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Research Article

Impact of Myopic and Hyperopic Chromatic Defocus on Retinal Response Using Multifocal Electroretinogram

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Abstract

Purpose: To examine the effect of optical chromatic defocus conditions on retinal activity using multifocal-electroretinogram (mf-ERG).

Method: Twelve emmetropic adults (aged 22 to 29 years) with normal ocular health participated in the study. Mf-ERG was performed six times on both eyes. The experimental conditions were: no defocus, positive defocus (+2D), and negative defocus (-2D) conditions with short-pass (blue), long-pass (red), and neutral density (ND) filters. A multifocal-ERG with hexagonal stimulus pattern subtended 60° horizontally and vertically at a working distance of 33 cm. The amplitudes and implicit times of wave components of mf-ERG responses were pooled into five concentric rings for analysis.

Result: Among the experimental conditions, the retinal P1 amplitude demonstrated a significant change between long-pass and short-pass (20.03 ± 12 nV/deg^2 and 15.14 ± 9 nV/deg^2, respectively) ($P < 0.05$). There was a significant interaction between color filters and type of defocus ($p < 0.05$). With the long-pass filter, myopic defocus showed a higher P1 amplitude (20.5 ± 10 nV/deg^2) compared to hyperopic defocus (18 ± 10 nV/deg^2), whereas the blue filter demonstrated a higher amplitude with hyperopic defocus (17 ± 8 nV/deg^2) than with myopic defocus (14 ± 10 nV/deg^2). Only central and paracentral retinal regions showed a significant amplitude change to chromatic blur. The implicit time was significantly lower (relatively faster) in peripheral retinal regions with no significant difference across all tested conditions.

Conclusion: Showed that chromatic blur caused small but significant changes in mf-ERG amplitudes that are limited to central and paracentral retina, where long-pass filters induced more mf-ERG amplitude under myopic defocus. To better understand whether the shift in the ocular chromatic aberration is one of the cues that the retina uses to differentiate myopic and hyperopic defocus, further studies that account for the posterior ocular shape, peripheral refraction, and off-axis ocular aberrations with a larger sample are required.

Keywords: *Chromatic; Defocus; Retinal Response; Electroretinogram; Myopia*

Abbreviations

MF-ERG: Multifocal Electroretinogram; LP: Long-Pass; SP: Short-Pass; ND: Neutral Density

Introduction

Most humans at birth are born with hyperopia due to a mismatch between the eye's optical power and its axial length. Human eyes undergo emmetropization process that occurs during the first six years of a child's life to bring ocular refraction towards emmetropia or low hyperopia through coordinated changes in the growth of the eye's refractive components (corneal curvature, lens power, and axial length) [1-3].

It is believed that emmetropization is a locally and visually guided mechanism. Disruption of early normal visual experience may lead to myopia in both humans [4,5] and animals [6-8]. Numerous studies that investigated the impact of different optical defocus conditions on chicks, monkeys, and guinea pigs on refractive error development demonstrated that imposed myopic defocus (positive) led to hyperopic refractive error, where imposed hyperopic defocus (negative) caused myopic refractive error [9-11]. It has been supported by findings from several animal studies that emmetropization is regulated by a local visually guided mechanism (i.e. within the eye), which is unlikely to require input from high cortical areas [12-14].

The short-term impact of imposed optical defocus has also been investigated in human eyes. Several rapid ocular responses were observed at the retinal and choroidal level following minutes to hours of defocus exposure. At the retinal level, studies showed that retina electrical activity showed different responses to myopic versus hyperopic defocus, where it was reduced with hyperopic defocus. On the other hand, choroidal responses to imposed optical defocus demonstrated a change in its thickness. Choroidal thickening occurs following short exposure to myopic defocus or after removing a diffuser from an eye, where hyperopic defocus causes the choroid to thin. This choroidal response is rapid and appears to be localized [15]. The observed rapid short-term ocular responses indicate that the retina has the ability to differentiate myopic from hyperopic optical defocus and reacts accordingly. However, the question that remains to be answered is what mechanism(s) the retina uses to recognize types of optical defocus.

