Received: 1 February 2021 | Accepted: 10 May 2021 | Published online: 11 August 2021

DOI: 10.1111/opo.12851

OPO THE COLLEGE OF OPTOMETRISTS

ORIGINAL ARTICLE

Dynamics of the accommodative response after smoking cannabis

Sonia Ortiz-Peregrina | **Carolina Ortiz** | **Franceso Martino** | **José J Castro-Torres** | **Rosario G Anera**

Department of Optics, Laboratory of Vision Sciences and Applications, University of Granada, Granada, Spain

Correspondence
Carolina Ortiz, Department of Optics, Laboratory of Vision Sciences and Applications, University of Granada, Granada, Spain.
Email: ortizh@ugr.es

Funding information
Ministerio de Ciencia, Innovación y Universidades, Grant/Award Number: FPU15/05571; European Regional Development Fund, Grant/Award Number: FIS2017-85058-R; Ministerio de Economía y Competitividad

Abstract

Purpose: Cannabis is the most widely consumed illicit drug worldwide. It has been suggested that cannabis could generate blurred vision during reading tasks. The goal of this study was to objectively assess the acute effects of smoking cannabis on the dynamics of ocular accommodation. The influence of other factors, including target distance and the direction of accommodation, as well as personal characteristics, were also analysed.

Methods: Nineteen young people who were occasional cannabis users participated in the study (mean age 22.53 [3.12] years). Their usage profiles were evaluated by means of the Cannabis Use Disorders Identification Test-revised (CUDIT-r). The dynamics of the accommodative response were evaluated using an open-field auto refractor (Grand Seiko WAM-5500). The participants completed two different experimental sessions, one week apart, and in random order (baseline session and after smoking cannabis). During these sessions, the amplitude of the response (D), mean velocity (D/s), peak velocity (D/s), response time (s), accommodative lag (D) and accommodation variability (D) were measured.

Results: The results indicated that cannabis use had a significant main effect on the mean accommodation/disaccommodation velocity ($F_{1,13} = 7.21$; $p = 0.02$; $\eta_p^2 = 0.396$). Cannabis consumption also interacted significantly with other factors. Response time showed a significant two-way interaction between condition × target distance ($F_{1,13} = 11.71$; $p = 0.005$; $\eta_p^2 = 0.474$) and condition × accommodation direction ($F_{1,13} = 8.71$; $p = 0.01$; $\eta_p^2 = 0.401$). For mean velocity, two-way interactions were found between condition × age ($F_{1,13} = 6.03$; $p = 0.03$; $\eta_p^2 = 0.354$), condition × CUDIT-r score ($F_{1,13} = 6.03$; $p = 0.03$; $\eta_p^2 = 0.356$) and condition × target distance ($F_{1,13} = 7.20$; $p = 0.02$; $\eta_p^2 = 0.396$).

Conclusions: These findings suggest that cannabis use can alter the accommodation process, although further studies should be carried out to explore the role of attention deficits. According to these results, certain daily activities that depend on an accurate accommodative function may be affected by cannabis use.

KEYWORDS
accommodation, accommodation dynamics, accommodative response, cannabis, cigarette, THC, vision

INTRODUCTION

Cannabis is one of the most commonly consumed illegal drugs in the world, although it should be noted that is not illegal in all jurisdictions. In Europe, around 18 million adults aged between 15 and 34 years (15%), and 25.2 million adults between 15 and 64 years (7.6%) used cannabis in 2019.[1] It is also the most widely used drug among the youngest population group (15–24 years), and around 20% used it in 2019. In Spain, cannabis is considered an illegal drug, but it is not illegal for personal use and possession. Thus, as well as being the most consumed substance after alcohol and tobacco, its use has been growing since 2011.[2] It is estimated that 37.5% of the adult Spanish population (15–64 years) has taken this drug at least once, and around 11% took it in 2019. Due to its widespread use and the fact that some countries are legalising it, cannabis consumption and the consequences of this has become a public health concern of enormous interest for both regulators and citizens.[3]

The two main compounds of *Cannabis sativa* are Δ^9–tetrahydrocannabinol (THC), responsible for its psychoactive effect and cannabidiol (CBD).[4-6] It is most commonly administered by inhalation in cigarette form, made by mixing cannabis and tobacco,[3] which causes it to rapidly arrive at the cannabinoid receptors (CB receptors) and other action targets, engendering its effect.[7] Cannabinoid receptors are densely distributed in various areas of the central nervous system (CNS), like the brain, including key locations in the visual system.[8] They are located along important visual information channels sending information to the visual cortex, such as the human thalamus (in the lateral geniculate nucleus (LGN)) and superior colliculus.[9,10] These receptors are also found in the retina and anterior segment structures, including the ciliary muscle, which is responsible for accommodation.[11] Ciliary muscle innervation is controlled by the autonomic nervous system (ANS), and one of the crucial modulators of its signalling is the endocannabinoid system, meaning that cannabis consumption could alter the accommodation process.[12-14] The parasympathetic branch of the ANS is principally responsible for accommodation control, although the sympathetic branch also plays a complementary role in inhibition.[15-17] Cannabis use stimulates the sympathetic nervous system and inhibits the parasympathetic nervous system.[18] In this context, the minimal data reported in the scientific literature indicate that cannabis use is associated with accommodative infacility and accommodative insufficiency.[19] Valk[20] reported a reduction in the magnitude of accommodation in five young users, who cited reading difficulties. Another study indicated a similar complaint from patients, although the author found no near vision problems during the assessments.[21] Later, González Pérez *et al*.[22] also found a markedly reduced accommodation amplitude in 15 drug addicts (16–36 years old), of whom 12 used cannabis. The authors argued that this effect could be due to the sympathomimetic effect of cocaine, nicotine and cannabis, although they admitted that it might depend on other factors, including the type of drug used, the duration of their addiction and gender, but they were unable to analyse these issues. Similarly, one of our recent studies demonstrated that smoking cannabis generated poorer accommodative accuracy (higher lags).[23]

Key Points

- Smoking cannabis seems to alter the dynamics of the accommodative response, significantly affecting the accommodation/disaccommodation velocity.
- Personal factors such as age, gender and cannabis use frequency/profile determine different effects on the accommodative response.
- Cannabis use may impact everyday tasks dependent on the accommodation function such as reading or driving.

Numerous studies have reported that cannabis use is associated with impaired cognition. Memory deficits are observed in chronic cannabis users; focused, divided or sustained attention is also impaired, showing a dose-dependent relationship.[24] Anderson *et al*.[25] studied the effects of marijuana in the Useful Field of View (UFOV) task, which allows the assessment of visual processing speed, divided and selective attention. The authors found that marijuana caused attention deficits in divided and selective attention tasks, but not in the sustained attention task, indicating that selective speed is specifically altered by cannabis. In addition, participants under the effects of marijuana overestimated the time required to complete the UFOV task. Indeed, Böcker *et al*.[26] showed that increased reaction time and poor performance accuracy were a function of memory load and THC-dose. However, other work has concluded that chronic cannabis users did not show deficits in the performance of the vigilant attention task, defined as the ability to respond to a stimulus without a cue.[27]

Attentional capacity is one of the non-blur driven stimuli of the accommodative response. Recent studies found that attentional distractors can alter the dynamics of ocular accommodation. Thus, performing tasks that required a higher mental load while fixating on a distant target produces a greater accommodative response. This might be a consequence of increased parasympathetic tone during cognitive effort.[28] In addition, auditory feedback enhances the accuracy of the accommodative response, with reductions in the accommodative lag.[29] Likewise, other factors that influence the accommodative response are the participant's characteristics such as age or pupil size,[30,31] and target configuration including luminance, spatial frequencies, contrast or colour.[32-35]

Despite previous work suggesting that cannabis does exert a possible effect on accommodation, to the authors' knowledge, no studies explore this issue further, and the potential impact of cannabis on the dynamics of accommodative response remains unknown. Moreover, it is important to assess the effects cannabis has on ocular accommodation objectively; if this drug produces significant changes, it may impede the precise and safe performance of daily activities for which vision is crucial. To address this informational gap, the goal of this work was to study the acute effects of smoking cannabis on the dynamics of ocular accommodation in an objective manner, controlling for other potentially influential factors, such as task distance, accommodation direction and personal traits including age, gender and usage profile.

