THE EFFECTS OF INTEROCULAR LUMINANCE DIFFERENCES ON THE BINOCULAR VER OF FUNCTIONAL AMBLYOPES: A COMPARISON STUDY

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Abstract

The effects of interocular luminance differences on the normal binocular VER have been examined by Trick, Compton, and Dawson in several experiments. This study has evaluated the effects of interocular luminance differences on the binocular VER of six subjects with functional amblyopia. Several interesting differences between the VER of these two groups has been established. In addition, a new objective test for functional amblyopia has been proposed.

Introduction to the VER

The processing of visual information at the visual cortex generates weak electrical currents which may pass through the bones of the skull. By placing non-invasive scalp electrodes over the visual cortex, these electrical currents can be relayed to electronic equipment for measurement and recording. When these currents are measured as a function of specific visual stimulus parameters, they are referred to as visual evoked responses (VER's) or visual evoked potentials (VEP's).

Various stimuli have been employed to generate VER's. The most common of these include a diffuse white light source, an alternating black and white grating, and a counterphasing checkerboard pattern. Of these, the counterphasing checkerboard pattern appears to yield the most reliable evoked response (Barret et al, 1976). In addition, this stimulus has the advantage over flash stimulation of providing a constant average luminance, while allowing only contrast changes.

A single visually evoked potential is quite small (approximately 5 μV), and is generally hidden in the relatively large potentials generated by the continuous inherent activity of the brain. To extract a visual response from this spontaneous cortical activity, an averaging technique is generally employed. Since the visual response is time locked to the stimulus, its characteristics will be enhanced by averaging, while contributions from random cortical activity will simultaneously be reduced. The characteristics of an averaged visually evoked potential are shown in figure 1.

Two attributes of the averaged visual evoked response are most frequently utilized in analysis. The first is the VER amplitude, defined as the difference in voltage between the peak of a major negative going potential (N_1) and the next maximum positive potential (P_2). VER amplitude has been shown to be dependent upon such optical conditions as visual acuity and refractive error, as well as visual system pathology and binocular anomalies. The other VER attribute is the response latency, defined as the time (in milliseconds) between the onset of the stimulus and the peak of the major positive potential (P_2). VER latency is quite consistent both among and between individuals and has been shown to be significantly altered in demyelinating diseases, such as multiple sclerosis (Regan, D., 1979).

Background

The mechanisms underlying normal binocular vision are poorly understood. While it has been demonstrated that normal binocular vision results from some form of synthesis of the individual monocular responses, the manner in which this is accomplished remains obscure. Furthermore, it is unclear how these mechanisms may be altered in cases of binocular anomalies.

One method, which has been employed to investigate these neural mechanisms involves the use of single unit recordings from the striate cortex of cats and monkeys (Hubel and Wiesel, 1963 and 1968). These experiments have demonstrated that deprivation of light or form may result in neurophysiological variations within the cortex. However, because of their invasive nature, these techniques have been necessarily limited to non-human subjects. Therefore, it is difficult to justify any generalizations made to human vision from these types of experiments.

An alternative approach which has been utilized to examine human binocularity involves recording pattern reversal VER's. In the past, pattern reversal VER's have been recorded for each eye individually and then for both eyes simultaneously, while altering such parameters as spatial and temporal frequency. Use of this approach has resulted in significant contributions to our knowledge (Srebro, 1978; Wanger and Nilsson, 1978). However, because of its limited design, the knowledge to be derived from this technique will also be limited. Furthermore, when this technique is employed to investigate binocular anomalies, such as functional amblyopia, conflicting reports are often generated among researchers (Arden et al, 1974; Tsutsui, 1973).

Clearly, a better method for evaluating the neural processes subserving binocularity would be to incorporate into the VER recording, a technique which would allow a more thorough manipulation of the variables influencing binocularity. One such technique involves the use of both similar (dioptic) and dissimilar (dichoptic) stimulus patterns for each of the two eyes. This procedure has been extensively employed in psychophysical experiments (Blake and Rush, 1980; Trick and Guth, 1980), but has had limited application in VER research (Harter et al, 1980; Lennerstrand, 1978; and Cobb et al, 1967). Following this line of reasoning, Trick, Dawson, and Compton (1980) have investigated the effects of interocular luminance differences on the binocular, pattern-reversal VER for subjects with normal binocularity.

Our previous investigations have been limited to subjects with normal binocularity and interests have been directed toward two goals. The first of these was to increase the knowledge about the mechanisms subserving binocularity. The second goal was to establish normal population trends for our particular paradigm; the significance being that if deviations from these trends should occur in cases of abnormal binocularity, then these deviations can be documented and in the future may become clinically significant.

This experiment will compare population trends for subjects with functional amblyopia to those previously determined for subjects with normal binocularity. Several interesting phenomenon have emerged from this experiment, as well as a potentially useful test in the clinical diagnosis of functional amblyopia.

Methods and Procedures

Six subjects were selected from the patient population at the College of Optometry, Ferris State College. All subjects had been diagnosed as having functional amblyopia. Four of the subjects were strabismic amblyopes and two were anisometropic amblyopes.

Each subject was required to sit for three one and one half hour sessions, thus theoretically generating three data sets per person. However, technical problems resulted in the use of one or two data sets per person.

VER's were differentially recorded between an active electrode (Ag-AgCl), attached with conductive paste, two centimeters above the inion on the mid-sagittal plane, and linked reference electrodes clipped to the ear lobes. A forehead electrode was used to ground the subject.

The potentials were evoked by an alternating black and white checkerboard pattern, generated on a television screen by a Nicolet visual stimulator (NIC-1006). At a one meter viewing distance, the television screen provided a 16.5 degrees by 12.6 degrees pattern, with each check subtending 14 ~~inches~~ minutes of arc. The mean luminance of the pattern was 26 cd/m^2, with a 74% contrast. The pattern was alternated at 3.75Hz, and a dark central spot served as a fixation target.

