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Vergence Driven Accommodation with Simulated Disparity in Myopia and Emmetropia

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Abstract

The formation of focused and corresponding foveal images requires a close synergy between the accommodation and vergence systems. This linkage is usually decoupled in virtual reality systems and may be dysfunctional in people who are at risk of developing myopia. We study how refractive error affects vergence-accommodation interactions in stereoscopic displays. Vergence and accommodative responses were measured in 21 young healthy adults ($n=9$ myopes, 22 to 31 years) while subjects viewed naturalistic stimuli on a 3D display. In Step 1, vergence was driven behind the monitor using a blurred, non-accommodative, uncrossed disparity target. In Step 2, vergence and accommodation were driven back to the monitor plane using naturalistic images that contained structured depth and focus information from size, blur and/or disparity. In Step 1, both refractive groups converged towards the stereoscopic target depth plane, but the vergence-driven accommodative change was smaller in emmetropes than in myopes ($F_{1,19}=5.13$, $p=0.036$). In Step 2, there was little effect of peripheral depth cues on accommodation or vergence in either refractive group. However, vergence responses were significantly slower ($F_{1,19}=4.55$, $p=0.046$) and accommodation variability was higher ($F_{1,19}=12.9$, $p=0.0019$) in myopes. Vergence and accommodation responses are disrupted in virtual reality displays in both refractive groups. Accommodation responses are less stable in myopes, perhaps due to a lower sensitivity to dioptric blur. Such inaccuracies of accommodation may cause long-term blur on the retina, which has been associated with a failure of emmetropization.

Keywords

Accommodation; Vergence; Myopia; Refractive Error; Virtual Reality

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Disclosure

Commercial relationships: Prevention and Treatment of Myopia, Patent Application US20160212404 A1, PCT/US2014/052398 (GM, PJB, FAVD).

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Introduction

The human visual system undergoes development into adulthood (Aslin, 1977; Banks, 1980; Fioravanti et al., 1995; Haynes et al., 1965; Yang and Kapoula, 2003). Disruptions to visual development may lead to, amongst other outcomes, incorrect eye growth and the development of refractive errors. Failure of normal emmetropization (eye growth towards the physiologically correct, or “emmetropic”, eye size and shape) may arise from predisposing genetic susceptibility and many environmental factors (Deng et al., 2010; Dirani et al., 2010; Dirani et al., 2009; Jones et al., 2007; Jung et al., 2012; Rose et al., 2008a; Rose et al., 2008b; Rosner and Belkin, 1987; Saw et al., 2002; Teasdale et al., 1988; Wu et al., 2001); for reviews see (Charman, 2011; French et al., 2013; Goldschmidt and Jacobsen, 2014; Saw, 2003).

Myopia (nearsightedness) is a common refractive error in which the lens fails to focus far objects onto the retina because the retinal surface is too far (i.e. the eye is too large or elongated). The key to understanding the initiation and progression of myopia requires an understanding of two mechanisms: (1) the environmental factors that disrupt the normal visual feedback loop that controls eye growth, and (2) the biological mechanisms that cause a remodeling of the posterior sclera (Summers Rada et al., 2006). We address only the first of these two mechanisms in this study. From animal models, we know that disrupting the visual feedback loop through pattern deprivation causes uncontrolled excessive ocular growth and myopia (Sherman et al., 1977; Troilo and Judge, 1993; Wallman et al., 1978; Wiesel and Raviola, 1977). Biasing visual feedback with lenses leads the infant animal’s eye to become myopic or hyperopic to compensate for the lenses, for a review, see (Wallman and Winawer, 2004). However, in humans, the use of plus lenses or lower power negative lenses to prevent or correct myopia does not control progression of myopia (Morgan et al., 2012; Walline et al., 2011).

There is a second visual mechanism, ocular accommodation, that demonstrates the human eye’s ability to respond to changes in retinal image quality and provides an alternative measure for investigating how we are able to alter focus in response to retinal image changes. Myopic children (Gwiazda et al., 1993) and adults (Abbott et al., 1998; Bullimore et al., 1992; Schmid and Strang, 2015) appear to have a decreased ability to accurately accommodate, e.g., greater lags and variability of accommodative responses compared to emmetropes (Allen et al., 2009; Harb et al., 2006; Langaas et al., 2008; Pandian et al., 2006; Price et al., 2013; Strang et al., 2011). Animal studies also show an association between inaccurate accommodation and myopia (Troilo et al., 2007; Troilo et al., 2009; Wildsoet et al., 1993). Such inaccuracies of accommodation may cause myopia due to retinal blur (Goss, 1991; Gwiazda et al., 2005; Gwiazda et al., 2004; Hampson et al., 2013; McBrient and Millodot, 1986; Millodot, 2015). Indeed, blur and depth sensitivity in the visual periphery may play a role in accommodation and emmetropization (for reviews see (Charman and Radhakrishnan, 2010; Smith III, 2013)). Causality may be reversed however, as decreased sensitivity to retinal blur in myopes may instead be the source of accommodation inaccuracies (Cufflin et al., 2007; Rosenfield and Abraham-Cohen, 1999; Vera-Diaz et al., 2004). Not all studies have found an association between myopia and accommodative

inaccuracies (Berntsen et al., 2011; Mutti et al., 2007; Rosenfield et al., 2002; Seidel et al., 2005; Taylor et al., 2009).

