On the Maintenance of Normal Ocular Dominance and a Possible Mechanism Underlying Refractive Adaptation

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Purpose. Do humans with uncorrected anisometropia who have not developed anisometropic amblyopia exhibit a shift in ocular dominance nonetheless, reflecting a more subtle form of deprivation? Also, is such a change in dominance, if it occurs, permanent or could it be rectified by an extended period of optical correction?

Methods. A total of 25 normal controls (27.5 ± 2.1 years; mean ± SD); 28 anisometropes (20.7 ± 5.6 years) who were fully corrected for more than 16 weeks prior to this investigation; and 24 anisometropes who had never been corrected (21.2 ± 9.8 years) participated in this study. Sensory eye dominance of observers was measured using the binocular phase combination paradigm to find an interocular contrast ratio at which the contributions of each eye to the binocularly fused percept were equal (i.e., the balance point measure of ocular dominance).

Results. Controls exhibited a balance point close to unity (0.91 ± 0.05), while the two groups of anisometropes exhibited a clear binocular imbalance (uncorrected anisometropes, 0.51 ± 0.28; corrected anisometropes, 0.70 ± 0.19); both were significantly different from controls ($P < 0.001$). The imbalance was less severe in corrected anisometropes compared with uncorrected anisometropes ($P = 0.004$).

Conclusions. We find that anisometropia is associated with an ocular imbalance even in the absence of amblyopia. This abnormality is weaker in anisometropes who have worn an optical correction for some time, suggestive that a better optical status leads to a better binocular status.

Keywords: anisometropia, ocular dominance, refractive adaptation

In humans, uncorrected anisometropia early in life can lead to anisometropic amblyopia in the more ametropic eye and result in a shift in ocular dominance toward the more emmetropic eye.[1] However, we don't know what comes first. We sought to answer the following questions: Does the anisometropic amblyopia produce the change in ocular dominance or is the change in ocular dominance produced by the anisometropia, which in turn leads to anisometropic amblyopia? Do humans with uncorrected anisometropia who had not developed amblyopia exhibit a shift in ocular dominance nonetheless, reflecting a more subtle form of deprivation for binocular vision? Such a result would suggest that the ocular dominance deficit might predate the amblyopia. If this is the case, then it raises an additional question: Is the deficit less severe in observers who have undergone a sustained period of optical correction? These questions have clinical implications for our understanding of the role played by spectacle adaptation in binocular vision.

We conducted a cross-sectional cohort study and quantitatively assessed the sensory eye dominance using a binocular phase matching task[2] in a group of uncorrected anisometropes who had never been corrected (except during the actual measurements) and a group of anisometropes who had been wearing their appropriate full refractive correction all day (and so were refractively adapted)[3] for at least 16 weeks prior to the investigation.

Methods

Participants

This study contains three groups: normal controls ($n = 25$, mean age: 27.5 ± 2.1 years); corrected anisometropes (having more than 16 weeks of refractive adaptation; $n = 28$; mean age: 20.7 ± 5.6 years); and uncorrected anisometropes (with no refractive adaptation; $n = 24$; mean age: 21.2 ± 9.8 years). Anisometropes were recruited from the department of ophthalmology of the First Affiliated Hospital of Anhui Medical University (Anhui, China); normal controls were students from Anhui Medical University.

A comprehensive eye examination was carried out by a clinician at the First Affiliated Hospital of Anhui Medical University, including: best-corrected visual acuity (BCVA) testing (Tumbling E chart); cycloplegic refraction; stereopsis (Random Dot Stereograms); and cover test at near and distance fixation. All participants had normal or corrected to normal visual acuity (no greater than 0.09 logMAR) in the two eyes; no anisometropic amblyopia (defined as a two-line or greater

