• Clinical Research •

Assessment of the effects of induced anisometropia on binocularity with glasses-free 3D technique

Xu-Bo Yang[1,2], *Wei-Dong Huang*[2], *Yong-Chuan Liao*[1]

[1]Department of Ophthalmology, West China Hospital, Sichuan University, Chengdu 610041, Sichuan Province, China
[2]Department of Optometry and Visual Science, West China School of Medicine, Sichuan University, Chengdu 610041, Sichuan Province, China
Correspondence to: Yong-Chuan Liao. Department of Ophthalmology, West China Hospital of Sichuan University, 37 Guoxue Xiang, Chengdu 610041, Sichuan Province, China. yongchuan2005@163.com
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Abstract

• **AIM:** To assess the effect of experimentally induced anisometropia on binocularity in normal adults with glasses-free three-dimensional (3D) technique.

• **METHODS:** Totally 54 healthy medical students with normal binocularity in the cross-sectional study were enrolled. Anisometropia was induced by placing trail lenses over the right eye, in 0.5 D steps including lenses of -0.5, -1, -1.5, -2, -2.5 D (hyperopic anisometropia) and lenses of +0.5, +1, +1.5, +2, +2.5 D (myopic anisometropia). The glasses-free 3D technique was used to evaluated not only fine stereopsis, but also coarse stereopsis, dynamic stereopsis, foveal suppression, and peripheral suppression in these subjects. One-way analysis of variance was used to compare quantitative data such as fine stereopsis, coarse stereopsis. Pearson's Chi-square test was performed to compare categorical data such as dynamic stereopsis, foveal suppression and peripheral suppression.

• **RESULTS:** The subjects showed a statistically significant decline in fine stereopsis, coarse stereopsis, and dynamic stereopsis with increasing levels of anisometropia (P<0.001). Binocularity was affected when induced anisometropia was more than 1 D (P<0.05). Foveal suppression and peripheral suppression were evident and increased in proportion to anisometropia (P<0.001).

• **CONCLUSION:** The relatively low degrees of anisometropia may have a potentially significant effect on high-grade binocular interaction. The mechanisms underlying the defect of binocularity seem to involve not only foveal suppression, but also peripheral suppression.

• **KEYWORDS:** anisometropia; binocularity; stereopsis; glasses-free 3D technique
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INTRODUCTION

Anisometropia is an ocular disorder characterized by asymmetry in refractive error between the eyes, which may be congenital, developmental or iatrogenic. The prevalence of anisometropia ranges from 1.9% to 18.8%, which is caused by different regions, races, ages, and diagnostic standards (anisometropia in these studies means that the refractive error difference between the two eyes is above 1.0 or 1.25 D)[1-4]. Anisometropia represents the interocular unequal growth, and is strongly associated with the development of some eye changes such as amblyopia, strabismus, aniseikonia and diplopia[5-7].

Under normal conditions, human beings see the world through both eyes. The disparate images of the two eyes can be fused into one integrated image in the brain, then the stereopsis arises. Stereopsis is the highest form of binocularity. Deficits in stereopsis will affect hand-eye coordination, fine and precise visual tasks and sense of distance, then cause various degrees of limitations on people's occupation and daily life[8].

Anisometropia will disturb binocularity, then cause deficits in stereopsis to different degrees[5,9-10]. Many studies verified that stereoacuity was easily damaged by the induced anisometropia, even in small degrees (as little as 1 D of spherical anisometropia)[11-16]. In those studies, fine static stereopsis was evaluated by printed stereograms such as TNO stereo test or Titmus stereo test, in which red-green glasses or polarizing glasses were needed to make two eyes work separately.

In this study, we use glasses-free three-dimensional (3D) technique to assess the effect of experimentally induced anisometropia on binocularity. More importantly, we evaluate the binocularity not only by fine static stereopsis, but also by coarse stereopsis, dynamic stereopsis, foveal suppression, and peripheral suppression.

SUBJECTS AND METHODS

Ethical Approval This study followed the provisions of the Declaration of Helsinki and was approved by the Ethics Committee of West China Hospital of Sichuan University (approval number: 2022[740]), and all participants provided written informed consent.

