Imbalanced Sensory Eye Dominance of Surgically Aligned Late-onset Acute Acquired Concomitant Esotropes with normal stereopsis

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Imbalanced Sensory Eye Dominance of Surgically Aligned Late-onset Acute Acquired Concomitant Esotropes with normal stereopsis

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Abstract

Background: Adults with late-onset acute acquired concomitant esotropia (AACE) have chance to develop normal binocular functions including a balanced ocular dominance before the onset of esotropia. For most patients, strabismus surgery re-establishing the ocular alignment indeed effectively restore stereopsis and visual acuity to the normal level. However, it is unclear whether they have already acquired balanced two eyes.

Methods: 11 surgically aligned patients with AACE (24.3 ± 1.5 years; mean ± SE) and 14 adults with normal vision (26.1±1.2 years) participated in our experiments. All patients had normal binocularity and stereopsis. Using binocular phase combination paradigm, sensory eye dominance was quantified as the interocular contrast ratio, termed balance point, at which the contribution of each eye to the perception of cyclopean grating were equal.

Results: Normal controls had a mean balance point value close to unity (0.95±0.01), while AACE group exhibited evident binocular imbalance (0.76±0.05), which was significantly different from control group ($t (10.45) = -3.485$, $p = 0.006$) . The balance point value didn't depend on the interval from AACE onset to strabismus surgery ($r = -0.357$, $p = 0.281$) or the interval from the surgery to examination of sensory eye dominance ($r = -0.105$, $p = 0.759$).

Conclusions: Although strabismus surgery effectively straightened AACE patients' ocular alignment and even conferred them normal stereopsis, late-onset AACE patients' two eyes were still not balanced. These results indicated that binocular imbalance might be a risk factor for adult AACE.

Key Words: acute acquired concomitant esotropia, strabismus surgery, sensory eye dominance, balance point

Background

Ocular alignment is not only necessary for cosmetic use but also clearly the first step to provide conditions crucial for re-establishing full binocular function in strabismus. Although there were several therapies for the treatment of ocular misalignment of strabismus such as refractive correction(1), eye exercises(2), botulinum toxin therapy(3), surgical alignment(4) and so on, strabismus surgery is a generally applied treatment especially for large deviation angle(5, 6). The benefit of surgical alignment to various binocular function have been reported for several types of strabismus. For example, better fusion was gained in adults with congenital esotropia after the surgery(7, 8) , which also improved stereoscope of patients suffering intermittent exotropia (9) as well as those with chronic acquired strabismus (10).

Strabismus surgery could effectively improve the binocularity and stereopsis (7, 11, 12), especially for patients who have no impediments in their early vision development (8, 13, 14). However, in recent studies, researchers quantified the sensory eye dominance using a phase combination paradigm(15) and found that the majority of surgically corrected intermittent exotropes even with normal stereopsis still exhibited significant interocular imbalance(16) and the surgical alignment did not present benefit to sensory eye dominance immediately or one year later after the surgery [16]. As a category of strabismus, intermittent exotropia was usually presented at childhood. It should be noted that, although intermittent fusion with proper ocular alignment at the early life stage might enable the development of normal binocular function, the residual part-time ocular deviation may still to some degree exert detrimental effect on sensory eye dominance of intermittent exotropes.

In contrast to intermittent exotropes, acute acquired concomitant esotropia (AACE), which was characterized by sudden onset of concomitant esotropia in older children and adults (17), was assumed to have opportunity to develop normal binocularity before the onset of esotropia. Although rare (14, 18) AACE appeared to rise in prevalence in recent years (19) due to excessive near work of modern people in everyday life, especially smart phone addiction(19). Surgical alignment is also proposed to be the principal therapy for AACE and has better stereopsis outcome than congenital or childhood esotropia (14, 20, 21). Thus, it is of great interest whether surgical

alignment could rebalance sensory eye dominance for late-onset AACE.

To test such possibility, we adopted the same paradigm to measure the sensory eye dominance of a group of surgically aligned adults with AACE who had clinically normal stereopsis and a group of normal adult controls. The sensory eye dominance was quantified as the interocular contrast ratio, termed balance point, at which two eyes contributed equally to cyclopean perception. We found that surgically corrected adults with AACE had significantly lower balance point comparing with the normal adult controls. Moreover, the balance point of adults with AACE had no relationship with the duration between onset of esotropia and surgery, or the interval from surgery to the examination of sensory eye dominance. Our results suggest that even for strabismus occurring since adulthood, straightening two eyes thorough surgery is yet not able to restore sensory eye dominance to normal level and binocular imbalance might be a risk factor for adult AACE.

