Artificially Increasing Intraocular Pressure Causes Flicker Sensitivity Losses

Vo Van Toi, P. A. Grounauer, and C. W. Durckhardt

It has been reported that psychophysical flicker sensitivity, electroretinogram (ERG), pattern electroretinogram (P-ERG), and visual evoked cortical potential (VECP) responses are affected by ocular hypertension and glaucoma. Moreover, it has also been revealed that artificially augmented intraocular pressure (IOP) impairs electrophysiologic responses. In this investigation the authors varied the levels of IOP of ten normal subjects and determined their flicker sensitivities at these levels. Temporarily elevated IOPs were produced by exerting pressure on the eyeball through the eyelids by a new type of ophthalmodynamometer. The results obtained showed that increasing IOP produced loss of flicker sensitivity. For an IOP of 27.2 ± 2.1 mm Hg, significant losses occurred in the range of frequencies lower than 20 Hz. For a higher IOP (40.7 ± 2.1 mm Hg) the loss was significant at frequencies higher than 5 Hz. However, the critical flicker frequency was not affected significantly at either level of IOP. The authors also discovered a phenomenon, called “curtain phenomenon,” in that for a critical level of IOP, a high flicker frequency stimulus could completely fade out. The authors' results suggest that the psychophysical flicker sensitivity measurement is a more sensitive technique for the investigation of the effect of the variation of the IOP and that the curtain phenomenon constitutes an interesting indication for additional study of the ocular hypertension mechanism.

Intraocular hypertension and glaucoma affect many people: consequently, accurate and early diagnosis and the comprehension of the mechanisms of these diseases are important. Several investigations have been devoted to these purposes.

In the psychophysical field, Breukin and Tyler reported that the temporal modulation transfer function plot (De Lange curve) of the human eye was affected by ocular hypertension and glaucoma. Tyler found sensitivities significantly reduced for stimuli of 30 and 40 Hz as compared with lower frequency ranges. The critical flicker frequency (CFF), by contrast, was normal in these patients. Parallel investigations indicated that electrophysiologic responses were also affected by these diseases. Papst et al. found that in patients with glaucoma the amplitude of the pattern electroretinogram (P-ERG) responses decreased when the intraocular pressure (IOP) was greater than 30 mm Hg and that there was no change when the IOP was less than 26 mm Hg. Wulfing and Benedikt et al. using mechanical devices such as Muller or Bailliart dynamometers to artificially increase the IOP, found that the amplitude of electroretinogram (ERG) and visual evoked cortical potential (VECP) responses diminished only when the IOP was greater than the diastolic pressure of the central artery of the retina.

Hence, these studies suggested that the De Lange curve is an attractive tool for investigating ocular hypertension and glaucoma and that artificially increasing the IOP by mechanical devices is an appropriate technique for simulating ocular hypertension. Although this technique has been widely used in many physiologic as well as clinical investigations in the electrophysiologic field, no such similar work has been performed in the psychophysical field. Further, existent instruments used in reported investigations require an eye anesthetic and may produce unpredictable deformation of the eyeball, which may influence the results. In this article we describe a new type of ophthalmodynamometer for temporarily increasing the IOP and report on the investigation of the loss of flicker sensitivity resulting from this increase. The results showed that the flicker perception threshold was sensitive to a temporary increase in the IOP.
Materials and Methods

The experiments were performed by means of two instruments: a visual stimulator (Papillometre; Metabo SA, 1049 Epalinges, Switzerland), which provides a sinusoidally modulated stimulus, and an ophthalmodynamometer, which artificially increases the IOP by exerting an adjustable force on the eyeball. The dynamometer was originally designed for measuring central retinal arterial pressure.16

The visual stimulator used here has been previously described in detail.17,18 Briefly, it consists of a stabilized light source that is modulated by means of a polarizer system. The frequency, modulation depth, color, and luminance of the stimulus, as well as the field size, can be adjusted independently and at will. The subject observes the stimulus through a Maxwellian view eyepiece on a dark background. The stimulus that then impinges on the subject’s eye is depolarized. The instrument is compact and handy-to-use because of the use of fiberoptic light guides instead of optical mirrors.