Subjects A total of 54 healthy medical students were recruited from West China School of Medicine, Sichuan University. All participants underwent a baseline ocular examination by technical professional workers, including assessments of best-corrected visual acuity (BCVA), anterior segment examination with slit lamp, fundoscopy, cover test, fine stereoacuity with Titmus. The inclusion criteria were defined as follows: BCVA of each eye is no less than 1.0, whereas the interocular difference is less than two lines of BCVA, and the Titmus score is not greater than 60 second of arc (sec arc). All subjects with any other ocular disease were excluded.

Induction of Anisometropia All subjects wore trial frames, which were used to correct their own ametropia and create the anisometropia. Anisometropia was induced by placing trail lenses over the right eye, in 0.5 D steps including lenses of -0.5, -1, -1.5, -2, -2.5 D (hyperopic anisometropia) and lenses of +0.5, +1, +1.5, +2, +2.5 D (myopic anisometropia). Therefore, each subject experienced 10 kinds of conditions of induced anisometropia.

Binocular Function Testing by Glasses-free 3D Technique The examination software was run on an autostereoscopic display (Shanghai EVIS Technology Co., Ltd.; a refraction-based, lenticular sheet on liquid crystal display) with a resolution of 3840×2160 pixels and a classical illuminance of 300 cd/m^2. The device automatically recognized the position of both eyes and presented a 3D vision by infrared eye tracking technology. The infrared camera could identify the ocular position and the dichoptic viewing was fulfilled by the optical barrier technology. The subject did not need to wear any dichoptic-viewing glasses. The examination software was developed by Guangzhou Medical Instrument Research Institute (Guangzhou, China). For each examination, the subject was required to be seated, with both eyes equal in height to the midpoint of the display, 80 cm apart (Figure 1). There was a five-minute break between each test to avoid fatigue. Meanwhile, to avoid accommodation, positive lenses were used first, and negative ones next. As to the avoidance of memorization, the presentation and orientation of stereograms were shown at random, and the measurement of stereoacuity was tested from the large degree of induced anisometropia to the minor one.

Fine stereopsis inspection It was measured by a random dot distribution map (54 cd/m^2) with a gray background (44 cd/m^2), with a size of 5°×5°, and an E optotype (3°×3°) consisting of random dots in the central part of the map with nonzero disparity of 400, 300, 200, and 100 sec arc, respectively, with peripheral dots as a reference and always relative zero disparity. Each patient needed to judge the opening direction of E-word in the figure, and press the arrow keys of the keyboard, or click the corresponding button on the interface as confirmation.

Figure 1 The experimental settings The participant is instructed to sit 80 cm away from the display, without any stereoscopic glasses.

Coarse stereopsis inspection It was measured by gray random dot stereograms (44 cd/m^2) presented on the monitor with the mean luminance of 34 cd/m^2. The size of each dot was 0.018°×0.018°. The maximum of both uncrossed and crossed disparity was 1800 sec arc. The minimum of them was zero. The relative disparity of the random points from top to bottom followed a sinusoidal variation. Subjects were instructed to state the convexity (crest) or concavity (trough) of random dot stereograms, and to press the arrow keys of the keyboard. Then the accuracy rate was recorded.

Dynamic stereopsis inspection It was tested by a central optotype (6°×6°) "E", which was made up of random dots with 800 sec arc disparity, with the background of different-speed movement. The density and size of dynamic random dots remained unchanged. Subjects were instructed to state the direction of the ''E'' by pressing the arrow keys of the keyboard. The 100% correctness of the answers to the test with the background of low-speed-movement was named as "pass-in-low-speed" in record and regarded as normal dynamic stereopsis. Otherwise, it was regarded as abnormal dynamic stereopsis, which was recorded as different categories ("pass-in-moderate-speed" and "pass-in-high-speed") respectively according to the different levels of dynamic stereopsis. The name "no-pass-in-high-speed" in record was regarded as absolute absence of dynamic stereopsis, meaning no correct answers to the test with the background of high-speed-movement.

