
Factors affecting visually evoked cortical potentials such as impaired vision of varying etiology

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Visually evoked responses produced by flickering light stimulation were recorded from the scalp over the occiput in normal subjects and patients with unilateral central visual loss due to various causes. It was necessary to use a digital computer so that the small evoked signals could be detected from larger extraneous potentials not "time locked" to the stimulus. The signal to noise ratio was also enhanced by using a narrow band pass frequency filter. Inter-subject comparisons of the evoked response obtained from central stimulation of one eye were limited by intersubject variability. However, there was much less variability in the evoked responses obtained from stimulation of each eye in the same subject. Impairment of vision in an eye with a central retinal lesion was indicated by a significant decrease in the size of the evoked response as compared to stimulation of the other normal eye and correlated roughly with the degree of visual loss. Uncorrected refractive errors and opacities of the media altered the magnitude of the visual evoked response much less than lesions directly involving neural tissue. An apparent decrement in evoked cortical response size with increasing age was found. The potential for determining macular functioning and the integrity of central visual pathways even with media opacities were discussed.

While recording visually evoked occipital potentials in a study of objective visual field testing,¹ it was apparent that considerably larger occipital potentials were evoked with central retinal stimulation than

with slightly peripheral stimuli. The greater magnitude of evoked potentials from central macular stimulation suggested a relationship might exist between these potentials and visual acuity. Therefore, this investigation was undertaken to determine if reduced visual acuity from different causes could be related to the magnitude of evoked occipital potentials.

In addition, considerable variability in the size of visually evoked potentials recorded from both the eye and cerebral cortex has been described, particularly when the responses obtained from different subjects are compared.²⁻⁴ Primarily, attention has been directed to recording techniques and response comparisons. Considerably less study has been devoted to the

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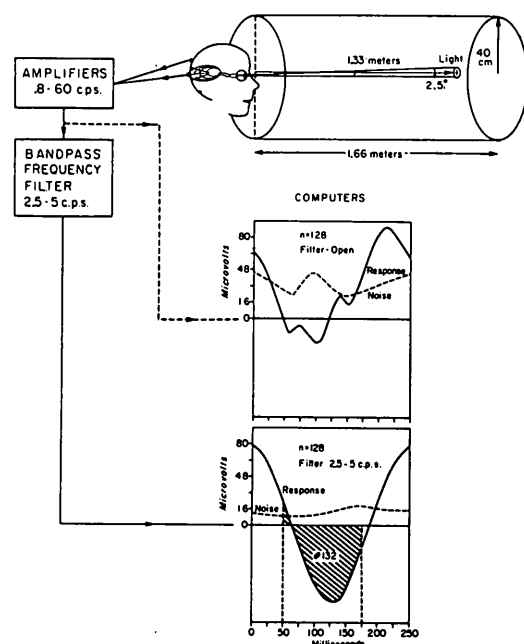


Fig. 1. Diagram indicating the method of ocular stimulation, recording, and actual tracings of evoked responses as obtained from the computer. The area of the filtered evoked response below the base line between 50 and 175 msec. is integrated to serve as a quantitative measure of the size of the evoked response. The "noise" (dashed lines) represents the averaged response with the light visually occluded but clicking.

alterations in evoked potentials caused by manipulations in stimulus parameters such as the background illumination, stimulus size, frequency of stimulation, etc. Even less attention has been paid to inherent subject variables such as visual acuity, the effect of spectacle corrections, state of adaptation of the retina, clarity of the optical media, and the presence or absence of ocular abnormalities. An exception has been the effect of pupillary changes on evoked responses, which has received considerable investigation.⁵ Therefore, it was also the purpose of this study to examine some of the causes of variability in visually evoked cortical responses relating to the importance of such factors as corrected visual acuity, optical imperfections, refractive error, and age.

Method

The essentials of the method are indicated in Fig. 1. The subject is seated with the head directed into a cylinder 40 cm. in radius and 1.66 M. in length. The head is steadied by a chin rest. The cylinder has the advantage of isolating the subject's head from extraneous distractions and supplies a more even background luminance (8 millilamberts). The stimulus light located 1.33 M. from the eye subtends a visual angle of 2.5 degrees. The stroboscopic xenon flash lamp has an energy of 0.3 joules and, with diffusors in place, an estimated average peak intensity of 53,200 lux. The duration of flashes was approximately 10 microseconds and the frequency of stimulation was always 3.8 c.p.s.

