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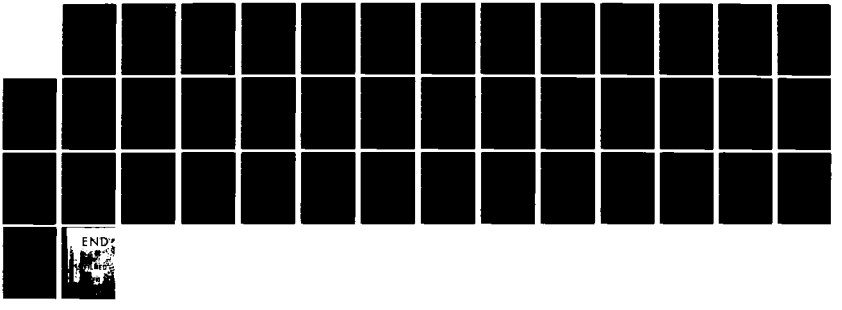

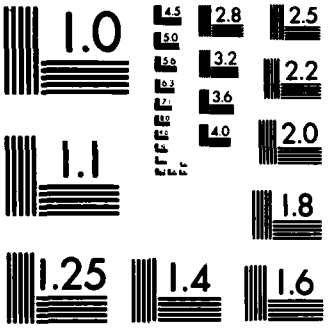

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PACIFIC UNIVERSITY
COLLEGE OF OPTOMETRY
FOREST GROVE, OR 97116

Dr. Robert L. Yolton

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Ten steady-state visual evoked responses (VERs) were recorded from each of 47 normal, adult subjects. For each subject, the mean and standard deviation for the ten VER amplitudes were calculated and used to determine amplitude variability. While some subjects produced extremely reliable VERs, data from the majority showed a considerable degree of variability. A number of factors including trend, Noise, attention, binocularity, accommodation, eye movements, artifacts and electrode placement were evaluated to determine their relative contributions to this variability. Noise and trend factors produced a large proportion of the variability (62%) while the other factors were found to be relatively insignificant.

SUMMARY OF RESEARCH WORK

AFOSR Grant 82-0160
Robert L. Yolton, O.D., Ph.D.
Pacific University College of Optometry
Forest Grove, OR 97116

STATUS OF RESEARCH

During the project period, the major goals described in the original proposal were reached. An assessment was made of the distribution of evoked potential variabilities found in the general population and a set of specific factors were evaluated to determine how much of the variability each produced.

REPORTS AND PUBLICATIONS

A preliminary report of this research was presented at the American Academy of Optometry Meeting in Philadelphia, December 1982, and a complete report of the work was presented at the School of Aerospace Medicine, Brooks Air Force Base, Texas.

A report of the research project which preceded this one (contract F49620-79-C-0038) will appear in the August, 1983 issue of the American Journal of Optometry and Physiological Optics and a report of the current work will be submitted to the same journal.

PROFESSIONAL PERSONNEL

Robert L. Yolton, O.D., Ph.D., Director of Research of Pacific University College of Optometry was the principal investigator for the research project. John Hagan, B.S., Optometry Degree Candidate, assisted Dr. Yolton. Drs. William Dunn and Dennis Engdahl and Mr. Sam Ashenberner developed programs for the computerized analysis of the evoked potentials.

INTERACTIONS

Preliminary results of this work were presented at the American Academy of Optometry Meeting in Philadelphia and a complete report was presented at Brooks School of Aerospace Medicine. During the project period, Dr. Yolton maintained close contact with Dr. Ralph Allen of the School of Aerospace Medicine.

NEW DISCOVERIES OR INVENTIONS

No patentable devices or new applications were developed in the course of this project.

ADDITIONAL INFORMATION

In this project, information was developed on the range and sources of variability that would be found in evoked potentials recorded from a general population of humans. Future projects can now be conducted to find ways to reduce this variability so as to make visual evoked potential recording a more useful technique for objectively assessing the status of the visual system in humans and animals.

EVALUATION OF FACTORS PRODUCING VISUAL EVOKED RESPONSE VARIABILITY

The visual evoked response (VER) is a gross electrical signal produced primarily by visual cortex cells as they respond to transients in visual space. In laboratory and clinical settings, these transients usually involve changes in the luminance and/or pattern of a stimulus, which is often a checkerboard. If the VER eliciting transient involves only a phase reversal of a checkerboard pattern, the amplitudes of the primary components of the response are determined by a number of factors including the size of the checks, the clarity of the image, and the adaptation state of the retina. These relationships have suggested the usefulness of the VER as an objective means for assessing a number of visual system parameters including acuity and refractive error. (1,2)

Unfortunately, repeated measures of the VER under constant, optimum conditions have demonstrated that VER amplitudes are somewhat variable (unreliable).(3) For many subjects, this lack of repeat-measure reliability limits the precision with which VER determined refractive error and acuity measurements can be made.(4) Occasionally, however, subjects can be found who produce extremely reliable VER data and these "selected subjects" are sometimes used in laboratories to develop VER measurement techniques, but problems can occur when these techniques are used with subjects who are drawn from the population at large and whose amplitudes are quite variable.

To provide information on how unreliable steady-state VER amplitudes are 10 separate, consecutive VERs were obtained from each of 47 normal, adult subjects. Variability found in the VERs

from these subjects provides an estimate of the range of values that would be encountered in the general population.

Factors which may be related to the lack of VER amplitude reliability were also considered in this study. These included noise, which is recorded along with the VER and not completely removed during signal processing, trend effects through which a subject's VER amplitudes increase or decrease in a sequential fashion, and physiological factors including changes in attention, accommodative and pupil states, artifacts, eye movements and blinks, binocularity, and recording electrode placement.

SUBJECT POOL

Forty seven subjects voluntarily participated in this project. Their mean age was 27.3 years (SD = 4.1, range = 21-39). Thirty-four were male and 13 were female. All were emmetropic or had visual corrections (glasses or contact lenses) which provided a minimum 20/20 visual acuity at distance and near. These corrections were worn during all phases of the study (except where noted). All subjects had normal binocular vision and were free from significant visual anomalies and/or pathologies.

