Comparison of the influence of alcohol and cannabis on the dynamics of the accommodative response

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Statements and Declarations

The authors declare that they have no competing financial interests.

ABSTRACT

Purpose: to assess and compare the changes produced by the two most commonly used substances, alcohol and cannabis, on accommodation dynamics.

Methods: **A total of 38 young participants (19 females) were enrolled in the study. They were assigned to two groups: a cannabis group (N = 19) and an alcohol group.** Participants in the cannabis group underwent two randomized sessions: a baseline session **and a session after smoking a cigarette. Participants in the alcohol group underwent three randomized sessions: a baseline session, a session after the intake of 300 ml of red wine (Alcohol 1), and other after the ingestion of 450 ml of wine (Alcohol 2)**. **For the accommodation assessment, the open-field autorefractor WAM-5500 was used.**

Results: The decrease of the mean velocity of the accommodative response produced by Alcohol 2 condition was significantly greater than that observed for Alcohol 1 and Cannabis ($p = 0.046$). The direction of the accommodation (near-distance and distance-near) had no effect on the deterioration of the accommodation dynamics following substance use. The target distance had a significant effect on the decrease of the mean velocity following substance use ($p = 0.002$). The decrease of the amplitude of the accommodative response was associated with a decrease of the peak velocity ($p = 0.004$) and the increase of the accommodative lag ($p < 0.001$).

Conclusions: a moderate-high dose of alcohol impairs accommodation dynamics to a greater extent that lower dose of alcohol or smoked cannabis. The deterioration of the accommodation mean speed was higher for a shorter target distance.

KEYWORDS: alcohol consumption, cannabis use, accommodation dynamics, accommodative lag, accommodative response, target distance.

1. INTRODUCTION

The accommodative system is one of the most important components of the visual function, as long as it enables sharp vision at any distance. A proper functioning of the accommodation dynamics is essential to perform tasks that require effective accommodative changes, such as driving, when we need to constantly change focus from distance (the road, signals, etc.) to near (speedometer, fuel indicator, navigator, etc.). The accommodation dynamics are controlled by the autonomic nervous system (ANS), mainly by the parasympathetic tone, although the sympathetic tone is also known to play a role [1]. The use of psychoactive substances such as alcohol or cannabis may trigger changes on the ANS, thus generating changes on the accommodative response. Alcohol was consumed daily by one in twelve adults (8%) in Europe during 2019, and 30% used it weekly (ec.europa.eu/Eurostat). According to the European Drug Report 2021, cannabis constituted the most tried illicit drug during that year, with 79 million people having used this psychoactive substance [2].

The effects of ingested alcohol on ANS are mediated through actions on different neurotransmitters, producing excitatory and inhibitory signals [3]. Given that alcohol inhibits the parasympathetic nervous system (PNS), responsible for accommodation [4], it seems reasonable that the accommodative response would be affected by this substance. In this line, some authors have reported an increase of the reaction time of accommodation following alcohol consumption [5]. Considering the accommodative response, Campbell and colleagues also observed that chronic alcoholism reduced static accommodation [6]; however Miller and colleagues found that ingested alcohol increased the accommodative response for near (30 cm) and distance (6 m) static targets [7]. Alcohol also interfere with the sympathetic nervous system (SNS), which takes part in the disaccommodation (near-distance) process [1]. It has been reported that the variability of the accommodative response is a consequence of the variation in heart rate and arterial pulse, controlled by the SNS [8, 9]. Alcohol rise both heart rate and blood pressure [10, 11], so the variability of the accommodative response would be altered as well.

It has been suggested that cannabis acts on the ANS, stimulating the SNS and inhibiting the PSN [12]. The main psychoactive compound of cannabis is the Δ-9-tetrahydrocannabinol (THC) that binds to cannabinoid receptors, located through the central nervous system. These receptors take part in the neurotransmission and are present in the retina and visual cortex, but also in important components of the accommodative system such as the ciliary muscle [13]. Therefore, the accommodative system could be altered by cannabis, however there is very little information about the influence of cannabis on the accommodative response. It has been reported that cannabis users indicate difficulties when reading under the effects of the drug [14, 15]. Also, it has been suggested that cannabis consumption may trigger accommodative infacility, accommodative insufficiency and reduced accommodative amplitude [16, 17]. In addition, a recent study carried out in cannabis smokers showed an increase of the accommodative lag under the influence of this substance [18].

Alcohol is a socially accepted substance and cannabis is often conceived of as a non-harmful drug. However, their effects on important functions as the visual system and specifically on the accommodative response, can be an impediment to performing everyday tasks safely, representing an issue of concern. Comparing the visual impairment derived from the use of these substances may help to better understand how they exert their effects on the accommodative system. Thus, the aim of this study was to assess and compare the effects of ingested alcohol and smoked cannabis on the accommodation dynamics.

