

Visual evoked responses in patients with multiple sclerosis¹

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SUMMARY The visual evoked response (VER) was evaluated in a series of multiple sclerosis patients and normal subjects. The data showed significant delays in wave peak latencies among the patient evoked responses. The prolonged latencies correlated closely with visual impairment; however, even patients with a previous history of visual impairment, but with no deficits noticeable on examination at the time of study, showed a delay in wave peak latencies. The results further suggest that the VER is primarily altered when there are central field defects.

The summated visual evoked response (VER) has been extensively reported in both normal subjects and patients with a variety of central nervous system diseases. Little effort, however, has been made to focus on the possible alterations of the VER in patients with a demyelinating disorder. Except for the reports of Rouher, Plane, and Solé (1969) and Richey, Kooi, and Tourtellotte (1971) the possible VER changes secondary to multiple sclerosis (MS) have not been particularly explored.

The variability of lesion location and severity, without a means of pathological-anatomical confirmation, makes interpretation of any CNS electrical phenomena in multiple sclerosis (MS) difficult, at best. A history of retrobulbar neuritis is usually easy to document, however, and the presence of optic atrophy on ophthalmoscopic examination does allow confirmation of at least this one lesion. For this reason, it was felt that a group of MS patients, homogeneous in that each had a history of monocular vision loss, could give reliable information on the effect of at least this one lesion on the VER.

METHOD

Twenty patients with multiple sclerosis and 20 nor-

mal subjects, matched for age and sex to the patient population, were used during this experiment. Each patient had a history consistent with at least one attack of retrobulbar neuritis and, in each instance, this was documented with impaired visual acuity and frequently by the demonstration of a central visual defect on tangent screen examination. No patient was considered to be in an acute exacerbation of their disease at the time of this study.

Patients were divided arbitrarily into three groups based on the visual acuity of each eye tested. Group I (mildly affected) had vision of 20/20 to 20/30, group II (moderately affected) had a visual acuity of 20/40 to 20/80, and group III (severely affected) had vision from 20/100 to finger counting. Patients were chosen carefully so that nystagmus was not a feature of their examination. By doing this, the possibility of contaminating the evoked response by involuntary eye movements was reduced.

All subjects were at rest in bed in an isolation room during the recording of the visual evoked response. While evoked potentials were recorded by stimulation of one eye, the other was covered by a black patch taped to the forehead and cheek. In all instances, the exposed eye was open during visual stimulation.

A standard Grass Model PS2 stroboscope was placed 35 cm before the subject's eye and a frosted diffusion screen was placed over the face of the lamp. Evoked responses were obtained using a full lamp face (diameter 13 cm) exposed to the patient and also with a metal diaphragm containing a 5 cm diameter aperture placed over the lamp face. The smaller aperture was used in an attempt to stimulate pri-

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marily the macular region. Since retrobulbar neuritis usually produces a central or paracentral scotoma, it was felt that the full strobe lamp might illuminate the retina excessively to obscure this central defect. Earlier studies in our laboratory had demonstrated that a light source of smaller diameter or a lamp position further from the eye produced a light source too small to be appreciated by many patients with a central field defect. When this happened, fixation was poor with loss of patient interest and a tendency for irregular eye movements. In these circumstances, reproducible VERs were difficult to achieve. Consistent and reproducible evoked potentials, however, were recorded in each tested subject with the described stimulus size and distance from the subject and with the ambient light as constantly maintained in our laboratory.

All summations were of 60 flashes at a one-second repetition rate. During each epoch of flash stimulation, a white noise generator was employed to mask the audible click from the stroboscope.

Brain electrical activity was detected by three electrodes placed on the scalp. The two active electrodes were placed symmetrically, each at a point 2 cm superior and 2 cm lateral to theinion. The reference lead was placed at the vertex. Electrodes on both ears were connected to ground.

All data were recorded on a Grass Model 4C Electroencephalograph and subsequently stored on an Ampex Model FM 100 tape recorder. On-line summation was performed by a Nuclear Data

computer Model 1024 and evoked responses were plotted on a Hewlett Packard XY Plotter.

All VER wave peak latencies were determined without knowing if the response was from a patient or normal subject and without knowing the visual acuity of the patient. In this fashion, it was hoped that any bias in determining wave peak latencies could be avoided.

In all instances, analysis was performed on the VER obtained from the electrodes placed on the scalp contralateral to the eye being stimulated.

