Predicting Visual Acuity From Visual Field Sensitivity in Age-Related Macular Degeneration

Jonathan Denniss,[1,2] Helen C. Baggaley,[2,3] and Andrew T. Astle[2]

[1]School of Optometry and Vision Science, Faculty of Life Sciences, University of Bradford, Bradford, United Kingdom
[2]Visual Neuroscience Group, School of Psychology, University of Nottingham, Nottingham, United Kingdom
[3]Optometry Unit, Ophthalmology Department, Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom

Correspondence: Jonathan Denniss, School of Optometry and Vision Science, University of Bradford, Bradford BD7 1DP, United Kingdom; j.denniss@bradford.ac.uk.

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Purpose. To investigate how well visual field sensitivity predicts visual acuity at the same locations in macular disease, and to assess whether such predictions may be useful for selecting an optimum area for fixation training.

Methods. Visual field sensitivity and acuity were measured at nine locations in the central 10° in 20 people with AMD and stable foveal fixation. A linear mixed model was constructed to predict acuity from sensitivity, taking into account within-subject effects and eccentricity. Cross validation was used to test the ability to predict acuity from sensitivity in a new patient. Simulations tested whether sensitivity can predict nonfoveal regions with greatest acuity in individual patients.

Results. Visual field sensitivity ($P < 0.0001$), eccentricity ($P = 0.007$), and random effects of subject on eccentricity ($P = 0.043$) improved the model. For known subjects, 95% of acuity prediction errors (predicted − measured acuity) fell within −0.21 logMAR to +0.18 logMAR (median +0.00 logMAR). For unknown subjects, cross validation gave 95% of acuity prediction errors within −0.35 logMAR to +0.31 logMAR (median −0.01 logMAR). In simulations, the nonfoveal location with greatest predicted acuity had greatest "true" acuity on median 26% of occasions, and median difference in acuity between the location with greatest predicted acuity and the best possible location was +0.14 logMAR (range +0.04 to +0.17).

Conclusions. The relationship between sensitivity and acuity in macular disease is not strongly predictive. The location with greatest sensitivity on microperimetry is unlikely to represent the location with the best visual acuity, even if eccentricity is taken into account.

Keywords: microperimetry, fundus perimetry, AMD, visual acuity, visual field sensitivity

Currently, much macular disease remains untreatable and results in permanent central vision loss. Functional rehabilitation of people with acquired macular disease aims to make the best use of remaining vision. Commonly, this involves the development and use of a nonfoveal preferred retinal locus (PRL) on which eye movements are centered and attention is deployed during visual tasks.[1,2] Because the PRL is extrafoveal, potential vision is limited by optical and neural factors,[3–5] as well as fixation instability.[6,7]

Fixation stability at the PRL in people with acquired macular disease can be improved through training, potentially leading to improved performance in visual tasks.[8–11] Similarly, fixation stability on a PRL chosen in the presence of a simulated central scotoma is improved by training in normally sighted people.[12–14] Commercially available microperimeters feature biofeedback tools that can be used in the clinic to train fixation at a chosen location. Although people with longstanding macular disease typically develop a PRL over time,[2] the choice of a location to train in people with newly acquired macular disease is nontrivial. Intuitive locations, such as above the scotoma or to the right of the scotoma for left-to-right readers, do not necessarily result in improved performance compared with other locations.[2,15] Further, the location in which PRLs naturally develop in those with established macular disease is highly variable between people.[2,15,16] A recent study in our lab has indicated that, although the polar direction of the naturally selected PRL relative to the scotoma and fovea is inconsistent between people, a consistent pattern of placing the PRL just foveal to (i.e., outside) the boundary of a region of relatively good visual field sensitivity (normal pattern deviation but not total deviation) can be observed.[16] Further, most participants in that study had a region of microperimetric sensitivity that was within normal limits at a similar eccentricity to their habitual PRL.[16] The study, therefore, suggests that people do not themselves select a PRL based on greatest visual field sensitivity.

Could functional vision be improved by principled selection and training of a new PRL? Previous reports of improved visual performance in patients with macular disease following fixation training on a new PRL have used intuitive or multifactorial approaches to selecting the new PRL. These include universal placement in the superior retina or the inferior retina when the superior retina is damaged,[9] choosing a superior retinal location with similar eccentricity to an existing PRL and the same or better microperimetric sensitivity,[8] and choosing a superior retinal location of 2° diameter based on microperimetric sensitivity.[11] A simple approach of choosing the most sensitive region on microperimetry has also been adopted in some studies and clinics.[17] Microperimetry has the clinical

