Binocular Inhibition of Reading in Macular Telangiectasia Type 2

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PURPOSE. To assess the presence of binocular gain in macular telangiectasia type 2 (MacTel) and its correlation to paracentral scotomas.

METHODS. Sixty-eight patients with MacTel were consecutively recruited for a cross-sectional analysis. Best-corrected visual acuity (BCVA), reading acuity, and reading speed were tested monocularly and binocularly. Macular retinal sensitivity was examined with fundus-controlled perimetry (microperimetry). Scotomas were quantified by their size, their depth, and their proximity to the fovea.

RESULTS. Binocular reading speed and acuity were lower than monocular reading speed and acuity in the functionally better eye (142 vs. 159 words per minute and 0.43 vs. 0.28 log reading acuity determination, $P < 0.001$). Magnitude of binocular inhibition of reading speed was correlated to the degree of interocular functional difference ($R^2 = 0.61$, $P < 0.001$). This correlation was not found for reading acuity or BCVA ($R^2 < 0.03$). Binocular reading speed was negatively correlated to size of right and left eye scotomas, with bigger effect size for left eye scotomas. The magnitude of binocular inhibition was correlated to size of left eye scotomas, but not of right eye scotomas. When both eyes had similar scotoma characteristics, the right eye was more frequently the better reading eye.

CONCLUSIONS. We provide evidence for the presence of binocular inhibition of reading performance in MacTel, likely due to binocular rivalry. This may result from the characteristic paracentral scotomas in noncorresponding retinal fields and, in particular, a disruptive projection of scotomas in reading direction arising from the left eyes. Patients may benefit from occluding one eye while reading.

Keywords: reading, binocular gain, binocular inhibition, macular telangiectasia type 2, scotoma

Macular telangiectasia type 2 (MacTel) is a bilateral neurodegenerative disease with additional vascular alterations. Characteristic structural and functional changes usually affect an oval-shaped area centered on the fovea, measuring 6° to 8° horizontal and 5° vertical diameter. A detailed description can be found in a recent review article.[1] Disease-related changes seem to first arise in the temporal parafovea, eventually leading to focal loss of photoreceptors and hence paracentral scotomas.[1-3] Paracentral scotomas were shown to be associated with reading difficulties and impaired stereoscopic vision[4-6] and can be visualized with fundus-controlled perimetry (microperimetry). Microperimetry enables a precise determination of retinal position, size, and depth of scotomas.[7,8]

An association of reading performance with presence of scotomas has been shown in a previous study, where monocular reading function has been evaluated.[4] So far, binocular reading performance has not yet been systematically analyzed in MacTel, although reading is typically a binocular activity. Visual performance can differ when performed with one or with two eyes. Commonly, binocular function is compared with monocular function of the better-seeing eye, and the difference is called "binocular gain."[9] If binocular function is better than monocular function then binocular gain is positive and may also be called "binocular summation," or it is negative and may be called "binocular inhibition." Binocular summation is a well-known phenomenon in visual acuity testing,[10] but there is currently no compelling evidence for binocular summation in reading.[11-13]

Kabanarou and Rubin[14] were not able to provide evidence for a significant binocular gain (neither negative nor positive) in patients with age-related macular degeneration (AMD).[14] People with MacTel have scotomas that are typically non-homonymous (i.e., not corresponding in their location in the visual field). With nonhomonymous scotomas, one might

predict binocular gain because either the missing information from one eye is provided by the other eye (binocular summation), or the missing information interferes negatively with the other eye (binocular rivalry). Interestingly, patients with MacTel frequently report that reading is easier with one eye closed (unpublished personal observation).

This study was designed to study the presence of binocular inhibition in people with MacTel. We further sought to explore the correlation of binocular inhibition to scotoma measures in both eyes.

METHODS

In this cross-sectional study, participants in the MacTel Natural History Observation and Registry Study (NHOR) with a confirmed diagnosis of MacTel were consecutively recruited from a single center (Department of Ophthalmology, University of Bonn, Germany). Exclusion criteria were extrafoveal or unstable fixation (as defined by fewer than 75% of fixation points falling within a 4° circle in microperimetry) and dyslexia.

