Temporal contrast sensitivity with peripheral and central stimulation in glaucoma diagnosis

Isabel M Velten, Matthias Korth, Folkert K Horn, Wido M Budde

Abstract

Aims—To evaluate temporal contrast sensitivity with full field, peripheral, and central stimulation and to determine the most sensitive corresponding retinal area for glaucoma damage.

Methods—Temporal contrast sensitivity was determined either with a full field, a peripheral annular area from 30° to 90°, or a central area from 0° to 30° at a frequency of 37.1 Hz. 232 eyes of 232 subjects were included. They were classified into four groups: eyes with ocular hypertension (OHT), n = 54), “preperimetric” glaucomas (n = 73) with glaucomatous optic disc abnormalities but no visual field loss, “perimetric” glaucomas (n = 53) with visual field loss, and 52 normals.

Results—In all four groups, temporal contrast sensitivity was almost equal with full field and peripheral, but significantly higher than with central stimulation (p <0.001). With regard to the diagnostic power of the three different stimulus areas, OHTs and glaucomas were found to be best discriminated from normals by peripheral stimulation.

Conclusions—According to these results, temporal contrast sensitivity seems to be determined by peripheral retinal areas. As the diagnostic power of the three different stimulus areas was best with the peripheral stimulation, this condition should be used for early glaucoma diagnosis.

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Temporal contrast sensitivity is thought to target mainly the functions of the magnocellular retinal ganglion cells (M type). The large retinal ganglion cells are known to be preferably damaged by glaucomatous optic nerve damage.

Subjects and methods

SUBJECTS

Subjects were recruited from our glaucoma service and from the hospital staff. Informed consent was obtained from each individual after an explanation of the nature and possible consequences of the study according to the...
Visual field indices as described by Flammer et al are calculated routinely by the Octopus 500 EZ program G1. Subjects performing in visual field testing with false positive and false negative responses of >12% were excluded. Normal visual fields were accepted even if the test was the first one for the subject. Abnormal fields (MD >2.8 dB, at least three contiguous test points 5 dB or more below the age corrected normal threshold) were accepted only if the subject had had at least two examinations with the Octopus 500 G1 perimetry.

The stereophotographies of the optic disc were interpreted and classified by one masked observer as already described. The stimulus of the used full field flicker test has already been described. A modified perimeter bowl was used to present a homogeneous full field diffuse white light stimulus. A sinusoidally flickering white light (frequency 37.1 Hz) was transmitted via glass fibre optics into the bowl of 58 cm in diameter providing a constant mean luminance of 10 cd/m². A modulatable 175 W high pressure xenon arc lamp (Cermax) was used for the illumination of the bowl. The lamp’s current provided by an appropriate power supply (PS 150–9, ILC Technology) was controlled by the sine wave of a digital function generator (DF 194, NF Instruments). The full field bowl was located in a darkened, isolated room. The linear and stable range of the light source was tested with a photodiode (SDC). The mean luminance (Lmean = [Lmax + Lmin]/2, with Lmax = luminance at the peak and Lmin = luminance at the trough of the sinusoid) was calibrated before each measurement with a digital photometer (Tektronix J 16, NIT’s probe J6503). Its value was adjusted to 10 cd/m² in each stimulus area by neutral density filters (Schott) for a pupil diameter of 4.5 mm. For all other pupil diameters the mean luminance was corrected as previously described so that the retinal illuminance was constant for all eyes. Pupil diameters for the full field condition did not differ significantly between the four study groups (unpaired t test, p >0.02, normals: 3.87 (SD 0.56) mm, OHTs: 3.67 (0.56) mm, “preperimetric” glaucomas: 3.62 (0.57) mm, “perimetric” glaucomas: 3.81 (0.85) mm). The temporal contrast is defined as C = (Lmax - Lmin)/(Lmax + Lmin) × 100%. With our light source, it could be varied from 10% to 58%.

The stimulus dimensions used were either the full field of 58 cm in diameter, a peripheral stimulus area from 30° to 90°, or a central area from 0° to 30°. Those areas not used for stimulation were screened by black cardboard except for that part of the bowl above the subject’s head where the light guide entered the perimeter. Thus, for central stimulation the 30° to 90° periphery was screened from illumination, while for peripheral stimulation a black 60° diameter disc covered the central area of the bowl (see Fig 1). In all three test conditions, the mean luminance of the stimulus areas was adjusted to the value determined before (see later). In order to check for possible

CLASSIFICATION OF SUBJECTS

The subjects were classified into four groups: normals, OHTs without any signs of glaucoma damage, “preperimetric” glaucomas, and “perimetric” glaucomas. The “preperimetric” and “perimetric” glaucoma groups included primary and secondary (pigmentary dispersion, pseudoxefoliation) open angle and low tension glaucomas.