In this study we examine how retinal image quality change in the peripheral visual field may alter accommodation. This approach is a result of animal research in myopia in which it is shown that defocus restricted to half the visual field causes axial elongation for only that half of the retina (Wallman et al., 1987). In addition, animal models show that eyes that had laser induced foveal ablation still become myopic in response to minus lenses (Smith III et al., 2007) and that this myopic response is as great as in animals with intact foveae (Huang et al., 2011). Thus, the near peripheral retina can clearly drive axial elongation and the development of myopia. With this in mind, manufacturers around the world are testing and marketing contact lenses with different refractive powers for the foveae and periphery in an attempt to decrease peripheral defocus and reduce the progression of myopia but with limited success (Berntsen et al., 2013; Gifford and Gifford, 2016; Hasebe et al., 2014). To understand how lenses that affect the peripheral retinal image focus may affect emmetropization, we must first determine how changes in image content affect retinal responses and how those changes affect accommodation. We therefore propose to measure accommodation responses to naturalistic stimuli spanning the retinal periphery.

In normal binocular vision, vergence and accommodation responses are tightly linked (Fincham and Walton, 1957). Vergence eye movements redirect the binocular gaze point to the physical distance of the visual target. Vergence is elicited primarily from a combination of retinal disparity and accommodative demand, while accommodation is driven mainly by retinal defocus blur and vergence demand. Thus, in normal vision, vergence and accommodation are tightly coupled. However, vergence and accommodation may become uncoupled when viewing 3D displays, in which depth, blur and disparity are usually independent (Hoffman et al., 2008; Rushton and Riddell, 1999; Wann et al., 1995). In virtual reality, disparity information can drive vergence away from the surface of a 3D monitor. However, focus cues drive accommodation toward the plane of the monitor, creating a cue conflict. Virtual reality technology is advancing, with recent interest focused on head mounted displays such as the Oculus Rift (Chessa et al., 2016). Given the complex interplay between vergence, depth, and focus cues (Maiello et al., 2014, 2015b), we must understand the influence of simulated depth information on accommodative responses as virtual reality systems become increasingly pervasive, particularly for young users whose visual systems may still be in development. One tantalizing idea is the possibility of employing virtual reality technology to manipulate vergence and accommodation stimuli in order to prevent refractive error development or treat its progression (Maiello et al., 2015a).

In this study we describe the vergence-accommodation link in myopes and emmetropes using a stereoscopic 3D system with simulated depth cues. First, we test whether the vergence-accommodation link (Fincham and Walton, 1957; Hoffman et al., 2008; Rushton and Riddell, 1999; Wann et al., 1995) has the same strength in both refractive groups. We have recently shown that myopes may be less sensitive to blur than emmetropes (Maiello et al., 2017), therefore myopes should rely less on focus cues and more on vergence cues to drive accurate accommodation responses. This finding would predict a stronger vergence-driven accommodation response in myopes. If myopes are less sensitive to blur but do not

adjust the strength of the vergence-accommodation link to compensate for their reduced sensitivity to blur, then this would result in smaller accommodation responses and therefore less accommodative vergence, thereby negatively impacting the vergence response in myopes. Furthermore, if myopes are less sensitive to blur, they may show greater accommodative inter-trial variability and microfluctuations of accommodation (Charman and Heron, 1988; Day et al., 2006).

Secondly, we assess whether the amount and consistency of vergence and accommodation vary with the consistency of focus, disparity and pictorial depth cues in the visual periphery. If blur in the peripheral retina can drive retinal growth (Smith III et al., 2007; Wallman et al., 1987), then it might be possible for the accommodative response to be influenced by depth cues presented to the near peripheral retina. Previous studies suggest that accommodation can also be elicited by near peripheral defocus (Ciuffreda et al., 2007; Lundström et al., 2009; Mathur et al., 2009; Pauné et al., 2016), and myopes may demonstrate less effective peripheral accommodation (Hartwig et al., 2011; Whatham et al., 2009). Studying the accommodation-vergence linkage with simulated depth in myopes and non-myopes is a necessary step to determine whether and how 3D display technology may impact the development of myopia.

Methods

Subjects

A total of 25 young adult subjects (mean $\pm$ sd age: 24 ± 2 years) were recruited for this study. Following a vision screening that comprised ocular health evaluation and ocular history questionnaire, 21 subjects who met the inclusion criteria were enrolled in the study. Criteria for inclusion were: (1) no history of surgery or eye disease, (2) within 18–32 years of age, (3) best corrected visual acuity (BCVA) 20/20 or better in each eye, (4) not using drugs that may affect their vision, (5) no current binocular vision or accommodative dysfunction, (6) contact lens wearer if myopic refractive correction was needed, (7) refractive error correction between +1.00DS of hyperopia and –14.00DS of myopia with 1.50DC of astigmatism and 1.00D anisometropia. One emmetropic subject who met inclusion criteria was nonetheless excluded from this study because the photorefractor we employed (see Apparatus subsection below) failed to produce measurements of the subject's accommodative status.

Subjects' refractive error correction (spherical equivalent, SE) was determined by non-cycloplegic binocular subjective refraction with binocular balancing and evaluation of the observer's best visual acuity. Objective refraction was measured with a Grand Seiko WR=5100K autorefractor and axial length measurements were performed with a Zeiss IOL Master optical biometer. These measurements are reported in the Supplementary Material. The refractive error correction of the observers included in the study ranged from +0.62D to –7.62D (mean $\pm$ sd SE: -1.50 ± 2.30 D). Of these, 9 subjects were myopes (mean $\pm$ sd SE: -3.60 ± 2.00 D) and 12 were emmetropes (mean $\pm$ sd SE: $+0.10 \pm 0.40$ D). Subjects were classified into the two refractive groups as follows: emmetropes were defined as having a SE in each eye between +1.00 and –1.00D; and myopes were those subjects with SE in each eye between –1.00 and –14.00D.

