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Early Age-Related Macular Degeneration Impairs Tolerance To Stimulus Degradation

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Abstract

Purpose—Pathologic changes of retinal photoreceptors associated with early age-related macular degeneration (AMD) have been well established, but the disease is usually asymptomatic at the early stage and traditional suprathreshold clinical tests often fail to reveal functional deficiencies. The aim of this study is to demonstrate subtle changes of one suprathreshold visual function in early AMD eyes.

Methods—The quality of pre-attentively discriminable texture stimuli was systematically degraded through random deletion of texture checks. The subjects' task was to make a forced-choice decision on whether two equally degraded patches contained samples of the same or different types of textures. Tolerance to texture stimulus degradation was measured in young and elderly normal controls and in patients with early AMD.

Results—Subjects were trained to perform the texture discrimination task until they made few errors in discriminating intact textures. Texture discrimination deteriorated with increasing stimulus degradation in all subjects. There was no significant difference between performance of young and elderly normal controls. Early AMD eyes showed significantly less tolerance to stimulus degradation than age-similar normal controls at a range of degradation levels. After controlling for visual acuity, normal subjects still performed significantly better than early AMD eyes around 22% check deletion. There was no significant difference between better eyes of early AMD patients and fellow eyes of late AMD eyes. Performance on the degraded texture task was not correlated with visual acuity. A mild blur of the stimulus had little effect on discrimination of degraded textures.

Conclusions—Early AMD may not directly affect suprathreshold visual functions when the stimuli are intact and contain redundant information, but may manifest itself as a reduction of tolerance to stimulus degradation in the form of localized information loss. The performance of patients with early AMD may be compromised when the visual stimulus contains less redundant information.

Keywords

age-related macular degeneration; texture discrimination; psychophysics; detection

Age-related macular degeneration (AMD) is one of the leading causes of adult legal blindness in the US ¹. It is in the late stages of AMD, when large patches of retinal cells in the macula are lost due to RPE destruction, neovascularization and retinal detachment, that

severe impairment of vision occurs. However, accumulating evidence suggests that neural damage begins in the very early stage of AMD. This study reports a type of spatial vision impairment that might be associated with early AMD.

Histopathological, psychophysical and electrophysiological studies have shown that a significant portion of parafoveal rods is lost in nonexudative AMD eyes; that rod sensitivity is reduced; that rod dark adaptation is delayed; and that the rod-mediated ERG is attenuated in early AMD patients^{2–10}. Early AMD patients sometimes complain about their vision in the dark. However, neural damage associated with early AMD may not be confined to rods. It has been shown that drusen, one of the most important clinical signs of early AMD, occur mainly within 0.5 mm from the foveal center, which is not in the 0.5 to 2 mm ring where rod degeneration was found^{6, 7, 11}. Johnson et al¹² found that drusen, including those too small to be detected by clinical fundus examination ($<65\mu\text{m}$), could distort the morphology of cone receptors, reduce cone density, and interrupt synaptic transmission. Therefore, even if affected cones are physically present, and thus contribute to an apparent normal receptor density, they may not function normally. Photo transduction may be attenuated due to distorted outer segments, neural signals may not be transmitted due to missing axon terminals, and local signs may be perturbed because the receptors may be displaced by drusen.

Psychophysical and electrophysiological studies also support the early involvement of cones in AMD. Reduced foveal contrast sensitivity¹³, poorer low luminance/low contrast near letter acuity^{14–17}, reduced color contrast sensitivity and discrimination^{18–25}, reduced flicker sensitivity^{26, 27}, delayed foveal dark adaptation^{10, 28}, delayed cone recovery function^{3, 29} prolonged glare recovery^{30–32} and attenuated amplitude and prolonged latency in cone-mediated first-order mfERG within central 2° and 6° fields (diameter)^{14, 33} have been documented in early AMD patients. However, these subtle changes in vision do not usually catch the attention of the patients, and do not seem to impact their daily activities. So far, visual function deficits associated with early AMD are largely demonstrated in threshold tasks. Conventional high contrast vision tests, such as distance visual acuity, do not correlate well with fundus features associated with early AMD, and are not included in most AMD classification systems^{34–36}. In 1052 early AMD patients (with ≥ 10 large drusen and visual acuity $\geq 20/40$ in each eye)³⁷, the total and sub-scale scores of the 25-Item National Eye Institute Visual Function Questionnaire were almost identical to those of 366 old subjects with normal vision (mean acuity 20/25).³⁸

