A Unified Rule for Binocular Contrast Summation Applies to Normal Vision and Common Eye Diseases

Ying-Zi Xiong,[1] Rong Liu,[2,3] MiYoung Kwon,[2,3] Ava K. Bittner,[4,5] Cynthia Owsley,[3] and Gordon E. Legge[1]

[1]Department of Psychology, University of Minnesota, Minneapolis, Minnesota, United States
[2]Department of Psychology, Northeastern University, Boston, Massachusetts, United States
[3]Department of Ophthalmology and Visual Sciences, University of Alabama at Birmingham, Birmingham, Alabama, United States
[4]Department of Ophthalmology, Stein Eye Institute, UCLA, Los Angeles, California, United States
[5]Department of Ophthalmology, Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, United States

PURPOSE. Binocular summation refers to better visual performance with two eyes than with one eye. Little is known about the mechanism underlying binocular contrast summation in patients with common eye diseases who often exhibit binocularly asymmetric vision loss and structural changes along the visual pathway. Here we asked whether the mechanism of binocular contrast summation remains preserved in eye disease.

METHODS. This study included 1035 subjects with normal ocular health, cataract, age-related macular degeneration, glaucoma, and retinitis pigmentosa. Monocular and binocular contrast sensitivity were measured by the Pelli-Robson contrast sensitivity chart. Interocular ratio (IOR) was quantified as the ratio between the poorer and better eye contrast sensitivity. Binocular summation ratio (BSR) was quantified as the ratio between binocular and better eye contrast sensitivity.

RESULTS. All groups showed statistically significant binocular summation, with the BSR ranging from 1.25 [1.20, 1.30] in the glaucoma group to 1.31 [1.27, 1.36] in the normal vision group. There was no significant group difference in the BSR, after accounting for IOR. By fitting a binocular summation model Binocular = $(\text{Left}^m + \text{Right}^m)^{1/m}$ to the contrast sensitivity data, we found that the same binocular summation rule, reflected by the parameter m, applies across the five groups.

CONCLUSIONS. Cortical binocular contrast summation appears to be preserved in spite of eye diseases that can affect the two eyes differently. This finding supports the importance of assessing both monocular and binocular functions, rather than relying on a monocular assessment in the better eye as a potentially inaccurate surrogate measure.

Keywords: binocular summation, contrast sensitivity, normal vision, eye diseases

In normal vision, contrast sensitivity with two eyes is better than with one eye, which is termed binocular summation.[1–3] In the eye clinic, binocular summation is important to consider since monocular visual functions are often compromised due to ocular disease.[4,5] Many people with eye disease have unequal visual function in the two eyes, making it tempting to evaluate visual function based on the capabilities of the better eye only. But if the visual mechanism underlying binocular summation remains intact in these patients, they may retain functional benefits of binocular viewing despite differences in their monocular vision. Thus, the current study was designed to investigate the extent and mechanism of binocular summation in individuals with or without ocular pathologies.

In normal vision, a classic probability summation model holds that the two eyes are independent of each other and the summation is purely statistical.[1] However, behavioral studies frequently report that binocular summation exceeds the prediction of probability summation, reflecting the physiological nature of binocular summation.[2,6–8] Electrophysiological studies have also shown that binocular neuron responses are observed in the primary visual cortex,[9] supporting the likelihood that binocular summation has a cortical origin.

The question arises as to whether the same binocular summation mechanism applies to patients with eye diseases. Early-onset forms of impaired vision may adversely affect visual development including binocular summation. For example, misalignment of the two eyes in early life could result in cortical suppression of the weak eye,[10] affecting binocular function, and may reduce binocular summation to a probability summation level.[11] Once normal binocular function has been established, late-onset forms of impaired vision with the primary pathology in the eye might leave cortical mechanisms of binocular summation unchanged, in which case the same binocular summation rule for normal

TABLE. Subject Demographics and Descriptive Summary of Monocular and Binocular Acuity and Contrast Sensitivity (Mean and Standard Deviation)

Clinical Values	Normal	Cataract	AMD	Glaucoma	RP
Sample size	243	448	121	166	57
Gender, F/M	115/128	169/279	42/79	95/71	35/22
Age, yrs, mean [SD]	63 [22.1]	76 [4.0]	81 [5.8]	71 [9.8]	49 [15.8]
VA, logMAR, mean [SD]					
Better VA	−0.04 [0.08]	0.08 [0.13]	0.10 [0.19]	0.05 [0.13]	0.23 [0.31]
Worse VA	0.03 [0.09]	0.22 [0.18]	0.30 [0.31]	0.22 [0.27]	0.45 [0.54]
Binocular VA	−0.07[*] [0.08]	0.03[*] [0.12]	0.04[*] [0.17]	0.02[*] [0.11]	0.23 [0.30]
CS, logCS, mean [SD]					
Better CS	1.70 [0.14]	1.61 [0.11]	1.53 [0.18]	1.59 [0.15]	1.26 [0.52]
Poorer CS	1.62 [0.14]	1.52 [0.12]	1.38 [0.30]	1.43 [0.30]	1.08 [0.62]
Binocular CS	1.80[*] [0.17]	1.70[*] [0.12]	1.63[*] [0.19]	1.67[*] [0.17]	1.34[*] [0.57]

Key: F = female, M = male, SD = standard deviation, CS = contrast sensitivity, VA = visual acuity.
[*] Significant binocular summation effect (all *P* values < 0.001).

vision may also apply to patients with eye diseases. However, imaging studies have shown that diseases of the eye can result in structural changes further along the visual pathway,[12] thus it is possible that the mechanism of binocular summation may be impaired even in patients with late-onset eye diseases.

The extent of binocular summation is usually quantified by comparing the contrast sensitivity between viewing with the better eye and viewing with both eyes. It is important to realize that the mechanism of binocular summation cannot be probed solely by an empirical measure of binocular summation. This is because eye diseases often cause asymmetric loss in the two eyes;[13–15] when there is a significant interocular difference in contrast sensitivity, the extent of binocular summation is expected to be decreased mainly due to a small contribution from the poorer eye.[8] However, the mechanism of binocular summation may remain intact.

