

REVIEW ARTICLE

Binocular visual function and fixational control in patients with macular disease: A review

Irina Sverdlichenko¹ | Mark S Mandelcorn^{2,3} | Galia Issashar Leibovitzh² |
 Efrem D Mandelcorn^{2,3} | Samuel N Markowitz^{2,3} | Luminita Tarita-Nistor² 

¹Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

²Krembil Research Institute, Donald K Johnson Eye Institute, University Health Network, Toronto, Ontario, Canada

³Department of Ophthalmology and Vision Sciences, Toronto Western Hospital, Toronto, Ontario, Canada

Correspondence

Luminita Tarita-Nistor, Krembil Research Institute, Donald K Johnson Eye Institute, University Health Network, Toronto, Ontario, Canada.

Email: lumi.tarita-nistor@rogers.com

Abstract

For normally sighted observers, the centre of the macula—the fovea—provides the sharpest vision and serves as the reference point for the oculomotor system. Typically, healthy observers have precise oculomotor control and binocular visual performance that is superior to monocular performance. These functions are disturbed in patients with macular disease who lose foveal vision. An adaptation to central vision loss is the development of a preferred retinal locus (PRL) in the functional eccentric retina, which is determined with a fixation task during monocular viewing. Macular disease often affects the two eyes unequally, but its impact on binocular function and fixational control is poorly understood. Given that patients' natural viewing condition is binocular, the aim of this article was to review current research on binocular visual function and fixational oculomotor control in macular disease. Our findings reveal that there is no overall binocular gain across a range of visual functions, although clear evidence exists for subgroups of patients who exhibit binocular summation or binocular inhibition, depending on the clinical characteristics of their two eyes. The monocular PRL of the better eye has different characteristics from that of the worse eye, but during binocular viewing the PRL of the better eye drives fixational control and may serve as the new reference position for the oculomotor system. We conclude that evaluating binocular function in patients with macular disease reveals important clinical aspects that otherwise cannot be determined solely from examining monocular functions, and can lead to better disease management and interventions.

KEYWORDS

AMD, binocular inhibition, binocular summation, binocular vision, central vision loss, fixation stability, PRL location

INTRODUCTION

Our two eyes view the world from slightly different angles, resulting in binocular disparity.¹ The brain receives signals from both eyes and with well-functioning binocular vision

can use these differences to perceive single objects in three dimensions.¹ Healthy binocular vision provides stereopsis and enhances depth perception.² Performance under binocular viewing conditions has consistently shown an advantage over monocular viewing, a phenomenon called

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binocular summation. For example, experiments comparing binocular and monocular performance found binocular superiority of visual functions such as contrast sensitivity and visual acuity. Broadly speaking, binocular summation can be attributed to either probability summation or neural summation. Probability summation assumes complete independence of the two eyes and predicts enhancement of binocular vision due to the statistical consideration that a binocular observer has two opportunities to detect weak signals.³ Neural summation is the result of binocularly enhanced performance that exceeds what would be expected from probability summation alone. It has been shown that the mechanism for binocular neural summation may be mediated, at least in part, by the same channels that provide stereopsis.⁴⁻⁶ Optimal binocular summation on resolution tasks and stereopsis are achieved from equal monocular foveal inputs in observers with a healthy visual system and proper eye alignment. However, these visual functions can be compromised in patients with pathological eye conditions, to the point that the binocular gain is negative (i.e., binocular visual performance is worse than monocular performance with the better eye, a phenomenon known as binocular inhibition) and stereopsis is completely damaged. For example, individuals with strabismus that have abnormal retinal disparity due to eye misalignment, and those with amblyopia that have unbalanced monocular inputs, exhibit poor or no stereopsis and impaired binocular summation.^{3,7} Although the asymmetric contributions between the two eyes can reduce binocular summation, the underlying neural mechanism of this function in the visual cortex may remain intact in pathologies such as strabismic amblyopia.⁸ This is because it has been shown that when visual input is enhanced in the affected eye to match the sensitivity of the fellow eye, binocular summation recovers.⁹

Central vision is important for tasks involving high spatial acuity, including recognizing faces, reading and driving.¹⁰ Visual information is acquired mostly when fixating briefly on targets with the fovea—the part of the central retina that provides the sharpest vision. Additionally, the fovea serves as the reference position for the oculomotor system;¹¹ precise oculomotor control with the two eyes is paramount for optimal binocular vision. The fovea is often damaged by irreversible macular diseases such as age-related macular degeneration (AMD), Stargardt disease, cone dystrophy or myopic macular degeneration. Among them, AMD is the most prevalent and the leading cause of blindness in individuals over 60 years of age.¹²

Macular diseases destroy central vision, leading to severe impairments in visual functions¹³ and disturbances in oculomotor control.¹⁴ Patients compensate by directing the image to a peripheral location on the retina that functions as a pseudo-fovea, called the peripheral retinal locus (PRL);¹¹ however, fixational oculomotor control with the PRL is worse than with the fovea, which may affect visual performance.^{15,16} An additional consequence of macular disease is that it usually does not affect both eyes equally, resulting in differences between the visual inputs received from each

Key points

- It is important to assess binocular vision in patients with macular disease because their binocular performance may be worse than monocular performance with the better eye, impacting daily living tasks.
- Asymmetric macular damage in the two eyes compromises binocular summation and stereopsis, adding to visual disability; therefore, impairments in binocular function should be evaluated and managed through appropriate rehabilitation techniques.
- Binocular fixational control is driven by the better eye, but more technological advances are needed to understand oculomotor adaptation during binocular viewing in patients with macular disease.

eye. This difference may arise from corresponding PRLs falling onto unequally functional retinal locations or from the PRL of the worse eye falling directly onto the scotoma when coming into retinal correspondence with that of the better eye during binocular viewing. For these patients, high interocular asymmetry,¹⁷ and possible abnormal disparity produced by eccentric locations of the PRL in the two eyes¹⁸ can affect binocular summation and stereopsis. Unfortunately, these binocular functions and oculomotor control of patients with macular disease are not well understood.

Given that patients' natural viewing condition is binocular, the goal of the present study is to review the differences in binocular and monocular viewing on visual functions and fixational oculomotor control in the context of macular disease. We highlight the importance of assessing binocular function for better disease management and interventions.

BINOCULAR VISUAL FUNCTION

In order to understand the influence of macular disease on binocular vision, two aspects of binocular visual function were examined: (1) differences in binocular and monocular viewing as well as prevalence of binocular summation and inhibition of various outcome measures and (2) stereopsis. The articles reviewed are presented in Table 1.

