Bi-directional Refractive Compensation for With-the-Rule and Against-the-Rule Astigmatism in Young Adults

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Purpose. The purpose of this study was to investigate the short-term effect of imposing astigmatism on the refractive states of young adults.

Methods. Nineteen visually healthy low-astigmatic young adults (age = 20.94 ± 0.37 years; spherical-equivalent errors [M] = −1.47 ± 0.23 diopters [D]; cylindrical errors = −0.32 ± 0.05 D) were recruited. They were asked to wear a trial frame with treated and control lenses while watching a video for an hour. In three separate visits, the treated eye was exposed to one of three defocused conditions in random sequence: (1) with-the-rule (WTR) astigmatism = +3.00 DC × 180 degrees; (2) against-the-rule (ATR) astigmatism = +3.00 DC × 90 degrees; and (3) spherical defocus (SPH) = +3.00 DS. The control eye was fully corrected optically. Before and after watching the video, non-cycloplegic autorefraction was performed over the trial lenses. Refractive errors were decomposed into M, J0, and J45 astigmatism. Interocular differences in refractions (treated eye – control eye) were analyzed.

Results. After participants watched the video with monocular astigmatic defocus for an hour, the magnitude of the J0 astigmatism was significantly reduced by 0.25 ± 0.10 D in both WTR (from +1.53 ± 0.07 D to +1.28 ± 0.09 D) and 0.39 ± 0.15 D in ATR conditions (from −1.33 ± 0.06 D to −0.94 ± 0.18 D), suggesting an active compensation. In contrast, changes in J0 astigmatism were not significant in the SPH condition. No compensatory changes in J45 astigmatism or M were found under any conditions.

Conclusions. Watching a video for an hour with astigmatic defocus induced bidirectional, compensatory changes in astigmatic components, suggesting that refractive components of young adults are moldable to compensate for orientation-specific astigmatic blur over a short period.

Keywords: astigmatism, compensation, adaptation, astigmatic defocus

Refractive astigmatism is a common cause of visual impairment affecting 20% to 30% of young adults, but its etiology remains elusive.[1] Without ophthalmic aids (spectacles or contact lenses) or surgical intervention, an astigmatic eye constantly suffers from retinal blur, because each point making up an object is refracted into two line foci oriented orthogonally at separate image planes, making it impossible for a fixed retinal plane to receive a sharply focused image of all orientations. The prevalence of this orientation-specific refractive error varies with age.[2] There is a high prevalence of astigmatism in young children, which disappears before school age,[3–8] whereas the prevalence of astigmatism in adults increases after 40 years of age.[9–12] The disappearance of infantile astigmatism before school age suggests that the ocular refractive components are moldable to minimize the difference in meridional power (i.e. toward a spherical refractive surface), but whether this "spherical-ization" process is a passive byproduct of natural eye growth or is actively remodeled by exogenous visual cues remains unknown.

Optical cues, including spherical and astigmatic defocus, can modify early refractive development. First reported in chickens,[13] spherical defocus provides directional growth signals to either accelerate or slow eye growth accompanied by corresponding changes in ocular structural components.[14–18] Importantly, recent studies in humans exposed to short-term (30 minutes to 2 hours) spherical defocus also showed similar ocular structural changes: hyperopic defocus (with diverging lenses) induced a longer axial length[19,20] and thinner choroid,[21,22] whereas myopic defocus (with converging lenses) resulted in a shorter axial length[19,20] and thicker choroid.[19–22] Compared to spherical defocus, the impacts of astigmatic defocus on refractive development are reported only in chicken and monkey models.[23] Specifically, by optically imposing astigmatism of different orientations using cylindrical (plano- or crossed-

cylinders) or sphero-cylindrical lenses, investigators have induced different degrees of compensatory refractive astigmatism with a specific axis counterbalancing the imposed astigmatism from various settings.[24–27] This cylindrical-lens induced refractive compensation is primarily attributed to corneal changes,[26] although the contributions of lenticular change and the relative alignment of refractive components with respect to the visual axis cannot be excluded. However, other studies using similar toric lenses failed to replicate the results in chicks[28,29] and monkeys,[30] indicating either methodological differences or idiosyncratic operational characteristics of the vision-dependent eye growth mechanism. To date, only one study in humans has shown short-term, bidirectional choroidal thickness changes in response to imposed astigmatism.[31] Whether and how human refractive states are responsive to optically imposed astigmatism has not been previously reported.

This study investigated how an hour of exposure to two common astigmatic conditions, with-the-rule (WTR; strongest refractive power along the vertical meridian) and against-the-rule (ATR; strongest refractive power along the horizontal meridian) astigmatisms, can affect the refractive state in young adults. Using the J0 astigmatic vector component that is sensitive to change in horizontal-vertical refractive power,[32] it was found that the treated eyes showed clinically significant bidirectional, compensatory changes in their astigmatic component to counterbalance the imposed astigmatism after only 1 hour of exposure to astigmatic blur.

Methods

Nineteen visually healthy young adults (age = 18–24 years) were recruited for this study. All participants fulfilled the following inclusion criteria: (1) spherical-equivalent error: 0 diopters (D) to −5.00 D; (2) cylindrical error ≤0.75 D; (3) best-corrected distant visual acuity better than logMAR 0 in both eyes; (4) anisometropia ≤1 D; (5) absence of ocular and systemic diseases; and (6) no history of any ocular surgery or myopia control interventions (e.g. orthokeratology, myopia control spectacles/contact lenses, and atropine). Before the study started, all participants underwent an eye examination to determine their refractive errors and rule out ocular anomalies. Refractive errors were measured by subjective refraction using the maximum plus/maximum acuity as the end point.[33] Contact lens wearers were required not to wear their contact lenses on the day of the experiment. This study was approved by the Human Subjects Ethics Sub-committee of the Hong Kong Polytechnic University (HSEARS20190410001), and written informed consent was obtained from each participant. The experimental procedures complied with the tenets of the Declaration of Helsinki.