The primary goal of the current study is to investigate the rule of binocular contrast summation in patients with ocular diseases. We chose four common eye diseases that affect different stages of visual processing in the eye, but all prior to binocular interactions in the cortex: cataract affects the crystalline lens and clarity of the ocular media, retinitis pigmentosa (RP) and age-related macular degeneration (AMD) damage photoreceptors and the retinal pigment epithelium, while glaucoma causes thinning of the retinal ganglion cell layer and the nerve fiber layer. We collected contrast sensitivity data from large samples of these four patient groups (*N* = 792) and a control group with normal ocular health (*N* = 243). We used a modeling approach to examine the mechanism of binocular summation in the presence of asymmetric contrast loss. We hypothesized that a unified binocular summation model can explain the extent of binocular summation in all groups as would be expected from an unaffected, common cortical site underlying binocular summation.

METHODS

Subjects

The current study included subjects categorized into groups based on four eye diseases: cataract, retinitis pigmentosa (RP), age-related macular degeneration (AMD), and glaucoma. Subjects with normal vision and no eye disease were also included for comparison. The data included in the current study were assembled from the raw data collected by the coauthors in studies published between 2001 to 2017 and an unpublished study in 2007–2009 by Bittner et al.[16–23] All studies were originally conducted for other research purposes, but included both binocular and monocular contrast sensitivity. All studies received IRB approval, and written informed consent was obtained from all subjects prior to data collection. Reanalysis of the data was approved by additional IRB review or was indicated in the consent form of the original studies.

In the current study, subjects were included only if they had monocular measurements in both the left and right eyes, as well as binocular measurement. Exclusion criteria included subjects who had other eye diagnoses, missing age, or age <18 years. The cataract group included only participants who were phakic in both eyes and did not have any previous cataract surgery. For other groups, pseudophakic participants were accepted. The final sample (*N* = 1035) included 448 subjects with cataract, 121 subjects with AMD (110 with cataract surgeries), 166 subjects with glaucoma (131 with cataract surgeries), 57 subjects with RP, and 243 subjects with no eye disease. The group characteristics are shown in the Table.

Assessments

Best corrected visual acuity was measured using the ETDRS chart[24] or its electronic version.[25] The acuity test was conducted at 3 m or a closer distance adjusted for subjects as needed if fewer than 10 letters were identified at 3 m.

Contrast sensitivity was measured with the Pelli-Robson chart at 1 m for all subjects.[26] Across all studies, the background luminance of the Pelli-Robson chart was confirmed by calibrated photometers (MINOLTA LS-100, MINOLTA LS-110 (Konica Minolta Inc., Tokyo, Japan)) to be within the recommended range (60–120 cd/m²). Sources of glare light were avoided during the test. It was scored on a letter-by-letter basis with each correctly reported letter worth 0.05 log units.[27] Larger log values indicate better contrast sensitivity. All subjects completed the contrast sensitivity test with either their habitual spectacle prescription or contact lenses or appropriate distance refractive correction using a trial frame and trial lenses for both monocular and binocular viewing conditions at the same visit. The measurements were terminated when no further letters were read correctly on a set of three letters with the same contrast. Subjects were encouraged to provide guesses when they were uncertain.
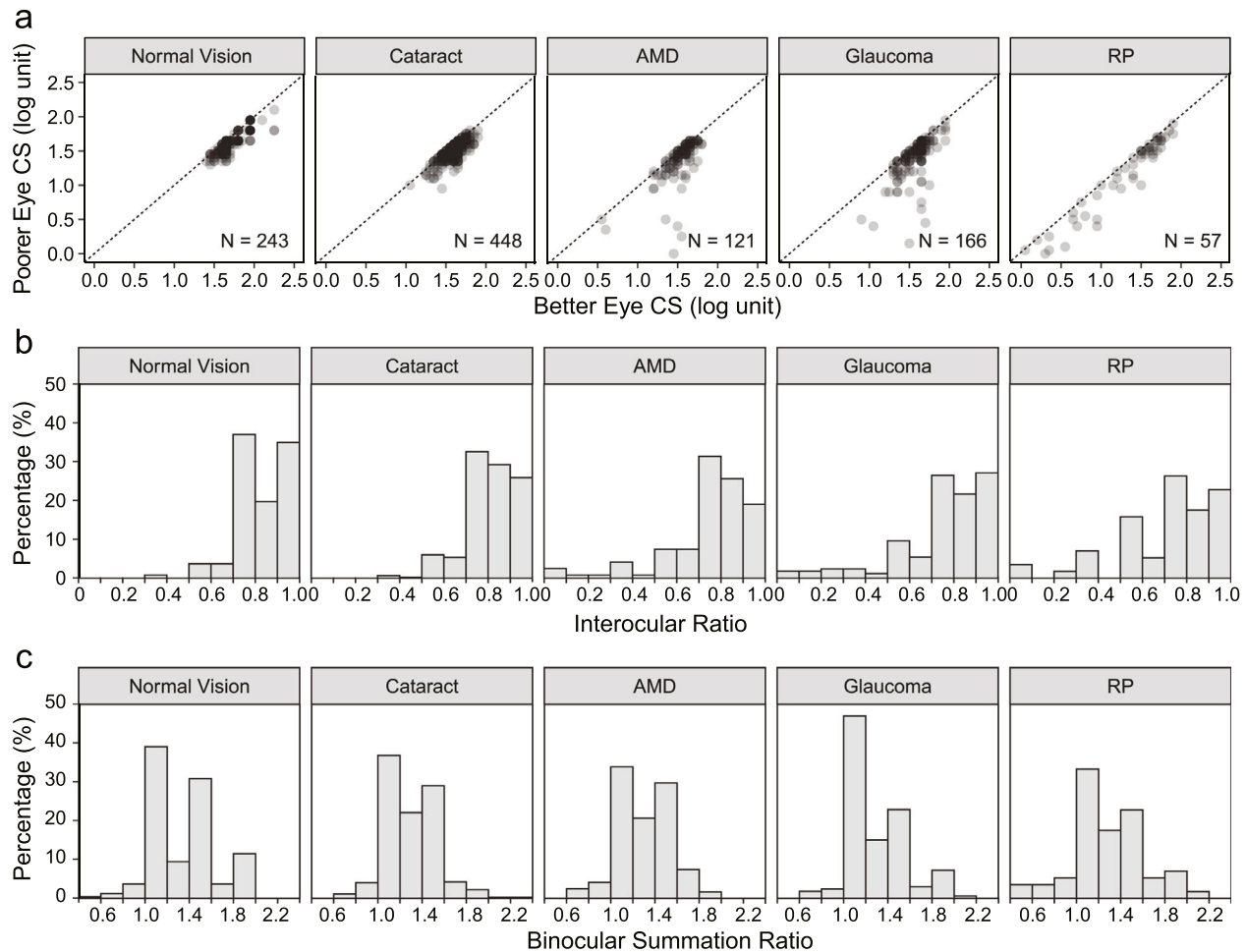
FIGURE 1. Monocular contrast sensitivity, interocular ratio (IOR), and binocular summation ratio (BSR). (**a**) Scatter plots of poorer eye contrast sensitivity as a function of the better eye contrast sensitivity for each of the five groups. (**b**) Histograms showing the distribution of the interocular ratio in each of the five groups. (**c**) Histograms showing the distribution of the binocular summation ratio in each of the five groups.