METHODS

Electrodes

In the experiments described below (exceptions are noted), VERs were recorded using standard techniques. Silver disc electrodes (1.0 cm diameter) were attached to each of the subject's earlobes and a 1.0 cm silver disc electrode was positioned 1.5 cm

above the inion on the mid-line of the head. Inter-electrode impedances were 5,000 ohms or less.

Stimulus

Subjects were comfortably seated in a darkened room and viewed a stimulus checkerboard made up of 15 arc min black and white checks (white checks 21.5 f-L, black checks 1.9 f-L). This check size was selected so as to elicit large amplitude evoked potentials from normal subjects.(1) The checkerboard was produced on a high contrast, high resolution video monitor (Tektronix Picture Monitor, Model 633) which was driven through a custom interface by an IEC Model F36 Function Generator. The monitor subtended an angle of 290 x 230 arc min at the 5.7 m viewing distance.

During VER recording, the checkerboard was sinusoidally phase reversed at a rate of 15.60 reversals per second by a sinusoidal driving signal from the function generator. No luminance fluctuations or other visually detectable artifacts were produced by the display.

Data Processing

Signals from the electrodes were amplified by a Gould Universal differential amplifier (frequency cut-offs of 0.3 and 100 Hz), analyzed on-line using a Data General NOVA 800 computer (5), and stored for re-analysis using a Vetter Model C-4 FM analog tape system. The computer was programmed to acquire 100 consecutive time-locked epochs (sweeps) of data with each epoch being 384 msec in duration. These 100 epochs were ensemble averaged and Fourier transformed to obtain a power spectrum from which an amplitude

spectrum was derived.(6) The analog-to-digital conversion rate (3.0 msec between successive conversions) and the total number of conversions in each 384 msec epoch (128) provided a Fourier bin resolution of 2.6 Hz, and placed the frequency of the primary VER response (15.6 Hz) in the center of an analysis bin. The amplitude of the 15.6 Hz response is referred to as the "VER" or the "Signal" in the discussions below.

Ten measurements of noise present at 15.6 Hz were also obtained during each recording session by ensemble averaging noise signals from subjects' electrodes during periods when the checkerboard display was visible but not phase-reversing. These signals were averaged and Fourier transformed in exactly the same manner as were the VER data and the resultant 15.6 Hz amplitudes are referred to below as "Noise".*

To record a single VER and Noise trial, the subject was alerted to the fact that the trial was about to begin and was asked to fixate on the center of the display. The checkerboard was then sinusoidally phase reversed at a counterphase rate of 15.6 Hz. Thirty seconds after the reversals were started, VER data acquisition began.(7) Thirty-eight seconds of data were ensemble averaged and Fourier transformed after which the pattern-reversal was stopped and the subject was instructed to relax for 1.0 min. Following this rest period, the subject was again asked to concentrate on the center of the stopped (non-reversing) checkerboard for an additional 38 seconds while Noise data were obtained and processed. A 1.0 min relaxation period followed after which the sequence was

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*The word "Noise" will be capitalized when it refers to only the 15.6 Hz portion of the entire noise spectrum recorded by the electrodes.

repeated until a total of 10 pairs of VER and Noise amplitudes were obtained from the subject.

For each of the 10 pairs of values, a Signal/Noise (S/N) ratio was determined by dividing the 15.6 Hz VER amplitude by the corresponding 15.6 Hz Noise amplitude. These 10 ratios were then used to calculate a mean Signal/Noise ratio for the subject.

Variability Indices (VIs) were also calculated for each subject. As defined by Yolton, et al. (3), the Variability Index is the standard deviation of the 10 VER amplitudes expressed as a percentage of their mean. An advantage of using VIs is that they are unaffected by increases or decreases in amplifier gain settings between subjects.

POPULATION PARAMETERS

In the course of this project, 10 VER and Noise amplitudes were collected from each of 47 subjects under standard recording and data analysis conditions (i.e. not involving a specific manipulation such as artifact rejection, etc.). These data can be used to draw conclusions regarding evoked potentials recordable from the general population of normal, young adults. Figures 1 and 2 present frequency histograms of the S/N ratios and VIs within the subject population. Although the majority of subjects have somewhat variable evoked potential amplitudes and low S/N ratios, some subjects do produce very reliable signals. Clearly, it is these latter subjects who would be candidates for use in psychophysical studies involving the need for reliable VER measurements.

Figure 1.

Frequency histogram showing occurrences of various S/N ratios in the population of normal subjects.