The evoked potentials were amplified by a low noise differential amplifier and actively filtered. The filtered signals were then averaged and recorded by a Nicolet CA-1000 signal averaging computer (see figure 4). The responses were averaged over 100 pattern reversals.

Each subject was seated in a chair at a viewing distance of one meter from the screen. Each experimental session included a standard binocular condition (OU), along with right eye (OD) and left eye (OS) monocular conditions. In addition, all sessions included a series of conditions in which one eye viewed the pattern through various neutral density filters (six filters ranging from 0.3-2.0), while the other eye viewed the unattenuated pattern. A pair of clear safety goggles was modified to hold the Wratten filters in position. The non-viewing areas of the goggles were covered with black tape to eliminate extraneous light. A set of conditions, in which the checkerboard pattern is monocularly viewed through the same set of Wratten filters, was included. Therefore, each session will be composed of 28 conditions: two monocular, one binocular, 12 binocular with one eye attenuated, 12 monocular with that eye attenuated, and one noise condition.

Results and Discussion

In order to better understand the significance of this experiment, a review of previous experiments for subjects with normal binocularity is needed. During these investigations, several attributes of the normal binocular VER have been determined. First, the mean amplitude during binocular stimulation exceeded the mean amplitude during monocular stimulation by a factor of approximately 1.4. This value is in good agreement with the $\sqrt{2}$ value reported in other VER research (Srebro, 1978); Sanger and Nilsson, 1978) and in psychophysical investigations of binocular brightness and contrast (Home, 1978); Fry and Bartley, 1933); and Blake and Rush, 1980). This phenomenon has been called binocular summation (Srebro, 1978).

When the VER amplitude is plotted as a function of the amount of attenuation of the stimulus during dichoptic viewing conditions, a complex interaction is revealed (figure 2). For small interocular luminance differences (less than 0.9 log units), the amplitude of the dichoptic

VER is greater than the amplitude of either monocular response. For larger interocular luminance differences (1.3-2.0 log units), the amplitude of the dichoptic VER is less than the amplitude for either monocular response. That is, when a large luminance difference is created between the two eyes, the amplitude of the response is less than when one of the eyes is completely occluded. This phenomenon has been suggested to be the cortical correlate of the psychophysical phenomenon of Fechner's paradox (Trick and Dawson, 1979).

Also from this graph it should be evident that the VER amplitude does not vary significantly across the levels of attenuation for either monocular response. This could be expected, since the range of neutral density filters utilized are not sufficient to prevent viewing of the stimulus. Finally, it should be noted that the monocular unattenuated amplitudes are nearly identical. This should be expected if each eye contributes equally to the binocular response.

In addition to the VER amplitude trends, various latency trends were obtained for the subjects with normal binocularity. In figure (4), VER latency can be seen to remain relatively constant across the range of attenuation as long as one or both eyes remain unattenuated. This is apparently because the contribution from one eye occurs at the same point in time regardless of the stimulus viewed by the other eye. However, when one eye is occluded and the stimulus for the other eye is progressively attenuated, the latency can be seen to rise to a statistically significant level ($p \leq .001$). This effect is likely due to the decreasing level of luminance of the stimulus.

In this experiment, the amblyopic subjects demonstrated several marked deviations from the normal population. In the first, the mean amplitude of the amblyopic and non-amblyopic eyes were significantly different (figure 5)

($p \leq .05$). Also, the amblyopic eye's amplitude was significantly reduced across the entire range of attenuation except for the 1.7 log unit condition. Recently, there has been much controversy over this finding. Some researchers have actually found amplitude to be larger for the amblyopic eye. Today it is generally agreed that the VER amplitude of the amblyopic eye is spatial frequency dependent. For our experiment, the spatial frequency was relatively high and the amplitude was significantly reduced.

Secondly, the amplitude of the unattenuated binocular response was 7.59 μV, which is not statistically different from the 6.39 μV value obtained for the non-amblyopic eye. While there may seem to be a small contribution from the amblyopic eye, it must be assumed that the majority of the binocular response originated from the non-amblyopic eye. The amblyopic eye's mean amplitude was 3.72.

When the binocular curve of the normal population is compared to the binocular curve of the amplyopic subjects, as in figure 6, an interesting phenomenon can be seen to be occurring. When the amblyopic eye is unattenuated and the non-amblyopic eye is attenuated over the log unit range, the curve can be seen to approximate the curve of the normal population. However, when the non-amblyopic eye is left unattenuated and the amblyopic eye is attenuated, the VER amplitude fails to decline to the level expected for the higher interocular luminance differences. This probably indicates a failure of the amblyopic eye to have a significant inhibiting effect on the non-amblyopic eye as was seen in normal subjects. Furthermore, one may be lead to suspect that there may be an inability to demonstrate a Fechner's Paradox phenomenon, although this experimentation was not done.

By far, the most clinically significant finding to arise from this experiment lies in the latency deviations from the normal population. As you may recall, VER latencies for the normal population remain relatively unchanged, as long as at least one eye remains unattenuated and is allowed to view the stimulus. This is not true for the amblyopic subjects (figure 7). When the amblyopic eye is left unattenuated and the stimulus to the non-amplyopic eye is increasingly attenuated; there is a significant rise in the latency values. In particular the 1.7-2.0 log unit conditions are statistically significant ($p \leq .05$). The mean latencies for these attenuation levels are in good agreement with the latencies found when one eye is occluded and the other is increasingly attenuated. This phenomenon can probably be explained by the dominancy of the non-amblyopic eye, but the mechanism is unclear.

