Rapid assessment of visual function: an electronic sweep technique for the pattern visual evoked potential

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We have developed an electronic spatial frequency sweep technique for electrophysiological assessment of visual acuity and pattern vision. The technique allows an accurate and reliable measurement of VEPs to a full range of spatial frequencies in just 10 sec. Because the measurements are so rapid, the technique suggests several new improvements in the assessment of visual function. Sweeping spatial frequency linearly and extrapolating the high-frequency region of the VEP spatial-tuning function to zero voltage allows an estimate of acuity which correlates highly with psychophysical estimates of acuity. Variants of the procedure are appropriate for the assessment of refractive error, determination of equality of visual function for the two eyes and of binocular interactions, and for sequential assessment of therapeutic conditions.

Key words: visual evoked potential, pattern vision, diagnosis, therapeutic evaluation, binocular interactions, visual acuity, refraction

Clinical assessment of visual function is relying progressively more on visual evoked potential (VEP) scalp recording as an objective indicator of visual system loss.[1-6] The classical technique of transient VEPs from flashed or pattern reversal stimulation is relatively slow, requiring stimulation times of the order of 1 min to obtain a single response average. Proportionately more time is required to estimate visual acuity or measure the range of stimulus patterns to which the visual system responds. This lengthy recording time is a great disadvantage for clinical assessment in young children or for screening purposes. The recording process can be greatly speeded by recording the synchronous VEP response at high temporal frequencies of stimulation.[7-10] The major information about response amplitude and phase can be obtained in a second or two using synchronous recording at 10 to 100 Hz rates.

This increase in recording speed allows the use of sweep techniques for presenting the full range of a stimulus variable in a single recording session. We have developed an electronic spatial-frequency sweep technique for electrophysiological assessment of visual acuity and pattern response. This enables us to measure the VEP to the full range of spatial frequencies in a 10 sec sweep with good resolution and reliability. A slower optomechanical version of this technique has recently been described by Regan.[6]

Methods

The electronic equipment consists of a visual display, a synchronous filter for the electroen-

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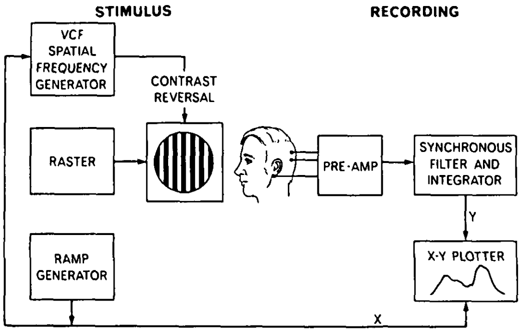

Fig. 1. Schematic of the electronic sweep stimulus and recording apparatus.

cephalogram (EEG), and a frequency-modulated waveform generator on an X-Y plotter (Fig. 1).

Stimulus. A sinusoidal or square-wave grating was presented on the face of a Hewlett-Packard cathode ray tube (CRT) display (Model 1332A, P31 Phosphor). The grating was counterphase modulated in contrast at a high temporal frequency and simultaneously swept in spatial frequency at a slow rate. The display appeared as flickering bars either continually increasing or decreasing in size.

A free-running 1 MHz triangle wave generated the fast sweep on the CRT vertical axis. The horizontal or X sweep was generated by a ramp function triggered by a master clock locked to a multiple of the alternation rate of the stimulus pattern. With the use of an Exact 507 lin/log sweep function generator, Z-axis modulation was produced by a triggered burst of the modulating waveform synchronized with the start of each X-axis sweep. The voltage-controlled frequency input (VCF) of the Z-axis generator was driven by a ramp function which continually varied the spatial frequency of the grating. The apparatus is quite flexible, allowing linear or logarithmic sweep over a range of up to 1000:1 with no change in other stimulus parameters such as luminance or contrast.

The mean luminance of the display screen was generally set at 46 cd/m^2 which gave a linear ($\pm$10%) control of contrast with input voltage up to 90%. Contrast, measured according to the standard definition,[11] was adjusted to 80%, unless otherwise specified.

Recording and data analysis. A bipolar electrode montage was employed with the recording electrodes placed 3 cm above the inion and 3 cm above and lateral; the ear served as ground.

The steady-state VEPs were extracted from the noise by a narrow-band synchronous filter technique.[7, 8, 10] Eliminating the need for computer averaging to obtain the signal from the scalp EEG, our filter was set at the temporal frequency of pattern reversal, with a bandwidth of 0.57 Hz and a time constant of less than 1 sec. The signal was rectified and fed to the Y-axis of the X-Y plotter, while the ramp producing the frequency sweep in the waveform generator controlled the X position. Thus the plotter displayed VEP amplitude as a function of spatial frequency of the alternating pattern.

