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Effect of Decreased Retinal Illumination on Frequency Doubling Technology

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Purpose: To investigate the effect of changes in retinal illumination on Frequency Doubling Technology (FDT).

Methods: Five eyes, of 5 adults who were free from identifiable ocular pathology, were examined using the Snellen chart and the Pelli-Robson chart, conventional automated perimetry, and the full threshold N-30 program of FDT. Each test was performed with and without a 0.9, 1.5, or 2.4 log unit neutral-density (ND) filter placed before the eye. Furthermore, the influence of pupil diameter on FDT test results was compared after treatment with pilocarpine or cyclopentolate with the influence of ND filters.

Results: All tests showed a decrease in sensitivity with decreasing retinal illumination. Frequency Doubling Technology showed an especially pronounced and significant decrease in sensitivity. The maximum mean threshold difference in FDT results with ND filter was 31.2 dB while that with the Humphrey Field Analyzer and the Pelli-Robson chart were 13.3 dB and 0.66 log contrast, respectively. The mydriatic state of the pupil increased the sensitivity of FDT and the miotic state decreased it to about the same extent as the the 0.9 ND filter.

Conclusion: The change in retinal illumination has more impact on FDT than on spatial contrast tests and conventional automated perimetry. It is important to take this into account in evaluating FDT results. **Jpn J Ophthalmol 2000;44:489–493** © 2000 Japanese Ophthalmological Society

Key Words: Contrast sensitivity, frequency doubling perimetry, temporal frequency, visual field glaucoma.

Introduction

The retinal ganglion cells are damaged in patients with glaucoma before visual field loss is detected by conventional light-sense perimetry.[1] Many tests for detecting early glaucoma have been reported and are being investigated to determine efficacy.[2–4]

The retinal ganglion cells of different sizes have distinct physiological functions. Small cells that project to the parvicellular layers of the lateral geniculate body belong to the "P-cell pathway," which conveys information on color, high spatial frequency, and pattern discrimination, while large cells that project to the magnocellular layer belong to the "M-cell pathway" dealing with motion detection, low spatial frequency and high temporal frequency.[5] Large optic nerve fibers (M-cell) are lost selectively in chronic experimental and human glaucoma.[1,6,7] Therefore, tests operating on the M-cell pathway, ie, flicker perimetry and motion detection test, were thought to have advantages for detection of early glaucoma.[2,8]

Furthermore, there are two subtypes of M-cell. One is the Mx-cell, which has linear characteristic summation in receptive fields and another is the My-cell, which has a nonlinear character. The My-pathway appears to be a strong candidate for an effective screening procedure for glaucoma because My-cells have a larger nerve fiber diameter and fewer redundancies than Mx-cells.[9] The My-cell represents only 3–5% of the total number of ganglion cells, indicating that the loss of even a single cell will lead to a distinct scotoma in the lattice of My-cell receptive fields.[9]

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When a low spatial frequency sinusoidal grating undergoes high temporal frequency counterphase flicker, its perceived spatial frequency is twice its actual spatial frequency.[10] This phenomenon, called frequency doubling illusion, is a result of the nonlinearity of the My-pathway in response to contrast.[11] Recently, several investigators reported that contrast thresholds for detection of frequency-doubled stimuli are effective in detecting early glaucoma.[9,12] Johnson and Demirel[13] report a higher sensitivity and specificity for detecting visual field loss with frequency doubling stimuli than with a steady sinusoidal grating or simple flicker stimuli.

The purpose of this investigation was to examine the effect of change in retinal illumination on Frequency Doubling Technology.

Materials and Methods

Subjects

Subjects were 5 adults (5 eyes), mean age 32 years (range, 23–42 years), who were free from identifiable ocular pathology. The diameter of pupils ranged from 3.5–4.5 mm. The test schedule was clearly demonstrated to the subjects. Only right eyes were tested, with their best spectacle correction in place.

