Comparison of the effects of alcohol and cannabis on visual function and driving performance. Does the visual impairment affect driving?

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Highlights

- Alcohol and cannabis are the most widely consumed psychoactive drugs.
- Both substances significantly impaired visual function.
- Driving performance was only significantly affected by the higher alcohol dose.
- The impairment in visual function was significantly associated with worse driving.
- Drivers were less aware of the negative consequences for cannabis than for alcohol.

Abstract

Background: Alcohol and cannabis are the most widely consumed psychoactive substances worldwide. This study compared the effects of alcohol and cannabis on visual function and driving performance, as well as self-perceived effects. Also, the relationship between visual effects under the influence and driving performance was studied.

Methods: Sixty-four young drivers, with a history of alcohol and/or cannabis use were included. Of these, 34 were allocated to the alcohol group and 31 to the cannabis group. All participants were evaluated in a baseline session. The alcohol group underwent two sessions: after drinking 300 ml and 450 ml of red wine (A1 and A2). The cannabis group attended one session after smoking cannabis (C). Visual function was evaluated at the contrast sensitivity, stereoacuity, and intraocular straylight level. Participants drove a driving simulator. A general score (overall visual score, OVS; overall driving performance score, ODPS) was obtained for both visual functioning and driving performance.

Results: The evaluation of visual function demonstrated a significant impairment in OVS for all conditions studied (A1, $p=0.005$; A2, $p<0.001$; C, $p<0.001$) with respect to the baseline session. General driving performance (ODPS) demonstrated a significant worsening for the A2 condition ($p=0.003$). Finally, a significant relationship between driving performance and visual function was found (rho=0.163, $p=0.039$ and $\chi^2 = 4.801$, $p=0.028$).

Conclusions: Cannabis and alcohol use negatively impact visual function. However, driving performance was only significantly affected by the higher alcohol dose. This impairment in visual function was significantly associated with worse driving performance.

Keywords: cannabis, THC, alcohol, driving performance, visual impairment, self-perceived effects

1. INTRODUCTION

Driving under the influence of alcohol or cannabis (DUIA and DUIC, respectively) constitutes a major road safety concern. Perhaps the most extensive monitoring program in Europe, which conducted roadside surveys in 13 countries and tested 50,000 drivers, revealed that alcohol was present in 3.5% of cases and illicit drugs in 1.9% (EMCDDA, 2012). Cannabis is the most widely detected illicit drug amongst drivers (Kelley-Baker et al., 2017). In Spain, a roadside study during 2015 found 11.6% of positives in 2744 drivers. The most commonly detected substance was cannabis (7.5%), followed by cocaine (4.7%) and alcohol (2.6%) (Domingo-Salvany et al., 2017). These data, and the latest trends suggest that, despite remaining a problem, DUIA has decreased recently whereas DUIC is increasing (Barry et al., 2021; Christophersen et al., 2016).

Driving a car is the primary mode of transportation. The integration of sensory information from a dynamic environment is essential in order to respond as quickly as possible to the road requirements, thereby maintaining an acceptable level of security. Although the effect of alcohol on driving performance has been well established (Martin et al., 2013), the evidence for cannabis is still limited despite the growing scientific interest it has attracted in recent years (Alvarez et al., 2021). The relationship between BAC (blood alcohol content) and driving impairment is linear, with values higher than 0.05% (the most commonly employed legal limit, equivalent to a BrAC of 0.25 mg/l) producing impairments in functions needed for driving (Martin et al., 2013). The psychoactive effect of cannabis is mediated by Δ9-tetrahydrocannabinol (THC), with cannabidiol (CBD) being the other main compound found in this substance. The relationship between THC concentrations and effect seems more complex given that blood concentrations and impairment do not appear to follow a linear relationship. Thus, detecting the presence of THC in blood or oral samples does not necessarily translate into impairment (Huestis, 2015). Cannabidiol (CBD) appears to produce a state of

mental and physical sedation (Zhornitsky and Potvin, 2012). The increasing use of CBD for the treatment of conditions such as epilepsy, anxiety or chronic pain, and the growing market of CBD wellness products at low doses, has brought the compound into the spotlight in recent research about driving (Zhornitsky and Potvin, 2012). In this line, Johnson et al. found that those drivers with high THC concentrations in oral samples who also tested positive for CBD showed higher incidence of risky acceleration behaviors (Johnson, 2019). Contrary, several studies combining THC and CBD have suggested no impairing effects of CBD in driving (Brands et al., 2021). A recent investigation did not find significant differences in lane weaving (standard deviation of the lateral position, SDLP) between a placebo condition and when driving after consuming vaporized CBD-dominant cannabis (Arkell et al., 2020).

The impairment that alcohol and/or cannabis is able to generate on driving performance is due to a reduction in different drivers' abilities, especially given that the use of such substances may also alter perception of the environment. During acute intoxication, both alcohol and cannabis have been shown to produce alterations in visual function for important parameters such as visual acuity, contrast sensitivity, depth perception, glare sensitivity, color discrimination and accommodation (Adams et al., 1976; Brown et al., 1975; Casares-López et al., 2020; Hill and Toffolon, 1990; Ortiz-Peregrina et al., 2021a; Watten and Lie, 1996). The deterioration of some of these parameters has been shown to negatively impact driving performance in subjects under the influence of alcohol and cannabis (Casares-López et al., 2020; Martino et al., 2021; Ortiz-Peregrina et al., 2020b), but also in subjects with other conditions such as eye conditions or Parkinson's disease (Ranchet et al., 2020; Uc et al., 2009; Wood and Black, 2016). Despite being the most widely used psychoactive substances worldwide, the effects of cannabis and alcohol on visual function, and its relationship with driving performance, have not yet been compared. Recent trends in the use of substances before

driving point to a need to gather more information concerning the use of alcohol and cannabis, and their effects on functions necessary for the performance of this task.

In light of the above, this study aimed to compare the effects that the use of alcohol and cannabis triggers in the visual function of users, as well as their perception of the changes generated by these substances. In addition, we aimed to compare the effect of alcohol or cannabis use on driving performance, and the relationship between those effects and visual function changes generated by these two substances.