As myopia prevalence and early onset among children increases dramatically, several effective optical treatments, such as multifocal contact lenses and overnight orthokeratology, have been shown to reduce myopia progression significantly in children [16]. These optical treatments mainly work on shifting the peripheral hyperopic defocus to myopic defocus, although the mechanism of such treatments is still unclear. Other evidence suggests that increasing children's time spent outdoors lowers the risk of developing myopia and myopia progression [17,18]. The mechanism of this effect is still unclear, but there are several proposed mechanisms. Generally, outdoor lighting, such as sunlight, differs in intensity and spectrum from artificial indoor lighting; the protective effect may be due to the intensity- or wavelength-dependent anti-myopia effect on the retina. With more outdoor sunlight exposure, retinal dopamine release increases, which may inhibit myopia eye elongation [19]. Since myopia progression rate differs per season, with significantly higher progression observed in winter compared to summer, it suggests that seasonal variation can be linked to outdoor light exposure activity [20,21].

Several studies tested the effect of imposed optical defocus on retinal electrical activities. The result of the study showed that the paracentral retinal area responded significantly less amplitude with negative lenses compared to the defocus created with positive lenses. The study concluded that human retina has the ability to distinguish positive from negative defocus; however, the mechanism is still unknown [22]. One of the possibilities is chromatic aberration.

Similar to any optical system, the human eye as any optical system suffers from a variety of aberrations, which reduce image quality. Chromatic aberration is one of them, in which every wavelength over the complete visible spectrum (400 - 700 nm) experiences a different index of refraction. As a result, each wavelength focuses on a different focal plane along the optical axis of the optical system, which is called longitudinal chromatic aberration (LCA). The human eye generates a range of LCA from 2 to 2.5 diopters [23].

The role of chromaticity in refractive error development has been demonstrated in animals [24-26]. Studies tested the status of refractive error development in chicks that were raised in red light or blue light. The conclusion was rearing chicks in red light led to myopia

progression, while raising chicks in blue light caused hyperopia progression. Also, the light-induced refractive error in chicks is reversible by changing the chromaticity of ambient light [24].

Unlike flash electroretinogram that provides the summed retinal response, MF-ERG allows the measurement of retinal responses in a topographical detail that can be divided into concentric retinal regions. In this study, we investigated the short-term effect of positive and negative defocus with short and long-pass filters on retinal activity in humans in different retinal regions using mf-ERG.

Materials and Methods

Subjects

Twelve young adults, seven males and five females, aged from 21 to 29 years (mean and standard deviation = 25 ± 2.1 years), with normal ocular health, were enrolled in the study. Individuals with posterior ocular diseases and/or ocular opacity were excluded from the study. All participants were emmetropic (spherical equivalent between -0.50 and +0.50 D), mean -0.23 ± 0.2 D. All participants had best corrected visual acuity of 0.00 logMAR or better, normal color vision, and astigmatism less than 1.00D. This study was granted ethical approval by the institutional review board and in accordance with the Declaration of Helsinki. After a detailed explanation of the study procedures, written consent forms were obtained from all participants prior to data gathering.

Data collecting procedure

The Diagnosys multifocal-electroretinogram (mf-ERG) (Diagnosys LCC, Lowell, MA) was used according to the manufacturer's protocol. The mf-ERG stimulus array consisted of 61 non-scaled hexagons that subtended 60 degrees horizontally and vertically that was presented at a working distance of 33 cm. The stimulus was presented on a 32-inch LCD monitor with 1000 cd/m^2 brightness and a 1000:1 contrast ratio. Each hexagon was alternating between bright and dark, based on a pseudo-random binary m-sequence stimulation.

Multifocal-electroretinogram was performed six times on both eyes of each participant. Each time was under a different experimental condition. There were three optical defocus [in focus (focused on retina), myopic defocus (+2 D), and hyperopic defocus (-2 D)] tested with short-pass (blue) and long-pass (red) filters.

