Temporal Frequency Modulation of Binocular Balance in Normal and Amblyopic Vision

Chenyan Zhou,[1] Jiawei Zhou,[1] and Seung Hyun Min[1,2]

[1]State Key Laboratory of Eye Health, Eye Hospital, Wenzhou Medical University, Wenzhou, China
[2]Department of Psychology, Zhejiang Sci-Tech University, Hangzhou, China

Correspondence: Jiawei Zhou, State Key Laboratory of Eye Health, Eye Hospital, Wenzhou Medical University, 270 Xueyuan West Road, Wenzhou, Zhejiang 325015, China; zhoujw@mail.eye.ac.cn.
Seung Hyun Min, Department of Psychology, Zhejiang Sci-Tech University, 928 Second Avenue, Xiasha Higher Education Zone, Hangzhou, Zhejiang 310018, China; sammin95@gmail.com.

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Purpose. To investigate how temporal frequency modulates binocular balance in normally sighted and amblyopic adults.

Methods. Twenty-three controls and 13 amblyopes participated in this study. The effects of temporal frequency differences and monocularly directed attention on binocular balance were measured using an onset binocular rivalry task with sinusoidally flickering gratings at varying temporal frequencies and static gratings with monocular attentional cues. For the flickering gratings, different combinations of temporal frequencies (2, 4, or 10 Hz in one eye vs. 2, 3, 4, 6, 10, 15, or 20 Hz in the other) were presented. Their effects were then compared, and their relationship was analyzed.

Results. There was no relationship between the shifts in balance from temporal frequency and monocularly directed attention in both controls and amblyopes. Intermediate temporal frequencies (8.9 ± 1.4 Hz) in one eye maximized its perceptual dominance, with a larger shift due to temporal frequency in amblyopes than in controls. While normally sighted observers experienced similar degrees of shift in balance from temporal frequency and attentional (active and passive) modulations, amblyopic observers experienced a larger shift from temporal frequency than from monocularly focused passive (but not active) attention.

Conclusions. Intermediate temporal frequencies in one eye, rather than a specific temporal frequency difference between both eyes, maximized its perceptual dominance in both normally sighted and amblyopic observers. This balance shift from temporal frequency modulation was larger in amblyopes than in controls. Finally, the effect of temporal frequency on balance was larger than that of monocularly directed passive attention in amblyopes.

Keywords: amblyopia, temporal frequency, binocular balance, onset rivalry, attention

During early visual development, the brain learns to combine signals from both eyes properly.[1,2] However, this developmental process can be disturbed if inputs from both eyes have spatial conflict, leading to severe abnormalities in visual perception and the organization of the primary visual cortex (V1), where inputs of two eyes get combined.[3–6] This mismatch can result from several factors, such as anisometropia, strabismus, and congenital cataract, creating a conflict between two eyes' inputs.[7,8] To resolve this conflict, the V1 area begins to ignore the input from the weaker eye and relies more heavily on the signal from the fellow eye,[5,9] forming a binocular representation of the world primarily through one eye.[10,11] This interocular imbalance from abnormal suppression can become permanent if there is no timely intervention, causing the affected individual to have impaired vision that cannot be optically corrected. This visual condition is known as amblyopia, a neurodevelopmental disorder that is characterized by significantly reduced visual acuity in the amblyopic eye, as well as impaired depth perception and binocular balance.[7,12,13]

Binocular balance can be quantitatively measured by eliciting binocular rivalry, a phenomenon that occurs when each eye is presented with a different image.[14,15] During binocular rivalry, the image from each eye alternately reaches conscious awareness.[14,16,17] Although these perceptual alterations are stochastic, the dynamics of binocular rivalry can reveal the state of interocular balance.[15,18,19] For example, if the right eye is more dominant, the image of the eye will reach conscious perception more frequently, while the input of the other eye will remain suppressed more persistently.[15,18,19] Binocular rivalry can be triggered between both eyes when they are separately shown with images that have sufficiently different colors,[20,21] shapes,[22,23] orientations,[21] spatial frequencies,[24] and temporal frequencies.[25] Binocular balance, as measured with binocular rivalry and other methods, can be shifted in favor of one eye by introducing higher contrast or luminance in the eye.[26,27] In dichoptic therapies, images shown to both the fellow and amblyopic eyes are spatially adjusted, such as their contrasts, so that observers can properly combine images from both eyes with equal weighting. This treatment method has been used to improve binocular vision of individuals with amblyopia.[28,29]

However, previous studies have only investigated how spatial differences between images presented to each eye, but not temporal differences, could modulate binocular balance, as demonstrated using various psychophysical tasks.[26,29–31] Interestingly, the human visual system favors high temporal frequencies over low temporal frequencies,[25,32–35] possibly through both a low and a high level of visual mechanisms. For example, there are at least two temporal channels: one tuned to low frequencies and the other to high frequencies, intersecting at around 6 to 8 Hz.[32,36–38] There is asymmetric inhibition between temporal channels, such that the high-frequency channel suppresses the response of the low-frequency channel but not vice versa.[32,33,36] Additionally, when a stimulus appears (onset), neurons in the visual pathway often show an increased firing rate.[39–41] If a stimulus flickers more frequently over time, there will be more rapid and frequent stimulus onsets within a given time period, thereby increasing the neural and perceptual response to the stimulus. Apart from low-level mechanisms, attentional selection may also potentially contribute to this preference for high frequency in temporal processing. Visual flicker can be categorized as a series of abrupt onsets, which can capture visual attention.[42–44] According to psychophysical studies, faster flicker can capture attention more effectively[35,45,46] possibly because it involves more frequent abrupt onsets.

Drawing from the idea that attentional selection may be involved in the asymmetric flicker influence, it follows that temporal frequency differences can potentially affect binocular balance through the attentional mechanism. Two types of attention can elevate the signal strength of the visual image. First, passive attention (i.e., bottom-up, involuntary) can be achieved by increasing the saliency of a visual target. For instance, binocular balance can be shifted in favor of the eye shown a +45° grating with monocularly directed cues rather than the eye shown only a −45° grating because the cues elevate the saliency of the +45° grating through passive attention.[47,48] Second, active attention (i.e., top-down, voluntary) requires deliberate, goal-oriented effort on a specific task and has been reported to significantly affect binocular balance more than passive attention during binocular rivalry.[48,49] To illustrate, when an observer views a +45° grating in one eye and a −45° grating in the other and is asked to perform a secondary visual task shown only to the eye seeing the +45° grating, this directs the observer's active attention to the +45° grating, thereby significantly shifting binocular balance. Flicker can elevate the saliency of a visual target as a function of its flickering rate because a faster flicker can better capture attention.[35,42–46] Thus, if one eye is shown with a +45° grating flickering quickly while the other eye is presented with a −45° grating flickering more slowly, it is possible that the eye with a faster flickering grating could become more perceptually dominant by recruiting attentional selection.

In the current study, we investigate whether temporal frequency differences between the two eyes could similarly alter binocular balance using an onset binocular rivalry task in normally sighted and amblyopic adults. In experiment 1, we first explore whether the eye with faster or slower flicker is perceptually more dominant. We hypothesize that the faster flickered eye would become more dominant. This prediction is based on previous studies showing that faster signals can asymmetrically suppress slower signals[32,33,36] and that higher flicker rates can capture attention more effectively,[35,42–46] which in itself can shift binocular balance.[47–49] To clarify whether temporal frequency modulates binocular balance through low- or high-level (e.g., attention-mediated) pathways, we compare the effect of attentional and flicker modulations and explore their relationship. We initially find that, in contrast to our hypothesis, the eye shown a slowly flickering grating is more perceptually dominant and that there is no relationship between these two modulations. In experiment 2, we test if a slower flickered eye is always more dominant. However, after testing a wider range of temporal frequencies of one eye, we find that intermediate temporal frequencies maximize eye dominance. In experiment 3, to further see if the absolute temporal frequency value in one eye or a specific value of temporal frequency difference between eyes depends on the shift in binocular balance, we test a range of temporal frequencies of both eyes and ultimately find that the eye with a temporal frequency of 8.9 ± 1.4 Hz (95% confidence interval) is most perceptually dominant, regardless of the temporal frequency of the other eye.

Methods

Participants

Twenty-three normally sighted observers (23.8 ± 1.9 years, 8 males; details in Table 1) and 13 individuals with amblyopia (25.4 ± 4.2 years, 9 males; details in Table 2) participated in this study. Some of them participated in more than one experiment (listed in Tables 1 and 2). We used the definition of amblyopia outlined in the Preferred Practice Patterns of the American Academy of Ophthalmology[8] to determine the criteria for subject recruitment. These criteria included interocular best-corrected visual acuity difference of two or more logMAR lines (≥0.2 logMAR) with no other ocular anomalies. All amblyopic subjects had been previously diagnosed, whose detailed clinical information is listed in Table 2. All subjects were asked to wear their prescribed optical corrections, if needed, during the experiment. Before their enrollment, they provided an informed consent form. Except for the primary author (CZ), all subjects were naive to the purpose of the study, which was approved by the Ethics Committee of Wenzhou Medical University and followed the tenets of the Declaration of Helsinki.