2. METHODS

2.1. Participants

The study included a total of 64 young participants (mean age ± SD; 24.3 ± 4.5 years; range: 19-43 years) who were alcohol and/or cannabis users. They were recruited via e-mail and advertising at the University of Granada facilities. The inclusion criteria were as follows: being an alcohol or cannabis user, being healthy at the time of the study, having held a driving license for more than one year and a monocular visual acuity of at least 6/6 (Snellen notation) with the habitual correction (if any). In addition, participants were excluded according to the following criteria: current or past medical illness; problematic or harmful alcohol or cannabis use evaluated by means of the Alcohol Use Disorder Identification Test (AUDIT) and the Cannabis Use Disorder Identification Test revised (CUDIT-r). These test has been validated as screening tools for this purpose by employing cutoff score values (AUDIT > 12 (women) or 14 (men), and CUDIT-r > 12) (Adamson et al., 2010; Babor et al., 2001). Other exclusion criteria included binocular vision problems; use of other drugs; pregnancy or breastfeeding; and simulator sickness. Participants were classified into two groups: alcohol or cannabis (parallel design). When volunteers indicated being co-users of cannabis and alcohol, they were randomly assigned with a 2:1 allocation ratio to participate in the cannabis and alcohol group,

as finding participants who were cannabis users were less frequent and they commonly also used alcohol. Thus, 33 participants were allocated to the alcohol group (mean age ± SD; 25.2 ± 3.7 years; 16 female) and 31 participants to the cannabis group (mean age ± SD; 23.4 ± 5.1 years; 11 female). Age differences demonstrated to be statistically significant between both groups (Z=2.690; p=0.007).

The study was carried out in accordance with the tenets of the Declaration of Helsinki and participants signed an informed consent. The University of Granada Human Research Ethics Committee prospectively evaluated and approved the study (921/CCEIH/2019).

2.2.Visual function assessment

Binocular contrast sensitivity (CS) was tested at 3 m using the chart included in the POLA Vista Vision Visual Chart System (DMD Med Tech srl. Torino, Italy) to obtain the contrast threshold (i.e. the minimum contrast necessary to detect a visual target grating over a uniform background). Different spatial frequencies were tested (0.75, 1.5, 3, 6, 12, and 18 cycles per degree (cpd), and the average contrast sensitivity was considered for analysis.

The stereoacuity, i.e. the ability to detect the spatial or three-dimensional location of objects, was measured at 5.5 m using the test included in the Vista Vision monitor. The stereoacuity test allows different disparities (from 300 to 10 arcsec) to be tested using rows of polarized vertical bars. Participants were asked to identify the bar which appeared to be "floating" with respect to the rest on the row.

We also measured the intraocular straylight (s), a parameter that quantifies the effect of scattered light in the optical media on the retinal image (van den Berg, 2017). This scattered light generates a veiling luminance over the retina (a veil of straylight), which reduces image contrast and increases glare. The C-Quant straylight meter (Oculus Optikgeräte GmbH,

Germany), which employs the compensation comparison method (Coppens et al., 2006), was used to measure the intraocular straylight, expressed as log(s).

The Overall Visual Score (OVS) was obtained from the individual visual parameters described in this section as an overall measure of visual quality. The procedure for obtaining this score is described in the statistical analysis subsection.

2.3. Driving performance assessment

A fixed-base driving simulator with three high-definition 27" screens was employed, providing a view of 180°. The software used for the driving simulator was the SIMAX DRIVING SIMULATOR v.4.0.8 BETA (SimaxVirt S.L., Pamplona, Spain). A detailed description of the driving simulator can be found in Ortiz et al. (2018).

Participants completed a route of about 12.5 km, which lasted for about 15 min. The route comprised three different sections: dual carriageway, mountain road and city. The dual carriageway had a speed limit of 120 km/h, two lanes of traffic in the same direction, straight segments, gentle curves and moderate traffic flow. The mountain road included speed limits of 40 and 90 km/h, a single lane in each direction (oncoming traffic) and moderate traffic flow. This section was more winding, with gentle but also sharp curves. Finally, the city section had speed limits of 40 and 50 km/h, one or two lanes of traffic in the same direction, several intersections, roundabouts, traffic lights, and pedestrians. The traffic flow was moderate.

The simulator generates different variables, of which the following were considered for analysis: mean speed (km/h), distance driven invading the opposite lane (m), distance driven on the hard shoulder (m), total distance driven outside the lane (m), standard deviation of the lateral position (SDLP) (m), standard deviation of the angular velocity of the steering wheel (rad/s), total time to complete the circuit (s) and reaction time (s). Reaction time was obtained from the braking response. The simulator generated three braking events in random locations

during the route of the mountain road. At this location, is common to follow lead vehicles. When this occurred and the driver reached a sufficient speed, the lead vehicle made a sharp braking stop. Reaction time was calculated as the time interval between the instant at which the leading vehicle turned on its brake light and the time at which the participant pressed the simulator brake pedal.

Finally, as an overall measure of driving performance, the overall driving performance score (ODPS) was computed. This general score was generated as in previous studies (Casares-López et al., 2020; Ortiz-Peregrina et al., 2020c, 2020a) and it is described in the statistical analysis subsection. To obtain the ODPS, mean speed and total time were not considered given that the speed selected did not represent better or worse performance. Similarly, on the mountain road only the total distance driven outside the lane was considered given that this parameter includes the distance driven on the hard shoulder and the distance driven invading the opposite lane. Z-scores were converted so that positive scores represented a better performance than the mean.

All participants underwent two training sessions with the simulator, using similar routes to those employed in the experimental sessions.

2.4. Procedures

The experimental procedure is described in Figure 1. Participants underwent from four to five visits to the laboratory, with one week between each. The two first visits were employed to check inclusion criteria, inform participants about the study procedures and perform the driving simulator training protocol. Once the training period had been completed, participants assigned to the cannabis group completed two sessions: a baseline session (B) and another after smoking cannabis (C) (in random order). Participants allocated to the alcohol group completed three experimental sessions: baseline (B), alcohol 1 (A1) and alcohol 2 (A2), also in random

order. Experimental sessions were conducted in the afternoon, between 4 and 8 pm. The visual tests and the driving simulator route were performed in random order during experimental sessions to avoid the influence of the time elapsed after consumption.