Experimental Procedures

Figure 1 illustrates the study procedures. The measurements, which were performed on 3 separate visits, were carried out between 9:30 AM and 4:30 PM. Each subject started the procedures at the same time for all three visits to avoid the potential influence of diurnal variation in ocular biometry.[34–36] At each visit, the same measurements were performed under one of three monocular optical defocused conditions, assigned in random sequence: (1) WTR astigmatic condition = +3.00 DC axis 180 degrees; (2) ATR astigmatic condition = +3.00 DC axis 90 degrees; and (3) spherical defocus (SPH) condition = +3.00 DS. The defocused conditions were imposed over the distance prescription obtained from subjective refraction. For each subject, one eye was selected randomly as the treated eye and the fellow eye served as the intrasubject control throughout the study. Full-aperture (38 mm) trial lenses were used during the treatment period. To prevent potential effects of pupil size and ocular accommodation on refractive measurements,[37] all participants were advised to avoid intensive near work and intaking caffeine-containing substances for at least 60 minutes before the procedure.

The measurements commenced with a baseline objective (auto-) refraction through the trial lenses under binocular viewing of a fixation target using an open-field autorefractor (NVision-K 5001, Shin-Nippon, Japan). The fixation target was set at 3 m from the eyes. Before commencing the measurements, the trial frame and lens position were checked to ensure alignment with the eyes. For each eye, five consecutive readings were taken and the representative value automatically generated by the autorefractor was used for further analysis. After this baseline measurement, participants wore the same pair of trial lenses and watched a self-selected video played on an LCD (size = 21.5 inches, resolution = 1920 × 1080, and refresh rate = 60 Hz) for an hour under normal room lighting (approximately 245 lux). The LCD was set at eye level, located 2 m from the subject, and subtending a maximum visual angle of 13.4 degrees × 7.6 degrees. The accommodative demand due to the 2 m working distance was neutralized by inserting a pair of +0.50 DS lenses binocularly. After 1 hour of video watching, the +0.50 DS lenses were removed and autorefraction was repeated through the corrective lenses.

Data Analysis

Refractive errors were decomposed into spherical-equivalent error (M), J0, and J45 astigmatic components using Fourier analyses.[32]

$$M = S + \frac{C}{2}$$
$$J0 = -\frac{C}{2}\cos 2A$$
$$J45 = -\frac{C}{2}\sin 2A$$

where S, C, and A represent the spherical error, cylindrical error, and axis, respectively.

Through Fourier analysis, astigmatism of different orientations and magnitudes can be expressed as a combination of vertical/horizontal J0 astigmatism (+ve = WTR astigmatism and –ve = ATR astigmatism) and oblique J45 astigmatism (+ve = astigmatism in 45 degrees axis and –ve = astigmatism in 135 degrees axis). Thus, J0 astigmatic component is more sensitive in reflecting the changes in vertical/horizontal meridians, whereas J45 astigmatic component is more sensitive for oblique meridians. As significant changes in J0 astigmatism were found in both WTR and ATR astigmatic conditions (as reported in the Results section), refractive errors for vertical (P_V) (i.e. 90 degrees) and horizontal meridians (P_H) (i.e. 180 degrees), were calculated from the equation 13.3 of Keating[38] to investigate how each meridian contributed to the J0 astigmatic changes.

$$P_V = S + C\sin^2(A - 90^\circ)$$
$$P_H = S + C\sin^2 A$$

Because the optical conditions (treated eye versus corrective eye) were imposed binocularly while watching the video and the autorefractions were performed sequentially with-