The lack of an observable impact on many daily activities in early AMD may be understood from the pattern of retinal lesions associated with early AMD and the visual stimuli in the daily environment. Because drusen are small focal abnormalities that are randomly distributed over the macula, any disturbance of photoreceptors caused by them is likely to be small-scale and randomly scattered. Such a pattern of lesions can be difficult to detect by conventional high contrast vision tests, such as visual acuity or Amsler grid, because patients can consciously or unconsciously direct intact parts of the retina to the small, isolated targets used in these tests. The effects of small-scale, scattered defects on vision can also be easily concealed by neural or perceptual filling-in when the stimuli are simple or familiar suprathreshold objects containing sufficient redundant information. The human visual system can easily recognize such objects and put them in use with only a fraction of the information in the stimuli. Conventional vision tests usually use such stimuli, and our visual environment is full of them.

We believe that in the early stage of AMD, pathological changes in the retina degrade the quality of visual input by attenuating or distorting the retinal image at random focal sites across the macula. Their impact is not felt by the patient because the redundant information

in many visual objects allows the neural, perceptual and cognitive mechanisms to function with only partial information. We hypothesize that when redundant information in the visual input is progressively removed through image degradation, early AMD patients will fail to perform a visual task earlier than age-similar controls, because lesions in their retina serve as an additional layer of stimulus degradation. To put it in a more explicit way, assume we systematically remove information from a visual stimulus until a threshold removal proportion d_n ($d_n < 1.0$) is reached at which a normal control can no longer perform the task. d_n quantifies the visual system's tolerance to degradation of input information, and $1 - d_n$ signifies the minimal amount of information required to perform the task. If the proportion of degradation is less than d_n , the visual system is able to compensate for the lost information, and no performance deficit will be noticed. Our hypothesis is that if a patient with early AMD undergoes the same test, his threshold removal rate, d_a , will be smaller than d_n . This is because the defects in the patient's retina add another source of stimulus degradation d_r . Now, the visual processing up-stream from the photoreceptors has to handle a compound degradation from both the stimulus (d_a) and the retina (d_r). Even if later visual processing can compensate for up to d_n degradation, the patient will show a reduced tolerance because of the additional source of degradation. We demonstrate in this study that early AMD patients indeed have impaired tolerance to the degradation of input information.

The suprathreshold task we chose was texture discrimination. Shown in Fig. 1a are samples of two classes of textures, even and random textures, developed by Julesz and colleagues³⁹. Because the difference between these two texture patches can be perceived instantaneously and without scrutiny, it is said that the discrimination is pre-attentive. Pre-attentive texture discrimination has been intensively studied, and has been used as a tool to understand early spatial visual information processing^{40–42}. Prior to the development of the even and random textures, it was conjectured that pre-attentive texture discrimination was possible only when textures were different in global properties of textures, such as luminance, contrast and spatial frequency components^{43–45}. The even and random textures showed that this conjecture was not valid. In the even texture patch on the left side of Fig. 1a, every 2×2 subsquare contains an even number (0, 2 or 4) of white checks. In the random texture patch on the right side of Fig. 1a, each check has an equal chance of being black or white. Intact even and random textures have the same luminance and the same contrast. They even have the same ensemble spatial frequency components^{39, 46, 47}. The fact that they are pre-attentively discriminable has led to the current understanding that pre-attentive texture discrimination is based on small, local conspicuous features such as oriented bars, blobs and terminations⁴¹, which are extracted in parallel over an extended field. When two texture patches have significantly different compositions of these local features, they become pre-attentively discriminable. These properties of pre-attentive texture discrimination make it a suitable task to test our hypothesis, because scattered retinal defects associated with early AMD may lead to distortion of local features of the texture stimuli, and the collective effect of these distortions may result in a discrimination deficit. Another advantage of this task is that texture stimuli are densely paved with features. Therefore, no matter which part of the retina the subject chooses to use for fixation, there will always be some features imaged on the retinal defects.