2. METHODS

2.1. Participants

A total of 38 participants were included in the study (mean age ± SD; 23.5 ± 3.5 years; range 19-33), of which 19 were female. The inclusion criteria covered the following aspects: being alcohol and/or cannabis user, monocular visual acuity of at least 20/20 (with best correction if necessary). Participants were excluded if they had any history or current illness, or binocular/accommodative problems, clinically significant disorders with alcohol or cannabis use according to the Alcohol Use Disorder Identification Test (AUDIT) [19] or the Cannabis Use Disorder Identification Test revised (CUDIT-r) [20], pregnancy or breastfeeding. They were classified into two different groups: alcohol and cannabis (parallel design). After classification, 19 participants were allocated in the alcohol group (mean age ± SD; 22.5 ± 3.1 years) and 19 participants formed the cannabis group (mean age ± SD; 24.5 ± 3.7 years). The results of the Mann-Whitney U test showed that the age of both groups did not differ significantly ($Z = 1.844$; $p = 0.075$).

The study was adhered to the tenets of the Declaration of Helsinki and an informed consent was obtained from all participants before enrolling the study. The University of Granada Human Research Ethics Committee prospectively evaluated and approved the procedures of this investigation (921/CCEIH/2019).

2.2. Procedure

All volunteers attended an initial visit where inclusion criteria were checked, and they were informed about the objectives and procedures of the study. Moreover, participants assigned to the alcohol group completed three experimental sessions in random order: Baseline, Alcohol 1 and Alcohol 2. Participants in the cannabis group completed two sessions in random order: Baseline and Cannabis. The criteria followed to assign participants to alcohol or cannabis groups were based on the substance they normally used. Most of the volunteers who indicated cannabis use were also occasional alcohol users, so we chose an allocation ratio of 2:1 in such cases, as finding participants who were cannabis users was more difficult.

Alcohol consumption simulated a social drink environment [21, 22] by consuming red wine with 13.5% alcohol content (Pago de Almaraes wineries S.L., Benalúa de Guadix, Granada, Spain). Experimental sessions were performed 2 hours after lunch, and participants drunk 300 ml in the Alcohol 1 session (≈ 32.4 g of alcohol) and 450 ml in the Alcohol 2 session (≈ 48.6 g of alcohol). Participants had approximately 40 minutes to complete the consumption and the breath alcohol content (BrAC) was controlled 30 minutes after, once the alcohol had been absorbed [23, 24], and every 20 minutes thereafter. The mean BrAC of such measurements was considered for analysis.

Cannabis use followed an *ad libitum* procedure. Participants underwent to the cannabis session 20 minutes after consuming a cannabis cigarette prepared and smoked as they usually do in their habitual use. Before starting experimental sessions, we checked cannabis or other drugs use and breath alcohol content with the Dräger DrugTest 5000 and the Dräger Alcotest 6820 breath analyzer (Dräger Safety AG & Co. KGaA, Lübeck, Germany), respectively.

2.3. Accommodative response assessment

At the initial visit, an optometric evaluation was made to check the inclusion criteria. If necessary, optical correction was adjusted. We measured the amplitude of accommodation with the push-up method to ensure normal values as a function of age [25]. Also, the near point of convergence was measured to discard convergence insufficiency, obtaining for all participants values of 5 cm or less [26].

The WAM-5500 (Grand Seiko Co. Ltd., Hiroshima, Japan) was employed for measuring the accommodative response dynamically. This is an open-field autorefractor, clinically validated for measuring accommodative response in its dynamic and static mode [27]. For measurements, we used the dynamic mode (HI-SPEED), with a sample frequency of 5 Hz and a sensitivity of 0.01 D. Subjects had to fixate a target binocularly and the device registered the spherical equivalent from one eye randomly selected. If they need optical correction, measurements were taken while wearing soft contact lenses.

During measurements, accommodation changes were triggered by changing participant's fixation between two different targets: one placed at 4 m and other at near distance (0.4 or 0.2 m). In this way, accommodation and disaccommodation steps of 2.25 and 4.75 D were generated. The fixation chart provided by the WAM-5500 manufacturer was employed as far target. This is a square (234 x 324 mm) chart comprising a 78 mm grid with a four-pointed star placed in the center. The near target was the same six-pointed black star, printed on a transparent slide. More information about the targets can be found in [18]. The room luminance was kept constant during measurements (150 lux), measured at the participant's corneal plane (T-10 illuminance meter, Konica Minolta). Participants were asked to change their fixation from one target to another every 10 s, guided by an audible alarm, starting at the far distance target (4 m). Participants were encouraged to make the changes as fast as possible, keeping the target in focus at all times and without blinking wherever possible. We measured 20 s of accommodation/disaccommodation cycles, and this was repeated three times, completing 60 s of measurement. The accommodation dynamics measurement procedure is summarized in Fig. 1.