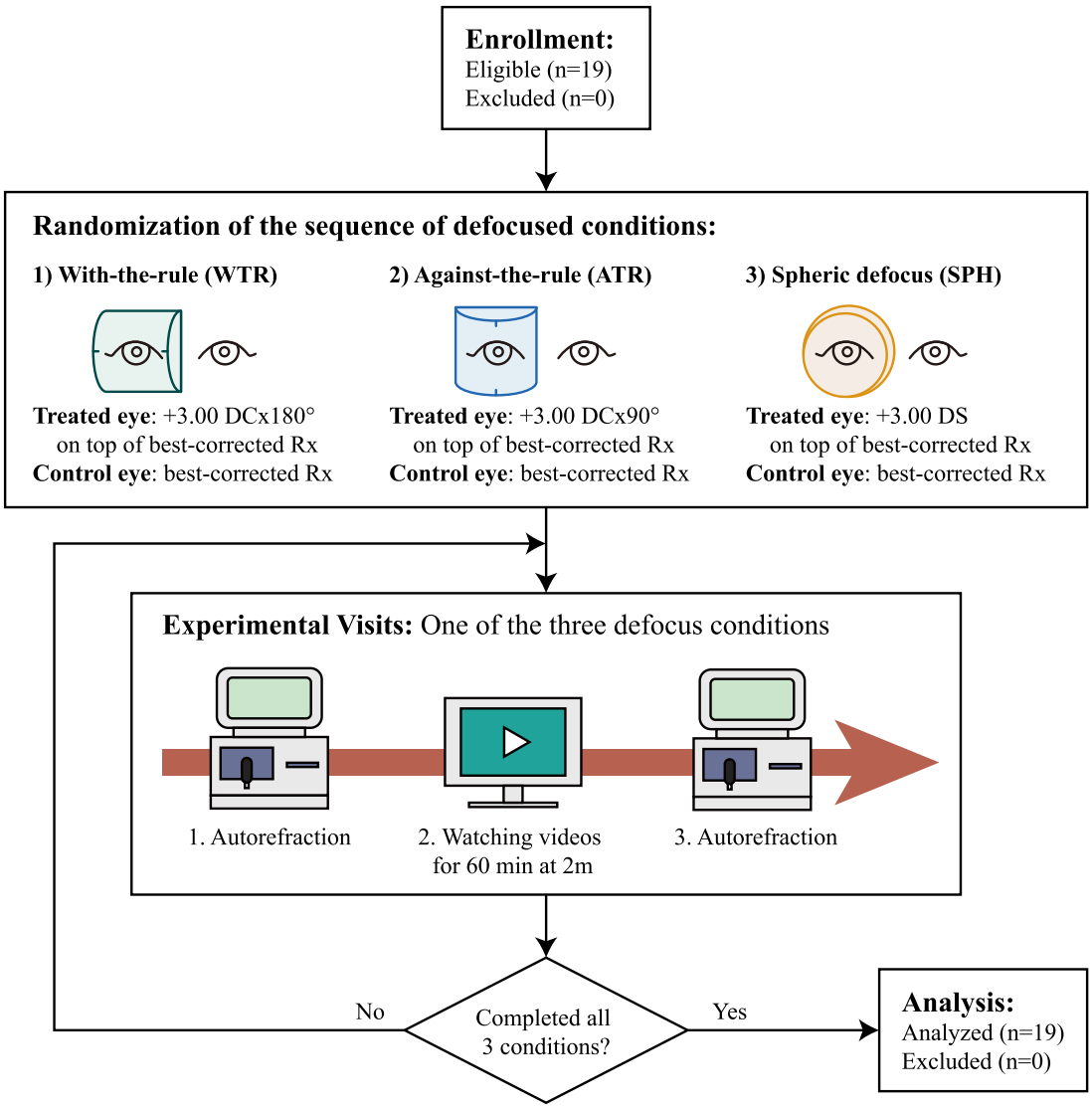

Figure 1. Flowchart of study procedures.

out closing one eye, it was considered that the effects of this binocular treatment would be best detected by subtracting the changes in the control eye from those in the treated eye. The interocular differences (i.e. treated eye – control eye) of refractive components were calculated as the primary outcome for statistical analysis to control for potential idiosyncratic responses arising from each eye and determine the specific effect of treatment over time. Paired *t*-tests were used to compare the interocular differences in refractive error before and after exposure to optical blurs in each defocused condition. Repeated-measures ANOVA was used to compare the extent of refractive changes (i.e. post – pre) among the three defocused conditions. Statistical analyses were performed using IBM SPSS Statistics 23 (IBM, Armonk, NY, USA).

Results

Refractive State Before Treatment

Table 1 presents participants' demographic information and the refractive state of their treated and control eyes before the lens treatments. At baseline, there were no significant differences in any refractive components between the treated and control eyes (all paired $t(18) \leq 1.792$, $P \geq 0.086$). The spherical and J0 astigmatic components of the two eyes were highly correlated (Pearson's correlation, all $r \geq 0.718$, all $P < 0.01$), in contrast to the cylindrical (Spearman's corre-

Table 1. Demographic Information and Refractive State of Treated and Fellow Eyes Before Lens Treatment (Mean ± SEM)

Age, y	20.94 ± 0.37	
M: F	9:10	
Refractive state (D)	Treated eyes	Control eyes
Spherical error	−1.29 ± 0.31	−1.33 ± 0.34
Cylindrical error	−0.25 ± 0.07	−0.38 ± 0.06
J0 astigmatic component	+0.01 ± 0.04	+0.05 ± 0.05
J45 astigmatic component	+0.03 ± 0.02	0.00 ± 0.02
Spherical equivalent error	−1.41 ± 0.31	−1.52 ± 0.35

No statistical differences were found between fellow eyes for any refractive components.

Table 2. Astigmatic and Spherical Defocus Induced Under the Three Experimental Conditions at Baseline

	WTR		ATR		SPH	
	Lens Power	Induced Blur	Lens Power	Induced Blur	Lens Power	Induced Blur
J0	+1.50	+1.53 ± 0.07	−1.50	−1.33 ± 0.06*	0.00	+0.12 ± 0.06
J45	0.00	+0.06 ± 0.07	0.00	−0.07 ± 0.10	0.00	+0.02 ± 0.05
M	−1.50	−1.66 ± 0.11	−1.50	−1.61 ± 0.13	−3.00	−3.14 ± 0.09

One-sample *t*-test between the induced blur and lens power: * $P < 0.05$.

The induced optical blur (mean ± SEM) is expressed as interocular difference (treated eye – fellow eye) in J0 and J45 astigmatisms and spherical-equivalent error (M).

WTR, with-the-rule; ATR, against-the-rule; SPH, spherical defocused conditions.

