Shape Discrimination in Age-Related Macular Degeneration

Yi-Zhong Wang,1,2 Elaine Wilson,1 Kirsten G. Locke,1 and Albert O. Edwards2,3

PURPOSE. Recent studies suggest that a global shape-discrimination task is sensitive to neural undersampling and/or irregular sampling, but is not affected by normal aging. In this study, the ability of patients with age-related macular degeneration (AMD) to perform the shape-discrimination task was examined.

METHODS. Twenty patients with AMD (age range, 66–81 years) were selected on the basis of Snellen visual acuity of 20/50 or better in at least one eye and prior clinical documentation. A control group consisted of 10 older subjects (age range, 61–93 years) with normal findings in a fundus examination. Radial frequency (RF) patterns were used as stimuli. A spatial paradigm and a temporal two-alternative, forced-choice (2AFC) staircase paradigm were used. In each trial, two RF patterns (one deformed and one undeformed) were presented, and patients were asked to identify the deformed pattern. The peak spatial frequency of RF patterns was 5 c/y/deg; the radial modulation frequency was 8 c/y/360°; mean radii were 0.5°, 1°, 2.0°, or 2.5°; and stimulus contrast was 80%. Thresholds for detecting the deformation were estimated by a maximum-likelihood fitting procedure.

RESULTS. Thirty-five of 40 eyes with AMD had 20/50 or better acuity. Among them, 29 eyes had early AMD (drusen, hyperpigmentation, hypopigmentation), 5 had extrafoveal geographic atrophy, and 1 had exudative AMD. With the spatial 2AFC, 91% (32/35) of eyes with AMD showed significant elevation of the threshold for detecting radial deformation of RF patterns when compared with normal control eyes. With the temporal 2AFC, 97% (31/32) of eyes with AMD showed significant threshold elevations, and the degree of the deficit in the shape discrimination did not correlate significantly with visual acuity loss (r = 0.3, P = 0.094). Comparison of the severity of AMD with shape-discrimination performance revealed that the average detection threshold of the eyes with extrafoveal geographic atrophy was significantly higher than that of the eyes with drusen only (P < 0.01), even though average acuity showed no significant difference.

CONCLUSIONS. Patients with AMD had significant deficits in performing the global shape-discrimination task. The dissociation of shape discrimination with visual acuity suggests that the shape-discrimination task may provide distinguishable information about the integrity of the photoreceptor mosaic in AMD.

AGe-related macular degeneration (AMD) is the leading cause of severe central vision impairment and blindness among older persons in the United States. AMD is thought to be associated with both environmental1–2 and genetic3–5 factors. Ongoing and future therapeutic trials of therapies designed to slow the rate of progression of AMD6–7 could benefit from a visual performance test that is more sensitive to the disease status of early AMD than is visual acuity. To design highly sensitive, noninvasive visual tests to help monitor early macular degeneration, the impact of macular degeneration on the central vision of patients must first be understood.

AMD leads to the dysfunction and death of the photoreceptors in the macula.8 The photoreceptor mosaic is the front end of the neural visual system, and human visual information processing starts with the sampling of the retinal image by the photoreceptor mosaic. Death or dysfunction of photoreceptors in macular degeneration causes structural changes in the mosaic that affect visual information processing, such as reduced density and/or increased irregularity of the mosaic. When damage to photoreceptors is severe, vision is lost. However, it is likely that at different stages of macular degeneration some visual functions are affected more than others.