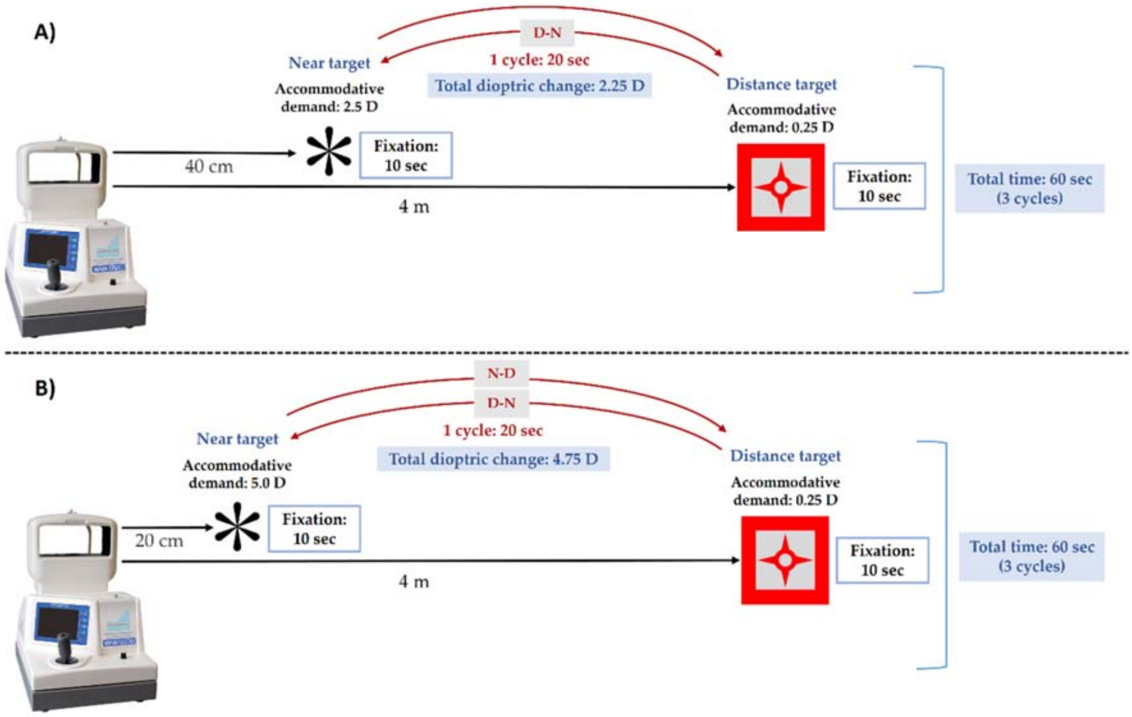

Fig. 1. Accommodation dynamics measurement process using WAM-5500 for both target distances: 40 cm (A) and 20 cm (B), and including near-distance (N-D) and distance-near (D-N) changes

Once the measurements were obtained, the data was divided into accommodation and disaccommodation cycles for subsequent analysis, allowing us to obtain the step response. Then, we calculated the amplitude of the response (D) as the maximum difference of the response. The mean accommodation/disaccommodation velocities (D/s) were also obtained as the absolute value of the dioptric change divided by the time over the interval 10%– 90% of the total step (80% of the absolute value). The absolute value of the maximum dioptric change by time unit was called the accommodation/disaccommodation peak velocities (D/s). These parameters have been obtained as in previous work [18, 28-30]. The response time was obtained as the time elapsed between the onset of the change in the accommodative response and when the accommodative response reached a steady-state level [28]. From the moment when the accommodative response reached a steady-state level, we obtained two more parameters: the accommodative lag (D) and the accommodative variability (D). The accommodative lag was computed by subtracting the mean focus point during the test (WAM-5500 refraction value) from the target distance (2.25 or 4.75 D) and adjusting the reference static refraction value (taken at 4 m) [31]. On the other hand, the variability of accommodation corresponds to the standard deviation of the accommodative response [18, 30, 32].

To compare the experimental conditions, the results of the different variables have been calculated as deteriorations, i.e. the absolute value in the baseline session minus the absolute value in other experimental condition (Alcohol 1, Alcohol 2 or Cannabis). Thus, a positive or negative value may indicate impairment in different variables (Table 1).

2.4. Statistical analysis

The SPSS Statistics v.26 software (SPSS Inc., Chicago, IL) was used for the statistical analysis. The mean deterioration values ± standard deviations (SD) were reported for all the variables analyzed. A significance level of 95% was considered in all tests. The Kolmogorov-Smirnov test was used to examine the normality of the residuals ($p > 0.05$). First, a t-test for independent samples was performed to verify that there were no age differences between the two groups (alcohol and cannabis). To analyze the effect of the experimental condition on the deterioration of the accommodative variables, a Kruskal-Wallis test was conducted, providing the H statistic and the p-value. To assess the effect of the target distance (20 and 40 cm) and the direction of the accommodation (N-D and D-N), a Wilcoxon test was performed, providing the standardized statistic (Z) and the p-values.

Finally, correlations between the deterioration of the different variables was assessed by a Spearman correlation test. The correlation coefficients index (ρ) and the associated p-values are included.

3. RESULTS

The mean BrAC obtained for Alcohol 1 condition was 0.20 ± 0.09 mg/l, and the mean BrAC for Alcohol 2 condition was 0.32 ± 0.13 mg/l.

