TITLE PAGE

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Effect of experimental conditions in the accommodation response in myopia

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STRUCTURED ABSTRACT

Statement of Significance: The accommodative response is more affected by the type of refractive error than the method of stimulation, field of view or stimulus depth.

Purpose: To analyze the effect of stimulation method, stimulus depth and field of view (FOV) on the accommodation response (AR) for emmetropes (EMM), late-onset myopes (LOM) and early-onset myopes (EOM).

Methods: Monocular AR was measured in 26 young observers (n=9 EMM, n=8 LOM, n=9 EOM) under 60 different viewing conditions that were the result of permuting the following factors: (1) stimulation method (free space or Badal lens viewing), (2) stimulus depth (flat or volumetric), (3) FOV (2.5⁰, 4⁰, 8⁰, 10⁰, 30⁰) and (4) accommodative stimulus (AS: 0.17 D, 2.50 D, 5.00 D).

Results: Mixed ANOVA for 2.50 D of AS resulted in a significant effect of refractive group (F=6.77, p<0.01) and FOV (F=1.26, p=0.04). There was also a significant interaction between stimulus depth and FOV (F=2.73, p=0.03) and among stimulation method, FOV and refractive group (F=2.42, p=0.02). For AS of 5.00 D, there was a significant effect of refractive group (F=13.88, p<0.01) and stimulation method (F=5.16, p=0.03). There was also a significant interaction of stimulation method, stimulus depth and refractive group (F=4.08, p=0.03). When controlling for all interactions: LOM showed larger lags than EMM and EOM, the AR did not significantly change for fields of 8⁰, 10⁰ and 30⁰, and it did not significantly differ for different stimulation methods or stimulus depth.

Conclusions: Previously reported differences in AR when using lens-based methods compared to free space viewing may be explained by the effect of other factors such as the FOV or the depth of the stimulus. Targets with a field of view of 8 or 10⁰ may be optimal for accurate accommodation responses.

Keywords: Accommodation, refractive error, field of view, periphery, Badal, depth.

TEXT

Accommodation is stimulated in laboratory or clinical settings either by changing the viewing distance of free space targets[1–10] or by optical means, i.e., Badal,[11–15] or ophthalmic positive[2,3] or negative lenses.[2,3,5] Free space targets usually offer a more naturalistic method of stimulating accommodation. On the other hand, lens-based methods are especially useful when applied to ophthalmic instruments. One important practical advantage of using lenses to stimulate accommodation is that this can be achieved in a compact space, which is of interest in emerging technologies such as stereoscopic virtual reality systems that demand optical solutions to overcome the convergence-accommodation mismatch.[16]

Previous studies have found poorer accommodative responses when accommodation is stimulated with lenses compared to free space targets.[2,3,14] Recently, Aldaba et al.[17] reported significantly more inaccurate accommodative responses to a Badal lens viewing when compared to free space. They suggested that the use of the Badal lens itself did not explain these differences and it was rather a combination of factors associated with closed-view Badal systems. They also suggested that the volumetric stimulation (i.e., interposition of objects in depth) and the size of the field of view could be important factors in controlling and providing accurate accommodative responses.

In most studies accommodation is stimulated with fixation targets smaller than 2º field, on a 2-dimensional uniform background.[1–13] The overall field of view available to the subject is not usually reported, even when using open-field autorefractors that allow for larger field of view (30º or larger horizontally) than the fixation target size. This means that the peripheral scene around the fixation target is not specified nor controlled, which can lead to one of three different conditions: (1) the overall field of view may be restricted to the size of the fixation target reported in the study; (2) the overall field of view may be much larger than the fixation target with a uniform background in the same 2-dimensional plane than the fixation target; or (3) the overall field of view may be much larger than the fixation target used in the study but

the peripheral scene has spatial information at multiple focal planes, being this latter condition the one closest to a naturalistic environment.

The accommodative response may be affected by all the previously mentioned experimental conditions, but also by the observer's refractive error. A large number of studies have attempted to disentangle the possible effect of refractive status in accommodative response (see Schmid and Strang[18] for a recent review). Some studies concluded that myopes accommodate significantly different than emmetropes[1–4,7,9,13,15] while others did not find a clear association between accommodation and refractive error.[6,8,10–12,14,19] Whether myopes accommodate more accurately than emmetropes or vice versa differed greatly among studies, especially when the myopic group was sub-classified as stable myopes or progressing myopes,[3,4,10–12] or more often, as early-onset myopes (EOM) or late-onset myopes (LOM).[1,3,6,8,9,13,14,19] Interestingly, the size of the fixation target was different in each of these studies, it ranged from 1' to 15º field. Also, most of these studies used only real targets in free space[1,4,6–9,19] or optical means[11–14], but not both.

A better understanding of the role of the experimental conditions on the accommodative response would help clarify the causes of inaccurate accommodative responses when accommodation is stimulated optically. By extension this may lead to improved lens-based methods to stimulate accommodation. Moreover, a study that includes an analysis of different refractive error groups and experimental conditions may help understand the causes of discrepancies among previous studies. The purpose of this study was to analyze the effect of field of view, stimulation method (either a real target in free space viewing or a target presented through a Badal lens), depth of the stimulus (either a flat, 2D, or a volumetric, 3D, stimulus), and their interactions, on the accommodative response in observers from different refractive error groups.

