Objective Assessment of the Effect of Optical Treatment on Magnocellular and Parvocellular-biased Visual Response in Anisometropic Amblyopia

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Purpose. Optical treatment can improve visual function in anisometropic amblyopia, but there is no electrophysiological evidence, and the underlying change in visual pathway remains unknown. Our aims were to characterize the functional loss in magnocellular and parvocellular visual pathways in anisometropic amblyopia at baseline and to investigate the effect of optical treatment on the 2 visual pathways.

Methods. Using isolated-check visual-evoked potential, we measured the magnocellular- and parvocellular-biased contrast response functions in 15 normal controls (20.13 ± 3.93 years; mean ± standard deviation), 16 patients with anisometropic amblyopia (18.00 ± 6.04 years) who were fully refractive corrected before and 29 (19.41 ± 7.41 years) who had never been corrected. Twelve previously uncorrected amblyopes received optical treatment for more than 2 months and finished the follow-up measurement.

Results. Both the magnocellular- and parvocellular-biased contrast response functions in the amblyopic eye exhibited significantly reduced response and weaker contrast gains. We also found that the uncorrected amblyopes showed a more severe response reduction in magnocellular-biased, but not parvocellular-biased condition when compared with those corrected, with a weaker initial contrast gain and lower maximal response. After optical treatment, 12 uncorrected amblyopes demonstrated improved visual acuity of the amblyopic eye and a significant response gain to magnocellular-biased but not parvocellular-biased stimuli.

Conclusions. We demonstrated deficits to both magnocellular- and parvocellular-biased stimuli in subjects with anisometropic amblyopia. Optical treatment could produce neurophysiological changes in visual pathways even in older children and adults, which may be mediated through the magnocellular pathway.

Keywords: visual pathway, optical treatment, amblyopia, visual plasticity

Amblyopia is a neurodevelopmental vision disorder, caused by abnormal visual input during the vision development period,[1] commonly due to anisometropia.[2] It is one of the most common causes of unilateral visual morbidity in children[3–6] and adults.[7] In addition to visual acuity loss, amblyopia is often accompanied by other visual abnormalities, such as defects in contrast sensitivity, stereoacuity, and interocular suppression.[8–10] Different patterns of the visual abnormalities in amblyopic individuals implies different anatomic and neurophysiological deficits occurring in visual pathways.[11–16] The presence and selectivity of functional loss in the 2 main streams of central visual pathway, magnocellular and parvocellular pathways, remain unclear and controversial.

Recent studies showed that full-time wear of refractive correction alone, also referred to as "optical treatment," could not only ameliorate refractive error immediately but also improve visual function long term.[17–26] Even for older children and adults, whose neuroplasticity is assumed to be limited for visual recovery, optical treatment could also be effective.[19,22,27] This simple intervention has now been widely recommended as the first step in amblyopic treatment, regardless of patient age. However, the underlying mechanism of the optical treatment is still unknown.

Isolated-check visual evoked potential (icVEP), which records the steady-state visual evoked potentials to isolated-check stimuli, offers an objective measurement of visual functions in magnocellular and parvocellular pathways.[28,29] This technique was developed based on the contrast response properties of magnocellular and parvocellular neurons[30,31] and has been widely applied in a range of mental and visual disorders such as glaucoma,[32–34] retinitis[35] and schizophrenia,[36–39] but scarcely in amblyopia. Recent studies have found that the 2 visual pathways still remained

Table. Summarized Clinical Details of the Participants by Group

Clinical Details	Corrected Anisometropic Amblyopes	Uncorrected Anisometropic Amblyopes	Normal Controls
Number	16	29	15
Age, y			
Mean ± SD	18.00 ± 6.04	19.41 ±7.41	20.13 ± 3.93
Median, n (range)	16 (11 to 29)	17 (10 to 30)	20 (12 to 26)
Sex			
Female, No.(%)	8 (50%)	15 (52%)	7(47%)
Male, No.(%)	8 (50%)	14 (48%)	8 (53%)
Best corrected visual acuity, logMAR			
Mean ± SD			
Dominant / fellow eye	−0.05 ± 0.06	−0.01 ± 0.05	−0.01 ± 0.05
Non-dominant / amblyopic eye	0.46 ± 0.22	0.71 ± 0.28	0.00 ± 0.02
Median (range)			
Dominant / fellow eye	0 (−0.1 to 0.18)	0 (−0.1 to 0.1)	−0.02 (−0.06 to 0)
Non-dominant / amblyopic eye	0.42 (0.14 to 0.82)	0.8 (0.18 to 1.0)	−0.02 (−0.04 to 0)
Interocular visual acuity difference, logMAR			
Mean ± SD	0.46 ± 0.23	0.71 ± 0.27	0.027 ± 0.01
Median (range)	0.4 (0.18 to 0.82)	0.8 (0.14 to 1)	0.02 (0 to 0.04)
Interocular spherical equivalent difference			
Mean ± SD	4.33 ± 1.85	4.61 ± 1.55	0.20 ± 0.2
Median (range)	3.75 (2 to 8)	4.0 (2.5 to 8.25)	0.5 (0 to 0.75)
Duration of refractive correction, month			
Mean ± SD	77.25 ± 38.69	N/A	108.23 ± 45.66
Median (range)	72 (12 to 144)	N/A	108 (12 to 168)

to be adaptive to changes in visual experience in human adults, although there is controversy about their different potentials for visual plasticity.[15,16,40–42] Given the effectiveness of optical treatment and the remaining plasticity of visual pathways, we hypothesized that the visual functions of magnocellular and parvocellular pathways could be altered by optical treatment in older children and young adults with anisometropic amblyopia.