This research followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Boards of Northeastern University and New England College of Optometry. Informed consent was obtained from all subjects after explanation of the nature and possible consequences of the study. All subjects were naïve as to the purpose of the experiment and received monetary compensation for their time.

Apparatus

The stimuli and experimental codes were programmed using the Psychophysics Toolbox Version 3 (Brainard, 1997; Pelli, 1997) in Matlab. Stimuli were presented on a gamma-corrected Acer GD235HZ 24" monitor with a resolution of 1920×1080 pixels (display dot pitch 0.2715 mm) running at 120 Hz from an NVidia Quadro FX580 graphics processing unit.

Subjects wore active stereoscopic shutter-glasses (NVIDIA 3D Vision) throughout the experiment. Figure 1 schematizes the geometry of the experimental setup. Observers' eyes were at 40 cm vergence (2.50 D) from the monitor with the head stabilized in a chin and forehead rest. At this viewing distance, the monitor subtended 66×40 degrees of visual angle.

Ocular vergence and accommodative status were recorded at 25 Hz employing a PowerRefractor (<https://plusoptix.com>), an infrared photorefractor (Choi et al., 2000; Schaeffel et al., 1993) positioned 1 meter from the observer. The PowerRefractor delivers infrared light into a subject's pupils and simultaneously records the reflection of the infrared light returned through the pupil from the back of the eye. From the pupil light distribution profile, the PowerRefractor determines instantaneous estimates of the refractive state of the eye (Roorda et al., 1997; Schaeffel et al., 1993), an indirect measure of accommodation. Vergence is computed as the difference in horizontal gaze position between the two eyes, with gaze position for each eye estimated using the relative displacement of the first Purkinje image from the center of the image of the pupil (Brodie, 1987; Riddell et al., 1994). Accommodation and vergence are measured with the same photorefractor images, so the two parameters were recorded synchronously with the same stimuli.

It is also worth noting that the PowerRefractor shows large inter-subject variability when calibrated to obtain absolute values of both vergence (Hasebe et al., 1995) and refractive state (Bharadwaj et al., 2013). Individual subject calibration or ethnicity specific calibration would provide more accurate measurements (Sravani et al., 2015). In this study we chose not to perform individual calibration of the PowerRefractor for each subject (Schaeffel et al., 1993) because we analyzed changes in accommodation and vergence responses, not absolute values. In addition, we did not expect there to be a relationship between individual calibration factors and the refractive error of the observers. To rule out the existence of such a relationship we employed data from Sravani et al. (2015), which indeed showed no significant correlation ($r^2=0.001$, $p=0.83$) between individual calibration factor and the refractive error of the eye. Furthermore, the accuracy of image-based vergence measurements is known to be dependent on pupil size (Jaschinski, 2016), and Schaeffel et al. (1993) directly showed that the calibration of the PowerRefractor is dependent primarily on pupil size. Pupil size is not correlated with myopia (Charman and Radhakrishnan, 2009;

Jones, 1990), and in our data pupil size does not correlate with the amplitude ($r^2=0.036$, $p=0.41$) nor with the variability of the accommodation response ($r^2=0.11$, $p=0.15$). Thus, the lack of individual calibration may have a slight effect on the individual absolute accommodation results, but all previous data suggests this effect is small and unlikely to affect our findings.

Because the PowerRefractor must have a straight ahead view of the observer's eyes, a dichroic mirror was positioned between the observers' eyes and the stimulus display, which allowed light from the monitor to be transmitted to the observers' eyes. At the same time, the dichroic mirror reflected infrared light from the PowerRefractor to the observers' eyes, therefore allowing for continuous recording of the observers' vergence and refractive state. The PowerRefractor was run from a dedicated pc. PowerRefractor measurements were synchronized with the stimulus presentation by providing an event trigger to the PowerRefractor pc, which stored the time of the beginning of the experiment in the PowerRefractor data file.

Stimuli

Step 1: Vergence driven Accommodation to Simulated Disparity—Stimuli to drive vergence without focus cues for accommodation were two green fixation dots (0.5 degree diameter each) rendered with -3.5 degrees of uncrossed disparity, as illustrated in Figure 2a. Each fixation dot was Gaussian filtered with a standard deviation of 5 pixels (12 arcmin) so as to contain no mid or high spatial frequency edge information and thus did not provide a reliable stimulus for accommodation at the surface of the monitor (Charman and Tucker, 1977). Given that the spatial structure of the Gaussian fixation dot was constant, any change in accommodation when a subject successfully fused the stimulus will be driven primarily by vergence (Okada et al., 2006). With a typical 63 mm interpupillary distance (Dodgson, 2004; Gordon et al., 1989; Smith and Atchison, 1997), the target was presented at a vergence/accommodation distance of 67 cm (1.50D).