Conclusions

This experiment has demonstrated sharp contrasts between the VER of subjects with normal binocularity and those with functional amblyopia. In several instances, it has demonstrated a relative inability of the amblyopic eye to influence its companion eye. In comparison, the non-amblyopic eye demonstrated strong tendencies to influence the binocular response. This tendency is not unlike that of normal monocular responses except to a much greater degree.

As has been previously demonstrated (Arden et al, 1974; Tsutsui, 1973; and Trick et al, 1980), the amplitude of the VER for the amblyopic eye is significantly different from that of its companion eye. The amount of difference can be expected to depend on both the spatial and temporal characteristics of the stimulus.

Clinically, a new test for amblyopia could soon be added to our repertoire. However, unlike most amblyopia tests which are subjective, this test is completely objective and, therefore, could prove valuable in the diagnosis of amblyopia in non-responders and malingerers.

The test would consist of comparing latencies for the binocular unattenuated condition to the condition when a 2.0 neutral density filter is placed over the suspected non-amblyopic eye. If a large difference in latency is found between these conditions, then amblyopia should be considered. Obviously, conditions of spatial and temporal frequency should be maintained at levels tested herein. As a precautionary measure, further clinical testing should precede any interpretation of these results.

An interesting follow-up experiment to this one would be to attempt to use this latency deviation technique to follow several amblyopes during amblyopia training. It could prove very valuable to our training procedures if this latency difference was seen to decrease with amblyopia training. It may also provide some information as to which techniques are most efficient. Finally, it would act to scientifically substantiate the need for amblyopia therapy.

Further experimentation needs to be done comparing the VER of persons with abnormal binocularity to those with normal binocularity. These comparisons may provide excellent clinical testing techniques, as well as input into the understanding of normal binocularity and deviations from it.

The use of the dichoptic viewing technique in VER research has proven to be an invaluable tool. Unlike other techniques in VER research, it allows a differential look at the monocular components of the binocular response to a controlled stimulus. In the future, this may provide valuable information in the understanding of binocularity and the summation process.

References

1. Arden, G.B., Barnard, W.M. and Mushin, A.S. (1974), "Visually evoked responses in amblyopia." Brit. J. Ophthal. 58, 183-192.

2. Barrett, G., Blumhardt, L., Halliday, A.M., Halliday, E. and Kris, A. (1976), "A paradox in the lateralization of the visual evoked response." Nature 261, (Lond.) 253-255.

3. Blake, R. and Rush, C. (1980, "Temporal properties of binocular mechanisms in the human visual system" Exp. Brain Res. 38, 133-140.

4. Cobb, W.A., Morton, W.B. and Ettlinger, G. (1967), "Cerebral potentials evoked by pattern reversal and their suppression in visual rivalry." Nature 216, 1123-1125.

5. Fry, G.A. and Bartley, S.H. (1933), The brilliance of an object seen binocularly." Am. J. Ophthal. 16, 681-693.

6. Harter, M.R., Conder, E.S. and Towle, V.L. (1980), "Orientation-specific and luminance effects: Interocular suppression of visual evoked potentials in man." Psychophysiology 17 (2), 141-145.

7. Home, R. (1978). "Binocular summation: A study of contrast sensitivity, visual acuity, and recognition." Vision Res. 18, 579-585.

8. Hubel, D.H. and Wiesel, T.N. (1963). "Receptive fields of cells in striate cortex of very young, visually inexperienced kittens." J. Neurophysio. 26 (6), 994-1002.

9. Hubel, D.H. and Wiesel, T.N. (1968) "Receptive fields and functional architecture of monkey striate cortex." J. Neurophysiol. 195, 215-243.

10. Hugonnier, R., Hugonnier, S.C., Strabismus, heterophoria, ocular muscle imbalance. Translated by S.V. Troutman. C.V. Mosby Co., (1969). pp. 155-179.

11. Lennerstrand, G. (1978). "Some observations on visual evoked responses (VER) to dichoptic stimulation." Acta. Ophthal. 56, 638-647.

12. Levi, D.M. (1975) "Patterned and unpatterned visual evoked responses in strabismic and anisometropic amblyopia." Am. J. Optom. and Physiol. Optics 52, 455-464.

13. Regan, D., "New Visual Tests in Multiple Sclerosis." In H.S. Thompson (Ed.) Topics in Neuro-ophthalmology. Baltimore: Williams and Wilkins, 1979.

14. Shapero, M., Amblyopia. Philadelphia, Chilton Book Co., 1971.

15. Sokol, S. and Shaterian, E.T. (1976) "The pattern-evoked cortical potential in amblyopia as an index of visual function." In Moore, S. and Main, Y., Eds. Orthopics: past, present, future. pp. 57-67. Stratten, New York.

16. Spekreijse, H., Khoe, L.H., van der Tweel, L.H. (1972) "A case of amblyopia: Electrophysiology and psychophysics of luminance and contrast." Recent Adv. Exp. Biol. Med. 24, 141-156.

17. Srebro, R. (1978) "The visual evoked response: Binocular facilitation and failure when binocular vision is disturbed." Arch. Opthal. 96, 839-844.

18. Trick, G.L., Dawson, W.W., and Compton, J.R. The Binocular VER: The Effect of Interocular Luminance Differences, XVIII the International Symposium on Electrophysiology and Pathology of the Visual Pathways, S. Karger, Basel, 1980.

19. Trick, G.L., Compton, J.R., and Dawson, W.W. Interocular Luminance Differences and the Binocular Pattern Reversal VER. Investigative Ophthalmology and Visual Science, 1981.

20. Trick, G.L., and Compton, J.R., Analysis of the Effect of Temporal Frequency on the Dichoptic Visual-Evoked Response. American Journal of Optometry and Physiological Optics, Vol. 59, No. 2, pp. 155-161, February, 1982.

21. Trick, G.L., Dawson, W.W. (1979), "The binocular VER: Facilitation, inhibition and a cortical correlate of Fechner's paradox."