To test the effect of degrading the input information, we used simple deletion, that is, randomly-selected checks of texture stimuli to be discriminated were set to black. For an $x\%$ of nominal deletion, there was an average of $(x/2)\%$ effective deletion, because half of the checks were already black. Figs. 1b–1d show results of 10%, 20% and 30% nominal deletion. The most noticeable effect of random deletion is a systematic disintegration of the conspicuous horizontal and vertical bars of the even texture. As more checks are deleted, the difference between the two texture patches becomes less distinct, and discrimination becomes more difficult. Fig. 1e shows the same texture pair with 7% of the checks randomly

switching positions with one of the nearest neighbors⁴⁸. This manipulation rendered the texture almost indiscriminable. Therefore, texture discrimination is more sensitive to positional scrambling of the stimulus. Fig. 1e also demonstrates why random check deletion is more preferable to randomly changing check colors, which inevitably introduces positional scrambling and thus significantly narrows the dynamic range of the test (see discussion).

METHODS

Texture discrimination performance was measured in 3 groups of subjects. Eighteen young normal controls (YN, 25–44 yrs, mean 32.7 yrs), 13 elderly normal controls (EN, 57–83 yrs, mean 66.8 yrs) and 17 subjects with early AMD (AMD, 60–89 yrs, mean 74.4 yrs) were recruited from the volunteer service and low vision clinic of Lighthouse International, New York, and from the Eye Clinic of VA New Jersey Healthcare System (NJHCS), East Orange, NJ. Table I shows characteristics of the AMD subjects (the asterisks indicate the tested eyes). The AMD group was older than the EN group ($t=2.40$; $p=0.012$). However, as will be shown below, the texture discrimination task we used was not affected by age per se. The YN and EN subjects had 20/20 or better vision. The dominant eye was tested. Early AMD eyes were determined by dilated fundus examinations, and were based on the presence of either soft indistinct drusen only or hard or soft drusen with pigmentary abnormalities, but the absence of geographic atrophy or exudative lesions. Seven of the 17 AMD patients had early AMD and 20/60 or better vision in the tested eye and advanced AMD with 20/200 or worse vision in the fellow eye. The other 10 AMD patients were diagnosed as having early AMD in both eyes. The eye with better visual acuity was tested. The mean visual acuity of the tested eyes of the 17 AMD patients was 0.19 ± 0.15 logMAR (between 20/20 and 20/60). Subjects with more than mild nuclear sclerotic or cortical changes of the crystalline lens or any posterior sub-capsular changes were excluded. Informed consent was obtained from the subject after explanation of the nature and possible consequences of the study. The research protocol was approved by IRB of the Lighthouse International in New York and VA NJHCS, and was conducted following the tenets of the Declaration of Helsinki.

The stimulus consisted of two 50-check $\times$ 50-check (each check was 6×6 arcmin in size) texture patches next to each other. Each texture patch subtended a 5×5 deg visual angle. In a test trial, one patch was a sample of the even texture and the other a sample of the random texture. Left and right positions of the patches were randomized trial by trial. In a catch trial, both patches were samples of the random texture. In each trial, two intact texture patches were first generated and then assembled into a stimulus. If check deletion was required, one deletion routine was applied to the whole stimulus. Therefore, the left and right texture patches in a stimulus were always equally degraded, so there were no luminance or contrast cues that might aid discrimination. The stimulus was generated on a PC computer and was displayed at the center of a mid-gray background on a 17 inch color monitor. All textures were generated on the fly during the experimental session. The luminance values of the background and the black and white checks were 30.5, 0.15 and 67 cd/m^2 , respectively. The experiment was conducted in a normally lit room.

The subject sat in front of the computer monitor, and was tested monocularly. A chin/head rest was used to ensure a 59 cm viewing distance. The subject wore his/her habitual distance refractive correction. For subjects who needed optical compensation for the viewing distance, a plus lens was attached to the subject's glasses with a Halberg clip. The stimulus was presented for 250 msec. The subject's task was to determine whether the left and right sides of the stimulus contained the same or different types of textures. To familiarize the subject with the task, a training session was given prior to testing. Textures pairs with 0, 10

and 20% of deletion were used. The subject was instructed to use two keys on the computer keyboard to make responses. Some older subjects found pressing keys distracting. In these cases, the subject was told to verbally report “same” or “different” in the ensuing tests, and the experimenter would press the keys according to the reports. The subject was ready for testing only when he/she could discriminate intact textures (0% deletion) correctly with a low overall false alarm rate (~10%).

Most subjects were able to perform the task correctly in a 30-trial training session. A few subjects showed high false-alarm rates because they paid attention to small, local variations of the textures. After they were told to pay attention to the global appearances of the textures, their false alarm rates were reduced. We chose to use a “same vs. different” judgment instead of a “which side is the even texture” decision because the experiment involves multiple levels of degradations of the textures. The subject would have to learn what an even texture looked like at all tested degradation levels.