One of the main symptoms associated with advanced AMD is the progressive loss of central vision and visual acuity.9 However, visual acuity may not be an effective test to quantify the early functional deficit in patients with AMD. In the early stages of macular degeneration, patients may experience visual problems while retaining normal visual acuity.10 Even at the late stages of AMD, patients may have relatively good visual acuity.11 Visual field tests have shown that the central visual field defects in AMD are predominantly parafoveal or paramacular.12 Therefore, in the early stages of AMD, patients may have a healthy enough fovea to retain normal visual acuity. It is well known that human foveal visual acuity (or resolution acuity) is limited by the density of the cone photoreceptor mosaic (or the spacing between adjacent cones).13 According to the sampling theorem,14 to decrease resolution acuity by one half (i.e., to reduce the spacing by 50%), the sampling density must be reduced by approximately 75%. Thus, a majority of photoreceptors in the fovea must become dysfunctional or die before a significant loss of visual acuity is noticed in macular degeneration.15 Furthermore, the human visual system undergoes many structural and functional changes with normal aging, resulting in decreased visual acuity and contrast sensitivity,16,17 that increase the difficulties of using visual acuity or contrast sensitivity for early detection or monitoring of AMD. Clinically, the Amsler grid test is often used to help detect signs of macular degeneration. Although the Amsler grid is a useful screening test, it also has inherent limitations. For instance, the test result is qualitative. It is difficult for some patients to describe what they see. Many patients with early AMD report no distortion on the Amsler grid.
Using a novel stimulus (radial frequency [RF] patterns; Fig. 1), Wilkinson et al.\textsuperscript{18} demonstrated that humans have very high sensitivity to sinusoidal deformation from circularity. The threshold for detecting radial deformation is a hyperacuity (0.10%) at low radial frequencies\textsuperscript{19,19} and shows little change with normal aging.\textsuperscript{20} It has been suggested that, to achieve optimal performance, a global shape-detecting mechanism is involved in processing such a task.\textsuperscript{18,21} Further studies show that strabismic amblyopes exhibit significant deficits in detecting radial deformation, implying that this global task may be sensitive to positional jittering or undersampling by neural arrays.\textsuperscript{19} Patients in the early stages of Stargardt disease (STGD) have significant deficit in detection threshold for radial deformation, but retain relatively good visual acuity.\textsuperscript{22} Given the clinical similarities between STGD and AMD, STGD could serve as a model for AMD in showing the effects of photoreceptor damage on visual function. Thus, changes in the cone mosaic structure in patients with AMD can be expected to disrupt the judgment of global shape. Because it involves integration across a wide retinal region, a global shape-discrimination task may be more sensitive than visual acuity to irregular sampling or undersampling caused by cone death or dysfunction, especially when patients have parafoveal or paracentral visual deficits. Hence, the purpose of this study was to quantify the performance of this global shape-discrimination task by patients with AMD.

METHODS

Subjects

Twenty patients with diagnosed AMD were recruited for the study (age range, 65–81 years; mean, 74 ± 5 [SD]). The criteria for patient selection were AMD with corrected Snellen visual acuity of 20/50 or better in at least one eye, an ophthalmic evaluation with photographic documentation by a retina specialist (AOE), no retinal disease other than age-related macular degeneration, and no concurrent systemic illness affecting the retina. AMD in these patients was characterized by the presence of one or more large drusen (≥125 μm) and drusen 63 μm or greater in diameter of sufficient number to have a drusen area estimated to be 393,744 μm\textsuperscript{2} or larger.\textsuperscript{5} Thus, all patients had substantial findings typical in early AMD\textsuperscript{23} and were at high risk for development of late AMD.\textsuperscript{24} Table 1 lists the patients and the results of their fundus evaluations.

Ten normal older volunteers (age range, 61–93 years; mean, 70 ± 9) served as the control group. The inclusion criteria for normal volunteers were corrected visual acuity of 20/32 or better, normal fundus photographs judged by a retinal specialist, and no concurrent systemic illness affecting the retina.

Subjects consented after the purpose of the study and the experimental procedures were explained to them. The study was in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center. To establish baseline measurement and to characterize the vision of patients with AMD, the following clinically available tests

### Table 1. List of Patients with AMD and Results of Their Fundus Evaluations

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Gender</th>
<th>VA (OD)</th>
<th>VA (OS)</th>
<th>CS (OD)</th>
<th>CS (OS)</th>
<th>Fundus Appearance (OD)</th>
<th>Fundus Appearance (OS)</th>
<th>Thh (OD)</th>
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<td>SF-D, EF-D/P</td>
<td>SF-D, EF-D/P</td>
<td>19.9</td>
<td>30.5</td>
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SF, subfoveal; EF, extrafoveal; D, drusen; P, hyperpigmentation; NG, hypopigmentation; GA, geographic atrophy; EXU, exudation; late AMD, geographic atrophy/exudation; VA, Snellen visual acuity; CS, Pelli-Robson letter-contrast sensitivity (in log units); Thh, detection threshold for radial deformation (in arcsecs) obtained in experiment 1.
were performed: corrected Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity, Pelli-Robson letter-contrast sensitivity (viewing distance of 1 m), Amsler grid test, and visual field test (central 10-2 on a visual field analyzer; Humphrey Instruments, San Leandro, CA). Both eyes were tested. In normal subjects, only one eye (the one with better acuity or the right eye if no difference) was tested. Subjects used current spectacle and contact lens corrections to perform the psychophysical tests.

