Published in final edited form as:
Ophthalmology. 2015 February ; 122(2): 431–433. doi:10.1016/j.ophtha.2014.09.006.

Prevalence, Patterns and Repeatability of Metamorphopsia in Macular Disease: A Statistical Analysis of 7,106 Amsler Grids

Emily Wiecek, MPhil[1,2,3], **Kameran Lashkari, MD**[1,2], **Steven C. Dakin, PhD**[3,4], and **Peter Bex, PhD**[1,2]

[1] Schepens Eye Research Institute, Massachusetts Eye and Ear Infirmary, Boston MA 02114, USA

[2] Harvard Medical School, Department of Ophthalmology, Boston, MA, 02114, USA

[3] Institute of Ophthalmology, University College London, 11-43 Bath Street, London EC1V 9EL, UK

[4] National Institute for Health Research (NIHR) Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust, 162 City Road, London, London EC1V 2PD, UK

Metamorphopsia (visual distortion) is experienced by patients with macular disease, and is a A-II symptom in the Preferred Practice Patterns for patient history, diagnosis, treatment intervention, and follow-up.[1] The Amsler grid is used to detect the presence of metamorphopsia in the clinic and at home. Patients fixate the grid centrally and note any lines that appear distorted or missing. In spite of its clinical significance, the prevalence, variation, and progression of metamorphopsia have not previously been reported. This study estimates the prevalence and magnitude of metamorphopsia in retinal clinic patients and provides statistical data to assist in the management of macular disease.

METHODS AND RESULTS

In a retrospective study, 1,495 anonymized ophthalmologic records were sampled from 5,661 retina patients at the Advanced Eye Center in Dartmouth, MA with Institutional Review Board approval. Certified ophthalmologic technicians showed patients a 4×4 inch (16°) printed Amsler grid monocularly and replicated the patient's drawing/description of distortion on a computer-based grid.

Table 1 shows the number of patients for six diagnoses considered: dry AMD, wet AMD, epiretinal membrane (ERM), central serous retinopathy (CSR), cystoid macular edema (CME), and diabetic macular edema (DME). Most patients were screened repeatedly

Correspondence: Emily Wiecek, emily.wiecek@meei.harvard.edu 20 Staniford Street Boston, MA 02118.

Meeting Presentation: Material was presented at the ARVO Annual Meeting 2014 in Orlando, FL.

Conflict of Interest: No conflicting relationship exists for any author

(average 6 month interval, maximum of 30 grids), and the final database included 7,106 monocular grids.

To quantify distortion, a binarized digital version of each grid was blurred with a Gaussian filter ($\sigma = 3$ pixels). Each individual's left eye grid was flipped horizontally and averaged with the right eye grid, and all images were averaged when multiple monocular grids from subsequent assessments were available.

A binary (present/absent) classification of distortion was used to estimate the odds of distortion for each individual. Table 1 lists the odds ratios with confidence intervals for experiencing distortion for each disease relative to dry AMD, where odds are listed. Dry AMD served as a reference because it was the largest group. For example, this analysis shows that wet AMD patients are 3.65 times more likely to experience metamorphopsia than dry AMD patients. A multivariate Wald test showed the overall effect of diagnosis was significant ($p = 0.0095$).

The area of distortion for each patient was quantified by taking the sum of drawn distortion pixels divided by the total number of pixels. An analysis of variance confirmed there was a significant difference in distortion area among groups ($p = 0.003$, $F = 3.7$) and multiple comparisons with Bonferonni adjustment showed that wet AMD patients had a significantly higher distortion area than patients with dry AMD ($p = 0.001$), CSR ($p = 0.03$), or ERM ($p=0.003$). This continuous distortion measure was used in a generalized linear model that included age, gender, acuity, and diagnosis as predictors. A generalized estimating equation accounted for the interdependence of samples between two eyes. Diagnosis ($p = 0.0013$), age ($p= 0.01$), and acuity ($p <0.001$) were significant predictors for the area of distortion.