Binocular summation and inhibition

Binocular summation and inhibition in patients with central vision loss were reviewed for contrast sensitivity, visual acuity and reading performance.

TABLE 1 Summary of included studies

| Study title and authors | Study design, country | N (diagnosis), Male: Female | Mean age \pm SD (years) | Outcome of interest | Measures used | Summary of findings |
|---|---|---|---------------------------|--|--|---|
| Properties of visual field defects around the monocular preferred retinal locus in age-related macular degeneration Demiss et al. ⁴⁷ | Retrospective and Prospective Case-series, United Kingdom | N = 185 (AMD) M: 54.2% (39) F: 45.8% (33) | Median = 80, 57–97 | PRL location | 4–2 Expert test of the MAIA micropertimeter | <ul style="list-style-type: none"> PRL tended to be located superiorly and nasally relative to presumed location of anatomic fovea In visual field space, PRLs were displaced to the left and inferiorly |
| Preferred retinal locus locations in age-related macular degeneration Erbezi and Ozturk ⁵⁰ | Case-series, Turkey | N = 72 (AMD) M: 54.2% (39) F: 45.8% (33) | 78 \pm 8.8 | PRL location | Optos SLO/optical coherence tomography/micropertimetry device to determine the location of the PRL | <ul style="list-style-type: none"> Locations of the PRLs on the retina were: <ol style="list-style-type: none"> 29.2% (42 eyes) nasal 2.5% (36 eyes) central 20.8% (30 eyes) temporal 18.1% (26 eyes) superior 1.4% (2 eyes) inferior In visual field space, PRL was located: <ol style="list-style-type: none"> Left visual field (27.8% right eyes, 40.3% left eyes and 34% both eyes) Right visual field (18.1% right eyes, 13.9% left eyes, 16% both eyes) Inferior visual field (19.4% right eyes, 16.7% left eyes, 18.1% both eyes) Superior visual field (2.8% right eyes, 1.3% both eyes) Central visual field (23.6% right eyes, 26.4% left eyes, 25% both eyes) |
| Binocular vision in older people with adventitious visual impairment: sometimes one eye is better than two Faubert and Overbury ²⁰ | A between-within repeated measures design, Canada | N = 49 (AMD) | 79.2 \pm 9.2 | Visual acuity Spatial contrast sensitivity | Spatial sine wave gratings generated using Nicolet Optonics 2000 contrast measurement system. Six spatial frequencies were tested: 0.17, 0.33, 1.0, 2.01, 3.81, and 7.63 cycles per degree of visual angle | <ul style="list-style-type: none"> Best monocular acuity was equal to binocular acuity 55% (27) showed summation/suppression (binocular contrast sensitivity function greater or equal to best monocular contrast sensitivity); 45% (22) showed binocular inhibition For binocular inhibition group, there was a binocular disadvantage for the medium to lower spatial frequencies (2nd, 3rd and 4th spatial frequencies) |
| Reading with central scotomas: is there a binocular gain? Kabanarou and Rubin ²¹ | Case series, United Kingdom | N = 22 (bilateral late-stage AMD) | 81.0 \pm 5.6 | Distance acuity Contrast sensitivity Reading acuity Reading speed | Distance visual acuity measured with ETDRS charts Contrast sensitivity was measured using the Pelli-Robson letter sensitivity chart Reading acuity measured using MNREAD acuity charts Reading time calculated in milliseconds for each sentence read orally using external computer software | <ul style="list-style-type: none"> No statistically significant difference between monocular and binocular visual acuity There was a slight benefit to binocular viewing for contrast sensitivity 18.1% (4) patients showed binocular summation for contrast sensitivity, and 9% (4) showed binocular inhibition There was no statistically significant difference between binocular and monocular reading acuity and MRS 63.6% (14) patients showed binocular summation for MRS and 13.6% (3) demonstrated binocular inhibition 18.1% (4) of patients showed binocular reading acuity summation, while 4.5% (1) showed binocular reading acuity inhibition |

(Continues)

TABLE 1 (Continued)

| Study title and authors | Study design, country | N (diagnosis), Male: Female | Mean age ± SD (years) | Outcome of interest | Measures used | Summary of findings |
|--|---|--|-----------------------|---------------------|--|--|
| Gaze changes with binocular versus monocular viewing in age-related macular degeneration Kabanarou et al. ⁵⁵ | Cross-sectional, United Kingdom | N = 29 (bilateral AMD) | 79.8 ± 5.6 | PRL location | SMI EyeLink eye tracker was used to record monocular and binocular eye movements | <ul style="list-style-type: none"> 3 patients demonstrated a significant shift distance in both eyes, whereas 17 patients showed a significant shift distance only in the worse eye The shift in gaze position of the worse eye was related to the distance between the 2 monocular PRLs, but there was no such association for the better eye |
| Characteristics of the preferred retinal loci of better and worse seeing eyes of patients with a central scotoma Kisilevsky et al. ⁴⁸ | Retrospective consecutive case series, Canada | N = 103 (AMD or Stargardt disease) | | PRL location | Fixation examination was conducted using MP-1 micropertimeter | <ul style="list-style-type: none"> 31% (27) of PRLs in the better eye occurred in the inferior visual field segment; 31% (27) occurred in the left visual field; 14.9% (13) occurred in the central visual field segment; 14.9% (13) occurred in the superior visual field segment; and 8% (7) occurred in the right visual field segment PRL distribution was not significantly different for the worse eye |
| Contrast sensitivity and binocular reading speed best correlating with near distance vision-related quality of life in bilateral nAMD Rossouw et al. ³⁸ | Prospective cross-sectional pilot study | N = 54 (bilateral neovascular AMD) M: 46.3% (25) F: 53.7% (29) | 79.6 ± 7.88 | MRS | Standardised high contrast 'sentence optotypes' Radner reading charts were used to test maximum reading speed | <ul style="list-style-type: none"> No statistically significant difference between binocular MRS and monocular MRS with the better eye ($p = 0.73$) |
| Changes in fixation stability with time during binocular and monocular viewing in maculopathy Samet et al. ⁵⁸ | Case-control, Canada | N = 17 (AMD) M: 52.9% (9) F: 47.1% (8) | 78.6 ± 8.1 | Fixation stability | EyeLink 1000 eye-tracker was used to measure fixation. Fixation stability was recorded binocularly and monocularly with each eye for duration of 15 seconds with fellow eye covered and analysed over 3 second consecutive intervals | <ul style="list-style-type: none"> For binocular viewing and monocular viewing with the better eye, fixation stability of fixed-duration intervals did not change; but improved linearly with consecutive fixed duration intervals when viewing with the worse eye |

