The Different Effects of Aging on Normal Sensitivity in Flicker and Light-Sense Perimetry

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Purpose. To verify whether or not an accelerated loss at an older age for normal sensitivity in the central visual field is present when using the stimulus configuration of conventional white/white automated light-sense perimetry and the stimulus configuration of the automated flicker perimeter developed by one of the authors (BJL).

Methods. One hundred thirty eyes of 130 normal subjects aged 9 to 86 years were tested with the Humphrey-Field-Analyzer 640, program 30-2, and our automated flicker perimeter. In addition, short introductory learning programs were used for both techniques. All tests were performed in random order.

Results. Mean critical flicker fusion frequency shows a linear loss over the entire age range (r = -0.5546, P < 0.0001, slope a = -0.3820 dB/decade), whereas mean light difference sensitivity decreases only slightly up to 46 years of age (r = -0.0118, P = 0.9226, slope a = -0.0153 dB/decade), with a marked acceleration above 46 years of age (r = -0.7304, P < 0.0001, slope a = -2.0640 dB/decade).

Conclusions. The absence of an accelerated loss at an older age for critical flicker fusion frequency (CFF) and the presence of such a loss for light-difference sensitivity (LDS) might be attributed to the independence of a flickering stimulus from disturbing effects induced by the ocular media at an older age as proposed by one of the authors. The different age effects for CFF and LDS could also be explained by different age-related losses at different sites and for different neuronal populations throughout the visual pathways. Investig Ophthalmol Vis Sci. 1994;35:2741–2748.
All eyes were tested with the automated flicker perimeter developed by Lachenmayr Ki:M using CFF as a reference to decide whether or not the age-dependent cell decrease is linear or nonlinear. Due to small sample size and enormous individual variability, however, the few currently available studies investigating age-induced cellular loss at different levels of the visual system do not provide convincing statistical evidence to decide whether or not the age-dependent cell loss is linear or nonlinear.

If the accelerated loss at an older age is due to preretinal factors, then a stimulus configuration largely independent of the ocular media should show no such media-induced accelerated loss. The automated flicker perimeter testing the distribution of critical flicker fusion frequency (CFF) in the central visual field, developed by one of the authors (BJL), provides a stimulus configuration that is resistant to disturbances of the ocular media. The flickering stimulus of 1° diameter largely eliminates the influence of light scatter, and the monochromatic yellow stimulus (wavelength 590 nm) minimizes the influence of lens absorption.

The present study aimed to answer the following questions: Is there an accelerated loss at an older age for normal sensitivity in the central visual field when using a stimulus configuration largely independent of preretinal factors, as in our automated flicker perimeter? Is there such an accelerated loss when using the stimulus configuration of conventional white-on-white automated light-sense perimeter? To answer these questions, normal sensitivity for automated flicker and light-sense perimetry was determined in 130 eyes of 130 normal subjects 9 to 86 years of age.

MATERIALS AND METHODS

Flicker Perimetry

All eyes were tested with the automated flicker perimeter developed by Lachenmayr using CFF as a threshold criterion. Yellow light emitting diodes (wavelength 590 nm) of 1° diameter served as stimuli (mean luminance of stimulus and surround = 50 cd/m²). The modulation of the stimulus was rectangular with a superimposed Gaussian onset and offset to rule out edge effects. For the present study, a grid was used testing 93 points up to 40° of eccentricity in the central visual field. The location of the test points is evident from the normal flicker field, which is demonstrated in Figure 1a. Stimulus presentation, registration of the responses, and calculation of the results were performed by a computer. For threshold determination, a two-fold bracketing procedure was used. The frequency values were transformed from the linear cycles per second (cps)/Hz scale into a logarithmic decibel scale according to the following formula:

\[ \text{CFF(dB)} = 20 \cdot \log \text{CFF (cps/Hz)}. \]

To rule out a possible learning effect, a short introductory program testing 13 points up to 30° was used before the standard program.

Light-Sense Perimetry

In addition, light-difference sensitivity (LDS) in the central visual field was determined for all eyes with the Humphrey-Field-Analyzer 640, program 30-2 (6° rectangular grid, 77 points up to 30° (Fig. 1b), full threshold strategy). The STATPAC printout of the Humphrey-Field-Analyzer was used for the statistical analysis. Again, a custom-made introductory learning program testing 13 points up to 30° was used before the standard program.