Table. Summarized Clinical Details for the Three Groups

Clinical Details	Corrected Anisometropes	Uncorrected Anisometropes	Normals
Number	28	24	25
Age, y			
Mean ± SD	20.7 ± 5.6	21.2 ± 9.8	27.5 ± 2.1
Median, *n* (range)	19 (12 to 36)	18 (10 to 43)	28 (22 to 30)
Sex			
Female	10	9	17
Male	18	15	8
Visual acuity without correction, logMAR			
Mean ± SD			
Dominant eye	0.6 ± 0.4	0.2 ± 0.4	0.3 ± 0.5
Nondominant eye	1.1 ± 0.4	0.9 ± 0.3	0.4 ± 0.5
Median, *n* (range)			
Dominant eye	0.6 (0 to 1.4)	0.05 (−0.08 to 1)	0.2 (−0.08 to 1.7)
Nondominant eye	1 (0.4 to 1.7)	1 (0.2 to 1.5)	0.2 (−0.08 to 1.7)
Stereoacuity, arcsecs			
Mean ± SD	198 ± 261	490 ± 332	40 ± 0
Median, *n* (range)	90 (40 to 800)	600 (40 to 800)	40 (40 to 40)
Refractive error: diopter of spherical			
Mean ± SD			
Dominant eye	−2.4 ± 1.6	0.07 ± 2.2	−1.6 ± 2
Nondominant eye	−5.9 ± 1.9	−3.7 ± 2.9	−1.8 ± 2.1
Median (range)			
Dominant eye	−2.75 (−5 to 0)	0 (−6 to 4.5)	−1 (−7.5 to 0)
Nondominant eye	−5.8 (−9.5 to −2.75)	−3.1 (−11 to 0)	−1 (−7.5 to 0)
Interocular refractive errors: diopter of spherical			
Mean ± SD	3.4 ± 1.4	3.7 ± 1.7	0.2 ± 0.2
Median (range)	2.9 (1.5 to 6)	3.4 (1.8 to 9)	0 (0 to 0.5)
Refractive error: diopter of cylinder			
Mean ± SD			
Dominant eye	−0.4 ± 0.7	0.04 ± 0.8	0 ± 0
Nondominant eye	−0.9 ± 1.1	−0.4 ± 0.86	0 ± 0
Median, *n* (range)			
Dominant eye	0 (−3 to 0)	0 (−2.5 to 1.5)	0 (0 to 0)
Nondominant eye	−0.6 (−4 to 0)	0 (−3.75 to 0)	0 (0 to 0)
Interocular refractive errors: diopter of cylinder			
Mean ± SD	0.5 ± 0.6	0.4 ± 0.6	0 ± 0
Median, *n* (range)	0.4 (0 to 2.0)	0 (0 to 1.8)	0 (0 to 0)
Correction duration, y			
Mean ± SD	4.9 ± 4.3	N/A	5.1 ± 6.4
Median, *n* (range)	3 (0.3 to 15)	N/A	0 (0 to 17)

interocular visual acuity difference [i.e., ≥ 0.2 logMAR units in BCVA]); no strabismus; and no history of eye pathology before the study. Normal controls had emmetropic eyes (i.e., spherical equivalent refractions under ± 0.75 diopters [D]) or had myopia in both eyes with less than 1.50 D interocular spherical difference. None of them had cylinder errors and all had normal stereo acuity (40 seconds). Anisometropes had 1.50 D or larger interocular spherical difference; their stereo acuity ranged from 40 to 800 seconds.

The uncorrected anisometropes had never been corrected (mainly because the uncorrected acuity in their dominant eye was near normal), but were fully corrected during the measurements made in the experiment. Since they had not been previously corrected, they were asked to wear and adapt to the glasses for 1 hour before the start of the measurement. The corrected anisometropes had been fully corrected for more than 16 weeks prior to this investigation. The Table summarizes the clinical details for the three groups. Individual details are also provided in Supplementary Tables S1 through S3. The two anisometropic groups were matched in age ($t[50] = -0.21$, $P = 0.84$, 2-tailed independent samples *t*-test) and the degree of anisometropia (spherical equivalent; $t[50] = -0.61$, $P = 0.54$). The control group was not age-matched with the two anisometropic groups, but the possible effect of age was controlled in our statistical analyses.

All subjects were naive as to the purpose of the experiment. A written informed consent was obtained from each of them or from the parents or legal guardian of participants aged less than 18 years, after an explanation of the nature and possible consequences of the study. This study complied with the