Color filters (short- or long-pass) were placed in front of the right eyes, while a neutral density (ND) filter that matched the transmitted similar luminance of the short- and long-pass filters was placed in front of the left eyes. MF-ERG recordings of both eyes were obtained simultaneously. To create the three defocus conditions, ophthalmic lenses on a frame were placed 15 mm vertex distance in front of each participant's eyes to create -2.0D, no defocus (0.0D), and +2.0D defocus conditions while stimulus placed at 33 cm from the participant's eyes. Both eyes received the same optical defocus in each ERG recording. The order of the six experimental conditions was randomized.

Recording DTL-Plus electrodes (Diagnosys LCC, Lowell, MA) were placed on the participants' cornea along the lower lid of both eyes after instilling a drop of proparacaine hydrochloride ophthalmic solution (0.5%). Gold cup electrodes were placed on the central forehead and 8 cm lateral to each outer canthus. All participants sustained a minimum of 7 mm pupil throughout the mf-ERG recording period. The testing was performed in dim room illumination. Prior to measurement commencement, two drops of Cyclopentolate (1%) were instilled at a 5-minute interval to ensure a steady cycloplegic effect throughout the recording period. The residual accommodation of both eyes was tested using the push-up method after 30 minutes of the first drop. Residual accommodation was measured. The power of the ophthalmic lenses was adjusted to compensate for any residual accommodation to ensure a constant level of optical defocus. The total mf-ERG recording time for each condition was less than 7 minutes.

Color filers Edmund Optics short- and long-pass filters were used in this study. The short-pass filter transmits all wavelengths between 300 nm and 490 nm with a wavelength cutoff of 500 nm (Figure 1a). On the other hand, the long-pass filter allows a wavelength range from 610 nm to 1650 nm and a cutoff of 600 nm (Figure 1b). Both filters were 5 cm in diameter with 5 mm thickness.

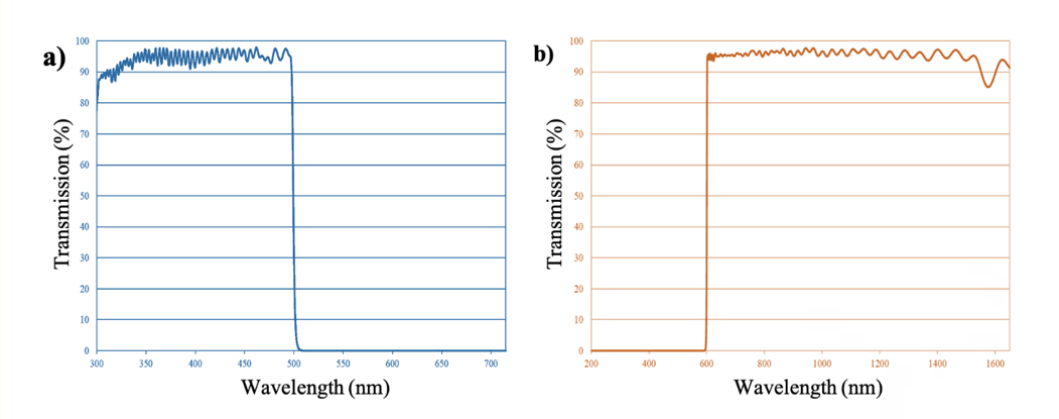

Figure 1: *The transmittance graph of the short-pass (a) and long-pass (b) filters used in the study.*

Statistical analysis

The data obtained from mf-ERG were pooled into five concentric rings (Figure 2). The P1 amplitude and implicit time of each ring were included in the analysis. The data analysis was performed using SPSS software (SPSS version 28.0, SPSS Inc., Chicago, IL, USA). Repeated measure analysis of variance (ANOVA) was used to test the effect of the defocus conditions on mf-ERG amplitudes and implicit times. Bonferroni adjustment was applied for multiple comparisons when appropriate. A p-value of ≤ 0.05 was considered statistically significant.

