Exploring the Relationship Between Binocular Imbalance and Myopia: Refraction with a Virtual Reality Platform

Zhengyang Tao, MM,1 Hongwei Deng, MD,1 Hang Chu, MD,2 Mark Wiederhold, PhD,3 Brenda K. Wiederhold, PhD,3 Huahong Zhong, MD,1 Zefeng Kang, PhD,4 Jun Zhao, PhD,5 Mei Xiong, MB,1 Minjuan Zhu, MM,1 Zhihong Lin, MB,1 and Jiao Wang, MM1

Abstract

To explore the relationship between binocular imbalance (BI) and the abnormal development of binocular refraction. BI data were collected by enrolling the first 1,000 adolescents and children aged 6–18 years in Shenzhen Eye Hospital from April 2020 to January 2021. In this cross-sectional study, the imbalance value (IV) did not show a statistical correlation with the spherical equivalent (SE) (oculus dexter [OD]: \( r = 0.022, p = 0.586 \); oculus sinister [OS]: \( r = -0.021, p = 0.606 \)), and had little correlation with the uncorrected visual acuity (VA) (OD: \( r = -0.084, p = 0.039 \); OS: \( r = -0.034, p = 0.408 \)). The proportion of binocular contrast imbalance (BCI) (the absolute value) maintained the highest level (from 54.42 to 79.17 percent) with the increase of bilateral SE difference in the four subcategories (binocular balance, monocular suppression, binocular rivalry, and BCI). From \(-100 \) to \(+100\) of IV, the SE of the left eye tends to increase negatively when compared with the right eye (from \(-95 < IV \leq -80\), SE difference \(-0.83 \pm 1.58\); \(-20 < IV \leq -10\), SE difference \(-0.14 \pm 0.61\); from \(10 \leq IV < 20\), SE difference \(-0.05 \pm 0.80\), to \(80 \leq IV < 95\), SE difference \(1.48 \pm 2.77\)). BI widely exists within the general pediatric population. The BI did not show significant correlation with the unilateral eye refractive state and the VA. However, the BI may be accompanied by imbalanced development of the eye refractive system. Furthermore, the SE of the dominant eye (from the prospective of BI) tends to be more negative than that of the opposite eye as the value increases.

Clinical Trial Registration number: ChiCTR2100045457.

Keywords: binocular imbalance, virtual reality, myopia, anisometropia, pediatric

Introduction

Binocular rivalry (BR), a psychophysical task with a clear link to cortical excitation and inhibition (E/I) balance, has been widely applied to the study of autism spectrum condition (ASC) characteristics.1–3 ASCs experience significantly higher levels of anomalous perception and have a slower rate of perceptual switching and a longer time spent on the mixed percept (lower rate of BR).4 Interestingly, some related concepts have also been recently studied in areas of ophthalmology and vision science.

Currently, nearly a third of the global population has developed myopia, becoming one of the leading causes of vision impairment worldwide.5,6 To achieve a high-quality image,
both eyes need to work properly and effectively in a synchronous manner. Binocular imbalance (BI), commonly referred to intermittent partial suppression of monocular vision during binocular fusion, is one of the conditions experienced during BR and binocular fusion. In common cases (in which the refractive system is corrected and nonpathological), BI may lead to a variety of visual problems. For example, the suppression of the weak eye in amblyopia leads to its poor corrected visual acuity (VA), and to a large extent becomes a factor of stereoscopic vision loss even if there is no structural abnormality in the refractive system of the suppressed eye.7

A recent cross-sectional study by Vera-Diaz et al. showed that BI was greater at high spatial frequency and low temporal frequency in patients with moderate myopia.8 A study by Li and colleagues showed that BI was common even in normal subjects.9 In this study, the BI test based on a virtual reality (VR) platform was used to quantify BI. To our knowledge, this is the first study to quantitatively compare BI in a population of children and teenagers with myopia. Through this exploratory study, the relationship between BI and myopia is clinically evaluated, and new clues for the role of visual perception abnormalities in the onset and development of myopia are examined.

Methods

Study participants

This study enrolled the first 1,000 adolescents and children aged 6–18 years who were admitted to the Strabismus and Pediatric Ophthalmology Department of Shenzhen Eye Hospital (Guangdong Province, China) from April 2020 to January 2021. Subjects were excluded for the following reasons:

- Poor compliance or do not understand the test
- Amblyopia (corrected vision <0.8, or previous diagnosis of amblyopia)
- Ocular position abnormality (including strabismus and nystagmus)
- Abnormality in color perception
- Receiving or had received (any kind of) myopia control before.