Foveal suppression check Under binocular vision, one eye saw the inverted letter L (0.33°×0.33°) and the other saw the inverted letter F (0.33°×0.33°). The examiner recorded

Table 1 Representation of binocularity at various levels of induced anisometropia mean±SD

Binocularity	Baseline value	Hyperopic anisometropia					Myopic anisometropia				
		-0.5 D	-1 D	-1.5 D	-2 D	-2.5 D	+0.5 D	+1 D	+1.5 D	+2 D	+2.5 D
Titmus score of fine stereoacuity (sec arc)	28.7±9.8	37.2±15.1	63.0±65.3	109.0±108.2[a]	147.3±127.5[a]	226.9±138.6[a]	37.4±22.6	52.3±35.5	83.7±69.0[a]	129.3±106.6[a]	227.5±147.3[a]
Glasses-free 3D score of fine stereoacuity (sec arc)	116.7±69.4	118.5±70.2	133.3±89.0	190.7±133.6[a]	268.5±135.7[a]	346.3±111.1[a]	116.7±69.4	142.3±99.7	194.4±133.8[a]	270.4±138.2[a]	359.3±98.1[a]
Accuracy rate of coarse stereopsis (%)	98.6±10.2	97.7±12.2	97.7±10.0	88.4±27.8[a]	79.6±35.0[a]	78.7±34.5[a]	95.0±19.7	91.8±24.1	89.4±26.9	84.3±27.6[a]	72.7±34.1[a]
The proportion of subjects with normal dynamic stereopsis (%)	96.3	96.3	90.7	75.9[a]	42.6[a]	20.4[a]	94.4	82.7	70.4[a]	46.3[a]	13[a]
The proportion of subjects with foveal suppression (%)	1.9	14.8[a]	37[a]	70.4[a]	79.6[a]	94.4[a]	12.2[a]	55.8[a]	87[a]	98.1[a]	96.3[a]
The proportion of subjects with peripheral suppression (%)	9.3	25.9[a]	35.2[a]	51.9[a]	57.4[a]	70.4[a]	20.4	51.9[a]	64.8[a]	72.2[a]	79.6[a]

SD: Standard deviation. [a]*P*<0.05 compared to baseline value. There were significant differences of fine stereoacuity between Titmus and glasses-free 3D technique in the baseline and all circumstances of induced anisometropia (*P*<0.05).

the results seen by the subject. When the total E could be seen, the result was normal without any foveal suppression. On the contrary, the inverted letter L or the inverted letter F represented foveal suppression and the result was abnormal.

Peripheral suppression check Under binocular vision, the subject was required to stare the central cross, which was surrounded by four squares (3°×3°). If no peripheral suppression exists, the four squares could be seen simultaneously. Similarly, if peripheral suppression exists, one or more than one squares could not be seen at the same time.

Statistical Analysis One-way analysis of variance was used to compare quantitative data such as fine stereopsis, coarse stereopsis. Paired *t*-test was use to compared fine stereoacuity between the glasses-free 3D technique and the Titmus test. Pearson's Chi-square test was performed to compare categorical data such as dynamic stereopsis, foveal suppression, peripheral suppression. The statistical analysis was conducted with SPSS software (Version 22.0; IBM, Armonk, NY, USA). *P* values < 0.05 were considered statistically significant.

RESULTS

Demographics of Subjects Totally 54 subjects (38 females and 16 males) were enrolled in this study. Mean age was 20.4 years old (range of 19-22y). Table 1 list the main testing data of all subjects in this study.

Fine Stereoacuity First, we used the Titmus test to measure fine stereoacuity. The Titmus score at baseline was 28.7 sec arc, and the value increased as the degree of anisometropia increased. The greater degree of anisometropia we induced, the worse score of fine stereoacuity we tested (F=33.797, P<0.001; Table 1, Figure 2). There were statistically significant differences between the Titmus scores of induced anisometropia (±1.5, ±2, ±2.5 D) and baseline (P<0.05), except anisometropia of ±0.5 and ±1 D (P>0.05). On the other hand, there were no significant difference between hyperopic and myopic anisometropia (+0.5 *vs* -0.5 D, +1 *vs* -1 D, +1.5 *vs* -1.5 D, +2 *vs* -2 D, +2.5 *vs* -2.5 D, P>0.05; Table 1).