Methods

Participants

Twenty three surgically aligned patients with AACE presenting to Wenzhou Eye Hospital were recruited and screened at least 7 days after the strabismus surgery, of which eleven patients who had ocular alignment successfully corrected and had normal clinical visual acuity and stereopsis were included in our study. A successful surgical alignment was defined as an esotropia or exotropia of no more than 10 prism diopters for both near and distance fixation using cover test. Normal stereopsis was defined as stereo acuity of less than 100 arc sec using clinical stereo tests (Titmus; Baoshijia, Zhengzhou, China). Patients with a history of other ophthalmic, a history of systemic or neurological disease, severe head trauma, cranial tumor and repetitive surgery were excluded. Another fourteen students from Wenzhou Medical Universities without any ocular abnormality other than refractive errors participated as controls. All treated patients and controls had normal or corrected to normal visual acuity (no more than 0.09 logMAR) in two eyes and exhibited normal ability of fusion assessed with the Worth’s 4 lights test. They had emmetropic eyes (i.e., spherical equivalent refractions under ± 0.75 diopters) or had myopia in both eyes with interocular spherical difference less than 1.50 diopters. Participants were required to wear their

prescribed optical correction, if needed, for data collections.

Apparatus

Visual stimuli used for measurement of sensory eye dominance were generated by a Mac computer running Matlab with PsychToolbox 3.0.9 extensions (22, 23) and displayed on a head mounted goggles (goovis G1, OLED) with 1024*768 pixels resolution and a vertical refresh rate of 60 Hz. The mean luminance of the OLED goggles was 160 cd/m^2. Luminance nonlinearities of the screen were corrected with an inverse gamma lookup table derived from careful calibration with a photometer, checked or recalibrated before each experiment.

Stimuli

The luminance profiles of the grating presented to the dominant and nondominant eyes as shown in Fig. 1 can be defined as following:

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

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

Where $L_0 = 160\ cd/m^2$ is the background luminance, C_0 is the base contrast in the nondominant eye, f is the spatial frequency of the gratings, θ is the interocular phase difference and δ is interocular contrast ratio. In our test, $C_0 = 100\%$; $f = 0.46\, cycle/°$; $\theta = 45°$ and $\delta = [0, 0.2, 0.4, 0.6, 0.8, 1.0\,]$.

Surrounding the gratings, a high contrast frame (width, 0.11°; length, 2.83°) with four white diagonal line (width, 0.11°; length, 2.83°) was displayed all over the test to help participants maintain fusion.

Procedure

The phase combination paradigm used for measuring the eye dominance has been described previously (24). As illustrated in Fig. 1A, observers were asked to view dichoptically two horizontal sinusoidal gratings with equal but opposite phase (± 22.5°) and estimate the perceived phase of the cyclopean grating. This process was repeated for various contrast ratios of dominant

to nondominant eye to evaluate the interocular ratio where two eyes made equal contributions to binocular combination. The ratio was termed "balance point" which quantified sensory eye dominance. In our study, the contrast of the grating presented to the nondominant eye was fixed at 100%, and the following interocular contrast ratios were used: 0, 0.2, 0.4, 0.6, 0.8 and 1.

To eliminate any potential bias, two configurations (Fig. 1B) were used for each interocular contrast ratio: in one configuration, the phase shift is +22.5^{o} for grating to dominant eye and was -22.5^{o} for grating to nondominant eye; In the other configuration, vice versa. The perceived phase was defined as half of the difference between perceived phases in these two configurations. Each configuration was repeated eight times and there were 8 Trials * 2 configurations * 6 interocular ratios, with 96 trials in total for each participant. All conditions were randomly intermixed. Participants normally finished the test in 25 to 30 minutes.

Fig. 1C illustrated the trial sequence in our experiment. Each trial began with an alignment task in which participants adjusted the positions of two monocular images to achieve better convergence till the images seen by two eyes were successfully combined into one steady cyclopean image. After the convergence was confirmed by pressing specified key, only surrounding high contrast frame was presented for 500 milliseconds. This was followed by the binocular phase combination task. Participants were instructed to indicate the perceived phase of cyclopean grating by moving a reference line to align it to the center of the dark stripe of the grating. The line was presented horizontally on both sides of monocular grating, with its initial vertical position (-9 to 10 pixels, relative to the center of the frame) randomly assigned in each trial. The line was moved up and down one pixel every step which corresponded to 4-degree phase angle of the sinusoidal grating. The stimuli were displayed continually till the end of trial. The next trial started immediately after participants confirmed the position of reference line by pressing specified key. Before the formal test, participants were allowed to get familiar with the task in a 5 to 10-minutes practice session.