The study was approved by the Ethics Committee of the University of Bonn and all subjects were treated in accordance with the Declaration of Helsinki. A detailed protocol of the NHOR study has been published previously.[15] In addition, reading acuity and reading speed were assessed monocularly and binocularly with Radner reading charts as described previously.[4] In short, standard Radner reading charts were used at a test distance of 40 cm and with best-corrected refraction for this distance. We used three different charts in order to test binocular reading, followed by monocular reading with the right eye and then with the left eye. The test sentences were covered with cardboard, and the investigator asked the patients to read each sentence aloud and without interruptions or corrections as soon as it was uncovered. Reading time was measured, and reading speed in words per minute (wpm) was calculated according to the manufacturer's instructions. Reading acuity was determined as the smallest print size at which the patient was able to read the sentence in less than 20 seconds, factoring in reading errors as proposed by the manufacturer. It was measured as logarithm of reading acuity determination (logRAD).

Reading speed between two eyes of one patient was defined as different when they were more than 25 wpm apart and reading acuity when more than 0.1 logRAD apart, corresponding to the reference range of test-retest variability.[16]

Macular retinal sensitivity was assessed in each eye with microperimetry (MP1; Nidek Technologies, Padua, Italy) as previously described.[7] In short, the test was conducted under mesopic light conditions with dilated pupils with a test grid of 83 test stimuli (Goldmann size III, 4-2 strategy, 1.27 cd/m^2 background illumination, stimulation time 100 milliseconds) within the central 8° of fixation. In particular, the central 4° × 8° degrees were covered by a grid of five rows of nine test points, each row and point 1° apart, thus resulting in a regular grid of 45 test points with a central row through the foveal center. The stimulus intensity ranged from 0 to 20 dB. A fixation target (red cross, 2° size) was provided, and fixation stability was monitored. Importantly, the device allowed for placement of additional stimuli after finishing the examination with the above-specified grid. In case a scotoma reached the margin of the central dense grid, we added further testing points (1° apart) around the scotoma. This procedure was repeated until we were able to outline the scotoma with a fringe of normal retinal sensitivity, allowing us to define the full extension of the scotoma and to limit the analysis of testing points to the central grid (Supplementary Fig. S1).

Scotoma Quantification

Scotoma size was defined as the largest horizontal diameter of the scotoma. It was obtained by counting the number of scotomatous points in the central row of the testing grid, thus reflecting the maximum horizontal diameter in retinal degrees as each testing point was 1° degree apart (Supplementary Fig. S1). The largest horizontal diameter was found in the central row of testing points in most cases, and we assumed it was suitable as a scotoma measure because in MacTel scotomas are typically monofocal and continuous.[8,17] Relative and absolute scotomas (see below) were considered equal for quantification of scotoma location and size.

Scotoma location was defined as the retinal location in degree of the nearest scotomatous point to the foveal center (Supplementary Fig. S1).

Scotoma depth was graded in three categories based on the lowest sensitivity value encountered in the exam instead of using sensitivity as a continuous variable. This means an eye with a single test location with an absolute scotoma would be graded as "absolute scotoma" for the analysis by virtue of this single test location. For linear regression, those categories were dummy coded (no scotoma = 1, relative = 2, absolute = 3). This approach was chosen due to the reduced dynamic range of the MP1 device, resulting in both strong ceiling and floor effects. Moreover, there is a 97% chance that pointwise sensitivity would fall in a range of 6 dB at retest.[18] The grading of presence of relative versus absolute scotomas was similar to a "local defect classification"[18] comparing the tested sensitivity with a normal sensitivity range. A relative scotoma was defined as retinal sensitivity lower than 2 standard deviations (SD) from an average sensitivity in healthy observers. We used previously published normal values[19] (mean 18.62 dB, SD 3.1 dB) creating a cutoff value for relative scotomas of 12 dB and lower. An absolute scotoma was defined as a test location where the brightest stimulus of the device was not perceived by the observer.

Statistical Analysis

Statistical analysis was performed using the R statistical software.[20] Paired *t*-tests were used for comparison of function of the better eye and binocular function. *P* values were corrected for multiple testing using Bonferroni correction. Pearson correlation coefficients for those variables were calculated with simple linear regression. To test the hypothesis that the magnitude of binocular gain might be correlated to the functional difference between eyes, we used simple linear regression models with binocular gain as the dependent variable and difference between eyes as the independent variable. Magnitude of binocular gain was defined as binocular functional performance minus monocular performance in the better eye. Multiple linear regression models were fitted to the data for exploration of the effect of scotoma characteristics on monocular and binocular visual performance. Model fits were compared with analysis of variance testing and based on the Bayesian information criterion. Statistical significance was set at the 5% level ($P = 0.05$).