Apparatus

All stimuli were generated by a Mac mini with MATLAB R2016a (MathWorks, Natick, MA, USA) and PsychToolBox 3.0.14 extension.[50] The stimuli were dichoptically presented using gamma-corrected head-mounted goggles (GOOVIS Pro, AMOLED display; NED Optics, Shenzhen, China). The goggles had a resolution of 1920 × 1080 pixels, a refresh rate of 60 Hz, a pixel density of 41.6 pixels per degree, and a maximal luminance of 150 cd/m^2.

Stimuli and Procedure

General Stimuli. In this study, an onset rivalry task was used to test initial eye dominance, which refers to the first eye that prevails in eye dominance during the measurement. In this task, two sinusoidal gratings with a size of 4.2 × 4.2 degrees and a spatial frequency of 1.4 c/deg were presented dichoptically to the two eyes (Fig. 1A). This spatial

Table 1. Details of Normally Sighted Observers

Observer	Age/Sex	VA (logMAR) OD/OS	Refraction OD/OS	RDS (Arcsecs)	Experiment
N1	21/M	0	−4.00/−0.75 × 5	30	1
		0	−3.75/−0.75 × 10		
N2	25/F	−0.02	−2.50/−0.75 × 177	25	1
		−0.06	−2.50/−1.00 × 166		
N3	24/M	−0.2	−0.75/−0.25 × 90	40	1
		−0.1	−0.50/−0.50 × 90		
N4	23/M	−0.02	−4.50/−1.25 × 30	20	1
		−0.08	−4.25/−1.00 × 165		
N5	23/M	−0.1	Plano	20	1
		−0.1	Plano		
N6	25/F	−0.04	−4.50/−0.50 × 108	30	1
		0	−4.50/−0.50 × 152		
N7	24/F	−0.1	−4.50	25	1
		−0.1	−4.25		
N8	25/F	−0.02	−4.25	40	1, 2
		−0.06	−4.00/−1.00 × 165		
N9	20/M	−0.1	−5.50/−0.50 × 83	40	1, 2
		−0.04	−5.50/−0.50 × 75		
N10	20/M	0	−2.25/−1.00 × 180	20	1, 2
		0	−1.25/−1.00 × 180		
N11	24/F	0	−5.00	25	1, 2
		0	−5.75		
N12	23/F	−0.02	−2.00	20	1, 2
		−0.08	−1.25		
N13	24/F	0	−5.25/−1.00 × 160	20	1, 2
		0	−5.00/−1.50 × 155		
N14	25/F	−0.06	−4.75/−0.50 × 5	25	1, 2
		−0.08	−4.75/−0.50 × 5		
N15	25/M	0	−1.50	20	1, 2, 3
		0	−2.00		
N16	23/F	−0.1	Plano	20	1, 2, 3
		−0.1	Plano		
N17	23/F	−0.1	−2.75	40	1, 2, 3
		−0.2	−2.75		
N18	25/M	−0.16	−2.50	20	1, 2, 3
		−0.16	−2.50		
N19	24/F	−0.2	−1.00	20	1, 2, 3
		−0.2	−0.50		
N20	25/F	0	−2.75/−0.75 × 100	20	1, 3
		−0.1	−2.75/−0.75 × 90		
N21	25/F	−0.02	−2.50/−0.50 × 180	20	2, 3
		−0.04	−2.25/−0.75 × 70		
N22	23/F	−0.1	Plano	20	3
		−0.1	Plano		
N23	29/F	−0.1	−2.75/−0.75 × 100	25	3
		−0.1	−2.50/−0.75 × 70		

F, female; M, male; OD, right eye; OS, left eye; RDS, randot stereotest; VA, visual acuity.

frequency was chosen where binocular imbalance in amblyopes is mild (below 2 c/deg) and their data are still reliable (unreliable at high spatial frequencies).[51] The gratings were surrounded by a circular cosine envelope (window = 2.8 × 2.8 degrees). One grating had an orientation of +45°, while the other eye's grating had an orientation of −45°. Two configurations of the orientations were used to eliminate response bias. In the first configuration, the dominant eye (DE) or fellow eye (FE) was presented with a grating at +45°, while the nondominant eye (NDE) or amblyopic eye (AE) was shown with a grating at −45°. In the second configuration, the orientation of the grating shown to each eye was reversed.

The method of constant stimuli was used to obtain a balance point (BP), which was where two eyes would be balanced. Specifically, gratings of the two eyes were shown at seven contrast ratios (α_{ratio}): 1/7, 1/3, 1/$\sqrt{3}$, 1, $\sqrt{3}$/1, 3/1, and 7/1 for adults with normal vision. Base contrast (β) of the grating was set at 0.37. The contrast of the gratings for DE and NDE was $\beta * \alpha_{ratio}{}^{1/2}$ and $\beta/\alpha_{ratio}{}^{1/2}$, respectively. In amblyopic observers, due to their severe imbalance, the contrast of the grating was fixed at 100% for AE and set at 100% * α_{ratio} for FE. We set seven individualized contrast ratios to obtain the BP as different subjects had different requirements for the contrast ratios, which were selected based on their performances from practice trials. Before each testing session, we ensured that subjects could clearly see the grating monocularly at all ratios. Each orientation configuration and interocular contrast ratio were repeated 10 times in one test block. Thus, there were 140 trials (2 orienta-

Table 2. Clinical Details of Amblyopes

Observer	Age/Sex	VA (logMAR) AE/FE	Refraction AE/FE	Squint	RDS (Arcsecs)	History of Treatment	Experiment
A1	19/M	0.3 −0.1	+4.00/−1.50 × 105 +1.00/−1.00 × 115	Ø	200	Detected at 5 years old, patched for 1 year	1
A2	24/M	0.34 −0.18	+3.00/−0.50 × 130 +0.25/−0.25 × 35	Ø	500	Detected at 9 years old, glasses since 18 years old, patched for several days	1
A3	30/M	0.42 −0.08	+1.00/−1.00 × 15 −4.75	Ø	400	Detected at 7 years old, patched occasionally for 1 year	1, 2
A4	30/F	0.36 −0.06	+3.00/−2.25 × 10 Plano	Ø	400	Detected at 18 years old, no treatment	1, 2
A5	28/F	0.18 −0.1	+2.00/−0.25 × 175 −2.00/−0.50 × 10	Ø	60	Detected at 11 years old, glasses since detection, patched occasionally for 3 years	1, 2
A6	18/M	0.4 0	−2.50 × 175 −8.25/−1.75 × 5	Ø	400	Detected at 9 years old, glasses since detection, patched for 1 year	1, 2
A7	23/M	0.3 −0.1	−5.00 × 175 −0.50 × 30	Ø	200	Detected at 7 years old, patched for 1 month	1, 2
A8	28/M	0.5 −0.1	+2.50/−0.50 × 30 −1.00	Ø	200	Detected at 4 years old, patched occasionally for 1 year	1, 2
A9	29/F	0.42 −0.1	+2.50/−2.00 × 155 −1.00	Ø	200	Detected at 13 years old, no treatment	1, 2
A10	25/M	0.4 −0.1	+4.00/−2.25 × 10 −0.75/−0.50 × 175	Ø	400	Detected at 20 years old, no treatment	1, 2
A11	28/M	0.34 0	+1.25/−1.00 × 24 −2.50/−0.50 × 45	Ø	200	Detected at 11 years old, patched occasionally for 6 months, glasses since 12 years old	1, 2
A12	20/M	0.4 −0.06	+2.00/−1.00 × 170 −0.75/−0.25 × 5	Ø	200	Detected at 5 years old, glasses since detection, patched for 3 years	2
A13	28/F	0.38 −0.14	+4.75/−0.50 × 20 −0.50	Ø	200	Detected at 14 years old, no treatment	2

F, female; M, male; AE, amblyopic eye; FE, fellow eye; RDS, randot stereotest; VA, visual acuity.

tion configurations × 7 interocular contrast ratios × 10 repetitions) in each test block. The order of the configurations and interocular contrast ratios was randomized throughout each trial.

In all experiments in the study, we flickered the grating shown to each eye by modulating its contrast in a sinusoidal on-off fashion (see video of a 2-Hz grating at https://www.smin95.com/grating2hz.MP4) because of its important advantage over square-wave contrast modulation. Previous studies on continuous flash suppression (CFS) report that sinusoidal flicker contains only one temporal frequency, whereas square-wave flicker can be decomposed into multiple low temporal frequencies even at high temporal frequencies.[46,52] In other words, the temporal energy of sinusoidal contrast modulation is specific. Sinusoidal contrast modulation of the two gratings shown to both eyes began at the same phase of the modulation, which was randomly selected across trials.

General Procedure. Each test block of the onset rivalry task included two parts. During the task, a surrounding frame composed of pixelated binary noise was shown to promote convergence between the two eyes. Participants were initially asked to perform an alignment trial first, during which they were asked to adjust the location of the two separate crosses into one composite cross using keyboard. Next, the test phase would follow, during which the two sinusoidal gratings were presented to the eyes dichoptically. The stimuli were presented briefly (see details later). After the stimulus presentation, subjects were asked to report the orientation of the initially perceived grating (clockwise or counterclockwise) using a keyboard (left or right key) for each response. Then, a next trial of the test phase would follow. It took about 3 minutes to complete one test block. Each subject completed two test blocks for each measurement condition. The data from the practice trials were used to determine which eye was dominant for each participant.