We conducted this comparative case-control study to test the hypothesis by (1) characterizing and comparing the baseline functional loss in magnocellular and parvocellular pathways for patients with anisometropic amblyopia; and (2) investigating the effect of optical treatment on functional changes in the 2 visual pathways. We anticipated that this study could provide objective evidence for the effect of optical treatment on visual pathways in older patients with anisometropic amblyopia.

Methods

Participants

This study consisted of 3 groups of participants, including normal controls (n = 15, mean age: 20.13 ± 3.93 years), corrected anisometropic amblyopes (CA; n = 16, 18.00 ± 6.04 years) who had been full-time refractive corrected for more than 6 months before this study, and uncorrected anisometropic amblyopes (UA; n = 29, 19.41 ± 7.41 years) who had never accepted any amblyopia treatment before but were newly refractive corrected. Participants were recruited through the Zhongshan Ophthalmic Center, Guangzhou, China. Clinical characteristics of the included participants are summarized in the Table. This study adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review boards of Zhongshan Ophthalmic Center, Sun Yat-sen University. Written informed consents were obtained from participants or their parents/legal guardians.

Inclusion criteria for normal controls were as follows: Participants had best-corrected visual acuity (BCVA) of at least 20/20 (0.00 logMAR) and a spherical equivalent refraction between −3.00 dioptric sphere (DS) and +3.00 DS in each eye, with a dioptric difference of less than 1.50 diopter (D) between 2 eyes, without any known ocular, oculomotor, or binocular abnormality. Amblyopia was defined as an interocular difference in BCVA of 0.2 logMAR or greater (≥2 lines), and with a logMAR acuity of at least 0.2 in the fellow eye. Anisometropia was defined as an interocular spherical equivalent difference of 1.50 D or more. Exclusion criteria were patients younger than 7 years old, those with strabismus, or those who were unable to cooperate with the eye or electrophysiological examinations, or with a BCVA of less than 1.0 logMAR in the amblyopic eye.

All participants underwent a comprehensive eye examination, including best corrected distance visual acuity (Early Treatment Diabetic Retinopathy Study numbers chart), cycloplegic refraction, cover tests at near and distance fixation, and slit-lamp and funduscopic examinations. Best refractive correction was determined by cycloplegic refraction. Cycloplegia was induced with 3–4 drops of 1% tropicamide instilled 10 minutes apart. After an additional 15 minutes, refractive error was first objectively measured after cycloplegia using both a table-mounted autorefractor (Topcon AR 8800; Topcon Medical Systems, Tokyo, Japan) and retinoscopy, and then determined by subjective refraction. For corrected amblyopes and normal participants, appropriate spectacles would be prescribed according to the refraction examination, if necessary, to achieve

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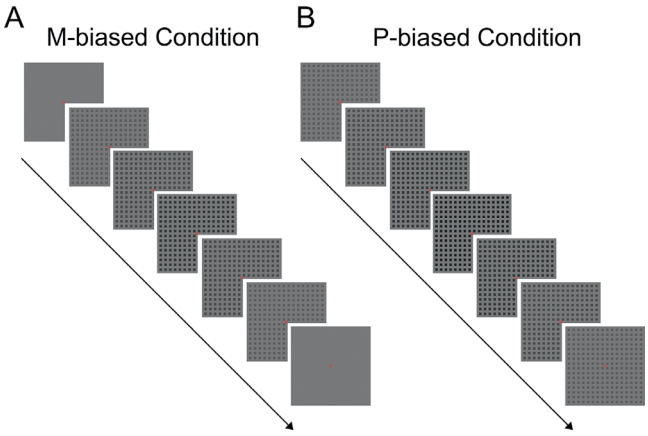

Figure 1. An illustration of sinusoidal modulation of the M- and P-biased isolated-check stimuli. For the magnocellular-biased (*M-biased*) condition, the depth of modulation (DOM) equaled to the pedestal making the stimuli presented in appearance-disappearance mode (**A**). For the parvocellular-biased (*P-biased*) condition, the pedestal was fixed at 48% level of Weber contrast, so that the stimuli checks never dropped below 16% contrast (**B**).

best-corrected visual acuity in both eyes. The dominant eye was identified with the hole-in-the-card test in normal participants.[43]

For the uncorrected amblyopes, spectacles were prescribed at the initial visit according to the following criteria: Anisometropia, astigmatism, and myopia were corrected fully, whereas hyperopia was either fully corrected or symmetrically undercorrected by ≤+1.50 D in both eyes. Patients were asked to adapt to their new spectacles for more than 12 hours before the baseline measurement. Full-time wearing of spectacles was required for all patients, and compliance was determined by self- or guardian-report.[19] Good compliance was defined as wearing spectacles for more than 50% of waking hours. Follow-up vision examination was performed 2–3 months after the baseline measurement. Only the patients who had a good reported compliance and finished both the baseline and follow-up examinations were included for the final analysis.