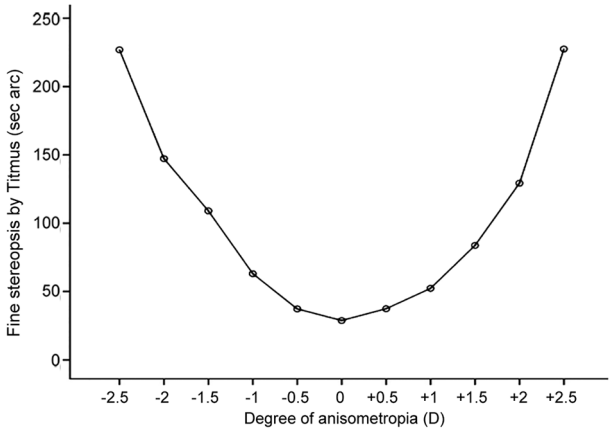

Figure 2 The relation between anisometropia and average fine stereoacuity measured by the Titmus test.

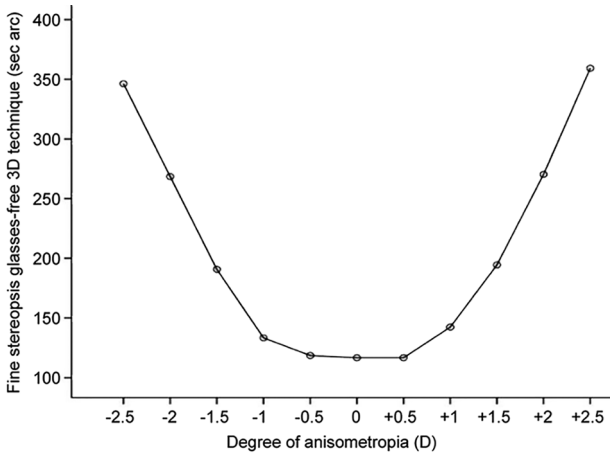

Figure 3 The relation between anisometropia and average fine stereoacuity measured by glasses-free 3D technique.

Second, we used the glasses-free 3D technique to measure fine stereoacuity. Similar to Titmus test, the glasses-free 3D scores of fine stereoacuity also increased as the degree of anisometropia increased, and the greater degree of anisometropia we induced, the worse score of fine stereoacuity we tested (F=39.247, P<0.001; Table 1, Figure 3). Similarly, there were statistically significant differences between the glasses-free 3D scores of induced anisometropia (±1.5, ±2, ±2.5 D) and baseline (P<0.05), except anisometropia of

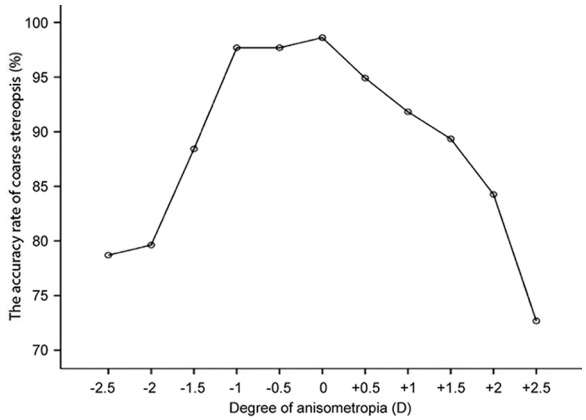

Figure 4 The relation between anisometropia and coarse stereopsis measured by glasses-free 3D technique.

±0.5 and ±1 D (P>0.05). Likewise, there were no significant difference (P>0.05) between hyperopic and myopic anisometropia (+0.5 *vs* -0.5 D, +1 *vs* -1 D, +1.5 *vs* -1.5 D, +2 *vs* -2 D, +2.5 *vs* -2.5 D; Table 1).

Coarse Stereopsis The accuracy rate of coarse stereopsis decreased as the degree of anisometropia increased (F=6.359, P<0.001; Table 1, Figure 4). The comparison of the accuracy rate of coarse stereopsis between baseline condition and induced anisometropia (±1.5, ±2, ±2.5 D) showed a significant change (P<0.05), except anisometropia of ±0.5 and ±1 D (P>0.05). Similarly, there were no significant differences between hyperopic and myopic anisometropia (+0.5 *vs* -0.5 D, +1 *vs* -1 D, +1.5 *vs* -1.5 D, +2 *vs* -2 D, +2.5 *vs* -2.5 D, P>0.05; Table 1).