Table. Clinical and Demographic Data for All Participants

Participant	Age, y	Sex	Eye	AMD Type	Beckman Classification	Diagnosed, y	Visual Acuity, logMAR	Visual Acuity, Snellen, 6/–	Refraction, Diopters
1	81	M	R	Wet	Late	3	0.54	20.8	+1.50/−0.50 × 100
2	69	F	L	Dry	Intermediate	20	0.18	9.1	−0.75/−0.25 × 85
3	78	F	L	Dry	Intermediate	11	0.42	15.8	+1.00/−1.50 × 90
4	73	F	R	Dry	Intermediate	8	0.16	8.7	+3.50 DS
5	78	F	L	Wet	Late	4	0.48	18.1	+1.00/−0.50 × 90
6	76	M	L	Wet	Late	16	0.42	15.8	+1.50/−1.25 × 90
7	65	M	R	Wet	Late	7	0.32	12.5	−0.50/−0.50 × 120
8	73	M	L	Wet	Late	4	0.22	10	+0.25/−1.00 × 65
9	67	M	L	Wet	Late	1	0.22	10	+6.50 DS
10	70	M	R	Wet	Late	3	0.5	19	+0.75/−0.50 × 70
11	72	F	L	Dry	Intermediate	14	0.28	11.4	+3.25/−1.25 × 100
12	83	M	R	Wet	Late	2	0.86	43.5	+1.00 DS
13	75	F	R	Dry	Intermediate	16	0.3	12	−1.00/−3.00 × 90
14	78	M	L	Dry	Intermediate	20	0.24	10.4	+2.00/−1.50 × 20
15	77	F	R	Wet	Late	6	0.52	19.9	+1.75/−1.25 × 90
16	72	F	R	Wet	Late	1	0.34	13.1	+2.25 DS
17	74	M	R	Wet	Late	2	0.16	8.7	+4.50/−1.50 × 90
18	82	F	R	Wet	Late	1	0.1	7.6	+0.75/−0.75 × 130
19	73	F	L	Dry	Early	2	0.04	6.6	−0.25 DS
20	80	F	R	Wet	Late	4	0.36	13.7	−1.00/−1.50 × 78

Snellen visual acuities given are converted from the measured logMAR acuities. Distance refraction is given as sphere/cylinder *x* axis. Where no cylinder was required refraction is given as sphere DS (diopter sphere).

advantage of providing a relatively fast assay of visual function across a range of locations that are registered to the retinal image, enabling repeat testing or training over multiple sessions. However, the task is quite unlike the daily visual tasks that people with macular disease have difficulty with, such as reading. It is not known how visual field sensitivity relates to other measures of visual function in macular disease that may be more strongly related to performance in tasks like reading, such as visual acuity. Whether microperimetry can be used as part of a principled PRL selection procedure, therefore, requires further consideration. Visual acuity may be a more ecologically relevant visual function for PRL selection, but it is difficult to measure clinically across the required range of visual field locations.

The purpose of this study was to investigate how well visual field sensitivity could be used to predict visual acuity in people with macular disease, and to assess whether predictions of acuity from sensitivity may be useful for the purpose of selecting an area with optimum acuity for fixation training.

Methods

The National Health Service National Research Ethics Service granted ethics approval for this study. The study adhered to the tenets of the Declaration of Helsinki, and all participants gave written informed consent to take part.

Participants

Participants ($n = 20$) were recruited from the database of a previous study.[16] Participants had a confirmed clinical diagnosis of AMD ($n = 13$ wet, $n = 7$ dry), no other known ocular pathology except for mild cataract and had stable foveal fixation according to a MAIA-2 (CenterVue, Padova, Italy) microperimetry "Expert" test in the previous study conducted median 5.5 months (range, 18 days to 11 months) prior. The Table shows clinical and demographic data for all participants, including grading of AMD severity according to the Beckman classification scheme.[18] Stability of fixation was confirmed by visual inspection of the fixation plots from the microperimetry test. Because stable foveal fixation was an inclusion criterion, no participants had central scotomas. Participants attended for two to three data collection visits. On the first visit refraction (monocular subjective with trial frame and loose lenses, Jackson cross cylinder technique), visual acuity testing (Early Treatment Diabetic Retinopathy Study chart at 4 m, scored by letters read correctly, stopping when <3 letters read correctly on a single line) and an additional MAIA-2 microperimetry test was conducted using a custom stimulus grid of 26 test locations within 10° of fixation, including the nine locations used in the psychophysical procedures. This test was used to confirm stable foveal fixation and to provide a starting point for measurement of visual field sensitivity. Psychophysical testing was then conducted as described below over the remainder of the first visit and subsequent visits that were all conducted within 1 month, except for one participant whose third visit was 7 weeks after their first.

Psychophysical Procedures

Participants undertook two psychophysical procedures to measure visual field sensitivity and visual acuity at nine spatial locations in the central visual field, including a central location (0°, 0°) and locations at 5° and 10° eccentricity in each of the cardinal directions (Fig. 1). Stimuli were generated using custom software written in PsychoPy[19,20] version 1.83.04, and presented on a gamma-corrected 32" calibrated LCD display system (Display++, Cambridge Research Systems, Kent, UK) with 100-Hz refresh rate, 1920 × 1080 resolution. Temporal dithering was used to enable 14-bit contrast resolution. Participants used a chin and forehead rest to maintain constant viewing distances of 3 m for the central acuity stimulus, 1.5 m for the acuity stimuli at 5° eccentricity, and 75 cm for the acuity stimuli at 10° eccentricity and the sensitivity task. The viewing distances necessarily varied in order to overcome limitations on maximum stimulus spatial frequency due to the pixel size of the display. Participants wore appropriate refractive correction