Step 2: Vergence and Accommodation Responses with Peripheral Depth Cues—Vergence and accommodation to the surface of the display were driven by 40×40 degree patches of “dead leaves” stimuli (Bordenave et al., 2006; Lee et al., 2001). Example stimuli are shown in Figures 2b–f. At the center of the stimulus, the same 0.5 degree green fixation dot as used in Step 1 was shown with zero disparity in order to drive vergence to the surface of the display. The dead leaves stimuli were constructed from a set of 3000 ellipses each assigned a center position, orientation, aspect ratio, and luminance drawn from pseudo-random uniform distributions. The mean luminance of the ellipses was equal to the display background (25 cd/m^2 through the shutter glasses) and the rms contrast was 0.5.

The size, blur and disparity of each ellipse was independently controlled to provide one or more simulated depth cues to simulate a surface slanted in depth with the superior area of the surface tilted away from the observer and the inferior area tilted towards the observer:

- a. Zero gradient (Fig 2b): mean ellipse size was constant (0.5 – 1.5 degrees), ellipse edges were sharp and disparity was zero. This stimulus appeared as a flat surface on a fronto-parallel plane anterior to the observer.

- b. Size gradient (Fig 2c): ellipse edges were sharp and disparity was zero. Mean ellipse size was constant (0.5 – 1.5 degrees) at the horizontal center of the stimulus. Below and above fixation the average ellipse size increased and decreased linearly to 1.5 and 0.5 degrees respectively. The pictorial depth cue of relative size provided the impression of viewing a flat picture of a surface slanted in depth.
- c. Blur gradient (Fig 2d): mean ellipse size was constant (0.5 – 1.5 degrees) and disparity was zero. Ellipse edge blur increased linearly above and below the fixation height. Individual ellipses were filtered in the frequency domain using a sync filter $\Gamma(\omega)$ defined as:

$$\Gamma(\omega) = \frac{\sin(\frac{\pi\omega}{\lambda})}{\frac{\pi\omega}{\lambda}} \quad (1)$$

Where λ determines the spatial frequency, ω , of the first phase reversal. To obtain a linear increase in blur away from the fixation height, the inverse of λ was linearly increased from 0.4 to 8 deg/cycle. The Sync filter was chosen because it both attenuates high spatial frequencies and introduces phase reversals typical of the modulation transfer function of an optical system with a circular aperture such as the human pupil (Murray and Bex, 2010). Because of the tilt shift effect (Vishwanath and Blaser, 2010), a stimulus with increasing levels of blur above and below fixation should be perceived as a near surface slanted in depth, with the top tilted away from the observer.

- d. Disparity gradient (Figure 2e): mean ellipse size was constant (0.5 – 1.5 degrees), and ellipse edges were sharp. Ellipse disparity increased from –1.4 degrees at the bottom (crossed disparity, ellipses before the screen) to +1.4 degrees at the top (uncrossed disparity, ellipses behind the screen). This disparity gradient provided a vivid impression of a surface slanted in depth, with ellipse elements popping out of the screen below fixation and instead appearing farther than the screen surface above fixation.
- e. Size, Blur and Disparity gradients (Figure 2f): ellipse size, blur and disparity varied together as in conditions b), c) and d).

Note that only conditions a) and e) contained no depth cue conflicts; the mean simulated depth of all depth gradients was centered on the display surface; and the horizontal midpoint of all stimuli was the same in all cases and specified depth on the surface of the display.

Procedure

Subjects who met inclusion criteria were asked to wear stereoscopic shutter-glasses and place their heads into the chinrest in front of the 3D monitor. Subjects underwent an initial training session of 5 trials during which all stimuli and tasks were demonstrated.

On each trial, subjects first completed Step 1, *Vergence driven Accommodation to Simulated Disparity*, then completed Step 2, *Vergence and Accommodation Responses with Peripheral*

Depth Cues. Subjects fused the blurred green fixation dot rendered with -3.5 degrees of uncrossed disparity on a uniformly gray background. When satisfied they were fusing the stimulus, subjects pressed a key on the keyboard in front of them, which initiated Step 1. The uncrossed disparity fixation dot was kept on screen for 0.5 seconds, and then Step 2 began where the disparity of the fixation dot was set to zero and one of the 5 dead leaves stimuli (Figure 2) was presented, at random across trials. The fixation dot and the horizontal center of the dead leaves stimuli drove vergence and accommodation to the surface of the display. Observers were instructed to maintain steady fixation onto the fixation dot at the center of the screen. After 5 seconds, the dead leaves stimulus was replaced once again by the disparity defined fixation dot onto a uniformly gray background, which signaled the end of the trial.

Once the subject had completed the training session, the experimenter verified that the subject understood the task and proceeded to the main test session. The test session was identical to the training session except that the test session consisted of 10 repetitions of each of the 5 peripheral cue conditions in random order, thus each subject completed 50 trials.

Data Analyses

For each subject, raw data were rescaled. We defined mean accommodation and mean vergence as baseline zero at the monitor distance when the subjects were viewing the Zero gradient dead leaves stimulus (Step 2, Zero gradient condition). Thus, all data are relative to the baseline level of accommodation when observers are viewing the flat image on the computer screen, which is like a typical computer use situation (these rescaling factors are provided in the Supplementary Material). Therefore, all results reported in this study are relative to the vergence/accommodative state of each observer when viewing the 2D monitor, and no conclusions may be drawn as to the absolute values of vergence and accommodation.

We further defined negative vergence values to signify vergence to uncrossed disparities (i.e. vergence to simulated depth beyond the surface of the monitor). Negative accommodation values also signify accommodation behind the surface of the monitor (diopters = 1/meters).