Procedure. The observers, resting comfortably in a supine position, viewed an overhead mirror image of the 20° by 15° CRT display which generally appeared at a distance of 37 cm. Ongoing EEG activity was monitored continuously to ensure observer vigilance and comfort. Observers fixated (when possible) a 0.3° star for the duration of the recording epoch (10 or 20 sec).

For comparison with the electronic sweep method under various conditions (see below), psychophysical estimates of acuity were also obtained. Using the method of adjustment, the observer varied the spatial frequency of the flickering gratings to threshold, and at least three separate settings were made to obtain the average threshold value.

Results and discussion

We describe the application of this technique to the measurement of several aspects of visual function. Variants of the procedure are appropriate for the measurement of visual acuity, assessment of refractive error, determination of equality of visual function in the two eyes, binocular interaction and suppression, and sequential assessment of therapeutic conditions.

Visual acuity. The object in measurement of visual acuity is to obtain an estimate of the highest spatial frequency to which the visual system will respond. As Regan[6] has pointed out in his version of the technique, the time constants of both the synchronous filter and the brain response tend to delay the response and hence to displace it in the direction of the sweep. This will result in either an overestimate or an underestimate of visual acuity, according to whether the sweep is increasing or decreasing in spatial frequency. We deal with this problem in two ways. The displacement is minimized if the response approaches the region of the acuity limit slowly.

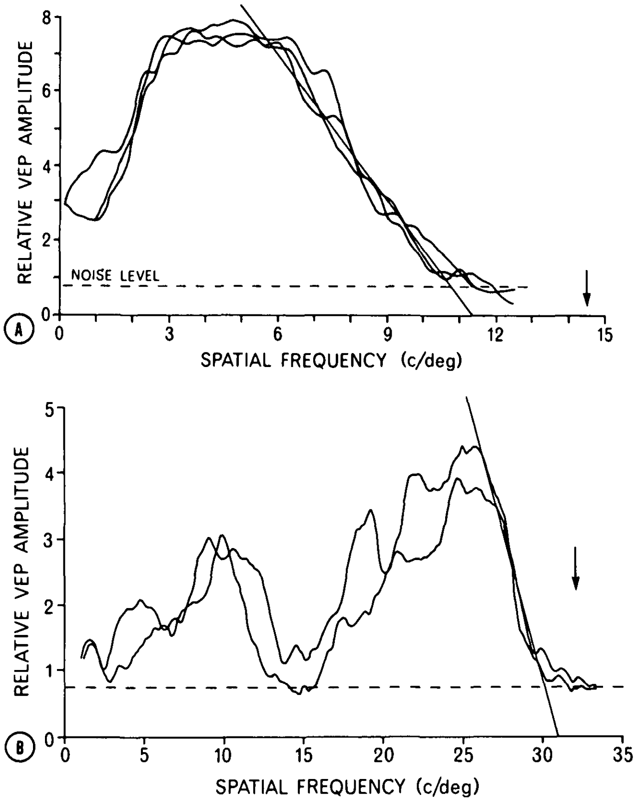

Fig. 2. VEP amplitude vs. spatial frequency for the linear sweep technique. A, Three separate traces are superimposed to show the repeatability of the data. The solid line is drawn by eye, and extrapolated through the noise (dashed line) to the 0 voltage level to determine the VEP acuity (see text for details). The psychophysical acuity is shown by the arrow (Observer D. L.). B, Same as in A, but with the following differences. The stimulus was within a 2° foveal disc, screen luminance was increased to 360 cd/m^2, viewing distance increased to 74 cm, and contrast was increased to 90% and set to square wave modulation.

We therefore use a linear, rather than a logarithmic, spatial frequency sweep. An overestimate is avoided by sweeping down in frequency. This results in a slight underestimate which, to be conservative, we use to correlate with measures of psychophysical acuity (see below).

In order to simplify the estimation procedure, we utilize the technique suggested by Sokol[12] of fitting the high spatial frequency portion of the VEP curve with a linear function and extrapolating down through the noise to give an estimate of the acuity at zero response level. This is based on the twin results of Campbell and Maffei,[13] who showed that near threshold the VEP amplitude is proportional to log contrast, and of Campbell and Gubisch,[14] who showed that log contrast sensitivity is linearly proportional to spatial frequency above about 5 c/deg. Taken together, these results imply that the VEP amplitude should be linearly proportional to spatial frequency near the acuity limit. An important advantage of this intercept method is that it is amplitude-insensitive. Thus it does not depend critically on a number of extraneous factors: thickness of skull, electrode localization, field size, etc.