Cannabis use

An *ad libitum* procedure was followed. Thus, participants underwent the cannabis session 20 minutes after smoking a cannabis cigarette. They prepared and smoked the cannabis cigarette as they normally would in their habitual consumption, with the only requirement to finish it in about 10 min. Before each session, participants underwent a saliva drug test with the Dräger DrugTest 5000 (Dräger Safety AG & Co. KGaA, Lübeck, Germany) to determine the consumption of cannabis, amphetamines, benzodiazepines, cocaine, methamphetamines, opiates, methadone, and ketamine. At the baseline session, they had to test negative for all the substances analyzed, and the same but positive for cannabis at the cannabis session. We also checked that participants had not been drinking alcohol by measuring their breath alcohol content (BrAC) using the Dräger Alcotest 6820 breath analyzer (Dräger Safety AG & Co. KGaA. Lübeck, Germany). Before the experimental sessions, participants were instructed not to use alcohol for 24 hours and cannabis or any other drug for 4 days.

Alcohol use

In order to simulate a social drinking environment (Casares-López et al., 2020; Munsamy et al., 2016), participants were given red wine with an alcohol content of 13.5% (Pago de Almaraes wineries S.L., Benalúa de Guadix, Granada, Spain). Participants were told not to consume caffeine or alcohol 24 hours before the experimental sessions. All experimental sessions were carried out two hours after lunch. Apart from the baseline session, the alcohol group underwent two sessions to determine the effects of alcohol: one after drinking 300 ml (low-moderate intake, equivalent to 32.4 g of alcohol approximately) and another after drinking

450 ml (moderate-high intake, equivalent to 48.6 g of alcohol approximately). At both sessions, they were given 40 min to drink the required quantity. Thirty minutes after finishing the dose the experimental session started after the breath alcohol content (BrAC) was measured (Luczak and Rosen, 2014; Paton, 2005). Every 20 min thereafter, the BrAC was measured again. For this purpose, we used the Dräger Alcotest 6820 breath analyzer (Dräger Safety AG & Co. Lübeck, Germany). If necessary, a second dose was provided during the session in order to ensure that the BrAC level did not vary by more than ± 0.05 mg/l. Four participants received the second dose. The amount of ingested alcohol that should be provided was calculated according to the Widmark equation, considering the mean BrAC recorded until then along with the weight (measured at their initial visit to the laboratory) and the distribution factor (0.60 for females and 0.70 for males) (Forrest, 1986). The BrAC (mg/l) was converted into BAC (g/l), as the conversion factor is approximately 2:1 (Jones et al., 1992).

$$BAC\left(\frac{g}{l}\right) = \frac{amount\ of\ ingested\ alcohol\ (g)}{weight\ (Kg) \times distribution\ factor}$$

The final BrAC level was the mean value of the four measurements taken over the session.

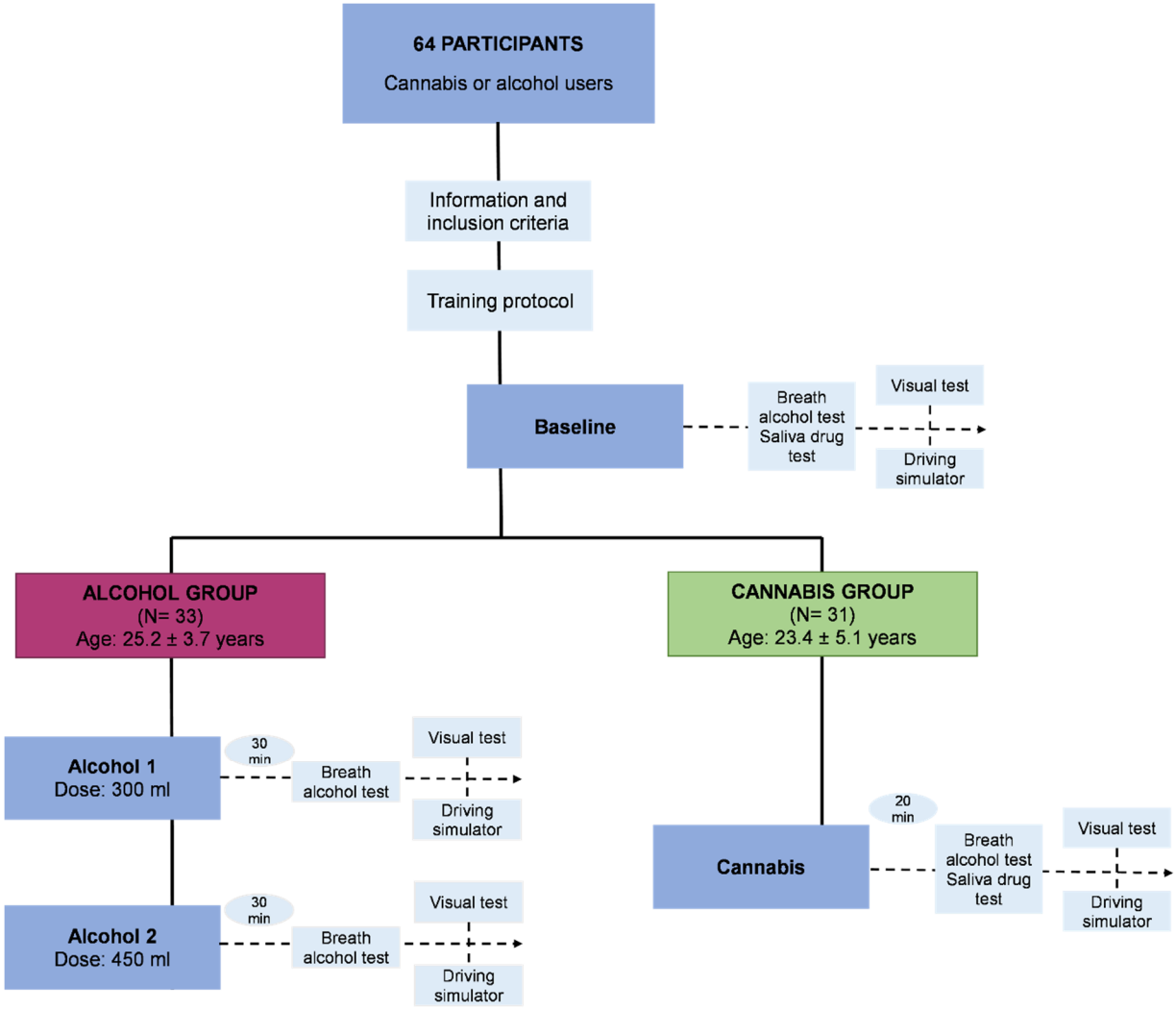

Figure 1. Schematic representation of the procedure employed in the study.