Both vergence and accommodation data were separately fit with a piecewise function, composed of a constant and an exponential (Beers and Van Der Heijde, 1994, 1996; Kasthurirangan and Glasser, 2005; Kasthurirangan et al., 2003; Yamada and Ukai, 1997), defined as:

$$D(t) = \begin{cases} d_0, & t < t_0 \\ d_0 + a \left(1 - e^{-(t-t_0)/\tau} \right), & t \geq t_0 \end{cases} \quad (2)$$

Where d_0 was the level of vergence/accommodation during Step 1 of each trial, when observers were fixating the blurred fixation dot with -3.5 degrees of uncrossed disparity on a blank background.

For each subject, we also separately computed the variability of accommodation and vergence during Step 1 as the standard deviation of the data prior to time. $t = 0$. We define time $t = 0$ as the start of Step 2; i.e. the onset of the dead leaves stimuli, during which the disparity of both the fixation and the center of the dead leaves stimuli was zero. The decreasing exponential function characterized the response with a delay t_0 , a response amplitude a , and an exponential half-life τ . An example of a function fitted to data from one condition from a representative observer is plotted in Figure 3. For each subject and each condition, for vergence and accommodation separately, we also computed the steady state response variability, which was defined as the standard deviation of the data from the time point $t_{ss} = t_0 + \tau * \log 20$, at which the exponential had reached 95% steady state.

For each subject, a single function was fit to the accommodation data from the left and right eye.

The refractive status data regarding level (d_0) and variability of vergence and accommodation during Step 1 were analyzed with a one-way between-subjects ANOVA. All data from Step 2, meaning parameters a , t_0 , and τ of the exponential fits as well as refractive status steady state vergence and accommodation variability, were analyzed with 2 (refractive status, between-subjects factor) $\times$ 5 (cue condition, within-subjects factor) mixed design ANOVA.

Results

Figure 4 presents group vergence responses as a function of time for myopes (red) and emmetropes (blue). Negative time points in each panel (dark gray shaded region) correspond to data for Step 1. Time 0 indicates the start of Step 2 (light gray shaded region) for each of the 5 depth gradient conditions (a–e). Red and blue shaded areas represent the 95% confidence intervals of the mean vergence trace, and solid lines show the mean best fitting piecewise function.

Figure 5 similarly presents group accommodation responses as a function of time for myopes (red) and emmetropes. (blue). Negative time points (dark gray shaded region) in each panel correspond to data for Step 1. Time $t=0$ indicates the start of Step 2 (light gray shaded region), for each of the 5 depth gradient conditions (a–e). Blue and red shaded areas are 95% confidence intervals of the mean accommodation trace, and full lines show the average fitted piecewise function.

Step 1: Vergence driven Accommodation to Simulated Disparity

Data from negative time points in Figure 4 show that both emmetropes and myopes verged away from the monitor depth in response to the disparity of the fixation target. Myopes' vergence response was on average -3.4 degrees [-2.7 , -4.2 ; 95% CI] away from the surface of the monitor, in agreement with the required -3.5 degrees of uncrossed disparity provided by the stimulus ($t(8)=0.26$, $p=0.80$). Conversely, emmetropes' vergence response was on average only -2.6 degrees [-1.9 , -3.3 ; 95% CI] away from the surface of the monitor, significantly less than the -3.5 degrees required to null the disparity of the fixation target ($t(11)= 2.76$, $p=0.019$). This might suggest that myopes responded more accurately to the

low spatial frequency disparity of the fixation target than emmetropes. However, vergence responses during Step 1 were not significantly different between the myopic and emmetropic groups ($F_{1,19}=3.0$, $p=0.10$). The variability in vergence responses during Step 1 was also not significantly different between myopes and emmetropes ($F_{1,19}=2.4$, $p=0.14$).

Data from negative time points in Figure 5 indicate that both groups, emmetropes and myopes, accommodated away from the monitor depth in response to the change in the disparity of the fixation target. Accommodation changes were consistent with an increase in depth of the fixation target in the absence of a reliable blur cue, in line with the vergence-accommodation linkage. However, although the fixation target was 1.00D away from the monitor, accommodation change was less than 1.00D in both refractive groups.

Figure 6a shows accommodation responses when the stimulus is away from the surface of the display during Step 1 for myopes (red) and emmetropes (blue). Myopes accommodation responses were on average -0.47D [-0.31, -0.61; 95% CI] away from the display surface, whereas emmetropes accommodated -0.27D [-0.20, -0.37; 95% CI] on average, showing 43% smaller accommodative responses than myopes ($F_{1,19}=5.13$, $p=0.036$). Given that the cue to depth change was disparity-driven vergence, the accommodation response during Step 1 was primarily driven by the vergence response. The larger accommodative responses found in myopes suggest that for a blurred target, the vergence-accommodation link is stronger in myopes than in emmetropes.

Figure 6b shows the variability of accommodation responses during Step 1 in emmetropes and myopes. Mean accommodation variability for was 0.17D [0.15, 0.22; 95% CI] for emmetropes and 0.24D [0.22, 0.26; 95% CI] for myopes. Thus, myopes exhibited a 35% increase in accommodation variability with respect to emmetropes ($F_{1,19}=12.91$, $p=0.0019$).