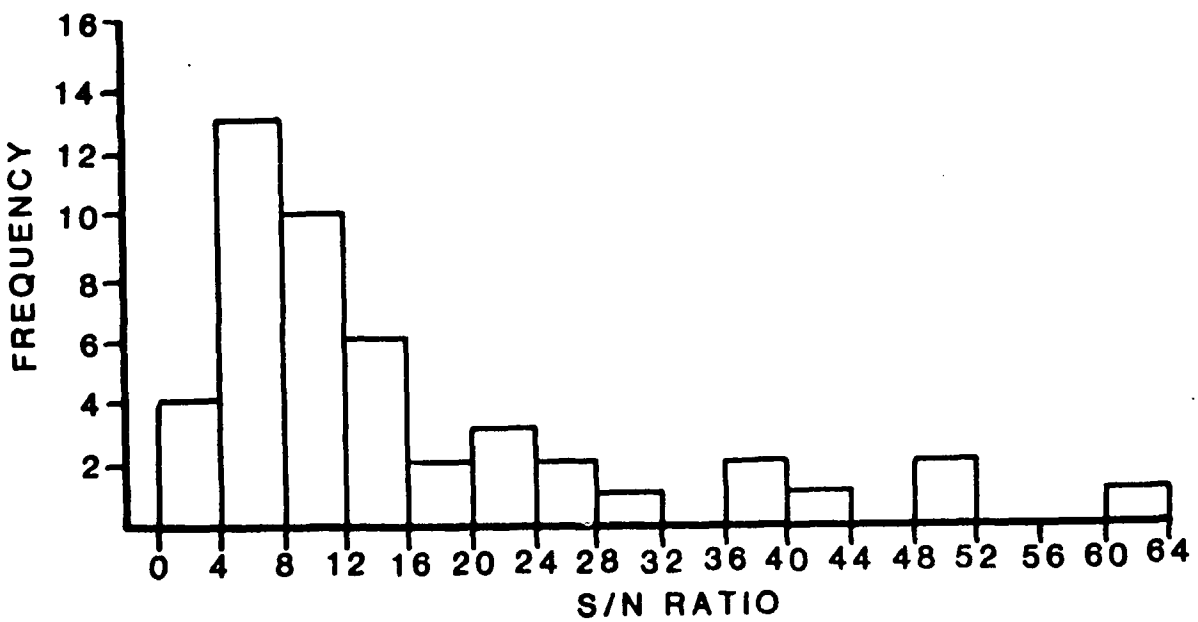
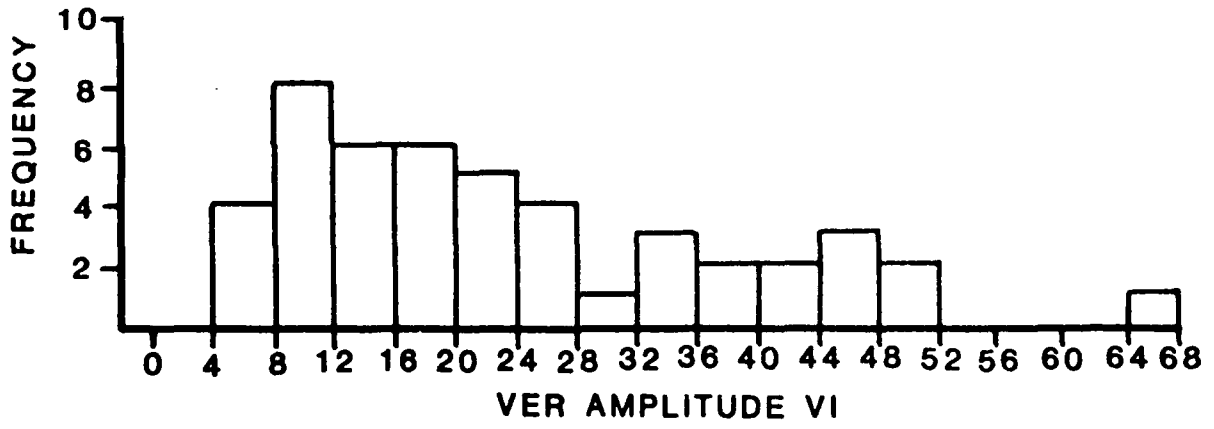


Figure 2.

Frequency histogram showing occurrences of various VI values in the population of normal subjects.



The reasons for the range of VIs and S/N ratios across the population is not known, but present speculations (8) include differences in bone thickness of the skull, core body temperature, and/or location of the foveal representation in the cortex with reference to the recording electrode site.

The classical wisdom that females produce larger and more reliable VERs than males was not supported by data from the experimental population. A t-test comparing S/N ratios for males versus females yielded a $t = 0.45$ ($df = 45$) which was not significant at the 0.05 level. A t-test for the corresponding male/female comparison of VIs ($t = 0.18$, $df = 45$) was also not significant. As a further demonstration of the fact that females do not necessarily produce the most reliable VER data, the subject with the highest S/N ratio and lowest VI was a male.

Intuitively, it would be expected that S/N ratios and VIs should be related with high S/N ratios being associated with low VIs (and vice-versa). Figure 3 illustrates that such a relationship does exist but that it is non-linear. The equation for the curve plotted on the Figure has the general form:

$$Y = \frac{1}{A + (B \star X)}$$

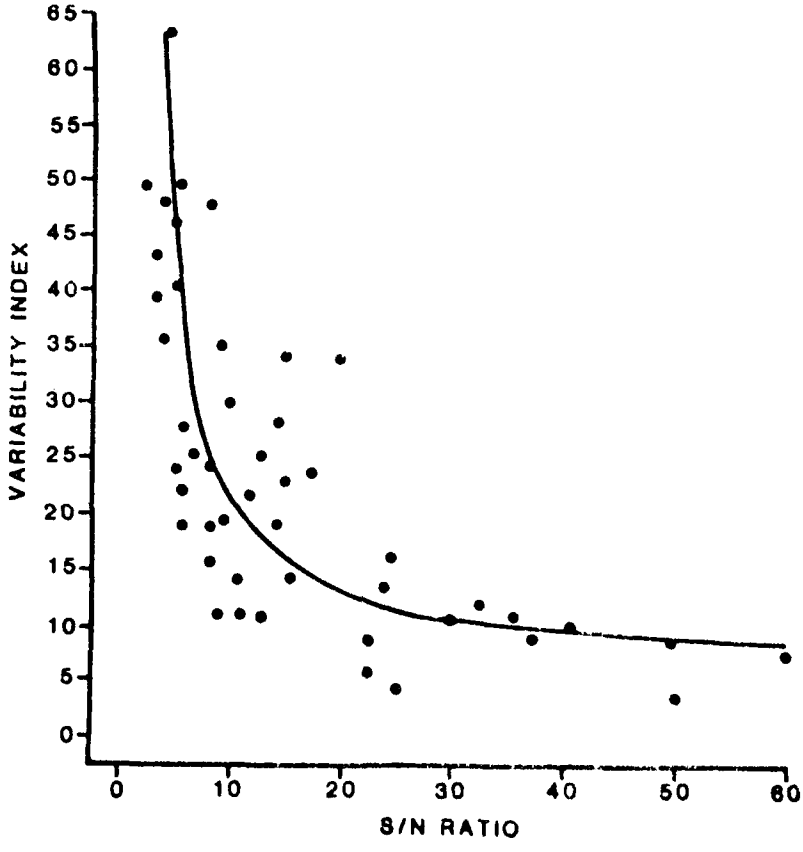
where Y is VI, X is S/N ratio, and A and B are constants.

FACTORS CONTRIBUTING TO AMPLITUDE VARIABILITY

Various factors have been suggested as possible causes of steady-state VER amplitude variability. Based on prior work and on a review of the available literature, several factors have

Figure 3.