22. Trick, G.L. and Guth, S.L. (1980), "The effect of wavelengths on binocular summation." Vision Research.

23. Tsutsui, J., Nakamura, Y., Takenaka, J. and Fukai, J. (1973), "Abnormality of the visual evoked response in various types of amblyopia." Jap. J. Ophthal. 17, 83-83.

20. Wanger, P. and Nilsson, B.Y. (1978), "Visual evoked response to pattern reversal stimulation in patients with amblyopia and/or defective binocular functions." Act. Ophthal. 56, 617-627.

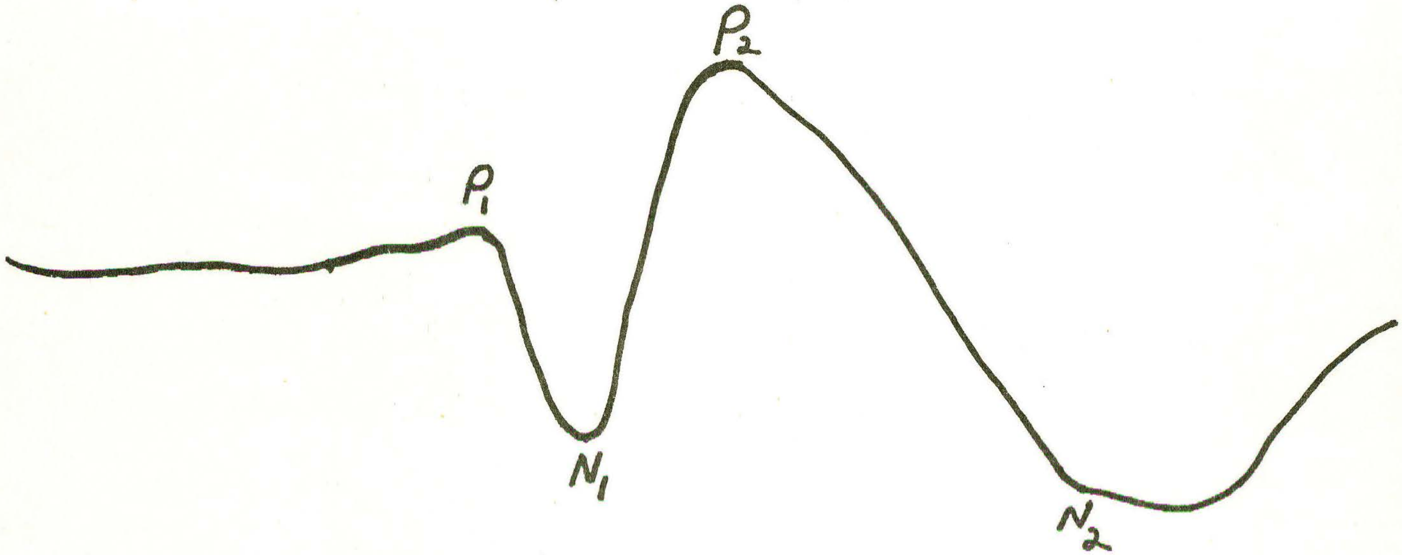


Figure 1. A typical VER waveform. See text for explanation of the characteristics.