Step 2: Vergence and Accommodation Responses with Peripheral Depth Cues

There was no significant difference in the amplitude of the vergence response across refractive groups ($F_{1,19}=1.62$, $p=0.22$) or across the various gradient depth cue conditions ($F_{4,76}=1.13$, $p=0.35$). There was also no significant interaction between refractive group and cue condition ($F_{4,76}=0.19$, $p=0.94$). Vergence responses were initiated on average 0.22 seconds [0.18, 0.27; 95% CI] after the onset of the dead leaves stimulus. The vergence response latency did not vary across refractive groups ($F_{1,19}=1.0$, $p=0.33$) or cue condition ($F_{4,76}=0.66$, $p=0.62$), and the interaction between refractive group and cue condition approached but did not reach significance ($F_{4,76}=2.4$, $p=0.057$). Thus, the presence of peripheral depth cues appears to have little or no effect on the onset or endpoint of vergence responses in myopes or emmetropes.

The exponential half-life of the fitted vergence response curves (τ) indicates the speed of the vergence response, with smaller values indicating faster responses. Mean, τ was 0.23 seconds [0.17, 0.31; 95% CI] for emmetropes and 0.41 seconds [0.27, 0.57; 95% CI] for myopes. ANOVA analyses revealed that myopes had significantly slower responses (78% larger τ) than emmetropes ($F_{1,19}=4.55$, $p=0.046$), as shown in Figure 7. ANOVA analyses also revealed no main effect of cue condition on τ ($F_{4,76}=0.48$, $p=0.75$), and no significant interaction between refractive group and cue condition ($F_{4,76}=0.27$, $p=0.90$).

Finally, vergence steady state variability was the same across refractive groups ($F_{1,19}=1.74$, $p=0.20$) and cue condition ($F_{4,76}=0.79$, $p=0.54$), with no significant interaction between refractive group and cue condition ($F_{4,76}=0.95$, $p=0.44$).

Because myopes relaxed accommodation to a greater extent than emmetropes during Step 1, myopes also had to execute larger accommodation responses to changes in target disparity ($F_{1,19}=8.63$, $p=0.0085$). However, there was no overall effect on accommodation response amplitude change of the specific peripheral depth cue condition ($F_{4,76}=0.2$, $p=0.94$), and no significant interaction between refractive group and cue condition ($F_{4,76}=0.80$, $p=0.53$). The accommodation responses were initiated on average 0.37 seconds [0.29–0.43, 95% CI] after the dead leaves stimulus onset. This response latency did not vary across refractive group ($F_{1,19}=0.14$, $p=0.71$) or cue condition ($F_{4,76}=1.29$, $p=0.28$) and no significant interaction was observed ($F_{4,76}=0.82$, $p=0.52$). The exponential half-life parameter of the accommodation response (τ) was on average 0.13 seconds [0.08–0.20, 95% CI]. ANOVA analyses show no main effect of refractive group ($F_{1,19}=0.33$, $p=0.57$) or cue condition ($F_{4,76}=1.07$, $p=0.38$) on τ , and no significant interaction between refractive group and cue condition was found ($F_{4,76}=1.38$, $p=0.25$). Thus, the presence of peripheral depth cues did not affect the accommodative responses of myopes or emmetropes in these conditions.

Figure 8 shows average accommodation responses steady state variability for myopes and emmetropes in each cue condition. ANOVA analyses found a significant main effect of refractive group ($F_{1,19}=6.24$, $p=0.022$), cue condition ($F_{4,76}=5.1$, $p=0.0011$), and a significant interaction between refractive group and cue condition ($F_{4,76}=2.7$, $p=0.037$). We therefore compared myopes to emmetropes for each cue condition using Wilcoxon rank sum tests. Myopes showed significantly higher steady state variability than emmetropes for the no cue condition (53% increase, $Z=2.38$, $p=0.017$), the relative size cue condition (43% increase, $Z=2.24$, $p=0.025$), the blur cue condition (37% increase, $Z=2.38$, $p=0.017$), and the disparity cue condition (48% increase, $Z=2.38$, $p=0.017$). In the condition where all cues were present, the difference in accommodation steady state variability between myopes and emmetropes was not statistically significant (25% increase, $Z=1.81$, $p=0.070$). Note that the presence of one outlier in the myopic group with much higher than average accommodation variability did not affect the pattern nor the statistical significance of the results.

Discussion

When viewing blurred targets presented with binocular disparity on a stereoscopic 3D monitor, myopes and emmetropes executed vergence eye movements of comparable magnitude to the stimuli. However, while the latency of vergence eye movements was not significantly different between refractive groups, the time constant of the vergence response in myopic observers was significantly slower than in emmetropes. Our observations are consistent with Vienne et al. (2014) who found that vergence responses were slower with conflicting disparity and blur cues, as well as with Semmlow and Wetzell (1979) who showed that binocular vergence movements are faster when disparity and blur are both available than when only disparity specifies a change in distance. Thus, slower vergence movements in myopes are consistent with the previous finding that myopes make less use of

retinal defocus information (Cufflin et al., 2007; Rosenfield and Abraham-Cohen, 1999) and extends this observation from the perceptual to the oculomotor system.