In all but one experiment (Fig. 2) the subject's attention was directed at a small black cross directly at the center of the light. Subjects were instructed to move as little as possible and maintain fixation accurately during recording trials. Each eye of each subject was tested separately (other eye occluded). Six trials were presented to each eye. A trial consisted of 128 flashes at 3.8 c.p.s. At the end of each trial the size of the summed evoked response was recorded and at the end of the test the six summed evoked responses obtained from stimulation of each eye were averaged. Thus, in most of the experiments a comparison of the mean evoked responses obtained from stimulation of one eye is compared to that obtained from the normal fellow eye to give a ratio. Data points shown in all figures are, therefore, representative of mean responses obtained from six trials presented to each eye separately. During testing the trials were presented to each eye in random order so as to minimize effects of such variables as distraction and habituation.

The evoked responses were recorded from the skin over the occiput via a differential set of electrodes. The silver disc electrodes were separated by two inches and oriented vertically with the lower electrode located over the inion. The electrodes were held in place by an elastic headband and EEG electrode jelly was injected under the electrodes to facilitate contact. The skin impedance between these electrodes was intermittently measured to establish adequate skin contact. An ear clip electrode was connected from the ear to ground. The potentials were then amplified through a system with a gain of 240,000 and a frequency response of about 0.8 to 60 c.p.s., i.e., 3 decibels down at .8 and 60 c.p.s. The amplifiers consisted of a Grass Model 5P5 condenser coupled amplifier connected to a Model 5 Grass D. C. driver amplifier. The signals were further amplified with a Tektronix type 122 low level pre-amplifier and a type 125 power supply. For the experiments shown here, the amplified potentials

were then passed through a Krohn-Hite narrow band pass frequency filter (Model 330 MR) with the filter settings at 2.5 to 5 c.p.s. A Syber Corporation digital computer then processed the neuro-electric activity by using well-known techniques to extract small signals from larger background noise. A Mnematron CAT computer and a Syber Corporation Neurac computer were also available to view the wave shapes.

In Fig. 1 a representative tracing obtained from the Neurac computer is displayed "filtered" and "unfiltered." The digital responses used in this study were obtained by integrating the area of the "filtered" wave form between 50 and 175 msec. below the base line (shaded area in Fig. 1, which was equivalent to 132 in this case). This integrated area was found to show good correlation with the magnitude of peak to peak amplitudes of the "filtered" evoked responses. The dashed lines represent the responses obtained when the light was occluded (noise).

Fifty-six subjects were examined during this study. The vision was checked in all subjects, refractions performed, and temporary corrections supplied where needed. Patients were sought who had abnormalities of central vision in one eye with normal vision in the fellow eye (corrected vision of 20/25 or better). Vision was recorded in subjects at 20 feet except when worse than 20/200. Patients received routine ophthalmologic evaluations such as refractions, ophthalmoscopy, and biomicroscopy with the facilities in the Ophthalmology Clinic of the University of Florida College of Medicine. Several trained observers were also repeatedly used for special experiments.

Results

Fig. 2 shows the magnitude of evoked occipital responses when a 2.5 degree stimulus light is located at different degrees off the visual axis in both the vertical and horizontal meridians. A trained observer was used because of the time-consuming nature of this experiment and the need for accurate fixation. Each point represents the mean of six trials (in each trial $n = 128$). The trials were presented in random order intended to minimize decrements in evoked responses known to accompany habituation. It is apparent that the evoked response obtained from central macular stimulation is about four times as great as that obtained when the stimulus light is located only 2.5 degrees off the visual axis.