The group means and standard deviations of the better eye, poorer eye, and binocular acuity and contrast sensitivity are provided in the Table. Scatter plots of worse eye contrast sensitivity versus better eye sensitivity for each group are provided in Figure 1a.

Data Analysis

Both binocular summation ratio (BSR) and interocular ratio (IOR) for contrast sensitivity were obtained from the Pelli-Robson contrast sensitivity scores. The Pelli-Robson scores were first converted into linear scales of contrast sensitivity, with a larger value representing better contrast sensitivity. BSR was then obtained as the ratio between measures of the binocular and the better monocular contrast sensitivity ($BSR = CS_{Bino}/CS_{Better}$). For example, a binocular CS of 10 and better-eye CS of 7.08 would correspond to a BSR of 10/7.08 = 1.41. Higher BSR values represent larger summation. IOR was obtained from measures of contrast sensitivity in the better and worse seeing eye ($IOR = CS_{Poorer}/CS_{Better}$). IOR ranges from 0 to 1, with smaller values representing larger interocular difference.

The statistical analyses were performed using R software.[28] Linear models were constructed to examine the group differences in BSR. Age was included as a covariate in all linear models. The significance of the fixed effects was examined by the anova function in the lme4 package.[29] Post hoc analysis was performed with Bonferroni corrections ("emmeans" package).[30] P values smaller than 0.05 were considered statistically significant. Nonlinear mixed effect modeling (NLME)[29] was performed to fit a binocular summation model (see Results section) of BSR as a function of IOR for each subject group. To account for the unbalanced sample sizes across the five subject groups, all confidence intervals were estimated by the bootstrap with resampling ($n = 1000$) method.[31]

RESULTS

Impact of Asymmetric Contrast Loss on Binocular Summation

Table provides the sample size, age, and gender distributions of each group. We first asked whether the groups with eye diseases showed asymmetric contrast loss. Figure 1b shows the distributions of IOR in each group. In the normal vision group, there were 35% of subjects who had equal contrast sensitivity in their two eyes (IOR = 1). In the four
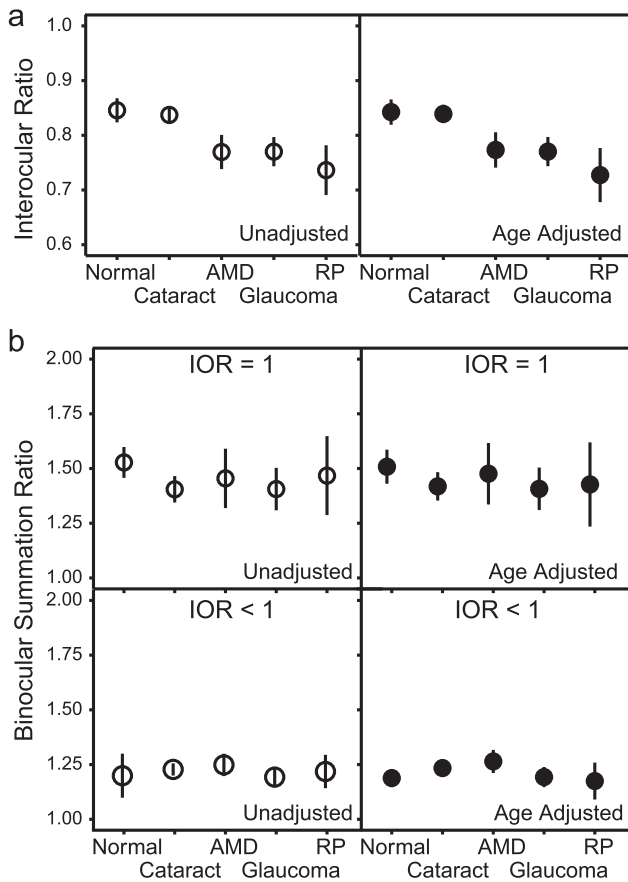
FIGURE 2. Interocular ratio and binocular summation ratio. (**a**) The group means and standard deviations of interocular ratio (IOR) in the five groups. The left and right panels represent unadjusted and age-adjusted results, respectively. (**b**) The group means and standard deviations of binocular summation ratio (BSR) in subsets of subjects with equal monocular contrast sensitivity (IOR = 1, upper panel) and unequal monocular contrast sensitivity (IOR < 1, lower panel). The left and right panels represent unadjusted and age-adjusted results, respectively.