S/N ratios versus Variability indices for the normal population. Dots represent data for individual subjects and the solid line is generated by use of the equation described in the text.



been selected for evaluation in this study. They are: trend, Noise, gross artifacts, eye movements and blinks, attention, accommodation and pupil changes, binocularity and recording electrode placement. The importance of trend and Noise effects can be assessed using data from the entire population of subjects, but the other effects require separate experimental manipulations to demonstrate their relative importances as sources of VER amplitude variability.

Trend Effects

When a series of VERs are recorded from a subject over a period of an hour or more, there is the possibility that fatigue (or other factors) could produce a systematic trend in the data. Such a trend would be shown by a correlation between the position in the sequence of the recorded VERs (eg. 1st, 2nd, etc.) and the corresponding amplitude. For all subjects in the pool, a mean correlation of $r = -0.04$ was calculated for the relationship between sequence number and the corresponding VER amplitude. While this value is not significantly different from zero, some individuals did show high plus or minus r values. Such high correlations could arise by chance factors alone, but it is also possible that some subjects behaved in a manner somewhat parallel to augmenters or reducers (11-13) and produced VERs that systematically increased or decreased with repeated measurements (even when a constant stimulus was used).

To determine the importance of the trend effect and its contribution to each subject's amplitude variance, correlations (as described above) were calculated for each subject. These correlations were then squared to determine the percentage of the variance within

the 10 VER amplitudes that could be accounted for by trend. The mean of these percentages was 25.3 (SD = 25.6) which means that across subjects about one-quarter of the total amplitude variance could be accounted for by trend effects. Since variances are additive, it also means that about 75% must be accounted for by other factors.

Noise

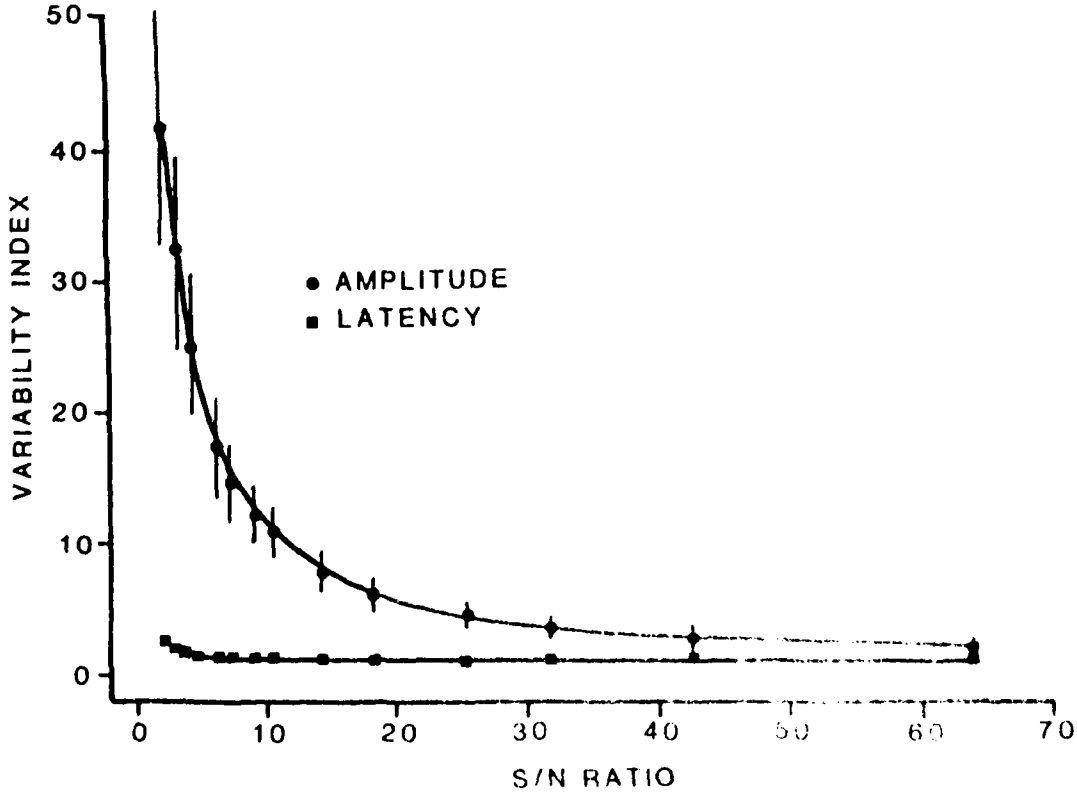
Yolton, et al. (3) and others (8,9) have developed models designed to explain how steady-state VER amplitude variability can be affected by Noise. In the models, it is usually assumed that VERs recorded from subjects are the sum of two components, a "true" VER sinusoid, and a Noise sinusoid, with each component having the same frequency. It is further assumed that the Noise is added to the "true" VER to produce the recorded VER, and that recorded VER variability is caused by, 1) fluctuations in the amplitude of the Noise (Noise VI), and 2) fluctuations in the phase relationship between the sine waves simulating the Noise and the "true" VER.

Figure 4 illustrates the VI predictions made by the model using different S/N ratios and a fixed Noise VI of 60% (which is approximately the median value for the subjects in the pool). The shape of the curve is the same as that for the data from the population of subjects as shown in Figure 3 and the equations of the curves in both Figures take the same form (but with somewhat different constants). This strongly suggests that Noise accounts for a

Figure 4.

The filled circles represent mean amplitude Variability Index predictions for different S/N ratios. The curve joining the points has the same general equation as the curve in Figure 3. This particular curve is derived by using a Noise Variability Index of 60% which is typical of the subjects in this study. The filled squares represent latency Variability Indices for different S/N ratios. These values are obtained by using a Noise VI of 60% and assuming a mean latency of 90 ms.