Tolerance to texture check deletion was determined by a constant stimulus procedure, in which 9 levels of check deletion, from 10% to 60%, were interlaced. The test started from 10% deletion because all subjects had practiced on intact textures, and had had near perfect performance before starting the test. Each experimental session consisted of 180 trials, 10 test trials and 10 catch trials for each level of deletion, and lasted about 6 minutes. Fifty test trials per deletion level were collected from most of the subjects. The hit rate (report “different” when the stimulus was made of an even and a random texture patches) and false alarm rate (report “different” when the stimulus was made of two random patches) at each deletion level were used to calculate a d' for texture discrimination: $d' = zScore(p_c) - zScore(p_f)$, where $zScore$ calculates the standard score or z-score of a probability, p_c and p_f are percent corrects and false alarms. p_c and p_f are adjusted for limited numbers of trials because if a subject makes no errors in 50 catch trials, it doesn't mean her false alarm rate is 0.0 ($zScore(0)$ is $-\infty$). She may make some errors if given more trials. A common adjustment is to replace the 0 with $1/(2*n)$, where n is the number of trials. So the p_f value used in calculating d' is not zero but 0.01. Similarly if the subject correctly discriminates all 50 stimulus trials, the p_c value used in d' calculation is not 1.0, but 0.99.

Two variations of the check textures in Fig. 1 were also used. In the first, a white check is made of a 2×2 pixel white dot, and a black check remained all black. Examples of the “dot” texture are show in Fig. 2a & b (0% & 30% deletion). The dot rendering of the texture prevented neighboring checks of the same color from merging into continuous bars, and might be more effective in “isolating the retinal contribution to form detection”⁴⁹. In the second variation, a 2-D Gaussian ($\sigma=2.04$ arcmin) was spatially convolved with the texture stimulus described above to create a mild image blur. Examples of blurred textures are shown in Fig. 2c & d (0% & 30% deletion). Blurred textures were used to estimate the effect of residual refractive error or mild cataract, which are common among older adults, on texture discrimination.

RESULTS

Tolerance to random texture check deletion for the EN and AMD groups (squares and stars) is compared in Fig. 3, where the mean d' is plotted as a function of % check deletion. The error bars show the standard errors of the means. For textures made of black and white checks (Fig. 3a), the average d' decreases with increasing % check deletion in both groups. However, at any given level of discrimination (d'), the AMD group could tolerate less deletion than the EN group. Similarly at any given deletion level, the EN group showed better performance than the AMD group (larger d'). Similar results were found using dot textures (Fig. 3b). A repeated-measures ANOVA was performed using deletion levels as the

within-subjects variable, and subject group as the between-subjects variable. For check textures, the main effect of deletion level was significant ($F_{8,224} = 300$, $p < 0.0005$), as was the group effect ($F_{1,28} = 17.9$, $p < 0.0005$). The deletion by group interaction was also significant ($F_{8,224} = 2.971$, $p = 0.004$), confirming the differential effect of check deletion on the AMD and EN groups. The difference between the EN and AMD groups was most pronounced at a moderate deletion level of 22.5% ($p < 0.0005$), and became insignificant at 53.75% deletion ($p = 0.311$). Similar analyses on the dot texture data also showed significant deletion level effect ($F_{8,224} = 266$, $p < 0.0005$), group effect ($F_{1,28} = 11.43$, $p = 0.002$), and deletion by group interaction ($F_{8,224} = 4.75$, $p < 0.0005$). The difference between EN and AMD groups was highly significant between 22.5 and 48% of deletion, but was not significant when there was too little or too much deletion. The p-values for group differences at the 9 levels of deletion are shown on Fig. 3a & b.