pathology groups, the proportions with equal contrast sensitivity were 25.9% (cataract), 19.0% (AMD), 27.1% (glaucoma), and 22.8% (RP). The normal vision group had an average IOR of 0.85 [0.83, 0.86] (mean [95% confidence interval with bootstrapping] here and below), while the groups with eye diseases had smaller average values of IOR ranging from 0.74 [0.67, 0.79] in the RP group to 0.84 [0.82, 0.85] in the cataract group (Fig. 2a). Linear modeling on IOR confirmed a significant group difference. Post hoc analyses showed that AMD, glaucoma, and RP groups, but not the cataract group, had significantly smaller IOR than the normal vision group (AMD: 0.07 [0.01, 0.13], $P = 0.010$; glaucoma: 0.07 [0.02, 0.12], $P < 0.001$; RP: 0.12 [0.04, 0.19], $P < 0.001$), indicating larger interocular differences on average.

Figure 1c shows the distributions of BSR in each group. All five groups exhibited a statistically significant amount of BSR (normal vision: 1.31 [1.27,1.36], $P < 0.001$; cataract: 1.27 [1.25, 1.30], $P < 0.001$; AMD: 1.29 [1.24, 1.34], $P < 0.001$; glaucoma: 1.25 [1.20, 1.30], $P < 0.001$; RP: 1.28 [1.18, 1.37], $P < 0.001$). To assess whether asymmetric loss of contrast sensitivity has an impact on binocular summation, we compared the BSR in subjects who had equal monocular contrast sensitivity (IOR = 1) to those who had unequal

monocular contrast sensitivities in the two eyes (IOR < 1). For the subset with IOR = 1, the average BSR ranged from 1.40 [1.35, 1.46] in the cataract group to 1.53 [1.45, 1.60] in the normal vision group (Fig. 2b, upper panel), which was close to the ratio (1.41) reported in the literature predicted by a quadratic summation rule.[7] For the subset with IOR < 1, the average BSR values were much smaller, ranging from 1.19 [1.15, 1.24] in the glaucoma group to 1.25 [1.20, 1.29] in the AMD group (Fig. 2b, lower panel), indicating less summation among those with unequal monocular contrast sensitivities between eyes than for those with equal monocular contrast sensitivities. The covarying nature of IOR and BSR was confirmed by significant correlations in all five groups ($P < 0.001$ in all groups, regression lines shown in Fig. 3). More importantly, we used a linear model to examine the group differences in BSR with IOR as a covariate but found no statistically significant group difference.

These results reveal three important messages: (1) AMD, glaucoma, and RP groups indeed exhibited larger interocular differences than in the normal control group, (2) larger interocular differences (smaller IOR) were associated with smaller BSR (less binocular summation), in both normal vision and in eye diseases, and (3) there was no group difference in BSR, when IOR was taken into account.

A Unified Rule of Binocular Contrast Summation

Next, we used a modeling approach to investigate whether the same binocular summation rule applied across the five groups. Behavioral studies of contrast sensitivity in conjunction with modeling approaches have described binocular summation using a canonical formula[7]:

$$\text{Binocular} = \left(\text{Left}^m + \text{Right}^m\right)^{1/m}. \tag{1}$$

where Binocular represents the binocular contrast sensitivity, Left and Right represent the monocular contrast sensitivities in the left and right eyes, and the exponent m characterizes the level of binocular summation. When the two eyes have the same contrast sensitivity, the BSR is simply $2^{1/m}$.

The exponent m is often regarded as an indicator of the mechanism of binocular summation. Higher m values correspond to less binocular summation. The value of the m for probability summation depends on the steepness of the associated psychometric function for contrast detection,[32] and was reported to be 3.5 for contrast sensitivity by Pelli et al. (1988),[26] predicting a BSR of approximately 1.22 ($2^{1/3.5}$). However, behavioral studies frequently report BSR to be close to or above 1.41 ($2^{1/2}$), exceeding the prediction of probability summation and suggests a physiological nature of binocular summation.[2,6–8]

To clearly demonstrate the impact of interocular difference on BSR, here we transformed Eq. 1 by replacing the contrast sensitivity of the poorer eye with the product of the better eye contrast sensitivity and IOR:

Binocular

$$= (\text{Better eye}^m + (\text{Poorer eye} : \text{IOR} \times \text{Better eye})^m)^{1/m},$$

