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Anisometropic Amblyopia: Interocular Contrast and Viewing Luminance Effects on Aniseikonia

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Purpose: To demonstrate an aniseikonia test for anisometropic amblyopia (ATAA) that uses variable viewing luminance at different interocular contrast levels.

Methods: The test consists of a direct size comparison task based on a computer. The subject is asked to adjust the size of a dichoptically dissociated paired square target. One square was always presented at 100% contrast to the amblyopic eye/nondominant eye, whereas its counterpart was presented to the fellow eye at six contrast levels. Measurements were performed at two luminance backgrounds: (1) a white square on a black background (WoB) and (2) a black square on a white background (BoW). To test the feasibility of this approach, 16 patients with anisometropic amblyopia and 23 normal controls were recruited.

Results: The Aniseikonia Index (AI) calculated from the ATAA increased when the difference in the interocular contrast increased in both the patients with anisometropic amblyopia and controls under BoW and WoB conditions. The mean AI differed dramatically between the BoW and WoB conditions in patients with amblyopia but not in normal subjects.

Conclusions: Our model predicted interocular differences in contrast to the measurement of aniseikonia. Execution of the AI in individuals with amblyopia should consider that their responses to different luminance viewing conditions could be asymmetric.

Translational Relevance: The ATAA has the potential to optimize optical correction for the management of aniseikonia in individuals with anisometropic amblyopia.

Introduction

Aniseikonia is a common binocular anomaly in which the right and left eyes perceive the same object as exhibiting a different size and/or shape.[1–4] This inequality in image perception between the two eyes can occur when there are large differences in the optics of the eye, in the distribution of retinal receptors, or in the magnification of cortical processing.[1,5–10] These differences can lead to visual discomfort[11,12] or even impair binocular functions, such as stereoacuity and interocular suppression.[4,13–17] The majority of instances of aniseikonia are induced when an anisometropic refractive error is corrected using spectacle lenses. There are clinical means that can minimize aniseikonia, including refractive surgery or the use of contact lenses.[5] Spectacle wear, however, is purposefully selected in children because it is noninvasive and can be easily modified as he or she outgrows the old refractive correction.[18–20]

Currently, the New Aniseikonia Test[21,22] and the Aniseikonia Inspector[17,23] are commercially available tests for the detection of aniseikonia. However, no tests assess the symptoms experienced by patients suffering from anisometropic amblyopia. Optical correction for any anisometropia is the first step in standard amblyopia treatment.[20,24] At least two-thirds of patients with amblyopia have anisometropia; thus, we may expect the true prevalence of aniseikonia in this population to be high. Aniseikonia assessment has therefore become an important tool to optimize optical correction in these cases, in which eye care practitioners can judiciously initiate patching and vision therapy

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(perceptual learning, video games) after prescribing optical correction for amblyopia management.

Anisometropic amblyopia is a visual neurodevelopmental disorder caused by abnormalities, including binocularity deficits and suppression.[25–27] Most aniseikonia tests use anaglyphic filters to disassociate targets.[28] These techniques work well on people with normal binocular vision; however, patients with amblyopia may struggle to see targets shown to the amblyopic eye, making direct comparison of image sizes difficult.[24] Recent research has shown that adjusting the contrast and/or luminance of the image presented dichoptically to each eye can overcome this suppression, allowing both targets to become simultaneously visible.[24–27] Furthermore, when background luminance changes, the difference in binocularity caused by amblyopia is likely to alter the difference in the image size between the two eyes. Here, we present a method for testing aniseikonia by varying the intraocular contrast differences and luminance backgrounds and preliminary evaluate the potential of this test for managing anisometropic amblyopia.

Methods

Apparatus

The programs used in the experiment run on a computer monitor (ASUS VG278HE, monitor size: 29 inches, refresh rate: 144 Hz, resolution: 1920 × 1080, luminance range: 1 cd/m^2–125 cd/m^2). Paired square targets were presented at 2.0-degree field eccentricity as the stimulus. To dissociate the right and left images, each eye viewed the target through a stereo shutter goggle (NVIDIA 3D VISION2). Subjects were seated 1.8 m away in front of the screen with the room lights off. A forehead rest was used to control viewing posture.

Heterophoria Calibration

An alignment task was completed before the aniseikonia test for anisometropic amblyopia (ATAA) was performed. Each eye saw one-half of a cross-shaped target. The targets were shifted relative to each other until a complete cross (+) was assembled. The subjects were encouraged to fixate on the central cross to avoid image fusion (Fig. 1).

The ATAA Test

All subjects wore their correction spectacles under three-dimensional shutter glasses during testing.

The square target was displayed against one of two possible backgrounds: total darkness (luminance: 1 cd/m^2) or pure white (luminance: 125 cd/m^2). In this study, maximum luminance was defined as 100% contrast displayed against a black background, while minimum luminance was achieved using a white background. We used relative values rather than Weber contrast to define the contrast ratio. The 100% contrast represents the extreme luminance (maximum or minimum) that the computer monitor could achieve.

The task required the subject to enlarge or shrink the dimensions of a square via a keyboard until the two squares were perceived to be equal in size. At the end of each adjustment, the subjects were instructed to press the space bar as a confirmation for the test program to change to the next comparison task. Measurements were repeated five times under each of the six contrast settings. All contrast settings, initial sizes, and positions of the square were randomly presented by the computer. The ATAA randomly displayed the two luminance backgrounds during separate measurements. The first measurements were not inspected until the second tests had been completed. Each subject completed a total of 60 sessions to achieve task completion consisting of 6 contrasts under 2 possible background settings.