It is possible that some factors other than the presence or absence of early AMD may account for the observed differences in tolerance to random deletion of texture elements. We evaluated the effects of age, blur and status of the fellow eye in the AMD group. To evaluate the effect of age, a group of 18 young subjects with normal vision (YN) was tested using the same protocol, and the results are shown in Fig. 4, along with results for the EN group. The curves for the two groups are very similar. Repeated measures ANOVA confirmed the difference between these two groups was not significant ($F_{1,29} = 0.072$, $p = 0.791$) although discrimination did significantly decrease with increasing deletion level in both groups ($F_{8,232} = 365$, $p < 0.0005$). In our AMD patients, the tolerance to texture degradation did not correlate with their age. Pearson correlations between patient's age and d' of the first five levels of deletion ranged from -0.061 to 0.311 , none of which was significant ($p = 0.224$ to 0.623). Because there was a small but significant age difference between the EN and AMD groups, an ANCOVA was conducted to compare the performance of the AMD and EN groups using the discrimination performance at a given texture check deletion level as the dependent variable, the Group as the fixed variable and the Age as a covariate. The results showed that even after adjusting for age, the difference in discrimination performance between the two groups was still significant at moderate levels of texture deletion. For example, when check deletion levels were 22.5% and 28.75%, the Age effects were not significant ($F_{1,27} = 1.49$, $p = 0.232$ and $F_{1,27} = 0.65$, $p = 0.428$, respectively) while the Group effects were significant ($F_{1,27} = 11.87$, $p = 0.002$ and $F_{1,27} = 6.30$, $p = 0.018$, respectively). The Group effect was not significant at other deletion levels. A further analysis was conducted to examine subjects in the EN and AMD groups who were 64 years or older. There were 8 and 15 subjects in the EN and AMD groups respectively who met this criterion. The mean ages of these "older" subgroups were 71.5 and 76.3, which were not significantly different ($F_{1,22} = 2.14$, $p = 0.158$). An ANOVA showed that the AMD subgroup performed the degraded texture discrimination task significantly worse than the EN subgroup ($F_{1,21} = 6.576$, $p = 0.018$). The difference between the two subgroups were significant at 22.5% and 28.75% deletion ($F_{1,22} = 6.63$ and 5.03 , $p = 0.018$ and 0.036 , respectively), but was not significant in other levels of deletions.

Among AMD patients we studied, tolerance to texture degradation did not correlate with visual acuity of the tested eye. Pearson correlations between d' of the first five levels of deletion and visual acuity ranged from -0.123 to -0.183 , none of which was significant ($p = 0.483$ – 0.635). This is not surprising, because the checks of the texture were fairly large (6 arcmin), and the features used for discriminating textures (blobs and oriented bars) were even larger. The AMD group had poorer acuity than the EN group. Impaired acuity might have contributed to the observed texture discrimination difference between these groups. An ANCOVA was conducted to compare the performance of the AMD and EN groups using the discrimination performance at a deletion level as the dependent variable, the Group as the fixed variable and the Acuity as a covariate. The results showed that even after adjusting

for acuity, the difference in discrimination performance between the two groups was still significant when 22.5% of checks were deleted ($F_{1,27}=5.96$, $p=0.021$). The group differences, after adjusting for acuity, were not significantly different at other deletion levels. The effect of Acuity was not significant at any deletion level.

Older patients with AMD might have more retinal image blur due to residual refractive error or mild cataract (even though patients with greater than mild cataracts were excluded). The effect of blur on texture discrimination was tested by repeating the protocol using the blurred texture stimuli similar to those shown in Fig. 2c & d. Fourteen YN, 6 EN, and 16 AMD subjects completed this experiment, and the results are shown in Fig. 5, where thresholds for sharp and blurred textures are shown by open and filled symbols, respectively. Image blur had no systematic effect on discrimination performance in YN and EN groups. Blurred textures appeared to be easier for AMD patients to discriminate at lower deletion levels. A repeated-measures ANOVA showed that the differences between sharp and blurred textures were not significant ($F_{1,31}=2.74$, $p=0.108$). The interaction between Stimulus Type (sharp and blur) and Deletion Level was not significant ($F_{1,31}=2.02$; Greenhouse-Geisser, $p=0.094$, Huynh-Feldt, $p=0.079$). If sphericity was assumed, the interaction would be marginally significant ($p=0.045$), but the sphericity assumption was not valid (Mauchly's Test of sphericity, $\chi^2=76.26$, $p<0.0005$). Our power to detect a significant difference may have been limited by the relatively small number of subjects.