$$0 <= \text{IOR} <= 1$$

the BSR can now be defined as the ratio between binocular contrast sensitivity and the better eye's contrast sensitivity,
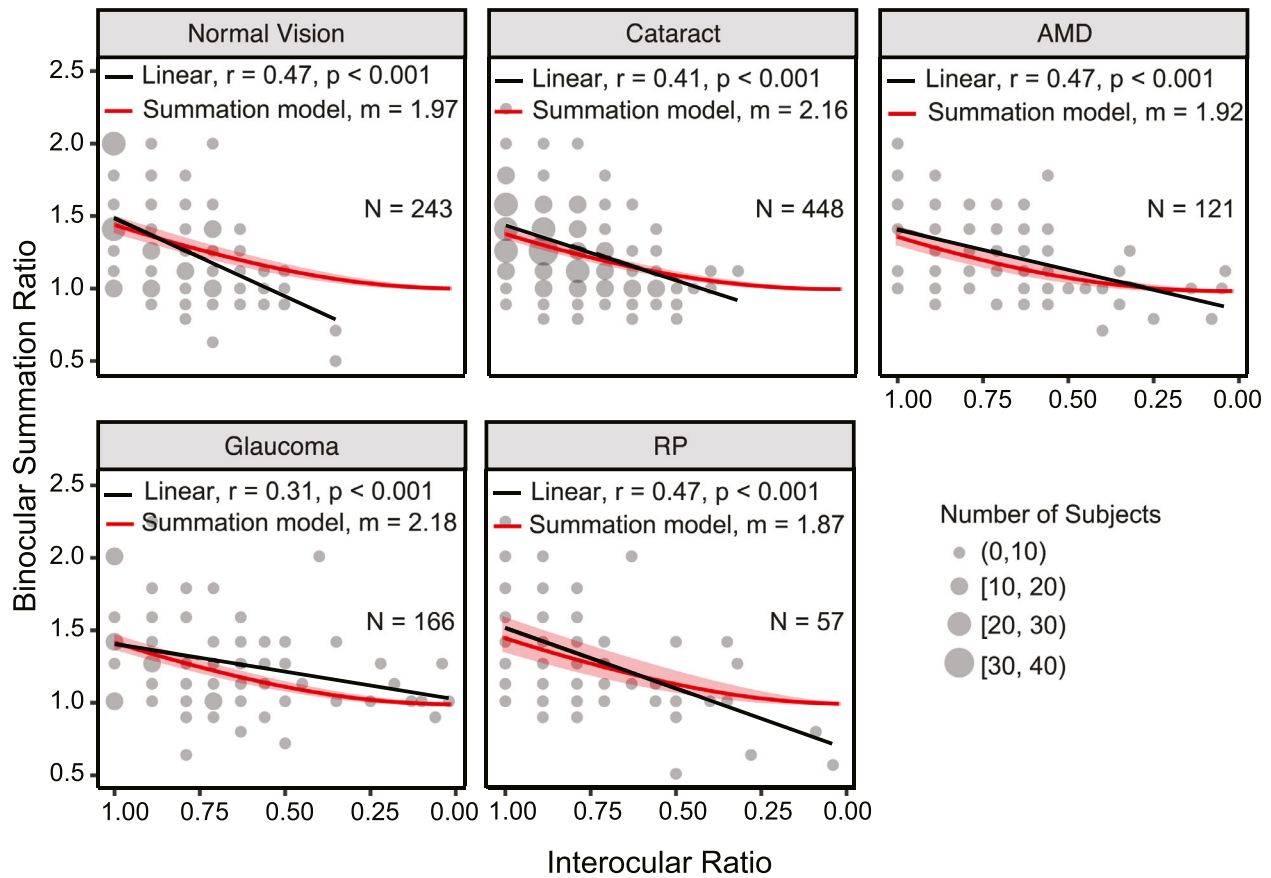
FIGURE 3. Scatter plots of binocular summation ratio as a function of interocular ratio in each group. The *black lines* are the linear regression lines, and the associated correlation index and *P* values are provided in the annotation. The *red curves* are fitted by Eq. 2, the exponent m that was determined by the fitted models are provided in the annotation, and the confidence interval of the fitted curves are shown as the *red shadows*.

and expressed as a function of the IOR:

$$\mathrm{BSR} = \left(1 + \mathrm{IOR^m}\right)^{1/m} \qquad (2)$$

Eq. 2 clearly shows that the BSR decreases as the IOR decreases (Fig. 4a), regardless of the value of m (i.e., the level of summation).

For each group, we used the BSR and IOR values from all subjects in Eq. 2, with m as a free parameter. Nonlinear models were constructed to obtain the m exponent for each of the five groups. For the normal control group, the best-fitted m value was 1.97 [1.82, 2.18]. For the eye-disease groups, the m values were also close to 2, ranging from 1.87 [1.57, 2.31] in the RP group to 2.18 [1.92, 2.51] in the glaucoma group. The fitted curves and confidence intervals are shown in Figure 3 (red curves). Recall that higher m values correspond to less binocular summation. The m values are consistent with the prediction of a quadratic summation model (m = 2) corresponding to BSR of 1.41.[7] which exceeds the prediction of a probability summation model (m = 3.5) corresponding to BSR of 1.22.

To further examine whether the relationship between BSR and IOR follows a quadratic summation model, we fitted the model in Eq. 2 again, with m fixed at 2 for each group. A comparison of the residual sum of squares between the full model with free parameters and the reduced model with the fixed m parameter showed no significant difference in any of the five groups (*P* > 0.05 for all groups), indicating that a reduced model with m = 2 is sufficient to explain the relationship between BSR and IOR across the five groups. Thus, this group level analysis confirmed similar binocular contrast summation rules for the five groups, which was beyond simple probability summation and close to a value of m = 2 representing quadratic summation.