**Normals**

Normals (n = 52, 29 females, 23 males, mean age 44.8 (11.8) years) had a maximum IOP above 21 mm Hg, a normal optic disc, and no visual field losses.

**OHTS**

Eyes with OHT (n = 54, 26 females, 28 males, mean age 44.8 (11.8) years) had no history of IOP above 21 mm Hg, a normal optic disc, and no visual field losses.

**“Preperimetric” glaucomas**

Eyes with “preperimetric” glaucomas (n = 73, 30 females, 43 males, mean age 46.5 (11) years) had early glaucomatous optic disc changes and no visual field losses. This group included 62 patients with maximum IOP above 21 mm Hg before treatment and 11 patients with “preperimetric” low tension glaucomas (LTG), presenting with a glaucomatous optic disc change only.

**“Perimetric” glaucomas**

The glaucoma category (53 eyes, 29 females, 24 males, mean age 51.4 (10.6) years) was defined by glaucomatous changes of the optic disc and glaucomatous visual field losses. This group included 31 patients with a maximum IOP above 21 mm Hg and 22 patients with LTG.

If both eyes were normal, one eye was chosen randomly. In glaucoma patients, the eye with the more advanced glaucoma damage was chosen. For both eyes in each subject the following examinations were conducted: best refracted visual acuity, perimeter with a computerised static projection perimeter (Octopus 500 EZ, program G1, three phases), slit lamp examination, gonioscopy, applanation tonometry, dilated fundus examination, and 15 degree colour stereophotography of the optic disc.
Peripheral
central stimulation

30°

Figure 1. A full field bowl (58 cm in diameter) was used to produce a homogeneous white flickering light. The areas to be tested were either the full field, a peripheral annular area from 30° to 90°, or a central area from 0° to 30°. Those areas not used for stimulation were screened by black cardboard.

different pupil sizes for the three different stimulus conditions pupil diameters were determined in a group of 16 normals. No significant differences were found between conditions (unpaired t test, p > 0.02). Thus, one may assume that all tests were carried out with comparable levels of retinal illumination under all conditions and in all subjects.

PROCEDURE
Without dark adaptation the participant was brought into the dark room and seated at the perimeter. No correcting lenses were used. For full field examination people were asked to look straight ahead into the perimeter. For testing the peripheral or the central areas the subject was instructed to fix one black (for the central stimulus) or white (for the peripheral stimulus) point in the centre of the bowl. The order of the three test conditions was chosen randomly for each subject. At the time of testing, all eyes had pupil diameters between 2 and 6 mm. The contrast of the whole field flickering stimulus was increased progressively in fixed steps of 0.1% until it was detected by the subject. Before testing the contrast threshold, a preview of the stimulus was given to each subject, and the test procedure was carefully explained. After one response, the flicker contrast was reduced to 0% for 5 seconds, and the threshold was tested twice more. Then the initial contrast was set about 25% above the contrast threshold found in the three previous tests. The flicker contrast was reduced in fixed steps of 0.1% until the subject noticed the flicker stimulus disappear. The six single values of the temporal contrast threshold were averaged and corrected according to Stiles Crawford effect for different pupil diameters as already described.15-17

The reciprocal of the resulting value is the temporal contrast sensitivity. Its log value was used for further evaluation.

In the normal eyes, log temporal contrast sensitivity decreased significantly (p < 0.01) with age (23–66 years). The OHT and “preperimetric” glaucoma group did not differ significantly from normals in mean age (p > 0.01), but there was a significant difference in the “perimetric” glaucoma group. Thus, before statistical analysis, the values of the temporal contrast sensitivities of all participants in the three different stimulus areas were age normalised by dividing each individual value by the equation of the linear regression of temporal contrast sensitivity to age and multiplying by the mean. For these calculations, the results of the 52 normals in the corresponding stimulus area were used as reference.

STATISTICAL ANALYSIS
Analysis among related samples was made using the Wilcoxon’s signed paired rank test and paired t test. Comparisons between groups regarding the diagnostic power of the three different flicker stimuli used the unpaired t test. Sensitivities and specificities were calculated to describe the diagnostic value of the three different test conditions. Sensitivity was defined as the proportion of positive test results in the OHT and the two glaucoma groups and specificity as the proportion of negative test results among the controls. To judge the percentage of correctly classified patients, the sensitivities in patient groups were calculated for a fixed specificity of 96%.

Results
The log temporal contrast sensitivities in the four groups with each of the three different stimulus areas are presented as box plots in Figure 2. In all four study groups, temporal contrast sensitivity was significantly (p < 0.001) higher with full field and peripheral compared with central stimulation. There was only a little difference between full field and peripheral stimulation in all study groups. It was not significant (p > 0.01) in the normals, the OHTs, or the “perimetric” glaucomas, but in “preperimetric” glaucoma group it was (p < 0.01). Table 1 shows the number of subjects obtained from a rank test and the results of the paired t test comparing the temporal contrast sensitivity between the three different stimulus areas.