In Fig. 3 the data from three groups of

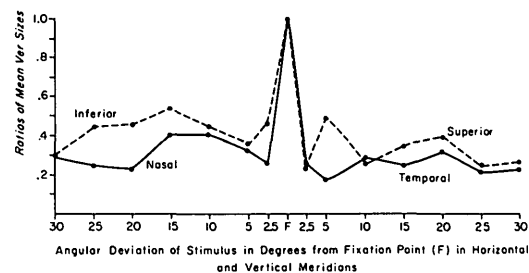


Fig. 2. The evoked occipital response is shown when the 2.5 degree diameter stimulus light is located at different points in the visual field of the right eye of one trained observer. Each point represents the mean of six trials ($n = 128$ flashes each trial) with all trials randomly recorded. The means are plotted as ratios of the peak response (fovea). Ver, visually evoked response.

patients are illustrated. The "neural" group consists of 18 patients with varying degrees of visual loss in one eye only. The term "neural" is used to indicate lesions affecting the macular or central optic pathways such as macular scars, tumors and degenerations, and retinal detachments with macular involvement. Patients with central scotomas from lesions in the optic pathways such as an optic neuritis were also included in this group. None of the patients studied had lesions behind the chiasm. All had one normal eye so that the mean evoked response obtained from stimulation of that eye could be compared to that from stimulation of the defective eye. Thus, the ordinate, Fig. 3, represents the ratio obtained by dividing the mean evoked response obtained from stimulation of the defective eye by that obtained from the normal fellow eye in the same subject. This ratio is plotted against the visual acuity in the defective eye on a log scale representing the reciprocal of visual acuity (numbers in parentheses) or the visual angle of resolution in minutes.

The "opacity" group refers to 11 subjects who had either a cataract, corneal opacity, or vitreous opacity in one eye only sufficient to reduce the Snellen visual acuity. Only patients were tested in whom it seemed apparent that neural tissue was

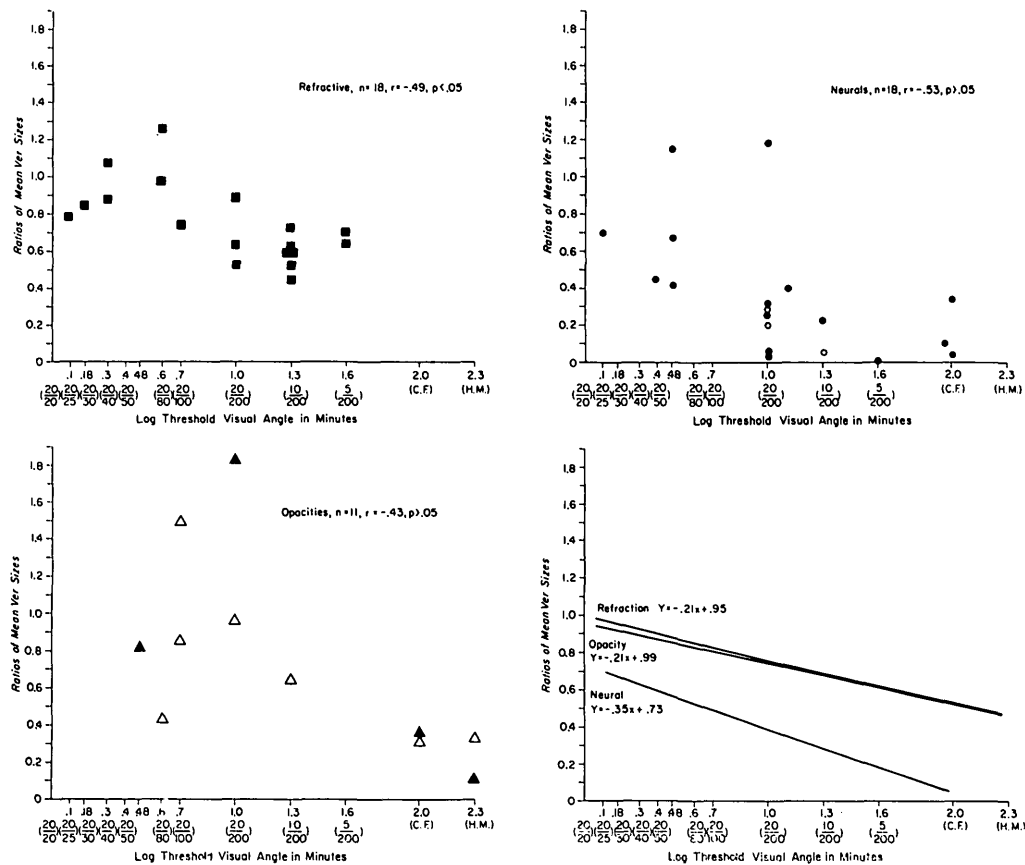


Fig. 3. The ordinate for the "neural" lesions and "opacity" of the media groups consist of patients in whom the evoked response obtained from stimulation of the abnormal eye may be compared to the normal fellow eye, and is expressed as a ratio, i.e., ratios of mean VER sizes equal mean VER obtained from stimulation of the abnormal eye divided by that obtained from stimulation of the normal eye. In the refractive error group the ratio refers to the mean VER obtained from stimulation of the eye, uncorrected, divided by the mean VER obtained from the same eye, corrected. The lines in the lower right hand corner of the figure represent the regression lines for each group. Ver, visually evoked response. Open circles and triangles equal dilated pupils.