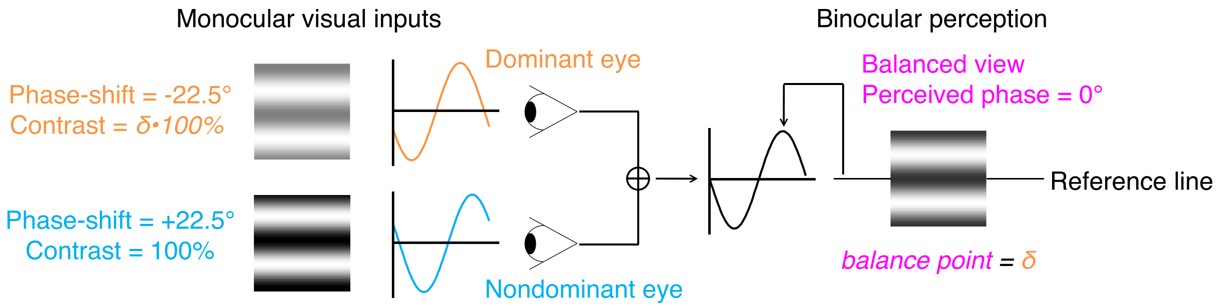

FIGURE 1. The binocular phase combination paradigm. Illustration of the method used to measure the relative contribution that each eye makes to the binocularly fused percept (ocular dominance) by estimating how stimuli of equal but opposite phase combine in the fused percept. Effective contrast ratio at balance point (or in short, balance point) refers to the extent to which the contrast has to be different in the two eyes before the contributions of each eye to the binocularly fused percept are equal.

tenets of the Declaration of Helsinki and was approved by the institutional review boards of Wenzhou Medical University, Anhui Medical University, and McGill University.

Apparatus

Experiments were conducted on a PC running statistical software (MATLAB; MathWorks, Inc., Natick, MA, USA) with extensions (PsychToolBox 3.0.9; MathWorks, Inc.).[4,5] The stimuli were presented on a gamma-corrected LG D2342PY 3D LED screen (LG Life Science, Seoul, Korea) with a 1920 × 1080 resolution and a 60 Hz refresh rate. Subjects viewed the display dichoptically with polarized glasses in a dimly lit room at a viewing distance of 136 cm. The background luminance was 46.2 cd/m^2 on the screen and 18.8 cd/m^2 through the polarized glasses. A chin-forehead rest was used to minimize head movements during the experiment.

Experimental Design

This was a cross-sectional cohort study examining the differences of sensory eye dominance between our two groups of anisometropic subjects (corrected and uncorrected) and our controls. The binocular phase combination task used to measure the eye dominance was as previously described.[6] Horizontal sine-wave gratings of equal but opposite phase (±22.5°) were seen by the two eyes. By having the observers estimate the perceived phase of the fused image one can determine the relative contribution from each eye (Fig. 1). This was repeated for a range of different dominant/nondominant eye contrasts to search for the interocular contrast ratio where the two eyes made equal contributions to binocular combination. This we term the "balance point"; it provides a quantitative measure of ocular dominance. In our study, the contrast of the grating in the nondominant eye was fixed at 100%, and the following interocular contrast ratios were used: 0, 0.1, 0.2, 0.4, 0.8, and 1.

In each trial, subjects first completed an alignment task. They adjusted the coordinates of images in their nondominant eye to make sure the images seen by the two eyes were perfectly fused. This was followed by the binocular phase combination task. Observers were asked to adjust the position of a binocular horizontal reference line to indicate the perceived phase of the fused sine-wave grating. They did so by aligning the line with the location of the center of the dark stripe of the grating. The reference line was presented on both sides of the gratings, with its initial vertical position randomly (–9 to 10 pixels) assigned relative to the center of the frame in each trial. The reference line was moved with a fixed step size of 1 pixel, corresponding to 4-degree phase angle of the sine-wave grating. During one trial, the stimuli were presented continually until subjects finished the phase adjustment task. The next trial started immediately after observers reported their results using a key press.

To cancel any potential bias, the perceived phases at each interocular contrast ratio were measured both when the phase-shift of the grating was 22.5° in the nondominant eye and –22.5° in the dominant eye (configuration 1), and vice versa (configuration 2). The binocular perceived phase was defined as half of the difference between these two configurations.

Each configuration was repeated eight times using the method of constant stimuli. The perceived phase and its standard error were then calculated from those eight measurements. In all, there were 96 trials in one measure (2 configurations × 6 interocular contrast ratios × 8 repetitions). Observers normally finished the test in 25 to 30 minutes. A 5- to 10-minute practice session was given to observers before the measurement to familiarize them with the task.