Apparatus and Stimuli

We measured magnocellular and parvocellular visual functions by using icVEP, which was performed by a Neucodia system (VeriSci Corp., Raritan, NJ, USA), including the stimulus generation and presentation, synchronized VEP recording, and raw data analysis. To obtain improved measurement of response, VEP sampling rate was at 480 Hz synchronized with the stimulus frame rate (60 Hz). Signals were amplified with a gain of 20,000, digitized and stored in a computer. All stimuli were presented in the center of a 17-inch organic light-emitting diode (OLED) screen (PVM-A170; Sony, Tokyo, Japan) with a 1920 × 1080 resolution. The background luminance was 50 cd/m^2.

Stimuli for VEP recording were based on those previously described.[39] Stimuli were isolated dark checks in 16 × 16 check arrays, subtending a total of 10 × 10 degrees of visual angle (Fig. 1). Each check subtended 18.75 minutes of arc of visual angle and was isolated from its neighbors by one check width. The space between checks was the background, whose luminance was constantly fixed instead of changing with the checks. Thus the checks covered one-quarter of the stimulus display field, and the background covered the remaining three-quarters of the field. Luminance of the checks was sinusoidally modulated at 12.5 Hz, above and below the static check luminance (pedestal) in 6 depths of modulation (DOM, 1%, 2%, 4%, 8%, 16%, and 32%). The VEP responses were biased toward magnocellular or parvocellular pathway by manipulation of different pedestals. For the magnocellular-biased (M-biased) condition, the DOM equaled to the pedestal making the stimuli presented in appearance-disappearance mode (Fig. 1A), which preferentially activates the magnocellular pathway. For the parvocellular-biased (P-biased) condition, the pedestal was fixed at 48% Weber contrast, so that the checks never dropped below 16% contrast (Fig. 1B). A 1 × 1 degree red cross was presented continuously in the center of the stimuli for participants to maintain fixation.

According to the International 10–20 System, we recorded VEP signals by Ag-AgCl electrodes, with one active electrode located at Oz (near the occipital pole), referenced to a second one at Cz (vertex) with a ground at Pz.

Procedure

Participants wearing the electroencephalography electrodes were seated in a shielded dark room with their head on the chin-forehead rest to secure position. They were asked to focus on the red cross from a distance of 57 cm through the corrective spectacles with the untested eye occluded by an opaque patch. Participants were instructed to focus on the red cross point and avoid blinking or moving eyes during the stimuli presentation. A camera on the top of the screen was used to monitor their eye movement and blinking. Eight independent runs (totally 48 seconds) for M-biased condition were obtained first and followed by 8 parvocellular-biased runs. To obtain reliable VEP signal, an individual run can be discarded automatically by the noise detection program built in the device software for signal saturation, excessive drift, or excessive line noise. Then another run will be repeated automatically until the 8 individual runs meet the criteria. For participants with amblyopia the fellow eye was always tested initially, whereas control participants always had their dominant eye initially tested. To avoid the effect of short-term patching, patients were asked to take off the eye patch and rest for 10 minutes between measurements for each eye.

Data Analysis

Amplitude and phase measures at the fundamental stimulus frequency (12 Hz) were extracted by a discrete Fourier transform for each run. As previously described,[32,37,39] vector average of amplitude and the 95% confidence region were obtained for 8 independent runs using the T^2_{circ} statistic, which is designed to analyze the signal produced by steady-state visual evoked potentials technique.[44] Noise was calculated as the radius of the circular 95% confidence region about the vector-average amplitude. Signal-to-noise ratios (SNRs), which was defined as the ratio between the averaged amplitude and the estimated noise, was derived as the dependent measure for the following statistical analysis.[32,37,39] The SNRs obtained from each eye were averaged for each condition and each DOM and were plotted as a function of DOM. The M-biased response curves, which are nonlinear, were fitted using the nonlinear Michaelis-Menten equation, whereas the linear P-biased response curves were

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fitted using a linear equation.[29,37,39] To further compare the contrast-response properties, 2 quantitative parameters were derived from the M-biased response curves, whereas 1 parameter was derived from the P-biased response curves. For M-biased condition, a measurement of initial contrast gain was calculated as the SNR changes from 4% to 16% DOM divided by the DOM change (12%), and the maximal response was calculated as the average of SNR at 16% and 32% DOM. For P-biased condition, we only calculated the initial contrast gain because there was no obvious response plateau.