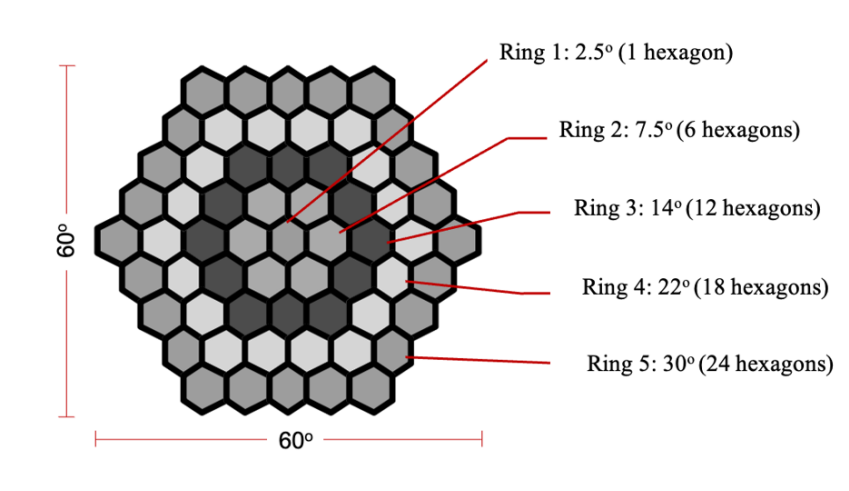

Figure 2: *The 61 hexagonal stimulus grouped into five concentric rings. Each ring boundary and number of hexagons are indicated in the figure.*

Results and Discussion

The amplitude and implicit time of the P1 component were analyzed under the chromatic optical defocus conditions (-2D, no defocus, and +2D) with short- and long-pass filters. The overall retinal response from all tested regions (P1 amplitude) under long-pass was 20.03 ± 12 nV/deg^2 compared to the short-pass filter (15.14 ± 9 nV/deg^2). The P1 amplitude was significantly reduced as eccentricity increased towards peripheral retinal (Ring 1: 36 ± 14 and Ring 5: 9 ± 2.5 nV/deg^2) regions with all experimental conditions.

A significant interaction between color filters and the eccentric retinal regions ($p < 0.001$) in P1 amplitude, which indicated the retina central retina showed significantly higher amplitudes with log-pass filters compared to short-pass (ring 1 and 2), whereas in paracentral and near-peripheral retinal regions (ring 3, 4, and 5) no significant difference in amplitude between the two-color filters (Figure 3). With the ND filter, there was a trend of reduced P1 amplitude in the overall measured retinal area with hyperopic defocus (- 2 D); mean of 12.5 ± 8 nV/deg^2 compared to myopic defocus and no defocused testing conditions (13.7 ± 8 nV/deg^2 and 13.8 ± 9 nV/deg^2, respectively) ($p = 0.1$) (Figure 3).