Stimuli

The gratings in the two eyes, as illustrated in Figure 1, were defined as:

$$Lum_{\mathrm{nonDE}}(y) = L_0\left[1 - C_0\cos\left(2\pi fy \pm \frac{\theta}{2}\right)\right] \quad (1)$$

$$Lum_{\mathrm{DE}}(y) = L_0\left[1 - \delta C_0\cos\left(2\pi fy \mp \frac{\theta}{2}\right)\right] \quad (2)$$

where L_0 is the background luminance, C_0 is the base contrast in the nondominant eye, f is the spatial frequency of the gratings, δ is the interocular contrast ratio, and θ is the interocular phase difference. In our test, $L_0 = 46.2$ cd/m^2 (on the screen); $C_0 = 100\%$; $f = 1$ cycle/°; $\delta = [0, 0.1, 0.2, 0.4, 0.8, 1.0]$ in different trails and $\theta = 45°$. Surrounding the gratings, a high-contrast frame (width, 0.11°; length, 6°) with four white diagonal lines (width, 0.11°; length, 2.83°) was always presented during the test to help observers maintain fusion.

Curve Fits

The functions of perceived phase (φ) versus interocular contrast ratios (δ), which we term "PvR functions" (e.g., Fig. 2), were fitted with a modified contrast-gain control model from Huang et al.[2]:

$$\varphi = \tan^{-1}\left[\frac{1-\left(\frac{\delta}{bp}\right)^{1+\gamma}}{1+\left(\frac{\delta}{bp}\right)^{1+\gamma}}\cdot\tan\left(\frac{\theta}{2}\right)\right], \quad (3)$$

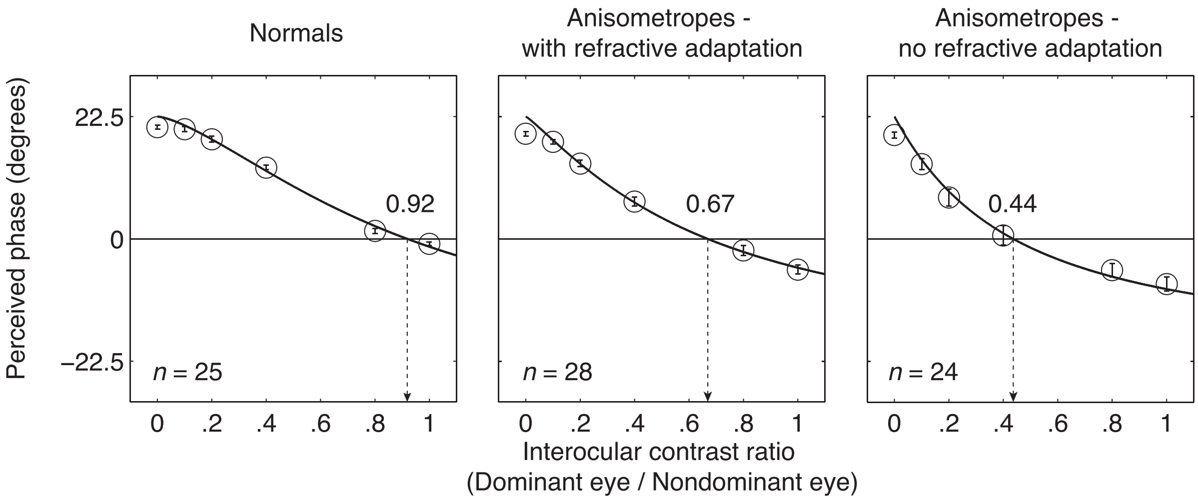

FIGURE 2. Averaged binocular perceived phase versus interocular contrast ratio (PvR) curves. The averaged results for the controls, corrected anisometropes (had been fully corrected for more than 16 weeks prior to this investigation), and uncorrected anisometropes (corrected at the time of these measurements but not having had long-term refractive adaptation). The *solid curve* is the fit derived from the contrast gain model. The point at which it crosses the zero line (where the two eyes contribute equally to the percept) is called the balance point. This is our measure of ocular dominance. *Error bars* represent standard errors.

in which bp and γ are two free parameters, bp represents the interocular contrast ratio that results in the two eyes making equal contributions to binocular combination (the balance point), and γ represents a nonlinear factor. Curve fitting was conducted in a computing environment (MathWorks) using the nonlinear least squares method to minimize $\sum(\varphi_{\text{theory}} - \varphi_{\text{observed}})^2$. The goodness-of-fit was statistically tested by computing the r^2 value:

$$r^2 = 1 - \frac{\sum(\varphi_{\text{theory}} - \varphi_{\text{observed}})^2}{\sum[\varphi_{\text{observed}} - \text{mean}(\varphi_{\text{observed}})]^2} \tag{4}$$