Test equipment

BI was assessed using a modified version of the dichoptic eye chart developed by the National Medical and Healthcare Appliance Engineering Technology Research Center implemented in a VR device (Vive by HTC Co.). The binocular contrast balance task is composed of sine bars. The images observed by the left and right eyes are divided into three quarters of a period of sine function as shown in Figure 1a, at a glance $y = \sin(x)(x = [0, 3\pi/2])$ grayscale image; as shown in Figure 1b, at a glance $y = \sin(x)(x = [\pi/2, 2\pi])$ grayscale image. In the initial stage, participants look at 100 percent contrast with both eyes, then the contrast is reduced from 100 to 5 percent at one eye, and the contrast is then decreased by 5 percent each time to find the balance point of the binocular integration. Figure 1c is the image after binocular integration is balanced.

Design and procedures

All patients were first asked to measure VA, which was done by two experienced technicians. The guardians of patients were then given a simple questionnaire about myopia control history before the outpatient visit. The ophthalmic tests with slit lamp biomicroscopy (Topcon SL-2G Slit Lamp, Japan) and color perception tests (Kechang Wang, Color Vision Test, China) were performed by three ophthalmologists. Next, the patients were asked to undergo the BI tests. The subjects were asked to wear a VR head mounted display while the researcher explained the procedure to them. The subjects were asked to click ‘‘+’’ or ‘‘−’’ with the mouse to adjust the size of the black and white grating in the image (Fig. 1). When the subject reported that the black and white areas are equal or when the subject could not see a fused image (black and white were dominant alternately), the test was completed. After the examination, there was a ‘‘contrast value’’ for each eye.

‘‘Contrast value (right eye) - contrast value (left eye)’’ was used to quantify the contrast signal between the two eyes, which was recorded as the Imbalance Value (IV). The positive IV means that the left eye contrast signal input is dominant in BI. Conversely, the right eye predominates. In this study, binocular balance (BB, or binocular contrast...
balance, BCI) was defined when the IV was ≤5 percent. Monocular suppression was defined when the IV was ≥95 percent. When subjects reported that the black and white pattern showed alternately, BR would be recorded. The remaining conditions are defined as binocular contrast imbalance (BCI).

Last, cycloplegic autorefraction was performed by the optometrist. A standard logarithmic tumbling E chart (WB-1112E; Wenbang, Co, China) was set at 5 m. Cycloplegia was induced in both eyes by the administration of 1 drop of tropicamide phenylephrine (Santen Pharmaceutical, Co, Japan) 10 minutes apart (3 drops in total) to obtain adequate mydriasis.

Myopia is defined as a condition in which the spherical equivalent (SE) refractive error of an eye is ≤−0.50 diopters sphere when ocular accommodation is relaxed.10

**Statement of ethics**

Guardians of the children were provided a clear and easy-to-understand explanation of the BCI test, including the purpose of the study and the safety of the test. And they also informed that the test may not have any impact on treatment. Any of the measurement results were recorded only with the informed consent of the parents. This study followed the Helsinki declaration and was approved by the institutional research ethics committee of Shenzhen Eye Hospital (20201230-07).

**Result**

This study included a total of 1,000 Chinese children (2,000 eyes) who visited Shenzhen Eye Hospital from April 2020 to January 2021. One hundred thirty-one patients who had received/were receiving myopia control (atropine eye drops: 36, orthokeratology lenses: 33, progressive addition lenses: 13, eye massage and acupuncture: 27, and vision training: 32) were excluded. A total of 15 individuals were excluded for strabismus, and 9 individuals were excluded for abnormal color perception, 57 individuals were excluded for BCI signal input.

Among these, BCI occupied the highest proportion and had no significant change with the increase of SE difference between the two eyes (from 54.42 to 79.17 percent).

**The proportion of BCI in bilateral SE difference**

Figure 3 shows the proportion changes of each subcategory as the bilateral SE difference gradually increases. It can clearly be seen that with the increase of the bilateral SE difference, the proportion of BR gradually increases, whereas the proportion of BCB significantly decreases. Among these, BCI occupied the highest proportion and had no significant change with the increase of SE difference between the two eyes (from 54.42 to 79.17 percent).

**The relationship between BCI and bilateral SE difference**

The absolute value of the SE difference (|SE [right] − SE [left]|) was used to indicate different states of the bilateral refractive system. The absolute value of IV (|IV|) was used to indicate the degree of difference in the binocular contrast signal input.