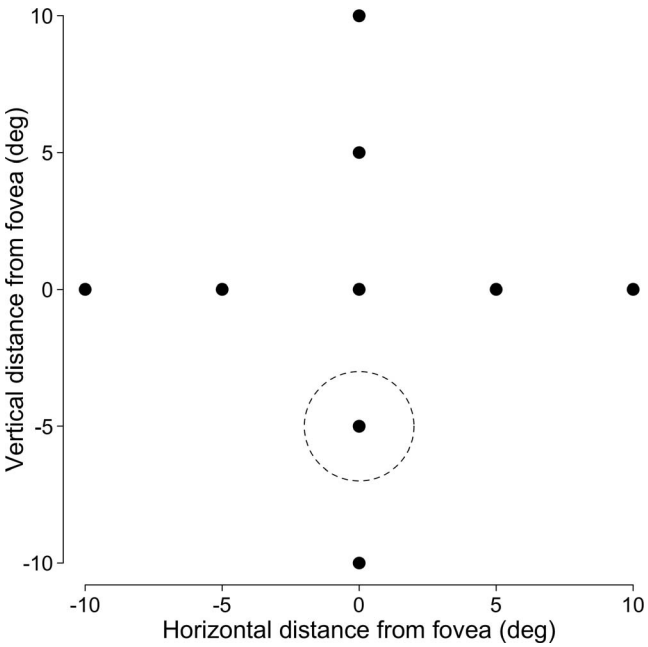

FIGURE 1. Stimulus locations. Points shown are to scale for the sensitivity task. The *dashed circle* shows the size of the grating stimulus for the acuity task.

for the screen distance in the form of wide aperture trial lenses held in a trial frame. The nontested eye was occluded with an opaque occluder.

For both tasks, participants were instructed to fixate carefully on the center of a fixation cross, and the experimenter monitored their fixation visually via a mirror. Each participant completed sufficient practice trials for the experimenter to be assured of their understanding of the task, and that their fixation was stable.

Sensitivity Task

The sensitivity task was used to measure visual field sensitivity at each location using stimulus conditions equivalent to the MAIA-2 microperimeter. To obtain accurate measurements of sensitivity at each location we measured frequency of seeing (FOS) curves; full psychometric functions for stimulus detection.

Stimuli were 0.43° diameter (Goldmann III) circular luminance increments presented for 200-ms duration, matching the stimulus of the MAIA-2 microperimeter and many other common perimeters. Frequency of seeing curves were measured using a method of constant stimuli, testing all spatial locations concurrently in a single perimetry-like experimental condition, whereby presentations were distributed randomly across spatial locations. Participants were instructed to press a button when they saw a stimulus at any location while fixating centrally. A white central broken cross was used to aid fixation, taking care to minimize structure in the immediate vicinity of the test stimulus to avoid masking effects.[21] Frequency of seeing curves were built up over multiple runs (each 3–5 minutes) with rest breaks in between until satisfactory psychometric function fits had been obtained with a minimum total of 175 presentations per test location. A minimum of nine contrast levels were measured per FOS curve, initially chosen based on the sensitivity recorded at the corresponding location of a MAIA-2 examination conducted at the first visit. FOS curves were examined after each run, and contrast levels were adjusted if needed to span the range from approximately 0% to 100% seen. Stimulus Weber contrast was measured using the same decibel scale as the MAIA-2 microperimeter, and background luminance was set to 4 cd/m^2, also to match the MAIA-2. Responses were collected within a window extending 1750 ms from stimulus offset; any responses outside of this window were deemed to be response errors and were ignored. Onset of the next stimulus was jittered randomly between 500 and 800 ms from the subjects' response, or the end of the response window if there was no response. Due to the rigorous nature of the method of constant stimuli, and because each included participant had completed several reliable MAIA-2 microperimetry tests prior to the study, we did not include catch trials for false responses.

Data from all presentations at each location were converted into percent seen at each contrast level. Frequency of seeing curves were fit to the data as a modified cumulative Gaussian function:

$$\psi(x,t) = (1 - fn)(1 - G(x,t,s)) \quad (1)$$

by maximum likelihood parameter estimation taking into account the number of presentations at each contrast level. In Equation 1, fn represents the false negative rate that defines the upper asymptote of the function, and $G(x, t, s)$ is the value at x of a cumulative Gaussian function with mean t and SD s. Sensitivity was defined as the 50% seen point on the fitted functions. Goodness-of-fit was assessed by comparing the model deviance of each fitted function to the deviance distribution of 1000 Monte Carlo datasets simulated from the fitted function.[22] This method derives empirical probabilities that a dataset generated by the fitted function with this number of presentations at each level would have deviance as large or larger than that observed. Higher probabilities therefore indicate a better fit. Frequency of seeing curves with goodness-of-fit $P < 0.05$ were excluded from analysis.