Experiment 1

The aim of the first experiment was twofold: to explore whether the faster or slower flickered eye would be relatively more dominant in normal and amblyopic vision and whether this change was related to active or passive attentional effect. Twenty normally sighted observers and 11 amblyopes participated in this experiment (see Tables 1 and 2).

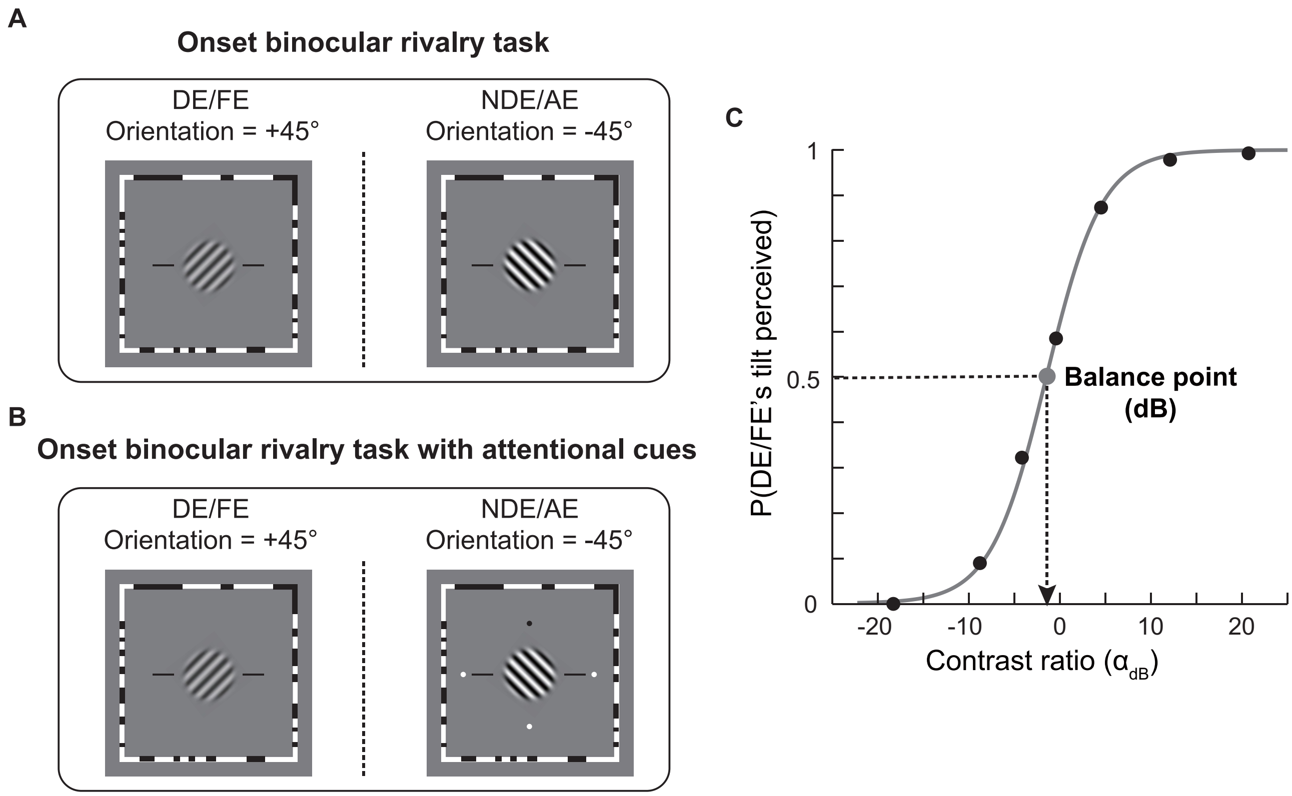

Figure 1. Stimuli and illustration of data analysis. (**A**) Onset binocular rivalry task. Two sinusoidal gratings were dichoptically shown to each eye. These two gratings have the same spatial frequency and size but different orientations relative to the horizontal axis (±45°). Subjects were required to press a key to report what they initially perceived. (**B**) Onset binocular rivalry task with attentional cues. Four dots (three *white dots* and one *black dot*) were added on the top, bottom, left, and right sides peripheral to the grating stimulus to direct attention to NDE/AE. (**C**) A psychometric function. The y-axis denotes the probability of the subject perceiving the DE/FE's grating. The x-axis denotes the interocular contrast ratio in log units (α_{dB}). A cumulative logistic distribution function was used to fit this psychometric curve. The BP indicates the point at which the two eyes had equal contribution to binocular vision.

Three types of stimuli were used in experiment 1, as shown in Figure 1A and 1B. First, for the baseline condition, two *static* gratings were dichoptically presented to both eyes for 0.75 seconds ("Baseline" in Fig. 2A). The gratings had a gradual appearance and disappearance—the contrast level varied as a function of a half-period sinewave, increasing from 0 to the maximum in the first one-third of the duration, remaining at this maximum for the middle one-third, and then decreasing to 0 in the last one-third. Second, two *flickering* gratings were dichoptically presented for 1 second, with contrast modulated sinusoidally ("Flicker" in Fig. 2A). The stimuli did not appear and disappear gradually. Third, two *static* gratings were dichoptically shown to both eyes for 1 second, which appeared and disappeared as those in the baseline, concurrently with attentional cues presented to NDE/AE only ("Active attention" and "Passive attention" in Fig. 2A). The cues, composed of three white dots and one black dot on the top, bottom, left, and right sides peripheral to the grating (Fig. 1B), were small enough to not distract the participants while they viewed the main grating. We were uncertain as to whether the visibility of cues or their ability to attract visual attention would be affected by the flickering grating. Therefore, we used static rather than flickering gratings in the attentional conditions to precisely measure the impact of attention, as previous studies did.[47,48] The position of the black dot was randomized in each trial. For the active attentional condition, subjects were asked to verbally identify the location of the black dot while they performed the main rivalry task. If participants had mislocated the black dot more than 10 times within one test block (140 trials), they were asked to be retested again. Most of the participants reached an accuracy of more than 95% (fewer than five incorrect responses). For the passive attentional condition, subjects were asked to focus only on the onset rivalry task. Although the stimulus duration varied between the baseline (first type) and experimental (second and third types) viewing conditions, this was not an issue because initial eye dominance could be induced within 300 ms when there was a contrast difference between both eyes.[53] The order of the three experimental conditions was randomized for each subject.

To introduce temporal frequency difference modulation ("Flicker" in Fig. 2A), we sinusoidally modulated the contrast levels of the left- and right-eye gratings at two different temporal frequencies—one slow and one fast (NDE/AE: 4 Hz; DE/FE: 20 Hz). We used a random-number generator to decide which eye was shown a faster flicker in each subject group, thereby avoiding expectancy bias. These two temporal frequencies were selected because they are sufficiently apart to be from unique temporal channels.[25,32] Additionally, they are still below the critical flicker fusion frequency,[54,55] which is a frequency value where observers stop perceiving flicker because it is too rapid. Before formal testing, we