Data Analysis

The perceived cyclopean phases for each interocular contrast ratio were calculated as the average of eight repeated measurements and fitted to a modified contrast-gain control model developed by

Huang et. al. (15):

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

where φ is the perceived phase; δ is interocular contrast ratio; θ is interocular phase difference (In our study, it is 45°); bp and γ are two free parameters, bp (balance point) representing for the interocular contrast ratio at which the two eyes contributed equally to the binocular combination and γ representing for transducer nonlinearity in the gain control pathway. All the model-fitting programs were implemented in Matlab (Mathworks, Inc., Natick, MA, USA) using the nonlinear least squares method to minimized $\sum(\varphi_{theory} - \varphi_{observed})^2$. The goodness-of-fit was evaluated by:

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

Independent-sample t test was used to test whether there was significant difference in balance point between surgically corrected AACE group and normal control group. Correlation analysis were also conducted to identify factors relating to AACE patients' postoperative balance point. All statistical computations were done in SPSS 13.0 (SPSS, Inc., Chicago, IL, USA).

Results

In total, 11 surgically aligned AACE patients (6 male; age, mean ± SE, 24.3 ± 1.5 years) which exhibited clinically normal stereopsis (stereo acuity was within 100 arc sec) and 14 normal adults (9 male; 26.1±1.2 years) were included in our study. These two groups were matched in sex (χ^2 (1)= 0.244, p = 0.622) and age (t(23) = -0.931, p=0.429). The clinical details of each patients in our study were provided in Table 1. Note that myopia is present for all patients except P8 and P10 who had emmetropic eyes (less than ±0.75 diopters). The refraction error on average was equal to a spherical equivalent of -3.47 diopters (range, -6.75 to 0.25 diopters; OD) and -3.41 diopters (range, –6.5 to 0.25 diopters; OS). All patients included was on average 22.7 years old (range, 14 to 30 years) when the esotropia manifested. Before surgery, the mean initial angle of esotropia was 33.6 prism diopters (range, 10 to 55 prism diopters) at near and 30.5 prism diopters (range, 10 to

50 prism diopters) at distance. Furthermore, 4 of 11 patients have equal near and distance esotropia. In the remaining 7 cases, the differences were within 5 prism diopters. The characteristics of most patients in our study met the diagnostic criteria of Bielschowsky type AACE defined by previous investigators (13, 19, 25), which was described as occurrence in adolescents and adults, varying degree of myopia and nearly equal angle of deviation at far and near distance (14, 20).

The perceived phase of cyclopean image versus interocular contrast ratio (PvR) functions for each surgically corrected patients with AACE and their average were shown in separate panels in **Fig. 2**. The shapes of all PvR functions were consistent with those documented in the literature: the phase depended strongly on the interocular contrast ratio and decreased monotonously from positive 22.5 degree to minus 22.5 degree with the ratio increasing. All data fitted contrast gain control model well with the average goodness of fit equal to 0.945±0.021 (mean ± SE) for treated patients and 0.968 ± 0.007 for normal controls. The average PvR function for fourteen normal controls was also shown in each panel and fitted to the contrast gain control model. The predictions of the best fitting model are plotted as smooth curves for both groups. The arrow marked the position of the balance point. Obviously, except for P2, P6 and P10, all other patients had arrows that were shifted leftward comparing with the average result of normal controls. The balance point for the average of patients with AACE was quite lower than that for the average of normal controls.

The average balance point for post-surgery patients with AACE and normal controls were shown in Fig. 3. Normal controls had an average balance point close to one (0.95 ± 0.01), indicating that a balanced contribution from each eye occurred when the image contrast in each eye was approximately equal. However, the post-surgery patients with AACE exhibited significant imbalance with an average balance point of 0.76 ± 0.05, which meant that balanced contribution from each eye occurred only when the signal strength in the dominant eye was on average 32% stronger than that of the other eye. A two-tailed independent samples t-test was conducted to compare the balance points between these two groups. The analysis showed that post-surgery patients with AACE had significantly lower balance point than normal controls (t (10.45) = -3.485,

p = 0.006).

The relationship between the balance point and two potential clinical features was shown in Fig. 4. The Pearson correlation analysis unraveled that the balance point were statistically independent of the interval from AACE onset to the surgery (r = -0.357, p = 0.281; Fig. 4A) and the interval from the surgery to the examination of sensory eye dominance (r = -0.105, p = 0.759; Fig. 4B). The Pearson correlation only describe the linear relationship between two variables. We also conducted spearman correlation analysis to test whether the balance point monotonously depended on these two features. No significance dependence was observed with both P>0.2.

Discussion

Here we conducted a cross-sectional cohort study to examine whether adults with AACE had balanced sensory eye dominance since the eyes have already been straightened through strabismus surgery. We quantified the sensory eye dominance by the effective contrast ratio of images presented dichoptically to two eyes, at which each eye made equal contribution to the binocular percept in a binocular phase combination task. Our results showed that post-operative patients with AACE yet have unbalanced eyes even when they had successfully corrected ocular alignment and clinically normal stereoscope.