METHODS

Subjects

The study, approved by the Ethics Committee of Hospital Mutua de Terrassa (Terrassa, Spain), followed the tenets of the Declaration of Helsinki and all subjects gave informed consent. Criteria for inclusion were: (1) best-corrected visual acuity of 0.10 logMAR (20/25 Snellen equivalent) or better in each eye, (2) between 13 and 28 years of age, to ensure good ability to accommodate, (3) spherical equivalent error measured with subjective refraction between -6.50 and +0.75 D, (4) amplitude of accommodation above the minimum given by Hofstetter's formula for Minimum Accommodation[20] (Amplitude = 15 − 0.25*Age), (5) no strabismus or amblyopia, and (6) no history of any ocular disease, surgery and/or pharmacological treatment that may have affected vision at the time of the study. Subjects with myopia were contact lens wearers and used their own disposable soft contact lenses for the study. The contact lenses prescription were within ±0.25 D of the subject's best correction in each meridian, determined by subjective refraction as explained below.

Subjects were divided into three refractive groups according to the classification suggested by McBrien and Millodot:[1] early-onset myopia group (self-reporting as becoming myopic before 15 years old), late-onset myopia group (self-reporting as becoming myopic at or after 15 years old) and emmetropia group. Emmetropia was defined as subjective refraction spherical equivalent between -0.25 and +0.75 D in each eye. Myopia was defined as subjective refraction spherical equivalent less than -0.25 D.

Instrumentation and setup

A binocular open field autorefractor, PowerRef II (Plusoptix Inc., USA), was used to measure accommodation responses. This autorefractor is based on the principle of dynamic infrared retinoscopy and it measures monocular spherical equivalent, pupil size and gaze position at a sampling frequency of 25 Hz.[21,22] Alignment between the PowerRef and the subject eye

was achieved through a 50-mm squared IR hot mirror placed 2.50 cm from the subject's pupil plane (figure 2).[23] Accommodation responses were measured for target distances, or equivalent positions in a Badal system, of 6 m, 0.4 m and 0.2 m, corresponding to accommodative stimulus of 0.17 D, 2.50 D and 5.00 D, respectively. These stimuli represent typical every day accommodation demands within 2/3 of the subjects' amplitude of accommodation.

Each subject observed a fixation target (Maltese cross) under 60 different conditions. These conditions were the result of permuting the following factors: (1) stimulation method (two configurations: free space or Badal lens viewing), (2) stimulus depth (two configurations: flat or volumetric stimulus), (3) field of view (five configurations, 2.5º, 4º, 8º, 10º and 30º) and level of accommodation stimulation (three configurations, 0.17 D, 2.50 D and 5.00 D).

The volumetric stimulus configurations were achieved by manipulation of three independent sections of the stimulus: left periphery, fixation target and right periphery (figure 1 D). The fixation target section comprised only the black Maltese cross, which subtended, in all configurations, 2º field. The positions of the fixation cross were related to the peripheral sections to determine the various accommodation stimulation levels (0.17 D, 2.50 D or 5.00 D). Both the right and the left periphery sections were composed of randomized phase spectra images of the black Maltese cross in the Fourier domain (figure 1 B, C, E, F). The peripheral stimulus was therefore an abstract image with the same spatial frequency content than the fixation target.[24]

When the three sections of the stimulus were in the same focal plane, a flat, 2-dimensional, stimulus was presented (figure 1 A). The volumetric, 3-dimensional, stimuli were achieved by moving at least one peripheral section to a different focal plane than that of the central fixation target. Notice that for all volumetric stimuli, the dioptric distance between the defocused peripheral plane and the fixation target was always 2.50 D. Luminance of the

stimulus was constant (3.7 cd/m^2 for the fixation black Maltese cross, 56.2 cd/m^2 for the central white area and 31.9 cd/m^2 for the grey area) for all configurations.

The field of view sizes chosen for this experiment (2.5º, 4º, 8º, 10º and 30º) aimed to stimulate differentiated regions of the retina (fovea, parafovea, perifovea and far periphery). A scaled version of the target for two field of view sizes in both flat and volumetric stimuli can be seen in figure 1 B,C,E,F. The field of view size was controlled by circular apertures positioned between the hot mirror and the Badal lens.

Examination Protocol

A monocular subjective refraction with endpoint criteria of maximum plus power that provides best visual acuity was performed to determine best optical correction. The dominant eye was chosen for the measurements and it was obtained with the distance hole-in-the-card test.[25] Monocular amplitude of accommodation was evaluated by averaging the values of two push-up and two push-down trials, to compensate for the bias of push-up to overestimate and push down to underestimate accommodation amplitude.[26]

Accommodative responses were recorded in the dominant eye (the contralateral eye was occluded with an eye patch) for a period of at least 5 seconds for each of the previously described 60 configurations randomly presented. All conditions were measured in one session that took approximately 45 minutes, including breaks. Subjects were allowed to take breaks as needed, although there was no systematic method to provide rests during the measurements. Randomization of configurations was rigorously applied to minimize potential learning or fatigue biases. During the accommodation measurements subjects were inside a booth with a chin rest and a viewing aperture (that did not limit the field of view for any of the configurations) allowed them to see outside. The targets were placed outside the booth. The viewing aperture was closed in between trials so that subjects were not aware of the exact changes made from one configuration to another.

Statistical analysis

The main analysis consisted on a mixed Analysis of Variance (with 3 within-subject factors and 1 between-subject factor) that was conducted for the accommodative response of 2.50 D and 5.00 D. The statistical analysis chosen allowed us, without losing statistical power, to investigate the interactions among factors and at the same time to include fewer participants than other experimental designs (e.g., direct pairwise comparisons). The accommodative response for the 2.50 D and 5.00 D stimuli were determined by subtracting the PowerRef measures for these stimuli from the measures for the 0.17 D stimulus.