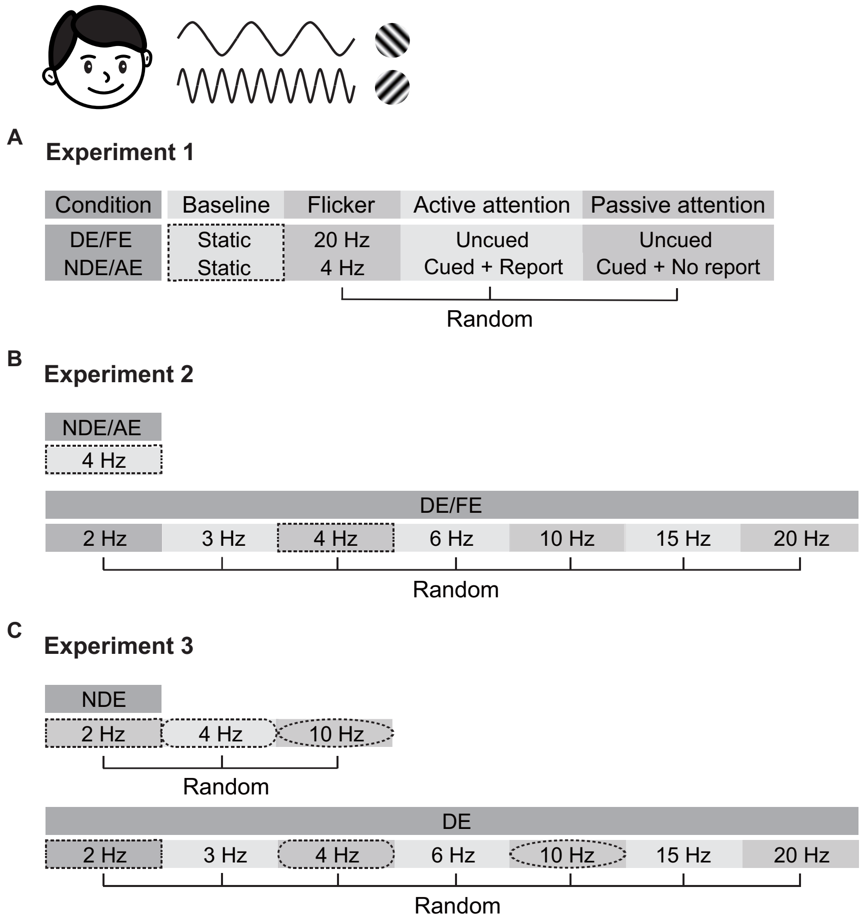

FIGURE 2. The experimental designs. (**A**) The experimental design of experiment 1. Binocular balance was measured when flicker, active attention, and passive attention were introduced. Baseline was set when static stimuli were shown to both eyes (marked with *dashed lines*). In the flicker condition, slow and fast flickering stimuli were separately shown to the two eyes (NDE/AE: 4 Hz; DE/FE: 20 Hz). In the attentional condition, additional cues were shown to NDE/AE with (active attention) and without (passive attention) asking subjects to respond to them. (**B**) The experimental design of experiment 2. Binocular balance was measured when NDE/AE was shown with a grating that flickered at only 4 Hz, while DE/FE was tested at different temporal frequencies (2, 3, 4, 6, 10, 15, and 20 Hz). Baseline was defined when both eyes viewed at 4 Hz (marked with *dashed lines*). (**C**) The experimental design of experiment 3. Binocular balance was measured when NDE was fixed at a frequency of 2, 4, or 10 Hz, while DE was shown at different temporal frequencies (2, 3, 4, 6, 10, 15, and 20 Hz). Baseline was when both eyes viewed at the same temporal frequency (2, 4, or 10 Hz in both eyes) (marked with *dashed lines* in different shapes).

made sure that the subjects were able to see the flickering grating monocularly at all contrast levels.

Experiment 2

The aim of the experiment was to test if various temporal frequency differences elicited a similar dominance shift in normally sighted and amblyopic observers as those from the frequency difference tested in experiment 1 (4 Hz vs. 20 Hz). Thirteen normally sighted observers (12 from experiment 1) and 11 amblyopic observers (9 from experiment 1) participated in this experiment.

There was only one experimental condition in experiment 2 (Fig. 2B). While NDE/AE was shown with a grating that flickered at only 4 Hz, DE/FE was tested at different temporal frequencies (2, 3, 4, 6, 10, 15, and 20 Hz). Its baseline condition was categorized when both eyes were viewing gratings that flickered at 4 Hz (no temporal frequency difference). Changes in binocular balance driven by different temporal frequency differences were quantified relative to the baseline condition. The order of the tested temporal frequency was randomized for each subject.

Experiment 3

The goal of this experiment was to see if a specific value of temporal frequency difference, regardless of the absolute temporal frequency values in both eyes, predictably shifted the binocular balance. Nine normally sighted observers (6 from experiment 2) participated in this experiment.

There were three experimental conditions (Fig. 2C). While DE was tested at different temporal frequencies (2, 3, 4, 6, 10, 15, and 20 Hz) as in experiment 2, NDE was shown with a grating that flickered at 2, 4, or 10 Hz. The baseline condition was categorized when both eyes were viewing gratings that flickered at the same temporal frequency (2, 4, or 10 Hz in both eyes). Shifts in binocular balance from different temporal frequency differences were computed relative to the baseline condition. The order of testing was randomized for each participant.

Data Analysis

A BP refers to a contrast ratio where both eyes contribute equally. The perceptual responses of the subjects at seven tested contrast ratios in each test block were converted to the probability of the subject perceiving the DE/FE's grating. The contrast ratios were converted into log scale first to achieve symmetry between eyes for further analysis by using the following equation:

$$\alpha_{dB} = 20 \times \log_{10}\alpha_{ratio}$$

where α_{ratio} is the contrast ratio of DE/FE to NDE/AE. When the stimulus contrast of DE/FE is twice than that of NDE/AE ($\alpha_{ratio} = 2$) to reach binocular balance state, it results in $\alpha_{dB} = 6$ dB.

Using the Palamedes toolbox,[56] we fitted the psychometric curve by a cumulative logistic function of the probability of perceiving the DE/FE's grating and interocular contrast ratios in log units to estimate the contrast ratio at the BP (Fig. 1C).[57,58] Specifically, when the probability of the participants perceiving the percept shown to DE/FE was 50%, the binocular balance state was reached, and the corresponding interocular contrast ratio was defined as BP. If two eyes were balanced, BP would always be 0. If BP < 0, the balance would favor DE/FE, while BP > 0 would indicate that NDE/AE would be more perceptually dominant.

Statistical Analysis

All analyses were performed with R software.[59] We used the Shapiro–Wilk test first to check the normality of the data and homogeneity of variance with Levene's test. In experiment 1, a two-way mixed-measures analysis of variance (ANOVA) and post hoc pairwise comparisons with Bonferroni correction were performed to examine whether changes in BP were different among flicker, active attentional, and passive attentional conditions and between two groups. A two-tailed Pearson correlation was used to determine whether flicker-driven changes in BP were correlated with active and passive attention-driven changes in BP for each group. For experiment 2, to explore the difference in temporal frequency effect between normally sighted and amblyopic observers, an unpaired Student's *t*-test and a Wilcoxon rank-sum test were performed separately for the normally and the nonnormally distributed data. In experiment 3, a pairwise *t*-test for paired groups with Bonferroni correction was performed to test whether there was a significant difference in the data among different experimental conditions. In the subsequent comparisons, a paired *t*-test was used to compare baseline BP in experiments 1 and 2, and a two-way mixed-measures ANOVA and post hoc pairwise comparisons with Bonferroni correction were performed to recompare the effects of temporal frequency and monocularly directed attention on binocular balance.

Results

Experiment 1: Can a Higher Temporal Frequency Shift Binocular Balance Through Attentional Selection?

First, we wanted to check whether our hypothesis that a faster flickered eye would be more dominant than a slower flickered eye was correct. This prediction was based on the idea that faster signals could asymmetrically suppress slower signals[32,33,36] and that faster flicker could attract attention more effectively.[35,42–46] There were three conditions in this experiment—flicker, active attention, and passive attention conditions (see Methods).

Opposite to our assumption, we found that the slower flickered eye at 4 Hz was more dominant than the faster flickered eye at 20 Hz, as shown in Figure 3A, where the positive value of change in BP indicates that NDE/AE has become more dominant relative to baseline. To further explore the relation between flicker and attentional modulations, we first performed a two-way mixed-measures ANOVA to compare their effects by designating experimental condition (flicker, active attention, and passive attention) as a within-subject factor and group (normally sighted and amblyopic observers) as a between-subject factor. The analysis revealed a significant effect of experimental condition ($F(2, 58) = 12.894$, $P < 0.001$) but not of subject group ($F(1, 29) = 1.425$, $P = 0.242$) or the interaction between condition and group ($F(2, 58) = 2.682$, $P = 0.077$). Post hoc pairwise comparisons with Bonferroni correction reported a significant difference in BP shifts between active and passive attentional conditions in both normally sighted ($P = 0.012$) and amblyopic ($P = 0.032$) groups, between flicker and active attentional conditions in controls ($P = 0.002$), and between two groups in the flicker condition ($P = 0.048$). These results indicate that the impact of active attention was greater compared to that of passive attention in both subject groups, and the impact of temporal frequency difference was significantly larger in amblyopes than in controls.

Even though we found that slower flicker rate leads to a greater perceptual dominance, it does not eliminate the possibility that temporal frequency differences and attention might still interact to affect binocular balance. For instance, 4 Hz could have captured more attention than 20 Hz due to some specific stimulus properties (e.g., apparent visibility) in our task. Therefore, we performed a correlation analysis to determine whether these changes in BP from temporal frequency difference and attentional cues had any relationships (Fig. 3B). According to a Pearson correlation test, no significant correlation was found between the effect of flicker and active attention in controls ($R = 0.053$, $P = 0.842$; Fig. 3B(i)) and amblyopes ($R = 0.55$, $P = 0.08$; Fig. 3B(ii)). Similarly, there was no significant correlation between the effect of flicker and passive attention in controls ($R = 0.28$, $P = 0.234$; Fig. 3B(iii)) and amblyopes ($R = 0.1$, $P = 0.76$; Fig. 3B(iv)). These results confirm that there is no link between changes in binocular balance driven by temporal frequency difference and those by monocularly driven attention.

Experiment 2: Is the Eye With a Lower Temporal Frequency Always More Dominant?