TABLE 1 (Continued)

| Study title and authors | Study design, country | N (diagnosis), Male: Female | Mean age ± SD (years) | Outcome of interest | Measures used | Summary of findings |
|---|--|---|-----------------------|---|---|---|
| Reading with central vision loss: binocular summation and inhibition Silvestri et al. ²² | Case series, Italy | N = 71 (AMD or Stargardt disease) M: 49.3% (35) F: 50.7% (36) | 63 ± 21 | Visual acuity Reading acuity Critical print size Contrast sensitivity MRS Stereoaquity Fixation stability PRL location | Visual acuity measured using ETDRS Reading acuity measured with Italian version of MINREAD acuity charts Contrast sensitivity measured using Pelli-Robson chart Stereoaquity measured using Stereo Fly Test Monocular fixation stability and PRL obtained using MP-1 Microperimeter | <ul style="list-style-type: none"> Binocular visual acuity did not differ from monocular visual acuity ($p = 0.30$) Contrast sensitivity for binocular viewing was statistically greater than monocular viewing ($p = 0.02$) MRS, critical print size and reading acuity did not differ significantly between monocular and binocular viewing conditions (smallest $p = 0.4$) 41% (29) of the sample showed binocular inhibition of MRS, 17% (12) of the sample had binocular equality and 42% (30) showed binocular summation Patients with binocular inhibition for MRS had significantly lower binocular MRS than the summation or equality group There was no difference in critical print size between binocular and monocular viewing conditions Residual stereoacuity found in 38% of cases in binocular inhibition group for MRS; 50% of cases in equality group and 73% of individuals in summation group Fixation stability was significantly better in better eye than worse eye. PRL distance from former fovea was significantly larger for worse eye than better eye in inhibition group ($p = 0.001$), but not in equality or summation group 92% of patients in equality group and 83% of patients in summation group had PRLs in corresponding locations in two eyes. 68% of patients in inhibition group had PRLs in non-corresponding locations PRL in better eye was inferior or superior to scotoma in equality group (75% of cases) and summation group (67% of cases); but in worse eye more patients had PRL temporal or nasal to scotoma (38%) Assuming that the PRL of the better eye stayed in the same location during monocular and binocular viewing, and PRL of worse eye moved into retinal correspondence with that of better eye in binocular viewing, in 52% (15) of cases of binocular inhibition, PRL in worse eye would fall on scotoma during binocular viewing |
| Identification of fixation location with retinal photography in macular degeneration Somani and Markowitz ⁴⁶ | Prospective, observational case series, Canada | N = 21 (AMD) M: 33.3% (7) F: 66.7% (14) | 78, 53–86 | PRL location | Retinal photography was performed with Zeiss fundus camera | <ul style="list-style-type: none"> In 17 (71%) of the 24 eyes with successful fixation location, preferred PRL was superior to macular scar; in 4 eyes (17%) it was to the left of the macular scar; in 2 eyes (8%) it was to the right of the macular scar; and in 1 eye (4%) it was inferior to the macular scar |
| Binocular interactions in patients with age-related macular degeneration: acuity summation and rivalry Tarita-Nistor et al. ³² | Case control, Canada | N = 17 (AMD) | 81.6 ± 6.8 | Visual acuity | Visual acuity measured with multiple tumbling E acuity test at three levels of contrast (86%, 32%, and 12%) | <ul style="list-style-type: none"> No difference between binocular and monocular visual acuity at any contrast level 39% of patients showed binocular inhibition for visual acuity, and approximately 50% demonstrated binocular summation |

(Continues)

TABLE 1 (Continued)

| Study title and authors | Study design, country | N (diagnosis), Male: Female | Mean age ± SD (years) | Outcome of interest | Measures used | Summary of findings |
|--|---------------------------------------|---|-----------------------|---|--|---|
| Fixation stability during binocular viewing in patients with age-related macular degeneration Tarita-Nistor et al. ³³ | Case-series, Canada | N = 20 (AMD) M: 50% (10) F: 50% (10) | 79.4 ± 8.3 | Visual acuity Fixation stability | Visual acuities were measured using the ETDRS chart Monocular fixation stability was recorded with the MP-1 microperimeter Binocular fixation stability was recorded with the EyeLink 1000 eye tracker | <ul style="list-style-type: none"> Monocular visual acuity of the better eye was not significantly different from binocular acuity When viewing binocularly, fixation stability of the better eye did not change between monocular and binocular viewing Fixation stability of the worse eye was 84 to 100% better in binocular than monocular viewing |
| Fixation patterns in maculopathy: from binocular to monocular viewing Tarita-Nistor et al. ³⁷ | Case-control, Canada | N = 12 (AMD) M: 33.3% (4) F: 66.7% (8) | 79.25 ± 7.31 | Fixation stability | Fixation stability was recorded using the EyeLink 1000 eye tracker | <ul style="list-style-type: none"> For the better eye, there was no difference in shift between better eye monocular viewing and binocular viewing For the worse eye, there was good coordination during binocular viewing, but greater shift with worse eye monocular viewing |
| Maximum reading speed and binocular summation in patients with central vision loss Tarita-Nistor et al. ³¹ | Prospective observational case series | N = 20 (AMD, cone dystrophy, myopic macular dystrophy) M: 40% (8) F: 60% (12) | 77 ± 12.9 | Visual Acuity Fixation stability PRL location | Visual acuity was measured using ETDRS chart Fixation stability and PRL location were recorded using MP-1 microperimeter | <ul style="list-style-type: none"> Binocular acuity was equal to monocular acuity of better eye. Acuity of worse eye was much poorer 6 patients in binocular summation group, 5 in inhibition group, and 9 in equality group Binocular MRS was lower in the inhibition group than the summation and equality groups |
| Identifying absolute preferred retinal locations during binocular viewing Tarita-Nistor et al. ⁵³ | Case control, Canada | N = 9 (bilateral central vision loss) M: 66.7% (6) F: 33.3% (3) | 73 ± 16 | PRL location | The MP-1 microperimeter was used to identify monocular PRL location The Vision 2020-RB eye-tracker was used to measure binocular PRLs | <ul style="list-style-type: none"> During binocular viewing, the PRLs were in corresponding locations, but this was not always the case in monocular viewing For patients with high interocular acuity differences, the monocular PRL of the worse eye would move into retinal correspondence with the PRL of the better eye during binocular viewing The PRL of the worse eye sometimes fell on the scotoma, while the PRL location of the better eye remained unchanged |
| Fixation stability and viewing distance in patients with AMD Tarita-Nistor et al. ³⁰ | Case-control, Canada | N = 30 (bilateral AMD) M: 40% (12) F: 60% (18) | 78 ± 8 | Visual acuity Fixation stability | Visual acuity measured using ETDRS chart Effect of viewing distance on fixation stability (40cm, 1m, 6m). Fixation stability was measured using MP-1 Microperimeter | <ul style="list-style-type: none"> There was no difference in visual acuity between better eye viewing and binocular viewing No effect of viewing distance on fixation stability of better or worse eye during binocular viewing (smallest $p = 0.1$) No effect of viewing distance on fixation stability of better eye during monocular viewing ($p = 0.3$); fixation stability was slightly worse at 40cm for worse eye viewing, but this did not reach significance ($p = 0.06$) |