Stimuli
RF patterns were used as stimuli. The contour of RF patterns has a cross-sectional luminance profile of the fourth derivative of Gaussian, which is band limited in the spatial frequency domain. Examples of RF patterns are shown in Figure 1. The main parameters describing an RF pattern include mean radius (i.e., the radius of the undeformed RF pattern), RF (the number of modulation cycles per circumference), amplitude of radial modulation (the amount of deformation), peak spatial frequency of RF patterns (determining the width of the contour), and stimulus contrast. The radial deformation is introduced by sinusoidally modulating the radius.

Stimuli were generated digitally on computer (MatLab; The MathWorks, Inc., Natick, MA) and displayed on a gamma-corrected, 8-bit, gray-scale monitor that was controlled by computer (PowerMac; Apple Computer, Cupertino, CA; running the Psychophysics Toolbox, which provides high-level access to the Gluage Video Toolbox). The mean luminance of the monitor was 73 cd/m², and the stimulus contrast was 80%. The stimulus screen subtended 18° × 15.5° at the viewing distance of 1.0 m.

Psychophysical Procedures
A spatial two-alternative forced-choice (2AFC) paradigm and a temporal 2AFC paradigm were used. For the spatial 2AFC, a deformed RF pattern was paired with an undeformed RF pattern on each trial. Two patterns were placed at the centers of the left half and the right half of the screen. The center-to-center separation between two patterns was 9°. The subject's task was to indicate, by using a joystick, which pattern was deformed. Stimulus patterns stayed on the screen until the response was registered.

For the temporal 2AFC, subjects were asked to look at a fixation target positioned at the center of the screen. In each trial of the temporal 2AFC paradigm, one interval contained a deformed RF pattern and the other interval contained an undeformed RF pattern. Subjects were asked to indicate which interval contained the deformed one. The duration of each stimulus interval was 0.5 second. Audio signals were used to prompt the subject before each interval and at the end of each trial, but no feedback was provided that indicated the correctness of responses.

The experiments were controlled by two-down, one-up staircase procedures and ended after eight reversals. A maximum-likelihood fitting procedure was used to fit a Weibull function to the data obtained from each experimental run. The estimated modulation threshold corresponded to 75% correct responses.

Data Analysis
To exclude the eyes with very-late-stage AMD or with severe media opacity, only data obtained from the eyes with AMD with 20/50 or better acuity were analyzed in this study (n = 35). Average detection thresholds for radial deformation of the control group and their 95% tolerance limits (±1.96 SD) were computed for the data obtained in experiments 1 (spatial 2AFC) and 2 (temporal 2AFC). A t-test was performed on the data from the control group to determine whether there was a significant difference between the outcomes of the two psychophysical paradigms. Detection thresholds obtained from the patients were compared with the tolerance limits of the normal control subjects. Correlation coefficients between thresholds for detecting contour deformation and visual acuity or letter-contrast threshold were calculated in the patients. The significance of correlation coefficients was tested using the t distribution.

The eyes with AMD were divided into different groups, based on the fundus features evaluated according to an international AMD classification. Psychophysical test results were compared with fundus features. Variance analysis was performed to determine whether there was any difference between mean thresholds of the eyes in different groups. The statistical analysis was performed on computer (Minitab; Minitab Inc., State College, PA).

Results

Experiment 1: Detection of Radial Deformation Using the Spatial 2AFC Paradigm
To determine the best overall performance of subjects in detecting radial deformation, a deformed RF pattern and an undeformed RF pattern were presented on the screen at the same time. There was no limit on viewing time and no control for eye movement. Subjects controlled the pace of the experiment.

