CHRONIC EFFECTS OF INTRAOCULAR PRESSURE IN NORMALS AS A FUNCTION OF RETINAL LOCATION.

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Sensitivity to sinusoidal temporal modulation (flicker sensitivity) for a uniform stimulus field is proving to be a valuable tool for in ophthalmological diagnosis. Flicker sensitivity has been shown in a variety of diseases to provide earlier detection than previously available tests;[1,2] to measure a reversible component of the visual susceptibility to disease;[3] provide differential diagnosis among conditions which are similar according to other tests;[4] to characterize the nature of the sensory deficit;[4,5] and to provide information as to which retinal mechanisms are affected by the disease.[4-6]

In previous work we have used flicker sensitivity to evaluate the temporal losses in patients with glaucoma, ocular hypertension and other optic neuropathies. In one study[7] we also looked at temporal sensitivity in normals as a function of their measured intraocular pressure (IOP). We found a significant association between IOP and sensitivity at 25 and at 40 Hz, for both central and 20° peripheral viewing conditions. While the correlations were statistically significant in most locations, they were not large, accounting for only about 25% of the variance or less. However, they left no doubt that IOP could influence sensitivity at high frequencies in peripheral retina.

One question raised by our previous study of IOP in normals was whether the flicker sensitivity losses were principally at mid-high temporal frequencies, as has been reported in glaucoma and ocular hypertension[1-3], or whether they showed a uniform temporal profile (or some other form altogether). A second question was whether the losses were a peripheral phenomenon, or whether they extended to foveal vision as well. The central target in our previous study was a 5° patch, so flicker sensitivity at 25 or 40 Hz could have been mediated largely by the peripheral rim of the stimulus rather than its foveal region.

To answer these questions, we designed a study to measure the full flicker sensitivity function in normals at range of retinal eccentricities from central fovea to 35° in the periphery.

METHODS

Participants

Normal observers were drawn from a population of hospital volunteers and respondents to local advertisements. Respondents over age 50 were excluded from participation. The average age of the fourteen observers was 38 $\pm$ 11.9 years. Informed written consent was obtained from each observer. The absence of ocular pathology was assessed by obtaining a clinical history and direct ophthalmic evaluation. It was considered optimal to use lenient inclusion criteria for normals, since this provides the most useful sample for clinical evaluation of the effective normal

population. The temporal visuogram performance of the normal observers has been fully documented elsewhere.[8,9]

Temporal Visuogram

The methods for measuring the temporal visuograms were similar to those in previous studies.[10,11] Briefly, amplitude thresholds were measured for flicker frequencies in half-octave steps from 2.5 Hz upwards, in addition to the critical fusion frequency (CFF). The sinusoidal flicker was presented in a half-second raised-cosine envelope. The stimulus consisted of a red, 660 nm LED array diffused to appear as a uniform red disk and set in an equiluminant white surround of 400 cd/m^2. This stimulus configuration has been developed for assessment of photopic vision across a range of retinal and optic nerve disorders[1-6]. It uses long wavelength light to isolate cone responses[12,13] and eliminate any rod contamination, while minimizing contamination from defocus, optical distortions, aging of the lens and early media opacities.[14,15]

To equate the peak sensitivity at a range of retinal locations, we scaled the stimulus area in proportion to estimated cone density as eccentricity was varied. Three retinal locations were used: central, 5° and 35° eccentricity. For the central stimulus, a foveolar size of 0.5° and a foveal size of 2° were used. Since the 0.5° central region of the foveal 2° stimulus was only 1/16th of its total area, a large proportion of this stimulus is eccentric to the foveolar 0.5° stimulus. It was felt that this was a better way to get at the rim of the fovea than attempting to rely on the observers' ability to fixate stably at an eccentricity of 1°. The diameters of the 5° and 35° stimuli were set at 2.5° and 5° respectively, chosen to equate the numbers of receptors stimulated with those of the foveolar 5° stimulus at about 4000 cones in each location. Field size was varied by appropriately setting the viewing distance.

The test procedure consisted of a YES/NO task for flicker detection with 20% blank trials as a check on the false-alarm response rate. The overall paradigm consisted of a cyclic interleaved staircase procedure, in which each of the staircases for all stimulus frequencies were interleaved in cyclic rotation. Each eye was tested separately, with the untested eye being occluded by an opaque patch. A typical test run would take about 10 minutes for 10 frequencies. The observers' IOP was measured within an hour of the temporal sensitivity tests.

The data were screened for reliability on the basis of the false-positive response rate. The test procedure included 20% blank trials as an indication of the observers' attention to the task and response criterion. This resulted in the presentation of an average of 8 $\pm$ 3 blank trials during a typical test run. The observers were allowed no more than 2 false positive responses for an acceptable performance. Pupil size was measured and the observer excluded if the pupil size lay outside the limits of 2.5 - 3.5 mm.

RESULTS AND DISCUSSION

The aim of the study was to determine which retinal locations are most susceptible to the effects of elevated IOP. The results were analyzed by sorting the individuals with IOP of 14-19 mm Hg to form the high IOP group (n=7) and those with 10-13 mm Hg to form the low IOP group (n=7); their average sensitivities and IOP difference functions are plotted as a function of temporal frequency (Fig. 1). The dashed lines above and below zero difference show $\pm$ 1 s.e.m. of the differences. Differences should be considered significant if points at two adjacent frequencies both fall outside the s.e.m. confidence interval.