Grating Acuity Task

Grating acuity was measured at the same spatial locations using a two alternative forced choice orientation discrimination task. For the acuity task, each of the three different eccentricities was tested under a separate experimental condition, such that in one condition stimuli were only presented centrally (0°, 0°), while in the other two conditions stimulus presentations were distributed randomly across four locations, one in each of the cardinal directions. A 2.8° diameter white fixation cross was positioned centrally, broken for the central condition. Stimuli were sinusoidal gratings within 4° diameter circular envelopes presented for 200 ms at 99% Michelson contrast, which was defined as (maximum luminance − minimum luminance) / (maximum luminance + minimum luminance). Mean luminance of the gratings was 100 cd/m^2, equal to the background luminance. We chose to use gratings contained within a circular envelope in order to restrict the spatial extent of the stimulus to a defined, localized area. Gratings were oriented randomly at either 45° or 135° on each presentation, and participants pressed one of two buttons to indicate the orientation of the grating, guessing if unsure. Grating spatial frequency was varied across presentations according to a 3-up-1-down staircase. Prior to the second reversal, spatial frequency was increased by 20% following three consecutive correct responses, and decreased by 20% after each incorrect response. These step sizes changed to 10% after the second reversal, and staircases terminated after six reversals. Psychometric functions were fitted by maximum likelihood parameter estimation to the data from all presentations of each staircase, taking into account the number of presentations at each spatial frequency. Fitted psychometric functions had the form

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$$\psi(x,t) = 1 - 0.5(G(x,t,s)) \quad (2)$$

where $G(x, t, s)$ is the value at x of a cumulative Gaussian function with mean t and SD s. Upper asymptotes were fixed at 1 due to minimal data being available from the staircases to determine a lapse rate. Acuity (cpd) was defined as the 75% correct point on the fitted functions. This was then converted to logMAR units for analysis using the formula logMAR = $\log_{10}$(60/2*cpd).

Predictive Modeling

Visual field sensitivity and acuity were measured at nine locations per subject. These measurements are independent between subjects but not within subjects. Further, both visual field sensitivity and acuity are known to vary with eccentricity.[5,23–25] A linear mixed model was constructed to relate measurements of acuity and visual field sensitivity, accounting for both within-subject effects and effects of eccentricity. Parameters were added to the model by a stepwise inclusion procedure, beginning with the most basic model that included only intercepts with random effects of subject and eccentricity. Parameters were added to the model one by one, beginning with fixed effects of sensitivity and eccentricity and continuing to random effects of subject on sensitivity and eccentricity and random effects of eccentricity on sensitivity. Parameters were retained only if the Akaike Information Criterion (AIC) decreased with $P < 0.05$ by χ^2 likelihood ratio test of the nested models. Models were fit to the data by maximum likelihood estimation.

The ability of the final model to predict acuity from sensitivity for a new patient was then tested by leave one out cross validation as follows: an individual subject was removed from the dataset and model parameters were refit to the remaining data. The newly fitted model was then used to predict acuity at each location for the removed subject from their measured sensitivities. For the left out individual, random effects of subject were assumed to be unknown and therefore were not included as predictors. Prediction errors were calculated as predicted − measured values. This procedure was repeated for all study participants to give an estimate of model performance in new patients.

Because our sample included only subjects with stable foveal fixation who may be uncommon among people with AMD, we also repeated the modelling after excluding data from the central (foveal) test location. In this subanalysis, we investigate how well acuity can be predicted from sensitivity in nonfoveal regions only. Both the model fitting with stepwise parameter inclusion and the leave one out cross validation were repeated after excluding foveal data.

Simulation of PRL Selection Application

Using the predictions of acuity from sensitivity from the leave one out cross validation procedure without the foveal test location, we performed simulations to determine whether predictions of acuity from sensitivity are likely to be sufficiently accurate and precise for use in predicting the nonfoveal visual field location with best acuity in a given subject. We ran the simulations excluding the foveal test location because our subjects were chosen specifically to have stable foveal fixation and are therefore likely to have relatively undamaged foveal areas, which are unrepresentative of the wider population with AMD. Simulations were performed as follows:

1. For each nonfoveal visual field sensitivity measurement, we took the prediction of acuity from the leave one out cross validation procedure (predicted acuity);
2. Sampled prediction error was then subtracted from this predicted acuity to give a simulated acuity. Prediction errors were sampled from the fitted density function of the prediction errors from the cross validation procedure, such that errors were selected from the distribution of prediction errors (predicted acuity − measured acuity) found in the cross validation procedure weighted by their probability of occurrence in that procedure. This was repeated 1000 times per location, per subject to produce 1000 simulated acuities per location for each subject (1000 sets of 8 simulated acuities per subject); and
3. Then, for each subject, we counted the number of occurrences within the 1000 sets of simulated acuities that the location with the best predicted acuity had the best simulated acuity. Where the location with best predicted acuity did not have the best simulated acuity we also calculated the difference in simulated acuity between the visual field location with the best simulated acuity and the location with best predicted acuity.

If model predictions were sufficient for predicting the location with the best acuity from visual field sensitivity then we would expect the location with the best predicted acuity to have the best simulated acuity in most cases. Where this is not the case, we expect the location with the best predicted acuity to have only slightly worse simulated acuity than the best possible location.

All model fitting, simulations and statistical analyses were carried out in the open-source software environment *R*,[26] version 3.4.0. The lme4 package[27] was used to fit linear mixed models.