METHODS

This observational study adhered to the tenets of the Declaration of Helsinki and was prospectively approved by the University of Granada Human Research Ethics Committee (921/CCEIH/2019). Prior to participating in the study, the volunteers were verbally informed of its details and possible consequences, and a signed informed consent was obtained from each of them.

Nineteen students from the University of Granada (mean age 22.53 [3.12] years; range 19–32 years), of which eight (42.1%) were female, voluntarily took part in the study. All of them declared that they were currently occasional cannabis users, i.e., self-reported cannabis use at least once but less than four times/week over the past three months.[36,37] Subjects were excluded if they currently or had previously used other recreational drugs (taken more than five times in their life); if their best-corrected visual acuity was >0.0 logMAR, they had any current or history of binocular/accommodation problems; had previously or were currently suffering any medical diseases and in the case of women were pregnant. Participants with refractive error were required to wear soft contact lenses for the experimental sessions, therefore, they had to have at least one year's experience of contact lens wear. To rule out alcohol use problems, we employed the Alcohol Use Disorders Identification Test (AUDIT).[38] In addition, to quantify cannabis use we employed the Cannabis Use Disorders Identification Test revised (CUDIT-r).[39] If the results of any of these tests indicated a disorder related to alcohol or cannabis use, those subjects were excluded from the study.

Participants attended two experimental sessions in the laboratory, a baseline session (with no cannabis use) and another after having smoked cannabis. The order of the two sessions was randomised, with a washout period of seven days between them. The experimental session under the effects of cannabis was performed 20 min after the participants had smoked a cannabis cigarette. The participants prepared the cannabis cigarette in the same manner as their habitual usage, and they smoked it in about 10 min. The testing sessions lasted approximately 45 min, guaranteeing that there was a considerable psychoactive effect throughout the session after having smoked cannabis, given that this tapers off within 2–3 h.[7] They were asked to abstain from cannabis use during the 4 days prior to each session, and not to drink alcohol in the preceding 24 h. To obtain objective confirmation of cannabis consumption, a saliva drug test was performed using the Dräger DrugTest 5000 (Dräger Safety, draeger.com). This device has been proposed as a highly sensitive, specific and efficient method for oral fluid cannabinoid detection,[40] and allowed us to ensure that no other substances had been used (e.g., amphetamines, benzodiazepines, cocaine, metanphetamines, opiates, methadone or ketamine). For cannabis, the Dräger test is able to detect concentrations higher than 12 ng/ml up to 8–14 h after consumption. To check that the participants had not consumed alcohol, we measured their breath alcohol content (BrAC) with the Dräger Alcotest 7110 MK-III (Dräger Safety, draeger.com).

Accommodative function assessment

Firstly, an optometric evaluation was made to ensure that the participants met the inclusion criteria. When necessary, optical correction was adjusted employing retinoscopy and subjective refraction. The normal amplitude of accommodation as a function of age was assessed using the push-up technique.

The dynamics of the accommodative response were then evaluated by means of an open field autorefractor, the Grand Seiko WAM-5500 (Grand Seiko, grandseiko.com), which has been shown to be reliable and valid for assessing accommodation in both static and dynamic modes.[41-43] We used the dynamic (HI-SPEED) mode, with a sample frequency of 5 Hz and a sensitivity of 0.01 D. The device also registered pupil size with a sensitivity of 0.1 mm. The measurements were taken from one eye (randomly selected),[44] while subjects viewed the target binocularly.[45] Before testing, on-axis measurements were ensured by seating the subject properly, supported on the chin rest and forehead strap and aligning them with the fixation target. Thus, the autorefractor was aligned with the measured eye, as well as with both stimuli (positioned at a viewing distance of 4.5 m and 0.4 or 0.2 m). We triggered changes in the accommodative response by asking the subjects to fixate on two different stationary targets: one placed 4.5 m away, and the other printed on a transparent slide at a near distance (0.4 m or 0.2 m); thus allowing the observers to see the far stimulus through the slide.[46] This way, we generated abrupt accommodative changes of 2.25 D or 4.75 D, respectively (which were evaluated in a randomised order).

The far target was the fixation chart provided by the WAM-5500 manufacturer (Michelson contrast = 53%). This was a 234 × 324 square chart comprising a 78 mm grid with a four-pointed star located in the centre. This star was made up of a ring (with a 60 mm and 35 mm outer and inner diameter) and four points which were 23 mm in width and 17 mm in length. This target is illustrated in Lockhart and Shi.[47] The near target was the same six-pointed black star as provided by the manufacturer for these particular distances, but printed onto a transparent slide (Michelson contrast = 70%). The luminance of the detail and background of each target were measured with a luminance meter (Topcon BM-5, topcon-medical.com). During data acquisition, the room illuminance was kept constant at approximately 150 lux, as measured at the corneal plane of the participant with a T-10 illuminance meter (Konica Minolta, konicaminolta.eu).

Participants were instructed to change their fixation from one target to another every 10 s, triggered by an audible alarm. They were asked to make these changes as fast as possible and to keep the targets in focus at all times. They started by looking at the far distance target (4.5 m), ignoring the first alarm, and changed their fixation when the second alarm sounded. This requirement was used as a control for attention and concentration. If a lack of attention or any error during the measurements was noted, the recording was interrupted, the participant was reminded of the instructions and the measurement repeated. Participants were encouraged to avoid blinking during the change in fixation and to blink as little as possible during testing to reduce artefacts in the accommodative response. In addition, participants underwent a training measurement session during the preliminary visit to help avoid learning effects; during this training session they made the changes in fixation described above following the experimenter's command, which was given at random intervals.

We measured 20 s accommodation/disaccommodation cycles, with three repetitions of each measurement, meaning that data for a total of 60 s was recorded. The device registered time, spherical equivalent and pupil size, and the results were exported to a computer. The data was then divided into accommodation and disaccommodation cycles (three of each class), and we calculated the mean step response. From this, we calculated the mean accommodation and disaccommodation velocities (D/s), and also the accommodation and disaccommodation peak velocity (D/s), as described by other authors.[48-50] Firstly, the amplitude of the response (D) was calculated as the maximum difference in the step response. The mean accommodation and disaccommodation velocities were 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 accommodation and disaccommodation peak velocity was analysed as the absolute value of the maximum dioptric change per time unit. The response time (s) was also obtained, as in Heron *et al.*[48] This parameter was calculated as the interval between the instant when the accommodative response started to change and that when the accommodative response reached a steady-state level. Steady-state accommodative response was evaluated by means of the accommodative lag (D) and accommodation variability (D). Accommodative lag was obtained in accordance with Poltavski *et al.*,[51] by subtracting the mean point of focus during testing (WAM-5500 refraction value) from the target distance (2.25 D or 4.75 D) and adjusting for the baseline static refraction value (taken at 4.5 m). In addition, the standard deviation of the accommodative response corresponded to the variability of accommodation.[42,52,53,54] In order to ensure that the accommodative response had a steady state, its variability was calculated for the 5 central seconds of the 10 s accommodation intervals in each cycle. Therefore, a total of 15 s of recording was used to obtain the mean accommodation variability in each measurement.

For each measurement, values deviating by more than ±3 standard deviations from the mean spherical equivalent were excluded as recording errors, possibly due to blinking. This criteria has been adopted previously by other authors.[54,55]

Statistical analysis

All the statistical procedures were performed with SPSS 26.0 software (IBM, ibm.com). Normal distribution of data was checked using a Kolmogorov-Smirnov test. Pupil size comparisons were performed with paired *t*-tests. Repeated-measures ANOVAs were employed for each accommodation variable, including condition (baseline and after smoking cannabis), target distance (0.4 and 0.2 m) and direction of accommodation (i.e., generating accommodation or disaccommodation) as within-subject factors. Gender was also included as a between-subjects factor, and age and CUDIT-r score were included as covariates to control their possible influence. A higher CUDIT-r score indicated heavy cannabis use, which could potentially influence the results since some subjects had a higher exposure to the drug than others. Repeated-measures ANOVAs were also performed for accommodative lag and variability, but in these cases the accommodation direction was not included as a within-subject factor. Additionally, for some variables where we found significant interactions, we performed bivariate correlation analyses in order to investigate the relationship between these specific parameters.