Figure 1 shows a spatial probability map of the likelihood that patients with a given disease experience distortion at a particular location in their visual fields. A bootstrapping technique (10,000 resamples with replacement) generated probability distributions to indicate if distortion would occur anywhere within each 2°× 2° cell of an individual's average binocular Amsler grid. Patients with wet AMD and CSR show higher probabilities of distortion centrally, and DME patients show higher probabilities peripherally. Similar patterns emerged when only the first documented grid from each individual was analyzed, to consider a patient's first clinical presentation.

Outer boundaries of distorted areas were identified with region of interest polygons. Figure 2A shows three consecutive grids for one wet AMD patient. We computed the change in area and centroid of distortion between all grid pairs for each individual to estimate the progression of distortion over time. Figure 2B and 2C shows the maximum difference in distortion area and centroid location as a function of time passed between two grids. There was no significant change over time in either area or location of distortion in any group ($p > 0.1$)

DISCUSSION

This study identified differences in the location and extent of metamorphopsia in patients with macular disease. Wet AMD patients experienced more distortion than dry AMD, DME,

or CME patients, and dry AMD patients had the lowest probability of distortion. Visual distortions were concentrated more foveally in wet AMD patients, but distributed more uniformly across the visual field in DME patients.

Metamorphopsia may be caused by disruption of the photoreceptors in the macula.[2] In wet AMD, photoreceptor disruption is caused by the accumulation of subretinal fluid or neovascularization[3] which may be linked to the central concentration of distortion in wet AMD. Alternatively, DME, caused by widening of retinal capillaries, can present focally, at the macula, or diffusely, [4] and may be correlated with more peripheral photoreceptor displacement and distortion. The CME diagnosis encompasses a broader range of cases involving localized “cystoids” of fluid accumulation, rather than a diffuse spread of leaky capillaries observed in DME.[5] These structural differences may underlie the functional differences in location of metamorphopsia.

We found no significant correlation between time passed between two grids and change in the area or location of distortion (Figure 2C and D). This supports one of two conclusions: Amsler grids are repeatable measures of metamorphopsia, or they are insensitive to measuring progression. Further research combining structural imaging data is needed to determine which conclusion is appropriate. Inter-rater differences among technicians recording Amsler grids across visits may contribute to variability in longitudinal data. However, the stability of distortion location over time (Figure 2c) suggests good agreement in metamorphopsia scoring.

Our analysis confirmed that Amsler grids indicate the progression from dry to wet AMD. The low prevalence of metamorphopsia in patients with dry AMD or ERM suggests that certain retinal defects, such as drusen in dry AMD and retinal shifts in ERM are unlikely to produce distortions. Differences in the spatial distribution of distortion substantiate speculation about localized retinal disruptions. Localized maps of metamorphopsia may help understand the retinal basis for distortion and provide statistical data to assist in the management of macular disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLDEGEMENTS

This work was conducted with support from Harvard Catalyst | The Harvard Clinical and Translational Science Center National Institutes of Health Award 1UL1 TR001102-01. This work was also funded by NIH grant R01EY019281 and author SCD is funded by the Wellcome trust.

REFERENCES

1. American Academy of Ophthalmology Retina/Vitreous Panel. Age-Related Macular Degeneration. American Academy of Ophthalmology; San Francisco, CA: 2011. Preferred Practice Pattern Guidelines.. Available at: http://one.aao.org/ppp. [August 20, 2014]
2. Krøyer K, Jensen OM, Larsen M. Objective signs of photoreceptor displacement by binocular correspondence perimetry: a study of epiretinal membranes. Invest Ophthalmol Vis Sci. 2005; 46:1017–22. [PubMed: 15728560]

3. de Jong PT. Age-related macular degeneration. N Engl J Med. 2006; 355:1474–85. [PubMed: 17021323]

4. Browning DJ, Altaweel MM, Bressler NM, et al. Diabetic Retinopathy Clinical Research Network. Diabetic macular edema: what is focal and what is diffuse? Am J Ophthalmol. 2008; 146:649–55. [PubMed: 18774122]