Results

Data from 16 test locations in total (from 8 participants; range, 1–5 per participant) were removed due to inability to obtain acceptable FOS curve fits ($n = 6$), the participant being unable to reliably detect the highest contrast stimulus available at that test location ($n = 7$), or the participant being unable to resolve the lowest spatial frequency grating presentable at that test location ($n = 3$). This left a total of 164 locations across 20 participants available for analysis.

Figure 2 shows the raw relationship between visual field sensitivity and visual acuity at each measured location of each subject.

The stepwise parameter inclusion procedure determined the parameters that were included in the final model separately for analysis including or excluding the foveal test location. Parameter selection began from a basic model that included fixed and random effects on intercepts only. When the foveal test location was included, adding fixed effects of visual field sensitivity and then eccentricity reduced AIC by 62 units for sensitivity ($\chi^2_1 = 64.3$, $P < 0.0001$) and a further 5 units for eccentricity ($\chi^2_1 = 7.3$, $P = 0.007$). Random effects of subject on sensitivity did not improve the model fit (AIC increased by 4 units, $\chi^2_2 = 0.06$, $P = 0.97$) so were not included. This indicates that the slope of the relationship between sensitivity and acuity was consistent between participants. Random effects of subject on eccentricity slightly improved the model fit (AIC decreased by 2.3 units, χ^2 (2) = 6.3, $P = 0.043$), indicating variation in the effect of eccentricity across subjects. Finally, random effects of eccentricity on sensitivity did not improve the model fit (AIC increased by 1 unit, $\chi^2_2 = 4.3$, $P = 0.12$) and so were not included in the final model. This indicates that the slope of the relationship between sensitivity and acuity is consistent across different eccentricities. The final model, therefore, included fixed effects of sensitivity and eccentricity,

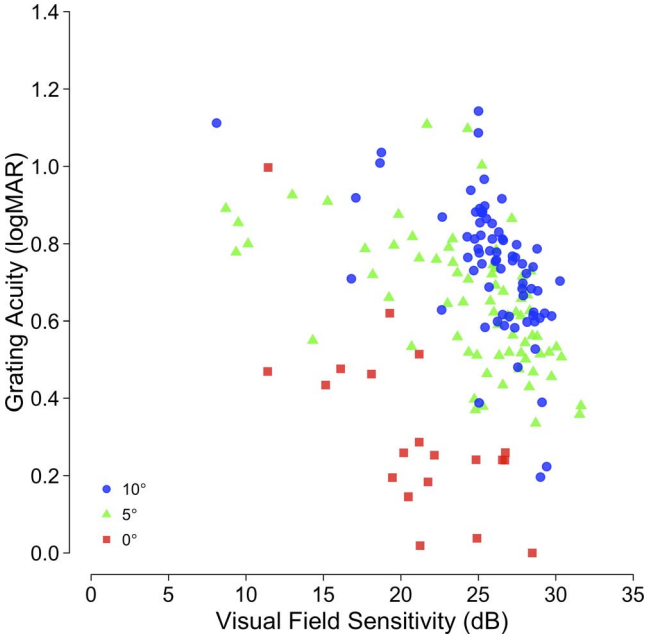

FIGURE 2. Visual field sensitivity versus acuity for all measured locations of all subjects. Different plotting symbols differentiate between tested locations with different eccentricities, given in the key.

random effects of subject on intercept and eccentricity, and random effects of eccentricity on intercept. The final model for eccentricity i of subject j is given by

$$Acuity = -0.020\ sensitivity + \left(0.053 + u_{1j}\right)\ eccentricity + \left(0.78 + u_{1i} + u_{2j}\right) + \varepsilon \quad (3)$$

where u_{ni} and u_{nj} denote random effects of eccentricity and subject respectively, and ε is an error term.

When the procedure was repeated with the foveal test location excluded, adding fixed effects of visual field sensitivity and then eccentricity reduced AIC by 50 units for sensitivity ($\chi^2_1 = 51.5$, $P < 0.0001$) and a further 5 units for eccentricity ($\chi^2_1 = 6.7$, $P = 0.0099$). Random effects of subject on sensitivity did not improve the model fit (AIC increased by 4 units, $\chi^2_2 = 0.1$, $P = 0.94$) so were not included. In this case, random effects of subject on eccentricity did not improve the model fit (AIC increased by 3 units, $\chi^2_2 = 0.8$, $P = 0.68$), indicating that the previously observed variation in the effect of eccentricity across subjects was not present when restricted to nonfoveal locations. Finally, random effects of eccentricity on sensitivity did not improve the model fit (AIC increased by 4 units, $\chi^2_2 = 0.1$, $P = 0.93$) and so were not included in the final model. The final model for only nonfoveal locations, therefore, included fixed effects of sensitivity and eccentricity, and random effects of subject and eccentricity on intercept. This model is given by

$$Acuity = -0.019\ sensitivity + 0.027\ eccentricity + \left(0.99 + u_i + u_j\right) + \varepsilon \quad (4)$$

where u_i and u_j denote random effects of eccentricity and subject respectively, and ε is an error term.