Dynamic Stereopsis The dynamic stereopsis worsened as the degree of anisometropia increased (P<0.001; Table 1, Figure 5). The comparison of the dynamic stereopsis between baseline condition and induced anisometropia also showed a significant worsening (P<0.05), except anisometropia of ±0.5 and ±1 D (P>0.05). Similarly, there were no significant differences between hyperopic and myopic anisometropia (+0.5 *vs* -0.5 D, +1 *vs* -1 D, +1.5 *vs* -1.5 D, +2 *vs* -2 D, +2.5 *vs* -2.5 D, P>0.05; Table 1).

Foveal Suppression The proportion of subjects with foveal suppression increased as the degree of anisometropia increased (P<0.001; Table 1, Figure 6). There were statistically significant differences between the foveal suppression of baseline and all induced anisometropia (±0.5, ±1, ±1.5, ±2, ±2.5 D, P<0.05; Table 1).

Peripheral Suppression The proportion of subjects with peripheral suppression also increased as the degree of anisometropia increased (P<0.001; Table 1, Figure 7). The comparison of the peripheral suppression between baseline condition and induced anisometropia also showed a significant change (P<0.05), except anisometropia of ±0.5 D (P>0.05; Table 1).

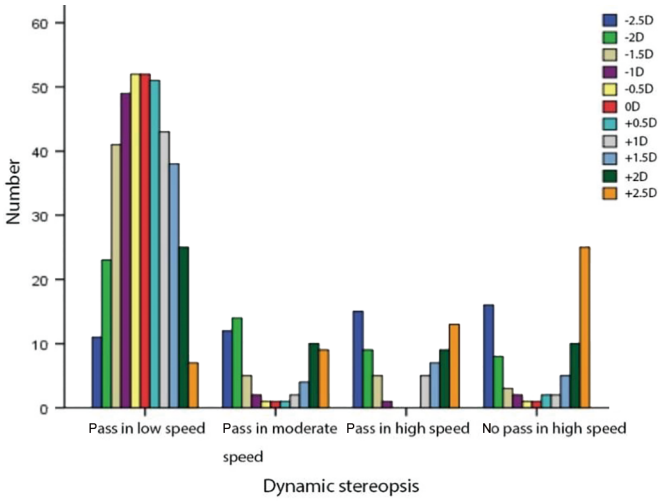

Figure 5 The relation between anisometropia and dynamic stereopsis measured by glasses-free 3D technique.

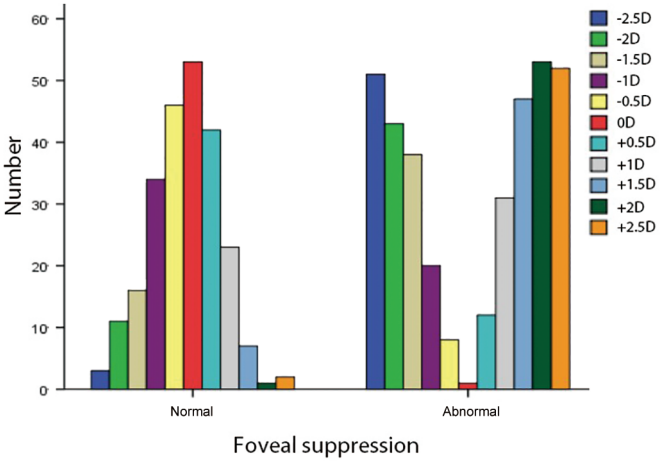

Figure 6 The relation between anisometropia and foveal suppression measured by glasses-free 3D technique.

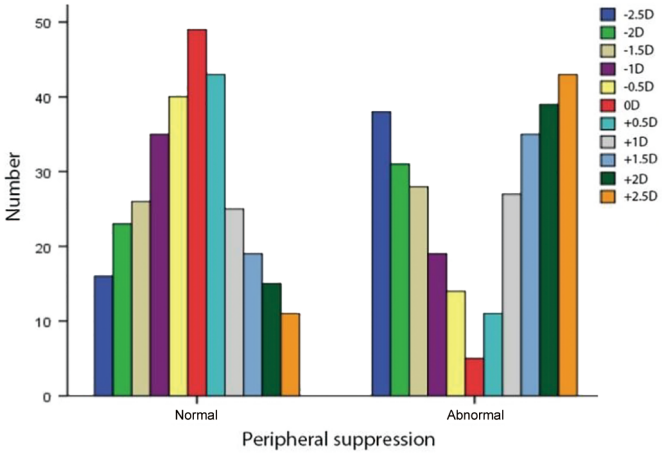

Figure 7 The relation between anisometropia and peripheral suppression measured by glasses-free 3D technique.