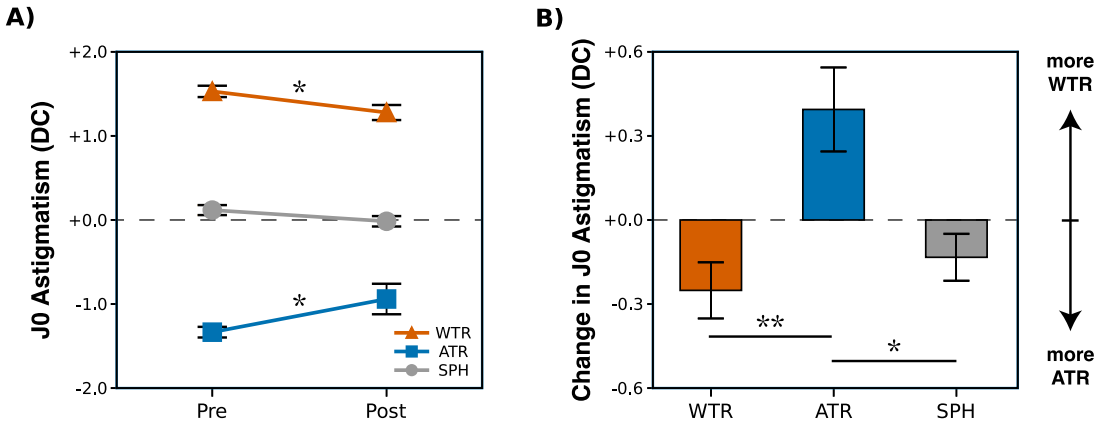

Figure 2. Effects of defocused conditions on interocular differences in J0 astigmatism (mean ± SEM). (**A**) Interocular differences in J0 astigmatism measured before (pre) and after (post) an hour of exposure to WTR, ATR, and SPH defocused conditions. (**B**) The change in J0 astigmatism (post – pre) under the three defocused conditions. Values above and below the dashed lines indicate WTR and ATR astigmatism, respectively. Paired *t*-tests and Bonferroni post hoc tests were used in **A** and **B**, respectively: * $P < 0.05$, ** $P < 0.01$.

lation, $\rho = 0.388$, $P = 0.100$) and J45 astigmatism (Pearson's correlation, $r = 0.160$, $P = 0.513$), which were not.

Astigmatic Defocus Imposed by Experimental Conditions

Table 2 presents the magnitude of induced optical blur under each of the three experimental conditions at baseline. As expected, cylindrical lenses induced obvious astigmatic defocus (+ve J0 for WTR and –ve J0 for ATR), whereas spherical lenses (SPH) induced a significant amount of spherical defocus (–ve M). In the WTR and SPH conditions, the magnitude of induced optical blur did not differ from the treatment lens powers for all three refractive parameters (one-sample *t*-tests, $t(18) \leq 1.98$, $P \geq 0.06$). Although the ATR condition also induced a significant amount of astigmatic defocus (J0 = −1.33 ± 0.06 D), the magnitude was slightly, but significantly lower than the lens power by 0.17 D (one-sample *t*-tests, $t(18) = 2.61$, $P = 0.02$).

Changes in Astigmatic Components After Watching Video Under Defocused Conditions

Watching a video for an hour through the spherical lens did not induce significant changes in the cylindrical error of the eye, but the same video task viewed through the cylindrical lenses resulted in bidirectional changes in astigmatic components that were compensatory to the imposed cylindrical axis. As shown in Figure 2 and Table 3, 1 hour of exposure to either WTR and ATR astigmatism caused statistically significant reductions in the magnitude of J0 astigmatism from both directions, but exposure to SPH condition did not produce a similar change (see Fig. 2A). In the WTR condition, the induced positive J0 astigmatism at baseline dropped significantly from +1.53 ± 0.07 D to +1.28 ± 0.09 D (paired $t(18) = 2.51$, $P = 0.02$); in the ATR condition, the induced negative J0 astigmatism became significantly less negative from −1.33 ± 0.06 D to −0.94 ± 0.18 D (paired $t(18) = -2.63$, $P = 0.02$). In contrast, exposure to spherical defocus only caused insignificant changes in J0 astigmatism (see Table 3; paired $t(18) = 1.59$, $P = 0.13$). Figure 2B shows the significant impact of defocused conditions on the directional changes in J0 astigmatism (post – pre; repeated-measures ANOVA, $F(2, 36) = 9.99$, $P < 0.001$), with ATR inducing significantly more positive J0 component than WTR and SPH conditions (Holm-Bonferroni post hoc tests; ATR versus WTR = paired $t(18) = 4.05$, $P < 0.001$; and ATR versus SPH = paired $t(18) = 3.03$, $P < 0.01$). There was no significant difference in J0 astigmatic change between the WTR and SPH conditions (Holm-Bonferroni post hoc tests, paired $t(18) = 0.96$, $P = 0.35$). For the change in J0 astigmatism (post – pre) in individual eyes, please refer to Supplementary Figure 1.

In contrast to the J0 astigmatic component, both M and J45 astigmatic components remained virtually unchanged after exposure to the 3 defocused conditions (see Table 3; paired $t(18) \leq 1.25$, $P \geq 0.23$). The changes in M and J45 astigmatism were also not significantly different among the

Table 3. Pre- and Post-Task Interocular Differences (Treated Eye – Fellow Eye) in Refractive Errors, and Changes (Post-Task – Pre-Task) in Refractive Components (Mean ± SEM)

	WTR			ATR			SPH		
	Pre	Post	Change	Pre	Post	Change	Pre	Post	Change
J0	+1.53 ± 0.07*	+1.28 ± 0.09*	−0.25 ± 0.10	−1.33 ± 0.06*	−0.94 ± 0.18*	+0.39 ± 0.15†	+0.12 ± 0.06	−0.02 ± 0.06	−0.13 ± 0.08
J45	+0.06 ± 0.07	+0.03 ± 0.09	−0.03 ± 0.09	−0.07 ± 0.10	+0.09 ± 0.13	+0.15 ± 0.12	+0.02 ± 0.05	+0.02 ± 0.07	+0.00 ± 0.06
M	−1.66 ± 0.11	−1.63 ± 0.11	+0.03 ± 0.08	−1.61 ± 0.13	−1.64 ± 0.19	−0.03 ± 0.10	−3.14 ± 0.09	−3.08 ± 0.10	+0.06 ± 0.08
P_V	−3.19 ± 0.14	−2.91 ± 0.16	+0.28 ± 0.16	−0.28 ± 0.16	−0.70 ± 0.26*	−0.42 ± 0.17†	−3.26 ± 0.12	−3.06 ± 0.12	+0.20 ± 0.13
P_H	−0.13 ± 0.12	−0.35 ± 0.12*	−0.22 ± 0.08	−2.95 ± 0.13	−2.58 ± 0.28	+0.37 ± 0.19†	−3.02 ± 0.09	−3.09 ± 0.11	−0.07 ± 0.11