An example of visual acuity measurement using this technique is shown in Fig. 2, *A*. The spatial frequency was swept from 0.2 to 12.5 c/deg with a linear sweep of 20 sec duration and a temporal alternation rate of 24 reversals per second (24 rps). Three separate

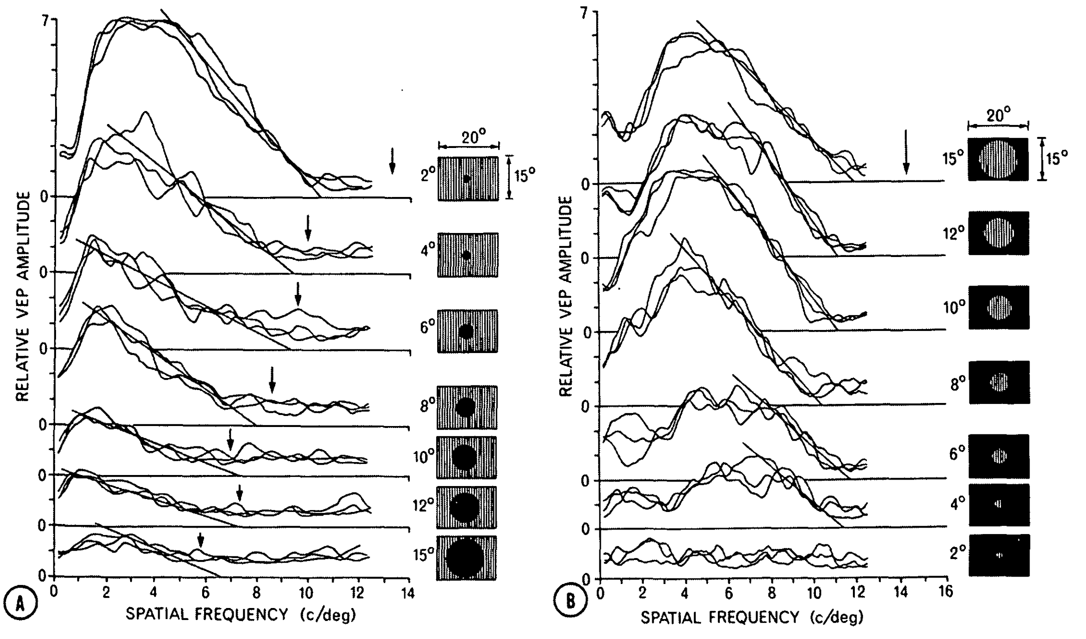

Fig. 3. **A**, Linear sweep VEP data for annular stimuli which ranged in inner diameter from 2° to 15° with a constant outer diameter of 20° by 15°. Estimated VEP acuity values are the intersection of the solid line with the 0 voltage level, and psychophysical acuities are shown by the arrows (details as Fig. 2). **B**, Linear sweep VEP data for disc stimuli which ranged in diameter from 2° to 15°. Estimated VEP acuity values are obtained as in **A**. The constant psychophysical acuity is shown by the arrow.

runs are superimposed. It is clear that in the higher spatial frequency region, the response falls approximately linearly with spatial frequency. A straight line may readily be fitted to these data by inspection, giving an extrapolated acuity in this case of 11.3 c/deg. We have fitted all the curves by inspection, but in principle the data can be digitized and the analysis performed automatically by an online computer. These values are quite similar to the comparable psychophysical acuity for this observer (shown by arrow). To obtain an equivalent complete psychophysical function takes about 20 min, as compared with 1 min for the three sweep VEP measures.

The VEP acuity value is low relative to the maximum acuity obtainable for this luminance level. One reason for this reduction is that the psychophysical acuity is itself reduced for the alternating grating relative to a static grating, but there is also a small error in the VEP estimate produced by the fact that the sweep is decreasing in spatial frequency, producing a delay of the response at each point of the sweep plot. The spatial resolution of the oscilloscope was an additional limitation because we required a short viewing distance (37 cm) to obtain a large field size.

To ensure that normal acuity estimates could be obtained if desired, we conducted a subsidiary test with three modifications to the apparatus. The area of the raster was reduced by a factor of 10, which increased the mean luminance obtainable to 360 cd/m^2. The viewing distance was doubled to 74 cm, and the stimulus was set to a square waveform with 90% contrast. The sweep was now run from 1 to 35 c/deg with a field size of 2°. Data for the observer of Fig. 2, *A*, under these high acuity conditions are shown in Fig. 2, *B*. Now the extrapolated VEP acuity increased to 31 c/deg and thus approximated the increased psychophysical acuity of 32 c/deg (arrow). This makes it clear that our low acuity estimates are due to technical limitations and that a high-luminance, fine-reso-