Figure 4a shows the trend of the mean value of IV variation with the increase of SE difference between the two eyes. With the increase of SE difference between the two eyes, the mean value of IV gradually increased (from 0.4 ≤ |SE difference| > 0, |IV| = 0.00 + 0.50, to 3.2 ≥ |SE difference| > 2.8, |IV| = 0.50 + 0.75). Figure 4b further showed the trend of the mean value of SE difference between the two eyes changing with the increase of |IV| (from 0 ≤ |IV| < 0, |SE difference| = 1.48 + 1.57, to 95 > |IV| > 80, |SE difference| = 1.63 ± 1.97).

**The analysis of dominant and inferior eyes in BI**

“SE difference” (SE [right] − SE [left]) was used to indicate the eye that tended to be more myopic. The more negative the value is, the more myopic refractive state of the right eye is.

| Table 1. Characteristics of the Participants in the Study |
|---------------------|---------------------|---------------------|---------------------|---------------------|
|                     | N       | Mean value | Upper limit | Lower limit | Maximum | Minimum |
| Age                 | 782     | 8.993606   | 8.783462    | 9.20375     | 18      | 6       |
| SE (OD)             | 757     | −1.636635  | −1.75276    | −1.5205     | 2.625   | −12.5   |
| SE (OS)             | 760     | −1.59391   | −1.71805    | −1.46977    | 2       | −14     |
| SE difference       | 752     | −0.0393    | −0.10649    | 0.027885    | 8.75    | −5.625  |
| |SE difference| 752     | 0.564501   | 0.510724    | 0.618279    | 8.75    | 0       |
| IV                  | 634     | −0.55205   | −2.72472    | 1.620621    | 90      | −90     |
| |IV| 634     | 18.4858    | 16.85837    | 20.11324    | 90      | 0       |

IV, imbalance value; OD, oculus dexter; OS, oculus sinister; SE, spherical equivalent.
Figure 5 shows that in the group with IV from $-10$ to $-95$, the SE of the right eye tends to be more negative than that of the left eye when the IV with more negative. The SE difference value gradually decreased with the dominance of the right eye becoming larger (from $-95 < IV \leq -80$, SE difference $= -0.83 \pm 1.58$, to $-20 < IV \leq -10$, SE difference $= -0.14 \pm 0.61$). Alternatively, when the IV in the population ranged from 0 to $+100$, the SE of the left eye tended to be more negative than that of the right eye, and the difference increased with the dominance of the left eye becoming larger (from $10 \leq IV < 20$, SE difference $= -0.05 \pm 0.80$, to $80 \leq IV < 95$, SE difference $= 1.48 \pm 2.77$).

**Discussion**

In recent years, BI has attracted more and more attention, especially in the field of dyslexia\(^1\) and autism.\(^3,12\) This is
dependent on the imbalance of BR as one of the external manifestations of E/I balance condition, and which can be observed and studied by various tests. However, the studies focused on BI in vision problems were relatively limited, especially with myopia.\textsuperscript{13–15}

The results indicated that larger IV did not mean a more negative SE (in both the right and left eyes), nor did it mean worse VA in the myopic population. According to the frequency chart, the frequency of BI maintained a high level in different levels of bilateral SE difference. This was consistent with the study by Li and colleagues, suggesting that BI is common within the population.\textsuperscript{9} With the increase of IV, it is more likely that bilateral SE difference will increase. This suggests that BI may be accompanied by imbalanced development of the ocular refractive system. In addition, we found that the dominant eye in terms of BI tended to have a more negative SE than the other eye. Moreover, from the perspective of myopia groups, the SE of the dominant side tended to be more negative as the predominance of this eye increased. This suggests that due to the higher efficiency of signal input, the eye at this side might be required to bear a greater load of binocular work, resulting in a greater degree of myopia than that of the opposite side.

There were some limitations in this study. First, some subjects reported BR because they could not fully mobilize the fusion function, resulting in the lack of quantified analysis. In future research, it would be worth examining whether the design of BI tests takes the duration cycle of binocular fusion and BR into account. Second, this study lacked systematic followup records. Whether a larger BI at baseline leads to greater difference of the refractive system development after a period of time remained unclear. Finally, the 95 percent CI of the data presented in the last two parts of the results were relatively large.

Recently, our team has obtained preliminary results in a small-sample study ($n=40$) showing that the BI could be improved by VR visual perception training. In the training (lasting 10 minutes), different contrast information is exchanged between the eyes in sinusoidal cycles (3 seconds per

**FIG. 4.** (a) The increasing trends in mean value of IV (the absolute value) along with bilateral SE difference (the absolute value) changing. (b) The increasing trends in mean value of bilateral SE difference (the absolute value) along with IV (the absolute value) changing. IV, imbalance value.