Surgical alignment commonly benefits various binocular functions for several type of strabismus (7-10). Recent studies(16, 26) showed that, after strabismus surgery, patients with intermittent exotropia although exhibiting visual acuity and even normal stereo still have imbalanced sensory eye dominance. It should be noted that binocular imbalance might be due to residual part-time ocular deviation of juvenile patients with intermittent exotropia. In contrary to congenital intermittent exotropia, AACE is an esotropia which occurred suddenly in adolescents and adults (25, 27). Apparently, binocular vision had developed normally before the onset of esotropia (13). Thus, the postoperative imbalance of eye dominance observed here unlikely originated from abnormal early visual experience. It has been demonstrated that adults with anisometropia tend to have unequal eye dominance(28). Indeed, the participants in our experiments almost all have myopia, a typical feature of Bielshcowsky type AACE, but none has anisometropia. Fawcett(29) proposed a critical window for misalignment in adults beyond which

recovery of binocular function is not possible. It seems that the long-term esotropia without surgical correction might make the interocular imbalance incurable. However, our results showed that the balance points did not depend on the interval from onset of AACE to strabismus surgery. This is consistent with previous studies which found that the duration of misalignment did not predict failure to recover stereo acuity (8, 10). In addition, several work (10, 30) also suggested that the recovery of binocularity may take several months to occur. Nevertheless, we found that the balance point was independent of the interval from surgery to the measurement of sensory eye dominance. Specifically, the patient whose sensory eye dominance was examined even two years after surgery still had a balance point of 0.63. Previous study(26) on intermittent exotropes gave the same results, in which the author examined the sensory eye dominance first 0.5 months after surgery and then 5 months after surgery and found no difference of binocular balance measured at different time.

The phase combination task have been applied in identifying the abnormality of sensory eye dominance in amblyopia(24), anisometropia(28) and strabismus(31). On assessing eye preference in binocular view, the traditional measurement e.g. the hole-in-the-card test (32) and the Worth-4-dot test (33) was convenient in clinical practice but only able to provide qualitative outcome of test. Thus the method we adopted here to some extent could detect binocular deficit that would be ignored in traditional crude test. Similar to binocularity and stereopsis, the binocular balance as reflected in the phase combination task has a cortical basis (34-37). It has been demonstrated that distinct binocular processes sharing a similar interocular contrast-gain control stage may have separate pathways (15, 38). Thus, it is possible that patients have deficits at different sites within the binocular pathway and this might explain inconsistencies in the surgery outcome of distinct binocular functions. In addition to phase combination, the asymmetry in other binocular visual function such as binocular orientation combination(39) , dichoptic motion coherence perception(40), dichoptic orientation coherence perception(41) and binocular rivalry(42) can also be determined quantitatively based on the paradigm used in phase combination task. Although results of these measurement were mostly consistent, there were still some difference possibly due to distinct cortical mechanism involved (43). It is of great value to investigate

whether ocular dominance in term of different binocular function would give the same result in future experiments.

Kushner et.al have demonstrated that the development of binocularity after surgery appears to be related to the stability of the postoperative ocular alignment. Kohli et.al (44) also pointed out that the development of binocularity and stereopsis is associated with the final postoperative alignment. Here we observed that the eye dominance after restoring ocular alignment was still abnormal. This indicate that binocular imbalance might be a risk factor for adult patients with AACE. Further research is needed to clarify whether postoperative imbalanced eye dominance induce the problem of ocular alignment in long term.

Conclusions

Post-operative patients with AACE yet have unbalanced eyes even when they had successfully corrected ocular alignment and clinically normal stereoscope. These results suggested that binocular imbalance observed here might be a risk factor for adult AACE.

Abbreviations

AACE: Acute acquired concomitant esotropia

SE: Standard error

Declarations

Ethics approval and consent to participate

This study was approved by ethics committee of Wenzhou Medical University and adhered to the tenets of the Declaration of Helsinki. A written informed consent was obtained from each participants after the nature and possible consequence of the study were explained. For participants under 16 years old, written informed consent would obtained from their parent or guardian.

Consent for publication

Not applicable.

Availability of data and materials

Data is obtained with the permission of the corresponding author.

Competing interests

The authors declare that they have no conflict of interest.

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Authors' contributions

Z.Y. and X.Y. conceived the project and designed the experiments. Z.Y., H.Y., B.C., and J.Z. performed the experiments and analyzed the data. Z.Y. , H.Y. and X.Y. wrote the paper. All authors had read and approved the manuscript.