The refractive group category (emmetropes, early onset and late onset myopes) was used as a between-subjects' factor. The three within-subject factors were: stimulation method (with two configurations, free space or Badal lens viewing), stimulus depth (with two configurations: flat or volumetric) and field of view (with five configurations: 2.5º, 4º, 8º, 10º or 30º). Where significance was obtained, a Bonferroni post-hoc test was made. Significance was set at $p < 0.05$.

A secondary analysis was used to evaluate whether changes in pupil diameter, fluctuations of accommodation and fluctuations of gaze position played a role in the main analysis (for 5.00 D stimuli). The same statistical methodology described above was used for this purpose, but using as dependent variables the pupil diameter, the within-subject standard deviation of refraction and the within-subject standard deviation of the horizontal gaze position.

Statistical power was assessed with the free open source G*Power 3.0.10.[26] Data from a similar previous study[17] was used to compute the required sample size for a statistical power of 0.8. Considering a significance of 0.05 and an Analysis of Variance model with 20 repetitions and 3 groups the required sample size is 6 for both the accommodative response at 2.50 D and at 5.00 D.

RESULTS

A total of 26 subjects were included in the analysis (n=9 emmetropes, n=9 early onset myopes, n=8 late onset myopes). The mean age ± standard deviation (24 ± 3 years) were not significantly different between the three refractive groups (one-way Analysis of Variance F=3.26, p=0.06). Although the difference approached significance because one subject within the emmetropic group was 13 years of age; most of the subjects were between 22 and 26 years of age. The statistical analysis was performed with and without this subject and results did not significantly change. In order to keep the statistical power as high as possible the 13 year old subject was included in the final analysis described below. The descriptive statistics for age in each group are shown in table 1.

Primary analysis: accommodative response for 2.50 D and 5.00 D stimuli

Figure 2 shows the main effects of each variable for the 2.50 D and 5.00 D accommodative stimuli. Mixed Analysis of Variance for the accommodative stimulus of 2.50 D resulted in a significant main effect of: (1) refractive group (F=6.77, p<0.01), with smaller accommodative lags for early onset myopes compared to late onset myopes and emmetropes (figure 2 A); and (2) field of view (F=1.26, p=0.04), with greater lags for a field of 2.5º (figure 2 D). There were not significant differences for stimulus depth (F=0.02, p=0.90, figure 2 C) or stimulation method (F=0.26, p=0.62, figure 2 B) when considered in isolation.

A significant interaction between field of view and stimulus depth (*Field of view*Depth*, F=2.73, p=0.03, figure 3) was found for the 2.50 D accommodative stimuli. Figure 3 shows mean accommodative responses for the 2.50 D stimulus for each field of view and for both flat and volumetric stimuli. To determine the nature of this interaction, the estimated marginal means (pairwise comparisons adjusted with Bonferroni correction) were computed and the statistically significant comparisons are shown in table 2. Accommodative responses

followed a similar trend across the different field of view sizes used, although for the 8 and 10^{0} fields the accommodative responses appear significantly more accurate than for the 2.5^{0} field in both the volumetric and flat stimuli.

Analogously, there was an interaction among stimulation method, field of view and refractive group (*Method***Field of view*RefractiveError*, F=2.42, p=0.02, figure 4) for the 2.5 D accommodative stimuli. Figure 4 shows mean accommodative responses for each field of view separated by stimulation method and refractive error group. As described above, we computed pairwise comparisons adjusted with Bonferroni correction to determine the nature of this interaction. The statistically significant comparisons are shown in table 3. Early onset myopes showed again more accurate accommodative responses compared to emmetropes and late onset myopes independently of the size of the field of view and the stimulation method used. The accommodation responses appear again to be more accurate for the 8 and 10^{0} fields of view than a 2.5^{0} field (particularly for free space viewing and early-onset myopes).

Similarly to the analyses reported for the 2.50 D stimulus, mixed Analysis of Variance for the accommodative stimulus of 5.00 D resulted in a significant main effect of: (1) refractive group (F=13.88, p<0.01, figure 2 A), with smaller accommodative lags for early onset myopes compared to late onset myopes and emmetropes (figure 2 A); (2) and stimulation method (F=5.16, p=0.03, figure 2 B), with significantly smaller lags for free space viewing. There were not significant differences for stimulus depth (F=2.68, p=0.12, figure 2 C) or field of view (F=2.13, p=0.12, figure 2 D) when considered in isolation.

For the 5.00 D stimuli, there was only a significant interaction of stimulation method, stimulus depth and refractive group (*Method*Depth*RefractiveError*, F=4.08, p=0.03, figure 5). Figure 5 shows mean accommodative responses for each stimulation method, stimulus depth and refractive group for accommodative stimulus of 5.00 D. The statistically significant comparisons are shown in table 4. The group of early onset myopes showed more accurate

accommodative responses than late onset myopes and emmetropes, independently of the stimulation method and depth of the stimulus. The accommodative response for flat stimuli was significantly larger in the early onset myopes group when using the Badal lens viewing method only. There were no significantly differences for stimulation methods across all conditions.