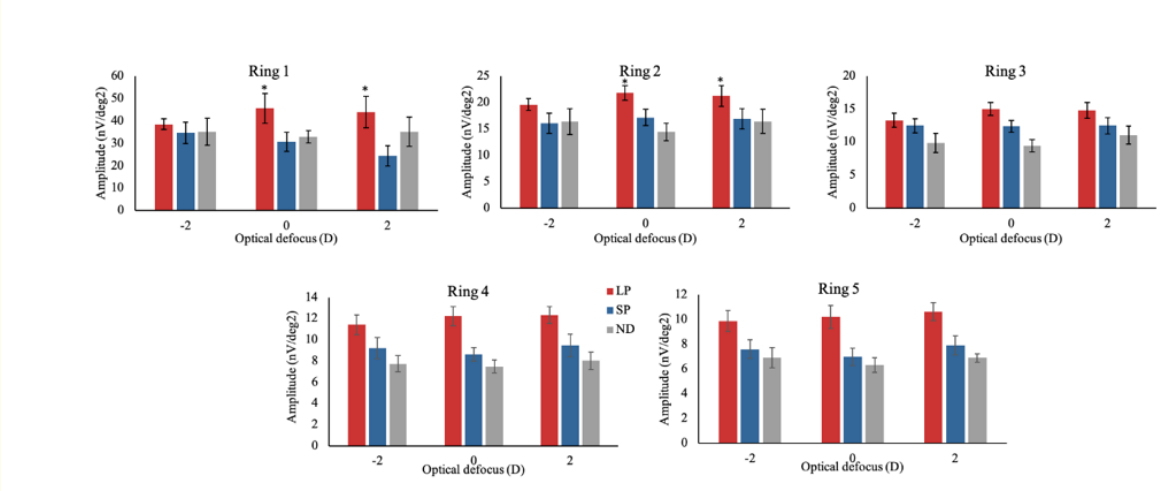

Figure 3: *P1 amplitudes under various chromatic defocus conditions for different retinal regions. Asterisk "*" indicate a statistically significant different from the in-focus (0) condition. The error bars indicate the standard error of the mean (SEM).*

In the central region (Ring 1) and with log-pass filter, the P1 amplitude of myopic defocus (+2D) was significantly greater (44 ± 10 nV/deg^2) than under 2D of hyperopic defocus (38 ± 7 nV/deg^2) ($p < 0.001$). On the other hand, a greater P1 amplitude was observed with the short-pass filter under hyperopic defocus (-2D) (35 ± 11 nV/deg^2) in comparison with myopic defocus (24 ± 10 nV/deg^2) with the same filter.

The overall implicit time of P1 was remarkably less (i.e., relatively faster) in peripheral regions (Ring 5: 31.8 ± 2 ms) compared to central retina (34.8± 5 ms). A statistically significant delay was observed with the short-pass filter (33± 4 ms) in comparison with the long-pass filter (31 ± 4 ms) ($p = 0.02$). Optical defocus conditions did not significantly impact the implicit time ($p = 0.12$).

In this study, we used single-power spherical ophthalmic lenses to induce optical defocus over the measured 60 degrees of mf-ERG retinal response. To our knowledge, this was the first to investigate the chromatic blur impact on human retinal mf-ERG activity. The

findings of different amplitude in the central retina with short- and long-pass filter is supported by the longitudinal ocular chromatic aberration (LCA). Normally, the human eye suffers from LCA that ranges from 2.0 to 2.5 diopter [23]. In myopic defocus, the long-pass filter showed increased amplitude, which can be explained by shifting the longer wavelength closer to the retina compared to the hyperopic defocus, where the long-pass filter showed a relatively reduced amplitude. Similar results were observed with short-pass filter where greater amplitude was seen under hyperopic defocus compared to myopic defocus condition. This finding diminished beyond central retinal regions (Ring 1 and 2).

The failure to detect a significant P1 amplitude in near-peripheral and peripheral retinal areas can be explained by three factors. First, the presence of yellow macular pigment in the central retinal region is likely contributing to blocking a part of the blue light, especially when the short-pass filter was used, which may lead to reduce amplitude with short-pass filter. Second, the small sample size of this pilot study was not large enough to detect changes in small P1 amplitudes generated by peripheral regions. Third, it can be due to the presence of the transverse chromatic aberration that increases in magnitude with increasing eccentricity. It has been reported that transverse chromatic aberration remained below ten arcmin within the central 40 degrees and exceeded 30 arcmin at 60 degrees of the field [27].

It has been demonstrated from animal models with experimentally induced myopia that defocus signals outside the central vision could contribute to sending signals that lead to myopia development or slow myopia progression rate [28,29]. The findings from several animal studies indicated that peripheral myopic defocus, through the use of two-zone concentric contact lenses, is more important than central defocus in refractive error development. In humans, it is believed that the hyperopic defocus created with the use of single vision lens in the paracentral and near-peripheral retina promotes ocular growth and leads to myopia development through axial elongation [30], whereas peripheral myopic defocus that is utilized by multifocal contact lens and overnight orthokeratology lead to a significantly lower rate of myopia progression in children [16].