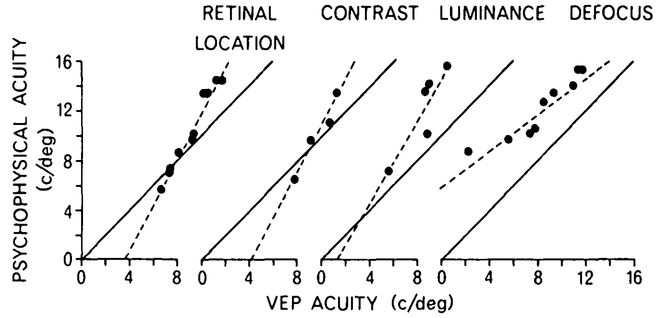

Fig. 4. Scattergrams of psychophysical acuity vs. VEP acuity for four different conditions: retinal location (annuli, 2° to 15°, see Fig. 3), contrast (0.1 to 0.8), luminance (0.5 to 46 cd/m^2), and defocus (0 to 3D, see Fig. 6). The solid lines show an absolute 1:1 correlation; the dashed lines are fit to the data by least squares regression (Observer D. L.).

lution display provides measures comparable to those obtained by other means. In addition, this control shows that good responses can be obtained from the foveal (2°) region under these conditions, whereas under our normal procedure foveal responses are rather small (Fig. 3, *B*).

For comparison with clinical conditions, a reduction in visual acuity was mimicked in four different ways: optical defocus, reduction in contrast, reduction in luminance, and stimulation of a series of peripheral regions of retina. In the case of the peripheral responses, we mimicked a central scotoma of varying size by presenting a series of annuli containing the flickering grating. The inner diameter of the annuli varied from 2° to 15°, and the outer dimension was constant at 20° by 15°.

A series of sweep data for the peripheral annuli from 2° out to 15° are shown in Fig. 3 *A*, which further illustrates the linear nature of the high-frequency fall-off and the ease with which a linear function may be fitted to it. The psychophysical acuities in each case are shown by the arrow. These show a reasonable fit for the more peripheral data, although the VEP sweep technique somewhat underestimates acuity in the more central regions.

The complementary series of foveal discs with an outer diameter from 2° to 15° is shown in Fig. 3, *B*. In this case, the psychophysical acuity is constant at approximately 14 c/deg (arrow), since the observer can always use the foveal region, and addition of the extra area of grating beyond 2° should not be expected to improve psychophysical acuity. However, such areal increases would be expected to increase the amplitude of the VEP at lower spatial frequencies, as can be observed in Fig. 3, *B*. This provides an important test of the high-frequency intercept method of estimating acuity, since it is designed to be insensitive to variations in VEP amplitude. The results certainly validate this method, giving acuity estimates which fall at 11 ± 1 c/deg at all field sizes despite the variation in VEP amplitude.

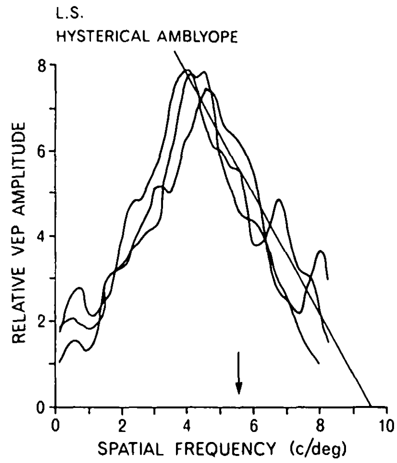

Fig. 5. Linear sweep VEP data for Patient L. S. (female, age 9). Note that the psychophysical acuity (arrow) is markedly reduced with respect to the VEP acuity (intersection of solid line and 0 voltage level).

