The Relation between Visual Sensitivity and Intraocular Pressure in Normal Eyes

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Intraocular pressure and flicker modulation sensitivity at 25 and 40 Hz were measured in 22 normal observers, with an age range from 20–71 years. Significant correlations up to 0.67 were found between intraocular pressure and flicker sensitivity at several points in the visual field. There was no correlation between flicker sensitivity and age of the observers. Thus intraocular pressure may affect neuronal function in the normal eye. Invest Ophthalmol Vis Sci 25: 103–105, 1984.

Losses in relative light sensitivity (as measured by clinical static and kinetic perimetry) may occur in conjunction with a sustained increase in intraocular pressure (IOP). It is probable that increased pressure is the direct cause of the visual sensitivity loss, although the actual mechanism is undetermined. It is, therefore, of interest to establish whether the loss of visual sensitivity is exclusively pathological, or whether it is the extreme manifestation of a normal retinal or optic nerve sensitivity to variations in IOP.

To investigate these possibilities, we employed a test of neuronal function that has been shown to be sensitive in the early stages of pathological increases in IOP. The stimulus was a flickering field, for which we measured the detection of sinusoidal flicker modulation at a fixed temporal frequency (see Methods). Under the photopic conditions used, this proved to be a more sensitive method than the critical fusion frequency (CFF), in which flicker frequency is increased to the maximum detectable rate. We therefore determined modulation sensitivity in normal observers at two fixed frequencies in the range of maximum loss for glaucoma, for three retinal locations, and compared these sensitivities with IOP measured on the same day.

Materials and Methods. The flicker apparatus consisted of an array of 25 high-luminance, light-emitting diodes. A steady DC signal maintained the mean luminance at 40 cd/m² and a 2-decade, 10-turn logarithmic potentiometer controlled the amplitude of sinusoidal modulation. An additional 1-decade range switch permitted control of the modulation from a maximum of 86%, down to 0.1%, which is important because good observers can give readings in the range of 0.3–0.5% under optimal conditions.

The field of 25 light-emitting diodes was set behind a circular diffusing sheet in a tube with a white inner surface, so as to produce a uniform field 2.5 cm in diameter. This field was centered in a large (40 cm) equiluminant steady field made by projection of four incandescent bulbs onto a diffusing surface. There was a 1-mm dark border around the flickering field. The apparatus was viewed from a forehead and chin rest at a distance of 28.5 cm, so that the flickering field subtended 5° in diameter.

Fixation spots were provided to allow the test field to be viewed at a peripheral eccentricity of 20° on the 45° meridians in the upper nasal and temporal quadrants, in addition to central observation.

Twenty-two observers were drawn from the population of workers and nonpatient visitors at the Ophthalmology Department of the Pacific Medical Center. All gave their consent to be tested after the procedure had been explained to them. These observers had an age range of 20–71 years (mean age 38), and all had visual acuities of 20/40 or better. None had any systemic disease or were on medication. The group consisted of 10 men and 12 women.

IOP was measured once in each eye by Goldmann applanation tonometry at a time between 10 AM and 4 PM on the same day as the flicker test. This should provide a representative measure of IOP, since previous studies have shown that diurnal variations are small, and that during this 6-hour period, remaining variation is randomly distributed.

For the flicker sensitivity test, thresholds were determined by the method of adjustment. In order to minimize flicker adaptation, modulation amplitude was reduced to well below perceptual threshold for a given test frequency, then slowly increased until flicker was first reported. Two readings of this point were taken for each retinal location. Both eyes of each observer were tested (except two who were tested only in the right eye). The testing staff had no knowledge of the IOP during performance of the flicker test.
Table 1. Correlations of flicker sensitivity with IOP.†

<table>
<thead>
<tr>
<th>Eye</th>
<th>Central</th>
<th>20° nasal</th>
<th>20° temporal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 Hz</td>
<td>-0.495*</td>
<td>-0.459*</td>
<td>-0.667*</td>
</tr>
<tr>
<td></td>
<td>(-0.47*)</td>
<td>(-0.52*)</td>
<td>(-0.65*)</td>
</tr>
<tr>
<td>40 Hz</td>
<td>-0.036</td>
<td>-0.356*</td>
<td>-0.313</td>
</tr>
<tr>
<td></td>
<td>(0.26)</td>
<td>(-0.37)</td>
<td>(-0.26)</td>
</tr>
<tr>
<td>Left</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 Hz</td>
<td>-0.439*</td>
<td>-0.412*</td>
<td>-0.458*</td>
</tr>
<tr>
<td></td>
<td>(-0.26)</td>
<td>(-0.27)</td>
<td>(-0.32)</td>
</tr>
<tr>
<td>40 Hz</td>
<td>-0.215</td>
<td>-0.312*</td>
<td>-0.452*</td>
</tr>
<tr>
<td></td>
<td>(-0.19)</td>
<td>(-0.49)</td>
<td>(-0.24)</td>
</tr>
</tbody>
</table>

* Significance at least $P < 0.05$ for single correlations on a one-tailed test.
† Upper values are product-moment correlations ($R$); lower values in parentheses are rank-order correlations ($p$). For right eyes, $n = 22$; for left eyes, $n = 20$.

All correlations were performed using the Pearson product-moment method, except those in parentheses in Table 1, which used Spearman’s rank-order method.