FIGURE 2

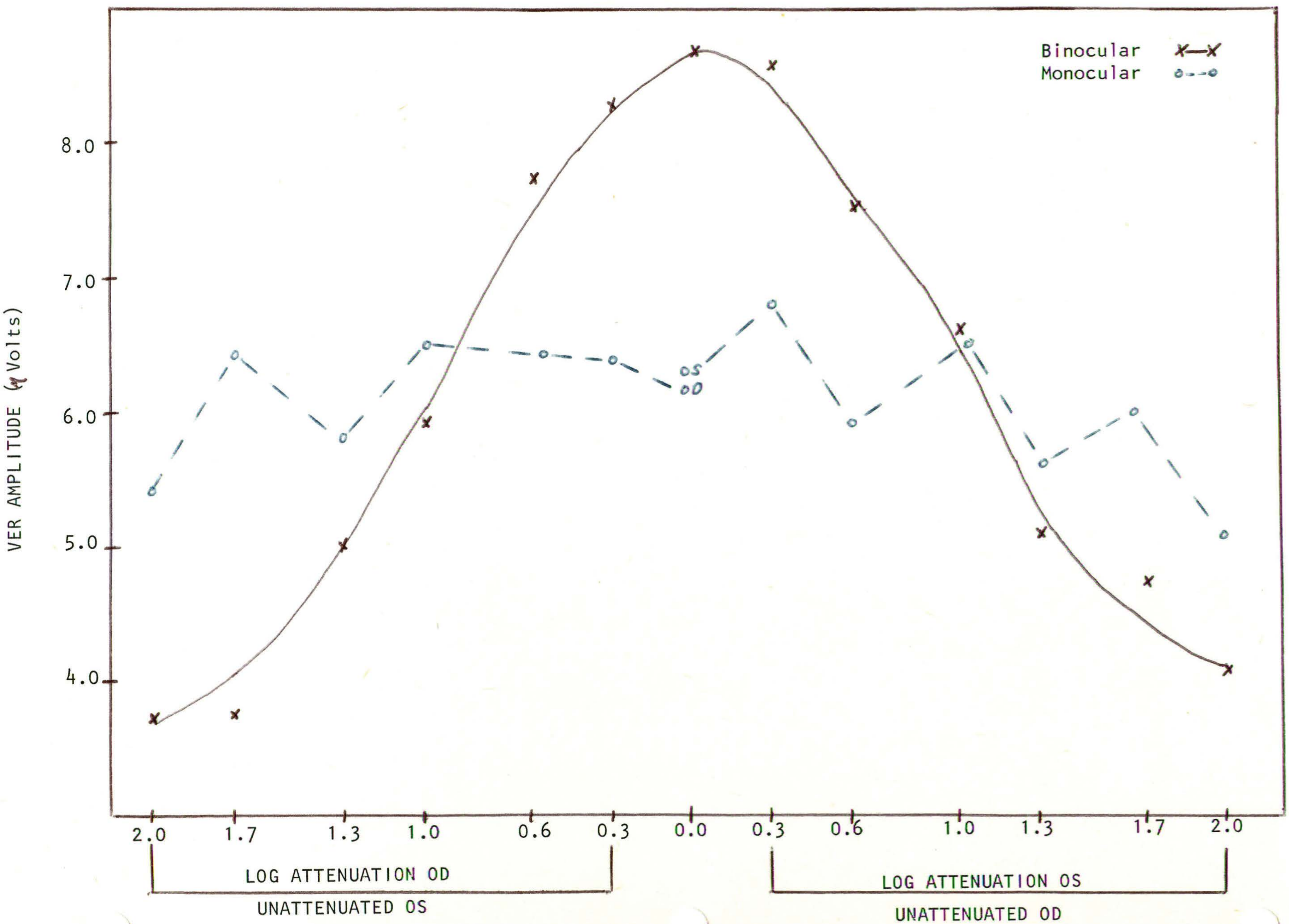

Binocular
Monocular
VER AMPLITUDE (μ Volts)
8.0
7.0
6.0
5.0
4.0
OS
OD
2.0
1.7
1.3
1.0
0.6
0.3
0.0
0.3
0.6
1.0
1.3
1.7
2.0
LOG ATTENUATION OD
UNATTENUATED OS
LOG ATTENUATION OS
UNATTENUATED OD