Results of the deterioration of the different accommodative variables in the three experimental conditions (Cannabis, Alcohol 1, and Alcohol 2) are shown in Table 2. The experimental condition had a significant effect on the decrease of the mean velocity, with pairwise comparisons indicating that the mean velocity following cannabis use was significantly lower than that observed for Alcohol 2 condition ($p = 0.045$). Mean velocity decreased 5.4% for Cannabis, 34.7% for Alcohol 1, and 37.3% for Alcohol 2 with respect to baseline condition. Peak velocity and the amplitude of the response decreased more for Alcohol 2 than for Cannabis and Alcohol 1 conditions, but the difference was not significant. The response time decreased after substance use, especially for Cannabis, but not significantly.

The accommodative Lag increased equally for Cannabis and Alcohol 1 conditions, while the variability of the response increased more for Alcohol 2 than for Cannabis and Alcohol 1 conditions.

Regarding the accommodation direction (distance-near and near-distance) for all substance use conditions (Alcohol 1, Alcohol 2, and Cannabis), no significant differences were observed for any of the variables analyzed (Table 3). Mean velocity deteriorated equally for both directions, while peak velocity decreased more for near-distance direction, but not significantly. Similarly, the response time increased more for near-distance step change, but the deterioration of the amplitude of the response was similar for both directions.

Considering the target distance (40 and 20 cm) for all substance use conditions (Alcohol 1, Alcohol 2, and Cannabis), mean velocity deteriorated significantly more for 20 cm than for 40 cm, decreasing 32.1% for 20 cm and 13.2% for 40 cm. The rest of the variables, however, did not show significant differences between the two target distances. Peak velocity and response time were slightly more deteriorated for 40 cm, while the amplitude of the response decreased more for 20 cm. The accommodative lag increased more for 40 cm, but the variability of the accommodation deteriorated similarly for both target distances.

The correlation analysis, considering the deterioration for all substance use conditions (Alcohol 1, Alcohol 2, and Cannabis), revealed a significant ascending association between the decrease of the amplitude of the accommodative response and the decrease of the peak velocity ($\rho = 0.199$; $p = 0.004$). Also, a descending correlation between the decrease of the amplitude of the accommodative response and the increase of the accommodative lag was observed ($\rho = -0.354$; $p < 0.001$). These correlations are represented in Fig. 2.

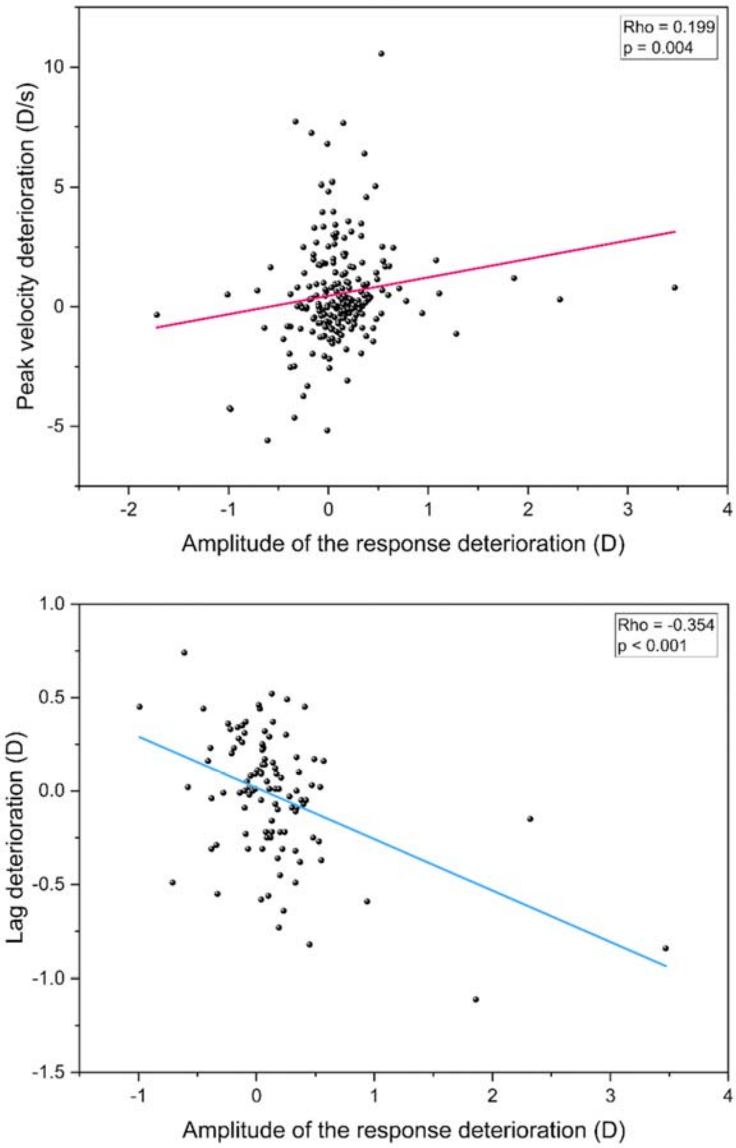

Fig. 2. Correlations between the deterioration of the amplitude of the response and the peak velocity and the accommodative lag.