Field tests were performed in random order for each individual. For the statistical analysis of the data performed with the SPSS-software, left eyes were projected onto the grid of a right eye.

Subjects

The study population consisted of 130 eyes of 130 normal subjects 9 to 86 years of age (mean, 43.1 years; median, 43.5 years). Subjects were excluded if one of the following criteria applied:

- corrected decimal visual acuity <0.8 (20/25);
- refractive error > ±5 D sph or 2 D cyl;
- intraocular pressure > 21 mm Hg;
- media opacities (for example, nuclear sclerosis or subcapsular opacifications detectable with the slit lamp by an experienced ophthalmologist and considered abnormal according to the subject's age);
- abnormalities of the fundus (for example, pigmentedary changes of the macula or sclerotic changes of the retinal vessels or the choroid, detectable with indirect ophthalmoscopy in mydriasis by an experienced ophthalmologist and considered abnormal according to the subject's age);
- severe ocular trauma or any ocular surgeries in the subject's history;
- family history of glaucoma or any inheritable ocular diseases;
- history of poorly controlled hypertension, diabetes mellitus, multiple sclerosis, cerebrovascular
attacks, epilepsy, or ingestion of any drugs that affected psychological function or mental state 24 hours before field testing.

For all subjects, a report of complete ophthalmologic status was provided including refraction, tonometry, examination of the anterior segment with the slit lamp, and examination of the fundus with indirect ophthalmoscopy in mydriasis. If both eyes of a subject were eligible according to these exclusion criteria (117/130), then one eye was randomly chosen for the study. Normal subjects with only one eye passing the exclusion criteria (13/130) were admitted to the study only if the reduction of decimal visual acuity below the limit of 0.8 (20/25) in the fellow eye was caused by a strictly unilateral disease; in this sense, only unilateral trauma or retinal detachment were accepted as strictly unilateral disease. The reliability criteria of the Humphrey 30-2 fields were as follows:

- **False-positives**
  - mean 4.3%, median 0%, mode 0%, SEM 0.6%, SD 6.7%, minimum 0%, maximum 31.3%;
- **False-negatives**
  - mean 2.8%, median 0%, mode 0%, SEM 0.5%, SD 5.2%, minimum 0%, maximum 27.8%;
- **Fixation losses**
  - mean 15.2%, median 8.3%, mode 0%, SEM 1.7%, SD 18.9%, minimum 0%, maximum 100%.

This research followed the tenets of the Declaration of Helsinki, and informed consent was obtained from all subjects before testing.

**RESULTS**

In a normal subject, CFF increases for our stimulus conditions from the fovea to the paracentral visual field, remaining at a high level up to eccentricities of 20° to 30° and dropping below the foveal value in the periphery. An example of an individual field in a 41-year-old subject is shown in Figure 1a. In this case, foveal CFF was 32 dB, increased to 34 to 35 dB between 10° and 25°, and dropped to 31 dB at 40°. In contrast to this, LDS decreased steadily from the fovea to the periphery, as demonstrated in Fig. 1b for the same subject. Foveal LDS amounted to 38 dB and dropped continually to values of 25 to 32 dB at 30° of eccentricity.

For all tested locations (93 for the flicker perimeter, 77 for the Humphrey-Field-Analyzer), CFF and LDS were plotted as a function of the subject's age. Both CFF and LDS show a loss of sensitivity with increasing age. For CFF, however, the loss of sensitivity is uniform over the entire life span, whereas for LDS there is a fairly distinct acceleration of loss from 50 to 60 years of age.

Global field indices were calculated as follows for each subject and field:

- **Mean critical flicker fusion frequency (MF)** = the average of all 93 CFF values of the flicker field.
- **Mean light-difference sensitivity (MS)** = the average of all 77 LDS values of program 30-2.

MF and MS as a function of age are shown in Figure 2. MF decreases linearly with age: \( r = -0.5546, P \)
< 0.0001, slope of the regression line \( a = -0.3820 \) dB/decade. Unlike MF, MS drops only slightly up to 46 years of age, and there is a marked increase of loss at an older age. Up to 46 years of age (index 1): \( r_1 = -0.0118, P = 0.9226 \), slope of the regression line \( a_1 = -0.0153 \) dB/decade. Older than 46 years of age (index 2): \( r_2 = -0.7304, P < 0.0001 \), slope of the regression line \( a_2 = -2.0640 \) dB/decade.