FIGURE 3

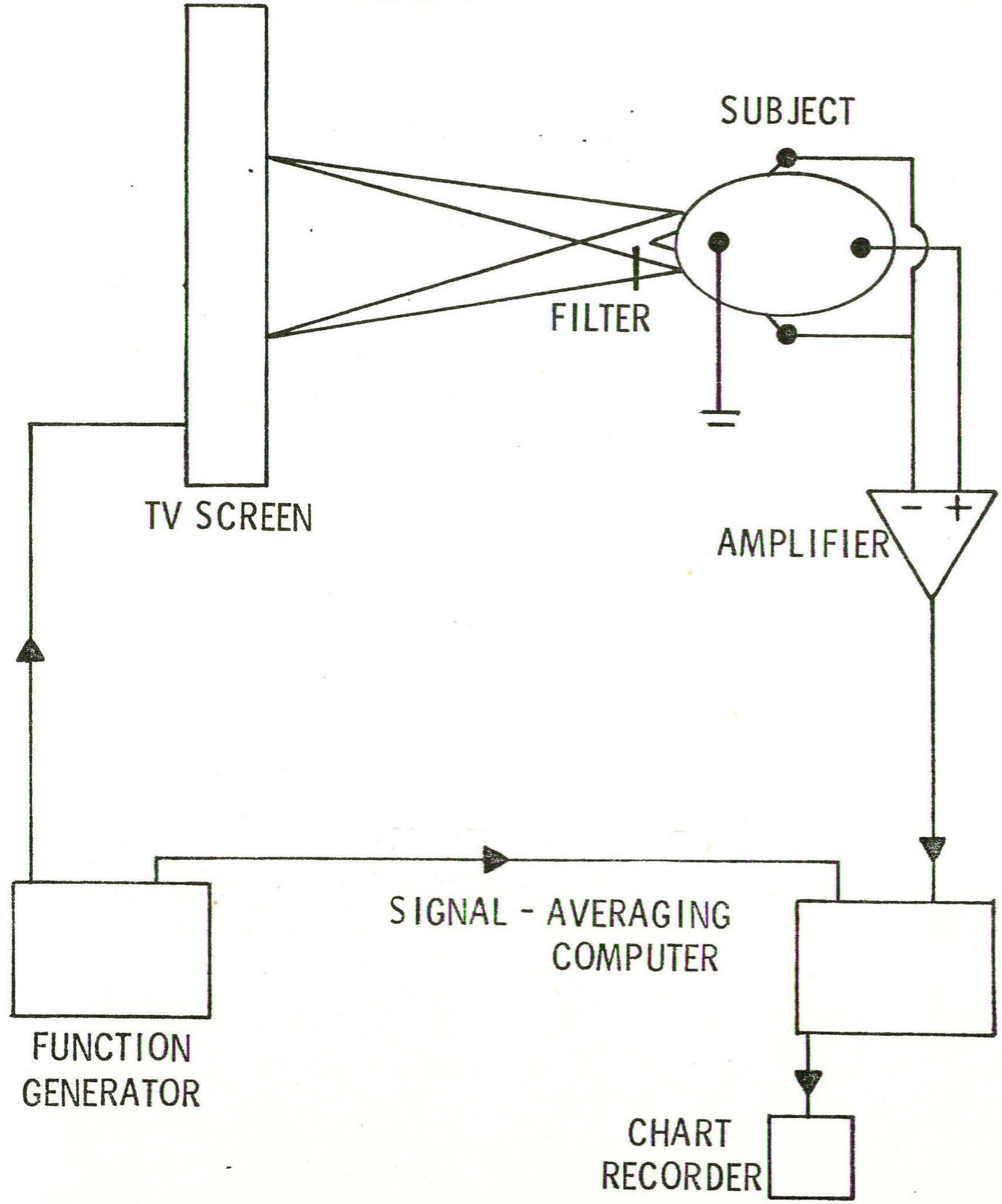