RESULTS

Seventy-two participants were examined. Four people did not meet the inclusion criteria and were excluded from analysis. Thus, 68 participants were analyzed (32 males, 36 females, mean age 62.7 years, SD 6.3; range: 52–78 years).

Monocular reading speed of the better eye (mean 159.79 wpm, SD 31.07) was faster than binocular reading speed (mean 142.13 wpm, SD 29.58, *P* < 0.001; Fig. 1A). Likewise, the
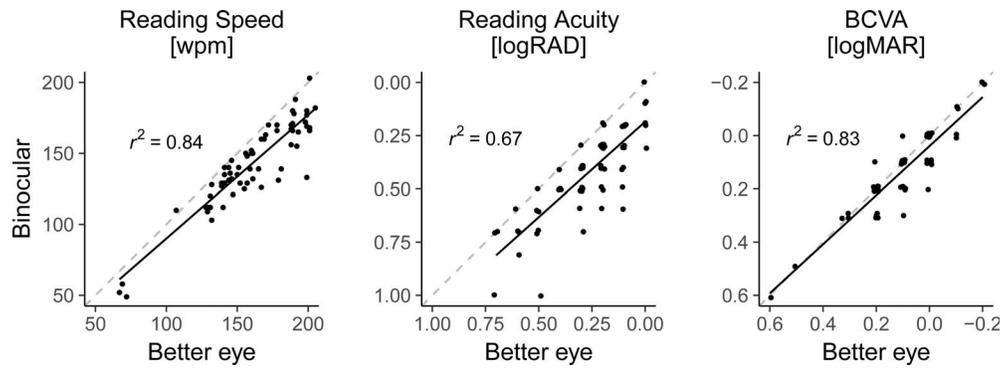
FIGURE 1. Binocular gain for reading speed, reading acuity, and BCVA. Reading performance was almost always better when performed with the functionally better eye (*x*-axis) than when performed binocularly (*y*-axis). Most of the values fall below the line of equality (*gray dashed line*). In BCVA testing, the values follow this line of equality very closely, corresponding to the small difference between both parameters. The regression line (*black line*) and coefficient (r^2) from simple linear regression models are shown. $N = 68$ patients.

better eye had higher monocular reading acuity (mean 0.28 logRAD, SD 0.19) and best-corrected visual acuity (BCVA) (mean 0.09 logMAR, SD 0.14) compared to binocular testing (mean 0.43 logRAD, SD 0.2, $P < 0.001$; mean 0.12 logMAR, SD 0.14, $P < 0.001$; Figs. 1B, 1C). Although this indicated the presence of binocular inhibition (negative binocular gain) in all tested functional parameters, the difference was small for reading acuity (0.15 log units) and very small for BCVA (only 0.03 log units) and thus was not clinically relevant for those measures.

The magnitude of binocular inhibition of reading speed was correlated to the interocular difference of reading speed ($r^2 = 0.6$, $P < 0.001$; Fig. 2A). Binocular gain of reading acuity and visual acuity were not correlated to interocular differences ($r^2 = 0$ and $r^2 = 0.03$; Figs. 2B, 2C, respectively). This indicated binocular rivalry as a possible mechanism for binocular inhibition in reading speed but not in reading acuity and visual acuity. We therefore focused on reading speed in our exploratory analysis on the correlation of scotoma measures with binocular inhibition.

Monocular reading speed in the right eye was correlated with scotoma size ($P < 0.001$) and scotoma depth ($P = 0.008$, Supplementary Table S1, left side). This changed when including BCVA as a covariate. In this case, scotoma depth was not a significant predictor in the model (Supplementary Table S1, right side). Scotoma location was not a significant predictor for monocular reading speed of right eyes in the explored linear models.

Monocular reading speed in the left eye was correlated with scotoma size ($P < 0.001$) and scotoma depth ($P < 0.001$,

Supplementary Table S2, left side). This did not change when including BCVA as a covariate (Supplementary Table S2, right side). Scotoma location was not a significant predictor for monocular reading speed of left eyes after adjusting for scotoma size and depth and BCVA.