Figure 3 shows measured acuity against acuity predicted by the fitted models from the corresponding visual field sensitivity for all locations of all subjects (Fig. 3A including foveal data, Fig. 3B excluding foveal data). Figure 3 represents the best possible predictive performance of the models, because predictions were made when all data were used to fit the models, and random effects of subject are known. In this case, 95% of acuity prediction errors (predicted − measured acuity) fell within the range −0.21 logMAR to +0.18 logMAR (median +0.002 logMAR) when foveal data were included, and 95% of acuity prediction errors fell within the range −0.17 logMAR to +0.21 logMAR (median −0.003 logMAR) when only nonfoveal locations were included.

The accuracy of model predictions for a new subject, estimated by the cross-validation procedure, is shown in Figure

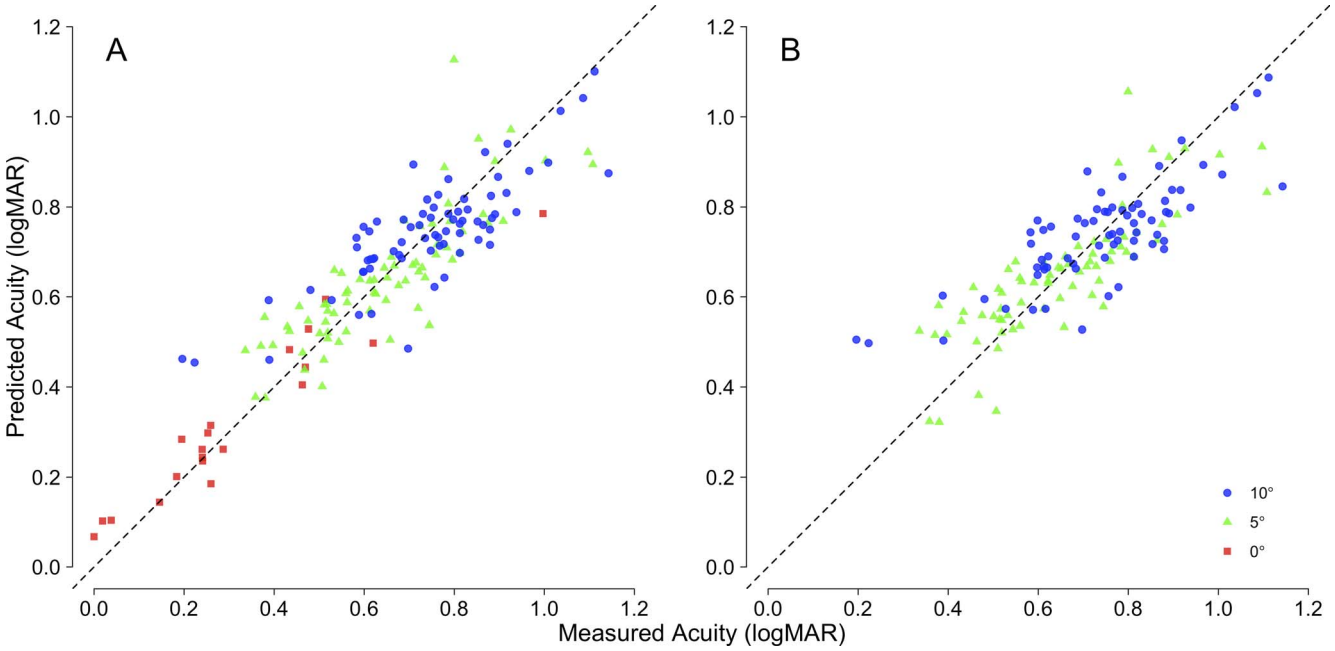

FIGURE 3. (A) Measured acuity versus acuity predicted from corresponding visual field sensitivity by the models when the models were fit using all available data for all test locations and all random effects were included. (B) As for (A) but with data from the foveal test location excluded from the model. The *dashed lines* represent unity. Different plotting symbols differentiate between tested locations with different eccentricities, given in the key.