**FIG. 5.** The trends in mean value of BCI along with bilateral SE difference changing.
cycle) to re-establish BB. Compared with the mean value of $|IV|$ in the control group, the mean value of $|IV|$ was significantly reduced in the training group after a training session. The mean difference of IV between the two groups was statistically significant (control group: $-0.25 \pm 2.55$, training group: $6.75 \pm 7.12$; $p=0.00$). Our team is now further conducting the study with a larger sample size and a longer followup period. The results will be published in the near future.

**Conclusion**

BI widely exists in myopia groups. In this study, the BI did not show a correlation with the unilateral eye refractive state and VA. However, the BI may be accompanied by imbalanced development of the eye refractive system. Furthermore, the SE of the dominant eye (from the perspective of BI) tends to be more negative than that of the opposite eye as the predominance increases.

**Acknowledgment**

We thank Yu Lin for assistance with data analysis that greatly improved the article.

**Authors’ Contributions**

H.D. and Z.T. conceived and designed the study. M.Z., M.X., and J.W. performed the data collection. M.Z., Z.L., and H.C. analyzed the data. Z.T. wrote the article. H.D., J.Z., H.Z., Z.K., M.W., and B.W. reviewed and edited the article. All authors read and approved the article.

**Author Disclosure Statement**

No competing financial interests exist.

**Funding Information**

The study was funded by International Science and Technology Cooperation Research Project of Shenzhen Science and Technology Innovation Committee (GHJZ2019 0821113401670), Sanming Project of Medicine in Shenzhen (SZSM201812090), and Shenzhen Fund for Guangdong Provincial High-level Clinical Key Specialties (no. SZGS P014). Yu Lin, Statistician, Shenzhen Withsum Technology Limited, was supported by Shenzhen Science and Technology Plan, grant no. CKCY20180323174659823.

**References**

1. Gao R, Penzes P. Common mechanisms of excitatory and inhibitory imbalance in schizophrenia and autism spectrum disorders. Current Molecular Medicine 2015; 15:146–167.
2. Skerswetat J, Bex PJ, Baron-Cohen S. Visual consciousness dynamics in adults with and without autism. Scientific Reports 2022; 12:4376.
3. Dunn S, Jones M. Binocular rivalry dynamics associated with high levels of self-reported autistic traits suggest an imbalance of cortical excitation and inhibition. Behavioural Brain Research 2020; 388:112603.
4. Milne E, Dickinson A, Smith R. Adults with autism spectrum conditions experience increased levels of anomalous perception. PLoS One 2017; 12:e0177804.
5. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology 2016; 123:1036–1042.
6. Modjahedi BS, Abbott RL, Fong DS, et al. Reducing the global burden of myopia by delaying the onset of myopia and reducing myopic progression in children: the academy’s task force on myopia. Ophthalmology 2021; 128:816–826.
7. Webber A, Schmid K, Baldwin A, et al. Suppression rather than visual acuity loss limits stereocuity in amblyopia. Investigative Ophthalmology & Visual Science 2020; 61:50.
8. Vera-Diaz FA, Bex PJ, Ferreira A, et al. Binocular temporal visual processing in myopia. Journal of Vision 2018; 18:17.
9. Xu L, Huang M, Lan J, et al. Assessment of binocular imbalance with an augmented virtual reality platform in a normal population. Cyberpsychology, Behavior and Social Network 2019; 22:127–131.
10. Flitcroft DI, He M, Jonas JB, et al. IMI—defining and classifying myopia: a proposed set of standards for clinical and epidemiologic studies. Investigative Ophthalmology & Visual Science 2019; 60.
11. Hussey E. Binocular visual sensation in reading a unified theory. Journal of Behavioral Optometry 2001; 12:119.
12. Karaminis T, Lunghi C, Neil L, et al. Binocular rivalry in children on the autism spectrum. Autism Research 2017; 10:1096–1106.
13. Kwon M, Wieck E, Dakin SC, et al. Spatial-frequency dependent binocular imbalance in amblyopia. Scientific Reports 2015; 5:17181.
14. Li J, Thompson B, Lam C, et al. The role of suppression in amblyopia. Investigative Ophthalmology & Visual Science 2011; 52:4169–4176.
15. Babu RJ, Clavagnier SR, Bobier W, et al. The regional extent of suppression: strabismics versus nonstrabismics. Investigative Ophthalmology & Visual Science 2013; 54: 6585–6593.

Address correspondence to:
Dr. Hongwei Deng
Department of Strabismus & Pediatric Ophthalmology
Shenzhen Eye Hospital Affiliated to Jinan University
Shenzhen University of Medicine
Shenzhen 518000
China
E-mail: dhw110@126.com