Binocular reading speed was correlated to scotoma size and depth in the left eye, but not to scotoma parameters of the right eye, when adjusting for BCVA in both eyes (adjusted $R^2 = 0.81$, $P < 0.001$). Table 1 shows the regression models with and without inclusion of scotoma parameters in the right eye; the fit was not significantly different between both models. Scotoma size in the right eye was a significant predictor in the model when excluding BCVA as a covariate, but the overall model fit decreased drastically in this case (not shown). Binocular reading speed plummeted to very low values in eyes where the scotoma affected the foveal center (Fig. 1A, the three dots in the bottom left, and Fig. 3, the bottom three lines), but scotoma location was not a significant predictor in linear regression models.

Binocular gain on the other hand did not show such a strong linear correlation with scotoma measures (adjusted $R^2 = 0.35$, $P < 0.001$, Table 2). The best model fit was achieved when including scotoma size of both eyes and, interestingly, including an interaction term of scotoma size in the left eye with presence of scotoma in the right eye. This interaction meant that the effect of scotoma size in the left eye was dependent on the presence of a scotoma in the right eye (Fig. 3, right side). This was not the case for the converse (Fig. 3, left side). Scotoma location, scotoma depth, BCVA of each
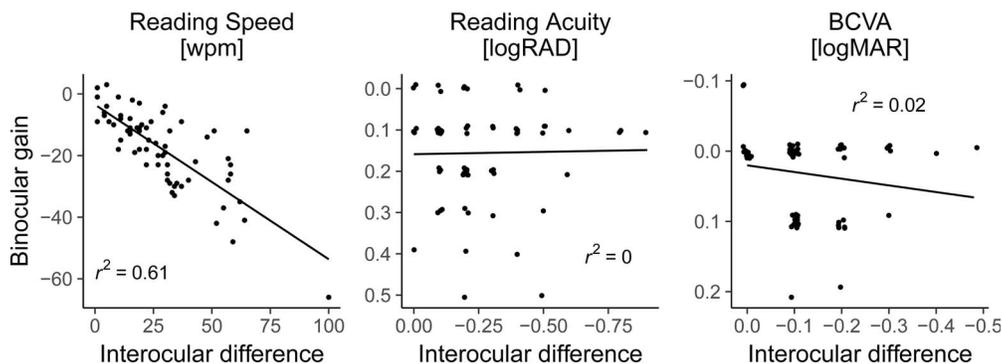

FIGURE 2. The functional difference between both eyes (interocular difference) was predictive of binocular gain in reading speed: the bigger the difference, the more negative was binocular gain, that is, the stronger was binocular inhibition. There was no similar correlation for reading acuity or visual acuity. The regression line (*black line*) and coefficient (r^2) from simple linear regression models are shown. $N = 68$ patients.

TABLE 1.   Summary of Multiple Linear Regression Models With Binocular Reading Speed as Outcome Variable

	Binocular Reading Speed					
	With RE Scotoma Measures			Without RE Scotoma Measures		
Predictors	Estimates	CI	P	Estimates	CI	P
(Intercept)	198.35	182.35 to 214.36	<0.001	197.12	184.43 to 209.82	<0.001
RE scotoma size	−1.18	−3.83 to 1.46	0.385			
RE scotoma depth	−0.37	−6.22 to 5.48	0.902			
RE BCVA	−54.14	−86.77 to −21.51	0.002	−59.53	−88.01 to −31.05	<0.001
LE scotoma size	−5.96	−9.04 to −2.88	<0.001	−6.29	−9.25 to −3.32	<0.001
LE scotoma depth	−11.56	−17.33 to −5.79	<0.001	−11.73	−17.39 to −6.08	<0.001
LE BCVA	−37.49	−67.64 to −7.35	0.018	−37.47	−66.76 to −8.19	0.015
Observations		68			68	
R^2/adjusted R^2		0.825/0.808			0.822/0.811	

On the left side, scotoma measures of the right eye (RE) were included. The model on the right side includes only scotoma measures in the left eye (LE), but also the model does not change significantly. The large effect of BCVA on the outcome measure is due to the nature of the linear model. The effect is evaluated for each log unit of BCVA. Bold *P* values indicate statistical significance. CI, confidence interval.

eye, and interocular BCVA difference were tested as independent variables and discarded as nonsignificant.