The ophthalmodynamometer consists of a pneumatic cylinder (Fig. 1) with the piston having two parallel “guides” (a) instead of one. Consequently, it induces only a translational motion of the “locker” (b). The locker carries the “stem” (c), which can be slid along its axis and locked securely if necessary. The stem carries a “ring” (d), having a diameter of 20 mm and a cross-sectional diameter of 2 mm. When compressed air is introduced into the cylinder through the “entrance” (e), it will cause the ring to advance. The ring will in turn exert a compressive force on the subject’s eye, thereby increasing its IOP.

Compressed air is generated by a manual pump as used in a sphygmomanometer. The operator controls the amount of compressed air and therefore can prevent the ring from excessively compressing the patient’s eye. A thin membrane inside the piston prevents any leakage of air inside the cylinder without constraining the motion of the piston. This motion is perfectly smooth because of the use of roller bearings. The pressure introduced into the cylinder can be read on a manometer and recorded on a chart recorder.

During use, the ophthalmodynamometer is fixed to one of the vertical rods of a forehead–chin rest and the ring form device is positioned in such a way that the ring will push on the upper and lower eyelids of the opened eye of the patient. In this way, the eyelids can be kept open without the use of an eye speculum, and the use of an eye anesthetic is not necessary. The eye will then have been subjected to a compressing force that is easily controlled and much safer and more homogeneous than if suction cup or Muller or Bailliart dynamometers19,20 had been used. Through the ring form device the subject can still see his or her surroundings, and the operator can continuously observe the fundus of the subject’s eye through a slit lamp. This constitutes an advantage with respect to the Hager dynamometer.21

Relationship Between Induced Pressure and IOP

To establish the relationship between the induced pressure and the corresponding IOP, a Goldmann applanation tonometer was used to measure the IOP for each corresponding pressure induced by our ophthalmodynamometer. The cone of the tonometer
was placed at the center of the ring (d). The results obtained from this calibration on two subjects showed that this relationship is linear according to the following equation:

$$Y = 1.35X + B$$

where $Y$ is the IOP in mm Hg, $X$ is the pressure in mbar induced in the ophthalmodynamometer and read on the manometer’s indicator and $B$ is the initial IOP in mm Hg of the subject. The value of $X$ can be considered as an incremental pressure index.

Numerous measurements indicated that our equation was accurate. Further, this equation agreed with the results reported in literature\textsuperscript{19–21}; therefore, it was used to determine the IOPs of our subjects in the investigation presented here.

In previous investigations, the retinal blood flow resulting from artificially increasing the IOP by using our ophthalmodynamometer was investigated and filmed. A study performed on 100 subjects indicated that the diastolic pressure of the retinal artery was approximately 50 mm Hg.\textsuperscript{16}

**Modification of Refraction Resulting From Induced Pressure**

Table 1 shows the spherical (S), cylindric (C), and axis (A) values of a subject’s eye at three different levels of IOP. The measurement was done by use of the Nidek refractometer.

**Experimental Procedure**

In the investigation reported here, the visual stimulator and the ophthalmodynamometer were installed in the following way. The dynamometer was fixed on a forehead–chin rest as previously described. The eyepiece of the stimulator was placed near the ring so that the stimulus was visible through the ring. Only one eye was tested, with the other eye being obstructed by a bandage (Fig. 2). The stimulus luminance used was 200 troland (td), achromatic with a field size of 20°. Three levels of IOP were tested: normal level, medium level (27.2 ± 2.1 mm Hg), and high level (40.7 ± 2.1 mm Hg). The normal IOP of each subject was measured by using the Goldmann applanation tonometer; the medium and high IOPs were deduced from the aforementioned equation. Although the normal IOP of the subjects were different, the incremental induced pressures were the same for every subject. The high-level pressure was chosen in such a way that it was slightly lower than the first appearance of the retinal arterial pulse (about 45 mm Hg), and consequently lower than the retinal central arterial diastolic pressure (about 50 mm Hg). The CFF and the following frequencies were measured: 5, 10, 15, 20, and 30 Hz. The fusion to flicker technique was used to determine the flicker thresholds. The measurement at each frequency was repeated three times and the order randomized.