Secondary analysis: pupil diameter and fluctuations of accommodation and gaze position

There was no significant effect and no interactions among the secondary factors: fluctuations of accommodation or gaze position. Pupil diameter was significantly associated only with the stimulation method (F=13.25, p<0.01), stimulus depth (F=5.16, p=0.03) and field of view (F=31.81, p<0.01) for all subjects. There was no association of pupil size with refractive error (F=3.36, p=0.06). Pupils were on average 0.30 mm (standard error=±0.08) larger for free space targets than Badal lens viewing; 0.08 mm (standard error=±0.04) larger for flat than volumetric stimuli; and a maximum pupil difference of 0.86 mm (standard error=±0.08) for a field of 2.5º when compared to 30º (being at 30º larger). Interactions among these factors were not statistically significant. The effect of pupil differences in the main analysis' results found in our study can be considered insignificant.[28–31]

DISCUSSION

This study investigated accommodative response accuracy as a function of the stimulation method used, as well as the depth and field of view of the stimulus, and the interactions of these three factors for subjects in different refractive error groups.

Effect of refractive error

In this study, accommodative response was significantly affected by refractive error group. Late onset myopes showed larger lags of accommodation at near than emmetropes and early onset myopes. Although significant interactions were found between refractive error and stimulus depth, field of view and stimulation method used, when controlling for stimulus depth, field of view and stimulation method, accommodative response differences among refractive error groups were still significant. However, from our results we cannot provide a definitive explanation for these differences among refractive error groups and a longitudinal study would be necessary to establish the mechanism. Our study aimed to determine how the experimental conditions may affect (or interact with) the accommodative response.[18] It is likely that the rate of myopia progression[3,11] (which was unknown in this study) might have biased the differences among refractive error groups. In addition, given that late onset myopes were in our study an average of 3.00 D less myopic than early onset myopes and that subjects with low myopia (less than |1.00| D) often use correction only for certain activities (e.g., driving), we speculate that the relationship between the magnitude of the refractive error and whether subjects wore correction during all day or just during some specific activities might have also been a confounding factor in our results.

Effect of field of view

When a higher accommodative stimulus was used (5.00 D), the effect of the field of view size was relatively small and not statistically significant, in agreement with the results of Yao et al,[35] who did not find significant differences in the accommodative response gradients (from 0 to 5.0 D stimuli, 1-D step) obtained for three different visual fields (2º, 8º and 44º) and using a flat, black Maltese cross.

For an accommodative stimulus of 2.50 D, representative of most near vision tasks, the accuracy of accommodative responses appeared to improve as the target's field of view increased from 2.5º to 10º, but no differences were found when the field of view increased to 30º. These results lead to an interesting question: Is there an optimum retinal image size for

accommodation stimulation? Physiologically, the macula is the zone richest in cone density with a sharp peak at the foveola and rapid decline up to about 10° to 15° eccentricity.[36] It is not known from our results how accommodative responses behave between this area of 10° to 30° eccentricity, but we can suggest that under photopic conditions the accommodation system appears to only use information from the visual field comprised within the perifovea.

This finding may have important implications in the development of myopia progression treatments such as novel multifocal contact lenses or orthokeratology in which there is an optical correction in the retinal periphery different to that in the foveola. The extent of the annular peripheral corrections may be optimized in these methods.

Effect of stimulus depth

When a subject is asked to look at a stimulus that comprises a range of spatial focal planes in the periphery (i.e., a volumetric stimulus), the accommodation system may respond two different ways. On one hand, peripheral blur provided by the out-of-focus plane may be used to better estimate the focal position of the fixation target.[32] On the other hand, the out-of-focus information in the retinal periphery may provide a conflicting stimulus and therefore bring the visual system towards its resting state of accommodation.[33]

There was no effect of the type of stimulus depth (flat or volumetric display) in the overall accommodative responses for 2.50 D or 5.00 D stimuli in our study. However, we did find that for 2.50 D stimuli, for a field of view of 4° and when using Badal lens viewing, volumetric stimuli resulted in larger lags than flat stimuli. Also, for 5.00 D stimuli, early onset myopes showed larger lags when using volumetric stimuli and Badal lens viewing. These specific conditions suggest that the extent of the effect of a volumetric stimulus in accommodative responses is yet to be determined. It is possible that decreasing the distance between the viewing planes, using more focal planes, or using additional peripheral depth cues besides blur may help to better disentangle the influence of volumetric stimuli in accommodation responses. Our results do show that flat and volumetric stimuli are equivalent if the fixation

target is rich enough to stimulate accommodation, as the Maltese cross used in this study. If there was an effect of depth in the accommodative response, a defocused plane in the periphery (with blur-only cues) could behave as a (weak) conflicting stimulus that brings the accommodative system towards less accurate responses. This is consistent with Hartwig et al.[34] results as they showed that retinal periphery is sensitive to defocus.

Effect of stimulation method

When an accommodative stimulus of 5.00 D was presented, larger accommodative lags were found for the overall group when using Badal lens viewing compared to free space stimulation conditions. However, no differences were found between the two methods when a 2.50 D stimulus was used. This result is in agreement with some previous studies in myopia that found larger accommodative lags when increasing the accommodative demand[2,3,13] and larger lags when stimulating accommodation by optical means (negative lenses) than when using free space conditions.[2,3,17]

The type of method used to stimulate accommodation showed a statistically significant interaction with the subject's refractive error group and size of the field of view for accommodation stimulation of 2.50 D and with the subject's refractive error group and depth of the stimulus for accommodation stimulation of 5.00 D. Interestingly, when controlling for refractive group, size of the field of view and depth of the stimulus, there were not statistically significant differences between the Badal lens viewing and free space viewing methods for either accommodation demand used. These results agree with Aldaba et al.[17] and may explain why previous studies have found significant differences between optically-induced and free space viewing accommodation. Aldaba et al. concluded that the differences between Badal lens viewing and free space could potentially (they did not measure in all conditions with a Badal lens) depend on the size of the field of view, the proximity of the instrument's cover, the angular size of the stimulus and the peripheral interposition of objects in depth. If one or more of these factors (field of view, depth or

refractive error group) were not controlled for in previous studies, differences in accommodative response between Badal lens and free space viewing could be explained if, for instance, myopes were more sensitive to flat stimuli and smaller fields of view than emmetropes.