Key Index Definition

The Aniseikonia Index (AI) was defined as the percentage difference in the actual sizes of the two square targets when the individual perceived that the two targets were equal in size. This value is calculated as follows:

$$AI = \frac{Adjusted\ size - Fixed\ size\ \ (125\ pixels)}{Fixed\ size\ \ (125\ pixels)} \times 100\,\%$$

Aniseikonia is a binocular phenomenon and therefore a relative condition. Having an image that is 5% larger in the amblyopic eye than in the fellow eye is approximately analogous to stating that the image in the fellow eye is 5% smaller than the image in the amblyopic eye. By definition, the AI is expressed as the perceived difference in the size of the image relative to that observed by the amblyopic eye. In normal controls, the AI is expressed as the perceived difference in the size of the image relative to the nondominant eye.

If the results revealed that the image viewed by the amblyopic eye was perceived to be larger, the AI measurement was recorded as a plus value (AI $>$ 0), whereas if the results revealed that the image viewed by the amblyopic eye was perceived to be smaller, a negative value was recorded (AI $<$ 0) (Fig. 2).

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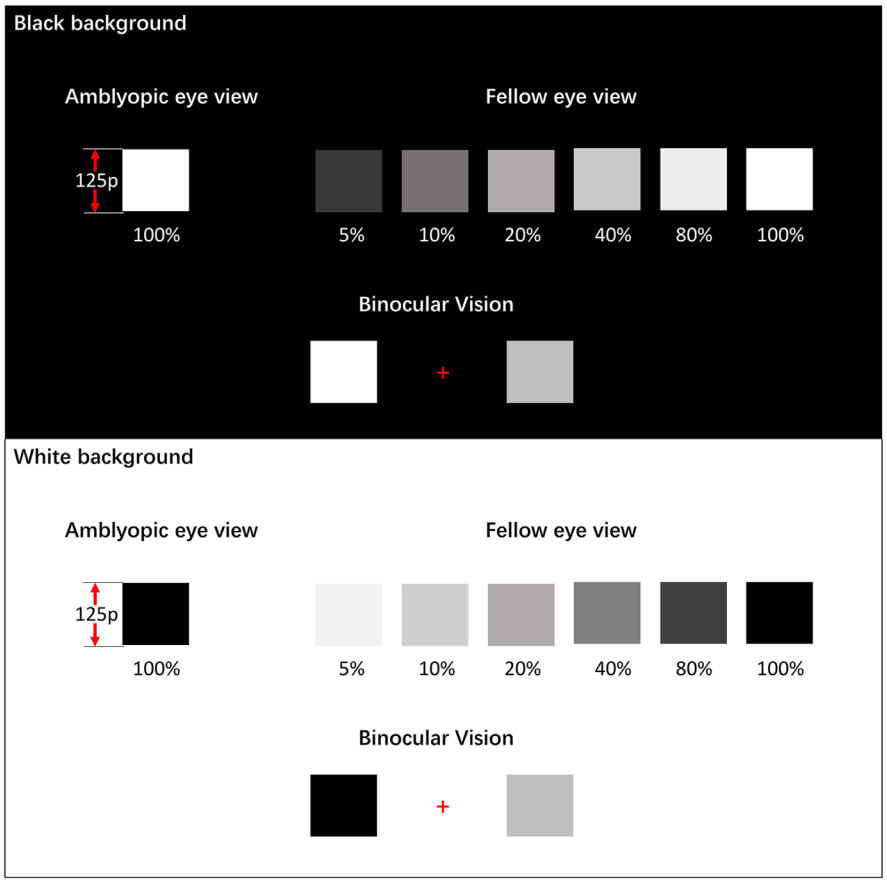

Figure 1. Schematic diagram of the ATAA. A white square on a black background (*top*) simulated the minimal viewing luminance condition, and a black square on a white background (*bottom*) simulated the maximum viewing luminance condition. During each presentation, one square with a constant size of 125 pixels was fixed at the 100% contrast and was viewed by the amblyopic/nondominant eye through a stereo shutter goggle while the fellow eye viewed squares with various contrast levels (5%, 10%, 20%, 40%, 80%, or 100%) with an adjustable size.

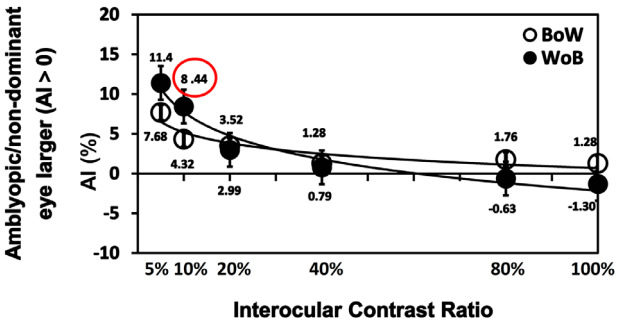

Figure 2. Example of aniseikonia assessment in a normal subject by the ATAA: The x-axis represents the contrast stimuli in the fellow eye, and the y-axis represents the averaged AI. When AI $>$ 0, the mean nondominant eye perceives images to be larger than they are in the dominant eye. As shown in the red circle, the AI in the 10% contrast under the WoB condition is 8.44, indicating that the nondominant eye perceived the image to be 8.44% larger than that observed by the dominant eye.