TABLE 1 (Continued)

| Study title and authors | Study design, country | N (diagnosis), Male: Female | Mean age \pm SD (years) | Outcome of interest | Measures used | Summary of findings |
|--|-----------------------------|---|----------------------------|----------------------|--|---|
| Effect of disease progression on the PRL location in patients with bilateral central vision loss Tarita-Nistor et al. ⁵⁴ | Case series, Canada | N = 51 (AMD or Stargardt disease) M: 51% (26) F: 49% (25) | 77 \pm 11 at first visit | PRL location | MP-1 microperimeter was used to measure monocular PRL location | <ul style="list-style-type: none"> For the better eye, PRL distance from the former fovea increased significantly between visits ($p = 0.03$) while maintaining a constant polar angle, whereas for the worse eye, this distance did not change significantly A decrease in PRL distance from former fovea was observed in 39% (20) of cases for the worse eye, and 24% (12) of cases for the better eye The PRL of the worse eye progressed to be in retinal correspondence with the new PRL of the better eye during visit 2, and would often land on the scotoma |
| Binocular contrast inhibition in subjects with age-related macular degeneration Valberg and Fosse ¹⁷ | Case control, Norway | N = 13 (AMD) M: 38.5% (5) F: 61.5% (8) | 75 \pm 6 | Contrast sensitivity | Spatial contrast sensitivity measured using horizontal sinusoidal gratings displayed on a calibrated (g-corrected) 30-bit videographic system (VIGRA) of 40 cd/m ² mean luminance | <ul style="list-style-type: none"> 8 out of 13 AMD subjects showed binocular inhibition for narrow or extended frequency band Average of integrated binocular contrast sensitivity was similar to the average for better eye |
| Depth perception and grasp in central field loss Verghese et al. ⁴⁴ | Case control, United States | N = 14 (maculopathy) | 77.2 \pm 10.5 | Stereoacuity | Stereoacuity was measured using the RanDot stereo test Peg-placement task was used as a task requiring depth perception | <ul style="list-style-type: none"> There was a significant benefit for binocular viewing for peg-placement time, errors and peg pick-up time For patients with measurable stereopsis, there was a binocular advantage for peg placement time and errors, but this was not statistically significant Among patients with measurable stereopsis, binocular advantage of peg-placement time was significantly correlated with stereoacuity |
| The oculomotor reference in humans with bilateral macular disease White and Bedell ⁴⁹ | Case-control, United States | N = 21 (AMD or Stargardt disease) | | PRL location | Image of the fixation target and 25° of the posterior pole of patient's preferred eye was videorecorded through a Zeiss fundus camera | <ul style="list-style-type: none"> In 85.7% (18) of patients, the preferred fixation area was in the superior hemiretina In 2/3 of remaining patients, the preferred fixation area was not far below the horizontal meridian |

Abbreviations: AMD, Age-related macular degeneration; ETDRS, Early Treatment Diabetic Retinopathy Study; MRS, Maximum Reading Speed; PRL, Preferred retinal locus.

Contrast sensitivity

Contrast sensitivity is a measure of how much contrast a person requires to see a target.¹⁹ Faubert and Overbury²⁰ assessed contrast sensitivity in patients with central vision loss across six spatial frequencies and found that 45% of patients showed binocular inhibition, while the remainder showed binocular summation or equivalence; binocular inhibition was more likely to occur at medium and lower spatial frequencies. Valberg and Fosse¹⁷ also found that in a sample of 13 patients with central vision loss, 8 exhibited binocular contrast inhibition; similarly, binocular inhibition tended to occur at lower spatial frequencies. Kabanarou and Rubin²¹ reported a benefit to binocular viewing for 18.1% of patients with AMD, while 9% of patients showed binocular inhibition. Lastly, Silvestri et al.²² reported a small but statistically significant binocular advantage for contrast sensitivity in a large sample of 71 patients with AMD and Stargardt disease.

It has been suggested that unequal monocular contrast sensitivities can lead to a decrease in binocular contrast summation. Faubert and Overbury²⁰ reported a large difference in the absolute contrast spatial frequency between the better and worse eye, with the binocular inhibition group having the poorest sensitivity. In line with this, Pardhan²³ used neutral density filters to vary binocular and monocular contrast sensitivities in the two eyes in healthy observers. In this study, binocular contrast summation was at a maximum when the sensitivities of the two eyes were equal but decreased with increased differences until binocular sensitivity dropped below monocular sensitivity. The occurrence of unequal macular scotomas in AMD may prevent adequate light stimulation of corresponding fixational points, and may be suggestive of Fechner's paradox.¹⁷ Furthermore, patients who exhibited binocular contrast inhibition were more likely to have non-corresponding monocular PRLs, as well as a greater distance from the former fovea in the worse eye compared to the better eye.²² It has been found that when PRLs are in non-corresponding locations, binocular contrast thresholds are below probability summation, at least for certain spatial frequencies.²⁴

One of the findings of the reviewed studies is that binocular inhibition in contrast sensitivity seems to occur more frequently in medium or lower spatial frequencies.^{17,20} Neural binocular summation arising from the cortical layer of VI is most easily demonstrated at low contrast.³ Thus, perhaps patients with asymmetric visual impairment, as in macular degeneration, show the greatest impairment in binocular viewing at low contrast.

Contrast sensitivity to medium and lower spatial frequencies is generally related to tasks such as orientation and mobility, that require this type of information.²⁰ Furthermore, contrast sensitivity has also been correlated with the ability to discriminate objects, recognize faces and judge distances.²⁵ Thus, patients with macular disease have

greater difficulty performing activities of daily living and may experience reduced quality of life.²⁵⁻²⁷ Considering these challenges, it is important for clinicians to consider both eyes when evaluating contrast sensitivity in patients with macular disease, as greater interocular differences may indicate more difficulty on daily tasks.