Statistical Analysis

Comparisons in SNR between eyes within the same group and between baseline and follow-up measures of the same eye were made using 2-way repeated measures analysis of variance. A 2-way analysis of variance was used to compare eyes from different groups. Paired *t*-testing was used to compare BCVA, initial contrast gain and maximal response between eyes within the same group. The effect of covariates such as age and degree of anisometropia on the main outcome measure of initial contrast gain and maximal response was assessed using a univariate analysis of variance. All statistical analyses were performed using IBM SPSS Statistics Version 20 (www.ibm.com).

Results

Comparison of Magnocellular and Parvocellular-biased Visual Responses between Amblyopic Patients and Normal Controls

Mean SNR for each DOM in different testing conditions are plotted in Figure 2A for the 2 groups. There was a variation in the M- or P-biased response curves between groups of eyes. The M-biased curves appeared to be markedly nonlinear, with a strong response rise and followed by a response plateau, whereas the shape of P-biased curves was primarily linear, with a shallow but steady slope over the full range of DOM. For normal participants, we found no significant differences in SNR between the dominant and nondominant eyes for both M-biased ($P = 0.93$) and P-biased conditions ($P = 0.55$), implying an interocular balance of magnocellular and parvocellular visual functions. Thus we averaged the SNRs between the 2 eyes for each DOM and condition to facilitate further comparison and analysis. A significant 2-way interaction between condition and DOM ($P = 0.003$) indicated that the SNRs to M- and P-biased stimuli increased as different functions of the DOM. These different patterns of response curves between testing conditions were further confirmed by a significant difference in initial contrast gain (mean [SD], 0.22 [0.11] vs. 0.08 [0.05], $P = 0.001$), suggesting a stronger response gain from low contrast for the magnocellular pathway.

For the 45 amblyopic patients taken together, SNRs in M- and P-biased conditions from the amblyopic eye were both significantly decreased compared with the fellow eye (M-biased condition: $P < 0.001$; P-biased condition: $P < 0.001$). In contrast, SNRs from the fellow eye were relatively normal when compared with the control (M-biased condition: $P = 0.61$; P-biased condition: $P = 0.29$). As shown in Figure 2B and C, the M-biased response curve from the amblyopic eye showed a significantly decreased initial contrast gain (mean [SD], 0.06 [0.06] vs. 0.17 [0.12], $P < 0.001$) and maximal response (mean [SD], 1.88 [0.97] vs. 3.46 [1.20], $P < 0.001$) when compared with the fellow eye. The P-biased curve also rises with a slower slope (mean [SD], 0.05 [0.04] vs. 0.11 [0.08], $P < 0.001$). Our results demonstrated that the amblyopic eye had substantial failure to response from the increasing contrast of both M- and P-biased stimuli.

Stronger Effect of Optical Treatment on Magnocellular-biased Visual Response in Anisometropic Amblyopia

To assess whether optical treatment could change the functional loss in magnocellular and parvocellular pathways, we analyzed the data from the UA and CA groups separately and compared the two groups. The amblyopic BCVA in the CA group was substantially better than that in the UA group. There is no significant difference in interocular spherical equivalent difference between the two groups (Table). For the fellow eye, there was no significant difference in response to M- and P-biased stimuli between UA and CA groups (M-biased: $P = 0.54$; P-biased: $P = 0.33$). However, the M-biased curve from the UA group exhibited a more severe SNR reduction than that from the CA group for the amblyopic eye ($P = 0.001$). This was not the case for the P-biased curve ($P = 0.11$, Fig. 3A). Furthermore, for the M-biased response curve, the initial contrast gain was significantly weaker (mean [SD], 0.05 [0.05] vs. 0.09 [0.04], $P = 0.044$, Fig. 3B), and maximal response was lower (mean [SD], 1.65 [0.86] vs. 2.29 [0.90], $P = 0.032$, Fig. 3C) in the uncorrected amblyopic eyes compared with the corrected ones. The difference in slope of the P-biased response curve was smaller and did not reach significance ($P = 0.070$). These results implied a more severe magnocellular deficit for the uncorrected amblyopic eyes than the corrected ones in anisometropic amblyopia.

Spectacles were prescribed to the 29 uncorrected amblyopic patients, who were scheduled for a follow-up examination 2 months after the initial visit. Eleven of them (37.9%) had poor compliance with use of spectacles and were excluded, generally because of spectacle or contact lens intolerance with good uncorrected visual acuity in the fellow eye. In addition, 6 of the patients (20.7%) were lost to follow-up. Thus follow-up data from the remaining 12 uncorrected amblyopic patients (41.4%) who received optical treatment for 2–3 months (mean [SD], 2.42 [0.40] months) were analyzed and compared with their baseline data. For the fellow eye, M- and P-biased response curves did not significantly change from baseline (M-biased condition: $P = 0.810$; P-biased condition: $P = 0.381$). For the amblyopic eye, a statistically significant improvement in BCVA (mean [SD], 0.16 [0.15] logMAR, $P = 0.008$) was observed. Seven of them (58.3%) achieved an improvement of $\geq$1 logMAR line, and 4 of them (33.3%) improved by $\geq$2 logMAR lines. A significant SNR enhancement was shown for the M-biased condition (M-biased condition: $P = 0.040$), but not for the P-biased condition (P-biased condition: $P = 0.430$; Fig. 4A). For the M-biased curve, the initial contrast gain was strengthened twice of that in baseline examination (mean [SD], 0.10 [0.03] vs. 0.05 [0.05], $P = 0.022$; Fig. 4C), along with an increase in the maximal response (mean [SD], 2.40 [0.97] vs. 1.67 [0.59], $P = 0.011$; Fig. 4B). As for the P-biased curve, the slope remained unchanged (mean [SD], 0.08 [0.06] vs. 0.06 [0.04], $P = 0.15$).