Vertical lines on the amplitude curve indicate plus and minus one standard deviation. The scale of the Figure does not allow standard deviations to be shown on the latency curve.



significant proportion of the amplitude variability in recorded VER data.*

Just as the sequence correlation coefficient predicted the proportion of each subject's amplitude variance accounted for by trend, the Noise model allowed prediction of the proportion of each subject's variance produced by Noise. Specifically, a computer (Nova 800) was programmed to first converge upon an amplitude for the sine wave which would best represent the subject's "true" VER. This was done by adding the subject's 10 actual Noise values (with phase randomized) to an arbitrarily selected "true" VER amplitude. The mean S/N ratio for the 10 simulated VERs was computed and the process repeated until 500 sets of 10 simulations had been produced. The overall mean S/N ratio for the simulated VERs was then compared to the S/N ratio from the subject's actual data, and, if these values were not equal, the amplitude of the "true" VER sine wave was adjusted, and the process repeated until the overall mean S/N ratio of the computer simulations was equal to the mean S/N ratio of the subject's actual data. In this way, the computer converged on a unique value for the amplitude of the "true" VER sine wave which could be held constant for all 10 VER simulations (as required by the Noise model).

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* As added support for this suggestion, the Noise model can be used to predict the phase variability of the recorded VERs. Since phase is used to determine the latency of the steady-state VER, VIs for latencies can be predicted just as amplitude VIs were. The lower line in Figure 4 shows latency VIs for different S/N ratios (assuming the same noise VI as was used for the amplitude data above). Clearly, the Noise model predicts that latencies will be much more reliable than corresponding amplitudes, which is in accord with numerous observations.(4,10) Thus, the Noise model not only predicts the shape of the curve for recorded VER amplitude VIs across S/N ratios, but it also correctly predicts that amplitudes will be much more variable than will be corresponding latencies.

Ultimately, the computer produced 500 sets of ten recorded VER amplitude simulations which met the mean S/N ratio requirement. The variance of each set of ten amplitudes was calculated and an overall mean and standard deviation of the variances obtained. For each subject, the standard deviation of the variances was typically quite large so that there was no unique value which could be used to estimate the exact proportion of the subject's VER amplitude variance which was caused by Noise. The mean of the predicted variances was determinded to be the best indicator available, however, thus it was used in the sections below as the proportion of the total VER amplitude variance which was due to Noise. Across subjects, Noise was found to account for an average of 36.4% (SD = 26.49) of the total VER amplitude variance. Trend and Noise effects, therefore, together account for approximately 62% of the total variance in the subjects' VER amplitude data. The remaining 38% of the variance must be accounted for by other factors.

Gross Artifact Rejection

Transient electrical events or shifts in the subject's body posture during recording can cause gross artifacts which could saturate amplifiers or exceed the limits of analog-to-digital converters. If there is a differential frequency of gross artifact occurrence across VER recording trials, apparent amplitude variability can result. To assess the effect of gross artifact removal, 10 VER and 10 Noise trials were recorded on FM analog tape for each of 10 subjects (mean age = 27; SD = 7.1). The taped data were then analyzed by the computer in the "Standard" manner described above

except that 50 epochs (instead of 100) were averaged for each VER and Noise value. This process produced the "Standard" data shown in Figure 5.

The "Artifact Rejection" data shown in the Figure were obtained by again analyzing the tape recorded data, but the computer was programmed to inspect each epoch of data and determine whether a gross artifact had occurred during the epoch. A gross artifact was deemed to have occurred if the signal amplitude exceeded preset upper and lower threshold limits. If such an event was detected, the entire epoch was rejected and the next epoch of data acquired from tape. The inspection/rejection process was repeated until 50 epochs of uncontaminated data had been obtained for analysis.

For the subjects in the study, on-line monitoring suggested that all gross artifacts could be eliminated if rejection parameters were set so as to reject approximately one-third of the epochs, thus threshold limits were set to cause approximately 16 epochs to be rejected for each VER trial. (In the actual experiment, a mean of 38 percent of all epochs were rejected).

In the left portion of Figure 5, mean S/N ratios and VIs are given for the 10 VERs recorded using "Standard" and "Artifact Rejection" procedures. The means were tested for significant differences using a one-tailed t-test for related measures. (A one-tailed test was used because the differences were tested only if they showed an increase in S/N ratio or a reduction in VI produced by gross artifact rejection. An adjusted significance level of 0.001 was used because of the number of t tests made in the study.)

Figure 5.

Summary data for "Gross Artifact" rejection procedure. Values in parenthesis are standard deviations. "Rejection" variances are based on data which were adjusted for each subject so as to equate the means of the "Standard" and "Rejection" VER amplitudes.

GROSS ARTIFACT REJECTION

CONDITION	MEAN VER AMPLITUDE	MEAN S/N RATIO	MEAN VER VI	MEAN TOTAL VARIANCE	MEAN VARIANCE ACCOUNTED FOR BY NOISE	MEAN VARIANCE ACCOUNTED FOR BY TREND	MEAN RESIDUAL VARIANCE
STANDARD	1,084.5 (924.8)	10.2 (3.8)	27.5 (15.8)	58,520 (57,921)	28,964 (27,032)	8,517 (12,318)	22,048 (32,617)
REJECTION	913.1 (952.1)	12.7 (8.8)	26.6 (15.5)	44,871 (41,291)	22,161 (17,530)	5,887 (12,564)	17,023 (27,783)
	t = 1.37 df = 8 p > .001	t = 0.99 df = 8 p > .001	t = 1.0 df = 8 p > .001	t = 2.04 df = 8 p > .001	t = 1.43 df = 8 p > .001	t = 0.59 df = 8 p > .001	t = 1.32 df = 8 p > .001

As indicated in the Figure, artifact rejection procedures did not produce significant improvements in S/N ratios or VIs.

In the right portion of the Figure, mean variances are presented for the "Standard" and "Artifact Rejection" VER amplitudes. In order to compare these variances directly, VER amplitudes for each subject's "Rejection" data were adjusted to make their mean equal to the mean of the subject's "Standard" data by multiplying each VER amplitude obtained using artifact rejection by a constant. The total variance (and the other variances) given in the Figure are then based on this adjusted set of amplitudes.