Results. The range of intraocular pressure was from 11-20 mm Hg. The range of flicker thresholds for central retina was 1.0-7.2% modulation at 25 Hz and 8.3-47.1% at 40 Hz. For peripheral retina the range was 1.3-16.6% at 25 Hz and 4.3-46.9% at 40 Hz. Thus, substantial variations in flicker sensitivity were found in this normal population under our testing conditions.

For most of the stimulus conditions, there is a significant product-moment correlation* between IOP and flicker modulation sensitivity (Table 1). The correlations have values from $-0.036$ to $-0.495$ for the central region of the retina, and from $-0.313$ to $-0.667$ for the peripheral locations. Except for the central retina at 40 Hz and one peripheral condition, these values are all statistically significant at or beyond the 5% level. In quantitative terms, the highest correlation ($-0.667$) for the temporal retina of right eyes at 25 Hz) represents a range of about a factor of three in the threshold amplitude of temporal modulation (see scattergram for this condition, Fig. 1) so that peripheral visual sensitivity shows a marked relationship with the normal range of IOP.

Another interesting measure is the comparison of differences in flicker sensitivity with differences in IOP between the two eyes of each observer. This comparison is close to the variability of the data because the IOP differences were only 1-2 mm Hg. For those observers with nonzero difference in IOP between the two eyes, a t-test for paired observations weighted by the IOP difference for each observer showed a significant depression (at $P = 0.05$) of flicker sensitivity in the eye with the higher pressure. Thus, even small differences in IOP between the two eyes seem to have a detectable effect on retinal function.

Discussion. The results of Table 1 demonstrate that, under many stimulus conditions, there is a significant negative correlation between visual sensitivity to flicker (expressed in terms of modulation amplitude) and intraocular pressure. The relationship appears to be stronger at 25 Hz than at 40 Hz in central retina, but not to favor either frequency or temporal versus nasal retina in the periphery.

A possible confounding factor is physiological change with age of the observers, independently controlling both IOP and flicker sensitivity (as opposed to there being a direct link between them). Such an effect is unlikely, since flicker sensitivity has been found to be independent of age, both in normal observers and in glaucoma patients. Furthermore, mean IOP varies by only 1 or 2 mm Hg in normal adults over the tested age range from 20-70 years of age. The absence of an age effect was confirmed in the present study for both variables. The correlation of IOP with
age was 0.09, and of flicker sensitivity with age was 0.00, both of which are well below statistical significance.

A second contaminating variable in studies of visual sensitivity is the size of the pupil. Under our experimental conditions the normal pupil had a size of about 4 mm in diameter. Pupil size determines the level of retinal illumination, which in turn is linearly related to high-frequency flicker sensitivity. To obtain the observed range of a factor of 10 in flicker sensitivity, retinal illumination would have to vary by about a factor of 50, and pupil diameter would have to change by the square root of 50, about a factor of 7 (from, say, 1–7 mm). Such a variation should affect central and peripheral sensitivities equally, and also have a similar effect at 40 and 25 Hz.

Our observers did not show such noticeable variations in pupil size, and the obtained product-moment correlations in central vision show significant differences between 25 and 40 Hz that cannot be explained by luminance variations. Even taking into account the total number of comparisons among all correlations (66), the difference of 0.631 between the right temporal 25 Hz correlation and the right central 40 Hz correlation is significant at \( P < 0.05 \). Since this difference is incompatible with a pupil size hypothesis, we conclude that pupil size does not determine the relation between IOP and flicker sensitivity.

It is always possible that there is a further variable that might exert control over both IOP and flicker sensitivity. Nevertheless, the presence of a significant correlation is of interest in identifying IOP as a potential risk factor for the neural deficit. The possibility of a direct effect of IOP on neural function (as represented by flicker sensitivity) merits further study.

Key words: intraocular pressure, flicker, visual sensitivity, retina


References


PMN Accumulation in Aqueous Humor and Iris-Ciliary Body during Intraocular Inflammation

Richard N. Williams and Christopher A. Paterson

The accumulation of polymorphonuclear leukocytes (PMNs) was determined in the aqueous humor and iris-ciliary body following an intravitreal injection of endotoxin in the albino rabbit. PMN accumulation in the iris-ciliary body was quantified by measuring myeloperoxidase (MPO) activity in homogenates of this tissue. Leukocyte appearance in the aqueous humor was determined by counting the number of PMNs in diluted aspirates of aqueous humor and also by measuring MPO activity in the same aspirates.

Twenty-four hours following an intravitreal injection of endotoxin, there was marked vasodilatation in the iris, breakdown of the blood-aqueous barrier, and infiltration of PMNs into the aqueous humor. There was, however, no correlation between MPO activity in the iris-ciliary body and the number of PMNs or the MPO activity in the aqueous humor. Furthermore, the number of PMNs in the aqueous humor did not increase with increasing amounts of intravitreally injected endotoxin, whereas MPO activity in the iris-ciliary body increased in a dose-dependent manner.

The results of this study suggest that quantification of leukocytes in the aqueous humor does not represent a meaningful index of intraocular inflammation. Invest Ophthalmol Vis Sci 25:105–108, 1984

Acute inflammatory responses in the eye are composed of a number of components, namely the accumulation of polymorphonuclear leukocytes (PMNs) in the ocular tissues and fluids, dilatation of blood vessels, and an increase in vascular permeability.