Paired *t*-tests on refractive components between pre- and post-exposure to optical defocuses: * $P < 0.05$.
Repeated-measures ANOVA with post hoc tests, significant difference compared to the other two defocused condition: † $P \leq 0.05$.
WTR, with-the-rule; ATR, against-the-rule; SPH, spherical defocused conditions; P_V, refractive errors for the vertical meridian; P_H, refractive errors for the horizontal meridian.

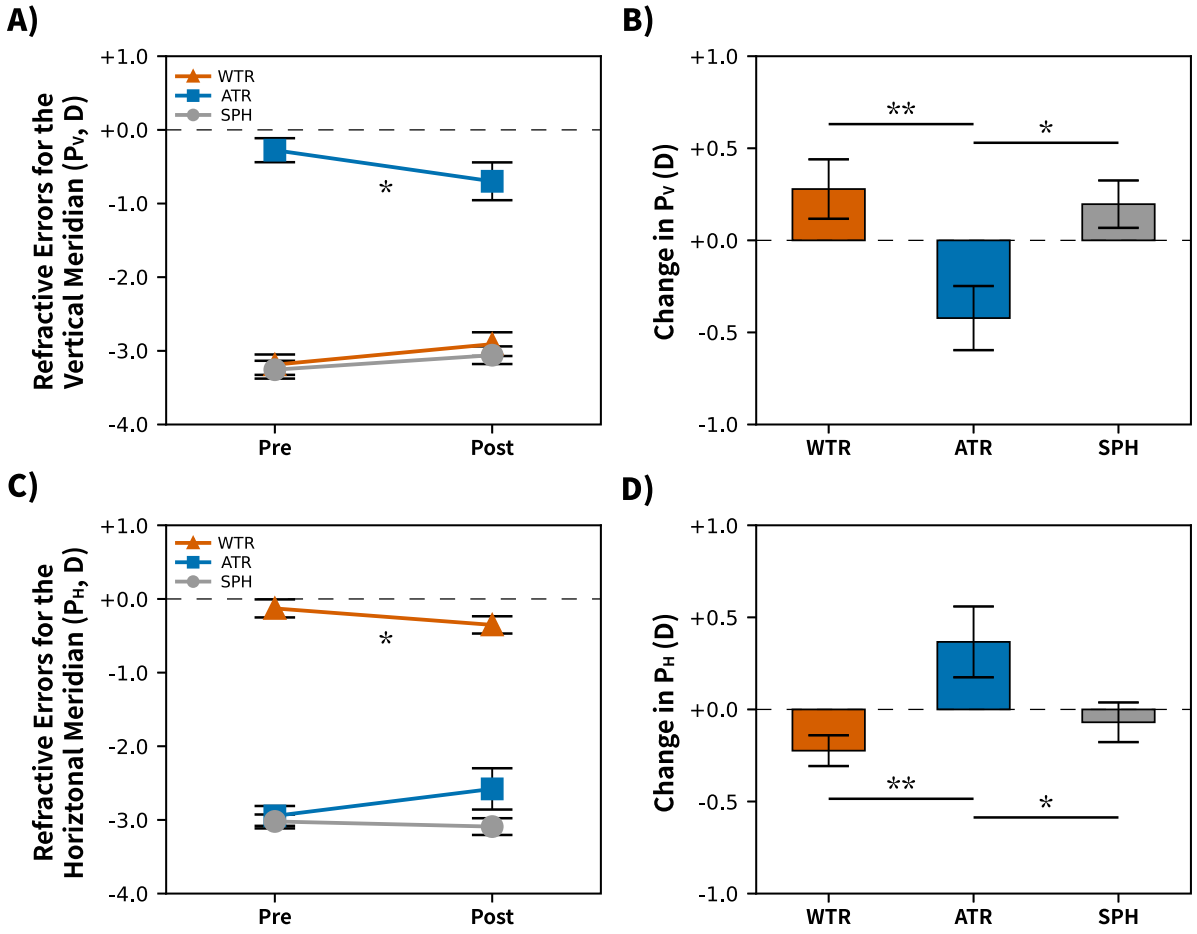

Figure 3. Effects of defocused conditions on interocular differences in refractive errors for vertical (P_V) and horizontal meridians (P_H; mean ± SEM). (**A, C**) Interocular differences in refractive errors for **A** vertical and **C** horizontal meridians measured before (pre) and after (post) an hour of exposure to WTR, ATR, and SPH defocused conditions. (**B, D**) The change in refractive errors for **B** vertical and **D** horizontal meridians (post – pre) under the three defocused conditions. Paired *t*-tests were used in **A** and **C** and Bonferroni post hoc tests in **B** and **D**, * $P < 0.05$, ** $P < 0.01$.

3 defocused conditions (repeated-measures ANOVA, $F(2, 36) \leq 1.02$, $P \geq 0.37$).