Procedure

In study 1, a total of 16 normal subjects underwent the ATAA and provided baseline results, and an additional 11 normal subjects and 10 individuals with amblyopia also finished the ATAA to determine whether it was feasible. First, the subjects repeated the test twice in two separate sessions at an interval of at least one day; this allowed us to estimate test-retest reliability. Second, we evaluated the validity of the test by comparing the measured aniseikonia percentages with the aniseikonia induced by lenses with magnifications of +1%, +3%, and +5% (PFO Global Inc., Dallas, TX). We verified that all of the lenses were correctly manufactured (the power factor was zero, and the shape factor was equal to the magnification). These lenses were inserted into the trial lens placed in front of the nondominant eye. The order of presentation

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Table 1. Clinical Details of Normal Participants

Observer	Age/Sex	Refraction	Correction Method	VA (RE)	VA (LE)	Dominant Eye
1	29/F	RE: −5.00–0.50 × 30 LE: −4.25–0.50 × 10	SP	0.00	0.00	RE
2	23/M	RE: −3.00–0.50 × 110 LE: −2.75–0.50 × 30	SP	0.00	0.00	RE
3	28/M	RE: −3.00–1.00 × 180 LE: −3.00–0.75 × 170	SP	−0.10	0.00	RE
4	28/M	RE: −5.00–0.50 × 160 LE: −5.00–0.50 × 30	SP	0.00	0.00	RE
5	29/M	RE: −0.50 LE: −1.50	SP	0.00	0.00	RE
6	20/M	RE: −3.00 LE: −2.25–0.75 × 165	SP	0.00	0.00	RE
7	21/M	RE: −3.75 LE: −3.50–0.25 × 95	SP	−0.10	−0.10	RE
8	26/M	RE: −3.50–0.25 × 80 LE: −2.50–1.25 × 160	SP	0.00	0.00	LE
9	23/M	RE: −3.00–0.25 × 90 LE: −2.75	SP	0.00	0.00	RE
10	21/M	RE: +0.25–0.25 × 15 LE: +0.50	SP	0.00	0.00	RE
11	21/M	RE: −0.25–0.25 × 15 LE: +0.50–0.50 × 170	SP	−0.10	−0.00	RE
12	29/M	RE: −0.50–0.25 × 145 LE: +0.25–0.25 × 115	SP	0.00	0.00	RE
13	14/F	RE: −4.50–0.25 × 90 LE: −4.25–0.25 × 125	SP	0.00	0.00	RE
14	15/F	RE: −5.50–0.25 × 180 LE: −5.25–0.25 × 170	SP	0.00	0.00	RE
15	13/F	RE: −1.00 LE: −0.25 × 120	SP	0.00	0.00	RE
16	23/M	RE: −4.00–1.00 × 10 LE: −5.00–0.25 × 180	SP	0.00	0.00	RE
17	13/M	RE: −1.50–0.75 × 175 LE: −1.25–0.75 × 165	SP	0.00	0.00	RE
18	12/F	RE: −2.25–1.00 × 90 LE: −2.50–0.50 × 115	SP	0.00	0.00	RE
19	13/M	RE: +0.50–0.50 × 5 LE: −0.50–0.25 × 135	SP	0.00	0.00	RE
20	14/F	RE: −3.00–1.00 × 180 LE: −3.00–0.75 × 170	SP	0.00	0.00	RE
21	15/F	RE: −1.25–0.50 × 180 LE: −1.75DS	SP	−0.10	0.00	RE

F, female; LE, left eye; M, male; RE, right eye; SP, spectacle; VA, visual acuity (LogMAR).

was randomized. In study 2, we evaluated the ATAA test in seven normal subjects who were subjected to monocular viewing conditions to eliminate the possible influence of monocular clues. In study 3, we evaluated the ATAA in 10 individuals with anisometropic amblyopia and compared the results with those obtained in the normal controls. In study 4, we evaluated the ATAA in six individuals with anisometropic

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Table 2. Clinical Details of the Subjects With Amblyopia

Case	Age/Sex	Refraction	Correction Method	VA (AE)	VA (Non-AE)	History
1	15/M	RE: +7.00–0.50 × 35 LE: +0.50 DS	SP	0.70	0.00	Glasses+patching
2	14/M	RE: +8.50–1.50 × 15 LE: +0.25 DS	SP	0.80	−0.10	Glasses+patching
3	16/M	RE: +5.75–2.50 × 170 LE: +0.25–1.00 × 175	SP	0.70	−0.10	Glasses+patching
4	14/M	RE: +1.25–0.50 × 180 LE: +9.00–1.75 × 180	SP	0.80	0.00	Glasses+patching
5	17/M	RE: +4.75–1.25 × 30 LE: Plano-0.50 × 5	SP	0.40	0.00	Glasses
6	28/F	RE: +4.75–0.75 × 20 LE: +1.00 DS	SP	0.70	0.00	Glasses
7	15/F	RE: +7.50–1.50 × 65 LE: +1.50–0.50 × 90	SP	0.40	0.00	Glasses+patching
8	21/F	RE: +3.75–0.75 × 110 LE: +1.25–1.00 × 45	SP	0.20	0.00	Glasses
9	17/M	RE: +7.50–1.75 × 25 LE: −0.25–0.50 × 175	SP	0.90	0.00	Glasses+patching
10	22/M	RE:+5.25+1.25 × 150 LE: −0.25–0.25 × 15	SP	0.80	0.00	Glasses

AE, amblyopic eye; non-AE, nonamblyopic eye.

Table 3. Clinical Details of the Subjects Who Use Different Correction Methods

Case	Age/Sex	Refraction	VA RE (SP)	VA LE (SP)	VA RE (CL)	VA LE (CL)
1	18/F	RE: −10.00–1.00 × 115 LE: −3.00DS	0.20	0.00	0.30	−0.10
2	10/F	RE: −2.50–0.75 × 170 LE: −13.50–1.50 × 140	0.00	0.30	0.00	0.20
3	15/F	RE: −14.50–2.00 × 5 LE: −8.00DS	0.10	−0.10	0.10	−0.10
4	15/F	RE: −2.00–0.75 × 95 LE: −9.50–2.00 × 15	0.00	0.40	0.00	0.30
5	8/M	RE: −5.75DS LE: −1.00DS	0.50	0.00	0.50	0.00
6	15/F	RE: −1.00–0.50 × 160 LE: −16.00–0.75 × 180	0.00	0.90	0.00	0.70

CL, contact lenses.

amblyopia; here, they were subjected to different refractive corrections.