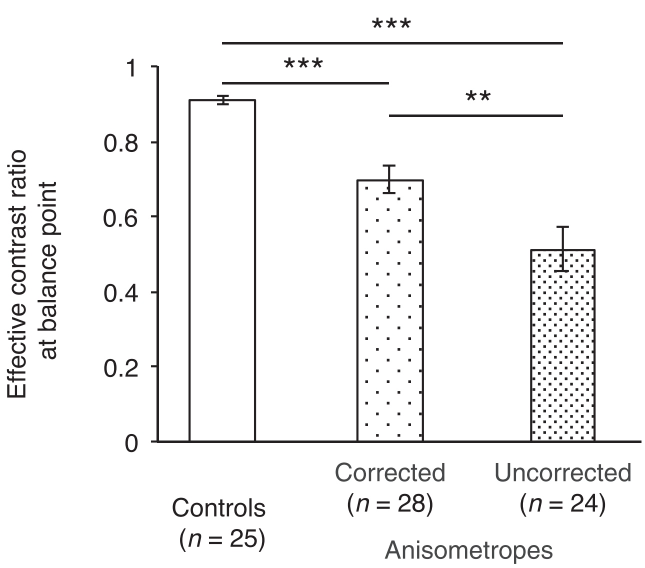

FIGURE 3. Average effective contrast ratio at balance point for the three groups. Averaged effective contrast ratios at balance points for the three groups. *Error bars* show standard errors. ** $P < 0.01$. *** $P < 0.001$. Statistical significances derived from ANCOVA test with the age factor controlled as a covariate and Bonferroni correction for the post hoc analysis.

Statistical Methods

An analysis of covariance (ANCOVA) test with the age factor controlled as a covariate and with Bonferroni correction for the post hoc analysis was used to assess whether the balance points were significantly different between groups. Partial correlation was used to assess the correlation between the correction time or the degree of anisometropia and the balance points.

RESULTS

Figure 2 shows the averaged PvR curves for the controls, corrected anisometropes, and uncorrected anisometropes. Compared with the normal controls, the PvR curves for both groups of anisometropes are shifted to the left. With the data averaged over the controls, the contrast ratio (dominant eye/nondominant eye) required to give a balanced contribution (perceived phase of 0°) from the two eyes is 0.92 (the balance point). In the anisometropes, it is necessary to give the stronger eye a lower physical contrast in order to achieve a perceptual balance. For corrected anisometropes the balance point was 0.67, and for uncorrected anisometropes it was 0.44.

We also fit the model to the data from the individual observers to obtain balance points for each of them. These are reported in Supplementary Figures S1 through S3, with the average balance points for each group shown in Figure 3. The controls had an average balance point close to one (0.91 ± 0.05; mean ± SD), indicating that a balanced contribution from each eye occurred when the input contrast in each eye was approximately equal. The uncorrected anisometropes exhibited a significant imbalance with an average balance point of 0.51 ± 0.28. This means that a balanced contribution from the two eyes occurred when the signal strength in the more ametropic eye was on average 95% stronger than that of the less ametropic eye (the more ametropic eye was much less dominant). In the corrected anisometropes this imbalance was much reduced (0.70 ± 0.19), meaning that a balanced contribution from the two eyes occurred when the signal strength in the more ametropic eye was 43% stronger.

A partial correlation analysis that controlled for age and degree of anisometropia (spherical equivalent) showed no significant correlation between the correction time and the balance point in the corrected anisometropes: $r_{partial} = 0.16$, $P = 0.43$. This is expected, as by 4 months, refractive adaptation should be asymptotic for most observers.[3] A partial correlation analysis with age and correction time controlled also showed no significant correlation between the degree of anisometropia and the balance point in the corrected anisometropes: $r_{partial} = -0.16$, $P = 0.45$. In the uncorrected anisometropes similar partial correlation analysis with age control also showed no significant correlation between the degree of anisometropia and the balance point: $r_{partial} = -0.23$, $P = 0.29$.

The anisometropic groups were age-matched with each other; however, the controls were not age-matched with the anisometropic groups. To compare the balance points between groups, we conducted an ANCOVA test with the age factor controlled as a covariate and with Bonferroni correction for the post hoc analysis. This showed that the balance points were significantly different between groups: $F(2, 76) = 23.84$; $P < 0.001$. The difference was also significant between controls and each of the two groups of anisometropes (all $P < 0.001$) and between the two groups of anisometropes: $P = 0.004$.