In contrast to our prediction, we observed that the slower flickered eye at 4 Hz was more perceptually dominant than the faster flickered eye at 20 Hz in experiment 1. However, whether a slower flickered eye would always be more dominant regardless of the other eye's frequency was unclear. Therefore, we conducted experiment 2 to test BP when one eye (DE/FE) was shown with a grating flickering at a wide range of temporal frequencies

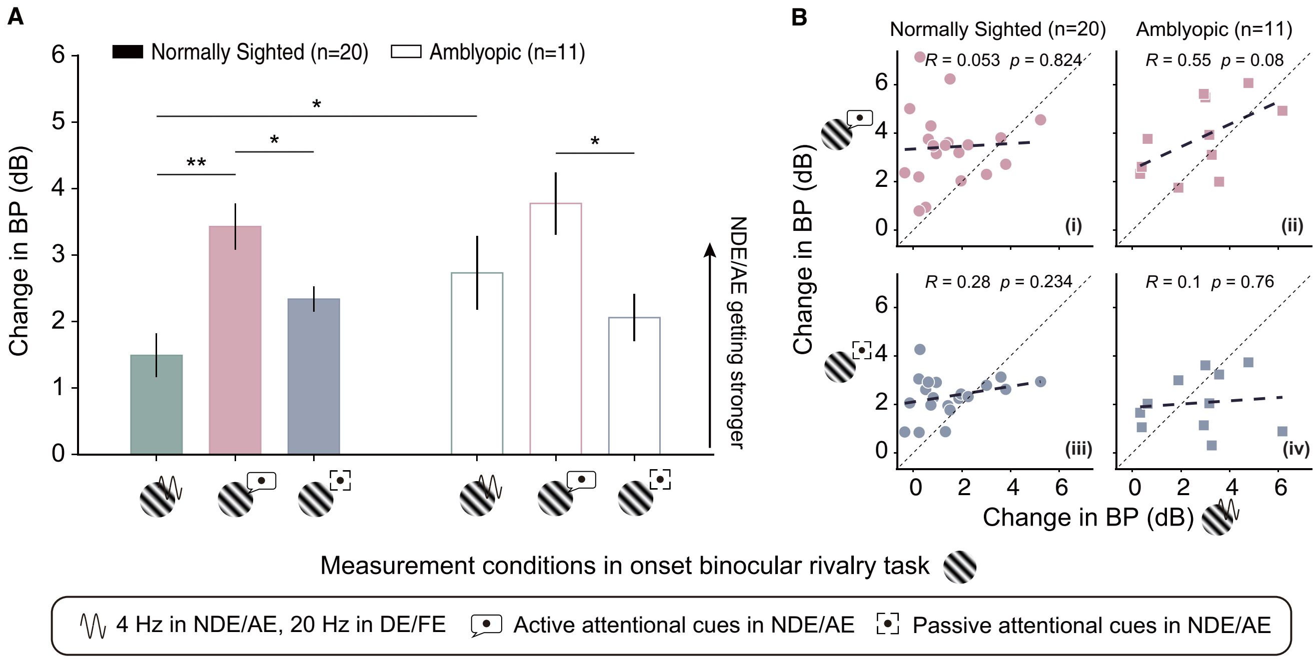

Figure 3. Results from flicker and attentional effects on BP in normally sighted ($n = 20$) and amblyopic observers ($n = 11$). (**A**) Changes in BP under different experimental conditions in the onset binocular rivalry task. The x-axis represents each experimental condition (flicker, active attention, or passive attention). The *filled* and *unfilled bars* represent normally sighted and amblyopic observers, respectively. In the flicker condition, two eyes separately viewed at low and high frequencies (NDE/AE: 4 Hz; DE/FE: 20 Hz). In attentional condition, additional cues were added to NDE/AE with (active attention) and without (passive attention) subjects' response. The *error bars* represent standard errors. The *asterisk* denotes a significant difference between two experimental conditions or groups (*$P < 0.05$, **$P < 0.01$). (**B**) Correlations between changes in BP measured in flicker and active attentional conditions (i, ii) and between changes in BP measured in flicker and passive attentional conditions (iii, iv). Individual data of normally sighted and amblyopic observers are plotted in points and squares, respectively. The *thin dashed line* represents no difference between changes in BP induced by flicker and attention.

(2 to 20 Hz) while the other eye (NDE/AE) was shown with a grating flickering at 4 Hz in both normally sighted and amblyopic observers. If our conclusion from experiment 1 was true, then we would observe that the eye at 2 Hz would be more dominant because it was the slowest among the tested frequencies. Changes in BP were computed relative to baseline when both eyes were shown at 4 Hz.

Similarly, we observed that when the temporal frequency of DE/FE was high (above 10 Hz) (Figs. 4A, 4B), it was weaker than during baseline when both eyes were shown at 4 Hz. However, we observed that when DE/FE was shown at 2 or 3 Hz, it would also become weaker, indicating that a low frequency could reduce perceptual dominance.

The data of both subject groups exhibited a tuning curve (Figs. 4A, 4B), which was fitted with a Gaussian function $G(x) = A \times \exp(-\frac{(x-\mu)^2}{2\sigma^2}) + \alpha$, where x = temporal frequency dimension, A = peak amplitude, μ = peak frequency, σ = standard deviation, and α = baseline offset. Amplitude, peak frequency, and bandwidth were calculated for each participant's tuning curve (Fig. 4C). According to the unpaired Student's t-test, the bandwidths ($t(22) = -0.626$, $P = 0.538$; Fig. 4C(ii)) and peak frequencies ($t(22) = 1.395$, $P = 0.177$; Fig. 4C(iii)) were similar between controls and amblyopes. However, a Wilcoxon rank-sum test revealed that the amplitudes were significantly different between controls and amblyopes ($W = 16$, $P = 0.001$; Fig. 4C(i)), suggesting that the magnitude of shift in balance from temporal frequency differences was once again larger in amblyopes than in normally sighted observers.

Experiment 3: Which Temporal Frequency Maximizes Perceptual Dominance of One Eye?

Results from experiment 2 indicated that the eye was the most dominant when it viewed at about 6 Hz while the other eye viewed at 4 Hz. There are two possibilities for why the peak was close to 6 Hz. First, where peak shift is induced can depend on whether two eyes have a small temporal frequency difference (e.g., 6 Hz in DE/FE and 4 Hz in NDE/AE). Second, the peak frequency can depend on the actual value of the temporal frequency in one eye regardless of the other eye's temporal frequency. To further identify it, we conducted experiment 3 by measuring BP in more conditions: the DE was shown at frequencies ranging from 2 to 20 Hz (as in experiment 2), while NDE was fixed at a frequency of 2, 4, or 10 Hz. Only normally sighted observers were recruited in this experiment because both subject groups had similar peak frequencies in experiment 2. If the temporal frequency difference determined the peak frequency, then the peak would be different at each of the three conditions (NDE at 2, 4, or 10 Hz) because it would depend on NDE's temporal frequency. However, if the absolute temporal frequency of each eye determined which eye was more perceptually dominant, then the peak would be similar across all three conditions.

As in experiment 2, we computed changes in BP relative to baseline (when both eyes viewed at the same temporal frequency: 2, 4, or 10 Hz). The results are shown in Figure 5 (NDE at 2 Hz in Fig. 5A(i); NDE at 4 Hz in Fig. 5A(ii); NDE at 10 Hz in Fig. 5A(iii)). The data (changes in BP) were

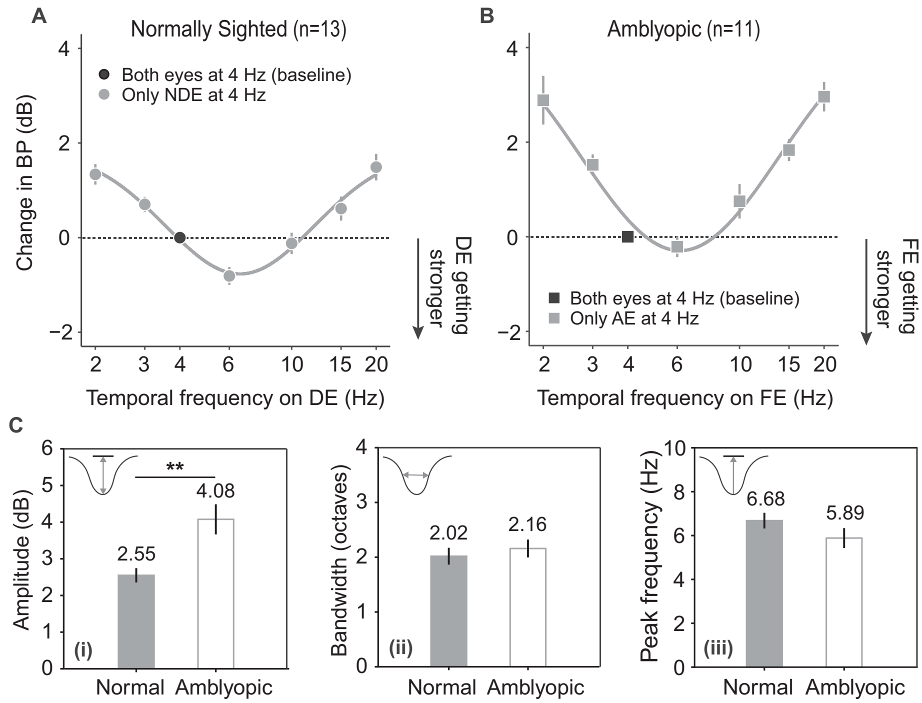

Figure 4. Results from effects on BP when NDE/AE viewed at 4 Hz and DE/FE viewed at 2, 3, 4, 6, 10, 15, and 20 Hz in normally sighted ($n = 13$) and amblyopic observers ($n = 11$). The changes in BP relative to baseline as a function of temporal frequency of DE/FE in normally sighted observers (**A**) and amblyopes (**B**). The *points* and *squares* represent normally sighted and amblyopic observers, respectively, and the *black* ones represent baseline. Continuous *solid lines* indicate the best-fitting Gaussians. The *error bars* in the figures represent standard errors. (**C**) The three parameters of the best-fitting Gaussian curves, including amplitude (i), bandwidth (ii), and peak frequency (iii). The amplitude was defined as the absolute height of the curve (i.e., the maximum change in BP minus the minimum). The bandwidth was the full width at half of the amplitude. The corresponding temporal frequency at the lowest point of the curve was peak frequency. The *filled* and *unfilled bars* represent normally sighted and amblyopic observers, respectively. The *error bars* represent standard errors. The *asterisk* denotes a significant difference between two groups (**$P < 0.01$).

