Computer-Based Test to Measure Optimal Visual Acuity in Age-Related Macular Degeneration

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PURPOSE. The authors present a computer-based method for evaluating the visual acuity of patients with age-related macular degeneration (AMD). It incorporates four features known to improve visual acuity: high contrast, white optotypes on a black background, proportional layout to reduce the effects of crowding, and multiple optotypes to minimize the effects of fixation instability and to maximize the likelihood of optotype detection.

METHODS. Experiment 1 evaluated the best-eye acuity of 24 patients with AMD using the ETDRS chart and three versions of the Tumbling E acuity test: multiple black optotypes on a white background, single white optotype on a black background, and multiple white optotypes on a black background. Experiment 2 compared the two White E optotype tests with the ETDRS in patients with AMD, and Experiment 3 measured probability summation in persons with normal vision.

RESULTS. Multiple white optotypes on a black background yielded the highest acuity estimates and the ETDRS the lowest. The Single E test yielded a lower estimate of acuity than the two Multiple E tests. The effect of polarity—white on black was better than black on white—was consistent with results found in persons with healthy retinas. For patients with AMD, acuity measured with the Multiple E test was independent of that measured with the ETDRS, but acuity measured with the Single E test decreased as acuity worsened. For the participants with normal vision, the differences between the Multiple and Single E tests were within the known limits of test–retest variability.

CONCLUSIONS. The multiple-optotype, reversed-polarity test provides a measure of the optimal visual acuity of which a person is capable and, in this sense, may be a useful tool for assessing rehabilitation progress. (Invest Ophthalmol Vis Sci. 2007;48: 4838–4845) DOI:10.1167/iovs.06-1240

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n age-related maculopathy both rods and cones deteriorate with disease progression, and the photoreceptor mosaic becomes irregular or less dense.1 Visual acuity is difficult to evaluate in patients with macular abnormalities because the reduction in acuity2–3 is not exclusively a function of the fact that peripheral acuity is lower than foveal acuity and is more susceptible to contour interactions.4 In addition to low acuity, distortions of shape,5 and diminished contrast sensitivity6 and color vision,7 the damaged fovea cannot generate the input for proper eye movement control and fixation stability.8–12 After the fovea is damaged by disease, the ocular motor system must acquire a new reference area in the retina where vision remains intact. Bilateral foveal damage in monkeys10 has shown that this adaptation involves two independent processes, the stabilization of fixation and ocular motor adaptation for searching and positioning the images of visual targets at a consistent location in the peripheral retina.13 An error of gaze selection or control of only 5 minutes arc could reduce the Snellen acuity of a person from 20/20 to 20/40.14

The criterion standards for clinical acuity measurement are the Bailey-Lovie15 visual acuity charts, whose design features were adopted by the National Eye Institute, National Institutes of Health for use in the ETDRS or Early Treatment of Diabetic Retinopathy Study.16 These charts have a number of advantages over some traditional charts17 in that they include a logarithmic progression of letter sizes whereas some charts have uneven size progressions, and lines of certain sizes are missing. They also have a standardized, proportional layout with letter spacing equal to the letter or symbol width and line spacing equal to the height of the lower line. In addition, each line contains five letters so that letter count scores are possible.

An important consequence of proportional layout with equal numbers of letters on each line is that relative crowding and contour interaction effects18–21 are similar for all lines, while only letter size changes. Because they are based on the logarithm of the minimum angle of resolution, ETDRS charts are also called logMAR charts although some charts with this feature lack a proportional layout. Alternatively, not all logMAR charts with a proportional layout consist of letters; some, for instance, consist of tumbling E optotypes,22 which, like the Landolt C, are resolution acuity measures and are preferred for use with observers not familiar with the Roman alphabet.

In 1984 the Visual Acuity Measurement Standard of the International Council of Ophthalmology selected the Landolt C (or Landolt broken ring) as the standard against which the recognizability of other tests should be calibrated.23 Not all the ETDRS optotypes are equally easy to identify,24 and identification and resolution acuity measures are not always comparable in persons with ocular abnormalities.25 Furthermore, compared with the ETDRS charts, the four cardinal orientations of the tumbling E result in a smaller, and therefore simpler, response set (in contrast to the 10-alternative forced choice of the ETDRS). With the exception of simulated simultaneous-contrast astigmatism, the resolution acuities derived from the tumbling E and Landolt C optotypes are similar.