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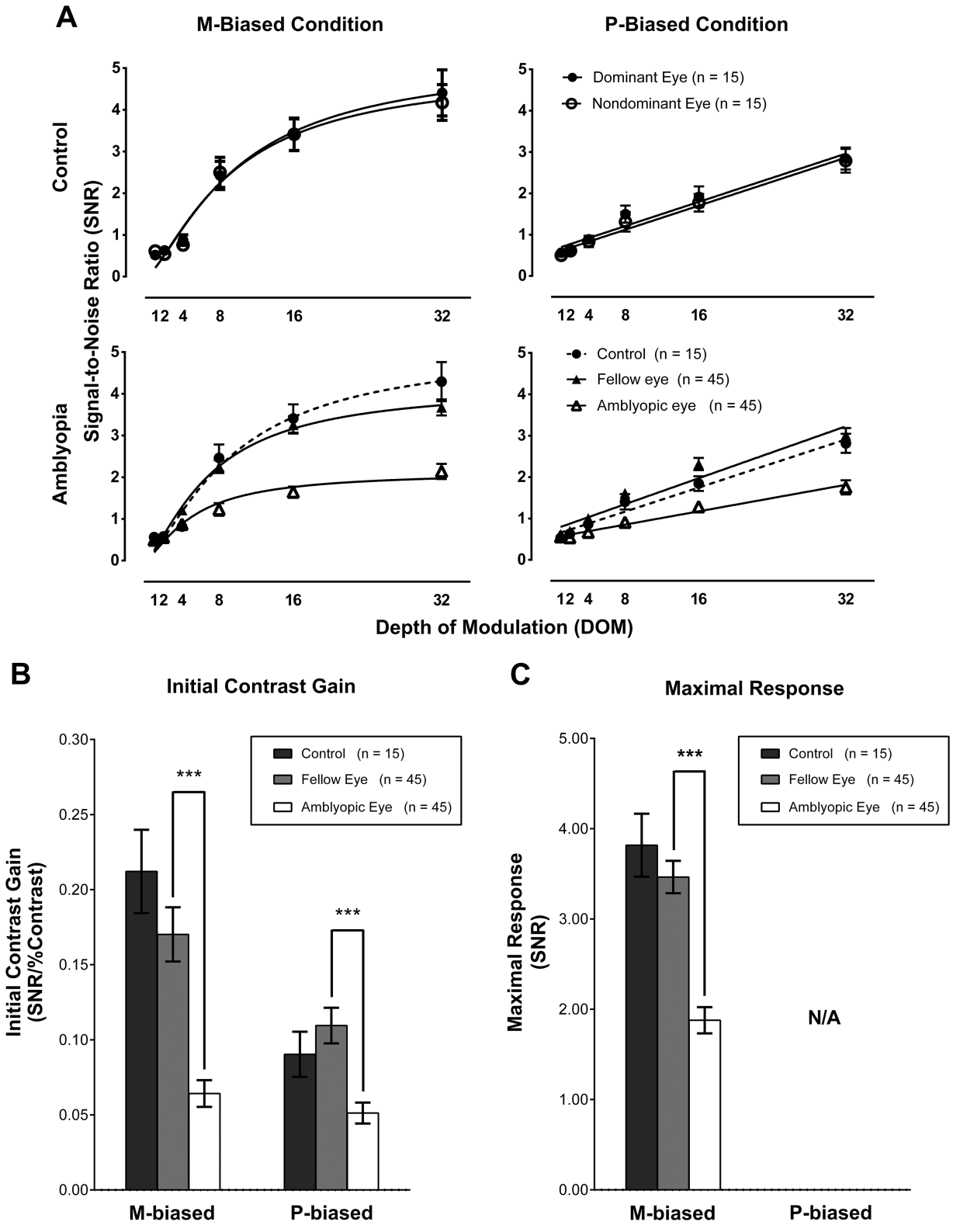

Figure 2. Steady-state visual evoked potential signal-to-noise ratios for both eyes of anisometropic amblyopes and normal controls measured with icVEP. (**A**) Magnocellular- (*M*-) and parvocellular- (*P*-) biased contrast response functions. Error bars represent ±1 SEM; (**B** and **C**) Comparisons of initial contrast gain and maximal response in amblyopic eyes (*AE*) and fellow eyes (*FE*) of anisometropic amblyopes and normal controls. Error bars give ±1 SD, *** $P < 0.001$.