2.5. Statistical analysis

All statistical procedures were performed using the SPSS v.26 software package (SPSS Inc., Chicago, IL). The normality of the data distribution was checked using the Shapiro-Wilk test. According to this test, the only parameter that was normally distributed was mean speed in the city. Before conducting comparisons between groups, we checked that participants allocated to the cannabis or alcohol arms of the study did not differ in terms of visual parameters and driving performance. To that end, t-tests or the Mann Whitney U test were used for independent samples, depending on the data distribution. Once it had been established that there were no

differences in the visual function and driving performance of participants in the cannabis and alcohol groups, comparisons were made between the different sessions. For normally distributed data (mean speed in the city), comparisons between groups (baseline, alcohol 1, alcohol 2 and cannabis) were carried out using a one-way ANOVA. Post hoc comparisons were performed by applying the Bonferroni correction. When the normality of the data distribution could not be assumed, a non-parametric test for several independent samples with pairwise comparisons was applied (Kruskal-Wallis).

To obtain the overall visual score (OVS) and the overall driving performance score (ODPS), Z-scores were obtained from the individual parameters. The average Z-score of the different visual variables was called OVS, and the average Z-score of the driving variables, ODPS. Z-score is defined as a measurement of how many standard deviations below or above the group mean an individual value is. In other words, it is a statistic used to compare the result of one subject with the result of the whole group. Thus, Z-score is computed as follows: $z = (x - \mu) / \sigma$ (where x is the variable value for a certain subject; μ is the mean for this variable in the whole group; and σ is the standard deviation of the variable in the whole group). Z-scores were converted in order to achieve that positive scores represent a better performance than the mean. To study the relationship between visual status and driving performance, a correlation analysis (Spearman) with the overall driving performance score (ODPS) and the overall visual score (OVS) was performed. Finally, to study the influence of other possible factors, such as age or biological sex, on the ODPS, we applied a Generalized Linear Model with the ODPS as dependent variable, condition and biological sex as factors, and age, frequency of alcohol or cannabis use and OVS as covariates. A significance level of 0.05 was set.

3. RESULTS

3.1. Frequency of driving under the effects of alcohol or cannabis and self-perceived quality of vision and driving performance

In general, the self-reported frequency of use was higher for cannabis than for alcohol (Table 1). Thus, while 24% of participants in the alcohol group reported consuming weekly (from 1 to 7 days a week), 55% of participants in the cannabis group used the drug with this frequency. Similarly, the self-reported frequency of driving under the influence (DUI) was generally higher in the cannabis group. Thus, while 55% of cannabis users reported having driven after using the drug 2-3 times or more than 4 times, the value for the alcohol group was 38%. In agreement with this finding, the question regarding the perceived effects of DUI showed higher risk awareness in the alcohol group. Thus, while 62% of participants in the alcohol group indicated that their driving performance is much worse under the influence of alcohol, the majority of cannabis users (68%) responded that their driving is only slightly worse under the influence of cannabis. In addition, 13% of participants in the cannabis group indicated that they feel no change or an improvement in their driving, while only 3% in the alcohol group indicated the same. A similar trend was observed when participants were asked if they perceived visual changes that could affect driving performance, as shown in Figure 2. In this case, the majority of participants perceived their visual quality for driving to be much worse during the daytime (50%) or at night (68%), whereas most participants in the cannabis group indicated that their vision was only slightly worse during the daytime (52%) and at night (58%). Moreover, the percentage of participants who perceived no change in their vision was higher in the cannabis group (32% and 26% for daytime and at night, respectively) than in the alcohol group (3% and 3% for daytime and at night, respectively).

Table 1. Participant's frequency of use, driving under the influence, and self-perceived visual and driving changes.

		Daily (%)	2-6 times/week (%)	2-4 times/month (%)	≤ once a month (%)
Frequency of use	Alcohol	3	21	50	26
	Cannabis	13	42	13	32
		Never (%)	Once (%)	2-3 times (%)	> 4 times (%)
Have you ever driven after having consumed alcohol/cannabis?	Alcohol	38	24	29	9
	Cannabis	32	13	19	36
		Much worse (%)	Slightly worse (%)	No change (%)	Improved (%)
Do you think that cannabis/alcohol effects affect your driving performance?	Alcohol	62	35	3	0
	Cannabis	19	68	10	3