As noted above, the total variance can be considered the sum of components produced by trend, Noise, and "residual" effects. Variance predictions based on trend and Noise were determined for each subject as described in previous sections, and subtracted from the total variance to obtain residual values. The means of these values are presented in Figure 5. None were found to be significantly affected by gross artifact rejection. Thus, artifact rejection was not shown to be a useful procedure for increasing the reliability of steady-state VER amplitudes. (This conclusion might have been very different, however, if children or adults who had a difficult time remaining still during the VER measurement periods had been used as subjects.)

Eye Movements and Blinks

Eye movements and blinks can cause the image of the checkerboard display to be removed from the fovea. If this happens during recording, a change in the amplitude of the evoked potential can

occur and this can produce variability. (12, 14-21) To evaluate the effects of these phenomena, eye positions and blinks were monitored using an Eye Trac (Model 106) infrared eye position detector. For 10 subjects (mean age = 26.3; SD = 4.9), analog data from the eye position monitor were recorded on magnetic tape along with the signals from the VER electrodes.

At the beginning and end of each recording session, eye movement calibrations were performed by asking the subject to move her/his eyes horizontally 1.0 degree from the center of the video display screen (approximately one-quarter of the width of the screen). The recorded magnitude of this eye movement was used as the rejection criterion in the procedures described below. The artifact produced by a blink was also measured, and this artifact exceeded the amplitude of the 1.0 degree eye movement for all subjects.

The tape recorded VER, Noise and eye position data were analyzed by using the "Standard" procedure and a "Rejection" procedure in which epochs were rejected on the basis of the occurrence or an eye movement or blink. Using the "Standard" procedure, VER and Noise data were taken from the tape just as they were recorded (ie., 50 consecutive epochs were averaged for the determination of each VER and Noise value). Using the "Rejection" procedure, the taped data were re-analyzed by processing the eye movement/blink signals along with the evoked potential data. Epochs of evoked potential and eye movement/blink data were obtained simultaneously by the computer and scanned to determine whether a blink or position change exceeding 1.0 degree had occurred during the epoch. If either of these two events was detected, the epoch during which it

occurred and the next epoch were rejected, and a new epoch of data was obtained from the tape. This process was repeated until 50 epochs of data uncontaminated by eye movements or blinks were obtained for analysis.

When a blink or eye movement was detected, it was necessary to reject two epochs because the mean latency for the visual system as measured under the recording conditions used in this experiment is about 90 ms (22). Thus, ocular events occurring in the latter part of one epoch might not be represented in the evoked potential data until the next epoch.

For all subjects, a mean of 28% of the epochs considered were rejected. Approximately 1/3 of these were rejected because of blinks and the remaining 2/3 were rejected because of eye movements.

Reference to the left portion of Figure 6 shows that the eye movement and blink rejection procedure did not improve S/N ratios or VIs. The right portion of the Figure shows that there were no significant reductions in variances produced by the rejection procedure. For the population of subjects used in this experiment, these results suggest that (contrary to expectation) eye movements and blinks did not contribute significantly to the overall variability of the steady-state visual evoked response.

Attention

A commonly suggested cause of variability in VER data involves changes in the degree of attention paid by the subject to the checkerboard display (23,24). Two approaches were utilized in assessing

Figure 6.

Summary data for "Eye Movement and Blink" rejection procedure. Values in parentheses are standard deviations. "Rejection" variances are based on adjusted data.

EYE MOVEMENT/BLINK REJECTION

CONDITION	MEAN VER AMPLITUDE	MEAN S/N RATIO	MEAN VER VI	MEAN TOTAL VARIANCE	MEAN VARIANCE ACCOUNTED FOR BY NOISE	MEAN VARIANCE ACCOUNTED FOR BY TREND	MEAN RESIDUAL VARIANCE
STANDARD	796.8	13.0	23.2	27,831	7,082	10,439	18,306
	(550.5)	(8.9)	(12.0)	(35,066)	(5,211)	(23,494)	(26,592)
REJECTION	794.1	12.0	25.0	29,129	7,108	11,435	10,586
	(548.1)	(8.0)	(12.7)	(29,816)	(5,218)	(22,038)	(8,046)
	t = 0.22 df = 8 p > .001						t = .10 df = 8 p > .001

the effects of such changes. First (as determined in the trend section above) correlation coefficients were calculated for each subject to determine the relationship between each VER amplitude and its position in the sequence of the ten gathered. The mean correlation coefficient of r = -0.04 is not significant at the .05 level, thus there is no reason to believe that a consistent drift in attention over the 1.5 hour recording period caused a systematic change in the VER data.

A second approach to the problem involved the actual manipulation of attention by the use of post-hypnotic suggestions. Through the use of these suggestions, attempts were made to relax the subjects and enhance their ability to attend to the stimulus, thus stabilizing any long or short term attentional fluctuations.

The use of hypnosis in VER recording has been explored by several authors (25,27). Most studies show little effect of hypnosis on the early components of the VER (which are usually associated with primary sensory events), however Beck and Barolin (25) did suggest that VERs appeared more stable when their subjects were hypnotized. This result, along with the apparent ability of hypnosis to alter attention and relaxation states in clinical settings, prompted an evaluation of its usefulness for reducing VER variability.

Twelve subjects were selected at random from the pool. Two declined and ten agreed to participate in the hypnosis phase of the study (mean age of subjects = 27.9; SD = 4.7). Prior to any recording, the hypnosis procedures were explained in detail. This explanation included assurances that no personal or emotional material would be dealt with in the hypnotic state and that the

sole purpose of the process was to encourage relaxation and facilitate concentration on the display screen. Following this explanation, recording electrodes were attached and ten VER and Noise amplitudes were measured using the "Standard" procedures described above.

Hypnosis was then induced by a trained hypnotist using a prewritten narrative. In this narrative (which took about 20 minutes to administer), three post-hypnotic suggestions were given to the subjects. Each was told that during the next two hours she or he would feel very good, would be physically relaxed, and would be able to attend closely to the VER display screen. The subject was then asked to return from the hypnotic state and ten additional VER and Noise amplitudes were measured.

Following recording of the final VER, an informal debriefing was held with each subject. All indicated that they had indeed been hypnotized, had enjoyed the experience, and had felt that the hypnosis had made it easier for them to attend to the display. (Subjects were also asked to report any lasting or unusual side-effects of the hypnosis to the examiners. Two subjects later reported feeling "cold" for about two hours following the hypnosis procedure but no other side-effects were reported.)