Participants

A total of 37 participants were enrolled: 21 normal individuals (Table 1) and 10 amblyopic individuals (Table 2). In study 4, the ophthalmological characteristics of 6 individuals with anisometropic amblyopia who wear contact lenses are shown in Table 3. The participants were recruited from the Zhongshan Ophthalmic Center. The study followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from the participants or their parents after the nature and intent of the study were explained.

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In this study, amblyopia was defined according to the Preferred Practice Protocol of the American Academy of Ophthalmology.[29] Anisometropia was defined hyperopic anisometropic amblyopia with an interocular spherical equivalent refraction (SER) difference of ≥1.50 D. Myopic anisometropic amblyopia with an interocular SER difference of ≥−2.00 D. The normal group comprised participants with a best corrected visual acuity of at least 0.00 logMAR in each eye with normal ocular motor functions, stereoacuity of at least 40 seconds of arc, and an interocular SER difference of ≤1.00 D. All the amblyopic subjects underwent a complete strabismus and amblyopia workup, and none showed signs of strabismus or anomalous retinal correspondence based on the results of a cover/uncover test and a major amblyoscope examination, respectively. All participants had worn their spectacles/contact lens with a full optical correction for a minimum of 3 months before data collection. For normal participants, ocular dominance was subjectively assessed using the hole-in-card[30] test before the measurement.

Data Analysis

We used the AI, which is derived from the ATAA, to analyze aniseikonia. First, the AI between the different groups (contrast, backgrounds) was performed using analysis of variance (ANOVA) and paired *t*-test analysis. A P value of <0.05 was defined as statistically significant. Second, the test-retest reliability of the ATAA after performance in normal and amblyopia groups was plotted on a Bland-Altman plot for analysis[31] (GraphPad Prism 8). Third, the Pearson product moment correlation coefficient was used to evaluate the association between the AI and either the induced magnification or the visual acuity.

Results

Study 1: Preliminary Evaluation of ATAA

A total of 16 normal individuals were included in study 1 (Table 1). The results showed that as the stimulus interocular contrast ratio increased from 100:100 to 100:5, the AI monotonically increased for both the black and white luminance backgrounds (Fig. 3). The difference in the stimulus became larger as the ratio increased (e.g., 100:100 vs. 100:5). Moreover, as the intensity of the stimulus increased, the perceived size difference increased. This implied that a target with a lower contrast and viewed by the dominant eye would require a size magnification to compensate for the aniseikonic effects induced by imbalanced interocular contrast. The interocular difference in size perception began at a 40% contrast on a black background and a 20% contrast on a white background. In other words, in normally sighted participants without anisometropia, aniseikonia did not occur until the difference in the stimulus of the interocular contrast increased. ANOVA showed that there was no significant difference between the 80% and 100% contrast ($P > 0.05$), but the variance among the other groups differed significantly ($P < 0.05$). There was no significant difference in the average AI between the two backgrounds ($P > 0.05$).

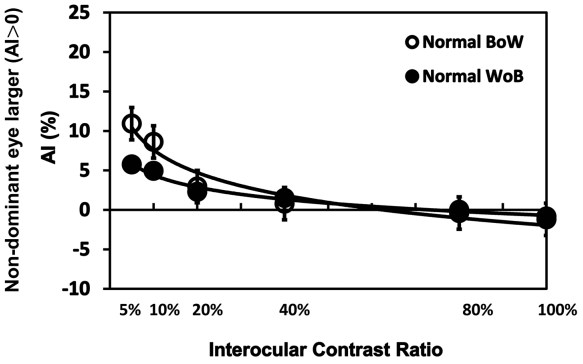

Figure 3. The AI measured in normal participants (N = 16) viewing the white background (BoW) and black background (WoB). The *black solid circles* correspond to the WoB results, and the *black hollow circles* correspond to the BoW results.

The Test-Retest Reliability of the ATAA

To examine the test-retest reliability of the AI values generated from the ATAA, 11 participants in the normal group and 10 participants in the amblyopia group underwent testing on two separate occasions. The results for the test-retest reliability are illustrated in a Bland-Altman plot, in which the differences (first test - second test) are plotted against the mean values for each subject.

In the normal group (Fig. 4), the mean differences between the first and second tests and the 95% confidence interval (CI) limits of agreement under the white square on a black background (WoB) at a contrast of 5%, 10%, 20%, 40%, 80%, and 100% were −0.582 (95% CI, 6.564 to −7.728), −0.044 (95% CI, 7.146 to −7.233), −1.396 (95% CI, 3.819 to −6.612), 0.16 (95% CI, 4.439 to −4.119), 0.466 (95% CI, 4.056 to −3.125), and −0.596 (95% CI, 3.832 to −5.025), respectively. The mean differences between the first and second tests under the black square on a white background (BoW) at a contrast of 5%, 10%, 20%, 40%, 80%, and 100%