once again fitted with a Gaussian function. We found that the balance was maximally shifted in favor of DE when the eye was shown at intermediate temporal frequencies regardless of NDE's temporal frequency. In other words, a temporal frequency difference between both eyes did not determine the outcome of perceptual dominance. This was confirmed by the fact that the peak was found to be near 7 Hz (of DE) when NDE was fixed at 2 and 4 Hz.

Interestingly, the characteristics of the Gaussian curves were quite different (Fig. 5B). Although the amplitudes were similar across the three conditions (NDE fixed at 2, 4, or 10 Hz) (Fig. 5B(i)), we observed that the bandwidth was narrower when the NDE was fixed at 10 Hz compared to when it was fixed at 4 Hz based on pairwise comparisons with Bonferroni correction ($P = 0.028$; Fig. 5B(ii)). The peak frequency was also the highest when NDE was fixed at 10 Hz (Ps ≤ 0.031 from pairwise comparisons; Fig. 5B(iii)). A broader bandwidth might be associated with decreased precision of the estimated peak frequency because, when one eye is fixed at a frequency that significantly weakens dominance (e.g., 2 Hz), multiple frequencies can be stronger than 2 Hz but without informing which of the stronger frequencies is the strongest. In other words, the narrow bandwidth at 10 Hz indicates that the estimated peak frequency is the most precise at this temporal frequency.

To confirm whether the peak temporal frequency would be different when one eye was fixed at a higher temporal frequency (beyond 10 Hz), we replotted the tuning functions for situations when one eye was fixed at 15 or 20 Hz using our data (DE at 15 Hz in Fig. 5A(iv); DE at 20 Hz in Fig. 5A(v)). The estimated peak frequency at each temporal frequency of the other eye is shown in Figure 5C. At higher temporal frequencies beyond 10 Hz, peak frequencies were still at intermediate temporal frequencies. However, as in the curves when NDE was fixed at 2 or 4 Hz, the bandwidths of the two replotted curves were wider than that when NDE was fixed at 10 Hz. This suggests that the precision of the estimated peak frequencies from the replotted curves was reduced. In short, the ultimate peak frequency seems to be close to 8.9 ± 1.4 Hz (95% confidence interval from t-distribution), showing that the eye with an intermediate temporal frequency, rather than the small temporal frequency difference with the other eye, becomes maximally dominant in sensory eye balance when both eyes are shown with flickering images.

Combined Analysis: Which Effect of Temporal Frequency or Monocularly Directed Attention on Balance Is Larger?

Findings from experiments 2 and 3 indicate that the full extent of temporal frequency modulation on binocular balance is not captured when one eye is shown at 4 Hz while the other eye is at 20 Hz (experiment 1). Therefore, our initial finding that the effect of temporal frequency difference is smaller than that of monocularly active attention in normally sighted observers is incomplete (Fig. 3A).

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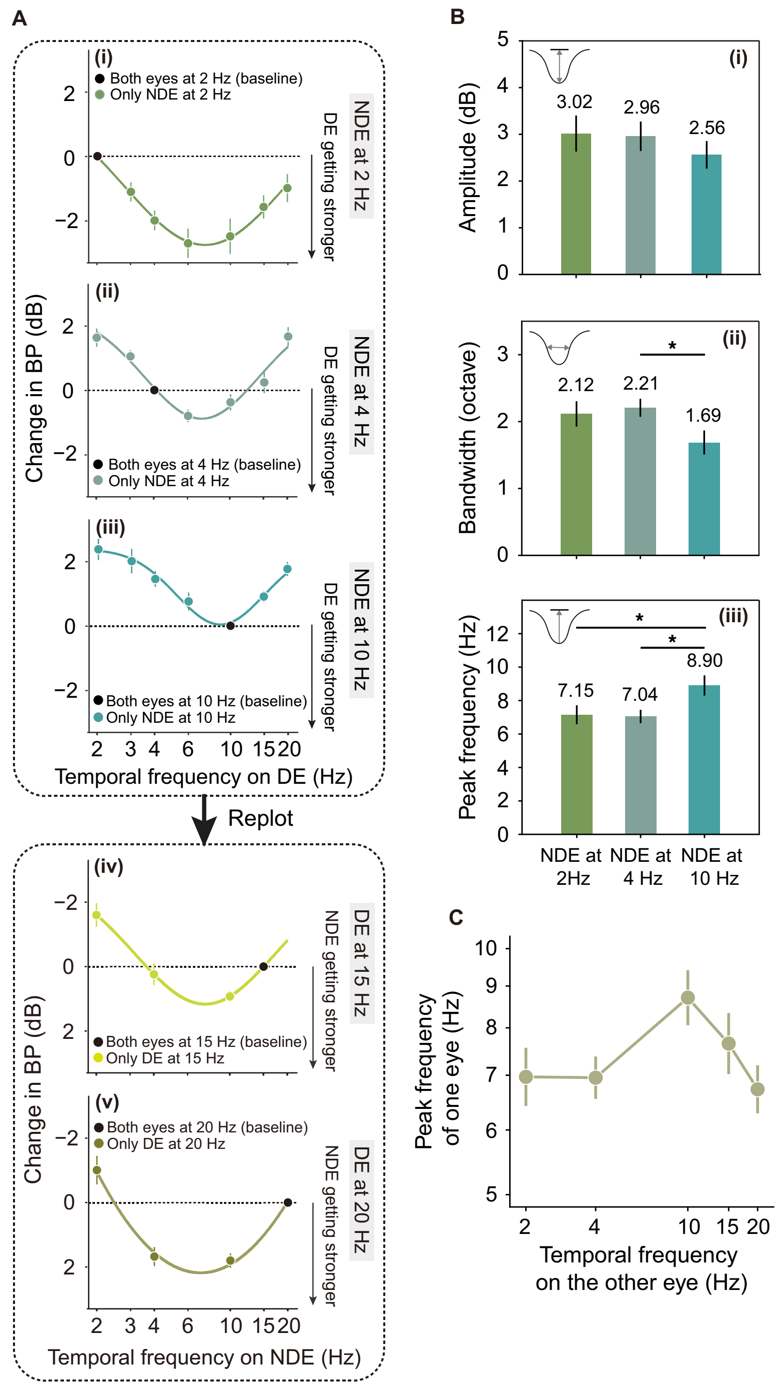

FIGURE 5. Results from effects on BP when NDE viewed at 2, 4, or 10 Hz and DE viewed at 2, 3, 4, 6, 10, 15, and 20 Hz in normally sighted observers ($n = 9$). (**A**) The change in BP relative to baseline as a function of temporal frequency of the DE when NDE was fixed at 2 Hz (i), 4 Hz (ii), or 10 Hz (iii). The data were replotted as the change in BP as a function of temporal frequency of the NDE when DE was fixed at 15 Hz (iv) or 20 Hz (v), with the y-axis reversed to better compare each curve. The *black points* represent baselines. Continuous *solid lines* indicate the best-fitting Gaussians. The *error bars* represent standard errors. (**B**) The three parameters derived from the best-fitting Gaussian curves, including amplitude (i), bandwidth (ii), and peak frequency (iii) when NDE was fixed at 2, 4, and 10 Hz. The amplitude was defined as the absolute height of the curve (i.e., the maximum change in BP minus the minimum). The bandwidth was the full width at half of the amplitude. The corresponding temporal frequency at the lowest point of the curve was peak frequency. The *error bars* represent standard errors. The *asterisk* denotes a significant difference between two conditions ($^*P < 0.05$). (**C**) Peak frequency of one eye as a function of temporal frequency of the other eye. Each *dot* represents the mean value. The *error bars* represent standard errors.

