdp.39.11.02

13. Maimaris, W., & McCambridge, J. (2014). Age of first drinking and adult alcohol problems: systematic review of prospective cohort studies. Journal of epidemiology and community health, 68(3), 268–274. https://doi.org/10.1136/jech-2013-203402
14. Crews, F. T., Vetreno, R. P., Broadwater, M. A., & Robinson, D. L. (2016). Adolescent alcohol exposure persistently impacts adult neurobiology and behavior. *Pharmacological Reviews*, 68(4), 1074–1109. https://doi.org/10.1124/pr.115.012138
15. Spear L. P. (2016). Consequences of adolescent use of alcohol and other drugs: Studies using rodent models. *Neuroscience and biobehavioral reviews*, 70, 228–243. https://doi.org/10.1016/j.neubiorev.2016.07.026
16. Ledesma, J. C., Rodríguez-Arias, M., Gavito, A. L., Sánchez-Pérez, A. M., Viña, J., Medina Vera, D., Rodríguez de Fonseca, F., & Miñarro, J. (2021). Adolescent binge-ethanol accelerates cognitive impairment and β-amyloid production and dysregulates endocannabinoid signaling in the hippocampus of APP/PSE mice. *Addiction biology*, 26(1), e12883. https://doi.org/10.1111/adb.12883
17. Tatarnikova OG, Orlov MA, Bobkova NV. (2015). Beta-Amyloid and tau-pro-tein: structure, interaction, and prion-like properties. *Biochemistry (Mosc)*. 80(13):1800-1819.
18. Pruznak, A. M., Nystrom, J., & Lang, C. H. (2013). Direct central nervous system effect of alcohol alters synthesis and degradation of skeletal muscle protein. *Alcohol and alcoholism (Oxford, Oxfordshire),* 48(2), 138–145. https://doi.org/10.1093/alcalc/ags113
19. Mocchegiani E, Costarelli L, Giacconi R, Malavolta M, Basso A, Piacenza F, Ostan R, Cevenini E, Gonos ES, Franceschi C, Monti D (2014). Vitamin E-gene interactions in aging and inflammatory agerelated diseases: implications for treatment. A systematic review. *Ageing Res Rev.* 14:81–101
20. Strohle A & Hahn A. (2009).Vitamin C and immune function *Med Monatsschr Pharm.* 32(2):49–54. 55-46
21. Rachdaoui, N., & Sarkar, D. K. (2017). Pathophysiology of the Effects of Alcohol Abuse on the Endocrine System. *Alcohol research : current reviews,* 38(2), 255–276.
22. Hall, W. (2010). What are the policy lessons of National Alcohol Prohibition in the United States, *1920-1933 Addiction*, 105(7), 1164–1173.https://doi.org/10.1111/j.1360-0443.2010.02926
23. Lees, B., Meredith, L. R., Kirkland, A. E., Bryant, B. E., & Squeglia, L. M. (2020). Effect of alcohol use on the adolescent brain and behavior. *Pharmacology, biochemistry, and behavior*, 192, 172906. https://doi.org/10.1016/j.pbb.2020.172906
24. Towner, T. T., & Varlinskaya, E. I. (2020). Adolescent ethanol exposure: Anxiety-like behavioral alterations, ethanol intake, and sensitivity. *Frontiers in Behavioral Neuroscience*, 14. https://doi.org/10.3389/fnbeh.2020.00045
25. Chung, T., Creswell, K. G., Bachrach, R., Clark, D. B., & Martin, C. S. (2018). Adolescent Binge Drinking. *Alcohol research : current reviews*, 39(1), 5–15.
26. Smart, R. G., & Schmidt, W. (1975). Drinking and problems from drinking after a reduction in the minimum drinking age. *The British journal of addiction to alcohol and other drugs*, 70(4), 347–358. https://doi.org/10.1111/j.1360-0443.1975.tb00048.x
27. Johnson, S. B., Blum, R. W., & Giedd, J. N. (2009). Adolescent maturity and the brain: the promise and pitfalls of neuroscience research in adolescent health policy. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine*, 45(3), 216–221. https://doi.org/10.1016/j.jadohealth.2009.05.016
28. Arain, M., Haque, M., Johal, L., Mathur, P., Nel, W., Rais, A., Sandhu, R., & Sharma, S. (2013). Maturation of the adolescent brain. *Neuropsychiatric disease and treatment*, 9, 449–461. https://doi.org/10.2147/NDT.S39776
29. U.S. Department of Health and Human Services. (2021, May). *Underage drinking.* National Institute on Alcohol Abuse and Alcoholism. Retrieved from https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/underage-drinking

30. DeJong, W., & Blanchette, J. (2014). Case closed: research evidence on the positive public health impact of the age 21 minimum legal drinking age in the United States. *Journal of studies on alcohol and drugs*. Supplement, 75 Suppl 17, 108–115.
31. Enstad, F., Evans-Whipp, T., Kjeldsen, A., Toumbourou, J. W., & von Soest, T. (2019). Predicting hazardous drinking in late adolescence/young adulthood from early and excessive adolescent drinking - a longitudinal cross-national study of Norwegian and Australian adolescents. *BMC public health*, 19(1), 790. https://doi.org/10.1186/s12889-019-7099-0