In summary, we show that previously reported differences in accommodative response when using lens-based methods compared to free space viewing may be explained by the effect of other factors such as the field of view or the depth of the stimulus, rather than the method to stimulate accommodation. The most accurate accommodative responses were obtained for fields between 8° and 10°, which suggests that there may be an optimum peripheral retinal image size for accommodation stimulation. The only factor that in isolation significantly affects the accuracy of the accommodative responses is the type of refractive error. According to these findings, the stimulation method, the depth of the stimulus and field of view should be controlled factors when measuring the lag of accommodation. In addition, it would be advisable in further studies of the lag of accommodation to include the refractive error as a covariate in all measurements to minimize the variability across subjects, which may mask some important findings.

ACKNOWLEDGEMENTS

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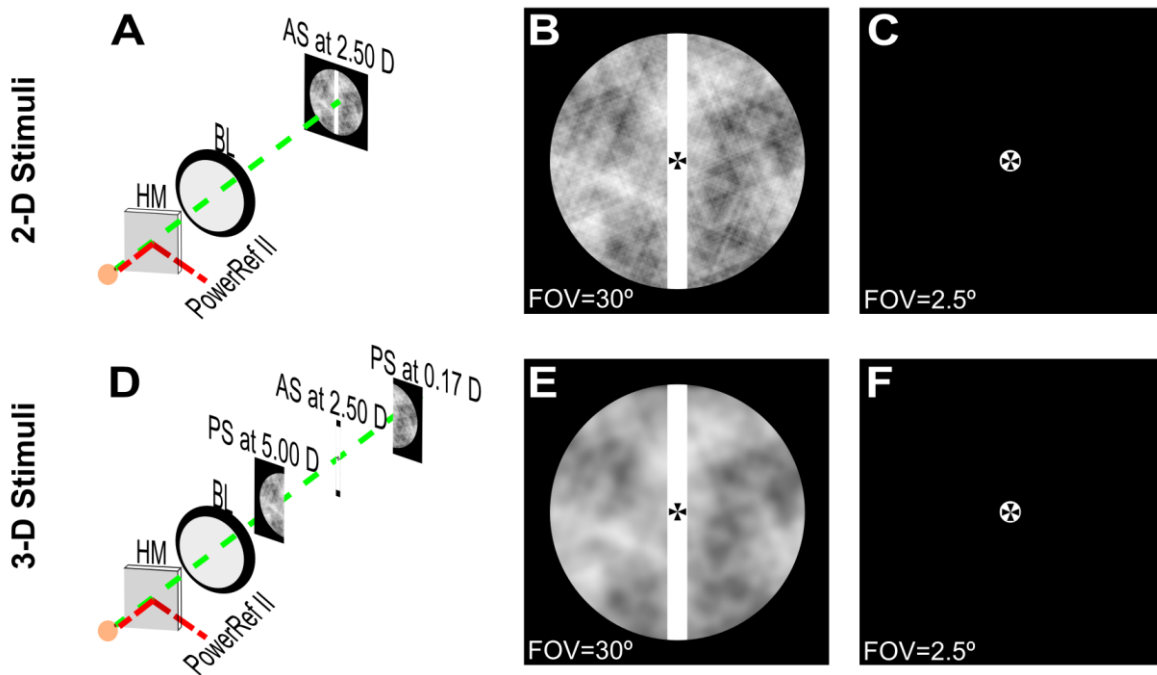
FIGURE LEGENDS