The diagnostic power of the three tests is evaluated by the receiver operating characteristic (ROC) curves in Figure 3 for “perimetric” glaucoma patients. Although there is only little difference between the three curves, a tendency towards best sensitivities with peripheral stimulation can be observed for high specificities between 90% and 100%. The next sensitive test condition is the full field stimulus;
Table 1 Comparison of temporal contrast sensitivity between full field, peripheral, and central stimulation

<table>
<thead>
<tr>
<th>TCS compared between different stimulated areas</th>
<th>Number of subjects of a rank test and results of the unpaired t test</th>
<th>Normals</th>
<th>Ocular hypertensives</th>
<th>Preperimetric glaucomas</th>
<th>Perimetric glaucomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central vs peripheral</td>
<td>t value (p)</td>
<td>15.16**</td>
<td>10.5**</td>
<td>13.34**</td>
<td>9.36**</td>
</tr>
<tr>
<td>Peripheral vs full field</td>
<td>t value (p)</td>
<td>15.82**</td>
<td>12.16**</td>
<td>14.19**</td>
<td>11.53**</td>
</tr>
<tr>
<td>Central vs full field</td>
<td>t value (p)</td>
<td>3.42</td>
<td>1.8 (ns)</td>
<td>3.01*</td>
<td>2.36 (ns)</td>
</tr>
</tbody>
</table>

ns = not significant; *p <0.01; **p <0.001.

Table 2 Diagnostic power of the flicker test with the three different stimulus areas for the three patient groups

<table>
<thead>
<tr>
<th>Sensitivities at a prefixed specificity of 96% and result of the unpaired t test</th>
<th>Ocular hypertensives</th>
<th>“Preperimetric” glaucomas</th>
<th>“Perimetric” glaucomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central stimulation</td>
<td>sensitivity (%)</td>
<td>11.1</td>
<td>20</td>
</tr>
<tr>
<td>p value</td>
<td>ns</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Peripheral stimulation</td>
<td>sensitivity (%)</td>
<td>24.1</td>
<td>37</td>
</tr>
<tr>
<td>p value</td>
<td>*</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Full field stimulation</td>
<td>sensitivity (%)</td>
<td>20.4</td>
<td>32.9</td>
</tr>
<tr>
<td>p value</td>
<td>*</td>
<td>**</td>
<td>**</td>
</tr>
</tbody>
</table>

ns = not significant; *p <0.01; **p <0.001.

Discussion

The high diagnostic power of the TCS test under the full field condition (Fig 3, Table 2) confirms our earlier results obtained with this stimulus. One important new finding in the present study, however, is that with the peripheral stimulation beyond 30° eccentricity, contrast sensitivity was not significantly different from full field stimulation in most patient groups (Fig 2, Table 1). This may suggest that even in the full field condition subjects’ responses were initiated from peripheral retinal areas. In fact, many subjects occasionally reported that with the full field stimulus flicker was noticed first in the far periphery of the visual field.

The most important result of our present study, however, is the rather unorthodox observation of a higher diagnostic sensitivity for glaucoma detection for the peripheral 30° to 90° eccentricity stimulation (Fig 3, Table 2). This suggests that in glaucoma diagnosis attention should also be paid to those peripheral retinal areas lying outside the conventionally tested central 30°.

A comparison of TCS between different locations within the visual field has been made in a few previous studies using flickering light...
spots. Thus, Tyler et al. found in normals with flickering targets of various sizes an increasing sensitivity and, consequently, increasing flicker fusion frequency (FFF) with increasing peripheral location (up to 45°) when high frequencies above 20 Hz were used. In OHT and even more pronounced in glaucoma patients, a higher proportion of significant losses occurred at 20° than in the centre of the visual field. In addition, a preponderance of high frequency losses (above 25 Hz) was noted with the more peripheral position while low frequency losses (below 25 Hz) were more common with foveal stimulation. A similar trend was observed by Stamper and Tytla across visual field. These variations in along all meridians leading to contour maps of eccentricity and increased with eccentricity varied with the meridian at a constant physiological inhomogeneities of the di...
probable for the other two ganzfeld stimuli mentioned above.

In summary, the present study suggests that in glaucoma diagnosis peripheral retinal areas outside the commonly tested 30° regions of the visual field should not be neglected. The TCS in these peripheral areas is significantly higher in all subject groups than in the central 30° area (Fig 2, Table 1) and it is rather similar to the full field results. The diagnostic power with the far peripheral stimulation is higher than with central stimulation (Fig 3, Table 2). For high specificities above 90% the peripheral stimulation is even more sensitive than the full field stimulation. This is true not only for the advanced glucomas but also for patients with optic disc damage but without perimetric defects and even for the OHT patients. Thus, the peripheral TCS test should be preferred.

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