In order to visualize the effect of scotoma measures on binocular reading speed, we plotted the horizontal scotoma size and location of both eyes on one horizontal line for each patient and then sorted the patients along the *y*-axis according to their reading speed, with the fastest reading speed on top (Fig. 4). There is an evident continuous increase of scotoma size in the left eye but a more random distribution of scotoma sizes in the right eye.

Figure 5 shows another visualization of the effect of scotoma measures on binocular reading speed (and binocular gain). We created subgroups based on scotoma distribution in both eyes and ordered those groups along the *x*-axis according to their reading speed, with the group with the best reading speed to the left. It might be possible to draw several conclusions based on this figure: (1) Decline in reading speed may correlate with the emergence of deep scotomas. Best reading speed was achieved by the person without scotoma (group 1), and reading speed fell with the emergence of absolute scotomas (groups 5–7). (2) Scotomas in the left eyes may have a stronger negative effect on binocular reading speed than scotomas in the right eyes (compare group 2 with 3 and group 5 with 6). (3) The highest degree of binocular inhibition was found in people who had a scotoma in their left, but not in

their right, eyes (group 3). (5) Visual acuity does not change clinically significantly between the groups (bottom graph). In those groups where scotomas were similar in both eyes (groups 1, 4, and 7), the better reading eye was almost exclusively the right eye (Supplementary Fig. S2).

DISCUSSION

In this study, we observed a significantly worse outcome for binocular reading speed, reading acuity, and visual acuity compared to measures in the better eye in patients with MacTel, suggesting the presence of binocular inhibition. Although statistically significant, the effect in BCVA and reading acuity was clinically negligible. The finding that the magnitude of binocular inhibition of reading correlated with interocular differences in reading speed is suggestive of binocular rivalry. Our exploratory analysis supports the hypothesis that in MacTel, this binocular rivalry might be related to the presence and characteristics of the typical paracentral scotomas. Although the statistical modeling proved to be quite challenging due to the abundance of predictive measures and the presence of multiple collinearities, as well as statistical interactions, the association of scotoma size with

FIGURE 3.   Binocular gain does not correlate with scotoma size in the right eye (*left graph*). It correlates with scotoma size in the left eye (*right graph*). There is a statistical interaction of scotoma size in the left eye and scotoma presence in the right eye. The effect of scotoma size on binocular gain is much higher when there is no scotoma in the right eye. RE, right eye; LE, left eye.

TABLE 2.   Summary of a Multiple Linear Regression Model With Binocular Gain (Binocular Inhibition) of Reading Speed as Outcome Variable

	Binocular Gain		
Predictors	Estimates	CI	P
(Intercept)	−15.76	−19.99 to −11.53	<0.001
RE scotoma size	2.53	0.55 to 4.51	0.015
LE scotoma size	−14.82	−20.54 to −9.09	<0.001
LE scotsize:RE scot	12.22	6.46 to 17.98	<0.001
Observations		68	
R^2/adjusted R^2		0.379/0.350	