Figure 1. A: schematic representation of the setup for the flat, 2-dimensional, Badal stimulation for the accommodative stimulus of 2.50 diopters and FOV of 30º. Panels B and C: subject's point of view for flat, 2-dimensional, stimuli for a FOV of 30º and 2.5º respectively. Similarly, panels D, E, F represent the same conditions but for a volumetric, 3-dimensional, Badal stimulation. FOV: Field of view. BL: Badal lens. HM: Hot mirror. PS: Peripheral stimulus. Note that the size of the diaphragm is scaled proportionally to the size of the fixation target (black Maltese cross) and that the blur shown in the peripheral stimulus of panel D is an approximation.
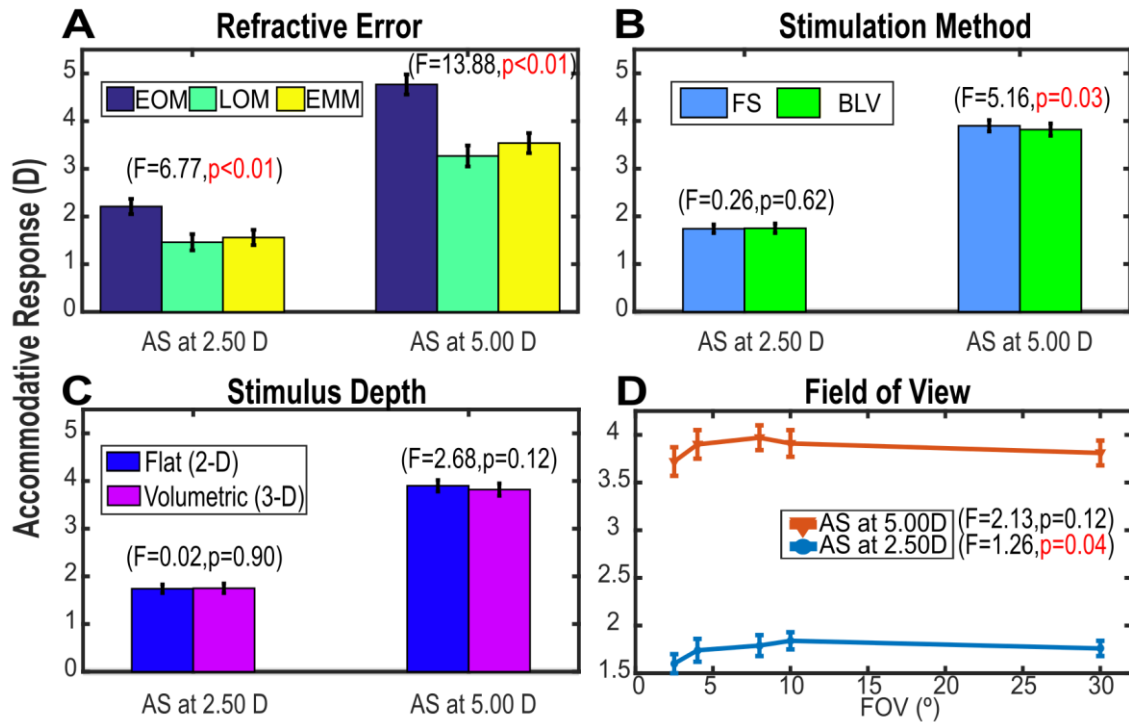
Figure 2. Mean accommodation response effect of each factor for the 2.50 D and 5.00 D accommodative stimuli. Panel A: main effects of refractive error (independently of the stimulation method used, field of view or depth of the stimulus). Panel B: main effects according to the stimulation method used (averaging all subjects, independently of the refractive error group, field of view or depth of the stimulus). Analogously, panel C and D: main effects of stimulus depth and field of view independently of the other of variables. Error bars correspond to the standard error of the mean. AS: Accommodative stimulus. EOM: early onset myopes. LOM: late onset myopes. EMM: emmetropes. FS: free space. BLV: Badal lens viewing. FOV: field of view.