In addition to smaller size progressions than standard charts, computer-controlled acuity tests have the advantage of more precise acuity measurements run by fast and efficient
psychophysical procedures. Compared with the ETDRS and Landolt C optotypes, Tumbling Es (also known as Albinis, illiterate, or rotatable Es) have the additional advantage of being easy to draw, and their proportions are simple to calibrate on a computer screen. The absence of round shapes allows small E optotypes to exhibit no pixilation at low screen resolutions, and the smallest E, if drawn with an aspect ratio of 1, only requires a $5 \times 5$ pixel matrix. Stroke lengths in multiples of 5 pixels allow for accurate aspect ratios, particularly in LCD screens, which are better than CRTs in terms of pixel linearity.

In 1985, Harris et al. published a Multiple E optotype test especially designed for persons with macular disease. Noting that the size of the macular defect cannot account for the low acuity in patients with AMD, the test was designed to simultaneously stimulate any functional retina in the posterior pole capable of better resolution in patients unable to use a suitable or stable preferred retinal locus. The test includes 10 white cards covered with an array of identical black E optotypes in sizes equivalent to $20/20, 20/25, 20/30, 20/40, 20/50, 20/60, 20/70, 20/80, 20/100,$ and $20/200$. Vertical and horizontal rows are spaced one-half letter width apart so that two letter widths separate adjacent Es, and the optotypes are staggered along $45^\circ$ diagonals to prevent pattern clues of their orientation.

Another Multiple optotype test, developed by Regan et al., for testing persons with amblyopia, consists of multiple identical target letters in the center of the chart, surrounded by letters randomly selected from the test’s pool of 10. Because letters adjacent to the empty spaces on the sides of charts are less affected by lateral interactions or masking, the surrounding letters eliminate differences between the optotypes as a result of their position and diminish the effects of probability summation. The Regan repeat letter chart, however, was designed for persons with amblyopia and deficient gaze selection or control who nevertheless have intact maculae. Given that the target optotypes are in the center, the Regan repeat letter charts could be confusing for a person with a diseased macula who has not yet learned to fixate eccentrically or who has poor fixation stability.

In observers with normal vision, white optotypes on a black background have been found, with Landolt Cs, and with an 18-letter chart, to yield higher estimates of visual acuity. This effect is likely due to a reduction in intraocular light scatter, which causes widening and flattening of the eye’s point-spread function, and is stronger in older observers.

Here we present a computer-based Multiple E optotype test for evaluating, under optimal viewing conditions, the visual acuity of patients with macular degeneration. The test incorporates four features known to improve visual acuity: high contrast, proportional layout to reduce the effects of crowding, multiple optotypes to increase the likelihood of identification and minimize the effects of fixation instability, and reverse polarity (white optotypes on a black background). It also has the same staggered arrangement as the test designed by Harris et al., and the optotypes have an aspect ratio of 1.

Experiment 1 compared the best-eye acuity measures of the Multiple White E test with the ETDRS, the Harris et al. test (or Multiple Black E test), and the Single White E test in patients with AMD. The ETDRS was chosen as a standard clinical test, the Multiple Black E test to compare the effects of polarity, and the Single E test as a control for the effects of lateral interactions and crowding.

Experiments 2 and 3 explored binocular summation using the Single and Multiple White E tests. When the same stimulus is simultaneously presented to two independent detectors, the probability that it will be detected is greater than when only one detector is stimulated. This effect is called probability summation. Visual tasks often show improvement in performance when two, rather than one, eyes are used. When the sensitivities of the two eyes are equal, binocular summation is defined as an increase in binocular performance compared with either of the two monocular performances. Probability and neural summation are two kinds of models used to explain binocular summation. Pirenne’s probability summation model predicts a maximum binocular superiority of 50%, but, adjusting for noise and guessing factors, other probability models predict smaller binocular superiorities. Binocular summation is often measured as the binocular ratio (BR) of the best monocular to binocular acuity.

Binocular improvement exceeding the values predicted by probability models is usually explained by neural summation models that can extend the prediction of binocular gain to more than double the monocular performance.