RESULTS

Participants reported a mean usage frequency of 5.38 (6.37) days per month, and the mean AUDIT and CUDIT-r test scores were 7.26 (3.74) and 6.44 (4.30), respectively (all scores below the cut-off limit that indicates a substance use disorder). *Table 1* shows pupil size data obtained during measurements for each distance evaluated. In general, pupil sizes were equivalent for both conditions.

Table 2 presents the results of the different parameters employed to assess the accommodative response dynamics for the two conditions (baseline session and after smoking cannabis). Descriptive results (mean (SD)) are presented for each condition, near target distance (0.4 and 0.2 m) and accommodation direction (accommodation and disaccommodation).

Repeated measures ANOVAs for the accommodative response dynamics revealed some significant main effects and interactions. For response amplitude, both target distance ($F_{1,13}$ = 9.57; p = 0.009; η_p^2 = 0.424) and accommodation direction ($F_{1,13}$ = 28.23; p < 0.001; η_p^2 = 0.685) had significant main effects. In addition, there were significant two-way interactions between condition × target distance ($F_{1,13}$ = 11.71; p = 0.005; η_p^2 = 0.474), condition × direction ($F_{1,13}$ = 8.71; p = 0.01; η_p^2 = 0.401) and target distance × direction ($F_{1,13}$ = 5.57; p = 0.04; η_p^2 = 0.300). Finally, a three-way significant interaction was found between target distance × direction × age ($F_{1,13}$ = 5.12; p = 0.04; η_p^2 = 0.283). On average, the amplitude of the response was 11.2% lower in subjects over 25 years of age, although we found no significant correlation between response amplitude and age.

The mean velocity revealed that condition had a significant main effect ($F_{1,13}$ = 7.21; p = 0.02; η_p^2 = 0.396). Moreover, we found significant two-way interactions between condition × age ($F_{1,13}$ = 6.03; p = 0.03; η_p^2 = 0.354), condition × CUDIT-r score ($F_{1,13}$ = 6.09; p = 0.03; η_p^2 = 0.356) and condition × target distance ($F_{1,13}$ = 7.20; p = 0.02; η_p^2 = 0.396). Older subjects and those with a higher consumption frequency (higher CUDIT-r scores) exhibited greater reductions in mean velocity after smoking cannabis, as confirmed by the correlations shown in *Figure 1*. Likewise, mean velocity was reduced when the near target distance was at 0.2 m in comparison with the 0.4 m viewing distance (*Table 2*). We found a significant three-way interaction between condition × target distance × age for this variable ($F_{1,13}$ = 6.60; p = 0.03; η_p^2 = 0.375).

Finally, gender had a significant main effect on mean velocity ($F_{1,13}$ = 5.86; p = 0.03; η_p^2 = 0.348). Being female significantly correlated with a lower mean accommodation/disaccommodation velocity after smoking cannabis, as shown in *Figure 1*.

For peak velocity, the results revealed a significant two-way interaction between target distance × age ($F_{1,13}$ = 5.23; p = 0.04; η_p^2 = 0.303) and a three-way interaction effect between condition × direction × CUDIT-r score ($F_{1,13}$ = 9.22;

TABLE 1 Descriptive statistics and comparisons (mean (SD)) of pupil size at the different distances evaluated in both conditions

Target distance (m)	Pupil size (mm)		
	Baseline	Cannabis	*p*-Value[a]
(4.5↔0.4)			
4.5	6.30 (0.98)	5.99 (0.94)	0.10
0.4	6.00 (0.98)	5.79 (0.99)	0.29
(4.5↔0.2)			
4.5	6.15 (0.97)	5.88 (0.87)	0.21
0.2	5.23 (1.15)	5.09 (1.08)	0.46

[a]Paired *t*-test.

TABLE 2 Descriptive statistics (mean (SD)) of the parameters describing the accommodative response dynamics in the baseline session and after smoking cannabis

Parameter	Target distance (near)	Accommodation		Disaccommodation		Significant main effects/interactions
		Baseline	Cannabis	Baseline	Cannabis	
Amplitude of response (D)	0.4 m	−2.20 (0.40)	−2.23 (0.50)	2.19 (0.45)	2.17 (0.47)	TD (p = 0.009) AD (p < 0.001) C × TD (p = 0.005) C × D (p = 0.01) TD × D (p = 0.04) TD × D × A (p = 0.04)
	0.2 m	−4.32 (0.50)	−4.31 (0.53)	4.36 (0.54)	4.18 (0.64)	
Mean velocity (D/s)	0.4 m	0.28 (0.17)	0.25 (0.21)	0.20 (0.06)	0.21 (0.10)	C (p = 0.02) C × A (p = 0.03) C × CS (p = 0.03) C × TD (p = 0.02) C × TD × A (p = 0.03) G (p = 0.03)
	0.2 m	0.72 (0.51)	0.66 (0.48)	0.55 (0.35)	0.36 (0.27)	
Peak velocity (D/s)	0.4 m	−5.59 (2.39)	−4.95 (1.51)	4.54 (2.44)	3.98 (1.15)	TD × A (p = 0.04) C × D × CS (p = 0.01)
	0.2 m	−7.42 (2.42)	−6.70 (1.84)	8.90 (3.25)	8.55 (3.96)	
Response time (s)	0.4 m	0.81 (0.60)	1.09 (0.55)	1.60 (0.75)	2.06 (0.94)	TD (p = 0.01)
	0.2 m	1.51 (0.50)	1.57 (0.49)	1.88 (0.96)	1.96 (0.62)	
Accommodative lag (D)	0.4 m	−1.06 (0.60)	−1.12 (0.54)	—	—	
	0.2 m	−1.52 (0.45)	−1.57 (0.55)	—	—	
Accommodation variability (D)	0.4 m	0.14 (0.06)	0.18 (0.08)	—	—	C × TD × A (p = 0.03)
	0.2 m	0.22 (0.08)	0.22 (0.10)	—	—	

Abbreviations: A, age; AD, accommodation direction; C, condition; CS, CUDIT-r score; D, direction; G, gender; TD, target distance.