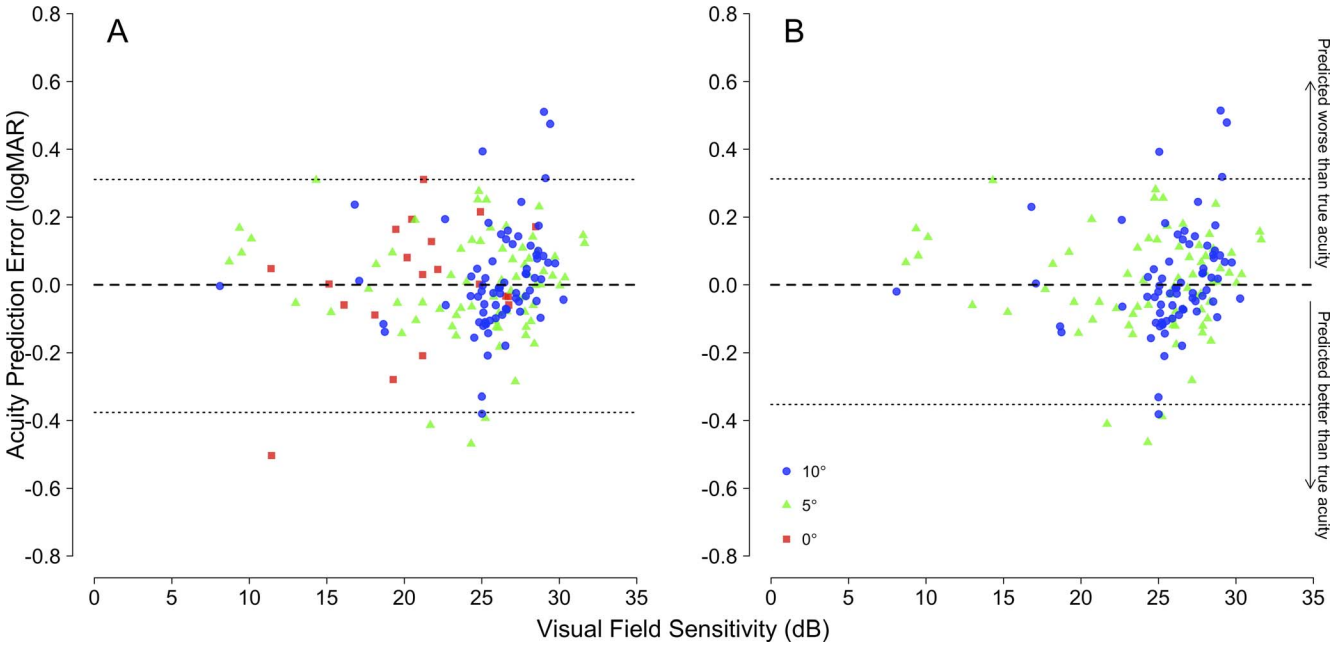

FIGURE 4. Errors in predicting acuity from sensitivity across the range of visual field sensitivity for (**A**) the model including data from all test locations and (**B**) the model excluding data from the foveal test location. Errors were calculated as predicted acuity − measured acuity. The *dashed horizontal lines* represent zero error, where predicted acuity exactly matches measured acuity. *Dotted horizontal lines* represent the central 95% range of acuity prediction errors. Different plotting symbols differentiate between tested locations with different eccentricities, given in the key.

4 (Fig. 4A including foveal data, Fig. 4B excluding foveal data). In this case, 95% of prediction errors (predicted − measured acuity) fell within the range −0.38 to +0.31 logMAR (median −0.002 logMAR) when foveal data were included. For the model without foveal data, 95% of prediction errors fell within the range −0.35 to +0.31 logMAR (median −0.008 logMAR). Predictions were within the range −0.2 to +0.2 logMAR on 86% of occasions for the model with foveal data and on 88% of occasions for the model without foveal data.

Simulations performed to establish whether predictions of acuity from sensitivity are sufficiently accurate and precise for predicting the nonfoveal visual field location with the best acuity indicated that this was not likely to be the case. Across all participants (1000 repeats per participant), the nonfoveal location with best predicted acuity was the location with the best simulated acuity on median 26% (range 18%–44%) of occasions. Median difference in acuity between the location with the best predicted acuity and the location with the best acuity for individual subjects was +0.14 logMAR (range +0.04 to +0.17 logMAR), indicating that a location was available within the tested region with acuity 0.14 logMAR better on average than the location with best predicted acuity.

DISCUSSION

Microperimetry provides a convenient, fast assay of visual function across a range of retinal locations in patients with macular disease.[28] Sensitivity estimates returned by microperimetry are useful in establishing the extent of functional damage, measuring PRL location and fixation stability, and potentially in monitoring disease progression and response to treatment. One further possible use for microperimetry is in choosing the location to train as a new PRL, either in newly affected patients or in those whose disease has progressed such that their existing PRL is no longer useful. Basing the choice of PRL for training at least partly on microperimetric sensitivity is a simple, clinically feasible approach, but whether locations with high microperimetric sensitivity represent an optimum choice for PRL training depends on how well visual field sensitivity relates to performance in daily tasks, such as reading. Because visual acuity may be more relevant than visual field sensitivity for these tasks,[29–31] we investigated how well visual acuity could be predicted from visual field sensitivity in the same locations.

Our results indicate that acuity in people with AMD is related to visual field sensitivity at the same locations, but the relationship is not strongly predictive. Predictions of acuity made from visual field sensitivity and eccentricity in people with AMD are typically only accurate to within ±0.2 logMAR, with larger errors occurring in some cases (Fig. 4). This accuracy is unlikely to be sufficient for clinical purposes, or for predicting performance in everyday visual tasks related to acuity. Further, our simulations show that the nonfoveal location with the best-predicted acuity based on visual field sensitivity and eccentricity is unlikely to be the location with the best true acuity. Simply taking the location with the best sensitivity, without taking account of eccentricity, is even less likely to result in selection of the location with the best visual acuity.