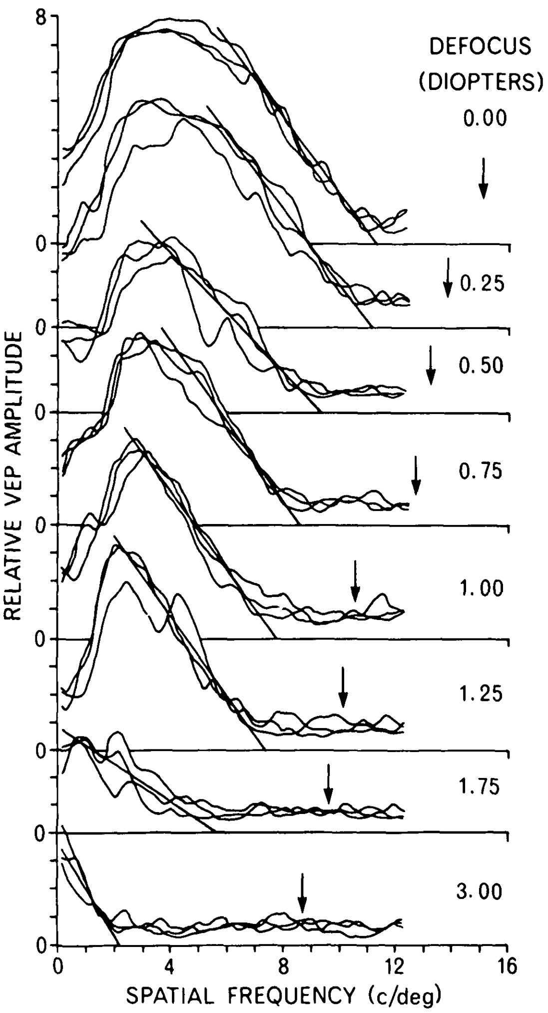

Fig. 6. Linear sweep VEP data for 0.00 to 3.00 diopters of optical defocus. Details are as in the other linear sweep data (see Fig. 2).

Similar series were obtained for central viewing of a 20° by 15° field with reductions in contrast, with reductions in mean luminance level, and with optical defocus. The full set of acuity estimates is plotted in the form of scattergrams between psychophysical and sweep VEP measures (Fig. 4). The correlations obtained between the psychophysical acuity and VEP acuity estimates for these four conditions are high ($r = 0.87$ to 0.99), but under our conditions, the sweep VEP tends to underestimate the higher acuity values by about 25% (0.1 log unit). The solid line in each scattergram indicates a theoretical absolute correlation between the two measures. The dashed lines have been fit to the data by least-squares regression. It is interesting that the slopes of the regression lines for the retinal location, contrast, and luminance conditions are quite similar, whereas the optical defocus data show a much flatter slope, suggesting that the VEP may be a more sensitive indicant of blur than is psychophysical acuity (see Refractive error).

An exception to this acuity underestimate in normal observers was found in the case of a patient with hysterical amblyopia (Fig. 5). This patient showed a significantly higher VEP acuity than that determined psychophysically (shown by the arrow) under precisely the same stimulus conditions (Fig. 5). In hysterical amblyopia, pattern VEPs are usually normal, and visual acuity is equally reduced bilaterally, probably due to psychogenic factors.[15, 16]

We conclude that linear extrapolation from the linear sweep VEP provides a useful technique for the estimation of visual acuity, not only of the over-all retina but also for localized regions of retina which may have suffered specific pathological losses. In these examples, we have limited the study to mild losses, but the technique may readily be adapted for extreme conditions by confining the total sweep to a smaller range, for example, 0.1 → 2 c/deg instead of 0.2 → 12.5 c/deg as has been shown here.

Refractive error. The linear sweep technique can be used for the reliable measurement of refractive error. There has recently been a series of claims and counterclaims as to the validity of VEP responses in refractive error.[17–21] These studies have all relied on the effects of blurring the edges of checks or bars of sizes which were well above the visual acuity limit. Typical sizes might be 10′ or 20′ checks, whereas tha acuity limit is reached with about 1′ checks. These authors also used low reversal rates.

Rather than picking a particular check size or spatial frequency, our approach utilizes the fast sweep technique to extrapolate to the effective acuity produced by refractive error. We find that the linear sweep technique is highly accurate and can objectively determine refractive state to within 0.25 diopter quite rapidly. This degree of accuracy results from the fact that the effects of blur are more marked at or near the acuity limit.[22]

The technique consists simply in recording the synchronous responses to the linear sweep, counterphase grating stimulus viewed through a set of refracting lenses. Each sweep takes 10 sec. The standard ophthalmic procedure of hill-climbing through spherical power, then astigmatic axis, and finally cylindrical power can be used by employing appropriately oriented gratings, except that the measure of visual acuity is now objective rather than relying on subjective discriminations. The main problem is to ensure that the observer's fixation remains in the center of the stimulus, so that a fair degree of cooperation is still necessary. In assessing infants and young children, a "peek-a-boo" technique (i.e., keeping the screen covered until immediately prior to recording) is quite effective in ensuring fixation on and attention to the visual display. With this procedure a basic assessment of refractive error has proved possible even in patients as young as 6 months of age.

The sensitivity of the linear sweep to induced refractive error is illustrated for a good observer in Fig. 6, which shows a series of sweeps with increasing spherical power, with the linear functions extrapolated to zero response amplitude. Note that there is little change in the response amplitude at low spatial frequencies (e.g., 2 c/deg). The data fall with a good approximation to linearity, and it is clear that a small change in lens power has a strong effect on the extrapolated value of the spatial frequency limit. It is probable that this extra loss in the VEP reflects the inability to accommodate continuously on the blurred stimulus, whereas short periods of good accommodation may be sufficient for psychophysical determinations.