We further investigated the level of summation for each subject and found results that were consistent with the group analysis just described. We used the monocular and binocular contrast sensitivities for each subject to estimate their value of m using Eq. 1. Figure 4b shows the distributions of m in each group. The average m value was 2.01 [1.85, 2.18] in the normal vision group. In the groups with eye diseases, the average m values were 2.28 [2.16, 2.40] in cataract, 2.11 [1.89, 2.37] in AMD, 1.87 [1.70, 2.05] in glaucoma, and 1.96 [1.65, 2.32] in the RP group. While the m values in the cataract group were significantly larger than 2 (by 0.28 [0.16, 0.40] *P* < 0.001), but only 9% (40) of the subjects in this group had m values indicating summation below the probability summation level. The m values in the other four groups did not show any significant difference from 2 (all *P* > 0.05).
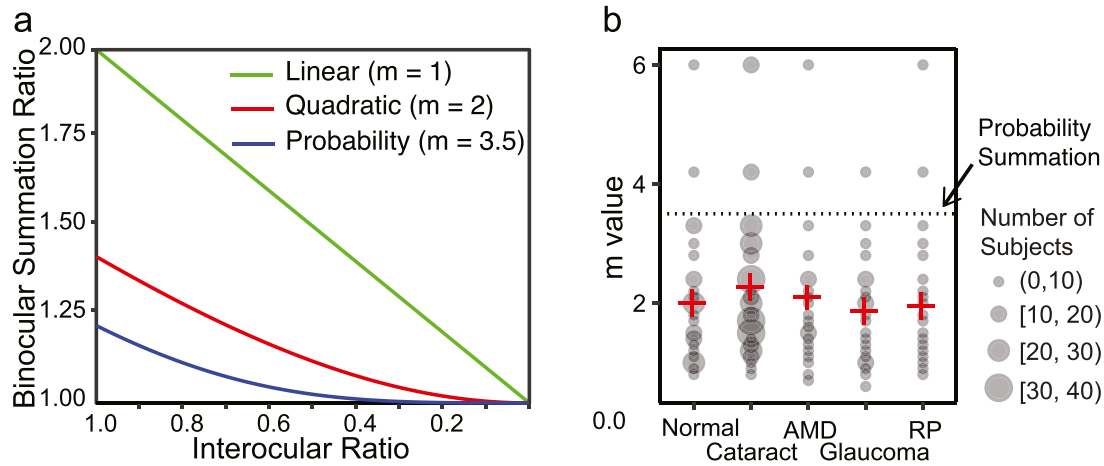
FIGURE 4. Binocular summation modeling prediction and results. (**a**) The relationship between binocular summation ratio and interocular ratio predicted by Eq.2, based on linear summation (*green line*, m = 1), quadratic summation (*red curve*, m = 2), and probability summation model (*blue curve*, m = 3.5). (**b**) The distributions of individual exponent m in each group. The *red crosses* represent the group means. The *dashed line* represents the value of m predicted by a probability summation model.

DISCUSSION

We found that larger interocular contrast differences are associated with smaller values of binocular contrast summation for individual subjects in all groups, but there were no significant group differences in the extent of binocular contrast summation, after accounting for the interocular differences. Using a modeling approach, we showed that the binocular contrast summation can be explained by a unified rule across all five groups, which is well described by a quadratic summation rule with m = 2, reflecting the physiological nature of binocular summation.[7] These findings suggest that the nature of binocular contrast summation is preserved in patients with the eye diseases we studied.

An important message conveyed by this finding is that a smaller BSR does not necessarily mean an impaired binocular summation mechanism. An interocular difference can induce reduced contrast summation simply due to an asymmetric contribution between the two eyes. Similar issues have also been reported in strabismic amblyopia.[33] People with strabismic amblyopia often have reduced contrast sensitivity in the amblyopic eye and show a smaller binocular summation effect. Baker et al.[33] found that when the contrast in the weaker eye is enhanced to compensate for the loss in contrast sensitivity, the strabismic patients showed a normal level of binocular summation.

The mechanism of binocular contrast summation is likely intact in our subjects with eye diseases, suggesting intact binocular processing in the visual cortex. Consistent with this possibility, previous contrast sensitivity studies have reported significantly higher equivalent input noise but relatively intact sampling efficiency in patients with glaucoma[34] and RP.[35] Sampling efficiency refers to how efficiently the visual system extracts and utilizes the available stimulus information. Thus, it is plausible that eye diseases significantly increase noise at the earliest stage of visual processing, but with minimal impact on later stages of visual processing. Moreover, in a clinical study of the light sensitivity across the visual field in glaucoma patients, Nelson Quigg et al. found that the same quadratic summation model provided the best relationship between the binocular and monocular light sensitivities. Their results also support intact binocular processing in glaucoma patients.[36]

Clinical studies have reported the existence of binocular inhibition (i.e., binocular function worse than the better eye) in unilateral cataract and AMD patients.[13,37,38] In our large subject samples, we found that only a small proportion of subjects showed binocular contrast inhibition. If we were to use a clinically significant difference as the criterion of binocular inhibition (0.15 logCS or a BSR of 0.71),[39] the proportion of our subjects with binocular contrast inhibition would become even smaller (i.e., 5% or three subjects with RP, <1% or two people with normal vision, <1% or one individual with glaucoma, and none in the cataract and AMD groups).

Comparing to Pardhan and Gilchrist's study which reported binocular inhibition in patients with unilateral cataract,[13] the reduced prevalence of binocular inhibition in our cataract group might be due to two reasons. First, Pardhan and Gilchrist's study focused specifically on patients with unilateral cataract, who might have larger interocular differences than our patient pool. Second, it is possible that the binocular inhibition primarily occurred for high spatial frequencies as shown in their study, whereas the Pelli-Robson test adopted in our study largely focused on patients' peak contrast sensitivity at low to mid spatial frequencies.[26]

We initially thought that AMD might differ from the other groups because the two eyes might use noncorresponding preferred retina loci (PRL) for monocular viewing. It is possible that during binocular viewing the scotoma of the worse eye would overlap with the better eye PRL,[14] in which case we would expect the binocular contrast sensitivity to be similar or even worse than the better eye. Binocular inhibition has been reported in AMD patients in previous literature.[37,38] However, in the current study, we did not observe a significantly smaller BSR for contrast sensitivity in the AMD group. One possibility is that our AMD subjects had relatively mild vision loss (i.e., mean contrast sensitivity of 1.53 and 1.38 logCS in the better and worse eyes, respectively) and may be less susceptible, while asymmetric scotoma might be more prominent in patients with more advanced vision loss.