To determine whether the influence of age on MF and MS is better described by a linear or a bilinear regression, the statistical approach of Owsley et al was used. These authors have developed a maximum likelihood procedure for comparing linear versus bilinear fits. Two candidate models are calculated. The first model consists of a linear fit, that is, a single straight line. The second model defines two straight-line segments that meet at a point. For each of the lines, the slope and the intercept are calculated. In addition, the breakpoint, that is, the value of the abscissa where the two lines intercept, is given. For both models the multiple correlation coefficient is derived as the \( R^2 \) value RSQ. A test is performed to decide whether the two-line model is necessary (likelihood ratio test). The computed value is compared to critical values of a chi-square random variable with 2 degrees of freedom. The null hypothesis is that two lines are not necessary, and this is rejected for large values of the calculated chi square. The application of this statistical procedure to our data gives a chi square of 43.24 \((P < 0.0001)\) for MS, and a chi square of 0.87 \((P < 0.6483)\) for MF. This implies that the MF versus age distribution is adequately described by a single-line model, whereas the MS versus age distribution requires a two-line model. For MS, a breakpoint of 46 years of age is calculated; this breakpoint was already used for the description of our data in the preceding paragraph.

The distribution of the underlying data is fairly normal for the CFF values of the 93 test locations (skewness: median \(-0.520\), mean \(-1.120\), minimum \(-6.543\), maximum 0.849; kurtosis: median 1.812, mean 6.852, minimum \(-0.434\), maximum 60.605) and MF (skewness \(-0.631\); kurtosis 0.832). For the LDS values of the 77 test locations (skewness: median \(-1.289\), mean \(-1.946\), minimum \(-3.280\), maximum 1.772; kurtosis: median 2.864, mean 3.898, minimum 0.189, maximum 15.720) and MS (skewness \(-1.452\); kurtosis = 2.470). There is, however, a pronounced deviation from a normal distribution. Because of this, in addition to the linear regression analysis of Figure 2, for MF and MS medians, 5th, 16th, 84th, and 95th percentiles were calculated after dividing the subjects into age brackets of 10 years each (Fig. 3). For both MF (Fig. 3a) and MS (Fig. 3b), the linear regression lines fall within the 16th to 84th percentile intervals and fit in well with the medians. Thus, the use of the regression lines seems to be permissible for the subsequent discussion of our data.

**DISCUSSION**

For the stimulus conditions of our flicker perimeter (1° diameter, 50 cd/m² luminance), maximum temporal resolution appears in the paracentral and midperipheral visual field. This confirms the data reported by Hartmann et al, who found an increase of CFF from the fovea to the periphery in the case of large stimulus diameter and high photopic adaptation level using a slightly different experimental setup. Earlier studies did not agree. Whereas Hylkema describes a similar increase of CFF from the fovea to the periphery, as was found in our study, various other authors report a decrease of CFF toward the periphery similar to the behavior of LDS. These studies, however, differ in stimulus size, stimulus luminance, adaptation level, stimulus duration (problem of flicker adaptation), and stimulus generation (projection technique). For the stimulus conditions of our flicker perimeter, a large area of the paracentral and midperipheral visual field has a high temporal sensitivity with a broad dynamic range in normal eyes. This is of clinical interest, especially for the early diagnosis of glaucomatous field loss, which frequently occurs at an early stage in the paracentral or midperipheral visual field. This could be one of the reasons for the high sensitivity of flicker perimetry or similar techniques for the early detection of glaucomatous field loss.

There are a few reports dealing with the influence of age on CFF in the central visual field of normal eyes. Wolf et al, using a 2° stimulus at an adaptation level...
of 3.4 cd/m², found a continuous decrease of CFF as age increases. Tyler described an increase of flicker sensitivity for normal subjects up to 16 years of age, with a slight but continuous loss of sensitivity at older ages for a 5° stimulus at 400 cd/m². The continuous loss of flicker sensitivity above 16 years of age is similar to the results of our study. We did not, however, find an increase of sensitivity for very young normal subjects, which could be due to the fact that there were few individuals younger than 16 years of age in our study population.