4. DISCUSSION

The dynamics of the accommodative response was clearly impaired by alcohol and cannabis use, as indicated by the deterioration values obtained for all the accommodative variables. The results of this study show a decrease of the mean velocity and the peak velocity of accommodation, along with an increase of the response time and a decrease of the amplitude of the response following alcohol and cannabis use. Although there are few reports on the effects of alcohol on the accommodative function, most of them point toward a decrease of the accommodative response and an increase of the response time [5, 30, 33]. Likewise, the few existing studies on the influence of cannabis on accommodation reported an impact on some visual functions related to accommodation, like phoria and binocular depth vision [34-36] and also on accommodative response and accommodation dynamics [18, 37].

Regarding the substance used (i.e. cannabis, low alcohol dose, or moderate-high alcohol dose), our results showed that the moderate-high dose of alcohol (Alcohol 2) induced a greater impairment than the low dose (Alcohol 1) and cannabis for most of the accommodative variables: the peak velocity, the amplitude of the response, the variability, and, especially, the mean velocity. It is noteworthy that, even though the mean velocity decreased more for the moderate-high alcohol dose, the response time (inversely related to the mean velocity) increased more for cannabis use. However, given that the amplitude of the response (directly related to mean velocity) also decreased more for the moderate-high dose of alcohol, these results would be reasonable. In fact, the deterioration of the amplitude of the response after smoking cannabis is almost nil (Table 2), thus indicating that the increase of the response time would be the main variable responsible for the decrease of the mean velocity in this case. The deterioration obtained in previous experiments for these variables following alcohol and cannabis use are in line with these results [18, 30]. An experiment carried out in rodents suggested that alcohol and cannabis act on the SNS through different mechanisms [38]. Indeed, according to previous studies, it seems that alcohol have a strongest effect on different visual functions than cannabis [34, 39], although it may vary depending on the concentrations of these substances and other factors such as the means by which cannabis is supplied, or the type of cannabis used.

When considering the direction of the accommodation (distance-near and near-distance), we obtained that the peak velocity and the response time were more impaired for the near-distance step change, while the amplitude of the response decreased more for distance-near step change, and the mean velocity deteriorated equally for both directions. Besides, these differences were not significant, indicating that the direction of the accommodation, in line with previous findings. Ortiz-Peregrina and colleagues only observed a significant effect on the accommodative direction on the amplitude of the response when smoking cannabis, being higher the deterioration for near-distance direction [18]. Other study showed no significant difference in the deterioration of the accommodation following alcohol consumption when considering the direction of the accommodation [30]. According to the literature, the PNS (responsible for the distance-near accommodative response) is inhibited by alcohol and cannabis, while the SNS (responsible for the near-distance accommodative response) is stimulated by these substances [10, 40-42]. Considering this, it could be hypothesized that the deterioration for the distance-near (D-N) accommodative response would be greater than that for near-distance (N-D) response. However, results do not show this tendency for most of the variables evaluated in this experiment. There are two reasons for that: first, there is the fact that the near-distance accommodative response is much slower than the distance-near response [1, 43], so a greater deterioration of the velocity and the response time would be expected for the near-distance accommodative response. Second, according to the literature, it seems that the contribution of the PNS to the ciliary muscle is much more important, being responsible for the dynamic changes of the accommodative response, while the sympathetic innervation operates in setting the tone of sustained accommodation at near [43].

The influence of the demand of the accommodative target was also analyzed. Our results revealed, after substance use, a greater deterioration for all accommodative variables when the demand of the accommodative target was higher, but the difference was significant only for the mean velocity. According to the literature, it seems clear that the demand of the accommodative target has an influence on the accommodative response, in such a way that the greater the demand, the higher the variability of the response [44] and the accommodative lag [45, 46]. Other authors also observed that peak velocity and mean velocity were lower when the step change less abrupt (i.e., when the accommodative target was less demanding) [28]. In the same line, Aldaba and colleagues reported a lower mean velocity for a greater accommodative demand in normal conditions [29].

Our results also showed that the peak velocity decreased and the accommodative lag increased significantly as the amplitude of the response decreases, thus indicating that the decrease of the amplitude of the response is responsible for the deterioration of the accommodation dynamics following alcohol intake, particularly the accommodative lag and the peak velocity. The deterioration of the dynamic aspects of the accommodation is an issue of concern when performing tasks that require an accurate and effective accommodation. In this sense, some authors have reported an association between a deterioration of the binocular vision and accommodation insufficiency and complex tasks, such as simulated driving and flight [47, 48].