Finally, did the condition of the fellow eyes, early vs. advanced AMD, make a difference in the tolerance to stimulus degradation? This was evaluated by comparing the 10 patients with early AMD in the fellow eye to the 7 patients with advanced AMD in the fellow eye. Fig. 6, which compares the average d' for these two subgroups of AMD patients, shows that the average d' was similar for the two subgroups with a hint of a greater loss of discriminability at lower deletion levels in patients with advanced AMD in the fellow eye. However, a repeated-measures ANOVA with subgroup as the between-subjects variable and deletion level as the within-subjects variable showed a highly significant main effect of deletion level ($F_{8,120} = 134$, $p<0.0005$) but insignificant subgroup effect ($F_{1,15} = 0.796$, $p = 0.386$) and deletion by subgroup interaction ($F_{8,120} = 0.287$, $p=0.969$). Because the number of subjects in each subgroup is relatively small, we may not have enough power to confidently state that there is no difference between the subgroups.

DISCUSSION

In this study, we used a texture discrimination task to demonstrate that early AMD manifests itself as reduced tolerance to stimulus degradation. Our results suggest that while early AMD patients may perform well when the viewing condition is optimal and when the visual stimuli contain amply redundant information, as in many daily activities, their performance may be less robust than that of normal subjects when stimulus redundancy is reduced by localized loss of information. This vulnerability may be used to develop new vision tests for AMD detection.

The reduced tolerance to stimulus degradation in patients with early AMD indicates that there may be loss of information in AMD retinas, as we hypothesized in the Introduction. At a given level of discrimination performance in Fig. 3a, for example, $d'=3.4$, AMD patients required more intact texture checks (83.6%) than older normal controls (71.8%). The difference, about 12%, may be considered as a proportion of information lost in AMD retinas. For several reasons, we don't intend to imply that there is a 12% loss of cones in the AMD eyes we studied. First, in order to explicitly link observed reduction of tolerance to stimulus degradation with photoreceptor loss, we need to know exactly how stimulus degradation is compounded with photoreceptor loss. We don't have that information.

Second, the deletion of our texture stimuli was in the unit of checks, which was much larger in size than a macular cone. Therefore, the effect of deleting one check might not be the same as the effect of losing one or a small bundle of cones. Third, intrusion of drusen or growth of a neovascular membrane may displace the photoreceptors from their original locations, and thus may perturb the cortical representation of the local signs of these photoreceptors. Fig. 1e shows that scrambling the positions of checks in a texture has a much stronger detrimental effect on texture discrimination than simply deleting checks⁴⁸. Therefore, the 12% may be considered a measure of the collective effect of all retinal defects in the AMD eyes expressed as the proportion of information functionally lost from the stimulus.

The potential impact of stimulus and neural redundancy on the sensitivity of vision tests for glaucoma detection was considered by Johnson^{50, 51}. It has been made clear that when the stimulus is manipulated to probe the spatially and functionally less redundant neural system, for example, the short-wavelength cones, more subtle loss of retinal ganglion cells may be detected. Several studies demonstrated that information loss caused by small, randomly scattered local deletions may be concealed by the human visual system. For example, Geller et al⁵² showed that normally-sighted subjects need only 5% of image pixels to make 90% correct judgment of the orientation of a square wave grating. In comparison, Seiple et al⁵³ showed that normal subjects needed 50% of image pixels to maintain a 90% correct performance in recognizing 11 arcmin Sloan letters. Frisen & Quigley⁵⁴ found that only 60% of the functional neural channels in the fovea were required for optic atrophy patients to reach 20/20 letter acuity. We showed that normal subjects could maintain a high level of texture discrimination performance when 30% of texture checks were deleted. Stimulus degradation in the form of random pixel/check deletion has been considered as a model of the fovea in retinitis pigmentosa (RP), because it is known that foveal photoreceptor density is reduced even in early RP⁵⁵. Turano & Wang⁵⁶ measured the smallest displacement that led to a correct judgment of motion direction ($d_{\min}$) for random dot patterns in 25 RP patients (logMAR -0.10 to 1.30). They found that $d_{\min}$ of RP patients was elevated comparing with that of normal controls, and $d_{\min}$ elevation was correlated with RP patients' visual acuity. These authors also simulated photoreceptor dropout in normal subjects by eliminating information from specified stimulus locations, and found that $d_{\min}$ started to increase when dropout rate was greater than 12%. Szlyk et al⁵⁷ tested 11 RP patients with symmetric and asymmetric patterns made of 30×30 arcmin blocks, and found that symmetry discrimination of RP patients was significantly lower than that of normal controls. They randomly deleted pixels from the test patterns and found that normal subjects' performance with 25% of intact pixels was similar to RP patients' performance with 100% of intact pixels. In both studies, the authors measured RP patients' sensitivity to intact stimuli.