DISCUSSION

In this study, we used glasses-free 3D technique to evaluate the effect of experimentally induced anisometropia on binocularity. It was shown that besides fine stereopsis, all other data including coarse stereopsis, dynamic stereopsis,

foveal and peripheral suppression were also affected by anisometropia.

In population-based studies, anisometropia is proven to be an important factor causing stereoacuity deficit. Levi *et al*[17] measured stereoacuity in 84 anisometropes and found that the stereoacuity levels were reduced in proportion to the degree of anisometropia. Jeon and Choi[18] investigated 107 children with anisometropia, divided them into non-amblyopic and amblyopic groups. They found that the mean degree of anisometropia was 2.54 D in the non-amblyopic group and 4.29 D in the amblyopic group, and the levels of stereoacuity in the amblyopic group were significantly worse than these in non-amblyopic group. Robaei *et al*[19] tested stereoacuity thresholds of 2343 Australian children, and indicated that presence of anisometropia was significantly associated with reduced stereoacuity. In all above population-based studies, binocularity was affected not just by anisometropia, but by many other factors, such as amblyopia, microstrabismus, and deprivation, so these studies haven't accurately revealed the relationship between anisometropia and binocularity as well as the levels of binocularity that might or might not be affected by various degrees of anisometropia. Therefore, studies on the effect of experimentally induced anisometropia on binocularity can analyze this issue precisely in small increments[8]. In 1996, Brooks *et al*[16] determined the effect of experimentally induced anisometropia on binocular function in 19 healthy adults. They concluded that relatively small degrees of anisometropia, as little as 1 D of spherical anisometropia, might cause significant defects in high-grade binocular visual functions in adults. Similar results were reported in several other studies and our study[11-15].

In those previous studies, printed stereograms were used to evaluate stereopsis and dichoptic-viewing spectacles were needed to measure the fine stereoacuity. However, in our study, a new glasses-free 3D technology was used to test binocular function of experimentally induced anisometropes. Theoretically, an autostereoscopic 3D display can be used to evaluate stereopsis because the fundamentals of a 3D display and the stereopsis measurement are all based on disparity. And some researchers have done studies in this field[20-21]. We chose glasses-free 3D displays because it was much closer to our natural visual experience. The glasses-free 3D displays used in this study adopted a light barrier, that was a parallax barrier technology[22]. A parallax barrier, which was placed in front of a liquid crystal display, could produce a series of ultrathin vertical grating pattern to divide images into both eyes, then show an autostereoscopic image without the need of wearing dichoptic-viewing glasses. Besides these, the autostereoscopic displays also constructed the light field better than 2D displays and resolved the conflict between accommodation and convergence in traditional 2D displays[23]. In 2019, Zhao and Wu[24] used an autostereoscopic smartphone to measure stereoacuity of 60 healthy adults, and proved that it was a useful tool to evaluate stereopsis qualitatively and quantitatively. In our study, the result of fine stereoacuity measured by glasses-free 3D technology showed a high-level agreement with traditional Titmus test (Table 1, Figures 2, 3). Our data indicated that anisometropia beyond 1 D, whether it be myopic or hyperopic, made a significant adverse effect on fine stereopsis (Table 1). Although the result of fine stereoacuity measured by glasses-free 3D technique was similar to that measured by Titmus, the scores of stereoacuity by glasses-free 3D technique were greater than Titmus scores (P<0.05; Table 1). The difference in scores of the above two tests might be caused by 3 factors. The first one was the different normal standards of above 2 tests in which Titmus test is 60 sec arc, and glass-free 3D test 100 sec arc; the second one was the possibility of the existence of monocular cues in Titmus test; the third one was the possibility of some restrictions of this glasses-free 3D technique in the test.