The thresholds for detecting the radial deformation of the RF pattern were plotted as a function of visual acuity in the patients with AMD and the normal volunteers (Fig. 2a). The mean (±SD) detection threshold of the normal control group was 8.6 ± 1.6 arcsec and is indicated by the solid horizontal line in Figure 2a. Among the 35 eyes with AMD with 20/50 or better acuity, 32 (91%) eyes showed significant elevation of the threshold for detecting radial deformation when compared

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**Figure 2.** Spatial 2AFC detection threshold for radial deformation as a function of visual acuity (a) and letter-contrast threshold (b). Data are shown for normal older subjects (n = 10 eyes) and patients with AMD (n = 35 eyes). The mean radius of the stimulus patterns was 1°. Each data point represents the estimate of the threshold in one eye. Solid horizontal lines: the mean detection threshold of the normal control group; dashed horizontal lines: 95% confidence limits (±1.96 SD) of the normal mean. Error bars, SEM of at least three threshold estimates.
with normal older control subjects. The other three eyes with detection thresholds falling into the normal range were those of three different patients. The mean detection threshold of the 35 eyes with AMD was 26.3 arcsec, which was significantly higher than the mean threshold of the control group ($t = 6.31, P < 0.001$). In addition, the mean detection thresholds of both the left and right eyes of every patient were significantly higher than the normal average. The degree of the deficit in shape discrimination did not correlate significantly with acuity loss ($r = 0.31, n = 35, P = 0.065$). For example, in eyes with AMD with visual acuity of 20/32 (Fig. 2a), the elevation of the threshold for detecting radial deformation ranged from 1.6-fold to 10-fold, with an average threshold elevation of 5.7-fold.

As a comparison, the detection thresholds for radial deformation shown in Figure 2a were replotted as a function of letter-contrast threshold (Fig. 2b). The detection threshold for radial deformation was significantly correlated with letter-contrast threshold ($r = 0.48, n = 35, P = 0.005$). However, the eyes with AMD with the same letter-contrast sensitivity (1.65 log units, or contrast threshold of 0.022) as those of the normal volunteers demonstrated a wide range of performance in detecting radial deformation. The detection threshold for radial deformation ranged from no significant difference from normal to a 7-fold elevation with average threshold elevation of 2.6-fold.

Comparison of the results obtained in left and right eyes of patients with AMD indicated that the performances of two eyes correlate significantly. However, the correlation appeared weaker for shape discrimination ($r = 0.58, n = 15, P = 0.024$) than for either visual acuity ($r = 0.74, n = 15, P = 0.002$) or letter-contrast sensitivity ($r = 0.76, n = 15, P = 0.001$).

**Experiment 2: Detection of Radial Deformation Using the Temporal 2AFC Paradigm**

One of the advantages of the spatial 2AFC paradigm is that the subjects could control the testing pace and did not feel rushed. This is especially important to older persons. The disadvantage of the spatial 2AFC is that there is no control for eye movement. This could become a problem when testing patients with AMD who typically have varied degrees of defects in visual field. Without the monitoring of eye position, it is difficult to determine which part of the retina a patient is using to perform the task. In addition, an experiment run could take a long time to finish for some patients, because there is no limit on viewing time.

In the second experiment, a temporal 2AFC was used for better control of the eye movement and the viewing time than in the first experiment. The subject was asked to fixate on a target during each experimental run. Each stimulus interval lasted 0.5 second. We found that 0.5 second was the interval length most older patients needed to make a comfortable judgment of the stimulus. In Figure 3, the detection thresholds for radial deformation obtained by using the temporal 2AFC paradigm were plotted as a function of visual acuity (Fig. 3a) or letter-contrast threshold (Fig. 3b). The mean radius of the stimulus patterns was $1^\circ$, the same size as that used in the spatial 2AFC paradigm to obtain the data in Figure 2.