not impaired, i.e., no evidence of macular disease or optic nerve disease. Again, the mean evoked response obtained from stimulation of the impaired eye was compared to that obtained from stimulation of the normal fellow eye.

The "refraction" group consisted of 9 subjects with normal eyes, except for varying degrees of refractive error. In these subjects the mean evoked response obtained from stimulation of each eye uncorrected was compared to the mean response obtained from the same eye corrected. Thus,

eighteen ratios were plotted from these subjects.

In a study of 18 normal subjects not shown in this figure, monocular stimulation resulted in no significant mean response difference between left and right eye stimulation or even binocular stimulation in the same subject. Therefore, the initial value would theoretically be a ratio of one for an infinitely large group. The average ratio in this group of normals was .88 with a standard deviation of .23. The intersubject variation with present techniques does

not allow absolute comparisons of response size as correlated with visual function, i.e., no correlation is present between absolute evoked response size and visual acuity in intersubject comparisons. However, as can be seen in Fig. 3, there is a significant correlation at the .05 level between visual acuity and the ratio of the evoked response obtained from stimulation of the impaired eye to that obtained from stimulation of the normal eye in the same subject. This was true for both the "neural" and "refractive" groups. It is apparent also that the "neural" and "refractive" groups are significantly different when the level and slope of the regression lines are examined. Neural lesions result in a much greater reduction in the evoked response when compared to a control eye than refractive errors for the same visual acuity reduction.

Examination of the "opacity" of the media group shows no significant correlation to visual acuities. However, inspection of the data suggests that cataracts or corneal scars do result in slight reduction of the evoked response obtained from stimulation of the abnormal eye as compared to the normal control eye in the same subject.

The question of the effect of pupillary dilation on the size of the evoked response was raised. In Fig. 4 the mean evoked response is plotted against different stimulus diameters and for two different artificial pupil sizes. The artificial pupils were located on the glasses of a trained subject (corrected vision O.D. of 20/15), 13 mm. from the cornea. The subject's pupil was dilated with Neosynephrine 10 per cent to 8 mm. in diameter. There is a definite increase in mean evoked response size when the larger aperture pupil is used for all stimulus diameters except the largest where no difference exists. Because pupil size affects the size of the evoked response, only patients were tested in whom the pupils were equally dilated so that the responses from stimulation of either eye could be compared. The results obtained from subjects with dilated pupils, as in Fig. 3, are indicated by open circles.

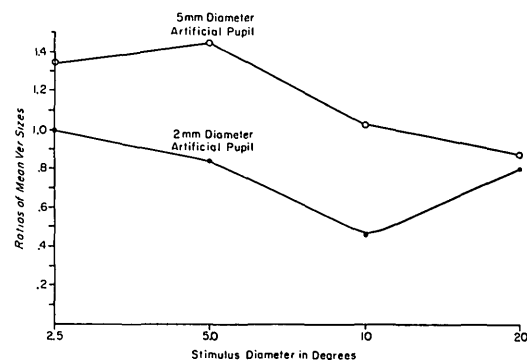


Fig. 4. The difference in evoked response size is shown with different stimulus diameters when an artificial pupil was worn 13 mm. in front of the cornea of a normal trained observer. The ratios represent the mean response sizes referred to that obtained with a 2.5 degree stimulus and a 2 mm. diameter artificial pupil. The observer fixated the stimulus lights centrally in all cases. *Ver*, visually evoked response.

In the same subject, stimulation through the right pupil (8 mm. in diameter) was compared to stimulation through the left (4 mm. in diameter) with the 2.5 degree diameter stimulus and the usual technique. The mean evoked response obtained from right eye to left eye stimulation was 1.22, which is an increase comparable to that found by slightly more than doubling the pupil diameter through the use of an artificial pupil, as in Fig. 4.