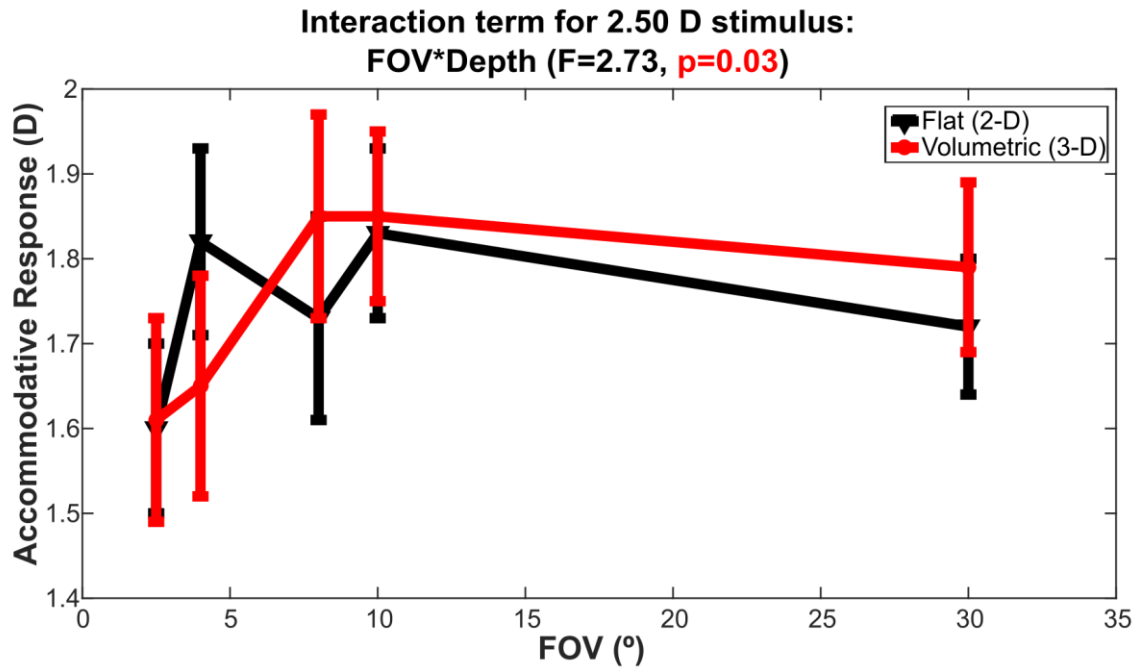
Figure 3. Group data accommodative response for the 2.50 D stimulus when observed with different fields of view (FOV) sizes. Black data points represent accommodation responses to 2-D flat stimuli and red data points represent 3-D volumetric stimulus (depth). Error bars correspond to the standard error of the mean.
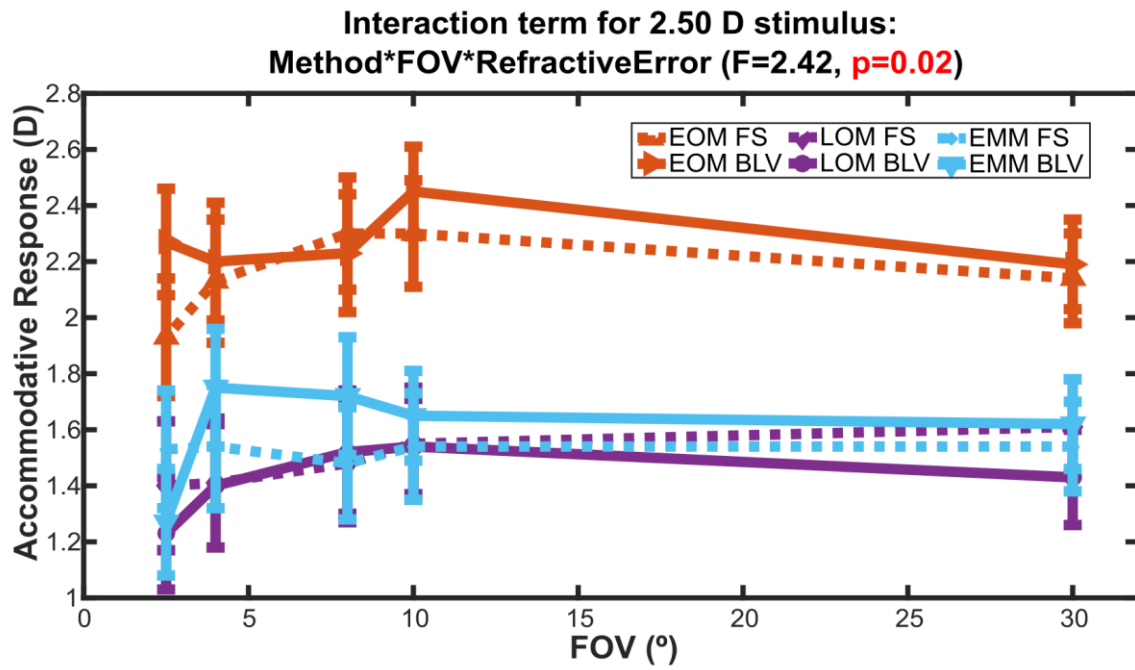
Figure 4. Group data accommodative response for the 2.50 D stimulus when observed with different fields of view (FOV) sizes. Orange lines represent data for the early onset myopes group (EOM). Purple lines represent data for the late onset myopes group (LOM). Blue lines represent data for emmetropes (EMM). Solid lines represent Badal lens viewing (BLV) and dotted lines represent free space (FS) viewing. Error bars represent the standard error of the mean.
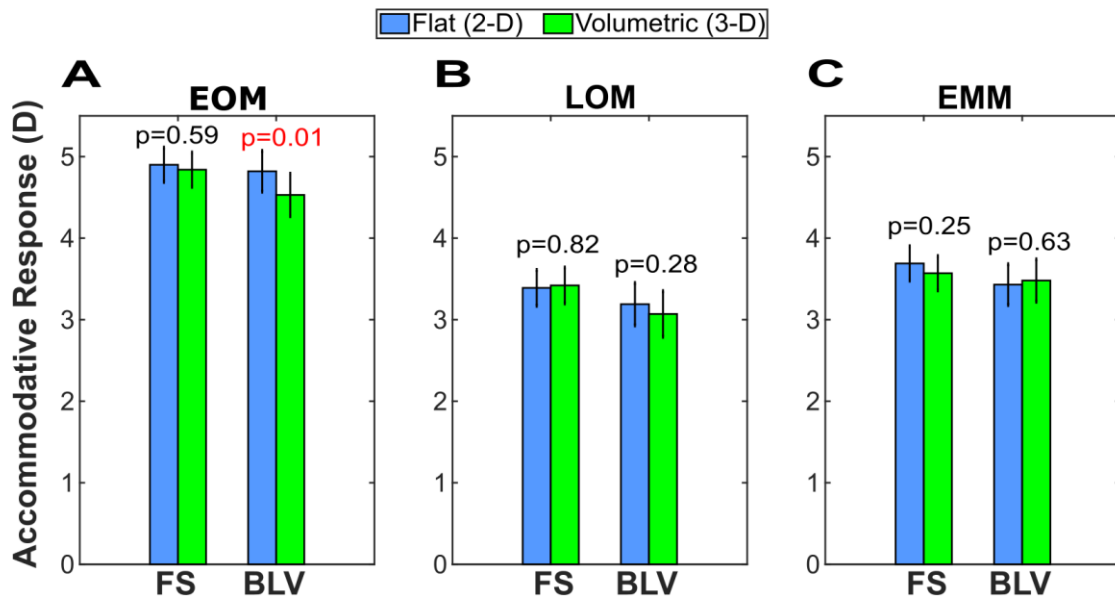
Figure 5. Group data accommodative response for the 5.00 D stimulus when observed with different Stimulation Methods (free space: FS, or Badal lens viewing: BLV) for both flat (2-D) and volumetric (3-D) stimulus (depth). Error bars correspond to the standard error of the mean. Panel A: shows data for early onset myopes (EOM), panel B for late onset myopes (LOM) and panel C for emmetropes (EMM).