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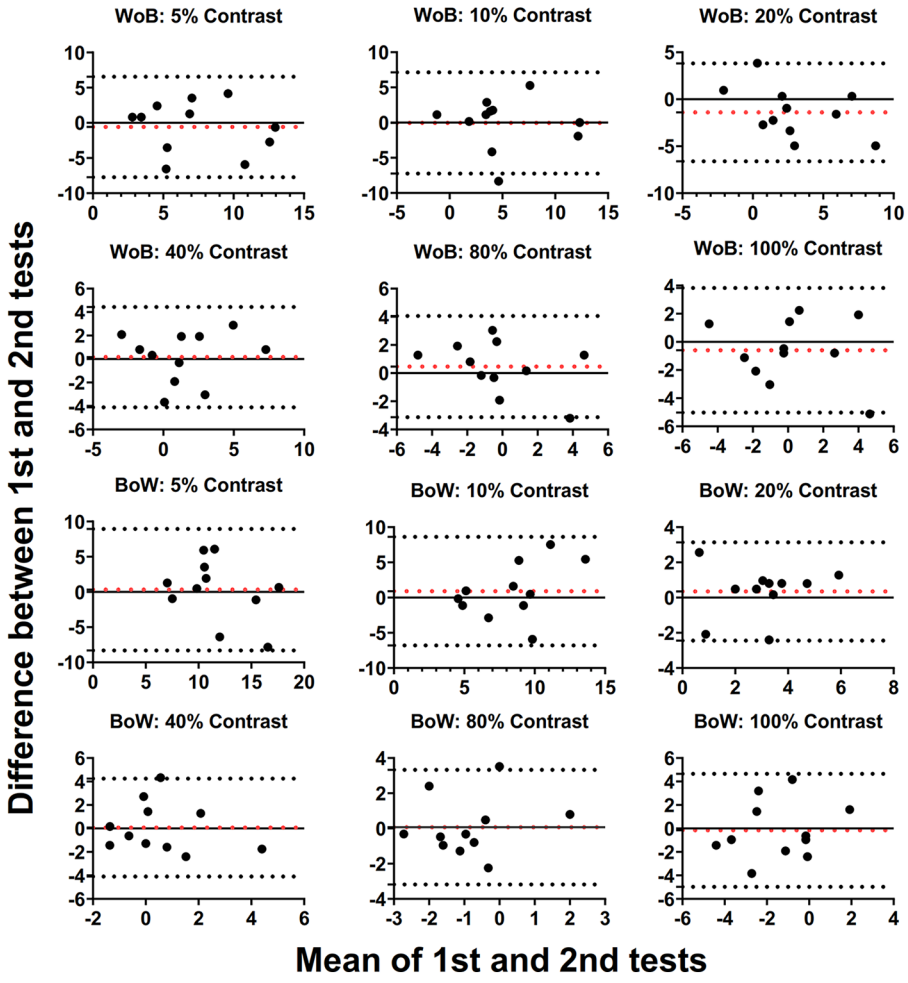

Figure 4. Bland-Altman difference plots of the normal group. Each *solid circle* indicates a date point from each subject. The *horizontal red dotted lines* represent a bias of the test, the mean difference value across normal participants.

were 0.32 (95% CI, 8.949 to −8.309), 0.916 (95% CI, 8.617 to −6.785), 0.349 (95% CI, 3.139 to −2.441), 0.073 (95% CI, 4.243 to −4.098), 0.073 (95% CI, 3.330 to −3.184), and −0.16 (95% CI, 4.658 to −4.978), respectively.

In the amblyopia group (Fig. 5), the mean differences between the first and second tests and the 95% CI limits of agreement under the WoB at a contrast of 5%, 10%, 20%, 40%, 80%, and 100% were −0.06 (95% CI, −7.126 to 7.006), 0.68 (95% CI, −7.539 to 8.899), −1.76 (95% CI, −8.912 to 5.392), −2.82 (95% CI, −12.03 to 6.387), −0.88 (95% CI, −9.502 to 7.742), and −1.76 (95% CI, −11.05 to 7.525), respectively. The mean differences between the first and second tests under the BoW at a contrast of 5%, 10%, 20%, 40%, 80%, and 100% were 2.81 (95% CI, −20.1 to 25.72), 2.391(95% CI, −13.77 to 18.55), −2.69 (95% CI, −10.29 to 4.906), −2.2 (95% CI, −16.92 to 12.52), −0.08 (95% CI, −8.589 to 8.429), and 0.51 (95% CI, −12.38 to 13.4), respectively.

Validity of the ATAA

The AI was measured by adding afocal size lenses (1%, 3%, and 5%) in front of the nondominant eye. The results showed that as the difference in interocular contrast increased, the AI induced by various power magnifications also increased under both WoB and BoW conditions, as shown in Figure 6. Although less pronounced, the same tendency was observed for agreements among the three afocal lenses as well as at baseline (without afocal lenses) when the AI was measured under both WoB and BoW conditions. We applied a linear regression analysis, and a strong negative correlation was found between the mean