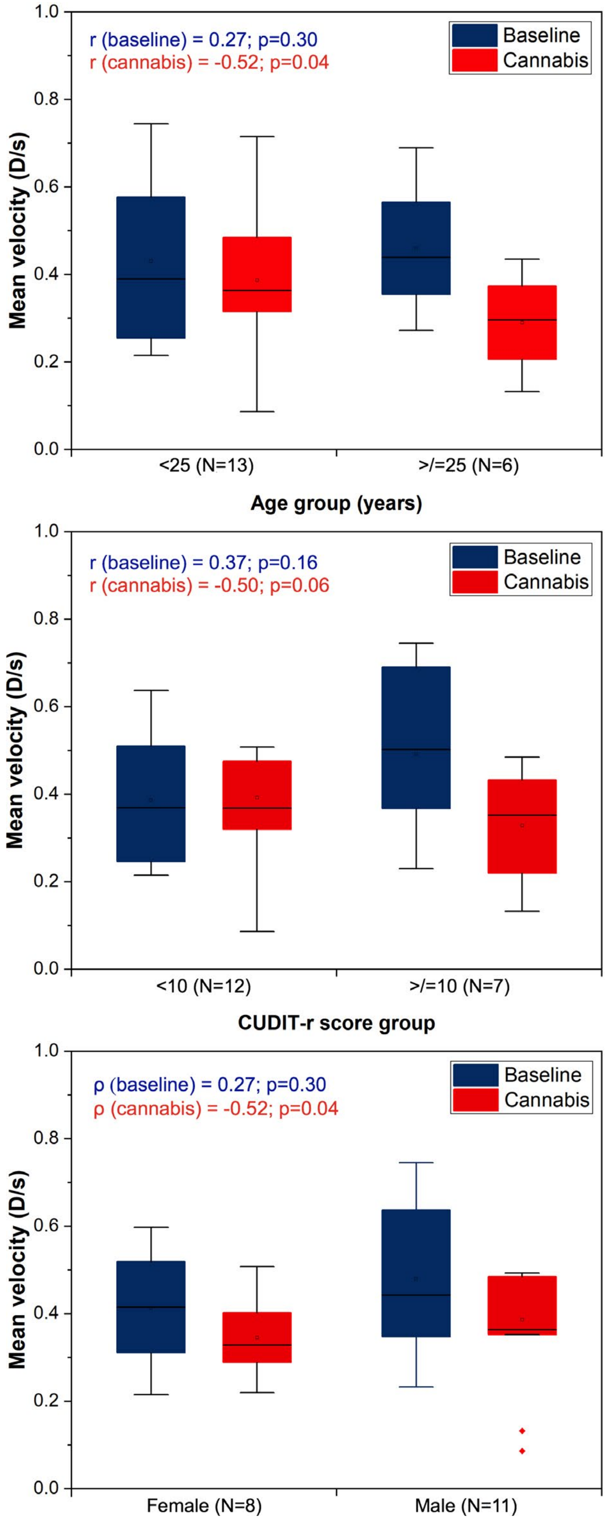

FIGURE 1 Mean velocity boxplots for participants categorized according to age, Cannabis Use Disorders Identification Test-revised (CUDIT-r) scores and gender. Results of bivariate correlations between mean velocity and age, CUDIT-r score and gender are also included for each condition

$p = 0.01$; $\eta_p^2 = 0.434$). As an example, in one participant as shown in *Figure 2a,b*, we obtained the velocity curves and spherical equivalent recordings for a period of 4 s, with the change in fixation target occurring after 2 s. This indicated a step response for accommodation and disaccommodation at the two target distances evaluated. It can be observed that the peak velocity is lower after cannabis use, although ultimately the accommodative response is similar in the two conditions.

Likewise, the response time for both directions of accommodation was longer under the effect of cannabis with respect to the baseline condition (*Table 2* and *Figure 3*). For this variable, we found that only target distance had a significant main effect ($F_{1,13} = 9.11$; $p = 0.01$; $\eta_p^2 = 0.432$). The average response time was 26.5% higher at 0.2 m compared with the response time at 0.4 m for both conditions.

In the case of the accommodative lag, we found that condition tended to exert an effect, but this did not reach statistical significance ($F_{1,13} = 4.18$; $p = 0.06$; $\eta_p^2 = 0.243$). For accommodation variability, a three-way significant interaction was found for condition × target distance × age ($F_{1,13} = 5.75$; $p = 0.03$; $\eta_p^2 = 0.291$). Cannabis use increased the accommodation variability only at 0.4 m, although the data demonstrates greater variability at the 0.2 m target distance compared with 0.4 m.

Finally, as an example, *Figure 4* presents dynamic accommodation measurements for one participant. This figure shows that under the effect of cannabis, and particularly at 0.4 m, the accommodative response is more variable and demonstrates decreased accuracy. However, the accommodative lag at 0.2 m is higher than at 0.4 m for both conditions. Cannabis use led to a greater accommodative lag at 0.2 m, but not at 0.4 m. However, the same effect did not occur when the stimulus was viewed at 0.4 m (top graph).

DISCUSSION

The aim of this work was to examine the acute effect of cannabis on ocular accommodation dynamics, controlling for other factors such as target distance, accommodation direction and personal factors including gender, age and usage profile. Although the amplitude of the response was similar in the two conditions, we found a decrease in both the mean and peak velocity after cannabis use, as well as longer response times. Likewise, during the steady-state response we found greater accommodative lags and response variability in subjects under the influence of cannabis.

Accommodation is controlled by the activity of the autonomic nervous system (ANS), and previous data suggests that THC acts on the ANS to induce sympathetic stimulation and parasympathetic inhibition.[14,18] Furthermore, CB receptors are located in the CNS, including the retina and the visual cortex, which play an important role in neurotransmission.[8] Changes in visual information processing could alter accommodative function due to input from the retina reaching the visual cortex more slowly, and subsequently the Edinger Westphal nucleus whose activity causes the ciliary muscles to contract.[56,57] CB receptors are also present in these muscles,[11,58] meaning that cannabis could also alter their contraction.[11] Although the pupil is also innervated by parasympathetic and sympathetic fibres, we did not find any significant changes in pupil size after cannabis use. This result is consistent with some previous findings,[23] although contradictory results have been published in the literature with regard to the effect of cannabis on pupil size.[59,60]

The presence of cannabinoid receptors in key structures for accommodative function may explain the reduced response found here. Although the effects of cannabis on the dynamics of the accommodative response were largely unknown, these results are in line with previous studies that reported near vision difficulties after using this drug.[20,21] Cannabis use had a significant main effect on the mean accommodation/disaccommodation velocities. This effect seems more marked in the direction of accommodation, for while we found a reduction in both near target distances in the case of positive accommodation, for disaccommodation the mean velocity was only lower for changes when the near stimulus was positioned at 0.2 m. This finding could be explained by the fact that the drug inhibits the parasympathetic branch of the ANS, responsible for stimulating accommodation, and although it also stimulates the sympathetic branch (whose role is inhibitory), this latter has less effect on the dynamics of the accommodative response, as suggested by others.[15] In general, the mean velocities found in this work are less than those reported by Adaba *et al*.[49] and Heron *et al*.[48,61] Although we employed the procedures described by these authors to obtain the parameters relative to the dynamics of the accommodative response,[48,49] the method used does have an influence. For example, when calculating the variable mean velocity, the duration of fixation time (10 s in this study) influenced the outcome, in such a way that longer fixation times led to lower mean velocities. Moreover, the autorefractor used could also be partially responsible for these differences, for example due to the sampling frequency.[49] Although it has been demonstrated that the strategy used to analyse the accommodative response dynamics does affect the outcome with regard to its descriptive parameters, there is still no standardised method for performing the analysis, leading to heterogeneous results.[62]

The peak velocity was also reduced after cannabis use in both accommodation directions and for the two target distances (*Figure 2a,b*). We obtained a higher peak velocity than in some previous studies,[48,49] but in line with that found by other authors.[31,63] This parameter is dependent on the response amplitude,[31] indicating that the magnitude of the accommodative change required by the fixation targets could influence the outcome, justifying the differences observed with regard to other works. Further, as noted above for mean velocity, the difference in peak velocities may also be attributed to the method of calculation. Notwithstanding, in line with previous studies, we also found greater peak velocities in the direction of disaccommodation,[62,63] but only for the greater accommodative demand, whereas for abrupt changes of 2.25 D the peak velocities were slightly higher during accommodation. Just as for the other parameters, response times were longer under the effect of cannabis, with the slowdown being more pronounced for disaccommodation. Heron *et al*.[48] also reported longer response times for disaccommodation, but in line with our results, they found no significant differences between the two accommodation directions. In general, our response times are longer than those reported by Heron *et al*.[48] for abrupt changes of about 1.00 D. This difference is likely to be due to the difference in the accommodative demand, as our own results demonstrate that target distance significantly affects response time. Thus, we found higher response times for abrupt step changes of 4.75 D compared with 2.25 D.