The current study focused on the binocular summation in contrast sensitivity. In clinical practice visual acuity is a more standard measure while contrast sensitivity is not often tested. In normal vision, binocular viewing has a small but significant advantage in acuity, with the summation ratio ranging from 4% to 7%.[2,6,40–42] Clinical studies have also reported binocular acuity summation in patients with eye diseases.[38,43] For example, Tarita-Nistor et al. found that a group with AMD showed similar overall BSR in acuity as elderly and young control groups.[38] Contrast sensitivity and acuity reductions have been found to covary across different eye diseases,[44,45] therefore, it is possible that clinical acuity measures could be used to predict binocular contrast summation. To examine this possibility, we conducted additional analyses to explore the relationship between acuity measured by the ETDRS letter chart and the BSR in contrast sensitivity. All groups showed significant binocular summation in acuity (BSR > 1, $P < 0.001$), except the RP group ($P = 0.90$). The BSR values in acuity were consistently smaller than the BSR values in contrast sensitivity. The mean BSR for acuity was 1.08 (1.5 letters) in the normal vision group and was 1.17 (3 letters) in the AMD group, 1.13 (2.5 letters) in the cataract group, 1.09 (1.5 letters) in the glaucoma group, and 1.03 (< 1 letters) in the RP group. We found that there were no significant correlations between BSR in acuity and BSR in contrast sensitivity (all $P > 0.05$). In addition, there were weak correlations between the IOR in acuity and BSR in contrast sensitivity for the AMD ($r = 0.27$, $P = 0.003$) and RP ($r = 0.34$, $P = 0.009$) groups, but not for the other three groups. These additional analyses indicate that clinical acuity measures are not effective predictors of binocular contrast summation, and that it is important to measure both acuity and contrast sensitivity in clinical practice. Moreover, the fact that both acuity and contrast sensitivity improve when two eyes are used reinforces the importance of measuring both monocular and binocular visual functions.

Several unexpected findings were found in the normal vision group. Interocular contrast differences were observed in some subjects despite the absence of eye diseases, which may indicate that the conventional refractive-error correction based on acuity is not sufficient to correct for interocular differences in contrast sensitivity. Moreover, the interocular difference was a significant predictor for the BSR, as in the groups with eye diseases. Such correlation between BSR and IOR in subjects with normal vision has previously been reported in Baker et al., 2018.[8] Using a similar modeling approach as in our current paper, Baker et al. (2018) reported a m value of 1.75 from a meta-analysis across 21 studies of binocular summation in normally sighted subjects, which was close to the m value reported in our study, and provided a consistent picture of the mechanism underlying contrast summation.

We acknowledge that there are limitations in the current study given the nature of our dataset amassed from various studies. To our best knowledge, the majority of patients did not have any major comorbidities. However, we cannot rule out that some patients might have had unknown ocular comorbidities, such as cataracts or other age-related vision loss. In addition, it would be more informative to compare binocular summation across patients at different stages of the eye diseases studied. However, this information was not available in our current dataset.

In summary, the current study shows a preserved binocular contrast summation mechanism across common eye diseases, including cataract, AMD, glaucoma, and RP. Our findings enhance our understanding of the cortical mechanism underlying binocular function and reveal the importance of considering binocular function in the treatment or rehabilitation of patients with eye disease. Our results also support the importance of improving contrast sensitivity in both eyes via medical treatments, refractive correction, or visual assistive devices to reduce the asymmetry between the eyes, which may result in a benefit for binocular visual functioning during daily activities.

Disclosure: **Y.-Z. Xiong,** (N); **R. Liu,** (N); **M. Kwon,** (N); **A.K. Bittner,** (N); **C. Owsley,** (N); **G.E. Legge,** (N)

References

1. Pirenne MH. Binocular and uniocular threshold of vision. *Nature.* 1943;152:698.

2. Campbell FW, Green DG. Monocular versus binocular visual acuity. *Nature.* 1965;208:191–192.

3. Blake R, Fox R. The psychophysical inquiry into binocular summation. *Percept Psychophys.* 1973;14:161–185, https://link.springer.com/article/10.3758/BF03198631.

4. Owsley C. Vision and aging. *Annu Rev Vis Sci.* 2016;2:255–271.

5. Legge GE, Chung STL. Low vision and plasticity: implications for rehabilitation. *Annu Rev Vis Sci.* 2016;2(1):321–343.

6. Home R. Binocular summation: a study of contrast sensitivity, visual acuity and recognition. *Vision Res.* 1978;18(5):579–585.

7. Legge GE. Binocular contrast summation II: quadratic summation. *Vision Res.* 1984;24(4):385–394.

8. Baker DH, Lygo FA, Meese TS, Georgeson MA. Binocular summation revisited: beyond $\sqrt{2}$. *Psychol Bull.* 2018;144(11), 1186–1199.

9. Poggio PG, Fischer B. Binocular interaction and depth sensitivity in striate and prestriate cortex of behaving rhesus monkey. *J Neurophysiol.* 1977;40, 1392–1405.

10. Levi DM. Linking assumptions in amblyopia. *Visi Neurosci.* 2013;30(5-6):277–287.

11. Dorr M, Kwon MY, Lesmes LA, et al. Binocular summation and suppression of contrast sensitivity in strabismus, fusion and amblyopia. *Front Hum Neurosci.* 2019;13:234.

12. Prins D, Hanekamp S, Cornelissen FW. Structural brain MRI studies in eye diseases: are they clinically relevant? A review of current findings. *Acta Ophthalmol.* 2016;94:113–121.

13. Pardhan S, Cilchrist J. The importance of measuring binocular contrast sensitivity in unilateral cataract. *Eye.* 1991;5:31–35.

14. Tarita-Nistor L, Eizenman M, Landon-Brace N, et al. Identifying absolute preferred retinal locations during binocular viewing. *Optom Vis Sci.* 2015;92:863–872.

15. Tzaridis S, Herrmann P, Charbel Issa P, et al. Binocular inhibition of reading in macular telangiectasia type 2. *Invest Ophthalmol Vis Sci.* 2019;60(12):3835–3841.

16. Owsley C, Stalvey BT, Wells J, Sloane ME, McGwin G, Jr. Visual risk factors for crash involvement in older drivers with cataract. *Arch Ophthalmol.* 2001;119(6):881–887.

17. Bittner AK, Haythorthwaite JA, Diener-West M, Dagnelie G. Photopsias are related in part to perceived stress and positive mood in retinitis pigmentosa. *Eye.* 2012;26(1), 101–108.