The relationship between visual field sensitivity and acuity at corresponding locations in AMD is multifactorial, and therefore a number of factors beyond simple measurement error contribute to the lack of a strongly predictive relationship. Optical and neural differences occur with eccentricity[3–5] and continue to limit maximum visual function at any given location in eyes with AMD. For example, a perfectly healthy retinal region at 5° eccentricity may still have worse acuity than a damaged foveal region due to these limitations. Metamorphopsia is well known to occur in AMD, and may have different effects on acuity and sensitivity.[32] The precise nature and severity of damage caused by AMD, and how these combine with underlying optical and neural limits may also cause different relative effects on sensitivity and acuity in different eyes. For example, it is possible that people with purely dry AMD may have a more consistent relationship

between sensitivity and acuity than people with wet AMD, where factors, such as edema and bleeding, may contribute; however, this remains to be tested.

Several previous studies have suggested that some people with central vision loss adopt multiple PRLs, perhaps for different tasks.[33–37] Shima et al.[38] proposed the concept of a "functional retinal locus," described as a region encompassing both the PRL and the region of highest sensitivity. This concept was based on the assumption that the optimum placement of the PRL would be to coincide with the region of highest sensitivity, and that the observed failures to achieve this in patients were due to deficiencies in oculomotor control.[38] It was suggested that a goal of functional rehabilitation of patients with central vision loss should be to align the PRL to the region of highest sensitivity.[38] However, our data suggest that the area with the highest sensitivity likely does not correspond to the area with the best visual acuity in damaged retinas. It could be further hypothesized that other visual functions may also be optimal at different locations to that with highest sensitivity. We therefore propose an alternative hypothesis, that patients do not develop PRLs at the region with highest sensitivity, not simply because of oculomotor deficiency, but because this is not the optimum location for all visual functions. It therefore follows that in some patients multiple PRLs may develop for use in different tasks or conditions, or a single PRL may develop as a compromise of performance across a variety of conditions and functions.

In this study it was necessary to use different stimulus sizes for the perimetric stimulus, that was chosen to match the stimulus of commercially available microperimeters, and the acuity stimulus, that needed to be of sufficient size to contain full cycles of the grating at reduced spatial frequencies where acuity was poor. Due to the difference in stimulus sizes, the extent of localized retinal damage may also differentially affect the two tested visual functions. For example, a small, localized region of damage on which the perimetric stimulus is centered could have greater effect on sensitivity than on acuity, which draws on a larger retinal area. Alternatively, if the same region of damage were offset slightly such that it does not coincide with the perimetric stimulus but does still overlap with the acuity stimulus, the opposite effect could be found. Further, sensitivity was measured against a 4-cd/m^2 background to match that of clinical microperimetry, while acuity was measured against a 100-cd/m^2 background. Again, it is possible that the retinal damage caused by AMD may cause functional defects that vary with luminance, and therefore background luminance may be another source of discordance between our measures. We posit that these differences in stimulus size and luminance are also reflected in the difference between clinical microperimetry and "real world" acuity-dependent visual tasks, such as reading and face recognition, and therefore the poorly predictive relationship found in this study may also reflect the relationship between microperimetry and many "real world" tasks. Further study is needed to investigate how microperimetry relates to performance in daily visual tasks and vision-related quality of life.

Aside from the necessary difference in stimulus sizes, a further notable limitation of this study is that the measurements of visual field sensitivity and acuity were not registered to a retinal image as in microperimetry; therefore, we cannot completely exclude the possibility of co-location errors in stimulus placement due to fixation changes. To minimize the possibility of fixation changes we deliberately selected participants who, despite their manifest AMD, still maintained foveal fixation as demonstrated by microperimetry. Fixation during testing was monitored visually by the experimenter, which we hypothesize allows detection of saccades greater than approximately 1° to 2°. The motivation to make eye movements was reduced by presenting stimuli at the same eccentricity in each of the four cardinal directions with equal probability on each run. In the perimetry task, all nine locations were tested within each run, while in the acuity task a maximum of four locations were tested within one run. As such, there was a slightly greater attentional demand in the perimetry task that may also have slightly affected our results. Our measurements were monocular, which replicates clinical microperimetry, but as with that technique may limit the applicability of our findings as most patients are binocular. The present data are also restricted to patients whose foveal fixation remained intact despite their AMD. It is possible, therefore, that these patients are atypical and the relationship between visual field sensitivity and acuity might be different in patients with damaged foveas. It is most likely, though, that the relationship and predictions would be worse in such patients due to decreased fixation stability, and so using visual field sensitivity to predict the location with best acuity would be even less likely to be successful.

The results of this study suggest that microperimetric sensitivity measurements are unlikely to be strongly predictive of acuity at the same locations in patients with macular disease. Further, in patients with macular disease, the visual field location with the greatest sensitivity on microperimetry is unlikely to represent the location with the best visual acuity, even if eccentricity is taken into account in predicting acuity. These findings call into question whether current microperimetry is a suitable basis for making a principled selection of a location to train as a PRL. Biofeedback training incorporating fixation monitoring by retinal image tracking during a visual task, as in current microperimeters, holds clear potential for use in training fixation on a chosen PRL. However, further work is needed to establish methods for selecting an optimal PRL in terms of "real-world" task performance and to establish whether there is a role for microperimetry in this selection.

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