Visual acuity

Visual acuity is the measurement of one's ability to discriminate between two stimuli separated in space at high contrast compared to the background.²⁸ Decreased visual acuity is a characteristic part of the macular disease process, since it can affect the fovea, which is responsible for high resolution acuity and colour vision.²⁹ Studies looking at aggregate data report no differences between binocular and monocular visual acuity in AMD,^{21,22,30-33} but subgroups of patients with compromised binocular summation have been identified. For example, using a computerised version of the multiple Tumbling E visual acuity test, Tarita-Nistor et al.³² found that 50% of patients with central vision loss demonstrated binocular acuity summation, and 39% binocular inhibition.³² The study found that binocular acuity showed a decline compared to monocular acuity of the better eye at low contrast. A later study by the same group found that out of 20 patients with central vision loss, 25% (5) experienced acuity inhibition, 30% (6) experienced acuity summation and 45% (9) showed equality on the Early Treatment of Diabetic Retinopathy Study chart.³¹

The literature suggests that when monocular acuities are similar, there is binocular summation,³⁴ but as the monocular acuities diverge, binocular equivalence or inhibition may occur.³⁵ However, Kabanarou and Rubin did not observe binocular inhibition in cases of central vision loss with large interocular acuity differences, but important clinical characteristics such as PRL locations in the two eyes were not reported for this sample.²¹ Nonetheless, even a small difference between binocular and the better eye's visual acuity can confer significant differences in other visual tasks such as reading performance. For example, a significant positive relationship between the binocular summation ratio for distance visual acuity and maximum reading speed has been reported.³¹ This implies that patients demonstrating binocular acuity inhibition would have greater difficulty with binocular reading regardless of their distance visual acuity.

Binocular acuity inhibition may result in difficulties performing distance and near vision activities, driving and facial recognition.^{36,37} Given the high prevalence of binocular acuity inhibition in this population, it is important to evaluate binocular function and its impact on activities of daily living. In particular, attention should be given to patients with interocular acuity differences because the monocular evaluation of their visual function in the clinic may underestimate the true visual impairment.

Reading

Reading function can be assessed by measuring maximum reading speed (MRS), critical print size (CPS) and reading acuity. In patients with central vision loss, aggregate data show no binocular advantage for MRS,^{21,22,38} although individual differences exist between patients. For example, Kabanarou and Rubin²¹ reported 63.6% of patients demonstrate a binocular advantage in MRS compared to 13.6% with binocular inhibition. Additionally, Silvestri et al.²² found a similar proportion of patients exhibiting binocular summation and binocular inhibition for MRS, at 42% and 41%, respectively. Patients with binocular inhibition also show a significantly lower binocular MRS than the summation and equality groups, as shown in Figure 1.^{18,25} Likewise, a similar pattern of results was found for CPS and reading acuity.^{21,22} For example, Kabanarou et al.²¹ reported that 18.1% of patients demonstrated reading acuity summation, and 4.5% showed reading acuity inhibition.

Reading difficulties are a significant complaint for individuals with macular disease. Although there seems to be no binocular advantage for reading when considering the whole sample, the subgroup of patients who experience binocular reading inhibition should be examined separately, because they have different clinical characteristics than those with binocular reading summation. For example, Silvestri et al.²² reported the PRL in the worse eye was at a larger eccentricity than the PRL of the better eye in the binocular inhibition group. The PRLs were also frequently in non-corresponding locations and situated temporal or nasal to the scotoma in the better eye, locations which can shorten the visual span required for reading. Consequently, the PRL of the worse eye may fall on the scotoma when moving into retinal correspondence with the PRL of the better eye, and text might disappear into the scotoma during binocular viewing.

Because reading is such an integral function of daily life, the primary goal for many patients attending low vision clinics is to improve their reading ability.³⁹ Considering

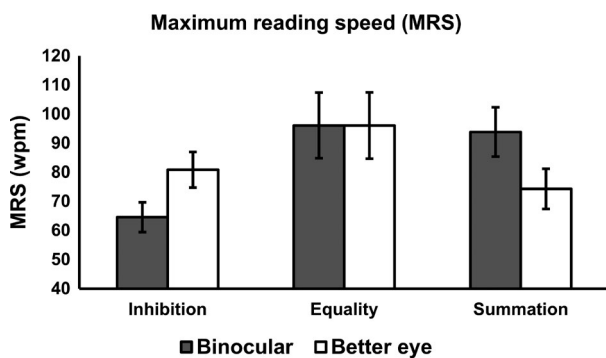


FIGURE 1 Maximum reading speed during binocular and monocular viewing with the better eye for patients with central vision loss who experienced binocular reading inhibition, equality, and summation. Error bars are ± 1 SE. From Silvestri et al.²² © 2020 The Authors. *Ophthalmic and Physiological Optics* published by John Wiley and Sons Ltd on behalf of College of Optometrists

that a proportion of patients experience inhibition, which is associated with a profound impairment in reading performance, methods for reading rehabilitation should focus on addressing disadvantageous fixation patterns that are characteristic for this subgroup.^{40,41}

Stereopsis

Stereopsis is the ability to perceive depth from binocular disparities. This function is severely disrupted in patients with central vision loss^{42,43} and this impairs other visual performances. For example, Silvestri et al.²² used the Stereo Fly Test to measure stereoacuity. They found that 38% of cases that showed binocular inhibition in MRS had residual stereopsis, as was also the case for 50% of patients in the equality group and 73% in the summation group. Verghese et al.⁴⁴ assessed the effect of central field loss on an eye-hand coordination task. The task was designed so that binocular depth cues were important for its performance. There was a significant benefit for peg placement time, errors and peg pick-up time in central field loss patients viewing under binocular conditions compared to monocular conditions. The authors also compared differences in binocular and monocular viewing for patients with and without measurable stereopsis. There was a benefit to binocular viewing for peg placement time and errors in the stereopsis group compared to the non-stereopsis group, but this difference was not significant. Among patients with measurable stereopsis, the binocular advantage of peg-placement time correlated significantly with stereoacuity.