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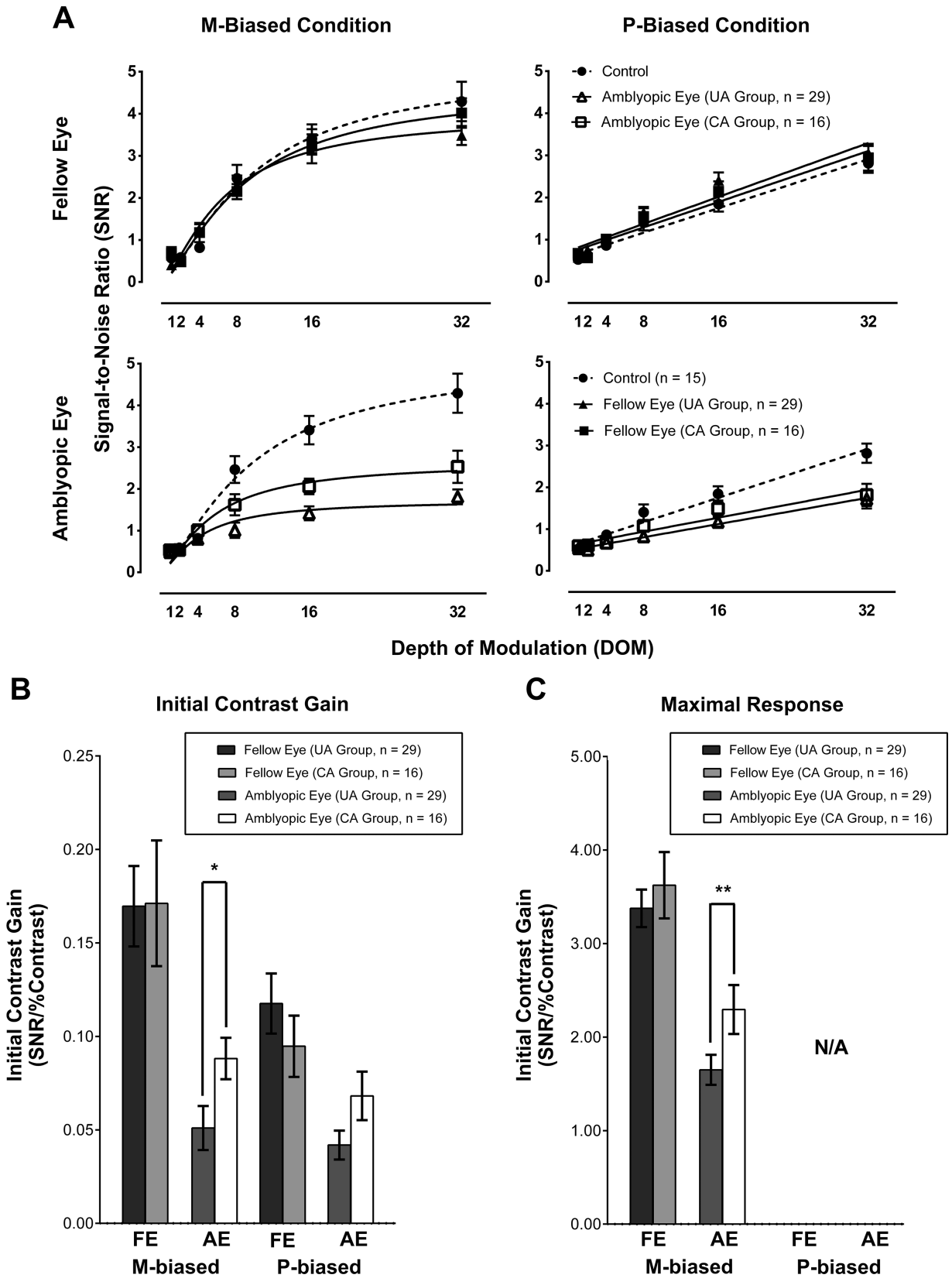

Figure 3. Steady-state visual evoked potential signal-to-noise ratios for both eyes of corrected (*CA*) and uncorrected anisometropic amblyopes (*UA*). (**A**) Magnocellular- (*M*-) and parvocellular- (*P*-) biased contrast response functions. Error bars represent ±1 SEM; (**B** and **C**) Comparisons of initial contrast gain and maximal response in amblyopic eyes (*AE*) and fellow eyes (*FE*) of amblyopes between 2 groups. Error bars give ±1 SD, $^{*}P < 0.05$, $^{**}P < 0.01$.