Changes in Meridional Refractive Errors After Watching Video Under Defocused Conditions

Further analysis of refractive errors for vertical (P_V) and horizontal meridians (P_H) revealed that the changes in J0 astigmatism in the WTR and ATR conditions were attributable to a bidirectional shift in meridional refractive errors, but this shift only reached statistical significance along the less myopic meridian (see Table 3). In the WTR condition, refractive errors for the horizontal meridian (i.e. less myopic meridian) became more negative, shifting from −0.13 ± 0.12 to −0.35 ± 0.12 D (Fig. 3C; paired *t*-test, paired $t(18) = -2.68$, $P = 0.02$). In contrast, refractive errors for the vertical meridian (i.e. more myopic meridian) became less negative, shifting from −3.19 ± 0.14 to −2.91 ± 0.16 D, although the

change was not statistically significant (see Fig. 3A; paired $t(18) = 1.727$, $P = 0.10$). In contrast, in the ATR condition, the refractive errors for the vertical meridian (i.e. less myopic meridian) became more negative (see Fig. 3A; from -0.28 ± 0.16 to -0.70 ± 0.26 D), whereas the horizontal meridian (i.e. more myopic meridian) became less negative (see Fig. 3C; from -2.95 ± 0.13 to -2.58 ± 0.28 D). However, only the change in the vertical meridian reached statistical significance (paired $t(18) = -2.42$, $P = 0.03$; horizontal = paired $t(18) = 1.91$, $P = 0.07$). The changes in refractive errors for neither the horizontal nor vertical meridian was significant under SPH conditions (paired $t(18) \leq 1.53$, $P \geq 0.14$).

Figures 3B and D illustrate the significant impacts of defocused conditions on the changes in refractive errors for the vertical and horizontal meridians (post – pre; repeated-measures ANOVA, $F(2, 36) = 6.462$ and 5.92, $P < 0.01$). The change for the vertical meridian was more negative in the ATR condition than in the WTR and SPH conditions (Holm-Bonferroni post hoc tests; ATR versus WTR = paired $t(18) = -3.29$, $P < 0.01$; and ATR versus SPH = paired $t(18) = 2.90$, $P = 0.01$), whereas the horizontal meridian was more positive in the ATR condition than in the WTR and SPH conditions (Holm-Bonferroni post hoc tests, ATR versus WTR = paired $t(18) = -3.32$, $P < 0.01$; and ATR versus SPH = paired $t(18) = 2.45$, $P = 0.04$). There were no significant differences in the changes in meridional refractive errors between the WTR and SPH conditions (Holm-Bonferroni post hoc tests, paired $t(18) \leq 0.87$, $P \geq 0.39$).

Discussion

This study revealed bidirectional, compensatory changes in the J0 astigmatic component after young participants were exposed to WTR and ATR astigmatic blur for an hour. The significant reduction in J0 astigmatism was equivalent to 0.50 DC (clinical cylindrical power) for the WTR condition and 0.78 DC for the ATR condition. In both conditions, the changes in J0 astigmatism exceeded the instrumental repeatability of Shin-Nippon open-field autorefractor (95% limits of agreement for J0 = $\pm$ 0.21 D),[39] suggesting that the findings were not simply due to instrumental variations between repeated measures. The changes in J0 astigmatism in both the WTR and ATR conditions were accomplished by a bidirectional shift of refractive power for the horizontal and vertical meridians, but, statistically, it was only significant for the meridian with less myopia. Apparently, astigmatism compensation and the shift in meridional refractive errors were more pronounced in the ATR condition than in the WTR condition. As shown in animal studies, the orientation of the imposed astigmatism is a factor influencing the magnitude of compensation, but the induced astigmatism in chicks was higher when rearing with WTR than with ATR astigmatic defocus, which is opposite to the trend observed in the current study.[25–27] However, it should be noted that the J0 astigmatism compensation, in terms of magnitude, was not significantly different between the two astigmatism conditions (Paired *t*-test, paired $t(18) = 0.720$, $P = 0.481$), so the effect of orientation on the rate of compensation cannot be concluded in the current study. To date, only one study has reported short-term, posterior anatomic change in human eyes after participants were exposed to monocular astigmatic blurs for 60 minutes.[31] Specifically, this study aimed to determine the choroidal thickness change in response to astigmatic blur and to correlate the choroidal change with axial myopia development. Thus, the current study provides the first evidence that in response to optically imposed astigmatic blur, treated eyes of young participants are capable of developing compensatory refractive change to partially counterbalance the cylindrical error within an hour.

The induced bidirectional, compensatory astigmatic change cannot be explained by the optical effects potentially arising from the misalignment of the tested eye and the trial lens. To exclude this possibility, the effect of lens tilt on the measured refractive astigmatism was calculated using Keating's equation.[38] This calculation presumed either a pantoscopic tilt (due to tilting the chin up/down or the trial frame slipping off the nose; Supplementary Figs. S2B, S2C) or a head tilt (i.e. two eyes were not leveled; Supplementary Figs. S3B, S3C) when performing autorefraction through the trial lenses. As shown in Supplementary Figure S2A, pantoscopic tilt has minimal effect on J0 astigmatism, with less than 0.25 D change in J0 astigmatism with as much as 20 degrees tilt. Likewise, it requires at least 17 degrees head tilt to create a 0.25 D change in J0 astigmatism (see Supplementary Fig. S3A). These theoretical estimations indicate that pantoscopic or head tilts are unable to explain the bidirectional, compensatory J0 astigmatic changes induced by the experimental conditions. We also tested the short-term repeatability (10-minute interval) of our refractive-error measurement approach using an independent sample ($n = 8$; see Appendix for experimental procedures and results). The indistinguishable differences in refractions before and after this 10-minute interval further confirmed that the compensatory astigmatic change observed was unlikely to be attributed to the measurement errors.