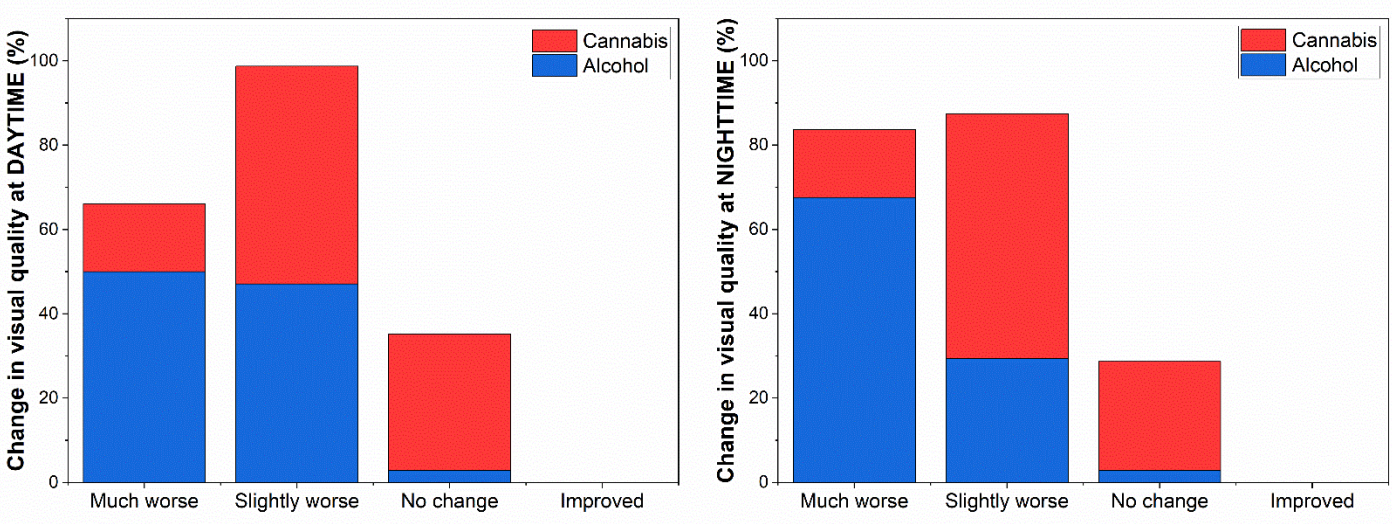

Figure 2. Self-perceived change in visual quality for driving after using alcohol and cannabis during the day and at night

3.2.Visual performance after alcohol or cannabis use

For the alcohol group, the mean BrAC reached for the alcohol 1 group (A1) was 0.19 ± 0.08 mg/l (range: 0.05–0.33 mg/l), increasing to 0.33 ± 0.12 mg/l (range: 0.12–0.60 mg/l) for the alcohol 2 group (A2). At these alcohol intoxication levels, as well as after smoking cannabis, visual function was significantly altered (Table 2). Although the mean binocular contrast sensitivity function decreased by 6% for A1 and 9% for A2, this parameter was only significantly decreased for the cannabis group (C), which exhibited a 12% reduction with respect to the baseline. Stereoacuity showed significant impairments for A1, A2 and C with respect to the baseline session, with increases of 77%, 128% and 210%, respectively. The straylight parameter was also significantly increased for A2 and C, whereas the A1 group did not show a significant increase with regard to baseline. Finally, the Overall Visual Score, as a general measure of visual performance, demonstrated significant impairments for all conditions (A1, A2 and C) with respect to the baseline (B). The greatest decrease in visual performance was found for cannabis use, followed by A2 and A1 (Table 2, Figure 3).

Table 2. Comparison of visual function parameters in the baseline session and under the effects of alcohol and cannabis. Median ± interquartile range are included.

	Baseline (B) (N=64)	**Cannabis (C)** (N=31)	**Alcohol 1 (A1)** (N=33)	**Alcohol 2 (A2)** (N=33)	Statistic (H)	p-value	Multiple comparisons
Binocular CS	152.00 ± 20.50	132.50 ± 28.50	140.75 ± 35.25	140.08 ± 32.88	17.392	**0.001**	B-C (p<0.001)
Distance stereoacuity (arcsec)	30 ± 40	150 ± 240	60 ± 75	120 ± 120	36.201	**<0.001**	B-A1 (p=0.013) B-A2 (p<0.001) B-C (p<0.001)
log(s)	0.82 ± 0.09	0.94 ± 0.23	0.89 ± 0.21	0.92 ± 0.15	16.599	**0.001**	B-A2 (p=0.001) B-C (p=0.026)
OVS	0.51 ± 0.62	-0.70 ± 0.95	-0.07 ± 0.91	-0.18 ± 0.92	47.956	**<0.001**	B-A1 (p=0.005) B-A2 (p<0.001) B-C (p<0.001)

CS: contrast sensitivity, s: straylight; OVS: overall visual score. According to the Shapiro-Wilk test, all variables followed a non-normal distribution and, therefore, a Kruskal Wallis test was applied.

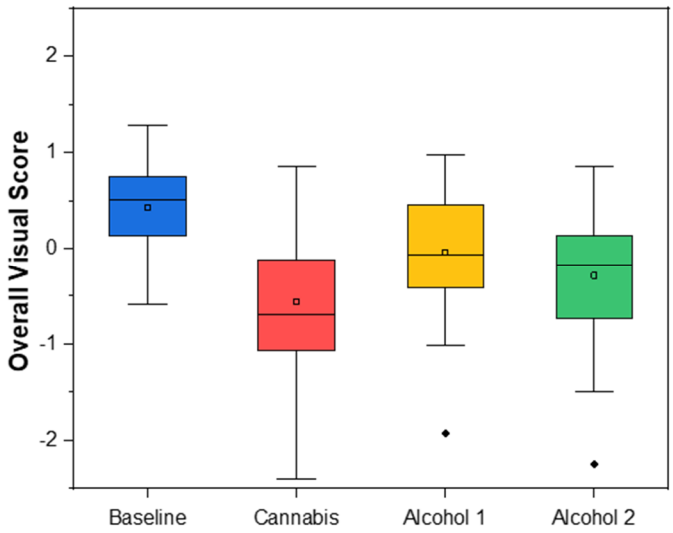

Figure 3. Overall visual score (OVS) obtained for each group.

3.3.Driving performance after alcohol or cannabis use

Table 3 summarizes all the parameters obtained during the driving performance analysis. For dual-carriageway driving, the group comparisons did not show any significant difference. However, driving performance on the mountain road revealed that the A2 group was the most affected. Lane-keeping was found to differ significantly as regards the distance driven on the hard shoulder, which was significantly longer for A2 compared to the baseline and C. Likewise, steering control was significantly impaired for A2 in comparison with the cannabis group, with the SD of the angular velocity of the steering wheel being 34% higher. In the city, the SD for the angular velocity of the steering wheel was significantly higher for A2 than for baseline or C. The variables in the total circuit analysis revealed that participants under the effects of cannabis required significantly longer to complete the circuit than both alcohol groups (A1 and A2). Moreover, the reaction time was significantly increased for A2 with respect to the baseline. The ODPS indicated a worsening of driving performance for groups

A1 and A2 with respect to the baseline group, whereas cannabis use only led to a slight worsening in the general score (Figure 4). Thus, the analysis indicated significantly worse driving performance for the A2 group with respect to B and C.