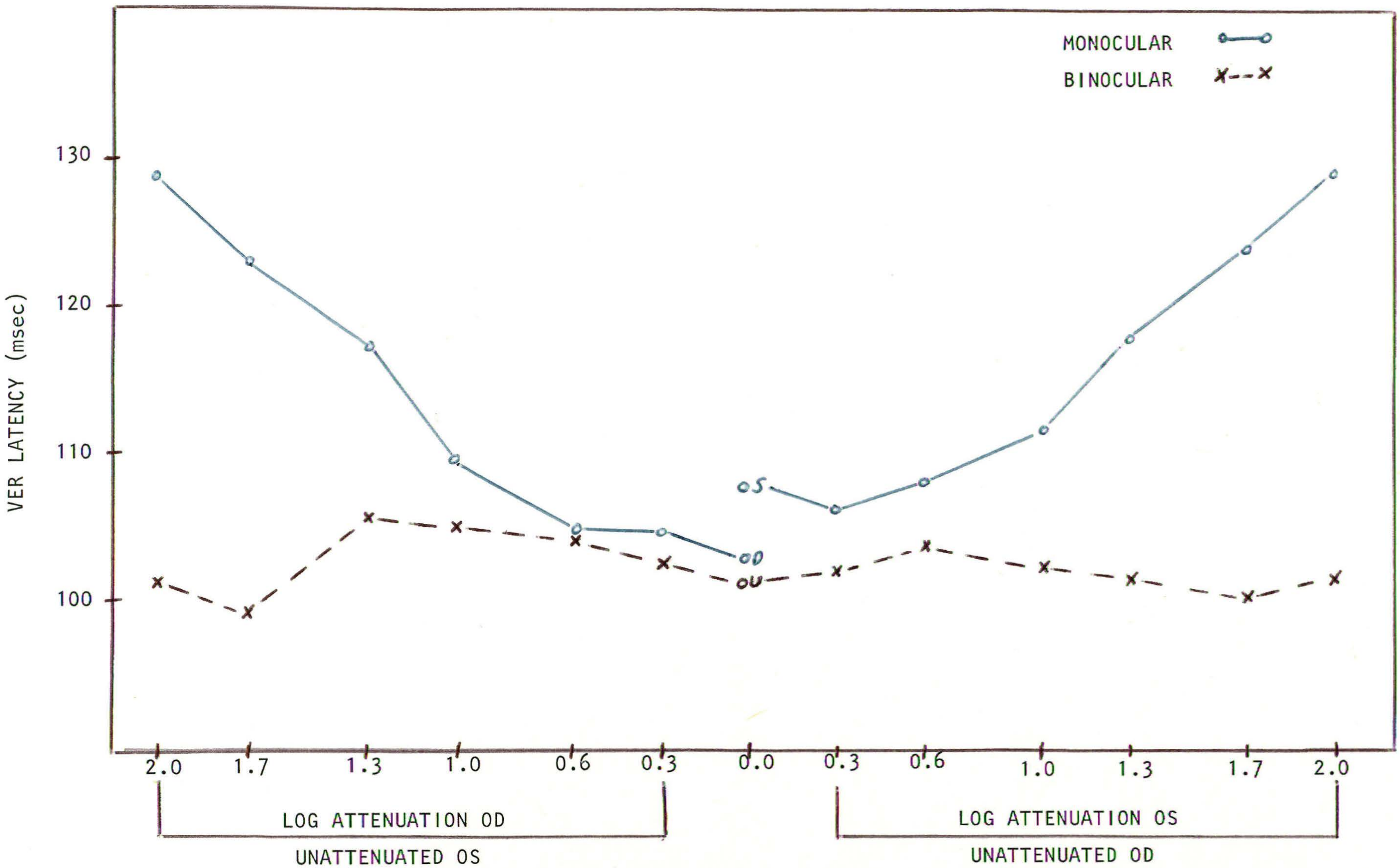
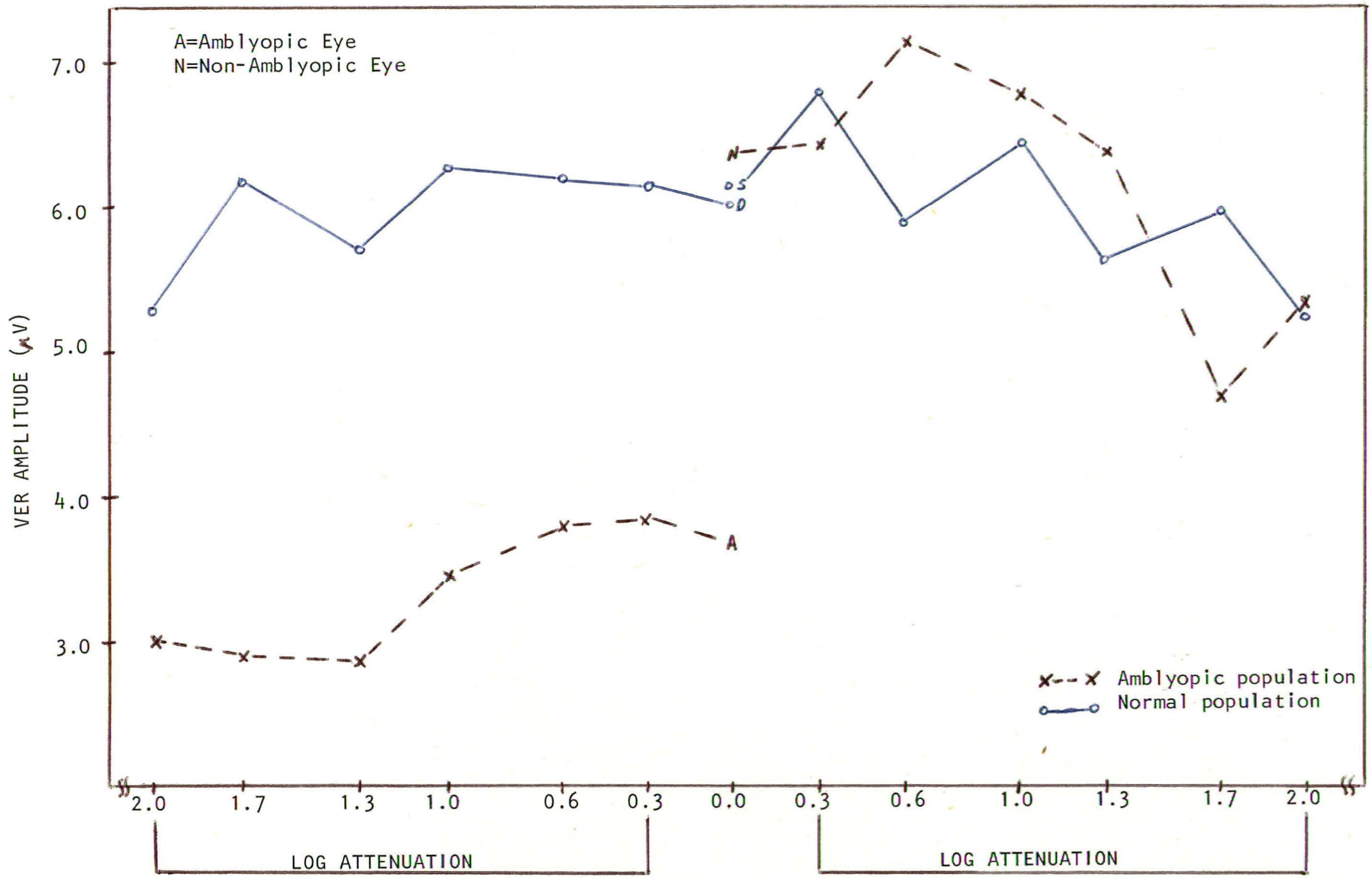