Stereopsis involves both fusion and suppression processes. The fusion process constructs a stereo percept by integrating the inputs from similar features in the images seen by the two eyes. At the same time, dissimilar inputs are suppressed to promote a single binocular percept. Poor or no stereopsis is observed in patients with macular degeneration, particularly those with large asymmetry in retinal damage between the two eyes.²² The potential for at least coarse stereopsis in these patients may depend on whether they have intact visual function in roughly corresponding points in the two retinas (i.e., the PRLs fall on functional retina and corresponding positions in the two eyes),⁴⁴ and if the distance between intact retinal locations is less than the upper disparity limit at the corresponding eccentricity.¹⁸

Coarse stereopsis in patients with central vision loss is important for performing tasks of daily living. The absence of stereopsis in patients with macular degeneration with bilateral vision impairment has been associated with reduced overall quality of life, with these patients scoring low on reading ability scores.⁴⁵ It has also been reported that reduced depth perception and stereoacuity confers a significant relative risk of multiple falls and hip fractures secondary to falls. Thus, it is not surprising that patients with residual stereopsis have better visual

function and motor skills than those who lose this function completely.⁴² There is potential for rehabilitation in some patients with stereopsis. For patients with an intact retina below the upper disparity limit, they can perhaps be trained to use alternate PRLs that fall within this limit to regain stereopsis.¹⁸ Therefore, it may be important to test for stereopsis during routine assessments in patients with macular disease to provide clarification on residual visual functions.

BINOCULAR FIXATIONAL CONTROL IN PATIENTS WITH MACULAR DISEASE

Patients with central vision loss develop a PRL that may serve as the new point of reference for the oculomotor system. To understand fixational oculomotor control of patients with macular disease, we reviewed two aspects of the PRL: its location on the retina and visual field, as well as fixation stability (see Table 1 for the included studies).

Preferred retinal locus (PRL) location

Monocular PRLs are determined during fixation tasks using imaging instruments such as microperimeters or scanning laser ophthalmoscopes. The literature reports a range of monocular PRL locations in patients with macular disease. It has been reported that over half of patients had a PRL superior to the macular scar, while the rest tended to have a PRL to the left or right of the scotoma.⁴⁶ Others found the most common monocular PRL location was superior and nasal to the anatomical fovea. Considered in visual field space, the PRLs tended to be displaced to the left and inferiorly.⁴⁷ Interestingly, PRLs often fell on or near a part of the retina with significant visual loss. Kisilevsky et al.⁴⁸ distinguished between the PRL in the better and worse eye; they reported that most patients with central scotomas had PRLs in the left and inferior visual field segments of the better eye, but in the worse eye, there was no favoured location. White and Bedell⁴⁹ found that most patients with macular disease had a PRL in the superior hemiretina. Silvestri et al.²² evaluated the PRL location for patients exhibiting binocular summation or inhibition of MRS and found that for the better eye, the PRL was most commonly inferior or superior to the scotoma in the equality group (75%) and summation group (67%). In the inhibition group, the PRL was temporal or nasal to the scotoma (38%). Finally, Erbezci and Ozturk⁵⁰ reported that the most frequent location of the PRL in the retina was nasal, or in the left visual field.

Cheung and Legge¹³ proposed three different hypotheses that may explain PRL location: (1) the function-driven PRL, (2) the performance-driven PRL and (3) the retinotopy-driven PRL. The function-driven hypothesis suggests that certain PRL locations might be more advantageous for performing visual functions, such as reading. However, many of the studies reported a PRL in the left visual field, which may

be maladaptive for reading performance as it can interfere with planning forward saccades and produces a limited visual span. In contrast, Somani and Markowitz⁴⁶ hypothesized that placing the PRL superior to the macular scar may offer advantages to ambulation and activities of daily living. The performance-driven hypothesis is based on the notion that when the macula becomes dysfunctional, the visual system places the PRL in that part of the retina having the best visual acuity. However, Denniss et al.'s⁴⁷ finding that the PRL was located in an area of the retina with less sensitivity does not fully account for this. Moreover, their finding aligns with other reports that show visual acuity and letter contrast sensitivity at the PRL are worse than that of visually healthy adults at the same retinal eccentricity.⁵¹ Finally, the retinotopy-driven hypothesis predicts a PRL at the border of the central scotoma. Indeed, among 883 eyes with different forms of maculopathy in Fletcher and Schuchard's⁵² study, 88.7% of the PRLs were within 3.5 degrees of the borders of the scotoma.

Currently, technological limitations prevent in-depth study of PRL locations during binocular viewing in patients with central vision loss. Using a combination of the microperimeter and a custom-made eye-tracker that does not require calibration, Tarita-Nistor et al.⁵³ found that the PRLs in the two eyes were in corresponding locations during binocular viewing, although this was not always the case for monocular PRLs (Figure 2, right panel). For patients with high interocular acuity differences, the monocular PRL of the worse eye would move into the corresponding position of the PRL of the better eye during binocular viewing. While the PRL of the worse eye fell on the scotoma, the location of the PRL in the better eye remained unchanged.

Silvestri et al.²² examined the monocular PRLs and fundus photographs of both eyes in patients with central vision loss. Assuming that the PRL of the better eye had the same location during monocular and binocular viewing, and that the PRL in the worse eye moved into retinal correspondence with that of the better eye during binocular viewing, the authors reported that the PRL of the worse eye would fall onto the scotoma in 52% of cases of binocular inhibition for MRS. Tarita-Nistor and colleagues also assessed longitudinal changes in PRL location in patients with central vision loss.⁵⁴ They found that, in the better eye, PRL distance from the former fovea increased with disease progression, while maintaining a relatively constant polar angle. For the worse eye, the PRL distance did not change on average, but for 39% of cases it decreased with time and often fell on the scotoma. Importantly, as the disease progressed, the PRL of the worse eye changed location relative to that of the better eye. These findings suggest that the referencing of the oculomotor system in macular disease is relative to the PRL of the better eye. In addition, relative change in PRL location when viewing condition changes from monocular to binocular can be inferred from eye position data recorded with eye-trackers during a fixation task. Kabanarou et al.⁵⁵ reported that more than half of the