Scotoma size in both eyes were significant predictors in the model, but the effect size was much bigger for scotoma size in the LE. Including an interaction term of scotoma size in the LE with scotoma presence in the RE (LE scotsize:RE scot) resulted in a significant improvement of model fit. The positive value (12.22) indicates that the overall binocular inhibition was less in eyes with scotoma in the RE. Inclusion of BCVA or scotoma location did not improve the model fit. Bold *P* values indicate statistical significance.
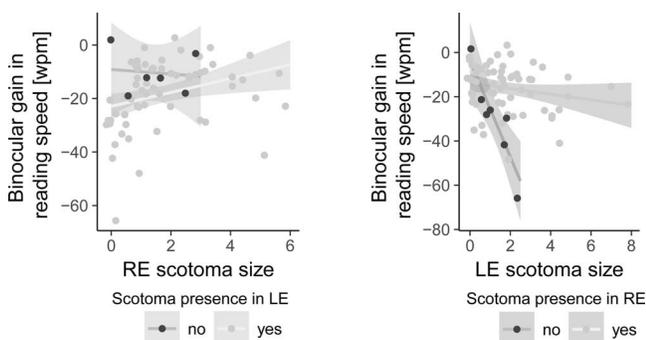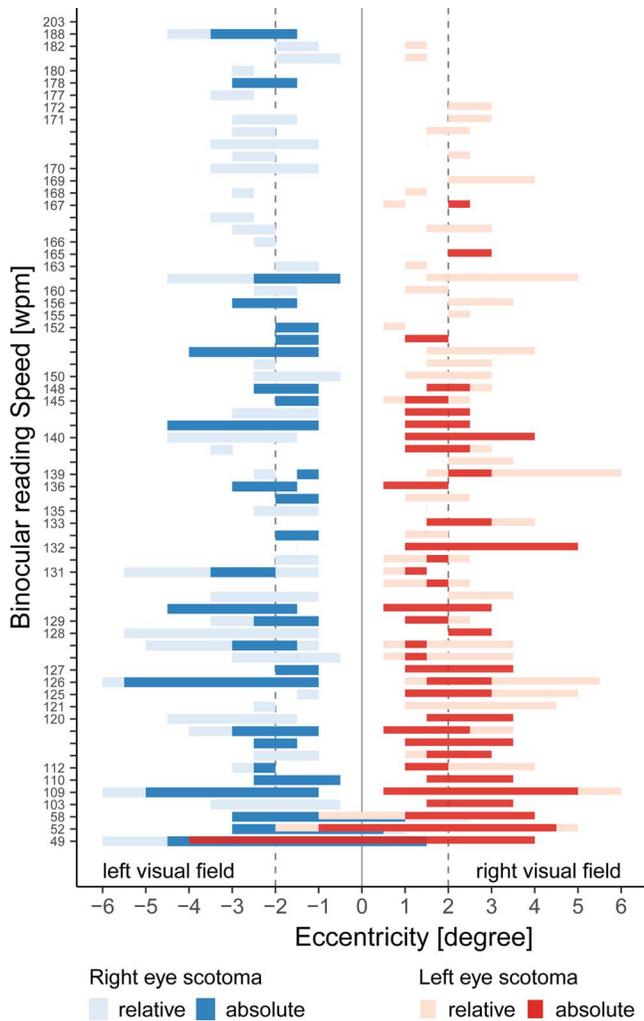
FIGURE 4. Horizontal scotoma size and location in both eyes of one patient were plotted on one horizontal line for each patient. The patients were sorted along the *y*-axis according to their binocular reading speed, with the highest reading speed on top. Axis ticks without labels have the same reading speed as the nearest lower label. Patients with the same reading speed were ranked randomly. The line at 0° represents the location of fixation. The *dashed lines* delineate the minimum visual field required for fluent reading.

binocular reading speed and binocular inhibition was consistently present in all models. Our data strongly suggested in multiple ways that scotomas in the left eye had a stronger effect on binocular reading speed than scotomas in the right eyes (Tables 1, 2; Figs. 3–5; Supplementary Tables S1, S2). Moreover, our data suggested that the magnitude of binocular inhibition was associated with scotoma measures in left eyes but not with scotoma measures in right eyes. An increase in scotoma size in the left eye resulted in a much stronger binocular inhibition in people without a scotoma in their right eyes than in those with a scotoma in the right eye (Fig. 3, right side). A similar effect was not found for scotomas in the right eyes (Fig. 3, left side). One explanation for this could be the observation that the right eye was more frequently the better reading eye, and thus binocular gain would more often depend on the reading speed in the right eye; that is, a lower reading speed in the right eye due to the presence of a scotoma would leave less room for impact of the scotoma in the left eye to make binocular gain. On the other hand, there seems to be a

larger observed effect size of left eye scotomas than of right eye scotomas on binocular reading speed in patients with unilateral scotoma (Table 2), which is generally in line with the concept of left eye scotomas having more impact on reading function than scotomas of right eyes.

A potential explanation for the different effect of scotomas in right and left eyes might be the relative location of the scotomas in the visual field (Figs. 4, 6). For fluent reading, a perceptual span of approximately 5° in the reading direction is required in order to guide the next saccade to the following text location and organize the switch between fixation and saccades during the reading process.[21] When reading from left to right, the visual field to the right appears to be of higher importance for reading performance than the visual field to the left side.[22] Scotomas of the left eye are projected on the right side of the fixated letter/word and hence in reading direction, thus interrupting the perceptual span required for reading (Figs. 4, 6). Interestingly, in our sample, left eyes had generally lower reading speed than right eyes, which would be in keeping with this idea (Supplementary Fig. S2). Accordingly, Sunness et al.[23] have found a trend to higher reading speed in patients with AMD when they were fixating to the right of their scotoma (resulting in a free visual field to the right).