1 TABLES

Table 1. Descriptive statistics of each refractive error group. SS: Sample Size. MO: Myopia Onset. SE: Spherical Equivalent in diopters. SD: Standard Deviation. Min: minimum value. Max: Maximum value.

Refractive Error	SS (n)	Mean Age ± SD [min;max]	Mean Age MO ± SD [min;max]	SE ± SD (D) [min;max]
Early-Onset Myopes (EOM)	9	24.4 ± 2.7 [21;28]	8.8 ± 2.9 [4;12]	-4.07 ± 1.71 [-6.5;-0.75]
Late-Onset Myopes (LOM)	8	26.1 ± 2.1 [21;28]	20.7 ± 3.1 [15;24]	-1.01 ± 0.74 [-2.5;-0.50]
Emmetropes (EMM)	9	22.1 ± 4.2 [13;27]	--	0.05 ± 0.19 [-0.25; 0.25]

Table 2. Simple main effects of stimulus depth and FOV (interaction *FOV*Depth*) for 2.50 D stimulus. Paired t
tests (with Bonferroni correction) are applied to all pairwise comparisons. SEM: Standard error of the mean. FOV:
Field of view.

Factor 1, Level	Factor 2, Pairwise Comparison	Mean difference (±SEM) [D]	p-value
FOV, 4º	Stimulus Depth, Flat - Volumetric	0.18 (±0.07)	0.03
Stimulus Depth, Flat	FOV, 10º-2.5º	0.23 (±0.07)	0.02
Stimulus Depth, Volumetric	FOV, 8º-2.5º	0.24 (±0.06)	0.01

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10 **Table 3**. Simple main effects of stimulation method, FOV and refractive group (interaction
11 *Method**FOV*RefractiveError) for 2.50 D stimulus. Unpaired t tests are applied to pairwise comparisons of
12 refractive error groups and paired t tests for any other pairwise comparisons. In all cases Bonferroni correction is
13 applied. SEM: Standard error of the mean. FS: Free space. BLV: Badal lens viewing. FOV: Field of view. EOM:
14 Early onset myopes. EMM: Emmetropes. LOM: Late onset myopes.

Factor 1, Level	Factor 2, Level	Factor 3, Pairwise Comparison	Mean difference (±SEM) [D]	p-value
Stimulation Method, FS	FOV, 30º	Refractive Error, EOM-EMM	0.60 (±0.23)	0.04
Stimulation Method, FS	FOV, 10º	Refractive Error, EOM-LOM	0.75 (±0.27)	0.03
Stimulation Method, FS	FOV, 10º	Refractive Error, EOM-EMM	0.76 (±0.26)	0.02
Stimulation Method, FS	FOV, 8º	Refractive Error, EOM-LOM	0.81 (±0.29)	0.03
Stimulation Method, FS	FOV, 8º	Refractive Error, EOM-EMM	0.82 (±0.28)	0.02
Stimulation Method, BLV	FOV, 30º	Refractive Error, EOM-LOM	0.76 (±0.23)	0.01
Stimulation Method, BLV	FOV, 10º	Refractive Error, EOM-LOM	0.91 (±0.23)	<0.01
Stimulation Method, BLV	FOV, 10º	Refractive Error, EOM-EMM	0.79 (±0.22)	<0.01
Stimulation Method, BLV	FOV, 4º	Refractive Error, EOM-LOM	0.80 (±0.30)	0.04
Stimulation Method, BLV	FOV, 2.5º	Refractive Error, EOM-LOM	1.04 (±0.27)	<0.01
Stimulation Method, BLV	FOV, 2.5º	Refractive Error, EOM-EMM	1.00 (±0.26)	<0.01
Refractive Error, EOM	Stimulation Method, FS	FOV, 10º-2.5º	0.38 (±0.09)	<0.01
Refractive Error, EOM	Stimulation Method, FS	FOV, 8º-2.5º	0.37 (±0.09)	<0.01

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19   **Table 4**. Simple main effects of stimulation method, stimulus depth and refractive group (interaction
20   *Method*Depth*RefractiveError*) for 5.00 D stimulus. SEM: Standard error of the mean. Unpaired t tests are
21   applied to pairwise comparisons of refractive error groups and paired t tests for any other pairwise comparisons.
22   In all cases Bonferroni correction is applied. SEM: Standard error of the mean. FS: Free space. BLV: Badal lens
23   viewing. EOM: Early onset myopes. EMM: Emmetropes. LOM: Late onset myopes.

Factor 1, Level	Factor 2, Level	Factor 3, Pairwise Comparison	Mean difference (±SEM) [D]	p-value
Stimulation Method, FS	Stimulus Depth, Flat	Refractive Error, EOM-LOM	1.50 (±0.30)	<0.01
Stimulation Method, FS	Stimulus Depth, Flat	Refractive Error, EOM-EMM	1.20 (±0.29)	<0.01
Stimulation Method, FS	Stimulus Depth, Volumetric	Refractive Error, EOM-LOM	1.42 (±0.30)	<0.01
Stimulation Method, FS	Stimulus Depth, Volumetric	Refractive Error, EOM-EMM	1.27 (±0.30)	<0.01
Stimulation Method, BLV	Stimulus Depth, Flat	Refractive Error, EOM-LOM	1.63 (±0.36)	<0.01
Stimulation Method, BLV	Stimulus Depth, Flat	Refractive Error, EOM-EMM	1.39 (±0.35)	<0.01
Stimulation Method, BLV	Stimulus Depth, Volumetric	Refractive Error, EOM-LOM	1.46 (±0.39)	<0.01
Stimulation Method, BLV	Stimulus Depth, Volumetric	Refractive Error, EOM-EMM	1.04 (±0.37)	0.03
Refractive Error, EOM	Stimulation Method, BLV	Stimulus Depth, Flat-Volumetric	0.30 (±0.11)	0.01

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