Ten normal voluntary subjects with no history of eye disease and taking no medication were selected. All subjects except one were naive and they all gave informed consent after the nature of the procedures had been explained fully. Before the experiment, the whole ophthalmologic check-up, including color vision, was performed and the humeral arterial pressure (BP) measured by a sphygmomanometer. The profile of all subjects is shown in Table 2. Nine were men (M); six were Asian (A) and four were white (W); six had normal vision (E) and four were myopic (M). The purpose of the experiment and the experimental protocol were fully explained to the subjects, and practice sessions were set up. In the first step subjects were trained to determine the flicker thresholds; in the second step they were exposed to the procedure for artificially increasing the IOP; and in the third step they were asked to determine the flicker threshold with a temporary increase in the level of IOP. Systematic experimentation was then performed in the following way: the subject was asked to look at the stimulus, the IOP was rapidly increased to the desired value, the flicker threshold was then measured, and the pressure was released as soon as the subject had indicated this value. Each measurement lasted approximately 1 min. The subject was allowed to rest for a couple of minutes between each measurement. The entire experiment took approximately 2 hr per subject. Only one eye was tested.

**Results**

The means and the standard deviations of the thresholds for each frequency were computed, and the curves were plotted. We found that, among ten subjects, one (subject 2) could not perform the experiment at the high level of IOP at any frequency and another (subject 10) at frequencies higher than 30 Hz because the stimulus faded out before they could determine the flicker threshold (see Curtain Phenomenon). Figure 3 shows the curves of subject 10 and that of another subject (subject 8) who completed the ex-

---

**Table 1.** Spherical, cylindric, and axis values of a subject’s eye at three different levels of IOP

<table>
<thead>
<tr>
<th>IOP (mmHg)</th>
<th>S</th>
<th>C</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 (normal)</td>
<td>-0.5</td>
<td>-0.75</td>
<td>1</td>
</tr>
<tr>
<td>24</td>
<td>-0.25</td>
<td>-1.75</td>
<td>161</td>
</tr>
<tr>
<td>38</td>
<td>+0.25</td>
<td>-2.75</td>
<td>23</td>
</tr>
</tbody>
</table>

S, spherical; C, cylindric; A, axis.
periment, as did most of the subjects. The solid line curves correspond to the normal IOP, the dashed line curves correspond to an IOP of 13.5 mm Hg above the normal level, and the broken line curves correspond to an IOP of 27 mm Hg above the normal level.

A statistical analysis that performs an analysis of variance was used to analyze the data. Tukey's studentized range, Duncan's multiple-range, and Box- and-Whisker plots procedures were compared. The results of this analysis showed the following:

1. When the pressure increased from the normal to medium value (27.2 ± 2.1 mm Hg), the flicker sensitivity for the range of frequencies between 10 and 20 Hz significantly decreased. In contrast, the variation of flicker sensitivity at other frequencies and of the CFF values was not statistically significant.

2. When the pressure increased from medium (27.2 ± 2.1 mm Hg) to high values (40.7 ± 2.1 mm Hg), the flicker sensitivity significantly decreased for the entire tested frequency range except at 5 Hz and the CFF values.

Furthermore, we processed the data in the following way. At each frequency and for each subject, we compared the thresholds at two levels of IOP. We arbitrarily accepted that the difference between the two sensitivities was valid if it was greater than the sum of their corresponding standard deviations. Table 3 indicates the number of subjects whose sensitivities at the normal level of IOP were greater than those at the medium level; the number whose sensitivities at the normal level were higher than those at the high level; and the number whose sensitivities at the medium level were higher than those at the high level.