We first employed blurred stimuli virtually located behind the monitor to degrade defocus blur cues to image depth and thus any change in accommodation during this first step was primarily driven by a change in vergence. Accommodation responses to the change in vergence were consistent with the change in disparity of the stimuli, providing additional evidence for the well-known coupling between vergence and accommodation (Fincham and Walton, 1957). While vergence eye movements to stimuli containing binocular disparity were generally comparable between emmetropes and myopes, there were significant differences in accommodative responses to these stimuli between the refractive groups. The magnitude of accommodative change in response to vergence change was significantly larger in myopes than in emmetropes. This finding suggests that the vergence-accommodation coupling is stronger in myopes than in emmetropes under the present conditions of degraded defocus information. It is possible that this is associated with evidence that myopes are less sensitive to image defocus than emmetropes (Cufflin et al., 2007; Rosenfield and Abraham-Cohen, 1999) and thus rely less on focus cues and more on vergence cues to drive accurate accommodation responses

We fit our data with a commonly employed exponential function to facilitate comparisons between our results and the existing literature. Indeed, the values of the fitted parameters in our study nicely conform to previous literature describing the characteristics of the accommodative response (Anderson et al., 2010; Beers and Van Der Heijde, 1994, 1996; Kasthurirangan and Glasser, 2005; Kasthurirangan et al., 2003; Yamada and Ukai, 1997). However, it is worth noting that the onset of both vergence and accommodative response is unlikely to be as abrupt as the exponential model imposes. Thus, the latency of the vergence and accommodative responses is likely to be slightly overestimated when employing this exponential model.

Adult myopes have been shown to have more variable accommodation responses with high contrast targets viewed monocularly (Day et al., 2006; Seidel et al., 2003) but not binocularly (Seidel et al., 2005). Adult myopes also show more variable accommodation when reading binocularly (Harb et al., 2006). In agreement with the more naturalistic reading task (Harb et al., 2006), but not with cross targets fixated binocularly (Seidel et al., 2005), we found that adult myopes have less stable accommodation than emmetropes when binocularly viewing high contrast, naturalistic depth defined stimuli. More specifically, when depth cues specified a flat perpendicular surface, and when depth cues were conflicting (some specifying a flat perpendicular surface and some specifying a flat surface tilted in depth), myopes exhibited higher accommodation variability than emmetropes. When a slanted surface in depth was simulated coherently by all cues, myopes and emmetropes exhibited statistically similar levels of accommodation variability, although on average myopes still exhibited more variable accommodation.

Previous work has shown that progressing myopic children underaccommodate to defocus blur cues but not to a target that changes its distance (Abbott et al., 1998; Gwiazda et al., 1993; Jiang, 1997), and that accommodation in myopes returns to the level of emmetropes

once myopia progression has stopped (Gwiazda et al., 1995). The improvement in accommodation may involve an adaptation process within the accommodative system that upregulates the gain of accommodation (Gwiazda et al., 1995; Vera-Diaz et al., 2004). An increase in the gain of the myopic accommodative system is consistent with the increase in the amplitude of accommodation to a blurred target and in the variability of accommodation observed in this study.

Our findings are all consistent with the notion that myopes are less sensitive to defocus cues and lend strength to the hypothesis that greater retinal blur signals may be an important factor in the development of myopia. Specifically, both vergence and accommodation differed across refractive groups when viewing simulated depth content on stereoscopic displays. Myopes executed slower vergence eye movements, exhibited a stronger vergence-accommodation link, and had more variable accommodation overall.

Our findings do not yet answer whether 3D stereoscopic technology influences myopia progression. The fact that the vergence-accommodation link is stronger in myopes suggests that the oculomotor system of myopes will behave differently to that of emmetropes in virtual reality displays. When the visual system is placed in unusual visual environments, it may alter or adapt the vergence-accommodation cross-link (Fisher and Ciuffreda, 1990; Judge and Miles, 1985; Miles et al., 1987; Wann et al., 1995). Our findings suggest that myopes may be less capable of adapting this linkage in simulated environments. Myopes may experience greater levels of visual blur in virtual reality displays because they do not uncouple vergence and accommodation as much as emmetropes. Future work should focus on precisely characterizing the relationship between the degree of myopia and oculomotor performance. Training the plasticity of the oculomotor system may then prove beneficial to promote normal emmetropization.

Investigating differences in the vergence-accommodation link across refractive groups is necessary to understand whether the advance of virtual reality technology might further exacerbate the increasing incidence of myopia, or whether we might turn this technology to our advantage to instead oppose the rise of refractive error development. One potential avenue of investigation in this regard is that inaccuracies of accommodation when viewing flat images (typical of indoor activities such as reading or computer use) may cause long-term blur on the retina, which may impede precise emmetropization. Having rich depth structure presented on virtual reality displays may instead be beneficial to stabilizing accommodation and promote normal ocular growth. Peripheral depth cues as used in our set up appeared however to have little influence on vergence and accommodation responses. Our findings do not support the notion that peripheral cues to depth may be employed to adapt the vergence-accommodation crosslink. However these cues might still play a significant role in regulating eye growth (Smith III et al., 2007; Wallman et al., 1987). It may be possible to exploit virtual reality technology to guide accommodation responses and the distributions of retinal blur in a fashion that minimizes the environmental conditions which are thought to trigger the development of myopia. To this end, virtual reality displays with coherent or near-correct depth and focus cues may be implemented in gaze contingent fashion (Duchowski et al., 2014; Maiello et al., 2014; Mauderer et al., 2014) with newly available low-cost eye tracking systems (Dalmaijer, 2014; Gibaldi et al., 2016), with

switchable lens systems (Love et al., 2009), and even as head mounted displays (Liu et al., 2010). An additional caveat to these display technologies is that the lens systems employed by head mounted displays may also induce adaptation of the vergence system (Henson and Dharamshi, 1982; Mon-Williams et al., 1993; North and Henson, 1981), which will in turn affect accommodation and retinal blur.