On the other hand, it should be noted that the assessment of accommodation dynamics is influenced by visual attention. Considering that alcohol and cannabis use have also an effect on visual attention, the deterioration of the accommodation dynamics obtained in this study may be influenced by this factor. In this line, it has been reported that alcohol has negative effects on vigilance tasks that require attention to changing stimuli [49, 50], as is the case of our experiment. Cannabis (specifically 9-Δ-tetrahydrocannabinol, THC) also leads to a decrease of the accuracy of visual attention tasks [51].

Some limitations should be considered when interpreting the results obtained. One limitation of this study is that participants were not randomly assigned to groups, since we followed the criteria stated above in the methods section. Also experimental sessions were not blind for the participants. As we used red wine to create a social drink environment, participants were aware of the condition under which they were performing the visual tests (alcohol or baseline). Other limitation is that the dose and type of cannabis used was not controlled (each participant smoked following their usual pattern), as long as we aimed to investigate the effects of recreational cannabis. Nevertheless, other authors have reported that there is no linear association between THC blood concentrations and the impairment caused by cannabis [52]. Finally, it should also be mentioned that a control group was not included in this experiment for two reasons: first, the aim of the study was to compare the impairment induced by these two substances (alcohol and cannabis) on the accommodative function and, for that, the difference between the baseline results and the results obtained following substance use was calculated for each individual, so the baseline session was performed by the same participants who underwent the alcohol sessions and the cannabis session. Second, we wanted to investigate the impairment of alcohol and cannabis on accommodation in occasional users. Although it would have been interesting to include a control group of non-users to compare their impairment with that of users, a different approach would have been necessary, including participants who were heavy users or with substance use-related problems instead of occasional users.

5. CONCLUSIONS

Alcohol and cannabis impair the accommodation dynamics, however the deterioration observed was not equal for the two substances. Overall, a moderate-high dose of alcohol produced a higher deterioration than cannabis, and the lowest effect was generated by a low dose of alcohol, but differences were significant only for the mean velocity of the accommodative response. Regarding the direction (near-distance or distance-near), no differences were observed. The accommodative demand generated by the target distance (20 and 40 cm) had a significant effect on the deterioration of the accommodation dynamics, but only for the mean velocity, showing a higher impairment for the target distance of 20 cm. The differences observed in the deterioration results for cannabis and alcohol could indicate that the mechanisms through which these two substances influence the accommodative system would differ at some point.

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Ethics approval

The study was adhered to the tenets of the Declaration of Helsinki and an informed consent was obtained from all participants before enrolling the study. The University of Granada Human Research Ethics Committee prospectively evaluated and approved the procedures of this investigation (921/CCEIH/2019).

REFERENCES

1. McDougal DH, Gamlin PD (2015) Autonomic Control of the Eye. Compr Physiol 5: 439-473 DOI 10.1002/cphy.c140014
2. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (2021) European Drug Report: In: European Drug Report: Trends and Developments, Luxembourg; 2021.
3. McIntosh C, Chick J (2004) Alcohol and the nervous system. J Neurol Neurosurg Psychiatry 75: 16-21 DOI 10.1136/jnnp.2004.045708

4. Sagawa Y, Kondo H, Matsubuchi N, Takemura T, Kanayama H, Kaneko Y, Kanbayashi T, Hishikawa Y, Shimizu T (2011) Alcohol Has a Dose-Related Effect on Parasympathetic Nerve Activity During Sleep. Alcohol Clin Exp Res 35: 2093-2100 DOI 10.1111/j.1530-0277.2011.01558.x

5. Levett J, Karras L (1977) Effects of alcohol on human accommodation. Aviat Space Environ Med 48: 434-437.

6. Campbell H, Doughty MJ, Heron G, Ackerley RG (2001) Influence of chronic alcohol abuse and ensuing forced abstinence on static subjective accommodation function in humans. Ophthalmic Physiol Opt 21: 197-205 DOI 10.1046/j.1475-1313.2001.00567.x

7. Miller RJ, Pigion RG, Martin KD (1985) The effects of ingested alcohol on accommodation. Percept Psychophys 37: 407-414 DOI 10.3758/bf03202871

8. Charman WN, Heron G (1988) Fluctuations in accommodation - A review. Ophthalmic Physiol Opt. 8: 153-164 DOI 10.1111/j.1475-1313.1988.tb01031.x

9. Winn B, Pugh JR, Gilmartin B, Owens H (1990) Arterial pulse modulates steady-state ocular accommodation. Curr Eye Res 9: 971-975 DOI 10.3109/02713689009069933

10. Iwase S, Matsukawa T, Ishihara S, Tanaka A, Tanabe K, Danbara A, Matsuo M, Sugiyama Y, Mano T (1995) Effect of oral ethanol intake on muscle sympathetic nerve activity and cardiovascular functions in humans. J Auton Nerv Syst 54: 206-214 DOI 10.1016/0165-1838(95)00022-p

11. Vallee A, Gabet A, Deschamps V, Blacher J, Olie V (2019) Relationship between Nutrition and Alcohol Consumption with Blood Pressure: The ESTEBAN Survey. Nutrients 11: 15 DOI 10.3390/nu11061433

12. Benowitz NL, Rosenberg J, Rogers W, Bachman J, Jones RT (1979) Cardiovascular effects of intravenous delta-9-tetrahydrocannabinol: autonomic nervous mechanisms. Clin Pharmacol Ther 25: 440-446.