How do our results compare with the normal data reported in the literature for the Humphrey-Field-Analyzer, program 30-2? Brenton and Phelps (102 eyes of 102 subjects) and Heijl et al. (74 eyes of 74 subjects) found a continuous loss over their age ranges. In contrast, in the study of Iwase et al. (147 eyes of 108 subjects), MS was almost independent of age up to approximately 40 years and showed an accelerated linear loss at older ages. Johnson et al. (124 eyes of 62 subjects) also describe a linear loss for their study population, despite the fact that the underlying data show a slight tendency to an accelerated loss above 60 years of age. Figure 4 summarizes the linear regression analyses of these studies using the regression data provided by the authors themselves and recalculating the data of Heijl et al. and it compares them to the results of our study. It is interesting to see that the regression lines of Iwase et al. fall within the 16th to 84th percentile intervals of our data up to 70 to 80 years of age. The data of Heijl et al. and Brenton and Phelps fit in well with our data up to 55 years of age. At older ages, there is a marked discrepancy. The regression line of Johnson et al. agrees least with our data and the data of the other authors.

Currently, it is unclear why some studies find an accelerated loss of MS at an older age and some do not. There are, of course, slight differences in the exclusion criteria, the recruitment of subjects, and their perimetric experience. These differences, however, cannot account for this discrepancy. When looking at the limits for visual acuity, for example, subjects were excluded from the study of Brenton and Phelps if decimal visual acuity was less than or equal to 0.67 (20/30) and from the study of Heijl et al. if decimal visual acuity was less than 0.67 (20/30) at 50 years of age and older, whereas in our study subjects were generally excluded if decimal visual acuity was less than 0.8 (20/25). In the study of Iwase et al., a decimal visual acuity of even 1.0 (20/20) was required! In fact, those studies reporting an accelerated loss at an older age...
age (Iwase et al and our study) used an even stricter acuity criterion.

The controversy concerning the presence or absence of an accelerated loss of sensitivity at an older age is also found in normal studies of other automated light-sense perimeters. Haas et al (203 eyes of 153 subjects) published normal data for the Octopus (Interzeag AG, Schieren, Switzerland) program JO (similar to the current program G1) and described a linear loss of sensitivity with increasing age. When looking at the underlying scatterplot, however, one can see that there is a tendency to an accelerated loss above age 65. A more recent normal value study for the new Octopus 1-2-3 performed by Hendrich et al (128 eyes of 128 subjects) demonstrates an accelerated loss of sensitivity above age 50 (—1.6 dB/decade, r = —0.6316, P < 0.001), with a slight but not significant loss at a younger age (—0.3 dB/decade, r = —0.2323). Another study with the Octopus 1-2-3, by Okuyama et al (203 eyes of 153 subjects) published normal data for the Octopus (Similar to the current program GL1) and described a linear loss as age increases. The underlying data, however, again show a slight tendency to an accelerated loss above age 65. Normal data for program GL1 of the Rodenstock Peristat 433 (G. Rodenstock Instruments GmbH, Ottobrunn-Riemerling, Germany) established by Viell et al also demonstrate an accelerated loss above age 57 (—2.5 dB/decade, r = 0.6259, P = 0.0002), with a slight but not significant loss at a younger age (—0.2 dB/decade, r = 0.1649). In this context, the review article of Johnson and Choy raises some interesting aspects for the definition of age-related normal data. Summarizing a number of normal value studies for various psychophysical and electrophysiological criteria, they concluded that visual function generally declines only slightly or not at all up to 50 to 60 years of age and is followed by rapidly accelerated loss at older ages. They attribute this accelerated loss to some kind of “subclinical pathology” that obviously may be present in older normal subjects. More specifically, the authors address the ocular media as a possible reason for this so-called subclinical pathology.

The most exciting observation of the present study is the simultaneous absence and presence of an accelerated loss of sensitivity at older ages in the same study population when using different perimetric threshold criteria. As already mentioned in the introduction, it is possible that different subsets of cells are responsible for these two psychophysical functions, and they may be subject to different age effects. At present, there is no histologic or neurophysiologic evidence available for such a hypothesis. Another possible explanation can be found in the characteristics of the two threshold criteria used in the present study. Measurements of LDS were performed with a white/white projection-type stimulus of 0.43° diameter and 100 msec duration of presentation at an adaptation level of 10 cd/m²; CFF was assessed by a flickering stimulus of 100% rectangular modulation, a diameter of 1°, and an overall stimulus duration of 3 sec at an adaptation level of 50 cd/m².