Scotoma presence and size might not be the only relevant factors for binocular reading speed and binocular inhibition in MacTel. In a previous study, Kabanarou and Rubin[14] were unable to provide evidence for binocular gain (summation or inhibition) in eyes with scotomas due to AMD. It is not trivial to explain this difference between AMD and MacTel. A possible explanation might be the nonhomonymous, binasal projection of the scotomas in MacTel, whereas scotomas in AMD might generally be more homonymously or randomly distributed. Binasal visual field defects result in a prefixational scotoma, which might interfere more with binocular vision than defects in more corresponding or more randomly distributed retinal areas. Our previous finding of an early impaired stereoscopic vision in MacTel would be in keeping with this concept.[6] Impairment of binocular fusion might also partly explain the phenomenon of "dancing" or "lost" letters, which is frequently reported by patients with MacTel (unpublished observation). Figure 6 attempts to simulate impaired monocular reading and impaired binocular fusion when reading. Another possible explanation of the difference between AMD and MacTel might also be different methodology in the studies. For example, sampling of a wider range of different scotomas in AMD might have obscured relevant effects in similar subgroups to MacTel. Furthermore, Kabanarou and Rubin[14] have performed a comparison of the better eye with binocular function but have not compared interocular differences with the magnitude of binocular gain and have not quantified scotomas.