**Experiment 1**

**Methods**

**Participants.** Participants were 24 volunteers with diagnoses of AMD and best-corrected visual acuity between $20/70$ and $20/200$ in their better eye (the right eye for 14) as measured by the ETDRS chart (Lighthouse International, New York, NY) at a distance of 1 m and obtained on a previous visit to the ophthalmologist. Their ages ranged from 70 to 92 years (mean, 82.4; SD, 7.03), and none had a history of neurologic disease or cognitive impairment. In this and the next two experiments, all participants provided informed consent, and the experimental procedure was approved by the Ethics Review Board of the University Health Network in accordance with the tenets of the 2004 Declaration of Helsinki.

**Apparatus and Stimuli.** Participants were tested in four high-contrast conditions that included the back-lit ETDRS and three versions of the illiterate E optotype test: the Multiple Black E test, the Single White E test, and the Multiple White E test. The latter two were presented on an LCD computer screen with a viewing area of $47 \times 40$ cm and a resolution of $1600 \times 1024$ pixels. The stimuli were generated, and the test was controlled by graphics generation and psychophysics testing software (VPixx Technologies, Inc., Montreal, QC, Canada) on a computer (Macintosh G4; Apple, Cupertino, CA). The white optotypes had a luminance of 193 cd/m$^2$ and the black background measured 0.46 cd/m$^2$, yielding a Michelson contrast $(L_{\text{max}} - L_{\text{min}})/(L_{\text{max}} + L_{\text{min}})$ of 99.58%.

**Procedure.** The order of presentation of the four acuity tests was counterbalanced so that each patient was assigned one of the 24 possible permutations of their presentation order. After complete clinical assessment, the best-corrected visual acuity of a patient was tested using the ETDRS, Single White E, Multiple White E (Fig. 1), and Multiple Black E tests in their selected order. All tests were performed at 1 m, with the exception of the Multiple Black E test, which was performed at 50 cm. The appropriate working distance lens was used for each test, and participants were tested monocularly with the fellow eye covered by an eye patch.

For the Multiple White and the Single White E tests, the computer program changed the letters’ orientation randomly from one trial to another, and thresholds were measured using a four-alternative forced-choice (4AFC) staircase. To approximate the thresholds obtained with the ETDRS and the Multiple Black E test, thresholds for the two white E tests were obtained with an adaptive psychophysical method in
which incorrect responses increased the size of the optotypes and correct ones decreased it by an amount (step size) of 0.1 log units. This kind of psychophysical procedure converges at thresholds around 50%. The staircase ended after eight reversals or 60 trials, and the acuity threshold was the average of the last four reversals. Trials were self-paced, and the participants viewed each E stimulus for 4 seconds. The Single and Multiple White E tests took place in a darkened room. The ETDRS and Multiple Black E tests were performed under normal lighting conditions. An alpha level of 0.05 was used for all statistical tests.

Results

Multiple white optotypes on a black background yielded the highest acuity estimates, and the ETDRS yielded the lowest (Fig. 2). A repeated-measures analysis of variance (ANOVA) with a Geisser-Greenhouse conservative $F$ statistic yielded a significant effect of tests ($F(3,39) = 8.47; P < 0.001$). Post hoc pairwise comparisons using the Holm sequential Bonferroni procedure found significant differences between the ETDRS and the Multiple White E test ($P < 0.01$) and between the Single and the Multiple White E tests ($P < 0.01$). Comparisons between the ETDRS and Multiple Black E tests and between the Multiple Black and Multiple White E tests also had associated probabilities smaller than 0.05, but these were larger than the critical values required by the Bonferroni correction. Assuming the same effect sizes (0.46 and 0.41, respectively), 46 and 41 cases would have been required to yield a more powerful (e.g., 0.70) test. The Tukey HSD test, which also offers protection against type 1 error, yielded the same results.

EXPERIMENT 2

Methods

Multiple and Single White E tests were compared to the ETDRS in monocular and binocular viewing conditions for patients with AMD. Binocular gain was also evaluated.