These studies revealed that the human visual system possesses the ability to compensate for local loss of stimulus information in a sense that normal performance is maintained when only partial information is available. These studies also showed that there were limits as to how much lost information could be compensated. Performance became impaired when available information was below the limit. Our study differed from the previous studies in that we tested AMD patients with degraded stimuli and compared their tolerance to stimulus degradation to that of normally sighted subjects. Our results indicate that early AMD patients require more intact texture information (or tolerated less degradation) than normal subjects in order to achieve the same level of performance. We believe that reducing information redundancy to defeat the built-in neural, perceptual and cognitive compensations of the visual system is the key in revealing latent visual deficiency in early AMD patients.

In our experiment, reducing redundancy was accomplished by randomly deleting texture checks. Other methods may achieve the same effect. In a recent paper, Bedell et al found that early AMD patients with normal visual acuity had more difficulty in judging the orientation uniformity of a patch of line segments than normal subjects⁵⁸. The key feature of this sensitive test was the selection of length of the line segments. The authors took advantage of a known phenomenon that the perceived orientation of line segments becomes uncertain when the line length is shorter than 0.3° ⁵⁹. The authors reduced the redundant information for orientation judgment by using 0.4° line segments, which contained just enough information for normal subjects to judge orientation correctly. The effect of small local lesions in early AMD can be detected because they either make the line segments shorter than required for reliable orientation judgment or perturb the line orientation.

Degraded texture discrimination may be used as an early detection test for AMD. An obvious advantage of using degraded high luminance, high contrast stimuli to measure visual deficits associated with early AMD is that the performance is less affected by normal aging of the pre-retinal components. It is well known that the aging of the pre-retinal optical components has direct impact on threshold tasks such as light detection, contrast sensitivity and color vision^{60–70}. Separating deficits associated with AMD and normal aging in these tasks can be difficult and tedious^{9, 28, 71–73}, and may raise theoretical concerns^{74, 75}. As shown in Fig. 4, the texture discrimination task is minimally affected by normal aging. This finding can be understood in two ways. First, the texture stimulus was made of high contrast features that are unlikely to be affected significantly by reduced pupil size, increased intra-ocular light scattering or yellowing of the ocular media. Second, the basis for the task we used is pre-attentive feature extraction. Several studies have shown that normal aging has minimal effect on subjects' ability to extract visual features in a parallel fashion, at least in an area the size of the macula^{76–82}. Another practical concern in detecting early AMD is the small amount of residual refractive error and mild cataract that are common in older adults, and that are known to interfere with visual functions such as contrast sensitivity and color discrimination^{83–86}. Fig. 5 demonstrates that a mild image blur did not have a significant effect on discrimination of degraded textures. We believe a mild blur may not reduce information redundancy of texture stimuli, because the basic elements for texture discrimination are visual features such as bars, blobs or terminations, which are robust against mild blur, but are more sensitive to local deletion or scrambling. We didn't study the effect of more severe image blur that may result from larger refractive errors or denser cataract because these conditions would be much more noticeable and should be corrected before retinal function is evaluated. Visual acuity might have some impact on texture discrimination, because fewer levels of deletion showed significant differences between the EN and the AMD groups after their acuities were taken into consideration. We don't know how visual acuity interacted with texture discrimination, because the texture checks had the size and contrast that were highly visible to our AMD patients. However, the fact that the EN group still perform significantly better than the AMD group around 22% of check deletion after the effect of acuity was controlled for suggested that texture discrimination could reveal some aspects of visual function impairment that did not manifest in visual acuity test.

Deleting texture checks to black has the side effect of reducing stimulus luminance. While deletion was done identically on both texture patches of any stimulus pair, and thus would not introduce luminance or contrast differences between texture patches, co-variation of luminance and visual feature degradation can be a legitimate concern. The discrimination of degraded textures is robust against large changes in luminance in normally sighted subjects. We conducted the same experiment on three young normal controls at three stimulus luminances (using 0, 0.8 and 1.25 log unit neutral density filters), three contrasts (98%, 50% and 20%) and in dark and normally lit rooms. The results from these conditions were all