Cannabis use also seems to alter accommodative function during the steady-state response, since we found an increased accommodative lag for both target distances, even though this effect was not significant ($p = 0.08$). Accommodative lags were similar to those found by a recent study in 31 young cannabis users for the baseline session and after smoking cannabis, although in that study cannabis use generated greater increase in the accommodative lag than in the present work.[23] In general, the lags observed here were comparable to those reported in recent studies employing the same optometer, although those works were not related to cannabis consumption.[46,50,52,54] In some cases, accommodative lag was employed to investigate the effect of another psychoactive substances. For example, Casares-López *et al*.[50] analysed the effect of alcohol on accommodation, and although the authors found slightly higher lags of accommodation at 0.4 and 0.2 m than were recorded here, they did not observe a significant effect of alcohol on this parameter. Additionally, other investigations evaluating the effects of caffeine on ocular accommodation found slightly lower lags than in our study. However, it was noted that caffeine intake did not affect accommodative lag,[52,54] even though it was shown that the autonomic stimulation caused by this substance increases the accommodative amplitude.[64] Caffeine enhances the activity of the sympathetic nervous system, which seems to have only a slight effect on the dynamics of the accommodative response.[15] In contrast, as discussed earlier, cannabis consumption triggers parasympathetic inhibition, which is consistent with the tendency towards higher accommodative lags found in this study. On the other hand, larger lags have been linked with poorer cognitive capacity and attention,[51] and this is a clear consequence of cannabis use. Several studies have suggested that THC impairs cognition (memory, divided and sustained attention and reaction time) in a dose related manner.[24,65] However, Ogourtsova *et al*.[66] found that only complex useful-field-of-view tasks (i.e., tasks of divided and selective attention) were significantly compromised 3 and 5 h after participants' usual dose of cannabis, especially when these were novel tasks. These authors did not find deterioration 1 h after use for recreational cannabis

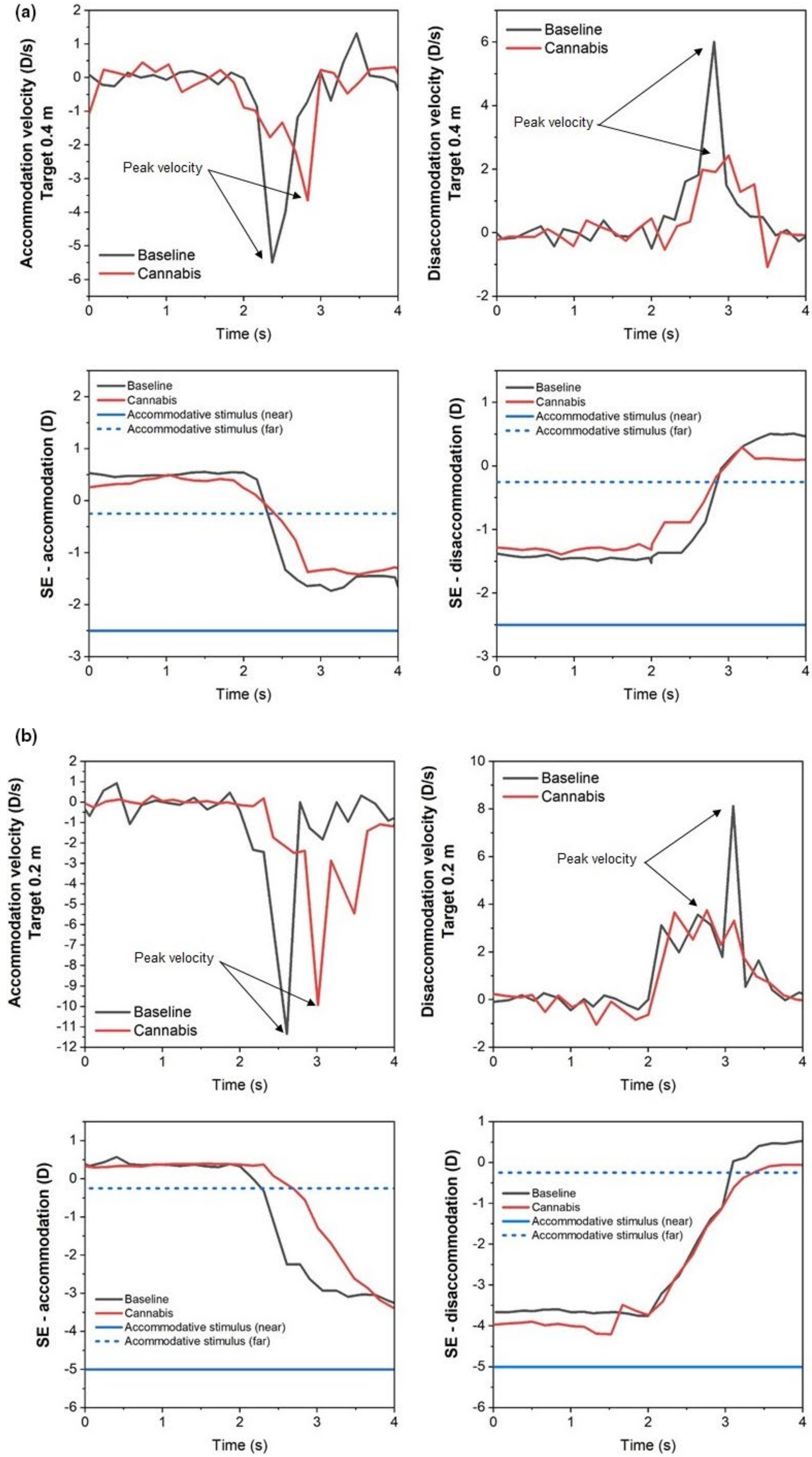
(a)
Accommodation velocity (D/s) Target 0.4 m
Peak velocity
Baseline
Cannabis
Time (s)
Disaccommodation velocity (D/s) Target 0.4 m
SE - accommodation (D)
Accommodative stimulus (near)
Accommodative stimulus (far)
SE - disaccommodation (D)
(b)
Accommodation velocity (D/s) Target 0.2 m
Disaccommodation velocity (D/s) Target 0.2 m

FIGURE 2 (a) Accommodation and disaccommodation processes in one participant during the baseline session (grey) and after smoking cannabis (red) for a 0.4 m target distance. The top images present the velocity curves (peak velocity is indicated) and the bottom images show the changes in the spherical equivalent during the accommodative response. (b) Accommodation and disaccommodation processes in one participant during the baseline session (grey) and after smoking cannabis (red) for a 0.2 m target distance. The top images present the velocity curves (peak velocity is indicated) and bottom images show the changes in the spherical equivalent during the accommodative response [Col

users. This result may suggest that the impairment in visual attention did not significantly influence the results we obtained in terms of the accommodative responses. In the same line, another study concluded that chronic cannabis users showed no performance deficits on the vigilant attention task.[27] However, given the importance of the attentional state for accommodative responses, this factor requires further research. Future studies should include tests of selective and sustained attention in the two experimental conditions (e.g., with a cancellation test). Another possibility would be to match attentional load in both sessions by introducing distractors in the baseline condition or by providing additional feedback during the cannabis session. Accommodative variability was only slightly reduced after cannabis use. This higher variability for near target distances is in line with previous data,[52] and the magnitude of the accommodation variability was comparable to that obtained in a previous work using the same autorefractor.[45]

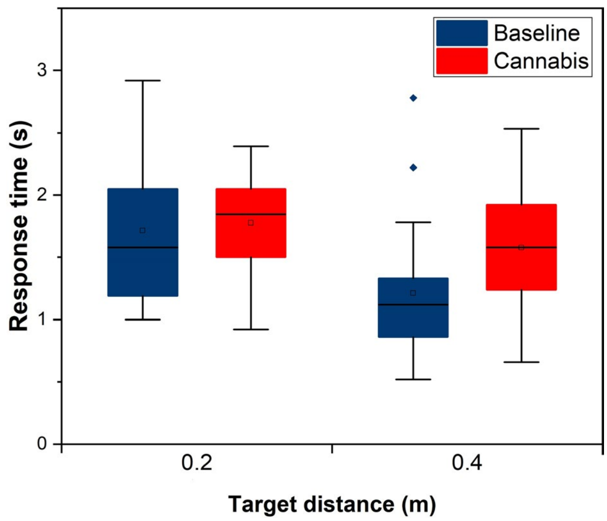

FIGURE 3 Response time boxplots for each target distance in the baseline condition and after smoking cannabis