RESULTS

A typical normal VER with our electrode placement scheme is shown in Fig. 1. This Figure also demonstrates the nomenclature adopted for labelling the various wave peaks. This method of wave peak identification is similar to that proposed by Gastaut and Regis (1965). We have found this to be a useful method of labelling, although our reference electrode was placed on the vertex in contrast to the chin or ear, as preferred by Gastaut.

Tabulation of the normal and patient data using the two light sources is presented in the Table. It can be noted that the wave peak latencies were shorter when the full stroboscope lamp face was used. This was a consistent observation for each wave peak identified.

TABLE
NORMAL AND PATIENT WAVE PEAK LATENCIES FOR EACH LIGHT SOURCE DIAMETER

Subject	Wave peak														
	N	III msec (mean)	SD	N	IV msec (mean)	SD	N	Va msec (mean)	SD	N	Vb msec (mean)	SD	N	Vc msec (mean)	SD
<i>Light source 13 cm diameter</i>															
Normal	39	50.6	5.58	40	65.6	7.82	29	74.8	8.82	30	86.4	9.54	40	113.6	8.20
Patients															
Group I (mild)	14	60.9	10.73	17	73.3	15.4	13	84.3	13.8	13	101.9	14.0	17	126.6	13.12
Group II (moderate)	7	58.7	12.1	9	76.3	11.5	8	90.5	12.5	10	107.6	11.7	11	136.6	13.4
Group III (severe)	6	63.0	7.3	9	80.9	11.5	6	93.0	13.9	7	111.0	16.2	12	134.7	14.6
<i>Light source 5 cm diameter</i>															
Normal	38	52.5	5.3	39	67.0	8.0	32	78.1	6.4	33	90.4	6.9	40	114.4	5.9
Patients															
Group I (mild)	16	51.7	12.0	16	73.3	15.1	13	86.8	12.6	13	103.4	13.5	17	129.9	15.6
Group II (moderate)	6	54.8	12.1	9	76.2	15.5	9	92.4	11.2	11	111.1	14.6	11	133.6	15.2
Group III (severe)	7	67.3	7.2	8	84.9	10.3	7	103.1	10.9	9	113.4	9.5	12	139.8	14.2

N = sample size.

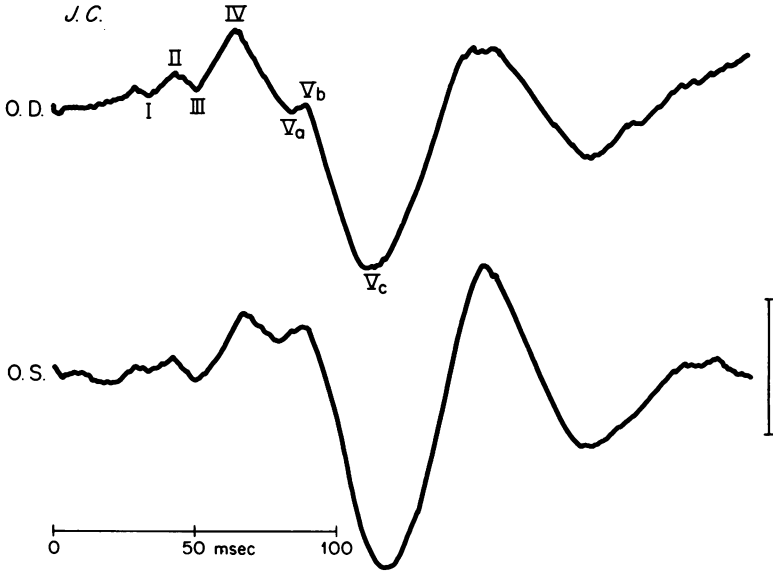


FIG. 1. Typical evoked responses from normal subject. Upper trace is the response from the left occipital region on stimulation of the right eye. The lower trace is the right occipital response on stimulation of the left eye.