From Ho., *et al*. investigation, the paracentral retina recognized positive and negative optical defocus. It is known that off-axis higher-order aberrations increase as eccentricity increases, such as radial astigmatism. In addition, peripheral refraction and transverse chromatic aberration become more significant with eccentricity. The effect of these components needs to be further investigated to understand their degree of impact on optical defocus in peripheral retina (i.e. beyond eccentricity of 20°). In terms of the retinal response with mf-ERG, Ho., *et al*. found that paracentral retina is the most reacted to optical defocus, which may indicate that paracentral vision possibly has a profound effect on ocular growth and refractive error development [22].

The current study had several limitations to be acknowledged. The study was conducted in a small cohort of emmetropic healthy young adults. The findings may not be generalizable to a larger population with a variety of ages and refractive errors (e.g. myopia and hyperopia). Therefore, research with a larger sample size is warranted to test the retinal response under different chromatic optical defocus conditions.

It is known that myopic and hyperopic eyes exhibit different posterior ocular shapes, whereas myopic eyes tend to be more prolate due to the associated axial elongation. Prolate-shaped eyes require more plus power in the periphery to create the same amount of myopic defocus as in emmetropic eyes. For the difficulty of precise measurement of the posterior ocular shape and its impact of optical defocus signal in the periphery, only emmetropic eyes were explored in this study. Future studies exploring the effect of chromatic blur on retinal activity of myopic eyes while taking into consideration the posterior ocular shape and peripheral refraction are warranted.

Conclusion

This work investigated the retinal electrical activity under various defocus conditions with LP, SP, and ND filters. Central and paracentral retina showed a response change to chromatic blur (greater amplitude with myopically defocused long-pass filter and reduced

amplitude under long-pass hyperopic defocus). Peripheral retinal regions did not show a significant change in response amplitude when comparing all chromatic blur conditions. Future studies, including both myopic and non-myopic eyes with a sufficient sample that account for peripheral refraction, posterior ocular shape, and off-axis ocular aberrations, is needed.

Bibliography

1. Mutti DO., *et al*. "Axial Growth and Changes in Lenticular and Corneal Power during Emmetropization in Infants". *Investigative Ophthalmology and Visual Science* 46.9 (2005): 3074.
2. Watanabe S., *et al*. "A longitudinal study of cycloplegic refraction in a cohort of 350 Japanese schoolchildren. Cycloplegic refraction". *Ophthalmic and Physiological Optics* 19.1 (1999): 22-29.
3. French AN., *et al*. "Comparison of Refraction and Ocular Biometry in European Caucasian Children Living in Northern Ireland and Sydney, Australia". *Investigative Ophthalmology and Visual Science* 53.7 (2012): 4021.
4. Hoyt CS., *et al*. "Monocular axial myopia associated with neonatal eyelid closure in human infants". *American Journal of Ophthalmology* 91.2 (1981): 197-200.
5. Nathan J., *et al*. "Disease-associated visual image degradation and spherical refractive errors in children.pdf". *American Journal of Optometry and Physiological Optics* 62 (1985): 680-688.
6. Hodos W and Kuenzel WJ. "Retinal-image degradation produces ocular enlargement in chicks". *Investigative Ophthalmology and Visual Science* 25.6 (1984): 652-659.
7. Smith EL., *et al*. "Form deprivation myopia in adolescent monkeys". *Optometry and Vision Science American Academy of Optometry* 76.6 (1999): 428-432.
8. Wallman J., *et al*. "Extreme myopia produced by modest change in early visual experience". *Science* 201.4362 (1978): 1249-1251.
9. Howlett MHC and McFadden SA. "Spectacle lens compensation in the pigmented guinea pig". *Vision Research* 49.2 (2009): 219-227.
10. Hung LF., *et al*. "Spectacle lenses alter eye growth and the refractive status of young monkeys". *Nature Medicine* 1.8 (1995): 761-765.
11. Norton TT and Siegwart Jr JT. "Animal models of emmetropization: matching axial length to the focal plane". *Journal of the American Optometric Association* 66.7 (1995): 405-414.
12. Choh V., *et al*. "Effects of interchanging hyperopic defocus and form deprivation stimuli in normal and optic nerve-sectioned chicks". *Vision Research* 46.6-7 (2006): 1070-1079.
13. Schmid KL and Wildsoet CF. "Effects on the compensatory responses to positive and negative lenses of intermittent lens wear and ciliary nerve section in chicks". *Vision Research* 36.7 (1996): 1023-1036.
14. Wildsoet CF. "Neural pathways subserving negative lens-induced emmetropization in chicks–insights from selective lesions of the optic nerve and ciliary nerve". *Current Eye Research* 27.6 (2003): 371-385.
15. Hoseini-Yazdi H., *et al*. "Regional alterations in human choroidal thickness in response to short-term monocular hemifield myopic defocus". *Ophthalmic and Physiological Optics* (2019).
16. Smith EL. "Optical treatment strategies to slow myopia progression: Effects of the visual extent of the optical treatment zone". *Experimental Eye Research* 114 (2013): 77-88.