5. Rotsos TG, Moschos MM. Cystoid macular edema. Clin Ophthalmol. 2008; 2:919–30. [PubMed: 19668445]

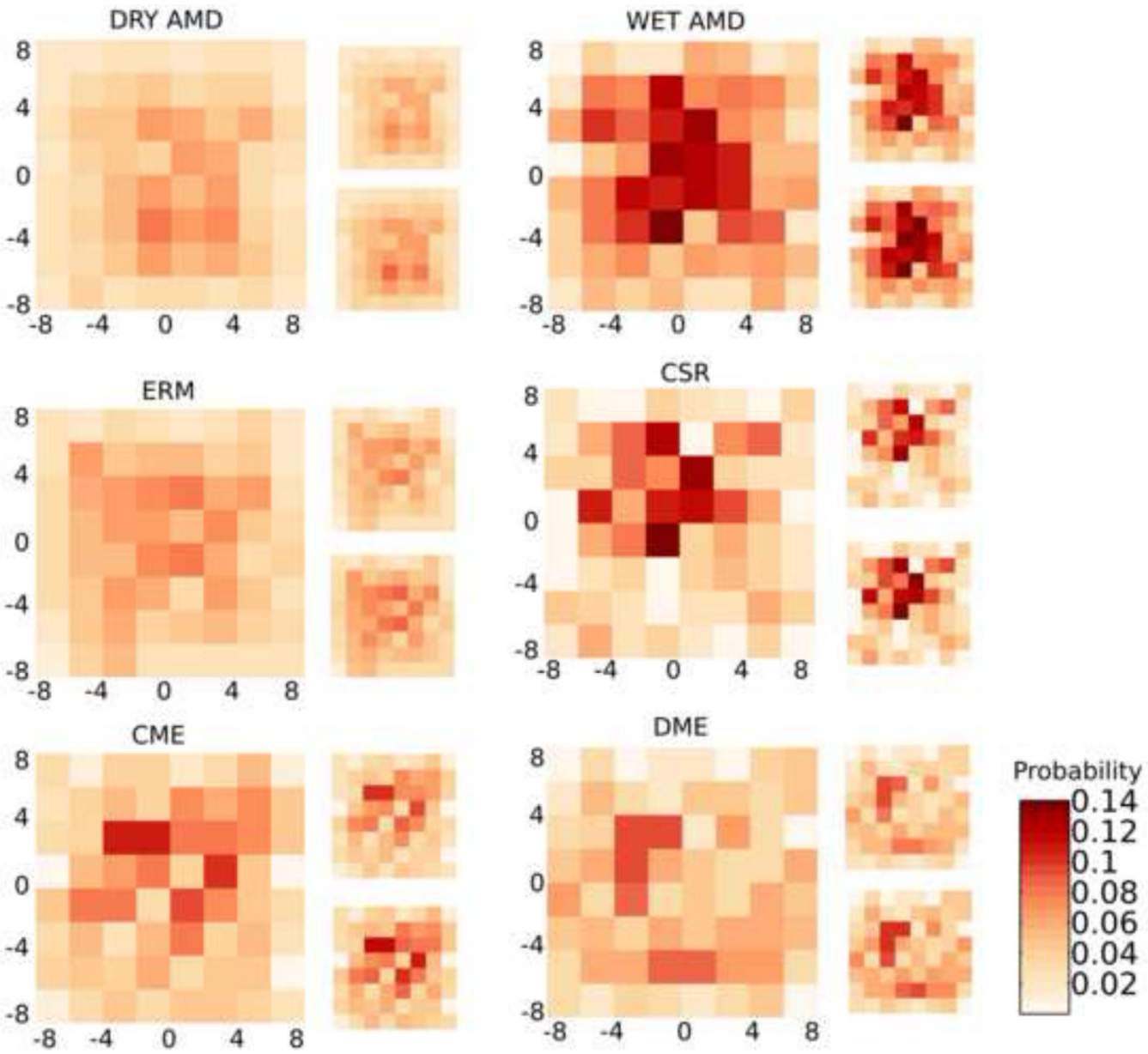

FIGURE 1.