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Figure Legends

Figure 1. The binocular phase combination paradigm. (A) Illustration of the stimuli and measurement. Two horizontal sine-wave gratings with equal and opposite phase-shifts of 22.5° (relative to the center of the screen) were dichoptically directed to the appropriate eyes. The perceived phase of the cyclopean grating was determined by the internal representations of the binocular inputs. Sensory eye dominance is quantified by the interocular contrast ratio at which the perceived phase of cyclopean sinusoidal grating was equal to zero, i.e., the balance point, where the two eyes are balanced. (B) Two configurations used in the measurement: (1) the phase-shift was +22.5° in the nondominant eye and −22.5° in the dominant eye; (2) the phase-shift was −22.5° in the nondominant eye and +22.5° in the dominant eye. (C) Trial sequence. Each trial started with an alignment task in which a cyclopean cross with four dots should be perceived with correct vergence. Once the vergence was achieved, a specified key was instructed to be pressed and then only the surrounding frames was displayed immediately. 500 milliseconds later, horizontal sine-wave gratings were presented to the two eyes. Subjects were asked to move the reference line to indicate the center of the dark stripe of cyclopean grating. After the observer finished the task, a blank screen was presented for 1000 milliseconds.

Figure 2. The perceived phase of cyclopean image versus interocular contrast ratio (PvR) functions for patients with AACE after surgical correction. Eleven patients' individual and average results are shown in separate panels as red circles. The average result for fourteen normal controls is also presented as green triangles in each panel for comparison. The red sold line and green dotted line are the fit derived from contrast gain control model for surgically corrected patients

and normal controls, respectively. The effective contrast ratio at balance point is denoted by the red arrow for patients and by the green arrow for normal controls. Error bars represent standard error.

Figure 3. Sensory eye dominance for patients with AACE after the surgery and normal controls. *Error bars* represented standard errors. ** P<0.01. Statistical significance derived from independent t-test.

Figure 4. The correlation between the contrast ratio at the balance point and (A) the interval from AACE onset to strabismus surgery and (B) the interval from surgery to the examination of sensory eye dominance. The red dotted line represented the best fit to the data. The Pearson correlation coefficients and their significances are indicated at the left lower corner of each plot.