Because of the relatively slight reduction in visually evoked response elicited by refractive errors in different subjects, an additional experiment was performed with a trained subject. The refractive error of the right eye was increased by the interposition of convex lenses causing an induced myopia. The left eye was always used as a control (*V* o.s. = 20/20 corrected). The formula⁶ used to determine the visual acuity for so many diopters of induced myopia is given in the legend and was employed primarily so that the results shown in Fig. 5 could be compared on a similar scale to the "refractive" group in Fig. 3. It appears that no significant reduction occurs in the evoked response ob-

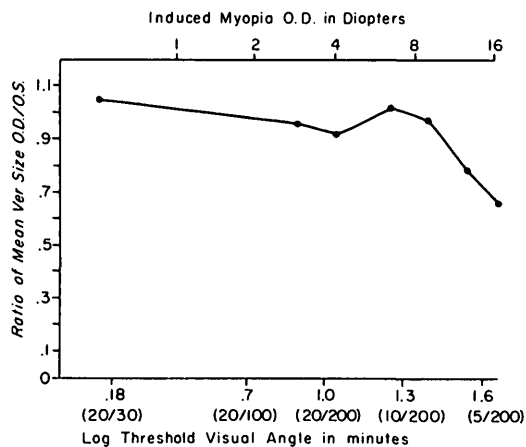


Fig. 5. The mean evoked response obtained from central stimulation of the right eye of a trained observer with varying degrees of induced myopia is compared to that obtained from stimulation of the normal corrected left eye ($V_{o.s.} = 20/20$). The myopia was induced with convex lenses of various dioptric powers. The visual loss induced is computed with the formula, $A = 2.8 M$, where A is the threshold visual angle in minutes and M is the diopters of induced myopia. Ver , visually evoked response.

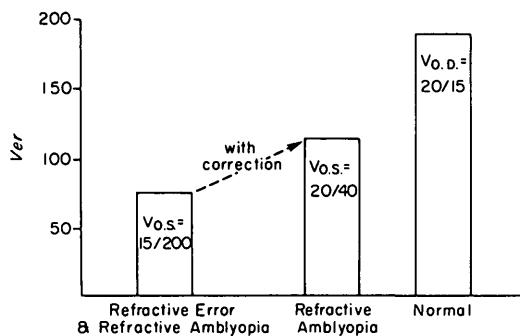


Fig. 6. Bar graph showing the results from a patient with a refractive error and neural lesion (refractive amblyopia) in one eye as compared to the normal fellow eye. Ver , visually evoked response.

tained from stimulation of an eye until the induced refractive error approaches about 10 D. The results are not exactly comparable to those of the "refractive" group in Fig. 3 since in the latter refractive error was not induced but presumably resulted from changes in the anterior-posterior

length of the eye as well as differences in the indices of the refracting media.

Fig. 6 displays the results obtained in one subject thought to be of particular interest. This young adult male had normal vision in one eye with no significant refractive error. In the other eye there was a significant compound myopic astigmatism ($-2.00 -3.00 \times 70$). However, full correction of the refractive error improved vision to only 20/40. Thus, it was felt that a refractive amblyopia also existed in this patient, resulting from the anisometropia. It is evident that the reduction in evoked response caused by the refractive error is significantly greater than expected and is of the magnitude expected for a "neural" lesion. It is believed that this reduction results, therefore, from the noncorrectable refractive amblyopia.

When the mean evoked response obtained from stimulation of 64 normal eyes is plotted against age, an apparent decrement in response size occurs with increasing age. Also, there appears to be more variability in the size of the evoked response in the young. Fixation was observed to be no worse in the older age group, particularly as compared to the children, and there appeared to be no significant differences between skin contact and impedance with age. The application of electrodes was facilitated by the baldness of many elderly subjects.