13. Schwitzer T, Schwan R, Angioi-Duprez K, Ingster-Moati I, Lalanne L, Giersch A, Laprevote V (2015) The cannabinoid system and visual processing: A review on experimental findings and clinical presumptions. Eur Neuropsychopharmacol 25: 100-112 DOI https://doi.org/10.1016/j.euroneuro.2014.11.002

14. Valk LEM (1973) Hemp in Connection with Ophthalmology. Ophthalmologica 167: 413-421 DOI 10.1159/000306985

15. Shapiro D (1974) The ocular manifestations of the cannabinols. Ophthalmologica 168: 366-369 DOI 10.1159/000307060

16. London R (1984) Accommodation. In: Barresi BJ (ed) Ocular Assessment: The Manual of Diagnosis for Office Practice. Butterworth- Heinemann, Boston, MA, pp. 123-130.

17. González Pérez J, Parafita Mato M, Segade García A, Díaz Rey A (1995) Intraocular motility, electrophysiological tests and visual fields in drug addicts. Ophthalmic Physiol Opt 15: 493-498 DOI 10.1016/0275-5408(95)00098-x

18. Ortiz-Peregrina S, Ortiz C, Martino F, Castro-Torres JJ, Anera RG (2021) Dynamics of the accommodative response after smoking cannabis. Ophthalmic Physiol Opt 41: 1097-1109 DOI 10.1111/opo.12851

19. Babor TF, de la Fuente JR, Saunders J, Grant, M. (2001) AUDIT - The Alcohol Use Identification Test: Guidelines for use in primary health care. World Health Organization.

20. Adamson SJ, Kay-Lambkin FJ, Baker AL, Lewin TJ, Thornton L, Kelly BJ, Sellman JD (2010) An improved brief measure of cannabis misuse: The Cannabis Use Disorders Identification Test-Revised (CUDIT-R). Drug Alcohol Depend 110: 137-143 DOI 10.1016/j.drugalcdep.2010.02.017

21. Munsamy AJ, Hamilton-Hoskins RS, Bero T, Ximba PP, Govender D, Soni M, Majola L (2016) The effect of acute ingestion of alcohol at 0.05% and 0.10% blood respiratory alcohol concentration on heterophoria. Afr Vis Eye Health 75: 7 DOI 10.4102/aveh.v75i1.342

22. Casares-Lopez M, Castro-Torres JJ, Martino F, Ortiz-Peregrina S, Ortiz C, Anera RG (2020) Contrast sensitivity and retinal straylight after alcohol consumption: effects on driving performance. Sci Rep 10 DOI 10.1038/s41598-020-70645-3

23. Paton A (2005) ABC of alcohol - Alcohol in the body. Br Med J 330: 85-87 DOI 10.1136/bmj.330.7482.85

24. Luczak SE, Rosen IG (2014) Estimating BrAC from Transdermal Alcohol Concentration Data Using the BrAC Estimator Software Program. Alcohol Clin Exp Res 38: 2243-2252 DOI 10.1111/acer.12478

25. Scheiman M, Wick B (2008) Clinical management of binocular vision: heterophoric, accommodative, and eye movements disorders. Lippincott Williams and Wilkins.

25. Scheiman M, Gallaway M, Frantz KA, Peters RJ, Hatch S, Cuff M, Mitchell GL (2003) Nearpoint of convergence: Test procedure, target selection, and normative data. Optometry and Vision Science 80: 214-225 DOI 10.1097/00006324-200303000-00011.

27. Sheppard AL, Davies LN (2010) Clinical evaluation of the Grand Seiko Auto Ref/Keratometer WAM-5500. Ophthalmic Physiol Opt 30: 143-151 DOI 10.1111/j.1475-1313.2009.00701.x

28. Heron G, Charman WN, Schor C (2001) Dynamics of the accommodation response to abrupt changes in target vergence as a function of age. Vis Sci 41: 507-519 DOI 10.1016/s0042-6989(00)00282-0

29. Aldaba M, Gomez-Lopez S, Vilaseca M, Pujol J, Arjona M (2015) Comparing Autorefractors for Measurement of Accommodation. Optom Vis Sci 92: 1003-1011 DOI 10.1097/opx.0000000000000685

30. Casares-Lopez M, Castro-Torres JJ, Ortiz-Peregrina S, Ortiz C, Anera RG (2020) Changes in accommodation dynamics after alcohol consumption, for two different doses. Graefes Arch Clin Exp Ophthalmol DOI 10.1007/s00417-020-04978-0

31. Poltavski DV, Biberdorf D, Petros TV (2012) Accommodative response and cortical activity during sustained attention. Vis Res 63: 1-8 DOI 10.1016/j.visres.2012.04.017

32. Sreenivasan V, Irving EL, Bobier WR (2011) Effect of near adds on the variability of accommodative response in myopic children. Ophthalmic Physiol Opt 31: 145-154 DOI 10.1111/j.1475-1313.2010.00818.x