Figure 7 shows that the post-hypnotic suggestions did not produce significant improvements in S/N ratios, VER variances for the subjects even though their comments [illegible] effectiveness of hypnosis in aiding attention indicated that improved VER reliability should have been found. This result is, however, consistent with reports by Yolton et al. (1) and Wilson, et al. (28)

Figure 7.

Summary data for "Hypnosis/Attention" procedure. Values in parentheses are standard deviations. "Hypnosis" variances are based on adjusted data.

ATTENTION/HYPNOSIS

CONDITION	MEAN VER AMPLITUDE	MEAN S/N RATIO	MEAN VER VI	MEAN TOTAL VARIANCE	MEAN VARIANCE ACCOUNTED FOR BY NOISE	MEAN VARIANCE ACCOUNTED FOR BY TREND	MEAN RESIDUAL VARIANCE
STANDARD	3,466	16.0	21.3	402,107	64,766	158,479	178,359
	(2,688)	(13.6)	(11.5)	(363,737)	(49,800)	(295,737)	(179,408)
HYPNOSIS	3,943	20.2	18.6	318,790	57,106	148,328	113,357
	(3,161)	(20.1)	(11.2)	(390,384)	(27,676)	(252,564)	(148,571)
	t = 1.94	t = 1.00	t = 0.76	t = .54	t = .61	t = .008	t = 1.45
	df = 8	df = 8	df = 8	df = 8	df = 8	df = 8	df = 8
	p > .001	p > .001	p > .001	p > .001	p > .001	p > .001	p > .001

who found no apparent correlation between subjects' reports of the degree of attention paid to the stimulus and the amplitude of the VER.

Accommodative and Pupillary Effects

After data had been obtained from the pool of 47 subjects, several reported that it had been difficult to maintain a clear image of the checkerboard stimulus for the 38 second viewing period. Obviously, accommodative fluctuations would lead to blurring of the retinal image and this would result in VER amplitude fluctuations (15,29,30). In a related phenomenon, several subjects reported that the display appeared to brighten and dim during the viewing period. Since the mean luminance of the display was constant, it is likely that the perceptual changes in brightness were caused by pupil size fluctuations (which may have been associated with changes in the accommodative system).

To assess the relative importance of these effects, VERs were recorded before and after the use of a cycloplegic agent. Ten subjects were selected at random from the pool for participation in this assessment (mean age = 26.9; SD = 3.5). For each subject, ten VER and ten Noise samples were obtained using "Standard" recording procedures. Then, following a ten minute rest, two drops of 0.5% Cyclogel (cyclopentolate) were instilled into the lower cul-de-sac of each eye. After twenty minutes, the subject's refractive error was determined and the appropriate distance correction lenses set in place in a phoropter. Ten additional VER and Noise values were then obtained by having the subject view the display through the phoropter lenses.

Reference to Figure 8 shows that the cycloplegic agent did not improve the S/N ratios, VIs or variances of the data significantly.

Binocularity

VERs recorded under binocular viewing conditions are typically larger in amplitude than VERs recorded monocularly.(2,30-32) It is possible, however, that when a checkerboard display is viewed in an otherwise darkened room, the status of the subject's binocularity can shift (2,30-32), possibly as the non-dominant eye is occasionally suppressed. Such changes would result in fluctuations in VER amplitudes and produce variability.

To determine whether binocular phenomena were indeed producing variability in the evoked potentials, ten subjects (mean age = 27.1; SD = 5.8) were selected from the pool and VERs were recorded under binocular and monocular viewing conditions.

To obtain monocular VERs, the subject's dominant eye was determined by a sighting task and the non-dominant eye was covered with an opaque patch. (33) For half of the subjects, the binocular data were obtained first with the order reversed for the other half.

The data from this phase of the project are summarized in Figure 9. Monocular viewing does not produce significant improvements in S/N ratios, VIs or amplitude variance of the VER data. This may mean that, for normal subjects, shifts in binocularity and/or alternating suppression phenomena do not contribute significantly to VER amplitude variability.

Figure 8.

Summary data for "Accommodation/Pupil" control procedure. Values in parentheses are standard deviations. "Cycloplegia" variances are based on adjusted data.

ACCOMMODATION/PUPIL

CONDITION	MEAN VER AMPLITUDE	MEAN S/N RATIO	MEAN VER VI	MEAN TOTAL VARIANCE	MEAN VARIANCE ACCOUNTED FOR BY NOISE	MEAN VARIANCE ACCOUNTED FOR BY TREND	MEAN RESIDUAL VARIANCE
STANDARD	3,242.4	12.8	23.0	920,784	78,921	337,324	504,519
	(1,550)	(4.1)	(13.8)	(1,798,880)	(81,491)	(778,107)	(987,581)
CYCLOPLEGIA	3,163.2	13.1	24.0	562,986	83,361	65,713	413,912
	(2,401.1)	(6.0)	(9.3)	(387,030)	(46,693)	(55,073)	(361,904)
	t = 0.21 df = 8 p > .001	t = 0.16 df = 8 p > .001		t = 0.65 df = 8 p > .001		t = 1.07 df = 8 p > .001	t = 0.31 df = 8 p > .001

Figure 9.

Summary data for "Binocular" versus "Monocular" viewing conditions. Values in parentheses are standard deviations. "Monocular" variances are based on adjusted data.