The probability of distortion at 2×2 degree intervals across the visual field for six diagnoses. Warmer colors indicate areas where there is a high probability for distortion to occur. The smaller plots to the right of each diagnostic probability map show the upper and lower 95% confidence intervals for the probability estimate at each location.

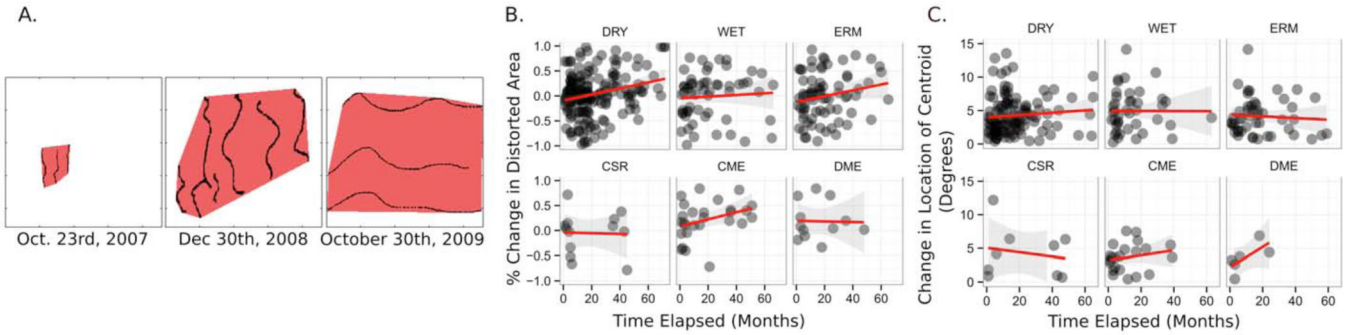

FIGURE 2.

Figure 2A. An example of the convex hull and distortions for one eye in an individual with Wet AMD. The dates indicate the time the Amsler was shown to the patient. Figure 2B. The maximum change in area across all pairwise comparisons of all grids within an individual plotted against the corresponding change in time (months) between the two grid assessments. The red line is the best-fit regression line. Each point represents the maximum change in one individual as a function of the time passed between the two grid assessments. Figure 2C. The maximum change in centroid location across all pairwise comparisons of all grids within an individual plotted against the corresponding change in time (months).

Table 1

The distribution of patients across the six different diagnostic groups examined including dry age-related macular degeneration (AMD), wet AMD, epiretinal membrane (ERM), central serious retinopathy (CSR), cystoid macular edema (CME), diabetic macular edema (DME).

Diagnosis	Total # Patients at Clinic	# of Random Samples	Total # of Grids (mean, max per patient)	Mean Age	Gender	# of Patients with at least one Distorted Grid	Odds Ratio with Confidence Intervals
Dry AMD	3216	789	3889 (5, 30)	84	534 F 259 M	468	1.46*
Wet AMD	505	119	830 (7, 41)	83	81 F 38 M	100	3.655 (2.24, 6.26)
ERM	1171	346	1448 (4, 18)	74	194 F 152 M	233	1.432 (1.10, 1.87)
CSR	120	53	234 (4, 18)	50	19 F 34 M	42	2.652 (1.39, 5.49)
CME	369	116	493 (4, 30)	72	68 F 48 M	86	1.991 (1.30, 3.13)
DME	280	72	212 (3, 14)	65	41 F 30 M	40	0.896 (0.55, 1.47)

*The right column for the Dry AMD group displays the odds of having distortion in that group. The right column for the remaining groups depicts the odds ratio calculated for each particular disease sample from a logistic regression model. Each odds ratio is relative to a reference group (Dry AMD). The odds ratio depicts the probability of distortion in a particular disease group relative to the probability of distortion in Dry AMD. Gender is coded as F(female) or M(male).