With the temporal 2AFC, the mean ($±SD$) detection threshold for radial deformation of the normal control group was $10.6 ± 5.0$ arcsec, which was significantly higher than the mean threshold of 8.6 arcsec obtained from the same group by using the spatial 2AFC ($t = 2.30, P = 0.056$). Of the 32 eyes with AMD tested that had 20/50 or better acuity, 31 (97%) showed significant elevation of the threshold for detecting radial deformation when compared with normal older volunteers. (We could not finish all tests from two patients. Patient 5897, who had severe deficits in shape discrimination when tested with the spatial 2AFC, was not tested with the temporal 2AFC. The other eye not tested, the left eye of patient 5875, also had a significantly elevated threshold when tested with the spatial 2AFC.) The mean detection threshold of these 32 eyes was 38.6 arcsec—significantly higher than the normal mean threshold of 10.6 arcsec ($t = 6.76, P < 0.001$). Similar to the findings in testing for spatial shape discrimination, the degree of deficit in eyes with AMD for temporal shape discrimination did not correlate significantly with acuity loss ($r = 0.30, n = 32, P = 0.094$), but correlated significantly with letter-contrast threshold ($r = 0.50, n = 32, P = 0.005$). The shape-discrimination deficits revealed by the temporal 2AFC method were comparable to (or slightly more severe than) those obtained by the spatial 2AFC. For example, the eyes with AMD with visual acuity of 20/32 had an average threshold elevation of 4.5-fold, and the eyes with AMD with the letter-contrast sensitivity of 1.65 log units had an average threshold elevation of 2.7-fold. The mean ($±SD$) time that patients spent on each threshold estimate was 177 ± 80 seconds when tested with the spatial 2AFC and 141 ± 42 seconds when tested with the temporal 2AFC.

When using the temporal 2AFC, the shape-discrimination performances of the left and right eyes of the patients did not correlate significantly ($r = 0.13, n = 13, P = 0.661$).

**Comparison of Fundus Features and Shape-Discrimination Deficits**

All 20 patients with AMD had color fundus photographs available for evaluation. Among the 40 eyes in which AMD was evaluated, 5 had visual acuity worse than 20/50. The results obtained in these 5 eyes were excluded from all analyses. Among the remaining 35 eyes, only 1 eye was had exudative AMD, and this eye was also excluded from the comparison analysis. Based on the evaluation of the fundus photographs, we could not find any obvious correlations between the disc margins and the detection thresholds of subjects with AMD.

**Figure 3.** Temporal 2AFC detection threshold for radial deformation as a function of visual acuity (a) and letter-contrast threshold (b). Lines have the same meaning as those in Figure 2. The mean radius of the stimulus pattern was $1^\circ$. 
the remaining 34 eyes with AMD were divided into the following four categories: (1) drusen only, (2) drusen with hyperpigmentation, (3) drusen with hyperpigmentation and hypopigmentation, and (4) extrafoveal geographic atrophy with findings also in category 3. Table 2 summarizes the mean log minimum angle of resolution (MAR) visual acuity and mean log contrast threshold for the patients in these four categories and in the normal control subjects. (category 0).

In experiments 1 and 2, we reported the shape-discrimination performance of the patients for one stimulus size (mean radius, 1°). The evaluation of fundus photographs suggested that the abnormal appearance of the macula of the patients with AMD was inhomogeneous. Whereas some parts of the macula had varied degrees of abnormality in most of the patients, other parts of the macula appeared normal. Because RF patterns of different sizes may assist in determining visual deficits in different areas of the macula, the thresholds for detecting radial deformation of different stimulus sizes were estimated, and the average detection thresholds for different stimulus sizes were compared with fundus features.

The histograms in Figure 4 illustrate the average detection thresholds for radial deformation for the control group (category 0) and for each of the four AMD categories listed in Table 2. With the spatial 2AFC, the detection threshold was measured for three stimulus sizes: 0.5°, 1.0°, and 2.0° mean radii. With the temporal 2AFC, the detection threshold was determined for two stimulus sizes: 1.0° and 2.5° mean radii. In general, the eyes with early AMD (categories 1, 2, and 3) had a lesser deficit in shape discrimination than did eyes with extrafoveal geographical atrophy (categories 4), even though their acuities were similar. Patients with extrafoveal geographical atrophy had greater difficulty in performing the shape-discrimination task with larger stimulus patterns.