The structural origin of the observed astigmatism compensation (i.e. cornea versus internal optics), was not determined in this study because objective refraction was performed directly over the trial lenses to avoid the potential decay of the induced refractive changes upon lenses removal. In this respect, it has been shown that although spherical defocus could induce bidirectional axial length changes, this ocular biometric change decreases rapidly, occurring within minutes after removing the defocus.[40] Furthermore, because this study included participants with spherical-equivalent errors which ranged from -4.75 to 0 D, it is unclear whether their uncorrected refractive error would interrupt astigmatism compensation had the corrective lenses been removed before performing autorefraction. Thus, a similar experimental setup to that of Delshad, Collins, Read, and Vincent[40] was adopted, in which the optical blur and/or optical correction was maintained throughout the entire experiment. The aim was to maximize the chance to detect even a minor change in the refractive state. However, because the objective refraction was conducted over the trial lenses, the keratometry readings obtained from the NVision-5001 autorefractor, which analyses the ring image reflected by the corneal surface,[41] could not reflect the participants' real corneal power as the image magnification (of the ring) induced by the trial lenses. Thus, the keratometry readings were not further analyzed in this study. Nevertheless, this study provides the first evidence of astigmatism compensation in human eyes. Future studies using custom optical systems that utilize beam splitters or hot/cold mirrors to bypass optical effect of the trial lenses could allow simultaneous measurement of refractive and corneal power changes and help to determine the structural origin of astigmatism compensation, as well as the time course of the compensation process.

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However, whereas more studies are warranted to investigate the structural origin of astigmatism compensation, according to evidence acquired earlier (see below), it is speculated that the astigmatism compensation is most likely attributable to changes in the cornea. Because population-based studies typically show high correlation between refractive and corneal astigmatisms in magnitude and vector components, refractive astigmatism is often believed to originate from the cornea.[12,42,43] As the cornea is the primary ocular refractive layer, contributing two-thirds of the total refractive power, a change in the anterior corneal surface, even in the order of microns as those observed in refractive surgeries[44] and orthokeratology,[45] can induce significant refractive changes. Nevertheless, the contribution of internal astigmatism, mainly originating from the crystalline lenses and partially from the posterior corneal toricity, should not be neglected. The disappearance of infantile astigmatism in human eyes[8] and refractive astigmatism development reported in animal eyes[26,27] were both shown to be accompanied by changes in corneal and internal astigmatism, suggesting the involvement of the cornea and crystalline lenses in astigmatism compensation.

Because corneal shape could be temporarily remodeled by the change in lid position associated with a downward gaze,[46,47] convergence,[48] and retraction with lid speculum,[49] it may be speculated that refractive astigmatism could be affected by the variation of eyelid tension during the experiment. However, we believe that lid tension could not explain the astigmatism compensation observed in the current study for several reasons. First, the magnitude of corneal astigmatic changes induced by downward gaze and convergence have been reported to be small (0.06 to 0.33 DC)[46–48] compared to the astigmatism compensation (0.50 DC and 0.78 DC for the WTR and ATR conditions, respectively) observed in the current study; second, during video watching, the screen was set at the eye level of the participants to maintain a straight gaze, preventing the potential effects of downward gaze; third, because baseline examination indicated all participants had healthy eyelids, the effect of lid position, if any, should have affected both eyes to the same extent; and, finally, because the control eye was corrected fully, no abnormal eye squeezing was observed during the experiment, nor did any of the participants report problems in seeing the screen.

In addition, whereas it is possible that monocular optical blur could disturb binocularity, deviation in ocular alignment, if any, cannot explain the astigmatism compensation. It should be noted that participants in this study had a low magnitude of heterophoria (mean = 2.1 ± 4.0Δ), and none had constant or intermittent heterotropia. A previous study has shown that ocular alignment determined by the Bagolini test was still preserved, even with the monocular imposition of up to three diopters of spherical or astigmatic defocus.[50] More importantly, horizontal ocular misalignment is the most likely direction of ocular deviation resulting from monocular optical blur due to a disruption of horizontal fusional vergence control. In this case, a relative ATR astigmatism would be induced in all three experimental conditions if objective refraction was determined at the horizontal peripheral visual field rather than the central visual field,[51] which cannot explain the bidirectional astigmatism compensation observed in the current study. Furthermore, as estimated by the second-order coefficient of the quadratic fit of peripheral J0 astigmatism,[51] 16 degrees of eccentricity (approximately 30 Δ of ocular deviation) are required to induce 0.25 D J0 astigmatism. To support our argument, our follow-up study also asked an independent group of participants to fixate either monocularly or binocularly during refractive-error measurement, and no differences were found between the two conditions (Appendix). Thus, the current results were unlikely to have originated from the induced off-axis astigmatism due to the disruption of binocularity.

Although the current experimental design cannot reveal the mechanism of astigmatism compensation, we speculate that the human retina may be capable of detecting orientation-selective astigmatic blur and alter its optical properties to compensate for the imposed astigmatism. A recent animal study, which involved destruction of retinal amacrine and bipolar cells by excitotoxin mixture, revealed that astigmatism compensation is mediated by the visual processing by the retina, as the cell obliteration confirmed halted astigmatism development.[52] It has been reported that the retina of many vertebrates, including primate,[53,54] cat,[55–57] rodent,[58–61] and rabbit,[62,63] comprises ganglion and amacrine cells that are orientation-selective, responding robustly to a preferred orientation, but weakly to the orthogonal one. Further studies are warranted to understand how the cornea, crystalline lens, and retinal signals interact and contribute to the refractive astigmatic changes after short-term exposure to astigmatic blur.