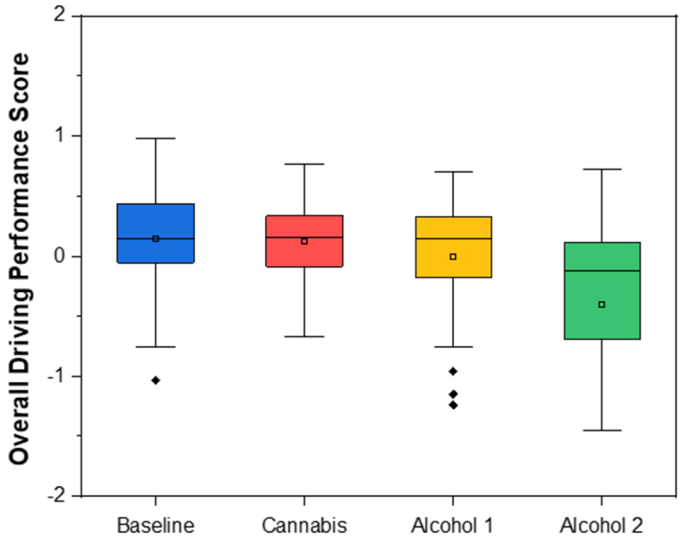

Figure 4. Overall driving performance score (ODPS) obtained for each group.

Table 3. Comparison of driving performance variables in the baseline session and under the effects of alcohol and cannabis. Median ± interquartile range is included except for the mean speed in the city, where mean ± standard deviation is presented.

		Baseline (B) (N=64)	**Cannabis (C)** (N=31)	**Alcohol 1 (A1)** (N=33)	**Alcohol 2 (A2)** (N=33)	Statistic (F/H)	p-value	Multiple comparisons
Dual Carriageway	Mean speed (km/h)*	116.96 ± 11.07	116.54 ± 13.26	119.50 ± 11.14	120.84 ± 13.28	4.492	0.213	
	Distance driven on the hard shoulder (m)*	53.41 ± 92.39	106.96 ± 116.06	78.96 ± 145.21	85.47 ± 124.92	7.866	**0.049**	*n.s. after Bonferroni correction*
	SD angular velocity steering wheel (rad/s)*	0.20 ± 0.09	0.18 ± 0.10	0.19 ± 0.11	0.23 ± 0.15	6.584	0.086	
Mountain Road	Mean speed (km/h)*	55.44 ± 1.99	55.68 ± 2.65	55.85 ± 2.31	55.28 ± 2.85	1.591	0.661	
	Distance driven invading the opposite lane (m)*	342.32 ± 279.62	321.91 ± 352.74	207.50 ± 239.96	195.79 ± 312.10	3.620	0.306	
	Distance driven on the hard shoulder (m)*	23.41 ± 52.19	30.00 ± 54.58	45.13 ± 103.52	83.36 ± 137.33	15.784	**0.001**	B-A2 (p=0.001) A2-C (p=0.041)
	Total distance driven outside the lane (m)*	376.12 ± 281.52	355.95 ± 340.60	303.64 ± 359.57	315.25 ± 406.23	1.117	0.773	
	SDLP (m)*	0.55 ± 0.15	0.57 ± 0.08	0.55 ± 0.17	0.60 ± 0.27	7.446	0.059	
	SD angular velocity steering wheel (rad/s)*	0.62 ± 0.24	0.58 ± 0.20	0.67 ± 0.27	0.66 ± 0.35	9.469	**0.024**	A2-C (p=0.030)
City	Mean speed (km/h)ǂ	32.06 ± 6.10	29.41 ± 4.89	33.62 ± 5.85	33.86 ± 6.70	3.775	0.072	
	SD angular velocity steering wheel (rad/s)*	1.11 ± 0.33	1.02 ± 0.16	1.10 ± 0.30	1.26 ± 0.39	15.729	**0.001**	A2-C (p=0.001) B-A2 (p=0.015)
Total circuit	Total time (s)*	764.81 ± 79.66	784.29 ± 82.10	742.89 ± 69.37	747.64 ± 88.33	10.566	**0.014**	A1-C (p=0.024) A2-C (p=0.033)
	Reaction time (s)*	0.90 ± 0.20	0.88 ± 0.24	0.95 ± 0.31	1.00 ± 0.22	9.687	**0.021**	B-A2 (p=0.020)
	ODPS*	0.15 ± 0.50	0.16 ± 0.42	0.15 ± 0.56	-0.12 ± 0.83	12.893	**0.005**	B-A2 (p=0.003) C-A2 (p=0.037)

SDLP: standard deviation of the lateral position; ODPS: overall driving performance score; n.s: non-significant. For multiple comparisons, only significant differences are shown. Bonferroni correction is applied. *Kruskal-Wallis test applied; ǂOne-way ANOVA test applied

3.4.Vision and driving: the effects of visual impairment after cannabis or alcohol use on driving ability

The results indicated that visual status and driving performance were significantly correlated including all conditions (rho = 0.163; p = 0.039). This relationship is shown in Figure 5. For each condition independently, we found a significant correlation between the ODPS and the OVS in the baseline (rho=0.265; p=0.034), but this correlation was not statistically significant for the rest of conditions (C, A1 and A2). The results of the GLM (Table 4) indicated that the condition had a significant main effect on the ODPS, with significant decreases only for the alcohol 2 group with respect to the baseline (reference category). Sex was also shown to be a significant factor, with estimates suggesting that being female represented ODPS 0.308 units less than being males. Finally, a significant main effect of the OVS was found, with estimates indicating that one unit of impairment in the OVS would result in an impairment of 0.16 units in the ODPS. Age and the frequency of cannabis or alcohol use did not show a significant main effect on the ODPS.