Fixed testing order or eye dominance might possibly have influenced our results. In a test-retest analysis of the applied reading test,[16] there was no evidence for a learning effect in reading speed, whereas there was a trend to mildly increased reading acuity at the retest. In our study, the right eye (test 2) consistently performed better than the left eye (test 3) and also consistently better than binocular function (test 1). If testing order were a confounder, this would have to be a combination of both learning effect (from test 1 to test 2) as well as a fatigue effect (from test 2 to test 3). This is, of course, not impossible, but we believe that it is rather unlikely to have occurred consistently in most observers. Several studies have failed to provide compelling evidence for effects of eye dominance on reading performance in healthy observers.[11–13] Nevertheless, the fixed testing order remains a potential limitation of our study.
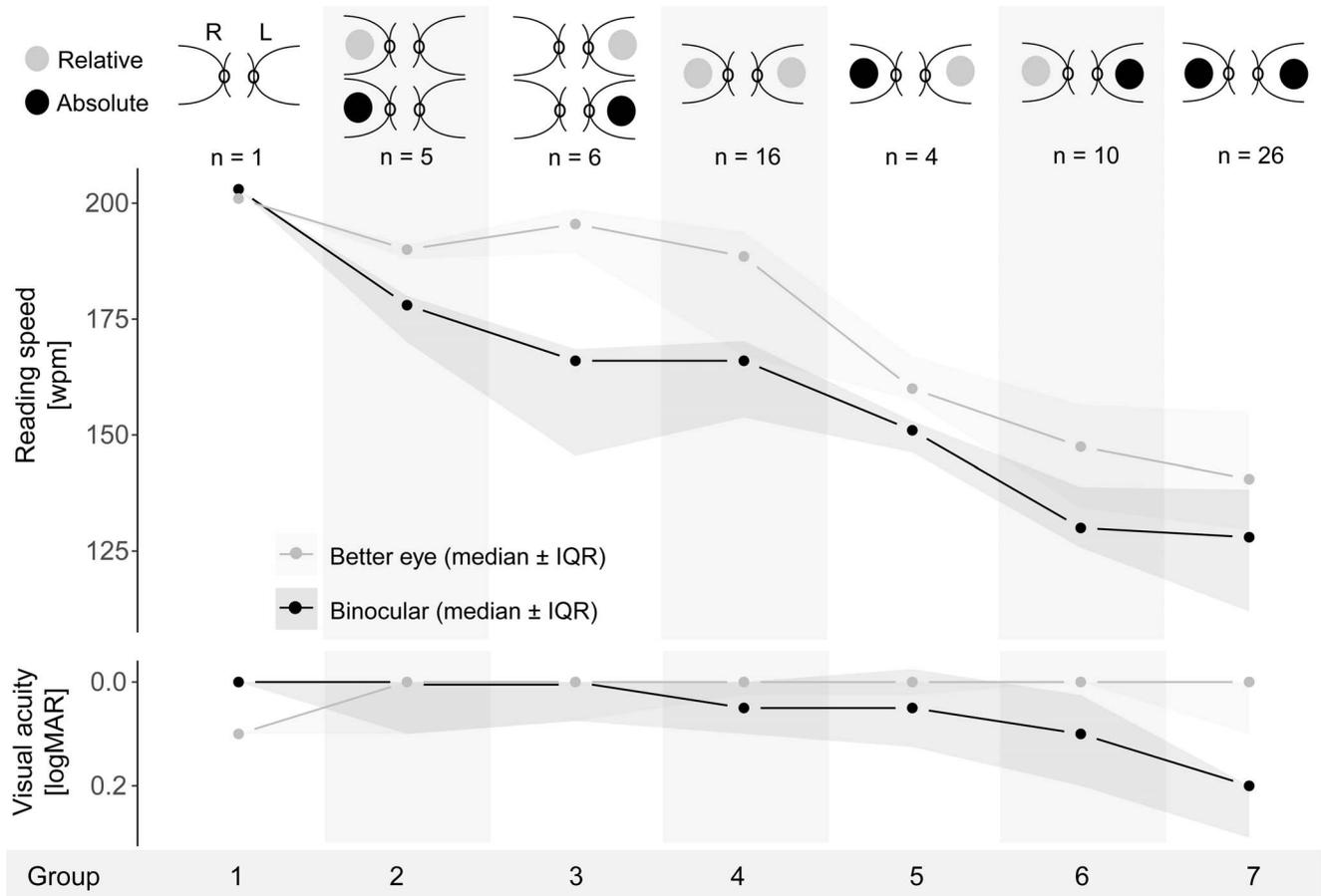
FIGURE 5. Subgroups were created based on the occurrence of relative or absolute scotomas in eyes. Decreasing binocular reading speed (arranged from *left* to *right*) was associated with more severe scotomata. The occurrence of absolute scotomas seemed to correlate with a drop in reading speed. For example, group 5 shows a markedly lower reading speed than group 4. Groups with more pronounced scotoma in the left eye seemed to have generally worse function (compare group 2 with 3 and group 5 with 6). The difference between *gray* and *black lines* indicates the magnitude of binocular inhibition. This was most pronounced in patients with a scotoma in their left eye, but without scotoma in their right eyes (group 3). Visual acuity in the better eye was similar across groups, and there was no clinically significant binocular inhibition. R, right eye; L, left eye.

It would be an interesting proof of concept and further evidence for our hypothesis if the effect was reversed when reading from right to left. A similar study, for example in Israel, where text is read from right to left, would be predicted to show that scotoma measures in right eyes were more relevant for binocular reading than scotomas in left eyes.

CONCLUSIONS

We provide evidence for the presence of binocular inhibition of reading performance in MacTel. The magnitude of binocular inhibition correlated with the difference in reading speed between eyes, possibly due to the characteristic paracentral scotomas in noncorresponding retinal fields and a disruptive projection of scotomas in reading direction mainly arising from the left eyes. People with MacTel may improve their visual symptoms by occluding their worse eye while reading.
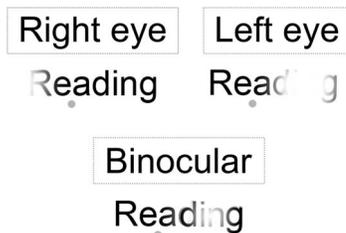

FIGURE 6. Simulation of possible monocular and binocular reading in eyes with MacTel. The *gray dots* denote the fixation location and can also be used as an aid for fusion of both images. The contemplator of this figure might get an impression of binocular reading vision of people with binasal paracentral scotoma due to MacTel. In the left eye, the scotoma projects in the reading direction. The scotoma in the right eye is not impairing the reading field but may impede finding the next line. The binasal scotoma results in a prefixational scotoma, which might interfere with fusion and result in the phenomenon of "dancing" or "lost" letters, which is often described by patients, thus challenging fluent reading.

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