A flickering stimulus minimizes the effect of lens scatter (adequately demonstrated by an experimental study using artificial media opacities), a monochromatic yellow stimulus minimizes the effect of lens absorption, and the higher adaptation level of 50 cd/m² reduces the possible influence of pupil size. Is a large, bright, static, yellow stimulus at a high adaptation level equivalent to a flickering stimulus in this respect? As can be derived from the study of Johnson et al, who compared three different stimulus conditions for automated perimetry in the central visual field, it is not. Even for a yellow stimulus of 1.72° diameter against a yellow surround of 200 cd/m² (“high” yellow/yellow condition), there is a tendency (perhaps not statistically significant) for an accelerated loss above age 60. By using a stimulus configuration that minimizes lens absorption effects, it is not possible to abolish completely accelerated loss at an older age. Only by using a flickering stimulus, as in the present study, is this acceleration effect gone. The differences observed for our two stimulus conditions cannot be explained by the slight differences in pupil size (10 cd/m² versus 50 cd/m²). Correcting MF for pupil size by multiple regression analysis reduces the slope from a = —0.3820 dB/decade to a = —0.3163 dB/decade (P < 0.0001). A similar correction of MS for pupil size changes the slope below age 46 from a = —0.0153 dB/decade to a = —0.0221 dB/decade (P = 0.8981) and above age 46 from a = —2.0640 dB/decade to a = —1.9985 dB/decade (P < 0.0001). The different age effects for MF and MS remain after correction for pupil size. Thus, we may conclude that the absence of an accelerated loss at an older age, as observed for our flicker perimeter, could be attributed to the use of a flickering stimulus that can eliminate the influence of scatter caused by the ocular media. This has also been demonstrated in the previously mentioned experimental study with artificial media opacities, where even slight opacities caused a measurable reduction of LDS with no effect on CFF.

Psychophysical data concerning glare sensitivity and measurements of lens absorption and scatter support the idea that retinal image quality is increasingly disturbed at an older age. This detrimental effect starts at approximately 50 to 60 years of age, depending on the criterion used for assessment, and increases rapidly in a nonlinear fashion as age increases. Thus, the study of Aulhorn and Harms, quantifying mesopic vision and glare sensitivity in a large normal population, shows a tremendous increase in glare sensitivity at 50 years of age, which, in this study population, can be attributed only to the disturbing influence of the ocular media. Various studies measuring lens trans-
mission, lens absorption, lens autofluorescence, and scatter show similar behavior, although there are some reports claiming a linear increase of optical density of the ocular media with age, as already mentioned in the introduction. Measurements of lens backscatter in normal eyes with the Opacity Lens Meter (Interzeag) demonstrate a clearly nonlinear increase of readings at an older age, with a marked acceleration at approximately age 50. Naturally, the increasing optical density of the ocular media at an older age with tremendous interindividual variability shows a gradual transition to subclinical pathology, as addressed by Johnson and Choy, or to actual pathologic conditions. Thus, any kind of threshold criterion that depends on retinal image quality should show some kind of accelerated loss of sensitivity at an older age. The results of the recent study of Curcio et al dealing with the aging of human photoreceptors are consistent with the hypothesis that visual deficits at older ages may be largely due to optical factors at high photopic levels.

In conclusion, we think the absence of an accelerated loss at an older age for flicker perimetry might be attributed to the independence of our CFF stimulus configuration from retinal image quality and, thus, from disturbing effects due to the optical media. This is another interesting aspect of our flicker technique, in addition to the experimental and clinical data acquired in the past. Whether or not the different age effects observed for CFF and LDS are due to preretal factors, that is, the ocular media, or to different age-related losses for different neuronal populations in the visual system cannot be answered unequivocally at the moment. More extensive morphologic and neurophysiologic examinations exploring the age effects at different sites and for different neuronal populations throughout the visual pathways are required.

Key Words
flicker perimetry, light-sense perimetry, normal data, age-related loss, visual field

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