Participants. Fourteen volunteers with diagnoses of AMD whose ages ranged from 51 to 89 years (mean, 80.86; SD, 9.80) participated. As in experiment 1, no participant had a history of neurologic disease or cognitive impairment, and all provided informed consent.

Procedure. The apparatus was the same as in experiment 1 for the Single and Multiple White E tests, but the psychophysical procedure was modified so that the size of the Es changed with participant responses using a one up/three down rule, which converges around a 79.4% threshold to obtain an estimate with lower variability. The staircase ended after eight reversals or 60 trials, and the acuity threshold was the average of the last four reversals. All participants were tested monocularly (right eye, left eye) and binocularly. Viewing conditions were assigned in random order, and testing was performed at a viewing distance of 1 m.

Results

ETDRS Versus E Tests (Monocular Tests). Figure 3 shows a Bland-Altman plot of the distribution of the residuals obtained by subtracting the acuity measured with each of the two E tests from the acuity measured with the ETDRS. The heteroscedasticity of the residuals, evaluated using Pearson correlation ($r$), showed that the differences between the ETDRS and the Single E test decreased as acuity worsened ($r(26) = 0.46, P < 0.05$) but that the differences between the ETDRS and the Multiple E test were independent of acuity ($r(26) = 0.06, P = 0.76$). Regression lines, their bivariate functional equations, and the limits of agreement (mean ± 2 SD) are also shown on the graph.

For monocular viewing, the acuity measured with the ETDRS was worse than that measured with the Multiple E test ($t(27) = 3.19, P < 0.01$) but was not significantly different from that measured with the Single E test ($t(27) = 0.35; P = 0.73$).

Single Versus Multiple E Acuity Tests. For the AMD group, the mean differences between the Single and the Multiple E tests were 0.10 (SD, 0.25) logMAR units for the better
eye, 0.31 (SD, 0.43) logMAR units for the worse eye, and 0.10 (SD, 0.27) logMAR units for binocular viewing. Figure 4 is a Bland-Altman plot showing the distribution of the residuals obtained by subtracting the Single E from the Multiple E acuity values for monocular and binocular viewing, shown as a function of the mean acuity. The difference between the two tests.

**FIGURE 4.** For the AMD group, differences between the Single and Multiple White E tests for monocular and binocular viewing as a function of mean acuity. The mean and limits of agreement (mean ± 2 SD) shown are for the monocular data and spanned 1.5 logMAR units.
increased as acuity decreased. The correlation (Pearson r) between the difference values and their mean was significant for the monocular viewing conditions ($r(26) = 0.46; P < 0.05$) but not for binocular viewing ($r(12) = 0.51; P = 0.06$); however, the latter result is from the smaller number of data points in the binocular condition. As Figure 4 shows, both functions have similar slopes and intercepts. Figure 4 also shows the regression lines and respective bivariate functional equations for the two viewing conditions.

Acuity values in logMAR units for the better eye, worse eye, and binocular viewing of the patients with AMD in the two tests were analyzed with a $2 \times 3$ repeated-measures analysis of variance using a Geisser-Greenhouse conservative $F$ statistic. There was a significant effect of test, with the Multiple E test yielding better acuity measures than the Single E test ($F(1,13) = 7.15; P < 0.01$) and a significant effect of viewing condition ($F(2,26) = 23.06; P < 0.001$) but no significant interaction between the two main effects. Post hoc tests using Bonferroni correction showed a significant difference between the acuity of the better and the worse eye ($t(13) = 5.27; P < 0.001$) and between binocular viewing and the worse eye acuity ($t(13) = 5.66; P < 0.001$) but no difference between the better eye and binocular viewing acuity ($t(13) = 1.54; P = 0.13$). Figure 5 shows the mean data.

**Results**

Acuity measures were analyzed with $2$ (Multiple and Single E tests) $\times 3$ (right eye, left eye, and binocular viewing) repeated-measures analysis of variance. Significant effects of test were observed, with better acuity measures for the Multiple E test ($F(1,19) = 73.60; P < 0.001$) and viewing condition ($2,38) = 19.13; P < 0.001$). There was an unexpected and significant ($P < 0.01$) superiority in acuity for the right eye (in 17 of 20 cases for the Single E test and in 15 of 20 cases for the Multiple E test); however, this superiority was above normal levels$^{42}$ in only one case for the Single E test and in only one, but different, case for the Multiple E test.