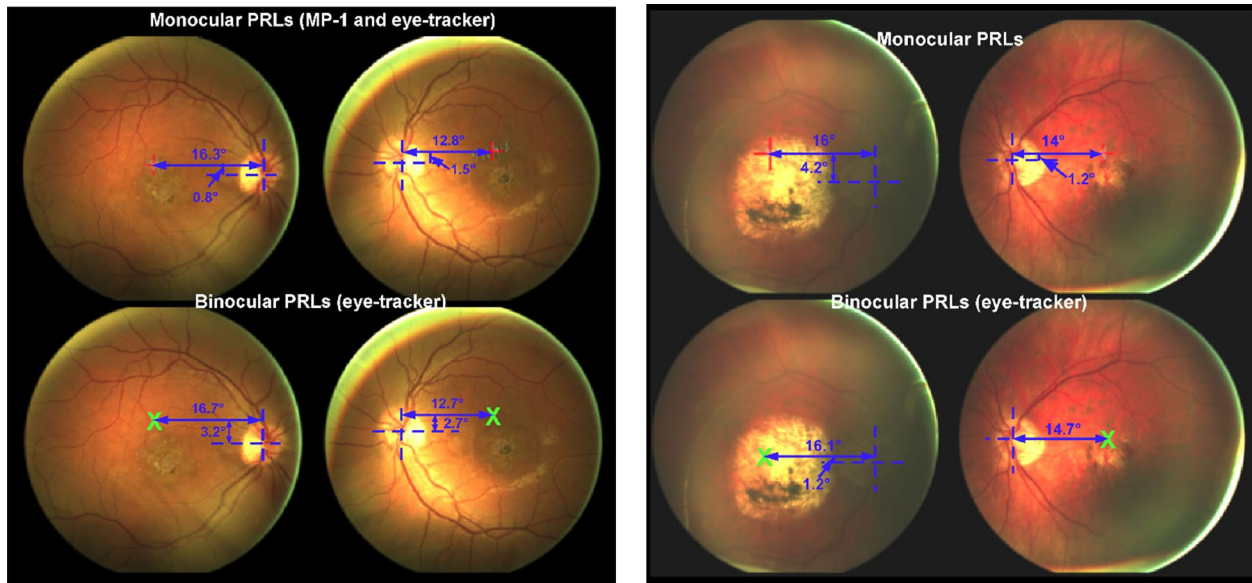


FIGURE 2 Monocular preferred retinal locus (PRLs) recorded with the microperimeter and binocular PRLs estimated from the eye-tracker recordings. Left panel shows that the locations of the PRLs were in the same location during monocular and binocular viewing conditions. Right panel shows that the monocular PRL in the worse eye changes location during binocular viewing. From Tarita-Nistor et al.⁵³

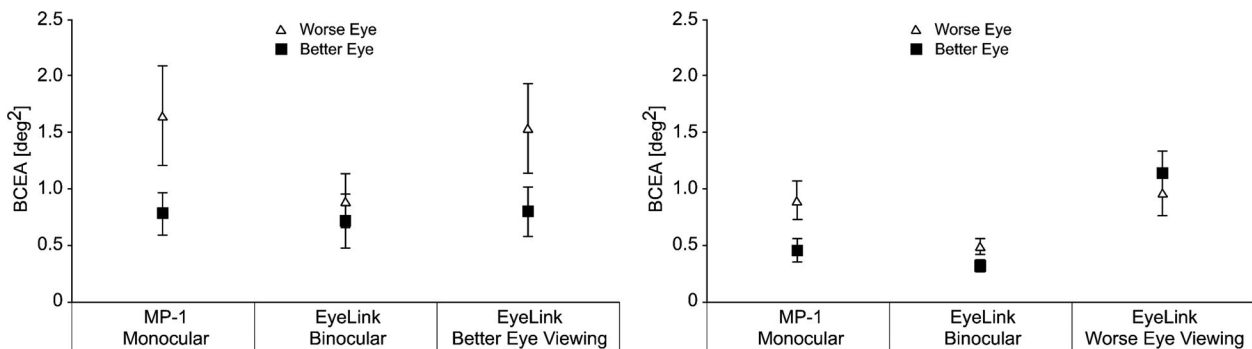


FIGURE 3 Means (SE) of fixation stability recorded with the MP-1 microperimeter and the EyeLink (binocular and better eye viewing [$n = 20$] and worse eye viewing [$n = 15$]). From Tarita-Nistor et al.³³ The Association for Research in Vision and Ophthalmology is the copyright holder of these figures

patients demonstrated a relative shift in gaze position in either one or both eyes when switching from monocular to binocular viewing. The magnitude of the shift distance in each eye reflected the amount of retinal correspondence and noncorrespondence of the monocular PRLs, suggesting that patients with macular degeneration who exhibit monocular PRLs in noncorresponding locations show gaze changes, especially in worse-seeing eyes, when viewing binocularly.

Fixation stability

Fixation stability is the precision of eye position when one fixates intently on a stimulus for a period of time. It has become an important outcome measure for treatment, intervention or disease progression in patients with central vision loss.⁵⁶ There are several ways to quantify fixation

stability, but the bivariate contour ellipse area (BCEA) is the most common measure, and is reported as an output of microperimeters. A larger BCEA corresponds to poorer fixation stability.¹⁶ Tarita-Nistor and colleagues evaluated fixation stability in patients viewing binocularly and monocularly.³³ The authors found that when viewing binocularly, fixational oculomotor control was driven by the better eye, such that fixation stability of the better eye did not change between monocular and binocular viewing (Figure 3).³³ However, fixation stability of the worse eye was 84% to 100% better in binocular compared to monocular viewing, and similar to that of the better eye.

Subsequently, Tarita-Nistor et al.⁵⁷ examined fixational control by observing characteristics of the shift in eye position from binocular to monocular viewing. For the better eye, there was no difference in shift when viewing binocularly or monocularly with this eye. For the worse eye, the eye traces revealed good coordination with the better eye

during binocular viewing, but a substantial loss of fixational control during monocular viewing (Figure 4).

Some studies examined the effects of factors such as viewing distance and time of examination recording on fixation stability across viewing conditions. Tarita-Nistor³⁰ examined fixation stability in patients with central vision loss during monocular and binocular viewing at a distance of 6m, 1m and 40cm. The authors found no association between viewing distance and fixation stability during binocular or monocular viewing with the better eye. For the worse eye, the BCEA was slightly worse at a near viewing distance, but this was not statistically significant. Samet et al.⁵⁸ examined changes in fixation stability with recording time. Fixation stability was recorded binocularly and monocularly with each eye for a duration of 15 seconds with the fellow eye covered, and data were analysed over consecutive 3 second intervals. For binocular viewing as well as monocular viewing with the better eye, fixation stability of fixed-duration consecutive intervals did not change. However, fixation stability improved linearly with consecutive fixed duration intervals when viewing with the worse eye. In this study, many patients had large interocular acuity differences, and the authors predicted that during monocular viewing with the worse eye, the patient uses a PRL in the functional peripheral retina that is not habitual (i.e., different from that in binocular viewing) that may take time to establish.