Frequency Doubling Technology

The contrast thresholds for detection of frequency-doubled stimuli were measured with the Frequency Doubling Technology (FDT) perimeter, produced jointly by Welch Allyn (Skaneateles Falls, NY, USA) and Humphrey Zeiss (St Louis, MO, USA).

The FDT presents frequency-doubling stimuli (10° × 10°) with low spatial frequency, co-sinusoidal grating (0.25 cycle/°) and high temporal frequency (25 Hz counter-phase flicker) on a square background display (40° × 40°, 100 cd/m^2). Stimulus duration (range, 200–400 ms) and inter stimulus intervals (range, 0–500 ms) are random. Contrast ranges of stimulus are 56 dB (0%) to 0 dB (100%) in log steps. Operation software version 1.02 has a Screening C-20 program for screening test, and Full Threshold C-20 and Full Threshold N-30 for the threshold test. Threshold tests give results of threshold (dB) plot, deviation plot with five probability level classifications based on age-related normative reference, MD (mean deviation) and pattern standard deviation statistical Global Indices values and reliability indices (Fixation, False positive, and False negative). The results of thresholds were divided into four zones for investigating eccentricity of the retina (Figure 1, left).

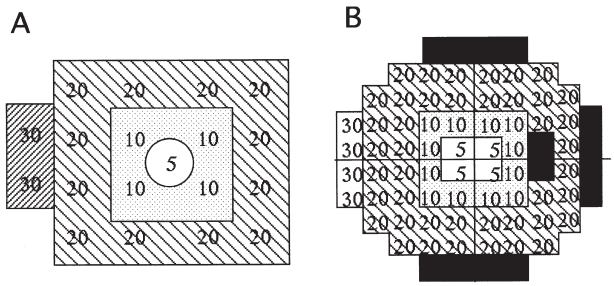

Figure 1. Zone of Humphrey Field Analyzer (HFA) and Frequency Doubling Technology (FDT). (**A**) Left figure shows 19 test locations of FDT Full Threshold N-30 program that were divided into four zones (5°, 10°, 20° and nasal 30°) for comparison. (**B**) Right figure shows 77 test locations of HFA central 30-2 program that were divided into five zones (fovea, 5°, 10°, 20°, and nasal 30°) for comparison.

Conventional Visual Field Test

Differential light sensitivity perimetry was performed with a Humphrey Field Analyzer (HFA), using target size III (0.43°) and Program Central 30-2. The test points were divided into four zones for comparison with FDT (Figure 1, right).

Contrast Sensitivity Test

Contrast sensitivity was tested with a Pelli-Robson chart.[14,15] This chart consists of letters of constant size arranged in 16 groups of three. Contrast ranges of the letters are 100% to 0.56% in 0.15 log unit steps. The chart was used at 1 meter at a mean luminance of 65 cd/m^2.

Procedures

The visual acuity test, Pelli-Robson chart test, HFA test, and Full Threshold N-30 of FDT were performed with and without a 0.9 or 1.5 or 2.4 log unit neutral-density (ND) filter placed before the eye. The eyes adapted to the filter after 5 minutes. Frequency Doubling Technology was performed twice to confirm that results could be reproduced. Furthermore, the influence on FDT results of pupil diameter after treatment with pilocarpine or cyclopentolate was investigated.

Results

Reproducibility of FDT

It takes 5.03 minutes to test 1 eye with the Full Threshold N-30 test. Mean difference of threshold without the filter is shown in Figure 2. The reproducibility of FDT was good even for a peripheral test field. The correlation coefficient of the first and second mean thresholds of FDT with and without ND

filter was 0.978 ($P < .0001$). There was good reproducibility in all test ranges (Figure 3).