Discussion

The major difficulty encountered in this study was the intersubject variability of the evoked visual responses. This variability has been previously described and the suggestion made that in spite of variability such responses might be useful in evaluating the individual visual system.² It is not possible from this investigation to draw any conclusions regarding central visual function from the size of the visually evoked response obtained from stimulation of any single eye. Perhaps the only exception would be the instance when the magnitude of the visual deficit is so great as to

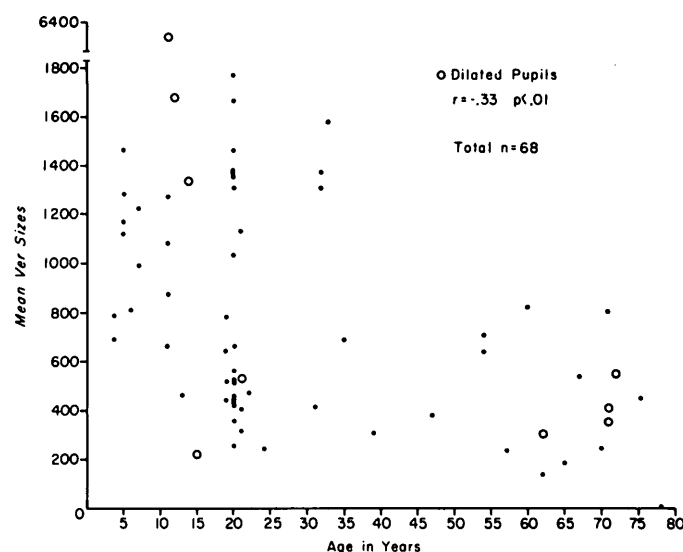


Fig. 7. Graph showing age range of 4 to 78 years plotted against mean VER size in normal eyes, corrected vision of 20/25 or better). Ver, visually evoked response.

approach complete blindness. In a malingerer feigning total blindness, for example, the presence of a good visual evoked cortical response from stimulation of the supposedly blind eye would be evidence that the eye was not completely blind.

A test such as this even in its present form suggests immediate clinical usefulness as an objective test in malingering, where unilateral visual loss is ordinarily feigned. However, the necessity of knowing visual function in one eye to make predictions about vision in the other is a pronounced limitation of such a technique. Similar attempts to evaluate objectively the visual field have avoided this problem¹ since the evoked response obtained from stimuli at various loci in the visual field of the same eye are compared, obviating the need for intersubject and even interocular comparisons with their consequent variability problems. This suggests the possibility of comparing the evoked response from central retinal stimulation to that obtained from more peripheral stimulation in the same eye as a more reliable means of predicting visual acuity. For example, it has been shown that a reduction in visual acuity, induced through the interposition

of convex lenses before an eye, affects central acuity greatly but peripheral visual acuity much less.⁷

It has been observed in this laboratory that visually evoked cortical responses may be detected at faster rates of flicker such as 16 c.p.s. from central macular stimulation, whereas signals are not apparently extracted from noise with more peripheral retinal stimulation when only 200 averages are made. It is interesting that with a higher rate of flicker (18 c.p.s.) and a 1 degree diameter orange stimulus light intended to favor photopic mechanism, the amplitude of the response from foveal stimulation is greater than that from peripheral retinal stimulation when recording evoked retinal potentials and using similar averaging techniques.⁸ These investigators did not find regional differences with slower rates of flicker (5 c.p.s.) and blue light flashes. It is probable, then, that our technique with xenon flashes (containing considerable blue light) at 4 flashes per second, and in spite of some background illumination, was stimulating scotopic mechanisms as well as photopic. Therefore, the probable reason in our study for the increased sensitivity of foveal stimulation

(Fig. 2) and the correlation of evoked response size to foveal functional integrity is the extensive area of foveal representation in the visual cortex lying in close proximity to the recording electrodes.

Higher rates of flicker, red light stimulation, and, perhaps, smaller stimulus sources might have further enhanced the correlations sought here. More intense stimulus background illumination would further suppress the irradiation of the retinal image of the stimulus, i.e., it is thought that about a 5 degree area of retina was actually illuminated rather than 2.5 degrees as suggested by blindspot experiments.

