The pattern reversal visual evoked response (VER) was recorded under conditions of artificially unbalanced visual input between two eyes, an aniseikonia induced by size lenses that alter the perceived retinal image size without changing refraction. At 3.0% aniseikonia binocular summation started to decrease, and at 5.0% aniseikonia there was no significant binocular summation. In higher aniseikonia (8.0–10.0%), binocular inhibition replaced binocular summation. The phase difference between binocular and monocular VER was largest at zero aniseikonia. When aniseikonia exceeded 5.0%, there was no significant phase difference between the two recording conditions. These results suggested that the binocular system can compensate for up to a 3.0% difference in perceived retinal image size (aniseikonia), but in higher aniseikonia the binocular system can no longer compensate for the difference and binocular inhibition takes place. These findings agree with previously reported subjective and psychophysical results. The authors suggest that this objective method of evaluation using the pattern reversal VER may be helpful in pediatric ophthalmology when subjective methods are of limited use. Invest Ophthalmol Vis Sci 27:601–604, 1986

Unbalanced visual input between the two eyes during development results in irreversible visual dysfunction. In the past two decades many studies, mainly in the fields of neurophysiology and psychology using animal models,1,2 have shown that this imbalance causes an irreversible change in the visual system. Light deprivation is a severe form of unbalanced visual input, and aniseikonia, a perceived retinal image size difference that usually accompanies anisometropia, is considered a less severe form.

Most studies concerning degree of aniseikonia and binocular function are based on subjective studies of unilateral cataracts or on psychophysical studies.3-5 Aniseikonia is usually determined with subjective methods such as the phase difference haploscope or the space eikonometer. However, in young subjects, particularly infants, the exact degree of aniseikonia is often difficult or impossible to determine with these methods.

In adult unilateral aphakia, binocular function can usually be restored considerably by use of a contact lens, size lens, intraocular lens, or a combination of these. In infancy and early childhood, a perceived image size difference between the two eyes can lead to irreversible impairment of binocular function.

Lovasik and Bishop6 studied the effect of simulated aniseikonia on transient pattern reversal visual evoked response (VER). They found that stimulations of unequal sizes given to each eye had no significant effect on transient pattern reversal VER. To study the sensitivity of binocular VER to perceived image size difference, we observed the effect of simulated aniseikonia induced by a size lens on the binocular summation of the pattern reversal VER.

**Materials and Methods.** Four normal subjects, including two males and two females ranging in age from 25–40 yr, participated in this study. They were all experienced subjects and had no ophthalmological abnormalities. The subjects were thoroughly familiar with the procedure and consented to participate. The binocular function as tested by the Titmus Wirt test was normal in all subjects.

VER was recorded using an 8-mm silver disc electrode. An active electrode was placed 3 cm above the inion on the midline, and the reference electrode was placed 10 cm above the inion on the midline. Ground electrodes were placed on both earlobes. A checkerboard pattern with square wave modulation was selected as the stimulus, and a 15-in television monitor was used as the stimulus display. Each element subtended a visual angle of 25.0 min from the viewing distance of 160 cm. The modulation depth (contrast) of the pattern was kept at the level of 0.30, as our previous study (Katsumi, Tanino, and Hirose, unpublished data) showed that a lower contrast pattern allows more sensitive evaluation of binocular function using the pattern reversal VER. The temporal frequency (alternating rate) was kept at 12 Hz, and the mean luminosity was set to 50 cd/m² (1.20 log foot-lambert). Responses were fed into the averaging computer (Cadwell 7400, Cadwell Laboratories; Kennewick, WA) with the high-cut filter set at 100 Hz and the low-cut filter at 1 Hz. There were 50 averagings, and the sweep time was 500 msec.

The amplitude of the pattern reversal VER was calculated individually for each subject by averaging the size of the peak-trough amplitudes of several waves (5–6) on the tracings. The value of the binocular summation was calculated from the ratio between binocular and monocular VER amplitudes.

To create the artificial aniseikonia, size lenses that enlarge the perceived retinal image size 2.0–10.0% (Hoya Lens Co.; Tokyo, Japan) were used (Fig. 1). The accuracy of the degree of aniseikonia was confirmed subjectively with the phase difference haploscope. The examination began with the lowest aniseikonia (2.0%) and progressed to the highest power in five steps, 2.0%, 3.0%, 5.0%, 8.0%, and 10.0%, successively. The size lens was placed in front of the dominant eye, which
was determined by the simple hole-in-card method. We considered the monocular response to be the VER obtained when the size lens was in place.

For statistical analysis, we used one-way analysis of variance.

**Results.** Figure 2 shows the binocular and monocular recording of VER. In low aniseikonia (2.0–3.0%), the binocular VER showed larger amplitudes, and each peak appeared earlier than that of the monocular VER. In mid-aniseikonia (5.0%), the binocular and monocular VERs showed similar amplitudes. In high aniseikonia (8.0–10.0%), the binocular VER showed smaller amplitudes than the monocular VER, and there were no significant peak time (phase) differences.

Figure 3a shows the mean binocular and monocular VER amplitudes. The monocular VER amplitude did not change significantly with alteration of image size over all the testing conditions. The binocular VER amplitude did not decrease significantly at 2.0% aniseikonia, but from 3.0% aniseikonia the amplitude showed a tendency to decrease, and at 5.0% aniseikonia the amplitude decreased significantly compared with zero aniseikonia (F = 7.26, SL = 0.017). When the amplitudes of the binocular and monocular VER were compared, the binocular VER was significantly larger than the monocular VER at 2.0% aniseikonia (F = 6.69, SL = 0.022). At 3.0% and 5.0% aniseikonia, the difference between the two recording conditions was not significant (F = 2.07, SL = 0.172 at 3.0%; F = 0.19, SL = 0.667 at 5.0%). At high aniseikonia (8.0–10.0%), the binocular VER amplitudes were smaller than in the monocular VER, especially at 10.0% aniseikonia, but the difference was not statistically significant.