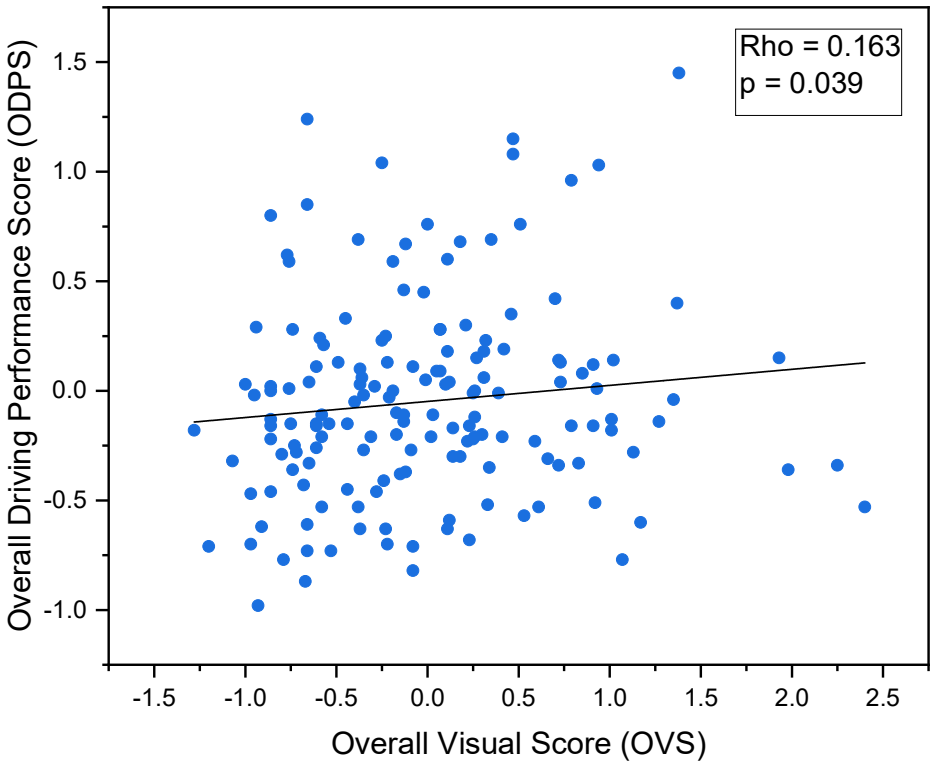

Figure 5. Scatterplot representing the relationship between the ODPS and the OVS.

Table 4. Results of the generalized linear model.

	B	*SE*	*Wald Chi-Square*	*p*-value	95% CI
Condition					
Baseline	----º	----º	----º	----º	----º
Cannabis	ns.	ns.	ns.	ns.	ns.
Alcohol 1	ns.	ns.	ns.	ns.	ns.
Alcohol 2	-0.418	0.129	10.470	**0.001**	[-0.672, -0.165]
Sex					
Female	-0.308	0.088	12.222	**<0.001**	[-0.480, -0.135]
Male	----º	----º	----º	----º	----º
Overall visual score (OVS)	0.160	0.073	4.801	**0.028**	[0.017, 0.302]
Intercept	0.219	0.085	6.613	**0.010**	[0.053, 0.385]
Number of observations	161				
AIC	279.342				
BIC	300.912				

----º Reference category; ns: not significant; AIC: Akaike's Information Criterion; BIC: Schwarz's Bayesian Criterion.

4. DISCUSSION

Several studies published to date have reported negative consequences for visual function under the effects of alcohol and cannabis. Nicholson et al. studied the change in contrast sensitivity after the ingestion of a low dose (mean BAC = 0.015%) and a moderate dose (mean BAC = 0.04%) of alcohol (Nicholson et al., 1995). These authors found a significant impairment in CS for the moderate dose, which is equivalent to the A1 condition in our study (BrAC 0.19 mg/l ≈ BAC 0.04%). Although the mean CS was reduced for groups A1 and A2, the difference was not statistically significant with respect to the baseline. Casares-López et al. found a similar effect on the CS, although these authors only found significant differences after alcohol use for 6 and 12 cpd (Casares-López et al., 2020). In the case of cannabis use, we found

a significant deterioration in the mean CS, in agreement with previous studies (Lalanne et al., 2017; Mikulskaya and Martin, 2018; Ortiz-Peregrina et al., 2021a). It has also been suggested that the perceived worsening in visual function under the effects of cannabis is modulated by the CS (Ortiz-Peregrina et al., 2021a), which could determine the decision whether to drive or not under its influence.

Alcohol and cannabis also affect the three-dimensional location of objects. All conditions evaluated significantly altered stereoacuity, although cannabis seems to affect it to a greater extent. This finding agrees with previous studies, which demonstrated that alcohol and cannabis affect binocular performance, with deleterious consequences for driving (Martino et al., 2021; Ortiz-Peregrina et al., 2020b). For the straylight parameter, the significant impairment for A2 and C agrees with previous studies (Casares-López et al., 2020; Ortiz-Peregrina et al., 2021a). Casares-López et al. found an increase in the log(s) after the intake of different doses of alcohol (the same as this study) (Casares-López et al., 2020). We did not find significant differences for the log(s) in the A1 group, the highest difference in our study was found for the A2 and cannabis groups, which were found to be similarly affected, thus meaning that subjects who smoke cannabis or drink a moderate to high dose of alcohol (in this case, 400 ml of red wine) may experience problems with glare at night. Finally, the OVS indicated an overall significant deterioration in visual function for all conditions (A1, A2 and C). It is interesting to note that, although cannabis use generated a much greater deterioration in the OVS than alcohol, participants indicated in their responses to the questionnaire that alcohol impairs vision to a greater extent. This result could indicate that there is an awareness that alcohol is more harmful than cannabis, which is often perceived as a soft drug (Galván et al., 2017), also for the visual system (Akano, 2017).