Table 2. Profile of subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Race</th>
<th>Vision</th>
<th>IOP (mmHg)</th>
<th>BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>M</td>
<td>A</td>
<td>E</td>
<td>12</td>
<td>120/80</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>M</td>
<td>A</td>
<td>M</td>
<td>14</td>
<td>115/80</td>
</tr>
<tr>
<td>3</td>
<td>22</td>
<td>M</td>
<td>A</td>
<td>E</td>
<td>12</td>
<td>115/75</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>M</td>
<td>W</td>
<td>E</td>
<td>16</td>
<td>120/75</td>
</tr>
<tr>
<td>5</td>
<td>22</td>
<td>M</td>
<td>A</td>
<td>M</td>
<td>15</td>
<td>120/80</td>
</tr>
<tr>
<td>6</td>
<td>28</td>
<td>M</td>
<td>W</td>
<td>E</td>
<td>16</td>
<td>120/80</td>
</tr>
<tr>
<td>7</td>
<td>26</td>
<td>M</td>
<td>W</td>
<td>M</td>
<td>14</td>
<td>120/80</td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td>M</td>
<td>A</td>
<td>E</td>
<td>16</td>
<td>105/70</td>
</tr>
<tr>
<td>9</td>
<td>33</td>
<td>M</td>
<td>A</td>
<td>E</td>
<td>10</td>
<td>120/70</td>
</tr>
<tr>
<td>10</td>
<td>28</td>
<td>F</td>
<td>A</td>
<td>M</td>
<td>12</td>
<td>120/80</td>
</tr>
</tbody>
</table>

BP, blood pressure; A, Asian; W, white; E, emmetropic; M, myopic.
Discussion

These results suggest that the sensitivities at low frequencies (below 20 Hz) were more susceptible to small variations in the IOP than the sensitivities at a higher frequency range. This fact may contribute to the belief that there are two mechanisms, one governing low frequency and one high frequency. In comparison with the results obtained by Wulfing and Benedikt et al, our results showed that the flicker-fusion sensitivity measurement is a much more sensitive technique to detect small and temporary variations in the IOP than the ERG or VECP technique. In comparison with the results of Papst et al, it is likely that the De Lange curve is as sensitive as the P-ERG recording technique.

It is unlikely that the modification of the eye’s optical characteristics resulting from the high induced forces affected our results because stimuli were presented in Maxwellian view. In addition, we did not find any noticeable difference between the results of emmetropic subjects and myopic subjects.

Our results are in agreement with those obtained by Tyler, who found that the CFF values of patients with glaucoma and ocular hypertension did not significantly change in comparison with those of normal patients. However, our results, by contrast, differed from those of Tyler in that Tyler found that the loss of flicker sensitivity occurred mainly for frequencies higher than 20 Hz. To verify Tyler’s results, we established the De Lange curve of a control group consisting of two patients with unilateral ocular hypertension. Both of them had normal IOP in one eye (approximately 20 mm Hg) and an IOP of about 40 mm Hg in the other eye. De Lange curves were re-

Table 3. Number of subjects at comparative levels of IOP

<table>
<thead>
<tr>
<th>Stimulus Frequency (Hz)</th>
<th>Normal &gt; Medium</th>
<th>Normal &gt; High</th>
<th>Medium &gt; High</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>9 (10)</td>
<td>8 (9)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>10</td>
<td>8 (10)</td>
<td>9 (9)</td>
<td>6 (9)</td>
</tr>
<tr>
<td>15</td>
<td>7 (10)</td>
<td>8 (9)</td>
<td>5 (9)</td>
</tr>
<tr>
<td>20</td>
<td>2 (10)</td>
<td>8 (9)</td>
<td>8 (9)</td>
</tr>
<tr>
<td>30</td>
<td>6 (9)</td>
<td>5 (9)</td>
<td></td>
</tr>
<tr>
<td>CFF</td>
<td>1 (10)</td>
<td>3 (8)</td>
<td>3 (8)</td>
</tr>
</tbody>
</table>

Number of subjects whose sensitivities at the normal level were greater than sensitivities at the medium level or at the high level of IOP, and the number whose sensitivities at the medium level were greater than those at the high level of IOP. Values in parentheses indicate the number of tested subjects. CFF = critical flicker frequency.
corded for both eyes without any artificial increase in IOP. The results obtained were consistent with those reported by Tyler. We suggest that this discrepancy could be attributed to the fact that patients with chronic ocular hypertension have had a long period of continuous and progressive increase in IOP whereas our subjects have had a temporary and abrupt increase in IOP. Chronic ocular hypertension and temporary ocular hypertension may affect the eye differently. The autoadaptation mechanism may contribute to this difference.