Although both WTR and ATR astigmatic conditions induced corresponding changes in refractive astigmatism, imposing spherical defocus with a plus lens (i.e. myopic defocus) did not cause a significant change in refractive components. This finding agrees with two previous studies, which showed that imposition of either +2.00 D myopic defocus over participants' distance refractive correction for 30 minutes,[64] or leaving mildly myopic participants (mean spherical-equivalent error = −1.85 D) uncorrected for 3 hours, thereby exposing the eyes to myopic defocus, resulted in no significant change in refractive error.[65] However, one human study reported that the axial length was temporarily shortened by 13 ± 14 μm after exposure to +3.00 DS myopic defocus for an hour,[19] and another recent study also found a significant change in choroidal thickness after exposing to +3.00 D myopic and astigmatic defocus (SPH = 8 ± 6 µm; WTR = +5 ± 5 µm; and ATR = −4 ± 6 µm).[31] Although axial biometry and spherical refractive errors were highly correlated,[66] the axial biometric changes reported in previous studies were too small to create a measurable spherical refractive-error change. Assuming every 100 μm change in axial length is correlated with a 0.24 D change in spherical-equivalent error,[67] a 13 μm shortening of the eyeball would result in approximately 0.03 D refractive change. Thus, even if human eyes do respond to imposed myopic defocus, the refractive magnitude correlated with ocular axial change is too small to be detected by autorefraction (minimum step size = 0.12 D). Our results suggest that whereas spherical defocus might only induce posterior biometric changes,[19,31] astigmatic defocus could temporarily modulate not only the posterior ocular biometry but also refractive astigmatism, which is likely to be originated from the anterior refractive components (i.e. cornea and crystalline lenses) as discussed above. More investigations on the anterior ocular biometric changes are required to ascertain our speculation.

This study demonstrated the short-term refractive changes of human eyes in response to imposed astigmatic defocus, but its generalizability may be subject to some limitations. First, this study tested WTR and ATR astigma-

tism, because they are the two most prevalent astigmatic subtypes observed in the Asian Chinese population.[68–71] Whether human eyes could also respond to astigmatism of oblique orientations remains unclear. Second, simple myopic astigmatisms (with plano-cylindrical lens) were imposed in this study, such that the induced astigmatic image foci were formed either on or in front of the retina, preventing possible ocular accommodation if the image plane fell behind the retina (hyperopic condition). However, infantile astigmatism is often accompanied by hyperopia.[5,6,8] Therefore, the study should be interpretated with caution with respect to generalizing the results to the disappearance of infantile hyperopic astigmatism during refractive development. Because the current study only investigated short-term refractive changes, whether the results could reflect a long-term refractive compensation is yet to be determined. Third, the imposed J0 astigmatism was significantly lower than expected by 0.17 D in the ATR condition. It should be noted that the power of the trial lenses required for each condition was calculated based on the subjective refraction data. The difference observed in the ATR condition could partly be related to the maximum plus/maximum acuity subjective refraction method, by which the astigmatic error (26% had WTR astigmatism and 53% had no astigmatism) could be underestimated compared to the autorefraction value. In addition, as the calculated trial lens powers were rounded to the nearest 0.25 D, the rounding errors might also contribute to the power differences. Nonetheless, the difference in J0 astigmatism was relatively small compared to the imposed astigmatism. Moreover, because the same set of trial lenses was used before and after video watching, it would not affect the interpretation of the results using a repeated measures experimental design. Finally, the participants were young myopic adults whose eyes should be fully developed. It is unclear whether children, whose eyes are still undergoing active structural changes, would exhibit similar astigmatism compensation as observed in the current study.

In conclusion, the bidirectional changes in the J0 astigmatic component induced by 1 hour of astigmatic blur suggest that the human eye can, at least partially, compensate for optically imposed WTR and ATR astigmatism. Given the fact that astigmatism in pediatric patients is often left uncorrected or only partially corrected,[72,73] further studies are strongly warranted in order to determine whether and how this short-term astigmatic compensatory response could interfere with refractive development in children.

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Appendix

Short-Term Repeatability of Autorefraction Under Different Defocus and Fixation Conditions

Eight young adults (female: male = 3:5; age = 19 to 25 years; spherical-equivalent errors = –1.91 ± 0.35 D; and cylindrical errors = –0.25 ± 0.09 D) were recruited for this short-term repeatability study. Open-field autorefraction was performed under four defocus conditions (fully corrected, WTR astigmatism = +3.00 DC × 180 degrees, ATR astigmatism = +3.00 DC × 90 degrees, and SPH = +3.00 DS) and two fixation conditions (binocular and monocular). In the monocular fixation condition, the non-testing contralateral eye was occluded during refraction. Identical to the study described in the main text, defocuses were imposed over the distance prescription obtained from subjective refraction in either the right or left eye (selected randomly), whereas the fellow eye was fully corrected. The sequence for defocus and fixation conditions were randomly assigned. All measurements were repeated after 10 minutes, and the change in interocular differences in refractive errors (second trial – first trial) was calculated as described in the Methods section. Supplementary Table 1 summarizes the results of J0 astigmatism, the primary measurement outcome of this study. One-sample *t*-tests indicated that none of the conditions was significantly different from zero ($t(7) \leq 1.65$, $P \geq 0.14$). Repeated-measures ANOVAs also showed no significant effect of defocus condition (repeated-measures ANOVA, $F(3,21) = 0.30$, $P = 0.82$), fixation condition ($F(1,7) = 2.29$, $P = 0.17$), nor their interaction ($F(3,21) = 0.84$, $P = 0.49$).

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