It is important to note that personal factors such as age, gender and cannabis use frequency/profile (CUDIT-r scores) demonstrated some significant main effects or interactions in our study. Age seems to influence mean velocity, response time and accommodative variability; all the subjects in our sample were young, ranging in age from 18 to 30 years, so we did not expect this parameter to be so influential. However, it is known that age influences the accommodative response dynamics, and its inclusion as a covariate allowed us to discover possible interactions with other factors such as cannabis use.[31] In this way, we were able to determine that the older the participant, the greater the impairment in mean velocity after cannabis use (*Figure 1*), and that the older the participant, the longer the response time. Heron *et al.*[48] did not find a relationship between increased age and response times, although both earlier and later studies have suggested this.[31,67,68] In agreement with the results of our study, Anderson *et al.*[31] showed that age interacted significantly with response accommodation variability. These authors found the greatest variability in the first decade of life and the least in the third decade. In contrast to our results, other

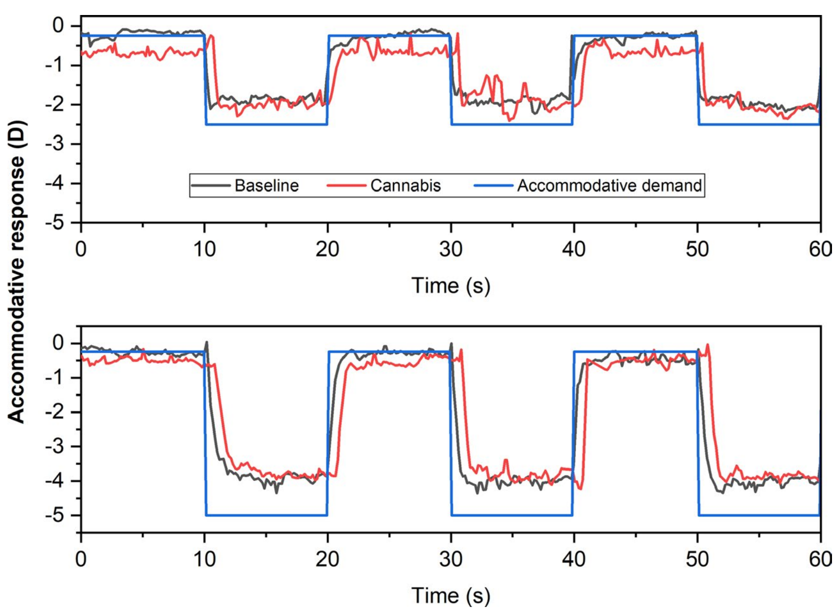

FIGURE 4 Accommodative response recorded for one participant in the two conditions (baseline and after cannabis use), for a stimulus at 0.4 m (top) and 0.2 m (bottom)

work has shown that age affects accommodation peak velocity, being fastest in the first and second decades of life.[31,63] However, these authors found no age differences in the disaccommodation peak velocity, which agrees with our findings. The disparate age ranges may explain the differences, since we did not include children or teenagers, unlike the other investigations cited. Surprisingly, gender demonstrated a significant main effect on mean speed, with females displaying slower accommodation velocities in both the baseline session and after cannabis use. This effect may be due, in part, to the drug having a greater effect on women, as demonstrated by the significant correlation between being female and the slower velocities observed in the cannabis condition. This drug could have a greater effect on a woman's accommodative function, since there are robust gender-related differences in the endocannabinoid system and metabolism of the drug.[69] Nevertheless, the females also showed lower mean velocities in the baseline condition, and while previous data has suggested lower objectively-measured amplitudes of accommodation in women,[70] there is no agreement with regard to gender differences in accommodative function. Accordingly, this question remains unresolved.[71-73]

However, the CUDIT-r score did interact significantly with other factors, affecting both the mean and peak velocity. Participants with higher questionnaire scores displayed lower mean accommodation/disaccommodation velocities, with this relationship being significant under the effect of cannabis. This result suggests that the frequency/profile of cannabis use could also determine the observed effect on accommodation, in agreement with studies on caffeine users, whose change in accommodative response after ingesting caffeine is dependent upon their habitual intake.[54] Our work only included participants who consumed cannabis less than four times a week, so further studies should explore the accommodation dynamics of more frequent users, as well as people with a longer duration of drug usage.

The results of the present study have a number of limitations that must be considered with regard to their interpretation, and these should also be addressed in future work. First, each participant consumed the THC cigarette in their usual manner, and since we did not measure their blood THC concentration, we are unable to establish a possible relationship between dose and effect. Nevertheless, it has been demonstrated that dose, blood concentration and effect do not follow a linear relationship,[7,74] and our goal was to study any effect that typical usage (i.e., that which the participants could be exposed to in a normal day) might have; thus allowing us to observe the effects of cannabis on accommodation from a real perspective. These results should serve as a starting point for future work involving varying doses or different administration routes. Second, the participants smoked the cannabis mixed with tobacco, and this second substance could also influence the accommodative function. It has been suggested that nicotine may increase parasympathetic activity after binding to nicotinic cholinergic receptors.[75] This increase in parasympathetic activity may be reflected as enhanced accommodative capacity, as demonstrated by Bardak *et al.*[76] who found increased objective accommodation after smoking cigarettes, with significant effects for 2 and 3D stimuli. Therefore, the effect of nicotine may have countered some of the effects of cannabis on the accommodation processes. This question should be analysed in future studies. Third, the size of the step and interval between steps was constant, thus generating changes that could be predictable, even though the participants were unaware of this information. This increases the possibility that the response is, to a lesser extent, driven by blur and is more likely to be affected by voluntary changes in accommodation.[61] Fourth, the sampling frequency of the autorefractor used in this study (5 Hz) was limited in comparison to other optometers. While the WAM-5500 allowed us to meet our goals for this work (comparison of the accommodative response under different conditions) the sampling frequency did not allow us to obtain parameters such as the response delay, which could be influenced by cannabis intake. Finally, both accommodative lag and response variability are influenced by cognitive performance (attention), and while caffeine consumption enhances cognitive performance, cannabis use has the oppose effect, i.e., impairing cognitive functioning. This impairment could further increase the accommodative lag and response variability. However, we observed a tendency towards higher accommodative lags after cannabis use, and found no association between cannabis consumption and greater accommodative variability. Future studies should explore this issue, assessing the extent to which cognitive impairment is responsible for changes in accommodation dynamics after cannabis consumption. As stated above, future work should assess selective and sustained attention in both experimental sessions, or alternatively the attentional state could be matched in the two conditions. Also, future studies should avoid the possibility of voluntary changes in accommodation due to subject anticipation. This could be avoided by using different time intervlas in the measured cycles. Unfortunately, because of the situation in our country resulting from the COVID-19 pandemic, it has been impossible at the present time to carry out this additional experimental work.

In summary, this study shows that cannabis use has an acute effect on accommodative function; specifically, we observed a significant main effect on the mean accommodation/disaccommodation velocity. We also found some interactions between cannabis consumption and one or more factors, including target distance, accommodation direction and personal characteristics such as age or CUDIT-r score. These affected the amplitude of the response, mean and peak velocity, response time and accommodation variability. Finally, cannabis use showed an effect on accommodative lag. These findings suggest that cannabis consumption can alter the accommodation process, and these variations could be due to the effect the drug has on the autonomic nervous system as well as the cannabinoid receptors present in the visual pathway and ciliary muscles. However, we did not observe changes in pupillary size, which is innervated by the same autonomic system as accommodation. Also, the impairments generated by cannabis use on attentional state might have influenced the accommodative responses of our participants. Therefore, although signs of a possible relationship between cannabis use and reduced accuracy of accommodation have been observed, this question remains to be analysed in future studies in order to draw more solid conclusions. These results have implications for daily activities that are dependent upon an accurate accommodative response, highlighting the importance of future work to explore the effects of cannabis on accommodative function further.

ACKNOWLEDGEMENTS

This work was supported by the Ministry of Economy and Competitiveness (Spain) and the European Regional Development Fund (ERDF) (FIS2017-85058-R), and by the Ministry of Science, Innovation and Universities (Spain) (Grant FPU15/05571). The authors thank Dräger Iberia for lending us the Dräger DrugTest 5000 and the Dräger Alcotest 7110 MK-III employed in this study. We also thank Trágora SCA for reviewing the English version of the manuscript. Funding for open access charge: Universidad de Granada/Consorcio de Bibliotecas Universitarias de Andalucía (CBUA).