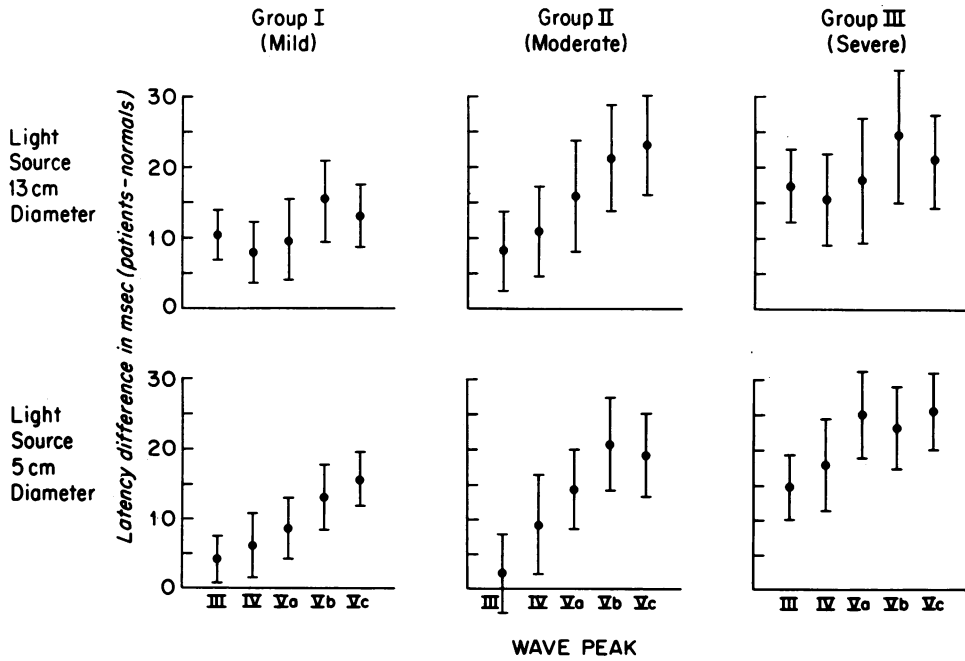


FIG. 2. Evoked response wave peak latencies plotted as a difference between patients and normals for each wave peak. 95% confidence intervals are indicated.

Figure 2 shows the differences between the patient and normal responses, plotted as latency difference for each of the wave peaks. Fiduciary limits are for a 95% confidence interval. The appearance of the earlier wave peaks (I and II) was quite variable in both the patient and normal populations and confidence for statistical purposes could be given only to the more easily discernible wave points III, IV, and Va, Vb, and Vc. That is, the earlier responses were frequently not present in some normal subjects and most conspicuously unidentifiable among the patient groups. This variability of appearance of the earlier portion of the VER has been previously stressed by Gastaut and Regis (1965).

As can be seen from Fig. 2, there was a significant delay of all portions of the patient VERs, irrespective of stimulus size, in all instances but one. The differences were most prominent when the responses from eyes 'severely' affected (group III) were compared with the normals; however, a significant difference was apparent even among those patients 'mildly' affected (group I). Even patients with normal vision at the time of study showed delays in wave peak latencies. The difference between the patient and normal responses was also consistently most apparent for the later wave peaks in comparison with the earlier wave peaks.

DISCUSSION

Our results demonstrate a correlation between latencies of the patient VER wave peaks and the degree of visual impairment. In addition, this observation appears relatively independent of the diameter of the light source used. The intention in using the smaller aperture was to achieve more selective stimulation of the macular region and, thereby, to bring about a greater differential between the patient and normal responses. This goal was not achieved and probably not needed. That is, although not universally accepted, it has been suggested that the VER is primarily of macular origin (DeVoe, Ripps, and Vaughan, 1969). In addition, Vaughan, Katzman, and Taylor (1963) have earlier stressed the importance of macular or central retinal projections to the cortex for the normal appearing VER. If this were true, lesions producing central vision loss would produce

alterations in the VER to a certain degree independent of the size of the light source, providing the stimulus were directed to the macular region. Such were the results of our experiment. This view that central visual defects are more likely to cause alterations of the visual evoked response has also been expressed by Richey *et al.* (1971).

The temporal dispersion of the VER and the delayed wave peak latencies would be consistent with delayed conduction across demyelinated areas of the visual system. Since all of our patients had visual impairment with a central scotoma either before or at the time of study, the most reasonable area for this delay in conduction would be in the optic nerve. Further, all wave peaks of the patient response were delayed, not merely the early or late components. While lesions in the non-specific projection system cannot be excluded, this observation would additionally imply that the delay in conduction occurred in the pathway common to all projection systems to the occipital area—that is, the optic nerve.

This study represents one phase of an ongoing investigational effort seeking neurophysiological correlates to the course of multiple sclerosis. The results are quite similar to previous studies (Namerow, 1968, 1970a, b) on the effect of demyelination in somatosensory pathways and in the pons. The latencies of the VER, however, appeared to be more variable than the results from these other pathways studied. This may reflect an increased difficulty in controlling pertinent parameters such as fixation in patients with central field defects and involuntary eye movements.

It was not our intention to investigate a possible diagnostic test for multiple sclerosis in this or previous studies. Rather, it was to gain understanding on the nature of conduction in patients with demyelinating disease. Such evaluation methods, however, clearly have potential clinical application as a means of obtaining objective data on MS patients and among these useful techniques one might possibly include the VER.

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