Differences between the left eye and binocular viewing ($P < 0.01$) and between the right eye and binocular viewing ($P < 0.05$) were also significant. There was no significant interaction between test and viewing condition.

As measures of probability summation, the mean differences between the Single E and Multiple E acuity tests were $0.08$ (SD, 0.06) logMAR units for the right eye, $0.10$ (SD, 0.06) logMAR units for the left eye, and $0.10$ (SD, 0.06) logMAR units for binocular viewing (Fig. 6). These data are similar to those of the AMD group for the better eye and binocular viewing but not for the worse eye, which had a mean of 0.31 logMAR units.

BR was calculated for each participant in each test for this and experiment 2. BR is the ratio of the best monocular to binocular acuity in minutes of arc. Because we did not have a measure of test-retest reliability for the multiple optotype test, we followed the definition used by Tarita-Nistor et al.$^{43}$ and used a range of 10% to define summation and inhibition values of BR. Summation was defined as a BR larger than 1.05, equality as a BR between 0.95 and 1.05 (1 ± 0.05), and inhibition as a BR < 0.95. Figure 6 shows that slightly more than half the participants in both groups exhibited binocular summation with the Single E test; with the Multiple E test, the proportions of AMD participants exhibiting summation and inhibition were identical.

In patients with AMD, no significant differences were observed between the BRs for the Single and Multiple E tests.
(t(13) = 0.01; P = 0.99), and the same result was found for the participants with normal vision (t(19) = 0.86; P = 0.40). Mean binocular gains for the AMD group in the Single and Multiple E tests were 14% for both tests, though the data for the Multiple E test were skewed by a single large outlier. Substituting this value by that of the group mean yielded a binocular gain of 7% (BR, 1.07), which is consistent with previous results using the same test. Substituting this value by that of the group mean yielded a binocular gain of 7% (BR, 1.07), which is consistent with previous results using the same test. 

**DISCUSSION**

Experiment 1 showed that multiple white optotypes on a black background yield the highest acuity estimates and that the ETDRS yields the lowest. The Single E optotype test, even in the absence of crowding effects and with the possibility of viewing with the preferred retinal locus, yields lower estimates of acuity than the Multiple E test and comparable values to the ETDRS. Lastly, the effect of polarity—white on black is better than black on white—is consistent with results found in persons with cataracts and persons without ocular abnormalities. For patients with AMD, experiment 2 showed that the differences between the ETDRS and the Single E test decrease as acuity worsens. With a different clinical population (patients with idiopathic macular hole), Wittich et al. found that resolution acuity measured with the Landolt C is more impaired than recognition acuity measured with the ETDRS and concluded that the component cues in letter optotypes help in their identification and lead to an overestimation of acuity in those patients. Patients with AMD in the present study might have used similar top-down cognitive processes, improving the acuity measured with the ETDRS in relation to the Single E test, as acuity worsened. The acuity measured with the Multiple E test, on the other hand, is independent of acuity when compared with the ETDRS.

As expected, the difference between the Single and Multiple E tests for the patients with AMD increased as acuity worsened. The evaluation of probability summation in persons with normal vision showed that the measured acuity was, on average, 0.10 logMAR units better with the Multiple E than the Single E test (Fig. 7).

**FIGURE 6.** By test and group, the proportion of participants exhibiting binocular inhibition (BR < 0.95), equality (0.95 < BR < 1.05), and summation (BR > 1.05). BR = better eye acuity/binocular acuity.

**FIGURE 7.** Box plots of the BRs of the AMD (n = 14) and control (n = 20) groups.
with the Single E test, and this value was within the limits of test-retest variability reported in the literature.45,46 These data indicate that for persons with normal vision, the presence of multiple optotypes does not improve measured acuity. For persons with AMD, on the other hand, the mean difference between the Single and Multiple E tests is 0.20 logMAR units, or two lines on a standardized chart, with large variability and limits of agreement that spanned 1.5 logMAR units. For patients with AMD, measurements of monocular and binocular acuity for the Multiple E test were higher than those for the Single E test, even though the latter test was free from the effects of crowding and lateral interactions. These data are in agreement with the values obtained by Harris et al.29 with the Multiple Black E test and a linear E test in patients with AMD and normally sighted controls tested with a plus lens that produced 20/70 or worse acuity on the linear test.29