CONFLICT OF INTEREST

The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

AUTHOR CONTRIBUTIONS

Sonia Ortiz-Peregrina: Conceptualization (equal); Data curation (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Resources (equal); Writing-original draft (equal); Writing-review & editing (equal). **Carolina Ortiz:** Conceptualization (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Resources (equal); Supervision (equal); Writing-original draft (equal); Writing-review & editing (equal). **Francesco Martino:** Formal analysis (equal); Methodology (equal); Writing-original draft (equal); Writing-review & editing (equal). **Jose Juan Castro-Torres:** Formal analysis (equal); Methodology (equal); Writing-original draft (equal); Writing-review & editing (equal). **Rosario G. Anera:** Conceptualization (equal); Investigation (equal); Project administration (equal); Supervision (equal); Writing-review & editing (equal).

ORCID

Carolina Ortiz https://orcid.org/0000-0003-0248-1699
Franceso Martino https://orcid.org/0000-0001-6812-1675
José J Castro-Torres https://orcid.org/0000-0003-0461-925X

REFERENCES

1. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) European Drug Report 2020: Trends and Developments. Luxembourg; 2020. Available from: emcdda.europa.eu/publications/edr/trends-developments/2020_en
2. Delegación del Gobierno para el Plan Nacional sobre Drogas y Observatorio Español de las Drogas Edades 2019/2020. Madrid (Spain); 2020. Available from: pnsd.sanidad.gob.es/profesionales/sistemasInformacion/sistemaInformacion/pdf/EDADES_2019-2020_resumenweb.pdf
3. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) European Drug Report: Trends and developments 2019. Luxembourg; 2019. Available from: emcdda.europa.eu/publications/edr/trends-developments/2019_en
4. Gaoni Y, Mechoulam R. Isolation, structure, and partial synthesis of an active constituent of Hashish. *J Am Chem Soc* 1964;86:1646–1647.
5. Mechoulam R, Gaoni Y. The absolute configuration of δ1-tetrahydrocannabinol, the major active constituent of hashish. *Tetrahedron Lett* 1967;12:1109–1111.
6. Mechoulam R, Shvo Y, Hashish I. The structure of cannabidiol. *Tetrahedron* 1963;19:2073–2078.
7. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet* 2003;42:327–360.
8. Schwitzer T, Schwan R, Angioi-Duprez K, et al. The cannabinoid system and visual processing: a review on experimental findings and clinical presumptions. *Eur Neuropsychopharmacol* 2015;25:100–112.
9. Glass M, Dragunow M, Faull RLM. Cannabinoid receptors in the human brain: a detailed anatomical and quantitative autoradiographic study in the fetal, neonatal and adult human brain. *Neuroscience* 1997;77:299–318.
10. Lalanne L, Ferrand-Devouge E, Kirchherr S, et al. Impaired contrast sensitivity at low spatial frequency in cannabis users with early onset. *Eur Neuropsychopharmacol* 2017;27:1289–1297.
11. Straiker AJ, Maguire G, Mackie K, Lindsey J. Localization of cannabinoid CB1 receptors in the human anterior eye and retina. *Invest Ophthal Vis Sci* 1999;40:2442–2448.
12. Rodríguez de Fonseca F, del Arco I, Bermudez-Silva FJ, Bilbao A, Cippitelli A, Navarro M. The endocannabinoid system: physiology and pharmacology. *Alcohol Alcohol* 2005;40:2–14.
13. Richards JR. Cannabinoid hyperemesis syndrome: a disorder of the HPA axis and sympathetic nervous system? *Med Hypotheses* 2017;103:90–95.
14. Benowitz NL, Rosenberg J, Rogers W, Bachman J, Jones RT. Cardiovascular effects of intravenous delta-9-tetrahydrocannabinol: autonomic nervous mechanisms. *Clin Pharmacol Ther* 1979;25:440–446.
15. Gilmartin B, Mallen EAH, Wolffsohn JS. Sympathetic control of accommodation: evidence for inter-subject variation. *Ophthalmic Physiol Opt* 2002;22:366–371.
16. McDougal DH, Gamlin PD. Autonomic control of the eye. *Compr Physiol* 2015;5:439–473.
17. Törnqvist G. The relative importance of the parasympathetic and sympathetic nervous systems for accommodation in monkeys. *Invest Ophthalmol* 1967;6:612–617.
18. Richards JR, Bing ML, Moulin AK, et al. Cannabis use and acute coronary syndrome. *Clin Toxicol* 2019;57:831–841.
19. London R. Accommodation. In: Barresi B, editor. Ocular Assessment: The Manual of Diagnosis for Office Practice. Boston, MA: Butterworth; 1984. p. 123–130.
20. Valk LEM. Hemp in connection with ophthalmology. *Ophthalmologica* 1973;167:413–421.