Discussion

We found that the two eyes of anisometropes were significantly imbalanced in binocular combination. This binocular deficit was reduced in anisometropes who had worn their spectacles for greater than 16 weeks. This binocular effect between recently corrected and long term corrected anisometropes cannot be explained by the age difference between the control and anisometropic groups, as the effect was still significant even after the age factor was controlled in the analyses. Such a binocular deficit in anisometropes could arise from either aniseikonia (optical origin)[7] or abnormal binocular neuronal responses (neuronal origin),[8] or both. Our data do not support the aniseikonia explanation, because: (1) partial correlation analysis in the anisometropic groups showed no significant correlation between the degree of anisometropia and the balance point; (2) the degree of anisometropia (and thus the degree of aniseikonia) was matched between the two anisometropic groups; and (3) the balance point became more balanced in subjects who had worn correction for 16 weeks even though the degree of aniseikonia would not have changed. We conclude that the deficit in binocular balance is neural in origin and results as a consequence of chronically uncorrected anisometropia.

This binocular imbalance is weaker in corrected anisometropes, whose correction has been worn for some time, than in anisometropes who had not been wearing correction. Such a difference cannot be explained by the age difference or the difference in the degree of anisometropia, as both factors were matched between the two anisometropic groups. There was also no significant correlation between the degree of anisometropia and the interocular contrast ratio at balance point. Nevertheless, our results suggest that a sustained optical correction plays an important role in balancing the contribution from each eye to the binocular sum and is therefore recommended.

It is interesting that this "sustained correction benefit" in dominance does not occur immediately after the anisometropia is corrected (as all our "uncorrected anisometropes" were corrected from 1 hour before measurements started). This might be expected as the improved contrast (especially at high spatial frequencies) would have occurred instantaneously due to a better focus. Instead a more balanced ocular dominance occurred only in the group with at least 16 weeks of full time correction. Since the only difference between these two anisometropic groups was the correction time, our results thus indicate that the improved contrasts resulting from the correction introduce a neuronal change at somewhere between 1 hour and 16 weeks of correction. This is consistent with an anisometropically induced shift in ocular dominance preceding, and potentially contributing to, the development of anisometropic amblyopia in the long term.

So far our conclusions are based on a controlled cross-sectional study comparing three groups (controls, uncorrected, and corrected anisometropes). This should ideally be followed up with a longitudinal study that would allow each anisometrope to act as their own control.

It would be interesting to know if an optically induced rebalancing of dominance also occurs in subjects whose uncorrected anisometropia early in life resulted in anisometropic amblyopia. If it did, which does not seem implausible on the basis of the current results, the beneficial visual effects of refractive adaptation in amblyopia[3] may have a binocular basis, being the result of rebalancing ocular dominance (and accompanying reduction in suppression by the amblyopic eye) that accompanies full correction of the anisometropia. This in turn would suggest, in the context of the current interest in active binocular therapy for amblyopia,[9] that refractive adaptation might be viewed as a passive form of binocular therapy.

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References

1. Li J, Thompson B, Lam CSY, et al. The role of suppression in amblyopia. *Invest Ophthalmol Vis Sci*. 2011;52:4167–4176.
2. Huang CB, Zhou J, Lu ZL, Feng L, Zhou Y. Binocular combination in anisometropic amblyopia. *J Vis*. 2009;9(3):17.
3. Stewart CE, Moseley MJ, Fielder AR, Stephens DA; MOTAS Cooperative. Refractive adaptation in amblyopia: quantification of effect and implications for practice. *Br J Ophthalmol*. 2004; 88:1552–1556.
4. Pelli DG. The VideoToolbox software for visual psychophysics: transforming numbers into movies. *Spat Vis*. 1997;10:437–442.
5. Brainard DH. The Psychophysics Toolbox. *Spat Vis*. 1997;10: 433–436.
6. Feng L, Zhou J, Chen L, Hess RF. Sensory eye balance in surgically corrected intermittent exotropes with normal stereopsis. *Sci Rep*. 2015;5:13075.
7. Lovasik JV, Szymkiw M. Effects of aniseikonia, anisometropia, accommodation, retinal illuminance, and pupil size on stereopsis. *Invest Ophthalmol Vis Sci*. 1985;26:741–750.
8. Smith EL III, Chino YM, Ni J, Cheng H, Crawford ML, Harwerth RS. Residual binocular interactions in the striate cortex of monkeys reared with abnormal binocular vision. *J Neurophysiol*. 1997;78:1353–1362.
9. Hess RF, Thompson B. Amblyopia and the binocular approach to its therapy. *Vision Res*. 2015;114:4–16.