SUBJECT
FILTER
TV SCREEN
AMPLIFIER
SIGNAL - AVERAGING
COMPUTER
FUNCTION
GENERATOR
CHART
RECORDER

FIGURE 4



LATENCY vs LOG ATTENUATION (NORMAL POPULATION)

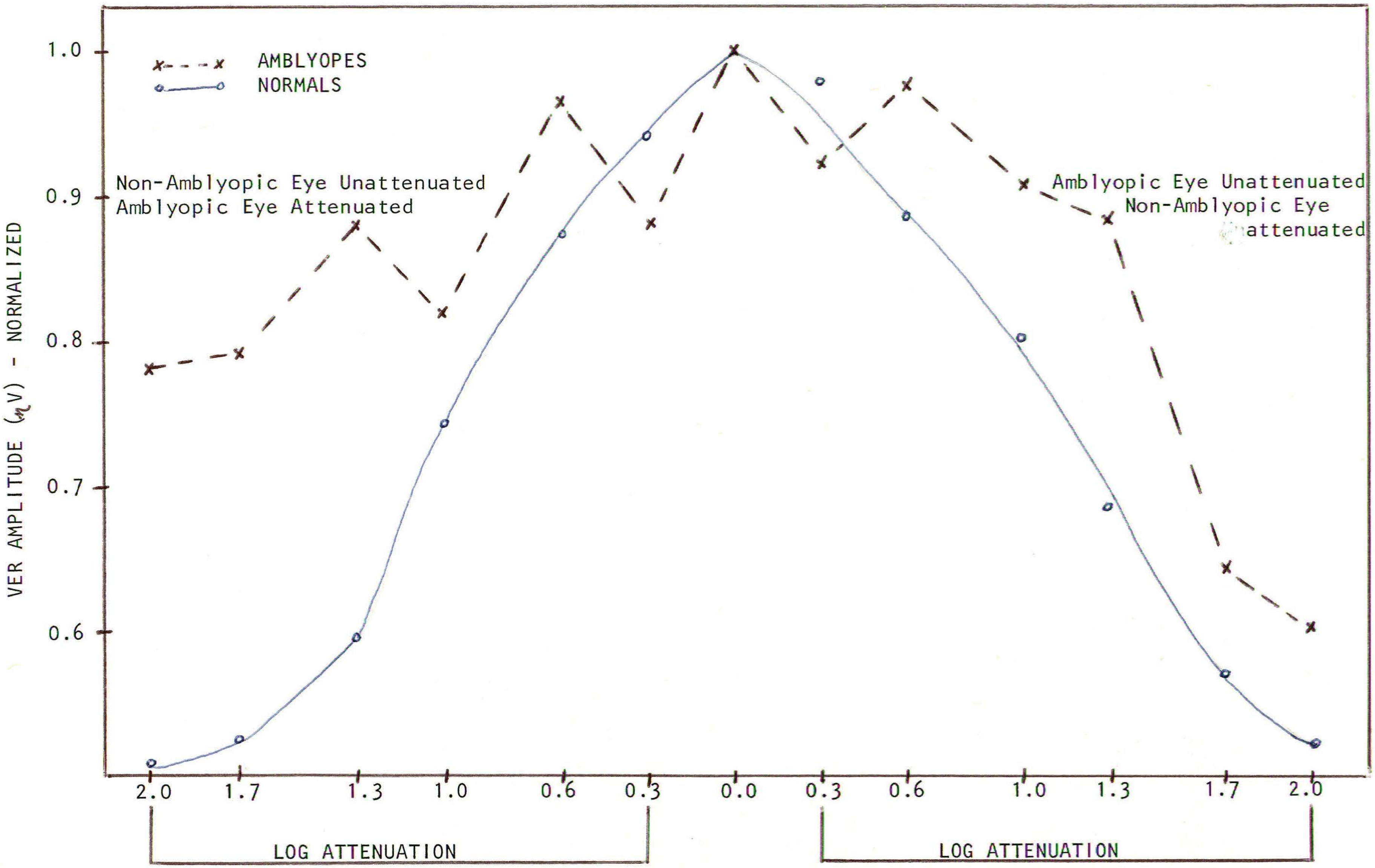
FIGURE 5



MONOCULAR ATTENUATION CURVES
NORMALS vs AMBLYOPES

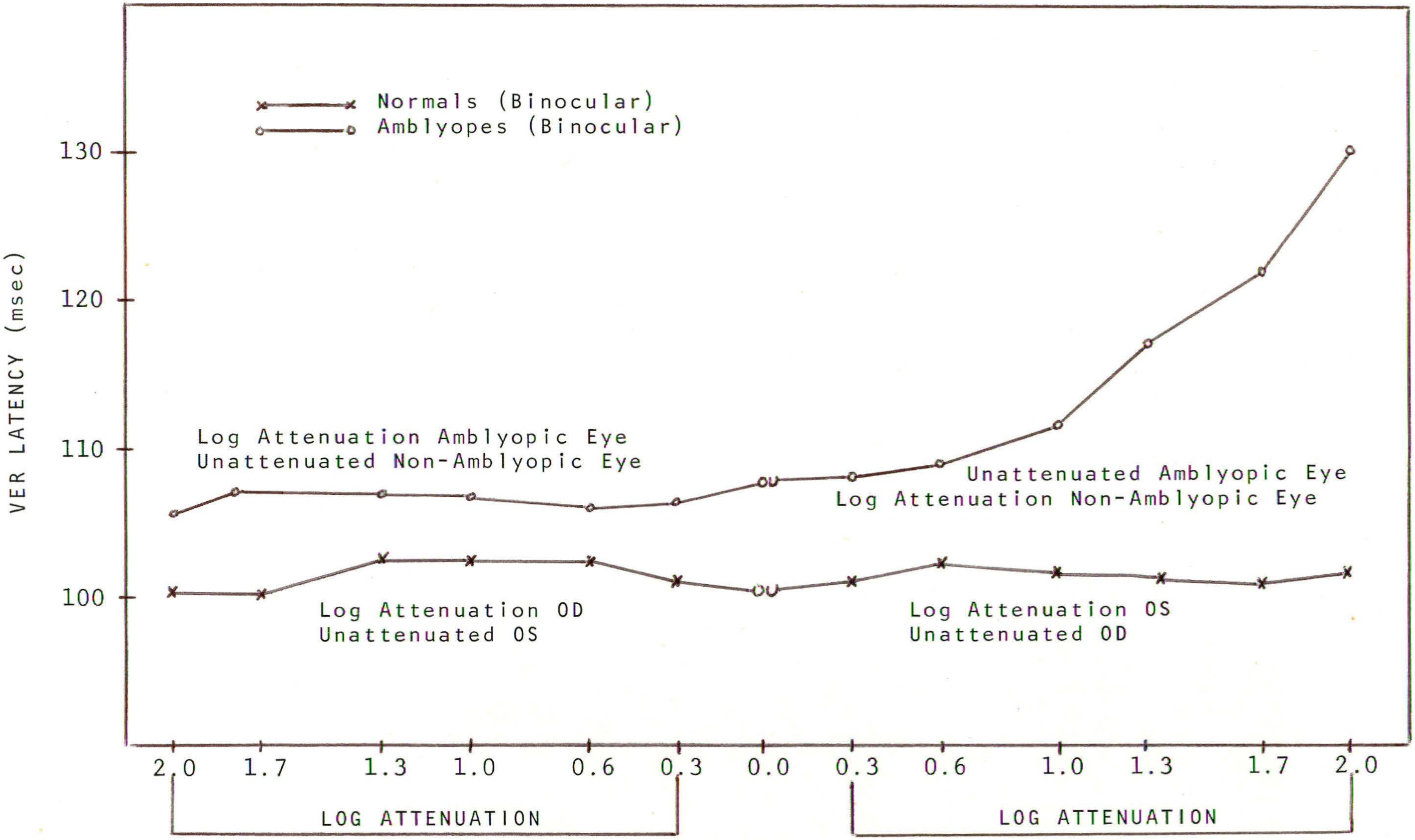
FIGURE 6

CURVES NORMALIZED TO O.U. CONDITION



BINOCULAR ATTENUATION CURVES
NORMALS vs AMBLYOPES

FIGURE 7


Normals (Binocular)
Amblyopes (Binocular)
130
120
110
100
VER LATENCY (msec)
Log Attenuation Amblyopic Eye
Unattenuated Non-Amblyopic Eye
Unattenuated Amblyopic Eye
Log Attenuation Non-Amblyopic Eye
OU
Log Attenuation OD
Unattenuated OS
Log Attenuation OS
Unattenuated OD
2.0
1.7
1.3
1.0
0.6
0.3
0.0
0.3
0.6
1.0
1.3
1.7
2.0
LOG ATTENUATION
LOG ATTENUATION

SUBJECT VISUAL ANALYSIS DATA

PATIENT	(20') B.V.A. (OD,OS,OU)	COVER TEST	STEREO.	ECCENT. FIX.	REFRACTION	
C.R.	40,15,15	3p.d. esop.	800"	Present	+3.75=-2.50x115 Pl=-0.25x140	OD OS
A.H.	15,30,15	Φ, 2p.d. rt. hypop.	140"	N/A	+0.50=-0.50x020 +1.25	OD OS
C.L.	30,70,30,	5p.d. Esot. (left)	200"	Present	+5.75=-0.50x035 +7.50=-1.00x155	OD OS
K.B.	200,15,15	6p.d. Exot. (right)	None	Present	-16.75=-1.50x180 -1.25=-0.50x155	OD OS
B.C.	40,15,15	10p.d.Lt. Exot.	None	Present	+0.50=-0.25x090 -1.25=-0.50x100	OD OS
T.S.	30^-,15 15	2p.d. exop.	N/A	None	+1.25=-1.25x005 -1.75=-0.50x003	OD OS