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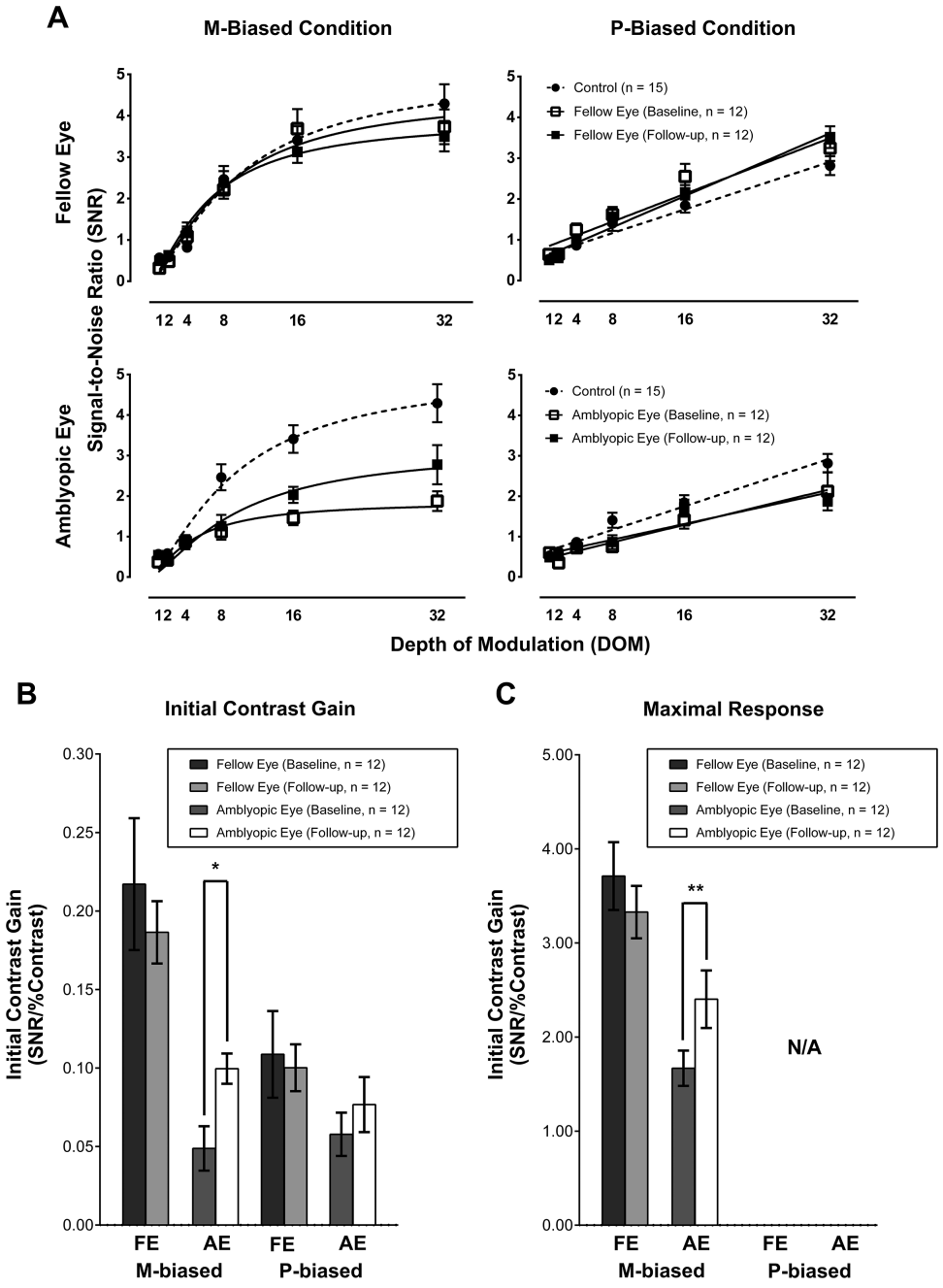

Figure 4. Steady-state visual evoked potential signal-to-noise ratios for previously uncorrected amblyopes before (*Baseline*) and after (*Follow-up*) optical treatment. (**A**) Magnocellular- (*M*-) and parvocellular- (*P*-) biased contrast response functions. Error bars represent ± 1 SEM; (**B** and **C**) Comparisons of initial contrast gain and maximal response in amblyopic eyes (*AE*) and fellow eyes (*FE*) of amblyopes between baseline and follow-up contrast response functions. Error bars give ±1 SD, $^{*}P < 0.05$, $^{**}P < 0.01$.

Discussion

This study found that VEP responses to both magnocellular and parvocellular-biased stimuli were reduced in the amblyopic eyes of patients with anisometropic amblyopia in comparison with their fellow eyes. In contrast, the fellow eyes remained relatively normal. More importantly, it demonstrated that there are differences in the patterns of response reduction related to the presence of optical treatment history, with a stronger response restricted to the magnocellular -biased stimulus for the corrected amblyopic eyes. In a subset of older children and adults with anisometropic amblyopia, we observed that optical treatment resulted in a VEP signal enhancement to magnocellular-biased stimulus rather than parvocellular-biased one, which implies a stronger effect of optical treatment on magnocellular visual function.