When we compared the eyes with AMD with the normal control eyes by one-way ANOVA, we found that eyes in the different categories did not have the same mean threshold for detecting the radial deformation of RF patterns, regardless of stimulus size (F > 5.58, P < 0.001). Tukey pair-wise comparisons suggested that the mean detection threshold of the eyes with AMD in any category was significantly higher than that of the normal control eyes, no matter what stimulus size was used (P < 0.05, Scheffé test). In contrast, the mean logMAR visual acuities of the eyes in AMD categories 2 and 3 were significantly worse than those of the normal control eyes (P < 0.009), whereas the mean logMAR visual acuities of the eyes in AMD categories 1 and 4 were not. Similarly, the Scheffé test indicated that the mean contrast thresholds of AMD categories 2 and 4 were significantly different from those of the normal control (P < 0.02), whereas the mean contrast thresholds of AMD categories 1 and 3 were not.

When comparing the performance among the eyes with AMD, one-way ANOVA indicated that, with stimulus sizes smaller than 2.0°, there was no significant difference between the mean detection thresholds of the eyes in four different AMD categories (F < 0.85, P > 0.480). For the stimulus size of 2.0° or larger, however, ANOVA indicated that the four AMD groups did not have a common mean threshold (F > 4.90, P < 0.007). Tukey pair-wise comparisons showed that the mean detection threshold of the eyes with extrafoveal geographic atrophy was significantly higher than that of the eyes with drusen only (category 1; P < 0.02). In contrast, the mean logMAR acuity of the eyes with extrafoveal geographic atrophy was not significantly different from that of the eyes with drusen only.

**CASE REPORTS**

The data reported in the previous sections demonstrate that patients with extrafoveal geographic atrophy showed greater deficits in shape discrimination than did patients with early AMD, although their visual acuities and contrast sensitivities were similar. The following case reports further substantiate this result.

**Case 1: Left Eye of Patient 5913 with Early AMD.** Figure 5a shows a fundus photograph of the left eye of a 69-year-old woman, and Figure 5b shows the corresponding visual field test result (10-2 in all case reports; Humphrey Instruments). The left eye’s visual acuity and letter-contrast sensitivity were 20/40 and 1.50 log units, respectively. The fundus appearance included subfoveal drusen, hyperpigmentation, and hypopigmentation and extrafoveal drusen and hyperpigmentation. The deficit in shape discrimination was approximately the same in response to stimulus patterns of different sizes, and the threshold elevations obtained with spatial and temporal 2AFC were comparable (Fig. 5c).
Case 2: Left Eye of Patient 6119 with Extrafoveal Geographic Atrophy. These data are from a 79-year-old male patient. Figures 6a and 6b show the fundus photograph and visual field test results, respectively, in the left eye of a 79-year-old man. Visual acuity was 20/25 and contrast sensitivity was 1.65 log units. In addition to subfoveal and extrafoveal drusen, hypopigmentation, and hypopigmentation, there was geographic atrophy appearing in the inferior macula of his left eye (arrow). The visual field test revealed a scotoma in the superior macula (Fig. 6b), which corresponds to extrafoveal geographic atrophy. The deficit in shape discrimination in this patient was approximately the same as that in the patient in case 1, for the small stimuli (Fig. 6c). However, the presence of the extrafoveal geographic atrophy increased the difficulty of performing a shape-discrimination test in which larger stimulus patterns were combined with short presentation times (temporal 2AFC).

Case 3: Right Eye of Patient 6110 with Extrafoveal Geographic Atrophy. The fundus photograph of the right eye of an 81-year-old man and results of the visual field test are shown in Figures 7a and 7b, respectively. Visual acuity was 20/32 and contrast sensitivity was 0.90 log units. The fundus photograph evaluation indicated that this patient had subfoveal hypopigmentation, extrafoveal drusen with hypopigmentation, and extensive extrafoveal hypopigmentation and geographic atrophy. The visual field test revealed a large parafocal scotoma (Fig. 7b). A profound deficit in shape discrimination was recorded, even for small stimuli (Fig. 7c). The patient had extreme difficulty in performing a shape-discrimination test in which stimulus patterns of extended size were used, although he had relatively good visual acuity.