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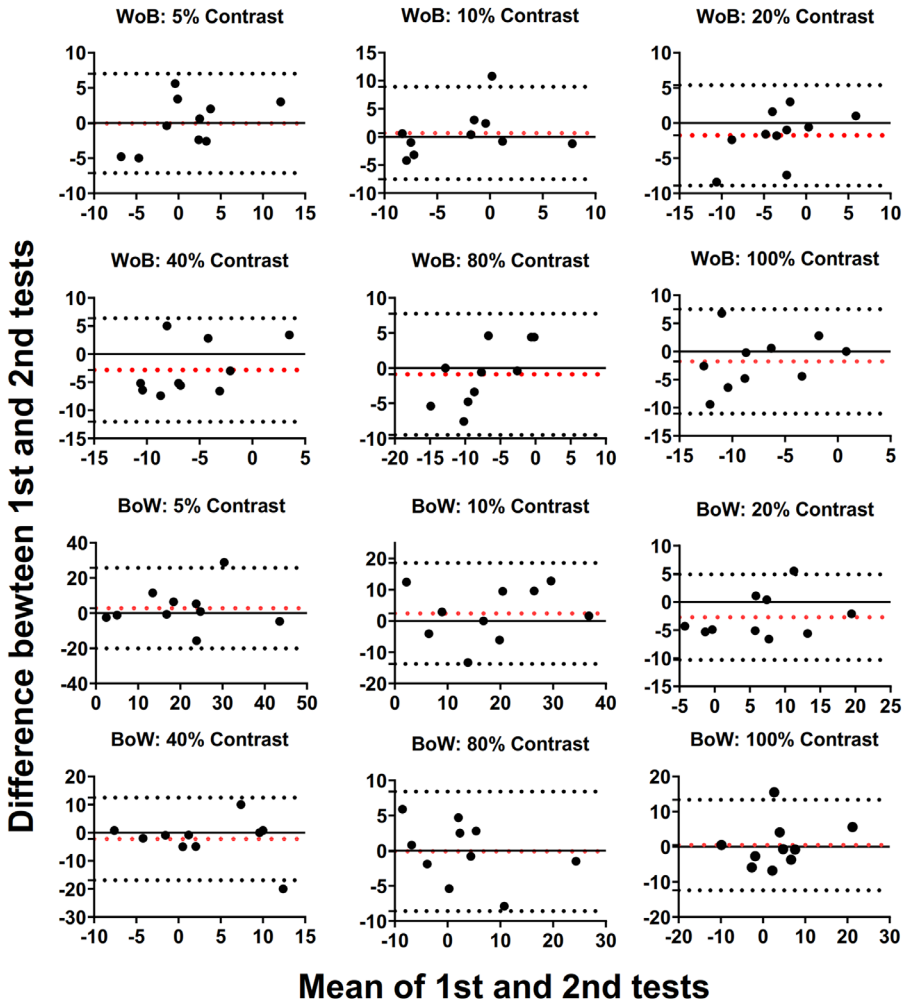

Figure 5. Bland-Altman difference plots of the amblyopia group. Each *solid circle* indicates a date point from each subject. The *horizontal red dotted lines* represent a bias of the test, the mean difference value across amblyopia participants.

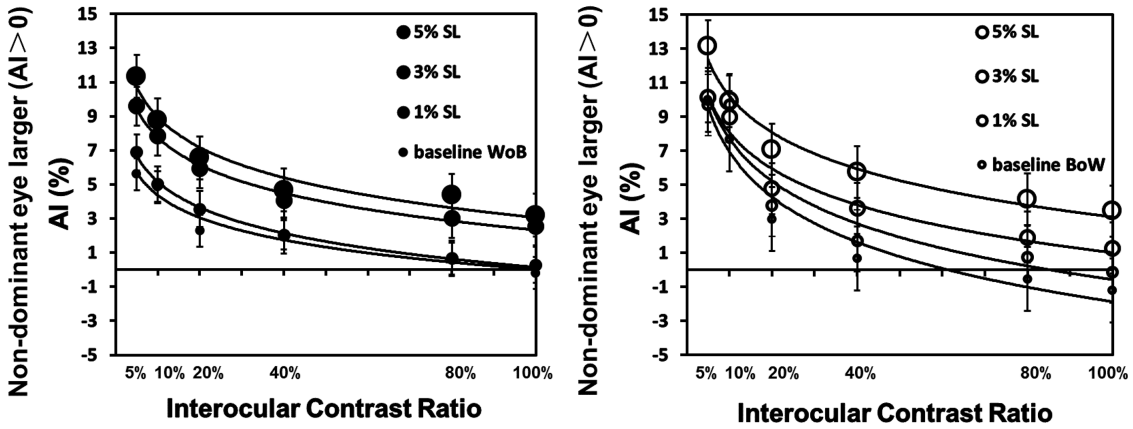

Figure 6. *Left*: Size lenses induced AI on WoB. *Right*: Size lenses induced AI on BoW.

measured AI and the induced magnification in the normal subjects; however, the slope deviated significantly from 1 at a 10% contrast on a white background ($P > 0.05$) (Table 4). When aniseikonia was induced through afocal lenses of known magnifications, the observed aniseikonic effects followed our expectations.

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Table 4. Aniseikonia Measurements vs. Lens-Induced Magnification

	Black Background						White Background					
Contrast	5%	10%	20%	40%	80%	100%	5%	10%	20%	40%	80%	100%
Mean slope	1.113	0.934	0.753	0.665	0.924	0.731	0.945	0.051	0.902	1.102	0.927	0.982
R2	0.985	0.92	0.901	0.904	0.975	0.905	0.849	0.038	0.949	0.999	0.967	0.986

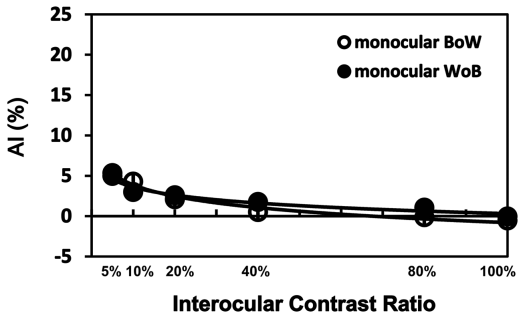

Figure 7. Measured AI in normal participants viewing both black and white backgrounds under monocular viewing conditions.

Study 2: ATAA Under Monocular Viewing Conditions

All subjects (N = 7, 14 eyes, age range: 13-29 years old, mean age: 21 ± 6 years) wore their corrective eyewear while one eye was occluded with a patch. The order in which eyes were tested was randomized. There was no significant difference in the average measurements obtained between the two backgrounds ($P > 0.05$) (Fig. 7).