This electrophysiological study implies a functional loss in both the magnocellular and parvocellular visual pathways. Normal participants in our study showed the characteristic contrast-response curves of the M- and P-biased stimuli, which are consistent with previous studies,[29,37,39] whereas patients with amblyopia exhibited decreased SNRs and depressed response curves in both M- and P-biased

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conditions. Similarly, a psychophysical study performed by Zele and et al.[12] showed that both the magnocellular and parvocellular-biased contrast sensitivity reduced in patients with anisometropic amblyopia, with a normal function in the fellow eye. Davis and et al.[15] also demonstrated that the peak time and amplitude of motion-onset and color VEP were abnormal in patients with strabismic amblyopia. However, an fMRI study examining 7 amblyopes provided controversial results with a greater signal reduction to the chromatic stimuli rather than the achromatic ones, suggesting a selective loss of parvocellular function in amblyopia.[11] The discrepancy is likely due to the different methodologies used and the fact that most participants tested in the MRI study were with severe strabismic or form-deprivation amblyopia, whereas our participants were patients with anisometropic amblyopia. It has long been proposed that different types of amblyopia may produce fundamentally different neurophysiological changes in visual pathways,[8,9,13] and these discrepancies deserve further investigation.

Our results have important clinical implications for treatment in older children and adults with amblyopia. Most patients beyond the age of critical period traditionally believe that they may not benefit from traditional amblyopia treatment, including optical treatment and discontinued wearing spectacles. However, there is a growing body of evidence that optical treatment alone could improve monocular and binocular visual functions in older patients in a long term manner.[19,22,27] The Binocular Treatment of Amblyopia Using Videogames Study finds that 16 weeks of optical treatment produces significant improvements in monocular and binocular visual functions in patients older than 7 years of age.[19] In our study, we demonstrated that a group of 12 previously untreated anisometropic amblyopes, all of whom were older than 7 years old, obtained improvement in VA (average of 0.22 logMAR) in their amblyopic eye after refractive corrected for more than 2 months (average of 2.42 months). Eight of them (66.7%) improved more than 1 logMAR line, the percentage of which was slightly higher than that reported by Gao and et al.[19]

The magnitude of response reduction was relatively smaller in the previously corrected amblyopic eyes than that in the uncorrected ones. This differential reduction occurred only in magnocellular-biased condition, rather than parvocellular-biased one, which implies that optical treatment may have a stronger effect on the magnocellular pathway. One concern is whether the difference we observed was due to the external factors such as skull thickness or electrode impedance. By comparing the data of fellow eyes from the 2 groups, we found no significant differences in either the magnocellular- or parvocellular-biased conditions, suggesting that absolute response between 2 groups were at the same level. Interestingly, when we further prescribed optical treatment alone to the uncorrected anisometropic amblyopes, a significant elevation of magnocellular-biased contrast-response function was still shown, with increased initial contrast gain and higher response plateau, whereas no changes in parvocellular-biased condition were observed. Thus the current study provides the first objective evidence that optical treatment could potentially cause neurophysiological changes, which may mainly occur in magnocellular pathway.

The stronger improvement of VEP response in magnocellular-biased condition may possibly be explained by the relatively high level of visual plasticity for magnocellular pathway. A previous fMRI study of perceptual learning may support this explanation.[41] In that study, normal adult participants, who had undergone a 30-day contrast detection training, showed improved contrast sensitivity, and most importantly, the increased fMRI signal specific to the trained eye and visual hemifield in magnocellular layers, instead of the parvocellular layers. The improvement of behavioral performance was significantly correlated with the increased neural response in magnocellular layers. In our study, the stronger effect of optical treatment on magnocellular-biased response for the amblyopic eyes is similar to that result, implying that the magnocellular pathway may be more modifiable and more sensitive to the changes of visual environment than the parvocellular pathway in adult humans, especially in patients with anisometropic amblyopia.

There are several limitations to our current study. One of the concerns is whether isolated-check stimuli could accurately identify responses origin from magnocellular or parvocellular pathway.[45] Indeed, it is not possible to obtain signal from a single visual pathway by VEP, but often mixed with that from other ones. However, the stimuli we used were based on the contrast response properties, which was found previously in animal studies,[30,31] and could therefore bias visual processing toward the magnocellular or parvocellular pathway. The characteristic contrast response function could also be expected to reflect the visual function of magnocellular or parvocellular pathway. Second, our findings cannot be generalized to patients with other types of amblyopia, such as strabismic amblyopia. Indeed, several studies found that optical treatment could also result in visual improvement in strabismic amblyopia, but the underling mechanism may be different, which deserves further investigation.

Conclusions

We measured magnocellular and parvocellular-biased contrast response functions for both eyes of anisometropic amblyopes by using icVEP. The signal-to-noise ratios for magnocellular- and parvocellular- biased stimuli presented in the amblyopic eye were both reduced. We found that optical treatment resulted in a response increase to the magnocellular-biased but not parvocellular-biased stimuli for the previously uncorrected amblyopic eye. Visual plasticity in older children and adults may be retained, especially in magnocellular pathway, and optical treatment should be recommended.

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Investigative Ophthalmology & Visual Science

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