Instead, the full magnitude of change in balance driven by temporal frequency can be captured as the amplitude of the Gaussian curve fitted to the empirical data as a function of multiple temporal frequencies of one eye while the other eye's flicker rate is fixed (Fig. 4). Note that in experiment 1, static stimuli were used as baseline to compute the effect of monocular attention on balance, while in experiments 2 and 3, stimuli flickering at the same rate were shown to

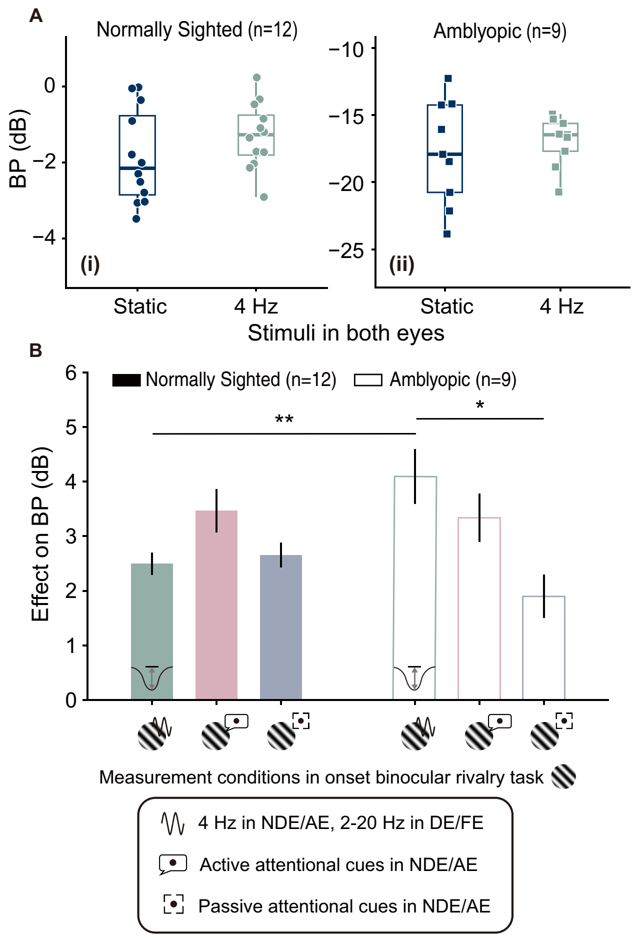

Figure 6. Results from comparisons between baseline BP in experiments 1 and 2 (**A**) and between temporal frequency and attentional (active and passive) effects on BP (**B**) in normally sighted ($n = 12$) and amblyopic observers ($n = 9$), who participated in both experiments 1 and 2. (**A**) Boxplots of BP under baseline conditions in experiment 1 (static stimuli) and experiment 2 (stimuli flickering at 4 Hz) in normally sighted observers (i) and amblyopes (ii). Individual data of normally sighted and amblyopic observers are plotted in *points* and *squares*, respectively. The *line* in the middle of box represents the median of the data. (**B**) Effects on BP under different experimental conditions. The x-axis represents each experimental condition (flicker, active attention, or passive attention). The *filled* and *unfilled bars* represent normally sighted and amblyopic observers, respectively. In the flicker condition, the effects on BP were represented by the amplitudes from the tuning curves in experiment 2. In two attentional conditions, the effects on BP were represented by the changes in BP from the same conditions in experiment 1. The *error bars* represent standard errors. The *asterisk* denotes a significant difference between two experimental conditions or groups (*$P < 0.05$, **$P < 0.01$).

both eyes for baseline measurement to quantify the effect of temporal frequency differences. Since we wanted to properly compare the effects of temporal frequency and monocularly driven attention, we first confirmed that these two baseline conditions resulted in similar states of binocular balance. Specifically, we compared BP in these two baselines from data of subjects who participated in both experiments. According to the paired *t*-test, no significant difference was found between them in normally sighted observers ($t(11) = -1.570$, $P = 0.145$; Fig. 6A(i)) and amblyopes ($t(8) = -0.936$, $P = 0.377$; Fig. 6A(ii)). The amplitude was also found to be similar regardless of the fixed eye's temporal frequency (Fig. 5B(i)), indicating that the impact of temporal frequency on binocular balance remains consistent and that the amplitude at 4 Hz can serve as a representative measure of the overall effect of temporal frequency modulation. Different vertical positions of the Gaussian fit (Fig. 5A) across the three conditions in experiment 3 are not critical for the value of amplitude, as they depend solely on the single-frequency flicker rate presented to the other eye. In summary, these preliminary analyses indicate that we could compare the amplitudes from the temporal frequency Gaussian curve from experiment 2 and BP shifts from attentional modulation from experiment 1 using data of controls and amblyopes who participated in both experiments (Fig. 6B).

First, a two-way mixed-measures ANOVA designating experimental condition (flicker, active attention, and passive attention) as a within-subject factor and group (normally sighted and amblyopic observers) as a between-subject factor revealed a significant effect of experimental condition ($F(2, 38) = 5.472$, $P = 0.008$) and the interaction between condition and group ($F(2, 38) = 5.219$, $P = 0.010$) but not of subject group ($F(1, 19) = 0.774$, $P = 0.390$). Furthermore, post hoc pairwise comparisons with Bonferroni correction reported a significant difference in effects on BP between two groups in the flicker condition ($P = 0.004$) and between flicker and passive attentional conditions in amblyopes ($P = 0.010$). Together, these results reveal that the degree of temporal frequency effect on binocular balance was similar to that of active and passive attentional effects in normally sighted observers, while it was larger than that of a passive (but not active) attentional effect in amblyopes. Additionally, as in experiments 1 and 2, the effect of temporal frequency was larger in amblyopes than that in controls.

Discussion

We sequentially conducted three experiments in this study. In experiment 1, we aimed to determine whether the eye with the higher temporal frequency would be more perceptually dominant, as previous research has shown that faster signals can asymmetrically suppress slower signals[32,33,36] and that faster flicker can more effectively capture attention.[35,42–46] Surprisingly, we found that the slower flickered eye (4 Hz) was more dominant than the faster flickered eye (20 Hz). Additionally, the shift in binocular balance due to monocular attentional cues was not correlated with the shift caused by the temporal frequency difference between the two eyes in both normally sighted and amblyopic observers. Overall, the first experiment demonstrated that in both normally sighted and amblyopic individuals, a temporal frequency difference influences binocular balance through a mechanism distinct from the one by which monocular attention modulates sensory eye dominance.

In experiment 2, we tested at a wider range of temporal frequencies in one eye while keeping the other eye fixed at 4 Hz to confirm whether the slower flickered eye would indeed be more perceptually dominant. However, we found that an intermediate temporal frequency (near 6 Hz) was the most dominant when the other eye was fixed at 4 Hz. In experiment 3, we examined whether the temporal frequency difference between both eyes or the absolute temporal frequency value itself in each eye determined the state of binocular balance. This was accomplished by showing various temporal frequencies in one eye (2 to 20 Hz) while fixing the other eye at three different temporal frequencies (2, 4, or 10 Hz). We observed that the value of temporal frequency in each eye, rather than the difference in temporal frequency between both eyes, determined the outcome of perceptual balance, with intermediate temporal frequencies (8.9 ± 1.4 Hz) maximizing eye dominance. Finally, we compared the magnitudes of the effects of temporal frequency and those of monocularly directed attention in both normally sighted and amblyopic observers by performing a combined analysis of the data from the first two experiments. We observed that the effect of temporal frequency was larger in amblyopes than in controls and that it shifted balance significantly more than monocularly directed passive attention.

The Onset Rivalry Paradigm With Sinusoidally Flickering Gratings

Several aspects of our experimental designs were deliberately chosen to investigate how temporal frequency modulates binocular balance. First, we chose to make the images flicker in both eyes, rather than keeping one eye static while the other flickered, to match the visual input energy between both eyes. Flicker can almost reduce stimulus energy by half because it can only be viewed for half the stimulus duration. So, if one eye sees a flickering stimulus but not the other eye, the former eye's input energy will be lower, potentially reducing its perceptual dominance. Second, we used sinusoidal contrast modulation to flicker the gratings because it can be decomposed into only one temporal frequency,[52] making the result more interpretable. Third, we used an onset rivalry task to measure initial dominance rather than a sustained rivalry task to measure the dynamics of interocular suppression. Previous research using a sustained rivalry task found that presenting a flickering stimulus to one eye significantly reduced its perceptual dominance but did not alter rivalry dynamics (i.e., the rate of perceptual alternation).[60] Additionally, we limited the response choices to two rather than three (excluding mixed perception) because the previous study reported that the proportion of mixed perception remained unchanged even when one eye's image is flickered.[60] This suggests that perceptual dominance in binocular rivalry is possibly the most significant marker for capturing the effect of temporal frequency differences between both eyes. As for measuring perceptual dominance, previous studies using static stimuli have shown onset rivalry is more sensitive than sustained rivalry[53,61] and has statistical power to be calculated by fitting psychometric function as the analysis method in our study.