Study 3: ATAA in Anisometropic Amblyopia

Similar to the control group, the amblyopia group (Table 2) showed an increase in stimuli (100% to 5%) as the AI increased (Fig. 8). At lower contrast, the amblyopic eye perceived the target to be larger than that viewed by the fellow eye. ANOVA revealed that there was no significant difference between 80% and 100% contrast ($P > 0.05$); however, the variance was significant among the other groups ($P < 0.05$) for different luminance backgrounds. We then compared the differences in the AI between individuals with hypermetropic anisometropic amblyopia and normal participants (Fig. 9). While the average AI differed dramatically between the WoB and BoW conditions in individuals with amblyopia ($P < 0.05$), no such difference was observed in the normal controls. This asymmetry of the AI was significantly different in groups between 80% and 5% contrast; 80% and 10% contrast; 40% and 5% contrast; 20% and 10% contrast; 20% and 5% contrast; and 40% and 10% contrast ($P < 0.05$).

Study 4: ATAA Under Different Correction Methods

Figure 10 shows the AI measured in all six observers (Table 3) who wore corrective contact lenses or spectacles. The results for contact lens wearers showed that the AI increased as the difference in the contrast increased under both WoB and BoW conditions. The average AI, however, differed dramatically under these two conditions ($P < 0.05$). A comparison of aniseikonia between corrective contact lenses and spectacles revealed that a small amount of aniseikonia was caused when wearing corrective contact lenses to view targets on either a black or a white background.

Visual acuity and AI

Pearson correlation analysis was used to compare the correlation between the difference in visual acuity (LogMAR) and image inequality in patients with anisometropic amblyopia. The results showed that there was no significant correlation between vision difference and the AI asymmetry in patients with hyperopic anisometropia amblyopia under the black and white background ($P > 0.05$) (Fig. 11).

Discussion

The aim of this study was to develop a novel test, the ATAA, to evaluate aniseikonia in patients with anisometropic amblyopia. In view of the potential benefits afforded by correction of aniseikonia, a recent study called for routine clinical assessment of aniseikonia in patient with anisometropic amblyopia.[24] Most of the common techniques require direct comparison of images seen by each eye thus cannot be applied in amblyopia. In the present study using the ATAA and carefully controlled interocular contrast, all participants with amblyopia perceived the targets simultaneously and finished the comparison test. When the interocular contrast changed, the same trend toward contrast-induced aniseikonia was share by participants with amblyopia and the normal control participants.

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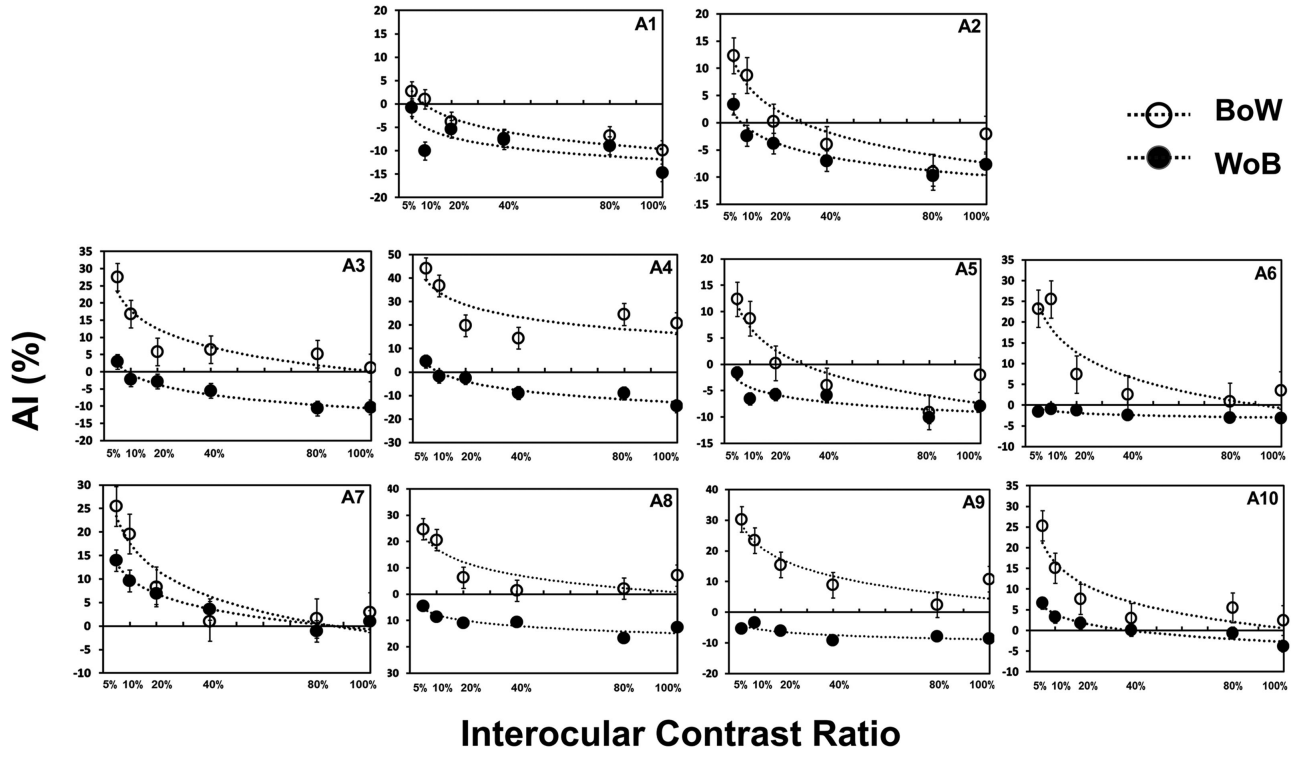

Figure 8. Estimated AI obtained with the ATAA, A1-A10, anisometropic amblyopia observers.