It is believed that through the introduction of such innovations and the fortuitous large representation of the fovea in the visual cortex immediately under the occiput, it may be possible to stimulate the retina diffusely as through closed lids and still primarily record foveal function. Even in this investigation a study of patients with unilateral cataracts suggested that a potential exists for testing macular integrity behind lens opacities sufficiently dense to preclude ophthalmoscopic examination. The relative lack of reduction of the evoked response when viewing the stimulus through a corneal or lens opacity is not thought to be related to the more diffuse area of retina stimulated through scatter. The interposition of translucent or ground glass filters in front of the eye of one normal trained observer and several patients with central chorioretinal scars did not result in larger evoked responses as would be expected if scattered light was an effective stimulus. For this reason, and others previously alluded to, it is believed that even though the stimulus light is dispersed as it passes through opacities of the media primarily macular integrity is being tested. Also, as shown in Fig. 4, the largest diameter stimuli do not necessarily give the largest evoked responses. Similarly, reductions in stimulus intensity do not always result in smaller visual evoked responses.^{3, 9}

This study does indicate that when the vision in one eye is known the visual acuity

may be roughly predicted in the other eye with such techniques. Further, the dramatic reduction in the size of the evoked response when neural tissue is diseased as compared to the slight reduction when only a refractive error exists for comparable reduction in visual acuity suggests such a technique may be potentially useful in distinguishing visual loss from refractive errors and opacities of the media from that caused by retinal and optic nerve diseases. The question may be raised as to whether the reduction in the size of the evoked response with decreases in visual acuity may be related to the inability of such subjects to fixate accurately the stimulus. This may be a legitimate criticism for visual reductions greater than 20/200, but would not explain the marked discrepancies between the "neural" and "refractive" groups.

Before this technique can become clinically useful, intersubject variability will have to be reduced. Differences in pupil size and fluctuations contribute to variability,⁵ as again demonstrated in this study. Artificial pupil apertures may reduce this variable.

Age is a variable requiring additional study before its effect can be accurately predicted. It is interesting that subjective studies of central visual function have previously shown decrements in function with age, especially as in this study where stimulus exposures are brief.^{7, 10, 11} It is our subjective impression that larger evoked responses were obtained from the elderly subjects who were more "alert" or exhibited more "curiosity" and "vitality."

Technical difficulties also contributed to the variability encountered in this study. For example, the area of the filtered response integrated beneath the base line does not correlate ideally with the peak to peak amplitude or the total area of the evoked response which would more accurately indicate the magnitude of responses. With narrow band pass frequency filtering, the evoked response approaches a sine wave in shape and phase shifts which sometimes occur, particularly in children, resulted in

an integrated area of the wave form, giving an inaccurately low representation of the evoked response as compared to peak to peak amplitudes. For this reason, evoked responses were even more affected by age differences than is evident in Fig. 7.

Myogenic potentials induced from the sound of the light click can be a source of contamination¹² and needs further investigation with our particular technique. Our "noise" readings or "controls" consist of recording trials with the stimulus light covered so that it cannot be seen by the subject. However, during such controls the discharge of the light is still audible. Such "controls" were performed in all subjects. As shown in Fig. 1, the "noise" readings are significantly smaller than the visually evoked responses. However, the "noise" varies in magnitude from subject to subject and such myogenic potentials may contribute to variability.

Continued attempts will be made to reduce variability so that intersubject comparisons may become possible. When this is accomplished it is believed that a useful tool will exist for assessing central visual function, particularly in young children, psychotic subjects, and some neurological patients unable to be tested through more conventional means. The problem of fixation in anesthetized and comatose subjects can be circumvented by accurately projecting flickering light stimuli onto the area to be tested through direct visualization employing an ophthalmoscope with a fiber optic bundle.

We wish to thank May Briscoe and Alan Plum for their assistance in data collection and analysis.

Discussion

Dr. Arthur Jampolsky, San Francisco, Calif. I wish to congratulate the authors in their attempt to shorten the lag time between new laboratory techniques which assess the visual apparatus and the possible clinical application to everyday problems.

Some perspective in this field may be provided

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to the uninitiated by posing the following questions:

What do recorded evoked potentials mean?

How far along are we in the attempt to determine objectively visual fields and visual acuity?

Are we on the threshold of being able to measure objectively visual functions formerly assessable only by psychophysical methods? The

most familiar and wearying psychophysical visual determination for this group is represented by the familiar question. "Which is clearer, lens number one or lens number two?"

Certain it is that a new era has been ushered in with the availability of new tools and new techniques.