21. Shapiro D. The ocular manifestations of the cannabinols. *Ophthalmologica* 1974;168:366–369.
22. González Pérez J, Parafita Mato M, Segade García A, Díaz RA. Intraocular motility, electrophysiological tests and visual fields in drug addicts. *Ophthalmic Physiol Opt* 1995;15:493–498.
23. Ortiz-Peregrina S, Ortiz C, Casares-López M, Jiménez JR, Anera RG. Effects of cannabis on visual function and self-perceived visual quality. *Sci Rep* 2021;11:1655.
24. Broyd SJ, Van Hell HH, Beale C, Yücel M, Solowij N. Acute and chronic effects of cannabinoids on human cognition - A systematic review. *Biol Psychiatry* 2016;79:557–567.
25. Anderson BM, Rizzo M, Block RI, Pearlson GD, O'Leary DS. Sex, drugs, and cognition: effects of marijuana. *J Psychoactive Drugs* 2010;42:413–424.
26. Böcker KBE, Hunault CC, Gerritsen J, Kruidenier M, Mensinga TT, Kenemans JL. Cannabinoid modulations of resting state EEG theta power and working memory are correlated in humans. *J Cogn Neurosci* 2009;22:1906–1916.
27. Nusbaum AT, Whitney P, Cuttler C, Spradlin A, Hinson JM, McLaughlin RJ. Altered attentional control strategies but spared executive functioning in chronic cannabis users. *Drug Alcohol Depend* 2017;181:116–123.
28. Iwasaki T. Effects of a visual task with cognitive demand on dynamic and steady-state accommodation. *Ophthalmic Physiol Opt* 1993;13:285–290.
29. Redondo B, Vera J, Molina R, Davies LN, Jiménez R. Accommodative dynamics and attention: the influence of manipulating attentional capacity on accommodative lag and variability. *Ophthalmic Physiol Opt* 2020;40:510–518.
30. Ward PA, Charman WN. Effect of pupil size on steady state accommodation. *Vision Res* 1985;25:1317–1326.
31. Anderson HA, Glasser A, Manny RE, Stuebing KK. Age-related changes in accommodative dynamics from preschool to adulthood. *Invest Ophthalmol Vis Sci* 2010;51:614–622.
32. Jiménez R, Redondo B, Molina R, Martínez-Domingo MÁ, Hernández-Andrés J, Vera J. Short-term effects of text-background color combinations on the dynamics of the accommodative response. *Vision Res* 2020;166:33–42.
33. Charman WN, Tucker J. Dependence of accommodation response on the spatial frequency spectrum of the observed object. *Vision Res* 1977;17:129–139.
34. Owens DA. A comparison of accommodative responsiveness and contrast sensitivity for sinusoidal gratings. *Vision Res* 1980;20:159–167.
35. Johnson CA. Effects of luminance and stimulus distance on accommodation and visual resolution. *J Opt Soc Am* 1976;66:138–142.
36. Hartman RL, Brown TL, Milavetz G, et al. Cannabis effects on driving lateral control with and without alcohol. *Drug Alcohol Depend* 2015;154:25–37.
37. Hartman RL, Brown TL, Milavetz G, et al. Cannabis effects on driving longitudinal control with and without alcohol. *J Appl Toxicol* 2016;36:1418–1429.
38. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. The Alcohol Use Disorders Identification Test. Guidelines for Use in Primary Care. World Health Organization, Department of Mental Health and Substance Dependence. 2001.
39. Adamson SJ, Kay-Lambkin FJ, Baker AL, et al. An improved brief measure of cannabis misuse: The cannabis use disorders Identification test-Revised (CUDIT-R). *Drug Alcohol Depend* 2010;110:137–143.
40. Desrosiers NA, Milman G, Mendu DR, et al. Cannabinoids in oral fluid by on-site immunoassay and by GC-MS using two different oral fluid collection devices. *Anal Bioanal Chem* 2014;406:4117–4128.
41. Jiménez R, Molina R, Jiménez C, Jiménez JR, Redondo B, Vera J. Dynamics of the accommodative response under artificially-induced aniseikonia. *Exp Eye Res* 2019;185:107674.
42. Jiménez R, Redondo B, Davies LN, Vera J. Effects of optical correction method on the magnitude and variability of accommodative response. *Optom Vis Sci* 2019;96:568–578.
43. Sheppard AL, Davies LN. Clinical evaluation of the Grand Seiko Auto Ref/Keratometer WAM-5500. *Ophthalmic Physiol Opt*. 2010;30:143–151.
44. Armstrong RA, Davies LN, Dunne MCM, Gilmartin B. Statistical guidelines for clinical studies of human vision. *Ophthalnic Physiol Opt* 2011;31:123–136.
45. Thiagarajan P, Ciuffreda KJ. Visual fatigue and accommodative dynamics in asymptomatic individuals. *Optom Vis Sci* 2013;90:57–65.
46. Win-Hall DM, Houser J, Glasser A. Static and dynamic accommodation measured using the WAM-5500 autorefractor. *Optom Vis Sci* 2010;87:873–882.
47. Lockhart TE, Shi W. Effects of age on dynamic accommodation. *Ergonomics* 2010;53:892–903.
48. Heron G, Charman W, Schor C. Dynamics of the accommodation response to abrupt changes in target vergence as a function of age. *Vision Res* 2001;41:507–519.
49. Aldaba M, Gómez-López S, Vilaseca M, Pujol J, Arjona M. Comparing autorefractors for measurement of accommodation. *Optom Vis Sci* 2015;1:1003–1011.
50. Casares-López M, Castro-Torres JJ, Ortiz-Peregrina S, Ortiz C, Anera RG. Changes in accommodation dynamics after alcohol consumption, for two different doses. *Graefes Arch Clin Exp Ophthalmol* 2021;259:919–928.
51. Poltavski DV, Biberdorf D, Petros TV. Accommodative response and cortical activity during sustained attention. *Vision Res* 2012;63:1–8.
52. Redondo B, Vera J, Carreño-Rodríguez C, Molina-Romero R, Jiménez R. Acute effects of caffeine on dynamic accommodative response and pupil size: a placebo-controlled, double-blind, balanced crossover study. *Curr Eye Res* 2020;45:1074–1081.
53. Sreenivasan V, Irving EL, Bobier WR. Effect of near adds on the variability of accommodative response in myopic children. *Ophthalmic Physiol Opt* 2011;31:145–154.
54. Redondo B, Vera J, Molina R, Luque-Casado A, Jiménez R. Caffeine alters the dynamics of ocular accommodation depending on the habitual caffeine intake. *Exp Eye Res* 2019;185:107663.
55. Tosha C, Borsting E, Ridder WH, Chase C. Accommodation response and visual discomfort. *Ophthalmic Physiol Opt* 2009;29:625–633.
56. Gamlin PDR, Reiner A. The Edinger-Westphal nucleus: sources of input influencing accommodation, pupilloconstriction, and choroidal blood flow. *J Comp Neurol* 1991;306:425–438.
57. Gamlin PDR, Zhang Y, Clendaniel RA, Mays LE. Behavior of identified Edinger-Westphal neurons during ocular accommodation. *J Neurophysiol* 1994;72:2368–2382.
58. Schwitzer T, Schwan R, Angioi-Duprez K, Giersch A, Laprevote V. The endocannabinoid system in the retina: from physiology to practical and therapeutic applications. *Neural Plast* 2016;2016:2916732.
59. Dawson WW, Jiménez-Antillon CF, Perez JM, Zeskind JA. Marijuana and vision-after ten years' use in Costa Rica. *Invest Ophthalmol Vis Sci* 1977;16:689–699.
60. Stark M, Englehart K, Sexton B, Tunbridge R, Jackson P. Use of a pupillometer to assess change in pupillary size post-cannabis. *J Clin Forensic Med* 2003;10:9–11.
61. Heron G, Charman WN, Gray LS. Accommodation responses and ageing. *Invest Ophthalmol Vis Sci* 1999;40:2872–2882.
62. Del Águila-Carrasco AJ, Esteve-Taboada JJ, Papadatou E, Ferrer-Blasco T, Montés-Micó R. Amplitude, latency, and peak velocity in accommodation and disaccommodation dynamics. *Biomed Res Int* 2017;2017:2735969. https://doi.org/10.1155/2017/2735969
63. Kasthurirangan S, Vilupuru AS, Glasser A. Amplitude dependent accommodative dynamics in humans. *Vision Res* 2003;43:2945–2956.
64. Abokyi S, Owusu-Mensah J, Osei KA. Caffeine intake is associated with pupil dilation and enhanced accommodation. *Eye* 2017;31:615–619.
65. Ehrenreich H, Rinn T, Kunert HJ, et al. Specific attentional dysfunction in adults following early start of cannabis use. *Psychopharmacology* 1999;142:295–301.
66. Ogourtsova T, Kalaba M, Gelinas I, Korner-Bitensky N, Ware MA. Cannabis use and driving-related performance in young

recreational users: a within-subject randomized clinical trial. *Can Med Assoc J* 2018;6:E453–E462.
67. Fukuda T, Kanada K, Saito S. An ergonomic evaluation of lens accommodation related to visual circumstances. *Ergonomics* 1990;33:811–831.
68. Sun FC, Stark L, Nguyen A, Wong J, Lakshminarayanan V, Mueller E. Changes in accommodation with age: static and dynamic. *Am J Optom Physiol Opt* 1988;65:492–498.
69. Bassir Nia A, Mann C, Kaur H, Ranganathan M. Cannabis use: neurobiological, behavioral, and sex/gender considerations. *Curr Behav Neurosci Reports* 2018;5:271–280.
70. Weng CC, Hwang DK, Liu CJL. Repeatability of the amplitude of accommodation measured by a new generation autorefractor. *PLoS One* 2020;15:e0224733.
71. Hickenbotham A, Roorda A, Steinmaus C, Glasser A. Meta-analysis of sex differences in presbyopia. *Invest Ophthalmol Vis Sci* 2012;53:3215–3220.
72. Hashemi H, Nabovati P, Yekta AA, et al. Amplitude of accommodation in an 11- to 17-year-old Iranian population. *Clin Exp Optom* 2017;100:162–166.
73. Yekta AA, Khabazkhoob M, Hashemi H, et al. Binocular and accommodative characteristics in a normal population. *Strabismus* 2017;25:5–11.
74. Hunault CC, Mensinga TT, de Vries I, et al. Delta-9-tetrahydrocannabinol (THC) serum concentrations and pharmacological effects in males after smoking a combination of tobacco and cannabis containing up to 69 mg THC. *Psychopharmacol*. 2008;201:171–181.
75. Lie TC, Domino EF. Effects of tobacco smoking on the human pupil. *Int J Clin Pharmacol Ther*. 1999;37:184–188.
76. Bardak H, Gunay M, Bardak Y. Evaluation of the acute changes in objective accommodation, pupil size and ocular wavefront aberrations after cigarette smoking. *Cutan Ocul Toxicol*. 2017;36:25–28.

How to cite this article: Ortiz-Peregrina S, Ortiz C, Martino F, Castro-Torres JJ, Anera RG. Dynamics of the accommodative response after smoking cannabis. Ophthalmic Physiol Opt. 2021;41:1097–1109. https://doi.org/10.1111/opo.12851