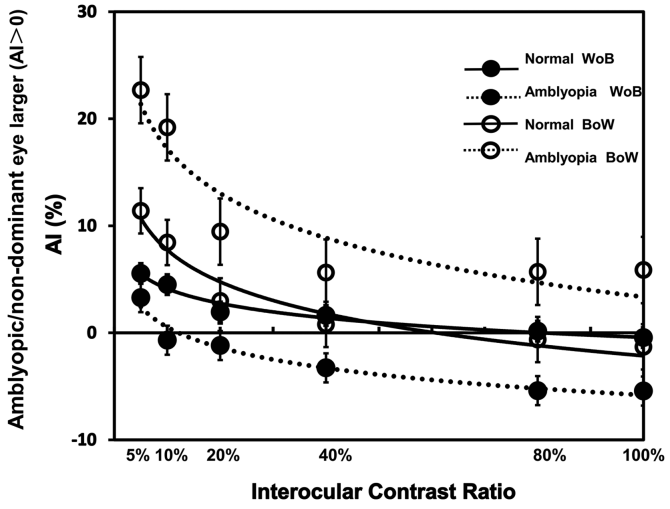

Figure 9. Comparison of the averaged AI between the amblyopia group (N = 10) and control group (N = 16) under WoB and BoW conditions.

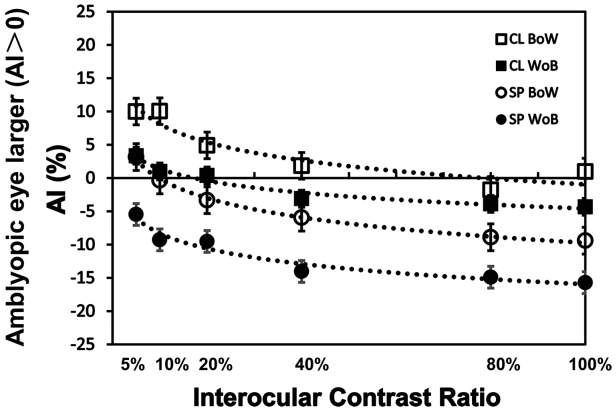

Figure 10. Comparison of the AI on WoB or BoW between individuals with anisometropic amblyopia who wear contact lenses or spectacles.

But the aniseikonia effects in the presence of black and white backgrounds differed in amblyopes.

Aniseikonia can arise from a variety of physiological, optical causes, retinal, and neurological.[1,5–10] This asymmetric response to different luminances could not be explained as an optical factor. Even after the refractive correction was changed, these results persisted. Luminance change as a postoptical factor related to "neuro-aniseikonia" seems to play an important role in amblyopia. It proves that even though the theoretical values of aniseikonia can be calculated from the formula, higher visual processing interprets this information beyond the scope of theoretical optics in the human eye. This is why subjective testing of aniseikonia is the only way to measure the overall perceived amount of aniseikonia. The expected magnification effects are difficult to estimate because the calculated theoretical

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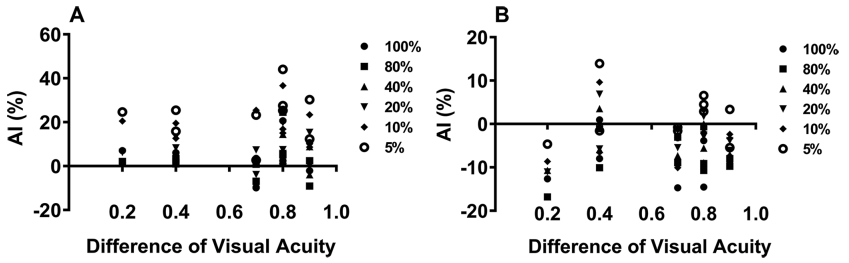

Figure 11. (A) Correlation between aniseikonia and the difference in visual acuity on WoB in individuals with amblyopia. (B) Correlation between aniseikonia and the difference in visual acuity on BoW in individuals with amblyopia.

values as an optical factor cannot represent actual performance. The cause of the perceived asymmetrical size differences under dark/bright target conditions in amblyopia is still unknown. We are aware that possibilities such as abnormal binocularity and interocular suppression play a key role in amblyopia.[32–35] Hence, the presentation of images with different sizes creates binocular rivalry between the two eyes. The interocular differences that produce rivalry can produce search asymmetries, but these effects are relatively weak.[36,37] Recently, Kremkow[38,39] proposed an attractive theory to explain the asymmetry in perceived size differences between dark and bright targets. Another potential explanation could be differences in the responses of an amblyopic visual system to dark or light exposure.[40,41] This novel finding indicates that when obtaining aniseikonia measurements in individuals with anisometropic amblyopia, clinicians should not simply consider a fundamental logical optical prediction.

The limitations of our study are as follows. First, the sample size was small. Second, our purpose was to measure aniseikonia in amblyopia, but in patients with severe suppression, aniseikonia could still be challenging to assess. Based on the results presented in this study, we propose that future work should explore this concept in contrast to the luminance-related aniseikonia paradigm in amblyopia. Obtaining additional information on the AI in a larger sample size and more diverse population groups with anisometropia would add fundamental value to the work presented here. Nonetheless, the study results open up new methods for testing aniseikonia with implications for future treatment of anisometropic amblyopia.

In conclusion, to the best of our knowledge, this is the first study to show a comprehensive method of measuring aniseikonia, which may be potentially used for clinical evaluation and applied in the optical treatment of patients with anisometropic amblyopia. The measurements obtained from the ATAA can also predict the amount of aniseikonia that could be experienced by amblyopic individuals during dichoptic contrast balance training. This will likely be an option for the treatment of anisometropic amblyopia to alleviate suppression.[42] However, we also suggest that there is potential to consider applying luminance differences to control aniseikonia effects when determining treatment outcomes.

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