Computer averaging techniques make it possible to record at various levels (retina or cortex) the responses evoked by visual stimuli, even when the response to be measured is very small relative to the interfering biologic electrical activity from which it is to be extracted. Computer averaging techniques allow this to be done if repeated stimulus-response measurements can be made in order to enhance the recognition of useful responses, and average out or throw away, the interfering "noise." The visual apparatus is ideally suited for repetitive stimuli, such as light flashes, and one can measure how the retinal nervous system handles this information, as well as measure its arrival at the visual cortex. Improved techniques are making it possible to use more discrete visual stimulus patterns, rather than gross ones.

As with any new technique, it takes time to understand fully the variables. Here the number of parameters are many. In recognizing this, the authors acknowledge that they have been more concerned with techniques than with the stimulus parameters, and are now attempting to elucidate more clearly the latter. They present evidence showing the effect of pupil size upon the evoked potential. They demonstrate a decrease of evoked cortical response with increasing age, and interestingly comment that the alertness or vitality of the elderly subject influences the results. The importance of the state of "attention" in psychophysical measurements has long been known. Presently the importance of the state of "alertness" in electrophysiologic assessments needs full exploration, since it is a variable that may change from moment to moment.

Indeed, the visual cells are capable of stimulation by many nonvisual inputs—from other sensory modalities—such as audible clicks from a changing light source as reported by the authors.

One time-honored way of avoiding many of the variables is to use the subject as his own control as best possible. The authors compare one eye with its fellow, or, in other instances, one retinal area with another.

Theoretically, the effectiveness of separating signal from noise increases with the number of responses added. The improvement is determined approximately by the square root of the number of flashes delivered. However, there are practical difficulties in that the subject becomes somewhat uncomfortable after a long series of flashes with consequent changing muscle potentials and other extraneous noise.

The authors found a difference in evoked cortical potential in "neural" compared to the "refractive" group. Some of these differences may be explained by the selected stimulus, since a flashing light may affect only certain visual cortical cells. Many cells that would respond to patterned stimuli or movement might not be affected by flickering light. Thus, refractive problems may not be best evaluated by the same stimulus, since the cells activated by flicker probably would not be primarily responsible for fine form or movement perception. The latter may be related to other cortical cells, responsive to other stimuli.

Of further interest was the finding that a patient with amblyopia was found to have a decreased evoked response similar to that found in neural lesions. Burian and Watson have described alterations in photic driving in amblyopic patients. James Miller, using binocular as well as monocular photic driving techniques, found changes associated with amblyopia only when binocular stimulation was used, and he remarked upon the possibility that binocular suppression mechanism in strabismic amblyopia might be of importance. Indeed, certain cortical cells fire only upon binocular stimulation.

The authors are to be commended for their justifiable caution in interpretation of results in terms of clinical problems. I am sure they will continue to elucidate the many parameters.

Even the diagnosis of malingering, or feigned blindness, must be made with caution utilizing this technique, since the recorded cortical evoked response heralds the arrival of the visual information, but as yet we know little of how—or indeed if—it is processed or integrated further into what one sees or perceives. But inroads here are also being made, and for the first time by understanding the components of the wave form representing the information processing stages, we can begin objectively to get at certain aspects of perception and learning. It is now becoming possible to record how the senses receive information, process it, store it, and relate it.

Professor W. A. H. Rushton, in the 1964 Prentice Lecture, made the following comment: "We who investigate the workings of the human eye occupy a quite special place in the body of science, for our concern is both with the objective and the subjective. The eye is the window in that wall which separates the body from the mind and we may look both out and in. Never in history has the view been more exciting than it is today when new techniques on every side invite us to explore gardens that for centuries have been locked to all but speculation.

"We need not be too dismayed at the great grasp of those giants that have preceded us. For by standing upon their shoulders we may reach what they could only envisage."

It took some time for electrocardiography to become an accepted clinical technique. One remembers when those who did not quite believe in it would ask those who did, as the latter studied an electrocardiogram, "and what do you believe the wild waves are saying to you today?"

We must be careful not to let our enthusiasm for new techniques race too far ahead of our ability to interpret the meaning of what we

measure and record. If one proceeds with caution, recognizing artifacts and variations, one will be able to make sensible some of the many wiggles produced by our giant computer with its pink jelly in its bony box. It will become possible to capture and identify and reliably relate the visual response which was formerly lost amidst the background roar of biologic noise.