33. Hill JC, Toffolon G (1990) Effect of alcohol on sensory and sensorimotor visual functions. J Stud Alcohol 51: 108-113 DOI 10.15288/jsa.1990.51.108

34. Stapleton JM, Guthrie S, Linnoila M (1986) Effects of alcohol and other psychotropic drugs on eye movements: relevance to traffic safety. J Stud Alcohol 47: 426-432 DOI 10.15288/jsa.1986.47.426

35. Emrich HM, Weber MM, Wendl A, Zihl J, Vonmeyer L, Hanisch W (1991) Reduced binocular depth inversion as an indicator of cannabis-induced censorship impairment. Pharmacol Biochem Behav 40: 689-690 DOI 10.1016/0091-3057(91)90383-d

36. Semple DM, Ramsden F, McIntosh AM (2003) Reduced binocular depth inversion in regular cannabis users. Pharmacol Biochem Behav 75: 789-793 DOI 10.1016/s0091-3057(03)00140-0

37. Ortiz-Peregrina S, Ortiz C, Casares-Lopez M, Jimenez JR, Anera RG (2021) Effects of cannabis on visual function and self-perceived visual quality. Sci Rep 11 DOI 10.1038/s41598-021-81070-5

38. Ng LKY, Lamprecht F, Williams RB, Kopin IJ (1973) Delta tetrahydrocannabinol and ethanol: differential effects on sympathetic activity in differing environmental setting. Science 180: 1368-1369 DOI 10.1126/science.180.4093.1368

39. Adams AJ (1978) Acute Effects of Alcohol and Marijuana on Vision. In: Cool SJ, Smith EL (eds) Frontiers in Visual Science. Springer Berlin Heidelberg, Berlin, Heidelberg, pp. 93-105.

40. Clark SC (1975) Marihuana and the cardiovascular system. Pharmacol Biochem Behav 3: 299-306 DOI https://doi.org/10.1016/0091-3057(75)90161-6

41. Johnson RH, Eisenhofer G, Lambie DG (1986) The effects of acute and chronic ingestion of ethanol on the autonomic nervous system. Drug Alcohol Depend 18: 319-328 DOI https://doi.org/10.1016/0376-8716(86)90094-3

42. Richards JR, Bing ML, Moulin AK, Elder JW, Rominski RT, Summers PJ, Laurin EG (2019) Cannabis use and acute coronary syndrome. Clin Toxicol 57: 831-841. DOI 10.1080/15563650.2019.1601735

43. Gilmartin B (1986) A review of the role of sympathetic innervation of the ciliary muscle in ocular accommodation. Ophthalmic Physiol Opt 6: 23-37 DOI 10.1016/0275-5408(86)90115-8

44. Miege C, Denieul P (1988) Mean response and oscillations of accommodation for various stimulus vergences in relation to accommodation feedback-control. Ophthalmic Physiol Opt 8: 165-171 DOI 10.1111/j.1475-1313.1988.tb01032.x

45. Nakatsuka C, Hasebe S, Nonaka F, Ohtsuki H (2005) Accommodative lag under habitual seeing conditions: Comparison between myopic and emmetropic children. Jpn J Ophthalmol 49: 189-194 DOI 10.1007/s10384-004-0175-7

46. McClelland JF, Saunders KJ (2004) Accommodative lag using dynamic retinoscopy: Age norms for school-age children. Optom Vis Sci 81: 929-933

47. Bernhardt KA, Poltavski D (2021) Symptoms of convergence and accommodative insufficiency predict engagement and cognitive fatigue during complex task performance with and without automation. Appl Ergon 90 DOI 10.1016/j.apergo.2020.103152

48. Martino F, Castro-Torres JJ, Casares-Lopez M, Ortiz-Peregrina S, Ortiz C, Anera RG (2021) Deterioration of binocular vision after alcohol intake influences driving performance. Sci Rep 11 DOI 10.1038/s41598-021-88435-w

49. Michel C, Battig K (1989) Separate and combined psychophysiological effects of cigarette-smoking and alcohol-consumption. Psychopharmacology 97: 65-73 DOI 10.1007/bf00443415

50. Fillmore MT, Vogel-Sprott M (1998) Behavioral impairment under alcohol: Cognitive and pharmacokinetic factors. Alcohol Clin Exp Res 22: 1476-1482 DOI 10.1097/00000374-199810000-00016

51. Bocker KBE, Gerritsen J, Hunault CC, Kruidenier M, Mensinga TT, Kenemans JL (2010) Cannabis with high Delta(9)-THC contents affects perception and visual selective attention acutely: An event-related potential study. Pharmacol Biochem Behav 96: 67-74 DOI 10.1016/j.pbb.2010.04.008

52. Grotenhermen F (2003) Pharmacokinetics and pharmacodynamics of cannabinoids. Clinical Pharmacokinetics 42: 327-360 DOI 10.2165/00003088-200342040-00003