The perception of impairment in vision or other functions after cannabis or alcohol use may predispose a user to drive under such circumstances, which is of special importance since our

results showed that different aspects of driving are significantly altered. Thus, driving performance has been shown to be significantly reduced, mainly for the A2 group. The review of Martin et al. concluded that there is scientific support for a BAC of 0.05% as the cut-off limit for impaired faculties in the driving task (Martin et al., 2013). As stated above, our main findings with regard to alcohol are for the A2 condition, which corresponds to a mean BrAC of 0.33 mg/l (BAC ≈ 0.07%). According to the conclusion of Moskowitz and Robinson, driving performance should also be significantly affected for the A1 group given that the mean BAC for this group is higher than the limit proposed by the authors (BrAC 0.19 mg/l ≈ BAC 0.04%). However, the mean BrAC found in our study for the A1 group is within the legal limit for driving in Spain and other countries, and agrees with the BAC limit identified in the review of Martin et al. (Martin et al., 2013). In contrast to the results found for alcohol, cannabis did not cause a significant impairment in driving performance. Driving under the effects of cannabis is illegal, and different methods are employed to detect impaired drivers (effect-based, zero-tolerance approaches, and *per se* limits; (McCartney et al., 2021)). There is no linear relationship between the blood concentration of THC, the psychoactive component of cannabis, and driving impairment, thus making it difficult to establish a legal limit as in the case of alcohol (Bondallaz et al., 2016; Sevigny, 2021). Some studies, mainly involving young and occasional users, have found that cannabis can negatively influence aspects such as longitudinal or lateral control in drivers (Hartman et al., 2016, 2015; Ortiz-Peregrina et al., 2020b). However, a recent systematic review concluded that there is currently only moderate to low confidence for the impact of this drug on driving performance (Alvarez et al., 2021). It is important to mention that, according to the questionnaire's results, participants think that their driving is more negatively affected by alcohol than by cannabis. In this sense, participants seem to be accurate in assessing the impairment produced by both substances, as we found a significant impairment in the ODPS only for the highest dose of alcohol, with an average BrAC

above the legal limit. Thus, the results obtained by other authors and the present study point to that the actual risk of driving under the influence of cannabis remains open to interpretation, and to the need for further research to clarify what kind of consumption/user profile could affect driving performance under the effects of cannabis.

The effect of alcohol and cannabis on key functions needed for driving (cognitive, motor, and sensory) can determine the assumed risk while driving under the influence. Visual status has been found to be significantly related to the ability to drive. The correlation found between the overall visual score (OVS) and the overall driving performance score (ODPS) was significant and positive, thus indicating that those drivers with worse visual status also had worse driving performance. Moreover, the GLM confirmed this finding, indicating the OVS to have a significant main effect on the ODPS. Driving is indeed a highly vision-dependent task, and any circumstance that affects this sensory mechanism can have repercussions for driving performance and safety (Owsley and Mcgwin, 2010; Wood and Black, 2016). Our findings agree with previous ones for alcohol and cannabis consumers. Thus, the study of Casares-López et al. found that the ODPS can be obtained as a function of retinal straylight and contrast sensitivity for drivers under the influence of alcohol (Casares-López et al., 2020). In the case of cannabis, a relationship between a worsening of stereoacuity and a loss of control of the vehicle's position in the lane has been reported (Ortiz-Peregrina et al., 2020b). Also for cannabis users, it has been suggested that a change in contrast sensitivity after smoking may be one of the factors determining changes in mean speed and the SDLP (Ortiz-Peregrina et al., 2021b). The importance of visual measures, such as the contrast sensitivity and retinal straylight, has also been demonstrated in healthy drivers, drivers with cataract and drivers with Parkinson disease (Ortiz-Peregrina et al., 2020a; Uc et al., 2009; Wood, 2002; Wood and Carberry, 2006). Specifically, the increase in the straylight level found after consuming cannabis or also alcohol means that these drivers would have more problems when driving at

night, with a higher incidence of glare and halo vision. Future studies should explore this question, assessing several night vision tests and relating them to nighttime driving performance. This is important given that in many cases, driving under the influence of alcohol or drugs occurs at night after social events.

Despite the results obtained, it should also be borne in mind that both groups (alcohol and cannabis) underestimated visual impairment. Although cannabis generated the greatest impairment in the OVS, this result did not translate into significant impairment in driving performance (ODPS). This would indicate that there are compensatory mechanisms for visual impairment during driving under the influence of cannabis, and not during driving under the influence of alcohol for which we found a worsening in driving performance. One of the mechanism employed to compensate for a decline in driving capabilities is speed self-regulation. If we observe our results, both in the dual carriageway and the city, the cannabis group adopted the lowest speed compared with the baseline, alcohol 1 and alcohol 2 groups. In general, drivers under the influence of cannabis have shown a decrease of driving speed under such circumstances (Brands et al., 2021). The study of Downey et al., compared driving performance under different doses of alcohol and/or cannabis. The authors found that subjects under the effects of cannabis had a greater likelihood of driving with longer following distances and slower speeds when entering the freeway, indicating a more cautious driving style (Downey et al., 2013). In addition, the cognitive impairment caused by cannabis use could influence the results obtained on visual test largely than in driving, which represents a more familiar task for participants. Future studies should include visual tests as objective as possible, and should control for cognitive and motor performance. In this way, the impact of motor, cognitive and visual effects on driving could be more concisely represented.

Finally, some limitations need to be considered when interpreting the results presented here. Firstly, participants smoked and prepared the cannabis cigarette as they usually do in their

habitual consumption. This did not allow us to establish dose-effect relationships. However, we aimed to simulate the real use of a cannabis smoker on a normal day, after which they could be prone to drive. Also, the fact that we included occasional but also more frequent cannabis users may have influenced the results. Future studies should include larger sample sizes in order to explore the possible tolerance effects (Sewell et al., 2009). Finally, studying driving performance by means of a driving simulator does not provide all the realism of actual driving, although it is a safe environment that allows driving in different situations and conducting a study of this type under controlled and safe circumstances (Brands et al., 2021).

5. CONCLUSIONS

Alcohol and cannabis consumption result in significant alterations to visual function, specifically to binocular contrast sensitivity, stereoacuity and straylight. Although cannabis generated the most significant deterioration in visual function, these consumers are less aware of the visual effect of cannabis consumption than those in the alcohol group. The driving performance results showed that only the higher alcohol dose (with a mean BrAC level over the legal limit) resulted in significant detrimental effects. Under such circumstances, drivers drove greater distances on the hard shoulder, exhibited a higher SD for the angular velocity of the steering wheel, and longer reaction times. In this case, participants in the alcohol group stated that their driving is more affected than those in the cannabis group when driving under the influence, with their responses being to some extent reflected by the objective data. Finally, the deterioration noted in visual performance after alcohol or cannabis use could have a significant impact on driving ability. As such, it is important to make consumers more aware of the negative effects of these drugs.

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