Discussion

In a prior study, the mean detection threshold for radial deformation of 28 normal older subjects was 9.0 arcsec, when the method of spatial 2AFC with mean radius of 1.0° was used. In the current study, the average threshold in the 10 normal subjects obtained with the same method was 8.6 arcsec, which is in agreement with the previous finding. When the method of temporal 2AFC was used, the average detection threshold in the normal older subjects was 10.6 arcsec for the mean radius of 1.0°, or approximately a 0.3% modulation of the mean radius, which also agrees with previous results obtained in normal young adults. These data further support the hypothesis that normal aging has little or no effect on the detection of radial deformation of RF patterns.

In the current study, patients with early AMD had significant deficits in performing shape-discrimination tasks when compared with normal older subjects, even though the patients had good visual acuity (≥20/32) or letter-contrast sensitivity (≥1.50 log units). Furthermore, the shape-discrimination performance of the patients did not correlate significantly with loss of visual acuity. The dissociation between shape discrimination and visual acuity suggests that the shape-discrimination task may provide distinguishable information about the integrity of the photoreceptor mosaic in AMD. However, we also found that shape-discrimination ability correlated significantly with letter-contrast sensitivity. This result may not be surprising, given that both the shape-discrimination test and the letter-contrast sensitivity test involve large-sized stimuli. At a 1-m viewing distance, a letter on the Pelli-Robson chart has a size of approximately 3°, and its recognition may also involve a global processing mechanism. The advantage of using the shape-discrimination test is that aging has little or no effect on the performance, whereas contrast sensitivity is significantly reduced with aging.

Could the poorer shape-discrimination sensitivity found in AMD arise from the reduction in contrast sensitivity? A previous study demonstrated that the shape-discrimination task used in this study is independent of the stimulus contrast (for contrast >10%), which suggests that a reduction of contrast sensitivity by up to four times (100%–25%) should not affect shape-discrimination sensitivity. Most of the eyes with early AMD analyzed in this study had a less than twofold reduction of letter-contrast sensitivity when compared with normal eyes. Hence, the reduction of contrast sensitivity may not account for the loss of shape-discrimination sensitivity in early AMD. This analysis was in agreement with our preliminary results that there was no significant change of shape-discrimination sensitivity in patients with early AMD when the stimulus contrast was reduced from 80% to 50%. In contrast, the eyes with late AMD typically had more severe reduction in contrast sensitivity, which could exacerbate the loss of shape-discrimination sensitivity in these eyes. Further studies are needed to determine in detail the impact of stimulus contrast on shape-discrimination sensitivity in both normal senior subjects and patients with AMD.

The sensitivity of the shape-discrimination task to early AMD suggests that this test can be useful for quantifying the early visual loss caused by macular degeneration. The comparable results obtained with the spatial and temporal 2AFC methods provide the foundation for designing shape-discrimination charts for the purpose of visual screening. In addition to being a potential screening tool, the global shape-discrimination task used in this study could serve as a test for monitoring the progression of AMD. Comparison of the fundus features with the performance of the shape-discrimination task indicates that the average threshold for detecting radial deformation tends to increase with the increased presence of different types of fundus abnormalities (Fig. 4). The statistical analysis of the results suggests that the patients with extrafoveal geographic atrophy had greater deficits in detecting radial deformation of larger RF patterns than did patients with drusen and pigmentation abnormalities, whereas visual acuity failed to uncover the difference in functional loss (examples shown in Figs. 5, 6, 7). However, it must be pointed out that the samples used in the statistical analysis had limited size. A small difference in acuity may not have been revealed because of the low power of the statistical test. Further studies are needed to verify the findings reported in this article.