17. French AN., *et al*. "Time outdoors and the prevention of myopia". *Experimental Eye Research* 114 (2013): 58-68.

18. Sherwin JC., *et al*. "The Association between Time Spent Outdoors and Myopia in Children and Adolescents". *Ophthalmology* 119.10 (2012): 2141-2151.

19. Rose KA., *et al*. "Outdoor Activity Reduces the Prevalence of Myopia in Children". *Ophthalmology* 115.8 (2008): 1279-1285.

20. Donovan L., *et al*. "Myopia Progression in Chinese Children is Slower in Summer Than in Winter". *Optometry and Vision Science* 89.8 (2012): 1196-1202.

21. Gwiazda J., *et al*. "Seasonal Variations in the Progression of Myopia in Children Enrolled in the Correction of Myopia Evaluation Trial". *Investigative Ophthalmology and Visual Science* 55.2 (2014): 752.

22. Ho W Cheung., *et al*. "Sign-dependent changes in retinal electrical activity with positive and negative defocus in the human eye". *Vision Research* 52.1 (2012): 47-53.

23. Bedford RE and Wyszecki G. "Axial chromatic aberration of the human eye". *The Joint Seat Allocation Authority* 47.6 (1957): 564-565.

24. Foulds WS., *et al*. "Progressive myopia or hyperopia can be induced in chicks and reversed by manipulation of the chromaticity of ambient light". *Investigative Ophthalmology and Visual Science* 54.13 (2013): 8004-8012.

25. Wang M., *et al*. "Effects of light of different spectral composition on refractive development and retinal dopamine in chicks". *Investigative Ophthalmology and Visual Science* 59.11 (2018): 4413-4424.

26. Rucker FJ., *et al*. "Signals for defocus from longitudinal chromatic aberration in chick". *Experimental Eye Research* 198 (2020): 108126.

27. Ogboso YU and Bedell HE. "Magnitude of lateral chromatic aberration across the retina of the human eye". *Journal of the Optical Society of America A* 4.8 (1987): 1666-1672.

28. Liu Y and Wildsoet C. "The Effect of Two-Zone Concentric Bifocal Spectacle Lenses on Refractive Error Development and Eye Growth in Young Chicks". *Investigative Ophthalmology and Visual Science* 52.2 (2011): 1078.

29. Benavente-Pérez A., *et al*. "Axial eye growth and refractive error development can be modified by exposing the peripheral retina to relative myopic or hyperopic defocus". *Investigative Ophthalmology and Visual Science* 55.10 (2014): 6765-6773.

30. Lin Z., *et al*. "Peripheral defocus with single-vision spectacle lenses in myopic children". *Optometry and Vision Science* 87.1 (2010): 4-9.

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