BINOCULAR/MONOCULAR EFFECTS

CONDITION	MEAN VER AMPLITUDE	MEAN S/N RATIO	MEAN VER VI	MEAN TOTAL VARIANCE	MEAN VARIANCE ACCOUNTED FOR BY NOISE	MEAN VARIANCE ACCOUNTED FOR BY TREND	MEAN RESIDUAL VARIANCE
STANDARD	1,368.3	11.2	30.2	121,854	25,077	31,016	65,762
	(1,640.4)	(8.3)	(19.0)	(116,229)	(19,448)	(68,640)	(90,812)
MONOCULAR	812.5	6.5	41.0	243,030	34,371	19,744	188,416
	(1,027.3)	(3.7)	(30.1)	(273,606)	(32,816)	(26,134)	(248,290)
	t = 2.69					t = .49	
	df = 8					df = 8	
	p > .001					p > .001	

Electrode Placement

Using "Standard" procedures, evoked potential data were recorded using a differential amplifier to remove common-mode noise present between the ear-to-ear and the ear-to-inion input channels. This is a commonly used electrode configuration since artifact (heart, respiration, etc.) rejection is reasonably good and very little of the VER signal itself is lost in the differential process. To determine whether a different electrode configuration (a "bipolar" configuration) would result in less variable data (34), recordings were made from ten subjects (mean age = 25.2; SD = 3.3) using the "Standard" electrode configuration and a "Modified" configuration in which electrodes were placed on one earlobe, at a point 1.5 cm above the inion, and on the midline of the skull one half of the distance from the inion to the vertex (approximately location P_Z). The placement of the electrode between the inion and the vertex was selected so as to minimize rejection of the evoked potential signals and maximize rejection of common-mode noise.

The evoked potential and noise data from both electrode configurations were recorded simultaneously using the FM analog tape system. Data from each electrode configuration were then analyzed separately by using identical ensemble averaging and Fourier transformation techniques.

Figure 10 shows that the modified electrode configuration did not produce VERs with significantly better S/N ratios, VIs or variances. This suggests that the use of this particular modification of electrode locations is not advantageous.

Figure 10.

Summary data for "Standard" and "Modified" electrode placements. Values in parentheses are standard deviations. "Modified" variances are based on adjusted data.

ELECTRODE PLACEMENT

CONDITION	MEAN VER AMPLITUDE	MEAN S/N RATIO	MEAN VER VI	MEAN TOTAL VARIANCE	MEAN VARIANCE ACCOUNTED FOR BY NOISE	MEAN VARIANCE ACCOUNTED FOR BY TREND	MEAN RESIDUAL VARIANCE
STANDARD PLACEMENT	537 (382.9)	8.9 (7.4)	46.5 (27.1)	85,984 (113,037)	14,610 (15,428)	29,489 (69,141)	41,884 (76,365)
MODIFIED PLACEMENT	709.3 (578.1)	12.2 (13.2)	36.3 (9.4)	55,834 (70,287)	12,884 (12,631)	18,477 (47,507)	24,473 (33,534)
	t = 1.41 df = 8 p > .001	t = 1.03 df = 8 p > .001	t = 1.40 df = 8 p > .001	t = 1.26 df = 8 p > .001	t = .48 df = 8 p > .001	t = 1.36 df = 8 p > .001	t = .79 df = 8 p > .001

DISCUSSION

The purposes of this study were to assess steady-state VER amplitude variability within a population of normal adult subjects and then to evaluate certain factors which might contribute to this variability. With respect to the population parameters, some subjects were found who produced very reliable VER data (Variability Indices of 0-8%), but, the typical subject in the population had a Variability Index of about 20%. This VI can be interpreted by assuming a situation in which the responses produced under two different sets of viewing conditions (check sizes, lenses, adaptation state, etc.) are to be compared. The relevant question is: "Did changing the viewing conditions make a significant difference in the amplitude of the VER?" To answer this question by using the techniques of this study, assume that 10 VERs are recorded with one viewing condition and that the mean and standard deviation of these VERs is determined. A second viewing condition is then used to obtain 10 more VERs and the mean and standard deviation of these amplitudes is determined. Has the change in viewing conditions made a statistically significant change in the mean amplitude of the VERs? To answer this question, a t-test can be used to determine how far apart the means must be for significance at the 0.05 level. If a two tailed t-test is used, the standard deviations of both sets of ten VERs are the same, and a VI of 20% is assumed (which is the VI for the typical subject), the difference between the means must be at least 20% of the first mean before it can be concluded that the change in viewing conditions has produced a significant change in the VER amplitudes. The requirement for such a large change in the mean of ten VERs makes it difficult to

assess the effects of relatively minor changes in viewing conditions, and this can make precise visual system status determinations difficult using the steady-state VER (at least as utilized in this study).

In the second part of the study, a number of factors which were presumed to contribute to VER amplitude variability were evaluated. Among these factors, sequential (trend) effects were found to account for 25% of the total variance in the subjects' data, and an additional 36% of the total variance could be accounted for by utilizing the Noise model. Thus, trend and Noise factors together can account for about 60% of the total variance in the subjects' data.

Even if all other factors which contribute to variability are eliminated, these two factors alone set limits on the reliability of VER data. The 40% of the total variability not accounted for by trend and Noise effects probably arises from various factors, but manipulation of the factors considered in this study (accommodation, eye movements, etc.) did not produce significant reductions in VER amplitude variability. These results might have been quite different (especially in the case of gross artifact and eye movement based rejection procedures) if less cooperative subjects had been used, but with normal adults these factors (taken individually) do not seem to contribute significantly to the overall variability of the VER.

The major conclusion that can be drawn from this study is that VER amplitude data from many subjects will be variable and this variability must be taken into account when interpreting the results

of VER testing. In most cases, the patency of the visual system can be assessed with confidence, but assessments that require more precision must be made with some caution and reports of VER determined visual parameters should include an indication of the reliability of the measurements being presented.

FUTURE STUDIES

If the reliability of the VER could be increased significantly, applications of the technique would increase correspondingly. To increase the reliability of amplitude data, perhaps the measurement of steady-state evoked potentials should be abandoned in favor of the use of transient stimuli to produce the evoked potentials. An earlier study (4) has, however, indicated that the variability of VER amplitudes produced using these two techniques is about the same so there does not seem to be a clear advantage in shifting to transient stimuli.

A more fruitful way of increasing reliability may involve reducing the effects of Noise through the use of analysis techniques (8,20,35-41) which are (in some ways) more advanced than the ensemble averaging and Fourier transformation procedures used in this study. Some of these new techniques are now being implemented and future studies should indicate whether or not they will increase the reliability of the steady-state VER to a point where it can be used to obtain highly reliable data from all subjects.

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