For both the central foveola (Fig. 1A) and the near periphery (Fig. 1C) show significant losses in the midfrequency region around 20 Hz, but show recovery at the highest testable frequencies. On the other hand, the 2° central location and the 35° peripheral location show no significant losses, but they show the high IOP observers having significantly greater flicker sensitivities for

high frequencies above about 40 Hz, and also in the low range below 10 Hz for the 2° central location. Thus, these tow locations may be characterized as showing a similar degree of loss, between midrange of frequencies and those both higher and lower, as do the other two locations. These results tend to confirm the report by Tyler, Ryu and Stamper[7] that IOP within the normal range can affect visual sensitivity; they extend it in showing that the sensitivity reduction is limited to the mid-frequency range at all retinal eccentricities. The surprising aspect of these results is that the strongest effect is seen in the central foveola at the intensity tested.

Supported by a grant from the Smith-Kettlewell Eye Research Institute.

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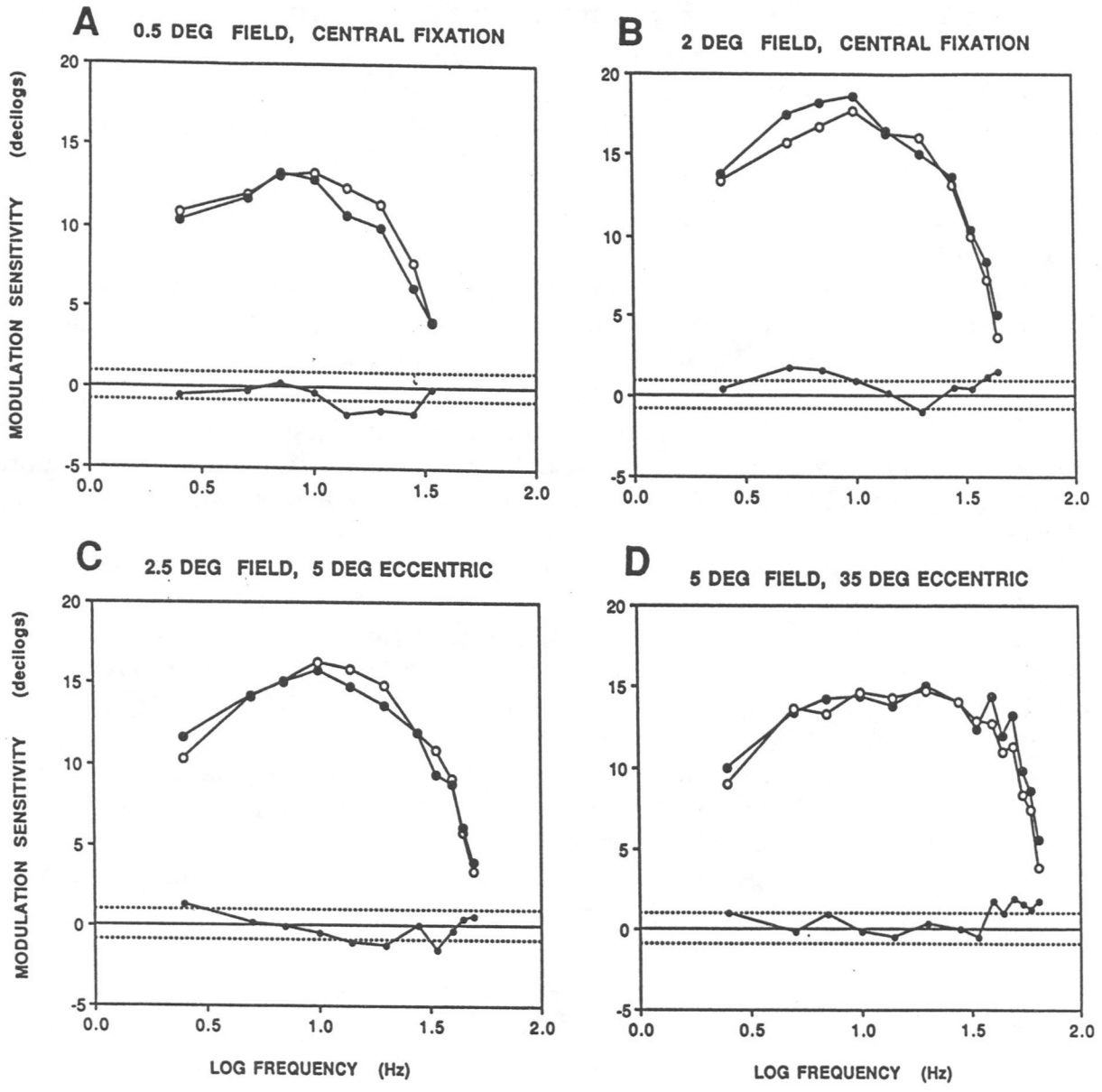

Figure 1. Temporal sensitivity functions for normals with low IOP (open circles) and high IOP (filled circles) at four retinal loci. Lower functions (points) show high - low differences for each condition, with confidence limits of $\pm$ 1 s.e.m. averaged across all frequencies indicated by the dashed lines around zero difference. Significant differences are present when two adjacent points exceed either confidence limit.