The present study has other limitations. The stimulus duration used in the temporal 2AFC was 0.5 second, long enough for two saccades. Some patients may have executed a saccade unintentionally during a stimulus presentation, so that the stimulus would fall onto the more healthy retinal area. This type of saccade could cause the underestimation of the deficit in shape discrimination. We also noted a large intersubject difference in performing the shape-discrimination task among patients within the same AMD category. This difference could be due to the limited sample size in the study for each category and/or the coarse classification of the fundus features of eyes with AMD. For instance, some patients with drusen only did not show significant deficits in shape discrimination. This may occur in very early AMD when only paracentral drusen are presented on fundus photographs (e.g., patient 6120). In this case, vision is still normal within the central 5° field. To determine the impact of extrafoveal drusen, the patient’s visual function in the paracentral area or near periphery must be evaluated, either by using larger stimulus patterns to cover the extrafoveal region or by presenting stimulus patterns in the near periphery. In addition, some eyes with extrafoveal and subfoveal drusen also showed no deficits (e.g., left eye of patient 6136). To better quantify visual loss in early AMD, further studies are needed to investigate the impact of different types of drusen on the shape-discrimination task by presenting visual stimuli directly to the area where drusen are located and carefully monitoring fixation with an eye tracker. A more...
FIGURE 5. (a) Fundus photograph of the left eye of 69-year-old female patient 5913 with early AMD (subfoveal drusen with hyper- and hypopigmentation and extrafoveal drusen with hyperpigmentation). (b) Corresponding visual field test result (10-2; Humphrey Instruments in Figures 5, 6, and 7); (c) Threshold elevation for detecting radial deformation of RF patterns of different sizes. Shaded area in (c), ± 95% interval of normal performance. VA, visual acuity; CS, letter-contrast sensitivity in log units.

FIGURE 6. (a) Fundus photograph of the left eye of 79-year-old male patient 6119, with late AMD (sub- and extrafoveal drusen with hyper- and hypopigmentation and extrafoveal geographic atrophy; arrow). (b) Corresponding visual field test result. (c) Threshold elevation for detecting radial deformation of RF patterns of different sizes. Shading and abbreviations are as in Figure 5.

FIGURE 7. (a) Fundus photograph of the right eye of 81-year-old male patient 6119 with late AMD (subfoveal hypopigmentation, extensive extrafoveal drusen with hyper- and hypopigmentation and extrafoveal geographic atrophy). (b) Corresponding visual field test result. (c) Threshold elevation for detecting radial deformation of RF patterns of different sizes. Shading and abbreviations are as in Figure 5.
detailed classification of fundus features in early AMD is also needed. Visual tests sensitive to early AMD are useful in identifying patients for preventative trials in the future. This study demonstrates that a shape-discrimination task can reveal visual deficits caused by AMD that are not identified by either visual acuity or letter-contrast sensitivity tests. The question is why shape discrimination is more sensitive than tests such as visual acuity in uncovering early visual loss in AMD. The evaluation of fundus images and the visual field test results in the eyes with AMD suggest that the retinal abnormality in the macula is usually inhomogeneous. Unless it is at a very late stage of the disease with complete loss of central vision, the macula of an AMD-affected eye may retain some healthy areas along with the regions affected by various degrees of abnormality. A patient may still be able to use a very small healthy area in the fovea to achieve normal performance on visual acuity tests or other types of tasks that require only localized visual processing.22

It should be noted that recent studies suggest that the shape-discrimination task used in this study involves a global pooling of contour information.18,21 Although a local mechanism can also detect the individual perturbations from circularity introduced by radial deformation, the optimal performance of this task (or lowest detection threshold) is ultimately limited by a global shape-detecting mechanism that requires visual integration or pooling of the area covered by the stimulus.21 Evidence has shown that the detection threshold for a fully modulated RF pattern is lower than that for a partially modulated, partially smooth RF pattern.21 Although it has been proposed that the site for processing this global shape discrimination may be in extraretinal cortex,22 this higher-level mechanism needs uncontaminated information from lower levels of the visual system to make optimal computation. Because the photoreceptor mosaic is the front end of the neural visual system, any defect at the level of photoreceptors can be expected to have a subsequent impact on later visual processing. In the case of AMD, if parts of an RF pattern fall on healthy macular areas and other parts on defective areas, the information rendered to the higher levels about the pattern is no longer optimal. Hence, the threshold for detecting radial deformation is elevated.

This analysis could also explain why the detection threshold was elevated in the eyes with AMD with good visual acuity when using the spatial 2AFC. Even though the patients could change their fixation to allow different parts of the retina to process the RF patterns, their detection threshold would remain elevated if they could not locate a large enough healthy area in the center of the macula to process the whole stimulus pattern. Visual search along the deformed circular contour by using a small healthy area in the fovea did not help patients to reach the optimal performance of shape discrimination.22 The deficient performance by patients with macular degeneration provides additional evidence to support the hypothesis that the optimal performance of shape discrimination is set by a global processing mechanism.

References