For patients with macular degeneration, multiple optotype tests minimize the effects of fixation instability and defective gaze selection by maximizing the likelihood that one of the optotypes will fall on the most sensitive part of the retina. A useful application of these tests is the estimation of potential visual acuity at baseline before training or surgery. For instance, an acuity chart for patients with macular hole using multiple Landolt C rings was found to be a better predictor of postoperative acuity than standard charts.37 Another experiment using the Regan high-contrast repeat letter charts found that persons with normal vision show similar acuity values when tested with single, line (eight letters per line), and repeat letter acuity tests, whereas patients with macular degeneration show higher acuity with the repeat letter chart compared with the line chart and higher acuity with the single letter test compared with the line test, indicating deficiencies of gaze selection and crowding, respectively.48 The data from experiment 2 show that the mean binocular gains of normally sighted persons and patients with AMD are similar to each other whether they are measured with the Multiple E or with the Single E test. It appears that the visual systems of patients with AMD maintain their ability to combine the inputs from the two eyes, resulting in a binocular gain similar to that of normally sighted observers, in spite of the fact that, typically, AMD does not affect the two eyes equally and that the two monocular acuities can differ considerably. The data agree with previous results showing that older persons with and without interocular acuity differences measured with the ETDRS acuity charts exhibit small binocular acuity gain.46

Sometimes binocular performance is worse than that of the best eye alone, resulting in what is known as binocular inhibition. Using contrast sensitivity as a measure, studies have found binocular contrast inhibition in a large proportion of patients with AMD for gratings of low and medium spatial frequencies.49,50 In a recognition task using the Multiple E test we present here, Tarita-Nistor et al.51 found that, although binocular ratios were similar for young and elderly observers with good vision and observers with AMD, evidence indicated that age rather than disease determines the number of persons exhibiting inhibition.

Although interesting, the data on binocular summation do not elucidate the mechanisms underlying the processes that integrate the information from the two eyes in persons with AMD; furthermore, the present models based on visually normal observers are based on the assumption that the inputs from both eyes are similar. Even less is known about spatial summation in these patients.

In form perception, local elements are first detected at early levels of visual analysis and then are integrated into contours and shapes at intermediate levels of processing which, in turn, are combined to constitute complex objects at higher stages of processing. Furthermore, information is integrated across space, as exemplified by spatial summation, wherein performance improves with increasing pattern size. This summation occurs over a limited spatial extent, after which, depending on stimulus contrast, performance stabilizes.52 At lower levels of processing, summation is indicative of center-surround interactions. At intermediate levels of processing, it offers a window on how information is integrated or pooled. In a study of the effect of age on spatial summation and suppression in humans, older observers were found to exhibit less suppression than younger observers, suggesting that center-surround interactions are modified by age.52 In addition, performance on contrast-defined stimuli declined more with age than performance on luminance-defined stimuli, suggesting that cortical involvement varies with age.53,54 At intermediate stages of processing, other results indicate that discriminating deviations from circularity for a subset of patterns is not affected by age54 but that performance worsens for observers with AMD, suggesting a deficit for global form perception.5 To date, no studies have evaluated the nature of spatial summation in patients with macular deficits.

Finally, low-contrast spatial vision is a better predictor of subsequent acuity loss with aging5.56 than standard high-contrast clinical tests. Psychophysical data from patients with AMD consistently show reduced function, not for the high-contrast, high-illumination targets of standard clinical acuity tests but for medium- and low-contrast targets.2,6,57 One further advantage of the computerized acuity test we present here is the possibility of varying contrast43 so that it can be used in the early detection of macular disease.

The results presented here indicate that typical clinical measures of acuity may underestimate the residual visual abilities of patients with AMD. The multiple-optotype, reversed-polarity test provides a measure of the optimal visual acuity a person is capable of; in this sense, it could be a useful tool for assessing rehabilitation progress.

Acknowledgments

The authors thank Linda Lillakas for her comments on the manuscript, and they thank Gillian Hurwitz and Emad Eskander for help with data collection.

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