Figures

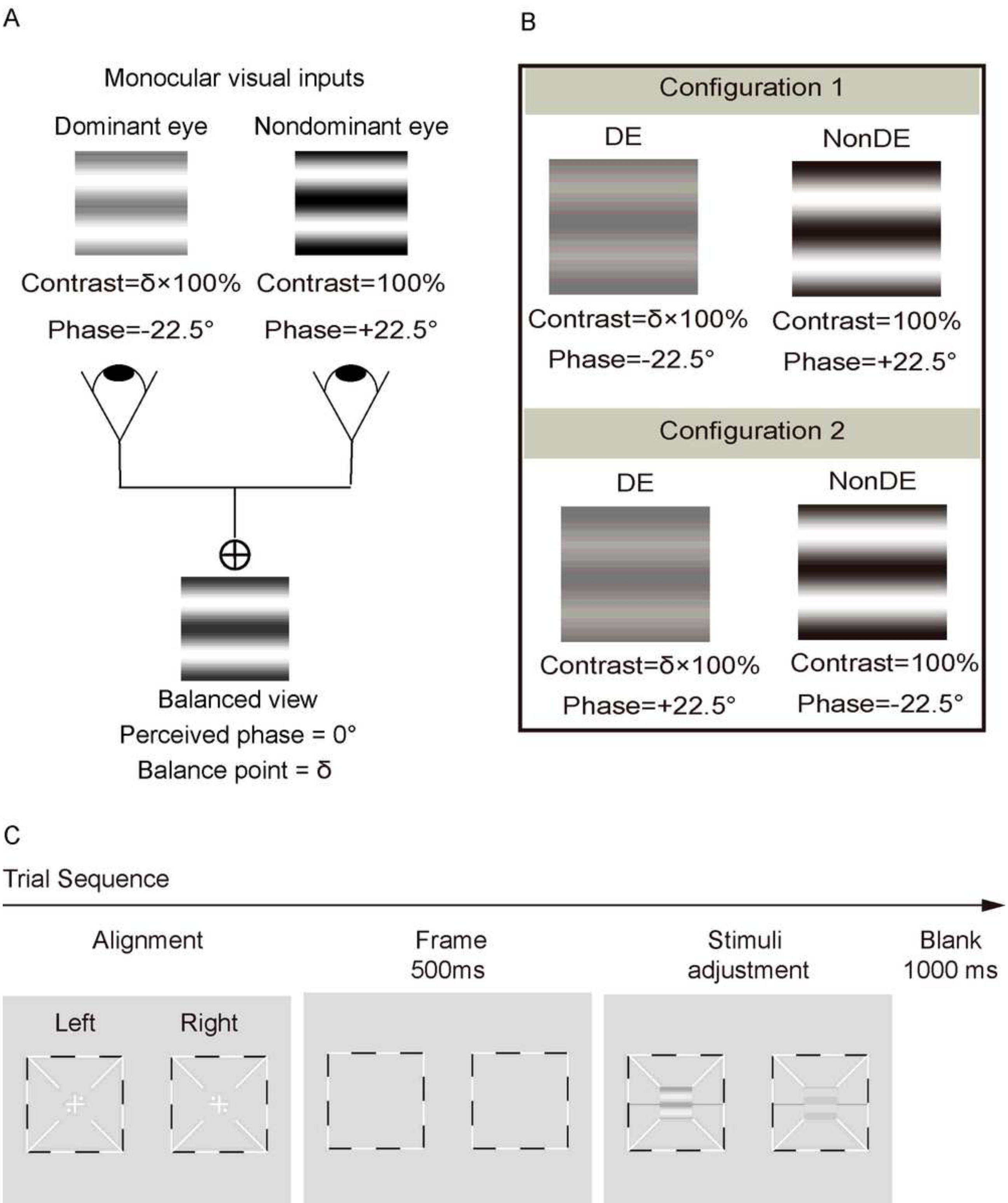

Figure 1

The binocular phase combination paradigm. (A) Illustration of the stimuli and measurement. Two horizontal sine-wave gratings with equal and opposite phase-shifts of 22.5° (relative to the center of the screen) were dichoptically directed to the appropriate eyes. The perceived phase of the cyclopean grating

was determined by the internal representations of the binocular inputs. Sensory eye dominance is quantified by the interocular contrast ratio at which the perceived phase of cyclopean sinusoidal grating was equal to zero, i.e., the balance point, where the two eyes are balanced. (B) Two configurations used in the measurement: (1) the phase-shift was +22.5° in the nondominant eye and −22.5° in the dominant eye; (2) the phase-shift was −22.5° in the nondominant eye and +22.5° in the dominant eye. (C) Trial sequence. Each trial started with an alignment task in which a cyclopean cross with four dots should be perceived with correct vergence. Once the vergence was achieved, a specified key was instructed to be pressed and then only the surrounding frames was displayed immediately. 500 milliseconds later, horizontal sine-wave gratings were presented to the two eyes. Subjects were asked to move the reference line to indicate the center of the dark stripe of cyclopean grating. After the observer finished the task, a blank screen was presented for 1000 milliseconds.