very similar. In comparison, at the level of deletion where the largest difference was seen between normal and AMD subjects (22% deletion, Fig. 3), the luminance reduction from intact textures was only 11%, or less than 0.1 log unit. While studies showed that AMD patients' performance on several vision tests were impaired by luminance reduction, the luminance changes used were in the order of log units. For example, Brown et al showed that the peak contrast sensitivity of AMD patients was reduced from 42 to 32 when stimulus luminance was reduced from 72 to 7.2 cd/m²⁸⁷. Bullimore et al found that in most AMD patients they tested the face recognition threshold changed 0.2–0.3 log unit when stimulus luminance was reduced from 100 to 1 cd/m²⁸⁸. Such large luminance changes inevitably involved different retinal pathways that could be selectively targeted by AMD, as acknowledged by some researchers⁸⁷. To produce that much luminance reduction, we would have to delete 90% to 99% of the texture checks. We are not aware of studies that demonstrate a significant performance change associated with a 0.1 or 0.2 log unit luminance change in the photopic range in early AMD patients. We are inclined to consider that the discrimination performance decay we observed with texture check deletion was associated with the disintegration of textons rather than the reduction of luminance. If an early detection test is to be developed based on degraded texture discrimination, the effect of luminance change will be tested on AMD patients to ensure that it has a minimal impact on test results.

An alternative method of degradation is to randomly change the colors (black and white) of texture checks. While this approach maintains the mean luminance of the stimulus, it introduces a different type of degradation. The net effect of changing check colors is positional scrambling. We used a more sophisticated method to introduce controlled positional scrambling into texture stimuli and demonstrated that compared with pure deletion, a much smaller percentage of check scrambling could result in significant performance reduction⁴⁸ (also see Fig. 1e). Although a test using scrambled textures may be more sensitive, it may have too narrow a test range to quantify visual deficits caused by different AMD severities. That was the reason we choose to use random deletion to degrade the stimulus.

The reduced tolerance to texture degradation observed in early AMD eyes may be used as a technique to screen for early AMD. For example, if a $d'=3.4$ screening criterion is set for 22.5% deletion so that a person scoring below this level on this test will be classified as a suspect of early AMD, then 11 of the 13 our older normal controls would be classified as normal and 14 of 17 of our AMD patients would be classified as AMD suspects (sensitivity=0.82, specificity=0.85). Because texture discrimination is very sensitive to positional scrambling⁴⁸, the degraded texture discrimination test may also find use in detecting the onset of neovascular AMD, which is known to perturb the positions of photoreceptors. More research will be conducted to explore clinical applications of this test.

To summarize, we present evidence that early AMD patients have reduced tolerance to stimulus degradation in a texture discrimination task. This reduced tolerance probably results from information loss associated with scattered retinal defects in the macula of early AMD patients. Using localized deletion of stimulus elements to reduce redundant information may be a viable method to develop new tests for early detection of AMD.

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Figure 1. Even and random check texture patches. **a)** through **d)** show the result of 0%, 10%, 20% and 30% of random check deletion. **e)** shows that scrambling of 7% of the checks can render the textures indiscriminable.

Figure 2. Even and random texture patches with 0% and 30% of random deletion. **(a)** and **(b)** are “dot” textures. **(c)** and **(d)** check textures blurred by a 2-D Gaussian ($\sigma=2.04$ arcmin).

Figure 3. Results of EN and AMD groups. Error bars indicate group standard errors of means. The numbers above errors bars are p-values of group comparisons. **(a)** used check textures and **(b)** used dot textures.

Figure 4. Comparing EN and YN groups. Error bars indicate group standard errors of means.

Figure 5.
Comparing sharp and blurred texture stimuli obtained from the YN, EN and AMD groups.
Error bars indicate standard errors of means.

Figure 6.

Comparing early AMD eyes and fellow eyes of late AMD eyes. Error bars indicate standard errors of means. The numbers above errors bars are p-values of group comparisons.

Table 1

AMD Subjects.

Subject	Age	Gender	VA (OD)	VA (OS)
001	64	F	20/30	20/25*
002	66	F	20/400	20/60*
003	73	M	20/40*	20/200
004	66	F	20/800	20/50*
005	85	F	20/400	20/30*
006	77	F	20/25*	20/40
007	82	F	20/40*	20/200
008	82	M	20/40	20/25*
009	81	M	3 FT/160	20/25*
010	79	F	20/30	20/20*
011	89	M	20/200	20/50*
012	72	M	20/25	20/20*
013	77	M	20/30*	20/40–1
014	78	M	20/30–1*	20/30+1
015	73	M	20/20*	20/20
016	61	M	20/30*	20/40
017	60	M	20/30	20/25*