18. Huisingh C., McGwin G., Wood J., Owsley C. The driving visual field and a history of motor vehicle collision involvement in older drivers: a population-based examination. *Invest Ophthalmol Vis Sci.* 2015;56:132–138.

19. Kwon M, Huisingh C, Rhodes LA, McGwin G, Jr., Wood JM, Owsley C. Association between glaucoma and at-fault motor vehicle collision involvement among older drivers: a population-based study. *Ophthalmology.* 2016a;123(1):109–116.

20. Kwon M, Liu R, Chien L. Compensation for blur requires increase in field of view and viewing time. *PLoS One.* 2016b;11:e0162711.

21. Chien L, Liu R, Girkin C, Kwon M. Higher contrast requirement for letter recognition and macular RGC+ layer thinning in glaucoma patients and older adults. *Invest Ophthalmol Vis Sci.* 2017;58:6221–6231.

22. Liu R, Patel BN, Kwon M. Age-related changes in crowding and reading speed. *Sci Rep.* 2017;7:8271.

23. Kwon M, Liu R, Patel BN, Girkin C. Slow reading in glaucoma: is it due to the shrinking visual span in central vision? *Invest Ophthalmol Vis Sci.* 2017;58(13):5810–5818.

24. Ferris FL, III, Kassoff A, Bresnick GH, Bailey I. New visual acuity charts for clinical research. *Am J Ophthalmol.* 1982; 94:91–96.

25. Beck RW, Moke PS, Turpin AH, et al. A computerized method of visual acuity testing: adaptation of the early treatment of diabetic retinopathy study testing protocol. *Am J Ophthalmol* 2003;135:194–205.

26. Pelli DG, Robson JG, Wilkins AJ. The design of a new letter chart for measuring contrast sensitivity. *Clin Vis Sci.* 1988;2:187–199, https://denispelli.com/pubs/pelli1988chart.pdf.

27. Elliott DB, Bullimore MA, Bailey IL. Improving the reliability of the Pelli–Robson contrast sensitivity test. *Clin Vis Sci.* 1991;6:471–475, https://www.researchgate.net/publication/246438668_Improving_the_reliability_of_Pelli-Robson_contrast_sensitivity_test.

28. R_Core_Team. *R: A Language and Environment for Statistical Computing.* Vienna, Austria: R Foundation for Statistical Computing; 2005.

29. Bates D, Maechler M, Bolker B. lme4: linear mixed-effects models using S4 classes. R package version 0.999999-0. Retrieved July 20, 2015; http://CRAN.R-project.org/package=lme4.

30. Piepho HP. An algorithm for a letter-based representation of all pairwise comparisons. *J Comput Graph Stat.* 2004;13(2):456–466, https://www.tandfonline.com/doi/abs/10.1198/1061860043515.

31. Efron B, Tibshirani RJ. *An Introduction to the Bootstrap.* Boca Raton, FL: Chapman & Hall; 1993.

32. Robson JG, Graham N. Probability summation and regional variation in contrast sensitivity across the visual field. *Vision Res.* 1981;21:409–418.

33. Baker DJ, Meese TS, Mansori B, Hess RF. Binocular summation of contrast remains intact in strabismic amblyopia. *Invest Ophthalmol Vis Sci.* 2007;48(11):5332–5338.

34. Liu R, Kwon MY. Increased equivalent input noise in glaucomatous central vision: is it due to understanding of retinal ganglion cells? *Invest Ophthalmol Vis Sci.* 2020;61(8):10.

35. McAnany JJ, Alexander KR, Genead MA, Fishman GA. Equivalent intrinsic noise, sampling efficiency, and contrast sensitivity in patients with retinitis pigmentosa. *Invest Ophthalmol Vis Sci.* 2013;54(6):3857–3862.

36. Nelson-Quigg JM, Cello K, Johnson CA. Predicting binocular visual field sensitivity from monocular visual field results. *Invest Ophthalmol Vis Sci.* 2000;41:2212–2221.

37. Faubert J, Overbury O. Binocular vision in older people with adventitious visual impairment: sometimes one eye is better than two. *J Am Geriatr Soc.* 2002;48:375–380.

38. Tarita-Nistor L, González EG, Markowitz SM, Steinbach MJ. Binocular interactions in patients with age-related macular degeneration: acuity summation and rivalry. *Vision Res.* 2006;46:2487–2498.

39. Pineles SL, Velez FG, Yu F, Demer JL, Birch E. Normative reference ranges for binocular summation as a function of age for low contrast letter charts. *Strabismus.* 2014;22(4):167–175.

40. Cagenello R, Arditi A, Halpern DL. Binocular enhancement of visual acuity. *J Opt Soc Am A Opt Image Sci Vis* 1993; 10(8): 1841.

41. Rubin GS, Munoz B, Bandeen-Roche K, West SK. Monocular versus binocular visual acuity as measures of vision impairment and predictors of visual disability. *Invest Ophthalmol Vis Sci.* 2000; 41: 3327–3334.

42. Azen SP, Varma R, Preston-Martin S, et al. Binocular visual acuity summation and inhibition in an ocular epidemiological study: the Los Angeles Latino Eye Study. *Invest Ophthalmol Vis Sci.* 2002;43: 1742–1748.

43. Pardhan S, Elliott DB. Clinical measurements of binocular summation and inhibition in patients with cataract. *Clin Vis Sci.* 1991;6:355–359, https://www.researchgate.net/publication/285534267_Clinical_measurements_of_binocular_summation_and_inhibition_in_patients_with_cataract.

44. KR Alexander, Derlacki DJ, Fishman GA. Visual acuity vs letter contrast sensitivity in retinitis pigmentosa. *Vision Res.* 1995;35:1495–1499.

45. Xiong Y-Z, Kwon M, Bittner AK, Virgili G, Giacomelli G, Legge GE. Relationship between acuity and contrast sensitivity: differences due to eye disease. *Invest Ophthalmol Vis Sci.* 2020;61(6):40.