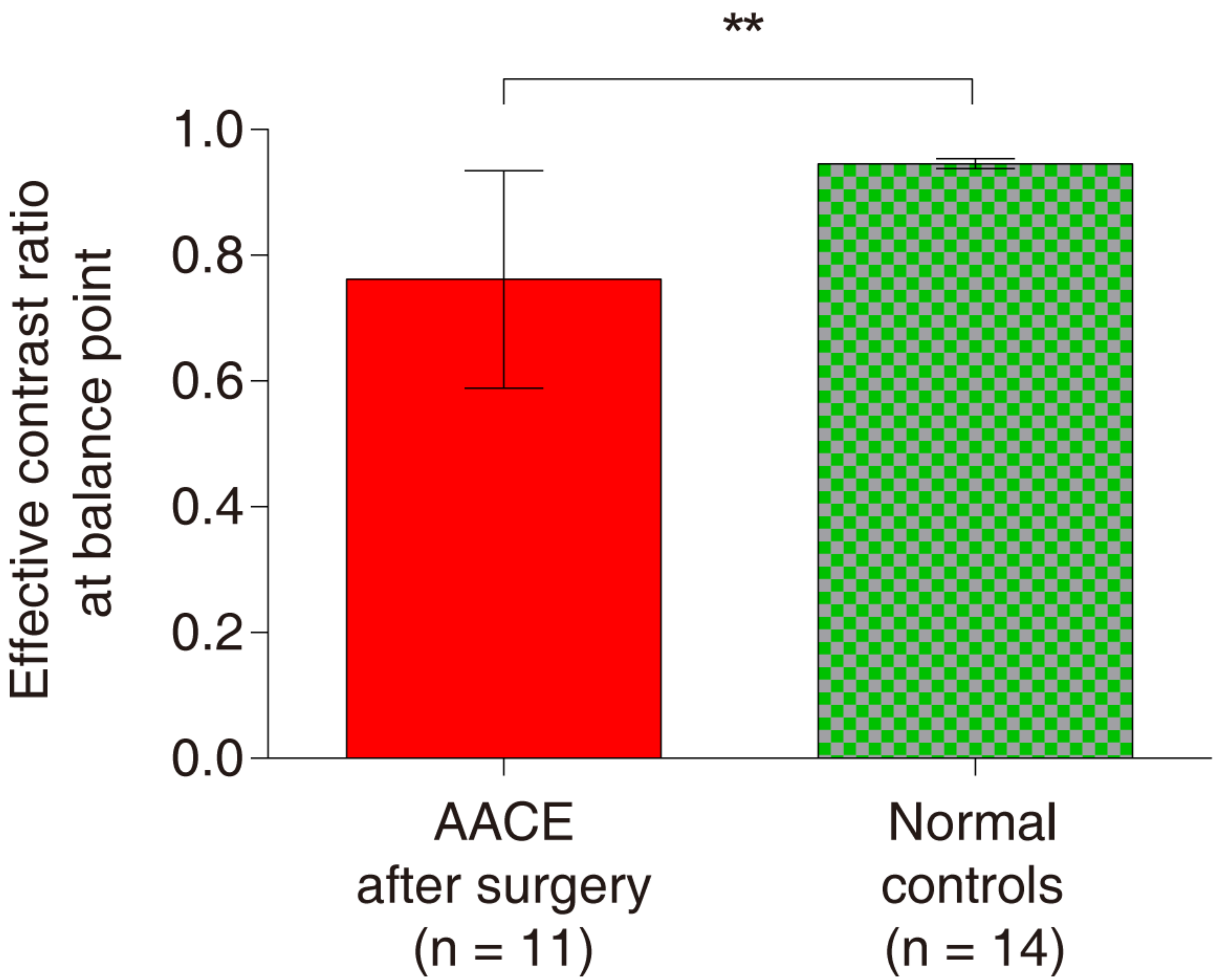

Figure 2

The perceived phase of cyclopean image versus interocular contrast ratio (PvR) functions for patients with AACE after surgical correction. Eleven patients' individual and average results are shown in separate panels as red circles. The average result for fourteen normal controls is also presented as green triangles in each panel for comparison. The red sold line and green dotted line are the fit derived from contrast gain control model for surgically corrected patients and normal controls, respectively. The effective contrast ratio at balance point is denoted by the red arrow for patients and by the green arrow for normal controls. Error bars represent standard error.

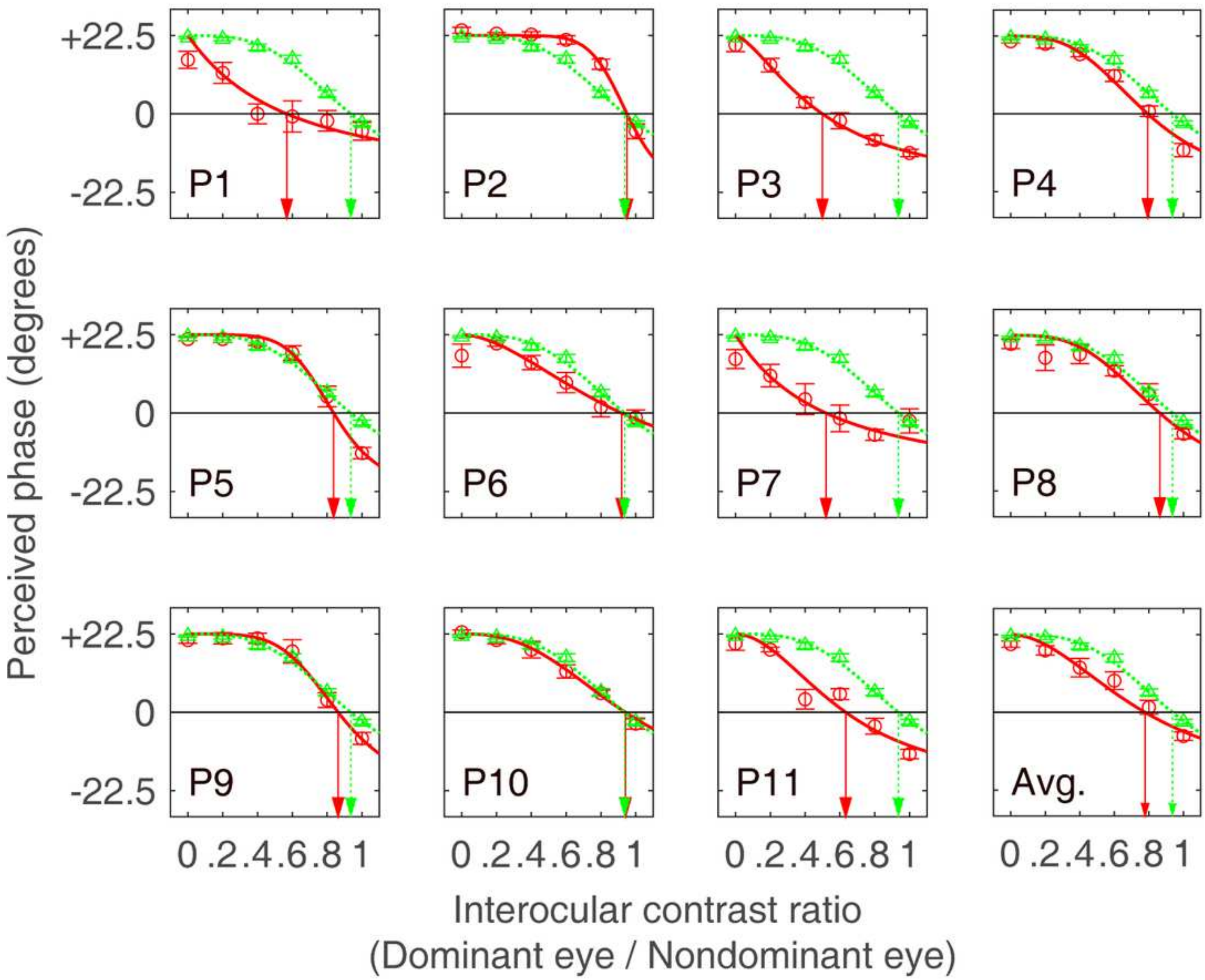

Figure 3

Sensory eye dominance for patients with AACE after the surgery and normal controls. Error bars represented standard errors. ** P<0.01. Statistical significance derived from independent t-test.