Overall, findings suggest that fixation stability is poor when viewing monocularly with the worse eye, but improves during binocular viewing because oculomotor control is driven by the better eye.¹⁵ Fixation stability affects the reading performance of patients with macular disease. Rehabilitative measures directed to fixational oculomotor control can improve daily visual function, including reading.

NEXT STEPS AND AREAS OF FUTURE INVESTIGATION

This review has summarised the impact of macular diseases on binocular visual function and oculomotor

control. There is strong evidence for subgroups of patients who demonstrate binocular summation and binocular inhibition on various outcome measures. In the clinic, visual function of patients with central vision loss is typically assessed monocularly; however, for these patients, it may also be important to assess binocular function and stereopsis, to get a better understanding of how the disease affects patients' daily function outside of clinic. With respect to oculomotor control, while information on fixation stability during binocular viewing exists, data on the PRL location in binocular viewing is scarce due to technological limitations. Tarita-Nistor et al.⁵³ developed a custom-made eye-tracker to track PRL location during binocular viewing; however, more advances are needed to evaluate PRL locations when viewing with both eyes. Lastly, there has been limited investigation of eye movement metrics in macular degeneration. As the oculomotor system needs to adapt to the new PRL-based reference frame, the eye movements of patients with central vision loss are expected to be less effective than for healthy individuals.¹¹ Such data can better help inform the relationship between oculomotor control in central vision loss and binocular visual functions. Therefore, more research on eye movements is needed to understand patients' search efficiency. Most importantly, it may provide crucial information necessary for better lens design and more effective smart glasses technology for patients with central vision loss.⁵⁹ The surprisingly weak assistive technology for patients with central vision loss may stem from incomplete knowledge about the basic mechanisms of binocular oculomotor control with central vision loss.

Finally, the information presented in this review may be particularly useful for clinicians, visual skills instructors or low vision therapists who are directly involved in supporting the rehabilitation of patients with central vision loss. Through rehabilitative efforts, visual therapists aim to optimise binocular visual function in their clients, as this is their natural viewing condition. Thus, the knowledge provided in this paper can be applied to further refine the rehabilitative interventions they use—for example, those related to eccentric viewing and biofeedback training—as well as to develop new research related to future techniques of vision rehabilitation.

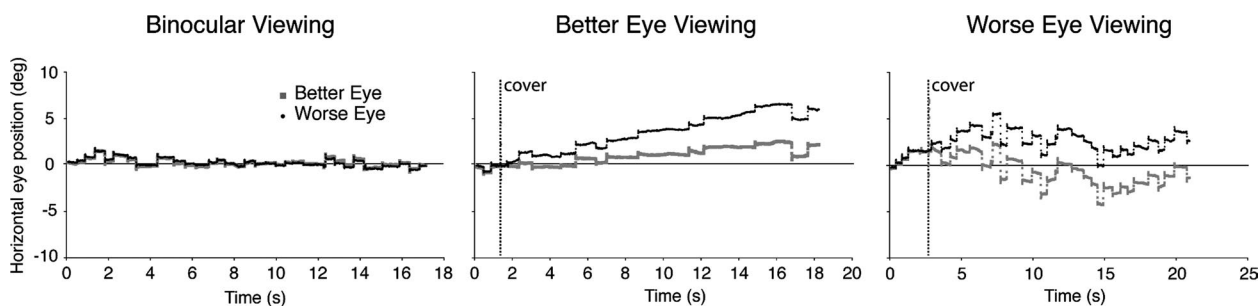


FIGURE 4 Loss of oculomotor control from binocular to monocular viewing with the worse eye, after the better eye was covered. There is also drift of the better eye during the better eye viewing condition that was associated with large phoria in the covered eye. From Tarita-Nistor et al.⁵⁷

CONCLUSION

Normally sighted individuals usually benefit from binocular vision, but this may not always be the case for patients with central vision loss. Our review of the literature compared binocular and monocular function of patients with central vision loss with respect to visual function and fixational oculomotor control. It showed that, when considering aggregate data, there is no difference between binocular or monocular viewing conditions for visual acuity or reading. However, certain subgroups of patients demonstrate binocular summation or inhibition depending upon the individual clinical characteristics of their eyes (i.e., correspondence of monocular PRLs, stability of fixation, asymmetric macular scotomas in the two eyes). With regards to monocular PRL location, most studies reported locations in the left and inferior visual space, and superior to the scotoma. These locations may offer advantages in visual acuity for PRLs in the lower visual field or to support ambulation and activities of daily living for PRLs superior to the macular scar. However, evidence regarding this remains mixed. When comparing monocular and binocular viewing, PRLs are not always in corresponding locations monocularly. In patients with high interocular acuity differences, the monocular PRL of the worse eye may move into corresponding position to the PRL of the better eye during binocular viewing, although this location can fall onto the macular scar. Lastly, binocular fixational stability seems to be driven by the better eye, as typically it does not change from monocular to binocular viewing with the better eye but is improved from monocular to binocular viewing with the worse eye. Overall, binocular visual function assessment—in addition to routine standard monocular measures available today—may result in an enhanced understanding of the impact of macular disease on patients' visual function, and therefore can lead to better intervention decisions and disease management.

CONFLICT OF INTEREST


The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

AUTHOR CONTRIBUTIONS

Irina Sverdlichenko: Conceptualization (lead); Investigation (lead); Methodology (lead); Project administration (lead); Visualization (lead); Writing – original draft (lead). **Mark S Mandelcorn:** Conceptualization (equal); Funding acquisition (lead); Resources (equal); Writing – original draft (supporting). **Galia Issashar Leibovitzh:** Conceptualization (equal); Supervision (supporting); Writing – original draft (equal). **Efrem D Mandelcorn:** Conceptualization (supporting); Funding acquisition (lead); Resources (equal); Writing – original draft (supporting). **Samuel N Markowitz:** Project administration (equal); Resources (equal); Writing – original draft (supporting).

Luminita Tarita-Nistor: Conceptualization (lead); Investigation (lead); Methodology (lead); Project administration (lead); Supervision (lead); Visualization (lead); Writing – original draft (lead).

ORCID

Luminita Tarita-Nistor  <https://orcid.org/0000-0002-4519-3868>

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How to cite this article: Sverdlichenko I, Mandelcorn MS, Issashar Leibovitz G, et al. Binocular visual function and fixational control in patients with macular disease: A review. *Ophthalmic Physiol Opt* 2022;42:258–271. doi.org/10.1111/opo.12925