Relevance to the Literature

Interestingly, Alais and Parker[25] observed consistent and reliable changes in the dynamics of binocular rivalry when the temporal frequency difference between the two eyes was at least two octaves apart (e.g., 3 Hz vs. 12 Hz) in the absence of spatial conflict. In other words, the dynamics of rivalry was found to be significantly altered only if the two frequencies belonged to separate temporal channels. Their findings further support the idea that the human visual system only has two[32,38] or three[62] temporal channels. In contrast, we observed that binocular balance, as measured using onset rivalry, shifted consistently in favor of the eye with an intermediate frequency, even when the temporal frequency difference between the two eyes was small. This could be because binocular balance, rather than the dynamics of binocular rivalry, could be affected more readily, with smaller temporal frequency differences. Previous studies using static stimuli have shown that initial dominance measured with an onset rivalry task can be a more sensitive measure to evaluate sensory eye dominance than a sustained rivalry task.[53,61] Another explanation for the difference in our and their results may be the spatial conflict in our study's stimuli (orthogonal gratings) but its absence in their stimuli. It is reasonable to presume that the presence of spatial conflict makes it easier for the early visual system to suppress one eye's image,[63–65] even if the two gratings flicker at temporal frequencies that belong to one temporal channel. In sum, our findings show that the human visual system can elicit a strong and robust shift in binocular balance in both normally sighted and amblyopic observers even if there is a small temporal frequency difference between the two eyes.

We found that absolute temporal frequency values modulated binocular balance: if one eye was shown at an intermediate temporal frequency (about 8.9 ± 1.4 Hz), it was more dominant regardless of the other eye's temporal frequency. Notably, this peak aligns with the temporal contrast sensitivity function (TCSF) peaks (6–10 Hz) in both normal and amblyopic vision reported in previous studies.[38,62,66–68] On one hand, this agreement between our findings and temporal contrast sensitivity results suggests that monocular stimulus visibility could account for the peak frequency in binocular balance. However, it seems that stimulus visibility at the threshold level (TCSF) does not fully account for other aspects of our findings. To illustrate, our tested range is similar to that of typical TCSF measurements, but the shapes of the curve appear different. Our fitted Gaussian curve is symmetrical around the peak (Fig. 5A), whereas TCSF is asymmetrical with significant tapering at higher temporal frequencies (above 10 Hz). In other words, if temporal contrast sensitivity fully accounted for our results, we would also have seen an asymmetric curve with similar tapering points from our Gaussian functions. Furthermore, although temporal contrast sensitivity is significantly higher at 2 Hz than at 20 Hz,[38,62,66–68] our findings using suprathreshold stimuli to measure binocular balance are contrary, as 20 Hz boosts ocular dominance more (Fig. 5A(i)). This discrepancy could be because the mechanism underlying binocular balance at a suprathreshold contrast level is not directly tied to contrast sensitivity differences between eyes (assessed at the threshold level).[11,69–72] For example, binocular imbalance at the suprathreshold level can be larger than that predicted from the contrast sensitivities or monocular perceived contrast of the two eyes at the threshold in both normally sighted and amblyopic observers.[70,71] Therefore, although temporal contrast sensitivity at the threshold level matches our peak frequency in ocular dominance using the suprathreshold binocular rivalry task, there are significant differences between them at outer temporal frequencies, suggesting that monocular stimulus visibility can only partially account for our results.

What could describe this discrepancy between the asymmetrical TCSF curve and our symmetrical Gaussian curves (Fig. 5A)? A typical TCSF measurement only concerns monocular or binocular stimulus visibility. However, a binocular rivalry task measures perceptual outcome from interocular suppression, which primarily manifests when two eyes view conflicting images, causing the visual system to prefer one eye's input to the other eye's input. According to our findings, temporal frequency might directly influence interocular suppression. This is because previous studies have found temporal frequency modulation of interocular suppression in CFS and masking experiments,[52,62,73] which cannot be accounted for by temporal contrast sensitivity.[52,62] In addition, both psychophysical[32,33,36] and neurophysiological[74] studies show asymmetrical suppression in temporal processing, where a high-frequency channel suppresses the response of a low-frequency channel. Likewise, in our study, a higher temporal frequency (e.g., 20 Hz) in one eye might asymmetrically suppress the signal at a slower temporal frequency in the other eye (e.g., 2 Hz). Considering that the channels intersect at about 6 to 8 Hz,[32,36,37] we can infer that the temporal frequency difference between the two outer frequencies (2 Hz and 20 Hz) was large enough to induce asymmetrical suppression between the two temporal channels. Alternatively, we observed the peak at an intermediate frequency (8.9 $\pm$ 1.4 Hz) because this is where two temporal channels intersect. In other words, our reported peak frequency might activate both channels, thereby maximizing ocular dominance. To better understand how temporal frequency affects binocular balance, future research should parse contributions of monocular stimulus visibility and interocular suppression.

Although rapid flicker can capture attention,[35,42–46] our findings show that eye dominance did not increase as a function of temporal frequency (Fig. 4). Moreover, there was no direct correlation between the impacts of flicker and attention (Fig. 3B), indicating that the mechanism that drives the effect of temporal frequency is different from those of active and passive attention, both of which can boost apparent contrast monocularly with cues.[47–49] Active attention operates through top-down mechanisms, prioritizing visual inputs based on internal goals, while passive attention is driven by bottom-up processes that respond to the salience of visual features.[75–77] Instead, rather than modulating stimulus visibility through attention, which is more susceptible to a faster flicker rate,[35,42–46] it seems more likely that temporal frequency modulates binocular balance through the interplay between stimulus visibility from temporal contrast perception and asymmetric inhibition between low and high temporal channels.

Intriguingly, we found that active attentional cues in one eye induced a stronger shift in binocular balance compared to passive attentional cues in both normally sighted and amblyopic observers (Fig. 3A), indicating that the pronounced shifts induced by both active and passive attention exist in visually intact and abnormal populations. This is consistent with the studies on attention in normally sighted individuals by Zhang et al.[49] and Wong et al.[48] However, it contradicts the recent finding in amblyopes by Wong et al.,[78] who observed that the monocular attentional effects are mainly stimulus-driven (passive). This discrepancy might be attributed to several factors. First, they measured sustained rivalry, while we examined onset rivalry, which is more sensitive when measuring eye dominance.[53,61] Besides, the cue stimuli and tasks used to attract attention also vary. The active attention task in our study was simpler as it only asked subjects to verbally locate the black dot among four dots, while the active cueing task in the study of Wong et al.[78] required subjects to report the color symmetry of dots surrounding the gratings using secondary button presses in addition to a primary continuous response (e.g., moving a joystick) of the sustained rivalry task. Along with our larger sample size (11 as opposed to 8 amblyopes in the study by Wong et al.[78]), the simplicity in our task might have allowed us to reduce measurement variability and increase sensitivity in detecting statistical significance between effects of active and passive attention in the amblyopic population (Fig. 3A). Our finding reports robust and similar effects of active and passive attention in both normally sighted and amblyopic populations for the first time, opening up new possibilities for binocular therapy in amblyopia. This finding is timely because previous studies show that luminance and contrast modulations elicit reduced benefits in binocular balance in amblyopes compared to controls,[26,79] as the suppression from the fellow eye to the amblyopic eye is significantly stronger than the suppression in the reverse direction.[10,11] Put together, our findings suggest that directing attention to the amblyopic eye's image can be an effective strategy in reducing severe amblyopic imbalance when images to both eyes are required to remain intact. This approach could be different and potentially more effective than dichoptic therapies that reduce brightness or contrast of the fellow eye's image to alleviate imbalance. This is because attentional modulation remains robust even under unequal interocular suppression in amblyopia (Fig. 3A), whereas the effects from changes in luminance and contrast can be weakened by that suppression.

Although attentional modulations induced similar degrees of changes in balance in both controls and amblyopes, the shifts from temporal frequency modulation were larger in amblyopes than in controls (experiments 1 and 2). The fact that a visual manipulation could introduce a larger change in amblyopes than in controls is novel, as previous studies showed that a much larger, severe manipulation of visual information (in luminance and contrast) is necessary to induce a similar degree of change in binocular balance in amblyopes.[26,27] Notably, the changes in binocular balance by temporal frequency were larger than the changes induced by passive attentional modulation in amblyopes but not in controls (Fig. 6B). This indicates that temporal modulation of visual input could be another avenue for dichoptic therapies to exploit in treating individuals with amblyopia.

Our study has a few notable limitations. First, only a low spatial frequency (1.4 c/deg) was tested. This was to remove the confounding effect of variability in binocular balance measurements at higher frequencies in amblyopes.[51] Nevertheless, with more trial counts, this problem could be alleviated. Hence, higher spatial frequencies should also be explored, especially because binocular imbalance becomes significant as a function of spatial frequency.[69,72] Second, all the patients recruited in our study were anisometropic amblyopes. Whether such an effect can be generalized to higher spatial frequencies and to individuals with other types of amblyopia apart from anisometropia (e.g., strabismic amblyopia) remains to be studied in the future.

In conclusion, our findings demonstrate how temporal frequency differences alter binocular balance in normally sighted and amblyopic observers. We provide the first evidence that the alterations in balance driven by temporal frequency differences do not share the same mechanism as those driven by monocularly directed attention. Additionally, our study reveals that intermediate temporal frequencies (about 8.9 $\pm$ 1.4 Hz) maximize the perceptual dominance of the eye regardless of the other eye's temporal frequency. The effect of temporal frequency is larger in amblyopia than in normally sighted adults and larger than that of monocularly directed passive attention in amblyopia. These results expand our understanding of temporal frequency modulation on binocular vision and provide a new potential approach to improve amblyopic vision.

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