Furthermore, using glasses-free 3D technique, we not only measured fine stereopsis, but also evaluated coarse stereopsis, dynamic stereopsis, foveal suppression and peripheral suppression in experimentally induced anisometropes.

Different from fine stereopsis, the coarse stereopsis serves as a type of backup mechanism, which is robust to large interocular differences in detail and luminance, and provides depth perception for stimuli at the upper limit of disparity processing[25]. In clinical studies, most of what we examine is static fine stereopsis, but most of the objects observed in daily life are dynamic. Dynamic stereopsis is valuable for people to perceive the depth of moving objects. Studies in psychophysics and neurobehavioral physiology have shown that stereopsis is processed on the dorsal, occipital, ventral, and occipitaltemporal channels. Dynamic stereopsis is more complicated than static stereopsis, and the main processing is the dorsal channel, while the static stereopsis is processed mainly in the ventral channel[26]. Zhong *et al*[27] found that individuals diagnosed as stereoblindness by traditional static stereograms had the potential for dynamic stereopsis. Therefore, compared with the traditional methods, our testing parameters of binocularity can provide more information and reveal the perceptual state of both eyes in the real world. In our study, similar to fine stereopsis, the coarse and dynamic stereopsis were also impaired by induced anisometropia. Our results showed that anisometropia beyond 1 D could bring a significant worsening of both coarse and dynamic stereopsis (Table 1, Figures 4, 5).

The precise mechanism in which anisometropia leads to decrease in stereopsis is not clear. Many studies supported that

foveal suppression in the defocused eye is the cause of reduced stereoacuity[14,16]. While some studies found that other factors, such as aniseikonia, contrast and density of fusional details, also play an important role on stereoacuity deficit[16,18]. The foveal and peripheral suppression results in this study clearly supported the presence of suppression in experimentally induced anisometropia. Our results indicated that as little as 0.5 D of anisometropia could cause a significant change of foveal suppression (Table 1, Figure 6). Besides foveal suppression, we also found that just 1 D of anisometropia could bring an obviously change of peripheral suppression (Table 1, Figure 7). The size of the suppression zone increased with increasing anisometropia, suggesting that binocular processing and fusion require greater interocular image symmetry. And the size of the induced suppression zone might account for the decrease of stereopsis.

Previous studies got different results on the influence of myopic and hypermetric anisometropia on fine stereoacuity. Nabie *et al*[11] suggested that stereoacuity was highly reduced in myopic anisometropia, while Rutstein and Corliss[28] detected that hypermetric anisometropia was a main reason of deterioration of stereopsis. In our study, the influence of myopic and hypermetric anisometropia on fine stereopsis were found the same，and the influence on dynamic and coarse stereopsis were the same too.

However, there are two limitations in this study. First, the age of the participants was different to the usual age of population-based anisometropia, especially in children and presbyopes. Second, the anisometropia was experimentally induced suddenly, the results may differ from uncorrected anisometropia with many years' adaptation. Further studies should be undertaken to more fully evaluate this issue. But our results do suggest that the effects of anisometropia on binocularity should be taken into consideration. Our study found that anisometropia beyond 1 D (both myopic and hyperopic) could bring a potentially significant adverse effect on fine stereopsis, coarse stereopsis and dynamic stereopsis. Thus, anisometropia beyond 1 D should be corrected in early years to avoid binocular rivalry and prevent anisometropic amblyopia in children, and the optimal value of monovision therapy for presbyopia might be about 1 D to avoid of decreased stereopsis and visual fatigue, which also have been confirmed by previous studies[11,29].

In conclusion, anisometropia beyond 1 D (both myopic and hyperopic) can bring a potentially significant adverse effect on fine stereopsis, coarse stereopsis and dynamic stereopsis. The mechanisms underlying the defect of binocularity seem to involve not only foveal suppression, but also peripheral suppression, and the extent of suppression is directly related to the degree of anisometropia.

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Authors' contributions: Yang XB and Liao YC designed the study. Yang XB drafted the manuscript. Huang WD and Yang XB collected patient data and analyzed the data. Liao YC revised the manuscript. Liao YC took responsibility for the integrity of the work.

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Conflicts of Interest: Yang XB, None; **Huang WD,** None; **Liao YC,** None.

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