Effect of ND Filter

All subjects had good visual acuity 1.5 without and with the 0.9 ND filter. It decreased to 0.67 with the 2.4 ND filter. Figure 4 shows the effect of each filter on the results of each test. All tests showed a decrease in sensitivity as retinal illumination decreased. Frequency Doubling Technology showed an especially pronounced and significant decrease in sensitivity. The maximum mean threshold difference with ND filter was 31.2 dB with FDT while the mean difference with HFA and the Pelli-Robson chart was 13.3 dB and 0.66 log contrast, respectively.

Eccentricity of the Retina

Figure 5 shows the effect of eccentricity of the retina in HFA and FDT tests. There is a 15-dB difference between fovea and nasal 30° in HFA. However, only a 2.5-dB difference between fovea and nasal 30° was seen in FDT. These differences due to eccentricity were smaller in dark illumination.

Effect of Pupillary Diameter

Mean diameters of the pupils instilled with pilocarpine or cyclopentolate were 1.7 and 8.3, respectively. Mydriasis increased sensitivity of FDT 2.90 dB ($P = .047$, paired t-test) and miosis decreased it 7.09 dB ($P = .027$, paired t-test), comparable to the effects of the 0.9 ND filter.

Discussion

In this study, we confirmed the significant effect of change in retinal illumination on the FDT. This effect was confirmed even when the diameter of the pupil changed. It is important how the diameter of the pupil affected test measurements. The effect was significant for FDT, however, much less so for HFA.

It is questionable if we can compare the thresholds (dB) of FDT and HFA directly, or not. The threshold of FDT is the minimum contrast of frequency-doubling illusion on one hand and the threshold of HFA is differential light sensitivity on a background of 31.5 apostilb (asb) on the other. To compare these thresholds fairly, we calculated the log contrast sensitivity of HFA and FDT with the same formula.

In FDT, the threshold is calculated with this formula:

$$dB = H\,10 \times log\,(2048/c) = -H \times 10 \times log(c/2048)$$

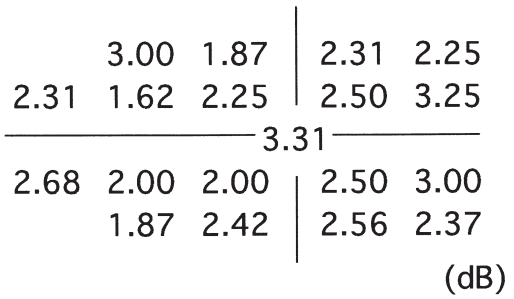

Figure 2. Mean intra-test difference of Frequency Doubling Technology (FDT). Each value shows mean of difference between first test threshold and second test threshold at respective 19 test locations of FDT in right eye measurement. Mean fluctuations ranged from 1.62 dB to 3.31 dB.

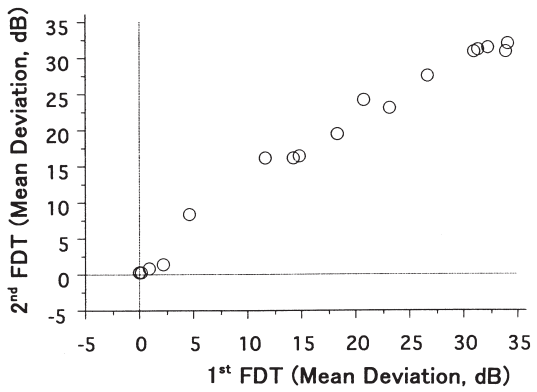

Figure 3. Reproducibility of Frequency Doubling Technology (FDT). Correlation coefficient between mean threshold of first measurement of FDT and that of second measurement is significant ($r = 0.978$, $P < .0001$).