In general, it is believed that intraocular hypertension impairs the blood flow to retinal and optic nerve tissues. With subjects in good health and about the same age as our subjects, Bill and Nilsson found that the retinal blood flow decreases when the pressure is about 40 mm Hg. Riva et al. found that the blood flow through the retinal macular capillaries is still constant, resulting from the autoregulation, for pressures of approximately 30 mm Hg. According to these results, we may conclude that the flicker sensitivity loss was probably caused by the retinal hypoxia resulting from the increase in IOP.

Grehn et al. recorded neuronal activities in the ganglion cells of cats under artificial increases in the IOP. They found that the ocular hypertension impaired the ganglion cell activities of cats. Quigley and Addicks found that pressures higher than 50 mm Hg disturb the axonal transport, and therefore the synaptic transmission of primates. Therefore, it is likely, as our results suggest, that the loss of flicker sensitivity may result from the disturbances in ganglion cell activities.

Further, Grehn et al. found that for cats, even after 3 hr under high pressure, ganglion cell activities recover completely within 5 min. Quigley and Addicks found that elevating the level of IOP of primates to 50 mm Hg for a period greater than 2 days may initiate degeneration of some ganglion cells. In our investigation, the highest level of IOP was less than the retinal diastolic pressure and was maintained for a period of no longer than 1 min. Therefore, it is unlikely that our experiment presents any potential risk to the subject. Further, one of the subjects (subject 9) has repeatedly performed this kind of experiment for many years and other subjects have performed it occasionally. None of them have reported any ophthalmologic problems.

Curtain Phenomenon

It is well known that high induced IOP produces temporary blindness (Craik Blindness phenomenon). During our experiments a different phenomenon that we call “curtain phenomenon” was discovered. To the best of our knowledge, it has not been previously reported. This phenomenon occurred under the following conditions: when the IOP reached a critical level and with the stimulus modulated 100% at 30 Hz, the subject, after about 10 sec, completely and abruptly lost his luminance perception. This loss moved from the peripheral to the central vision field and took over the whole field in less than 1 sec. The subject reported that it felt as though a dark curtain had suddenly fallen in front of his eyes. The loss of luminance sensitivity, once it occurred, continued until the pressure was released. The recovery was then instantaneous. For the same level of IOP, the phenomenon, by contrast, did not occur if the flicker frequency was less than 20 Hz. This phenomenon differs from Craik Blindness phenomenon by the fact that it occurs at a lower level of IOP and depends not only on the IOP, but also on the characteristics of the stimulus.

In the experiments described previously, if possible, the part of the De Lange curve greater than 20 Hz was established before the curtain phenomenon occurred. One subject (subject 10) could not determine the CFF fast enough. Another subject (subject 2) was particularly more vulnerable than the others, in that the phenomenon occurred as soon as the IOP reached the high level and regardless of the frequency of the stimulus. By contrast, another subject (subject 4) was not affected by this phenomenon. Both IOP and arterial pressure of these subjects were normal (see Table 2).

A more elaborated investigation of this phenomenon was performed on one subject (subject 9). To check the validity of his results, other subjects were asked to perform only part of the experiment. In this investigation, parameters such as IOP and flicker frequency were varied systematically. Table 4 indicates the field size, frequency, and modulation depth of the stimulus. IOP, experimental time, and number of subjects tested. In Table 4, where it applied, the experimental time corresponds to the time when a diminution of luminance perception was perceived or when the curtain phenomenon occurred.