These data show that, contrary to the conclusion of Bostrom et al.,[21] it is possible to use the VEP for estimation of refractive error if the technique involves stimulation by high spatial frequencies and higher temporal frequencies than have typically been used. However, it is unlikely that such a technique would be of much clinical advantage for determining refractive error, since a retinoscopic determination is easy, even in relatively uncooperative, nonverbal patients. The great sensitivity of the sweep VEP to refractive error serves as a caution to ensure that accommodation is appropriate for the stimulus if an accurate assessment of visual acuity is required. Nevertheless, the effect of varying lens power may be useful in differentiating between optical and neural anomalies in clinical conditions such as amblyopia.[19, 23]

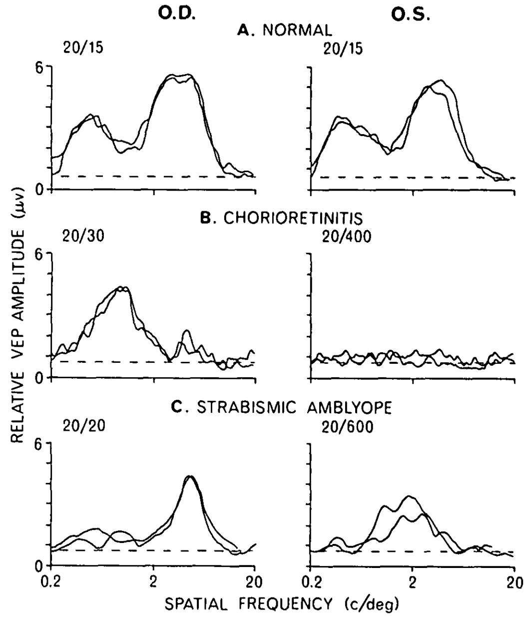

Fig. 7. Monocular comparisons with logarithmic sweep VEP. A, Normal observer (D. L.) O.D., 20/15, O.S. 20/15. B, Patient with chorioretinitis (R. D.), O.D., 20/30, O.S., 20/400. C, Strabismic amblyope (B. B.), O.D., 20/20, O.S., 20/600.

Assessment of monocular function. Our previous studies[10, 24] have emphasized the nonhomogeneities in VEP amplitude across spatial frequency of the stimulus. In view of this nonhomogeneity and the large individual differences in response profile, we do not recommend the use of absolute VEP amplitude as an indicant of specific loss (except at the acuity limit, where it appears to be quite stable).

This problem may be overcome by the use

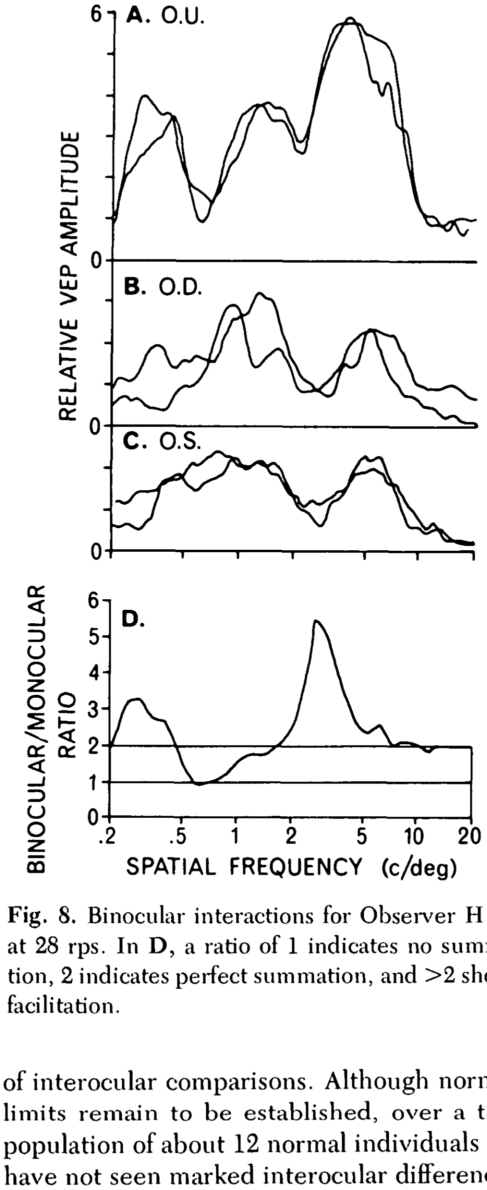

Fig. 8. Binocular interactions for Observer H. S. at 28 rps. In **D**, a ratio of 1 indicates no summation, 2 indicates perfect summation, and >2 shows facilitation.