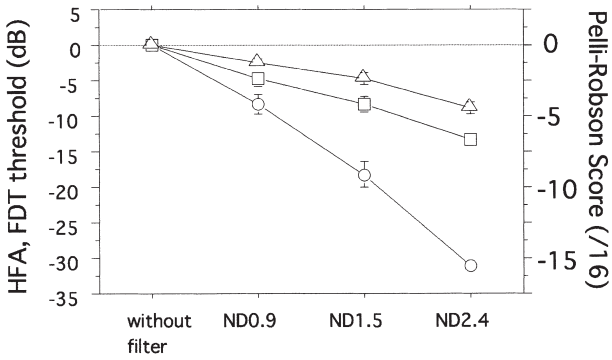

Figure 4. Effect of neutral-density filter. Circles, squares, and triangles show thresholds of Frequency Doubling Technology (FDT), Humphrey Field Analyzer (HFA) and score of Pelli-Robson chart, respectively. Bars show one standard error. FDT showed especially pronounced and significant decrease in sensitivity with decreasing retinal illumination.

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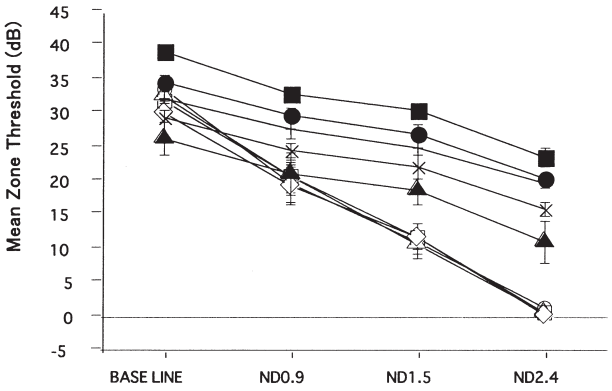

Figure 5. Effect of eccentricity and illumination of retina. Mean zone thresholds of Frequency Doubling Technology (FDT). △:5°; ○:10°; □:20°; ◇:nasal 30°. These similar values were decreasing with neutral-density (ND) filters. Mean zone thresholds of Humphrey Field Analyzer (HFA). ■: fovea, ●:5°; +: 10°; ×:20°; ▲:30°. These wide-ranged thresholds of HFA were decreased by ND filter, keeping the difference in thresholds.

where H is approximately 2. The c ranges from 0–2048. The $c/2048$ means a minimum perceptive contrast.

Contrast is often defined by a formula:

$$contrast = delta\ L / L_{AVE}$$

where *delta L* is the difference in luminance between the peak and the average luminance. L_{AVE} is the average luminance.

In sinusoidal grating, this formula is:

$$contrast = delta\ L / L_{AVE} = (L_{max} - L_{min}) / L_{max} + L_{min}$$

where L_{max} is maximum luminance of stimulation. L_{min} is minimum luminance of stimulation.

This formula is known as Michelson's formula.[16] We know that the $(L_{max} + L_{min})$ is always 200 cd/m^2, and $(L_{max} - L_{min})$ is the variable in FDT.

Therefore,

$$\log contrast = log[L_{max} - L_{min})/(L_{max} + L_{min}] = log(c/2048) = -dB/20$$

Likewise, we postulate, even though HFA does not have a sinusoidal grating, that modulation of HFA is as follows:

$$log\ contrast = log[\{(Lstm + Lbg) - Lbg\}/\{(Lstm + Lbg) + Lbg\}] = log[(Lstm + 2Lbg)/Lstm]$$

where L_{stm} is the luminance of the stimulus. L_{bg} is the luminance of the background.

In HFA, the stimulus ranges are 10 asb to 10,000 asb in 0.1 log unit steps. The stimulus of HFA is L_{stm}(asb) = 10(4 − dB/10)(asb). The background luminance of the HFA is L_{bg} = 31.5 asb.

Figure 6 shows the contrast sensitivity curve of three tests. In all tests, especially in FDT, there is a decrease in contrast sensitivity with decreasing retinal illumination. This phenomenon is not caused by a change of the contrast on the retina. Modulation of the illumination at the retina never changes with the ND filter, because the filter decreases both L_{max} and L_{min} at the same ratio.