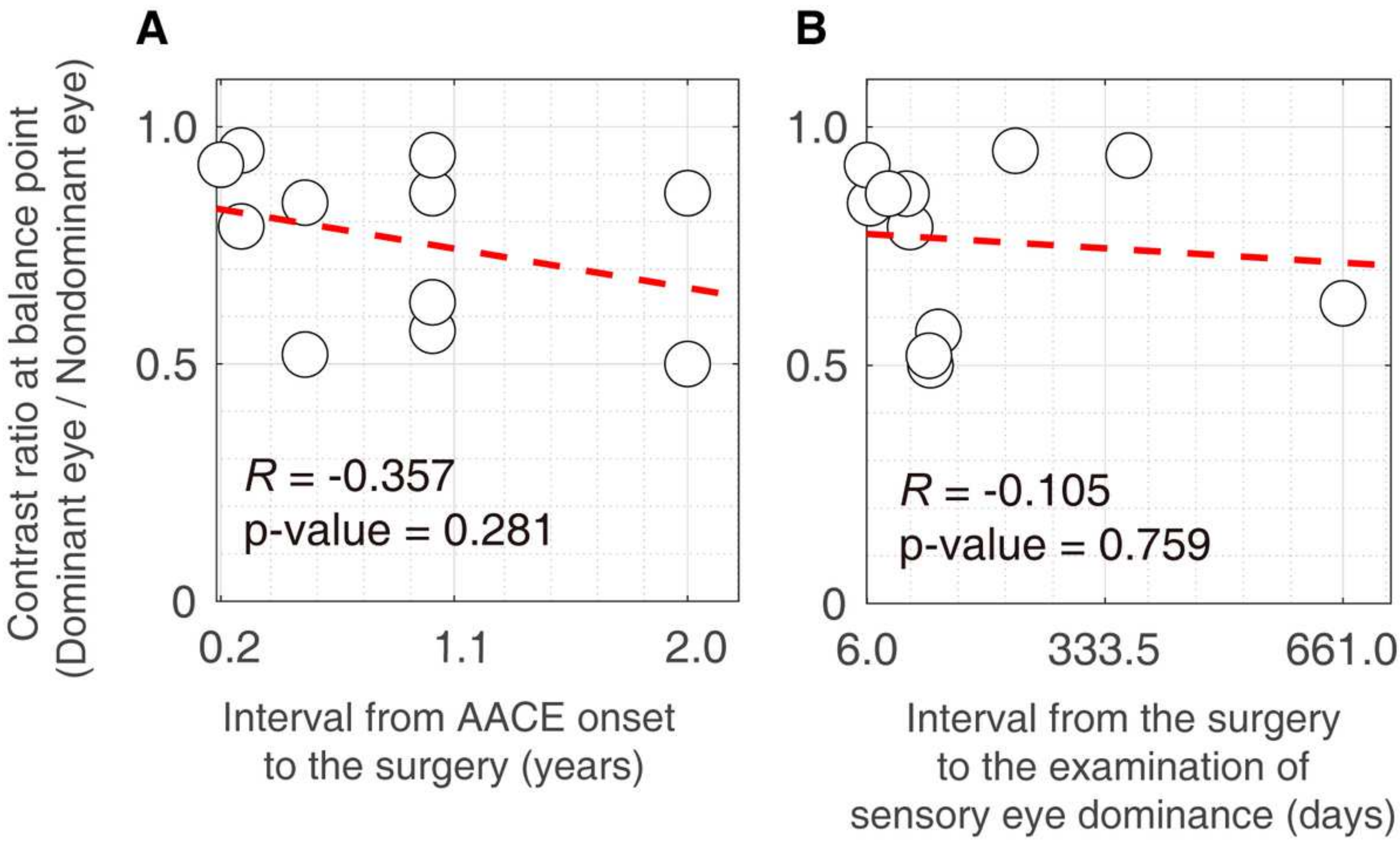

Figure 4

The correlation between the contrast ratio at the balance point and (A) the interval from AACE onset to strabismus surgery and (B) the interval from surgery to the examination of sensory eye dominance. The red dotted line represented the best fit to the data. The Pearson correlation coefficients and their significances are indicated at the left lower corner of each plot.