of interocular comparisons. Although normal limits remain to be established, over a test population of about 12 normal individuals we have not seen marked interocular differences in the VEP. Both the amplitudes and phases of the responses are typically similar between the two eyes at all spatial and temporal stimulus frequencies. On the other hand, most patients with some diagnosed monocular pathology show large differences between the pattern of responses from the two eyes. Interocular comparison is therefore a useful diagnostic tool and has been extensively utilized for pattern-evoked potentials in the past.[4, 6, 23, 25] The interocular comparison technique may now be extended to a full range of pattern vision by the use of a version of the spatial-frequency sweep technique. This is of particular importance because it has recently been shown psychophysically that pathological conditions can affect some spatial frequencies and not others.[26-28] Furthermore, there may be residual function at low spatial frequencies even when acuity is severely degraded.[25, 29-31]

In order to give appropriate weight over the range of spatial frequencies, a logarithmic sweep of spatial frequency is optimal for determining the structure of the spatial-frequency tuning function. A logarithmic sweep gives equal weight to each octave of spatial frequency in order to correspond with the tuning functions obtained psychophysically.[32, 33] A two-decade range 0.2 to 20 c/deg appears adequate, and it is preferable to use a 20 sec sweep time if the attention span of the patient allows it. We have found that a temporal frequency in the region of 24 rps is a good compromise between high rate and good signal-to-noise ratio.

Examples of data from a normal observer and two types of visual dysfunction (chorioretinitis and strabismic amblyopia) are shown in Fig. 7. What is clear from these data is that the curves from the right and left eyes of the normal observer (Fig. 7, *A*) are highly similar both in shape and amplitude even though the characteristic specificity of tuning to spatial frequency is present. Note that these separable spatial frequency peaks are often not visible with the linear sweep because the low and medium frequencies are swept rapidly and peaks and troughs integrated by the 0.8 sec time constant. The logarithmic sweep allows more time at these frequencies, but it correspondingly reduces accuracy in the high-frequency region and hence is unsuitable for acuity measurement.

Fig. 7, *B*, shows data from a patient who had long-standing chorioretinal lesions. The right eye showed some mild involvement, which appears to be reflected in the slightly reduced Snellen acuity (20/30), and the fact that the VEP did not show a strong response at high spatial frequencies. The left eye showed large areas of involvement and markedly reduced acuity (20/400) and exhibited drastic VEP losses across the entire frequency spectrum. In contrast, the data for a strabismic amblyope (Fig. 7, *C*) with even greater visual acuity loss in the left eye (20/600) show a much more selective pattern of loss and even an increase in response relative to the normal eye at spatial frequencies around 1 c/deg. We have observed such abnormalities in other amblyopes,[25] and similar changes have been reported by Sokol.[31] The losses are of course to be expected, but the amplitude increases in the amblyopic eye at particular spatial frequency regions are suggestive of some kind of functional reorganization in the pathways of the amblyopic eye. Two possible processes are suggested by the data. In most cases, the response increases appear as a downward shift of the peak seen in the normal eye to lower spatial frequencies for the ambylopic eye. Thus, if the peak is produced by some kind of resonant response to specific spatial and temporal frequencies, the space/time constants may change to some larger value, resulting in a peak shift.

The other possibility is that the response is derived from some active inhibitory or suppressive mechanism. In this case, the presence of a response might reflect the suppression of function rather than the presence of some function. This kind of process is exhibited in the ubiquitous alpha-rhythm, which appears when over-all visual function is under suppression. Certain pattern VEP peaks could correspond to similar or related processes operating specifically on the suppressed (amblyopic) eye. We have not tested one of these two hypotheses vs. the other as yet.

Assessment of binocular function. A neglected aspect in the VEP diagnosis of visual function is the assessment of binocularity. Although retinal losses must have a concomitant effect on the binocular response, under some conditions (e.g., strabismus), a binocular loss may occur in the absence of retinal losses. We have found that in normal observers the binocular response may vary from zero summation, in which the binocular response equals the mean monocular response, to facillation, in which the binocular response is greater than the sum of the two monocular responses. The degree of binocular interaction is highly specific and is dependent upon such stimulus dimensions as spatial and temporal frequency.[24] Given this degree of specificity, testing binocular function under only a few stimulus conditions may be inappropriate. In this regard, the sweep VEP has a great advantage because it can be exhaustive with respect to spatial frequency and thus permits an extremely rapid exploration of the complex details of binocular interactions over a wide range of stimulus conditions. As an illustration of the application to binocular interaction, we show the binocular responses of a normal observer at 28 rps (Fig. 8, *A*). Fig. 8, *B* and *C*, show the responses for the right and left eye obtained under the same stimulus conditions. It is apparent that the binocular response is considerably larger than its monocular components but has the same general form. The comparison is facilitated by plotting the ratio of the binocular to the mean monocular response as a function of spatial frequency (Fig. 8, *D*). For this observer the degree of binocular interaction