Generally, it is well-known that contrast sensitivity on the same spatial frequency is higher in bright conditions than in dimmer conditions.[5] The amount of decreasing sensitivity caused by the lower light level is greater at high spatial frequency than it is at low spatial frequency.[5,17] In one report, the log contrast sensitivity of the low spatial frequency (0.5 cycle/°) in bright light level (107 cd/m^2) and dark light level (0.107 cd/m^2) is −1.799 and −1.397, respectively[17]). This report supports the results of our study except that the threshold of FDT decreases disproportionately.

This significant sensitivity loss for FDT was thought to be caused by a different mechanism of spatial contrast sensitivity than for other tests. We postulate that rod-cone interaction is responsible for this phenomenon.

The background luminance under 0.9, 1.5, and 2.4 ND filter is 39.55, 9.935, and 1.251 asb, respectively. The background of the 0.9 ND filter is in the photo-

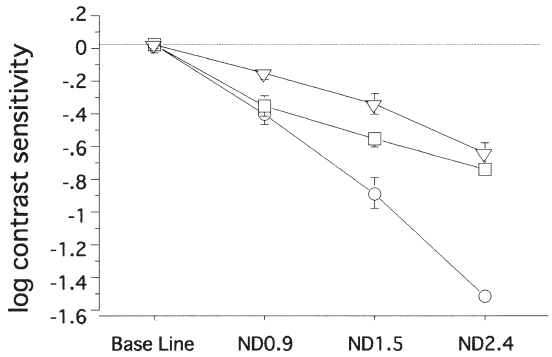

Figure 6. Change in log contrast sensitivity caused by neutral-density filter. Log contrast sensitivity was calculated for Frequency Doubling Technology (FDT), Humphrey Field Analyzer (HFA), and Pelli-Robson chart. Circles, squares and triangles show thresholds in FDT and HFA tests and score with Pelli-Robson chart, respectively. Bars show one standard error. FDT showed especially pronounced and significant decrease in sensitivity with decreasing retinal illumination.

pic range, but that of 1.5 ND and 2.4 ND filters are in the mesopic range. In the mesopic function, cone-detected thresholds are influenced by rods. This phenomenon is thought to affect all tests. However, FDT has one more disadvantage, that rods cannot detect flicker stimulus of 25 Hz. It was reported that rods interfere with cone sensitivity in the detection of flicker.[18] Both sensitivity loss of spatial contrast and flicker in the mesopic condition influence FDT. The dramatic sensitivity loss of FDT in the mesopic situation is evidence to support our hypothesis.

The effect of small pupil or medial opacity is clinically important in this test. We confirmed in 3 subjects that the significant effect of the smaller pupil with pilocarpine is the same as with the 0.9 ND filter. This is a reasonable change as an effect of decreased retinal illumination. A small pupil affects not only retinal illumination but also refraction error and diffraction. This study reveals that the effect of change in retinal illumination on the FDT is significant. In the case of mydriatic eyes, the increasing sensitivity of FDT supports the importance of retinal illumination in FDT.

It is difficult to determine what Hz of frequency doubling illusion is useful in glaucoma diagnosis. However, we can estimate it by the properties of both temporal and spatial contrast sensitivity in glaucomatous eyes, because the frequency doubling illusion is produced by low spatial frequency and high temporal frequency. There were two types of reports about temporal modulation transfer function properties in glaucomatous eyes. One is a sensitivity reduction at 30 and 40 Hz,[19] and the other is a sensitivity loss center at 15 Hz.[20] In normal eyes, the temporal modulation transfer function of higher frequency is more susceptible to dark illumination and aging than that of low frequency;[21] that is to say, a lower temporal frequency is more stable than a higher one. Therefore, we theorize that lower frequency, such as 15–20 Hz, is better for glaucoma diagnosis, because the frequency doubling illusion requires 15 Hz or more temporal frequency.[10]

The software of FDT is expected to improve in several stages.

We would expect that there will be improvements to take into account the pupil diameter, and to include a choice of temporal frequencies and a number of test points.

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