Future work should thus focus initially on understanding defocus sensitivity in virtual reality displays. The method we have devised employs simulated disparity to drive and continuously monitor accommodation. This method may be employed in future research to study natural dioptric defocus perception using an observer's own optics without the need to construct custom volumetric (MacKenzie et al., 2010) or multiplane display rigs (Sebastian et al., 2015). Future investigations should also include children at risk for myopia and young progressing myopes to evaluate possible causative or preventative effects of simulated visual environments on refractive error development.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights to

- Vergence and accommodation are disrupted in virtual reality systems.
- Vergence-driven accommodation is stronger in myopes than in emmetropes.
- In myopes vergence is slower and accommodation is less stable.
- Accommodation inaccuracy causes retinal blur, which may be associated with myopia.

Figure 1. Schematization of the Experimental Setup. Observers wore NVidia 3D vision shutter glasses and viewed the 3D monitor through a 45 degree tilted dichroic mirror. The Power Refractor camera was placed above the mirror and viewed the observers' eyes reflected in the mirror.

Figure 2.

Stimuli to Drive Vergence and Accommodation. (a) In Step 1, a Gaussian blurred dot with -3.5 degrees of uncrossed disparity was used to drive vergence behind the surface of the display. Its blurred structure eliminated spatial cues for accommodation. (b–f) In Step 2, dead leaves stimuli were used to drive vergence and accommodation to the surface of the display. At central fixation, zero disparity and sharply focused images specified vergence and accommodation at the depth of the monitor, and the potential influence of the visual periphery was assessed by presenting 5 simulated depth cue configurations in the peripheral visual field: (b) No Depth Cues (c) Relative Size gradient (d) Blur gradient (e) Disparity gradient (f) Size, Blur and Disparity gradient. In figures (e,f) stereoscopic disparity may be viewed using red-cyan anaglyph glasses. See main text for a detailed description of stimuli and stimulus generation procedures.

Figure 3.

Accommodation as a function of time for a representative observer in which Step 2 was a “Zero gradient” stimulus. Cyan circles represent raw accommodation data and the magenta line is the best fitting accommodation curve (equation 2). Step 1 (Vergence driven Accommodation to Simulated Disparity, dark gray shaded area) occurs before time $t=0$ s and specifies a target at 1 diopter away from the monitor (green line). Step 2 (Vergence and Accommodation Responses with Peripheral Depth Cues, light gray shaded region) begins at time $t=0$ s, and specifies a target on the surface of the monitor.

Figure 4.

Vergence Response Curves. Shaded regions bounded by dotted lines are 95% bootstrapped confidence intervals of mean vergence as a function of time for myopes (red) and emmetropes (blue). Negative time points correspond to Step 1, and time 0 indicates the start of Step 2. Filled lines are piecewise functions fitted to the raw data and then averaged across observers in each refractive group and each peripheral cue condition: (a) Zero gradient (b) Size gradient (c) Blur gradient (d) Disparity gradient (e) Size, Blur and Disparity gradients. The convention employed in this study places the monitor at 0 degrees of vergence, with divergence beyond the surface of the monitor specified as increasingly negative values. The disparity defined fixation dot in Step 1 specifies vergence at -3.5 degrees away from the surface of the monitor (here highlighted by the green lines). Note that because fitted piecewise functions and raw vergence data are averaged separately, filled lines representing piecewise functions need not pass through the middle of the raw vergence data shaded regions.

Figure 5.

Accommodation Response Curves. As in Figure 4 except for Accommodation Responses. Shaded regions bounded by dotted lines are 95% bootstrapped confidence intervals of mean accommodation for myopes (red) and emmetropes (blue). Negative time points correspond to Step 1, and time 0 indicates the start of Step 2. Filled lines are fitted piecewise functions averaged across observers in each refractive group and each peripheral cue condition: (a) Zero gradient (b) Size gradient (c) Blur gradient (d) Disparity gradient (e) Size, Blur and Disparity gradients. Negative time points refer to Step 1, where accommodation is specified by vergence stimulus to be 1D behind the display. Step 2 began at $t=0$ s and the fixation and center of the stimulus specified accommodation at the distance of the monitor. Note that the y-axis direction is flipped to facilitate graphical comparison to Figure 4: more negative dioptric values mean accommodation to farther distances (diopters = 1/meters). Note that because fitted piecewise functions and raw accommodation data are averaged separately, filled lines representing piecewise functions need not pass through the middle of the raw accommodation data shaded regions.

Figure 6.

Accommodation and Accommodation Variability During Step 1. (a) Mean value of d_0 of the fitted accommodation response curves averaged across emmetropes (blue) and myopes (red). (b) Mean variability of accommodation during Step 1 averaged across emmetropes (blue) and myopes (red). Error bars are 95% bootstrapped confidence intervals. Circles are individual subject data. * $p < 0.05$, ** $p < 0.01$

Figure 7.

Exponential half-life τ of the fitted vergence response curves averaged across myopes (red) and emmetropes (blue) and across cue conditions. Error bars are 95% bootstrapped confidence intervals. Circles are individual subject data. * $p < 0.05$

Figure 8.

Accommodation Steady State Variability averaged across myopes (red) and emmetropes (blue) for each cue condition. Error bars are 95% bootstrapped confidence intervals. Circles are individual subject data. * $p < 0.05$