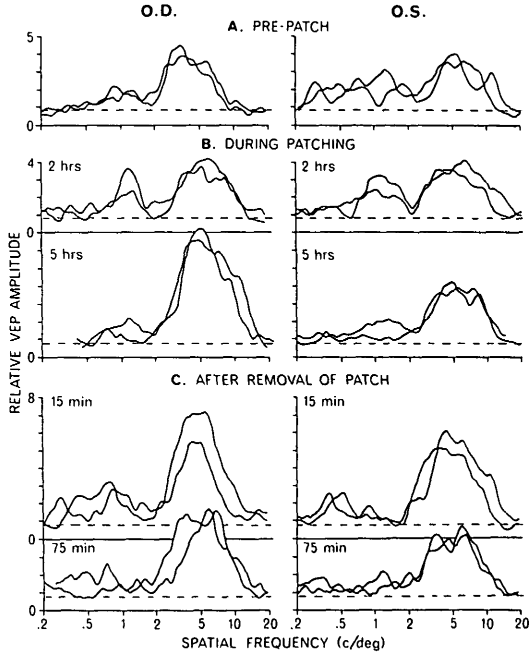

Fig. 9. Effect of patching left eye for logarithmic sweep VEP for Observer D. L. at 24 rps.

varies from no summation at approximately 0.6 c/deg to dramatic facilitation in a narrow region around 3 c/deg, where the binocular response is approximately 5.5 times the mean monocular response.

As is usual in observers with normal vision, the binocular response does not fall below the mean of the monocular responses. Since the variations seen in binocular interactions are complex, requiring exploration over a wide range of spatial and temporal frequencies, we conclude that the sweep VEP technique provides a rapid method for comprehensive identification and study of binocular interactions which should be of value in the analysis of disorders involving abnormal binocular function.

Therapeutic assessment. The rapidity of the sweep technique makes it valuable for sequential monitoring of the effects of therapeutic techniques on visual function and visual acuity. As an example of a therapeutic technique which could easily be transposed to the laboratory, we chose a simple monocular patching regimen such as might be used in the treatment of amblyopia. The monitoring procedure is equally applicable to the effects of topical or systemic drug treatments, surgical procedures, or even optical manipulations.

The procedure consisted of occluding the left eye of a normal observer for 5 hr while he ambulated in a normal visual environment (except for the brief test periods). The sweep VEP was measured for each eye alone and for both together, to determine the changes in monocular function and binocular interactions. Measurements were taken prior to patching, once an hour during patching, and at regular intervals after removal of the patch to determine the effects of recovery. The logarithmic sweep was used because we were interested not so much in visual acuity as in the general effects of patching on the various frequency regions.

Sample results are shown in Fig. 9 for the spatial tuning functions obtained prior to patching (Fig. 9, *A*), at 2 and 5 hr following application of the patch to the left eye (Fig. 9, *B*), and 15 and 75 min after removal of the patch (Fig. 9, *C*). After 2 hr of patching, little change is evident; after 5 hr, there is a dramatic doubling of the amplitude of the high-frequency peak in the exposed eye, accompanied by little change in the patched eye. Such an increase in the nondeprived eye has been reported recently in this journal[34] and must be a neural effect since no patching was applied to this eye.

Removal of the patch produced the first major effect on the patched eye, which was a dramatic response increase reminiscent of a postinhibitory rebound (Fig. 9, *C*). The unpatched eye's response was decreased again by removal of the patch; by 75 min after removal, the responses of the left eye were back to the baseline level, while the right eye still showed some elevation. Curiously, no interesting changes were observed in the binocular response, which remained at about 0.8 of the sum of the monocular responses throughout all conditions. Similar results have been found during patching with transient VEP recording,[34] but the rapid sweep technique allows examination of the post-patch period over the entire range of spatial frequencies.

The data presented here are intended to show that the sweep VEP technique is sensitive to visual changes produced by this therapeutic patching regimen. In addition, the sweep technique allows the effects of patching to be assessed with great rapidity, thus minimizing exposure during the testing sequence.

Conclusion

The electronic sweep technique described provides a rapid and useful method of VEP assessment of several aspects of pattern vision. The speed and reliability of assessing pattern vision by sweeping spatial frequencies, as well as other stimulus dimensions, are of great value for both clinical and research purposes.

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