Figure 3b shows the amount of binocular summation in all testing conditions. The highest binocular summation of 1.513 was observed at zero aniseikonia. Binocular summation was 1.416 at 2.0% aniseikonia, but decreased to 1.119 at 3.0% aniseikonia, 1.058 (almost zero summation) at 5.0% aniseikonia, 0.909 at 8.0% aniseikonia, and to 0.888, the lowest binocular summation, at 10.0% aniseikonia.

Figure 4 shows the change in phase difference between the two testing conditions in various aniseikonia. The phase difference between the binocular and monocular VER decreased above 5.0% aniseikonia. In high aniseikonia, the phase difference decreased further.
Fig. 3. (a) Mean VER amplitude of binocular and monocular recordings. The monocular VER amplitude did not change significantly over all conditions. The binocular VER decreased significantly from 3.0% aniseikonia. At 5.0% aniseikonia there is no significant difference between the two recording conditions and at 10.0% aniseikonia, the binocular VER was slightly smaller than the monocular VER. (b) Mean binocular summation value. The upper horizontal line at 1.40 indicates a value used as a reference by many investigators, and the lower horizontal line at 1.00 indicates the level of zero summation. The highest binocular summation was observed at zero aniseikonia (1.513). At 5.0% aniseikonia, there was zero summation (1.058). At 10.0% aniseikonia, there was binocular inhibition (0.888).

Fig. 4. Mean peak time (phase) difference. The horizontal line indicates the level of 10 msec, which we consider to be the phase difference between the binocular and monocular VER at 0.30 contrast with no aniseikonia with steady-state stimulation (unpublished data). The phase difference was largest at zero aniseikonia. It decreased with increasing aniseikonia and in high aniseikonia, there were no significant phase differences between the two recording conditions.

Discussion. Using the random dot stereogram, Campos and Enoch\(^7\) concluded that fine central stereopsis cannot be obtained when the degree of aniseikonia exceeds 5.0%. Wesson,\(^8\) using a psychophysical method, suggested that aniseikonia greater than 8.0% interferes with normal development of binocular function. Using the phase difference haploscope, Isomura and Awaya\(^9\) reported that the aniseikonia tolerance for fine stereopsis was between 4.0% and 7.0%.

In clinical studies, the degree of aniseikonia in unilateral aphakia is reported to be approximately 20% when corrected with glasses,\(^3\) 10% with a contact lens,\(^3\) and 2.0–2.5% with an intraocular lens implant.\(^5\) The use of an intraocular lens implant resulted in relatively good binocular function.\(^4,5,10,11\)

In our study, the binocular system seemed capable of fusion of up to 3.0% aniseikonia, but at 5.0% aniseikonia there was no significant binocular summation in any of the subjects. In high aniseikonia (8.0–10.0%) the binocular VER amplitudes were smaller than those of the monocular VER, and this may be associated with the binocular inhibition due to the large difference in the perceived retinal image size. The binocular sys-
but when the difference exceeds a certain level, the binocular system is unable to fuse these perceived image differences and may function as binocular inhibition resulting in a smaller binocular than monocular VER amplitude.

Our results show that the binocular system may be able to compensate for a perceived retinal image size difference between two eyes of up to 3.0%. Although a direct comparison cannot be made, our results are in good accordance with those obtained from psycho-physical and clinical studies.

Whereas Lovasik and Bishop\(^6\) reported that simulated aniseikonia did not affect the amplitude and implicit time of transient pattern reversal VER, we found steady-state pattern reversal VER very sensitive to the perceived retinal image size differences between two eyes. An abnormal degree of binocular summation suggests defective binocular function. However, asthenopia and headache can be observed in patients with passable VER examination. Further clinical studies are required to clarify these findings. We suggest that pattern reversal VER may be helpful in evaluating visual function, especially binocular function of pediatric subjects in whom subjective methods are of limited use.

**Key words:** aniseikonia, binocular interaction, binocular summation, binocular vision, pattern reversal VER

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**Human Basement Membrane Components of Keratoconus and Normal Corneas**

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Using immunofluorescence techniques, we analyzed the distribution of glycoproteins in normal and keratoconus corneas of humans. Laminin, bullous pemphigoid antigen, fibronectin, and fibrin/fibrinogen were all found in the epithelial basement membrane of normal corneas. Keratoconus corneas produced similar results, except that staining for fibrin/fibrinogen was weak. Fibrin/fibrinogen was absent from normal corneal basement membrane in animal models studied previously. Keratoconus may be the result of the lysis of fibrin or may involve impeded elaboration of fibrin. Invest Ophthalmol Vis Sci 27:604–607, 1986

Normal corneal basal epithelial cells are anchored to the stromal substratum at the basement membrane zone (BMZ) through hemidesmosome attachment complexes. Endothelial cells are anchored by hemidesmosomes to their basement membrane, Descemet's membrane. These basement membranes are similar to epidermal basement membrane, including ultrastructurally identifiable electron dense (lamina densa) and electron lucent (lamina lucida) zones. Bullous pemphigoid antigen\(^1\) has been localized to the lamina lucida, while laminin,\(^2\) Type IV collagen,\(^3\) and fibronectin\(^4\) have been localized to the lamina densa.

Ultrastructural derangements of these zones of the BMZ have been reported in keratoconus.\(^5\) Keratoconus, a central, noninflammatory, usually bilateral

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**References**