From this investigation we found the following:

1. For an IOP of 24 mm Hg, the curtain phenomenon did not occur regardless of the values of other parameters.
2. For an IOP of 38 mm Hg and a frequency of 20 Hz with 100% modulation, the subjects, after a period of 5 sec, experienced a significant diminution of luminance of the whole vision field and they also perceived their retinal vessels.
3. For an IOP of 38 mm Hg and a frequency of 30 Hz with 50% modulation, the same phenomenon of diminution of luminance perception occurred. If the modulation depth was increased to 100%,
the curtain phenomenon occurred after a period of 6 sec. This phenomenon also occurred when the frequency was 65 Hz (slightly higher than his CFF value of 60 Hz). By contrast, the curtain phenomenon did not occur when the frequency was 80 Hz (much higher than the CFF).

4. For an IOP of 45 mm Hg, the temporary blindness occurred despite the flicker frequency (Craik Blindness phenomenon).

5. It seems that the curtain phenomenon does not depend on the field size.

6. The time corresponding to the diminishment of luminance perception and the occurrence of the curtain phenomenon for all tested subjects are of the same order.

We can conclude that the curtain phenomenon depends on three factors: the IOP, the flicker frequency, and the modulation depth of the stimulus. At the critical level of IOP (38 mm Hg) the curtain phenomenon occurs only when the frequency and the modulation depth reached a critical value (20 Hz for the flicker frequency and 50% for the modulation). This critical value of pressure likely depends on the individual subjects. However, it is unclear on what mechanism this value depends.

So far, the origin of the curtain phenomenon is unknown. The IOP of 38 mm Hg is lower than the retinal diastolic pressure. An observation of the eye's fundus at that pressure did not show visible ischemia of the retinal central artery. Further, Bill and Nilsson reported that the reduction in blood flow started only when the pressure was about 40 mm Hg. Even if we accept that the retina undergoes a diminution of the blood flow at 38 mm Hg, it is unlikely that a hypoxy would cause a complete loss of the luminance as observed in the curtain phenomenon.

In studying the Troxler effect, Schiecting and Spillman found that a stimulus of 3° size projected on the peripheral retina faded away after 35 sec. The fading time is proportional to the modulation and the stimulus diameter but is inversely proportional to the retinal eccentricity and flicker frequency. The difference between these results and ours suggested that the curtain phenomenon is different from the Troxler effect.

Brockhuijsen and Veringa reported that they applied a sinusoidally modulated electrical current on a subject's eye while the subject was observing a steadily illuminated screen with a 35° field size. This stimulation considerably darkened the visual field of the subject. The effect was maximal when the stimulus frequency was 90 Hz and the screen luminance was 0.01 cd/m². It is unclear whether there is any relation between this phenomenon and the curtain phenomenon.

We also found that the curtain phenomenon may not recur when the experiment is repeated many times. A higher pressure was needed to produce this phenomenon again. However, to preclude the possibility of discomforting the patient with repeated exposure to a very high IOP, there was no systematic attempt to determine this value. This observation suggests the existence of an autoadaptation mechanism and also of a difference between the chronic ocular hypertension or glaucoma mechanism and the artificial ocular hypertension mechanism.

Conclusions

In the study of ten normal subjects whose IOPs have been temporarily increased, we have determined a relationship between the flicker sensitivity and the IOPs. The loss of flicker sensitivity depends on the IOP and also on the flicker frequency. This loss occurred at an IOP as low as 27.2 ± 2.1 mm Hg.
This allows us to conclude that the De Lange curve technique is a sensitive psychophysical tool for the detection of the loss of luminance perception resulting from a temporary increase in IOP. However, the mechanism of chronic ocular hypertension and glaucoma may differ from the mechanism of temporary ocular hypertension.

The curtain phenomenon, the complete loss of the luminance perception of the eye, depends on three factors: the IOP, flicker frequency, and modulation depth of the stimulus, with the pressure being the dominant factor. This phenomenon may constitute important information for additional physiologic as well as clinical investigations of the ocular hypertension and glaucoma mechanisms.

Key words: ocular hypertension, artificially increased IOP, flicker sensitivity, De Lange curve, ophthalmodynamometry

Acknowledgments

The authors thank Dr. P. E. Grumbach for his support, Durwood Marshall and Guy Van Mell for their assistance in the statistical analysis, and Richard Heckbert for his assistance in the preparation of the manuscript.

References