Principles and Practice of Clinical Electrophysiology of Vision

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Pattern Visual Evoked Cortical Potential in Multiple Sclerosis

Emiko Adachi-Usami

In contrast to the flash evoked potential, the pattern evoked potential shows very little variation in the P100 latency of different subjects. Therefore the usefulness of the pattern response is greater than the flash stimulus. The present chapter deals with the literature pertaining to pattern response in multiple sclerosis (MS) only. It began with the pioneering work of Halliday et al.,[9] from which subsequent studies were derived. They collected 51 patients of definite, probable, or possible MS. Of the 51 patients with MS, 24 had a past history suggestive of optic neuritis in one or both eyes. All 24 proved to have delayed pattern responses. Twenty-seven other patients had no history of visual impairment, but of these no fewer than 25 turned out to have delayed pattern responses, and there were only 2 patients with normal responses in the whole group. Thus from their data 96% of the patients with MS can be expected to have delayed responses, as can 93% of the patients with no clinical history of optic neuritis. The percent incidence of delayed pattern responses in subsequent published papers of MS varied from 50% to 96% for overall detection rates. The cases with a history of optic neuritis showed higher detection rates that ranged between 82% and 100%, while the cases without a history of visual impairment had rates that were the lowest, between 36% and 93%. On the other hand, no significant delay of pattern disappearance response in MS without a history of optic neuritis has been reported[19] (Fig 113–1).

The reasons for the various rates of delayed pattern responses among different authors might be related to the patients selected and stimulus conditions used. Nonetheless, the percentage of detecting delayed pattern responses in MS is generally acknowledged to be higher than with that found in other diseases.

HOW CLOSE IS THE RELATIONSHIP BETWEEN DELAYED VISUAL EVOKED CORTICAL POTENTIAL AND SUBJECTIVE VISUAL DYSFUNCTION IN MULTIPLE SCLEROSIS?

Visual Acuity Decrease

An attack of optic neuritis starts with a sudden vision loss and decreases to a very low visual acuity level such as light perception by the end of the first week. At this acute stage, the pattern visual evoked cortical potential (PVECP) is found to be flat or, in other words, "nonrecordable." When visual acuity is less than 1/10, a nonrecordable PVECP is observed with 100% certainty.[1] Nonrecordable PVECP occurs not only in optic neuritis caused by MS but also in optic nerve lesions caused by tumors, injuries, vascular ischemia, and degeneration. Delayed PVECP is generally found in patients with visual acuity remaining higher than 2/10.

It is known that delayed PVECP recovers to normal with time[3] in accordance with the recovery of visual acuity, although VECP improvement was found to lag in the recovery of subjective vision and its recovery was incomplete after relapses in MS cases.[13]

Neima and Regan[15] compared VECP results with an analysis of grating contrast sensitivity. Diseases

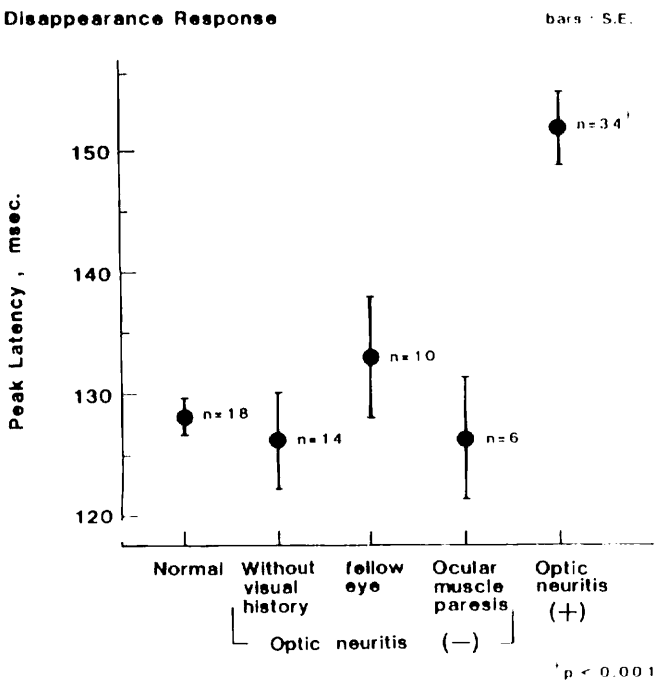

FIG 113–1.
Mean peak latencies of the positive components of the disappearance response in eyes of MS patients. A significant prolongation of peak latency in eyes with a history of optic neuritis as compared with that of normal eyes was observed, although no significant differences were found in eyes without this history and those with a history of ocular muscle paresis as compared with normal eyes. (From Toyonaga N, Adachi-Usami E, Kakisu Y: *Neuro-ophthalmology* 1988; 8:81–86. Used by permission.)

that depressed sensitivity for high spatial frequencies alone were associated with depressed visual acuity and attenuated VECP amplitude for a smaller check size pattern, but the VECP latency was less closely correlated with abnormalities in contrast sensitivity. These results do not agree with the widely accepted works of many authors who found that VECP abnormality is not closely related to sensory visual loss in patients with MS, i.e., abnormally delayed PVECP is often found even in the subclinical stage of optic neuritis.

Sanders et al.[18] reported that VECP amplitude is related to visual acuity while a correlation with the change in VECP latency is barely significant; they concluded that VECP latency was more concerned with the extent of demyelination. Using the critical fusion frequency (CFF), Salmi[17] reported that VECP delay was more frequent in patients with long-standing MS, the frequency of VECP delays relative to changes in CFF increasing in MS. As described above, data for comparing visual acuity and VECP are still far from sufficient.

Color Sense Abnormality

In MS an acquired red-green color vision defect is frequent. Pinckers and Verriest[16] carried out comparative studies of VECPs and color vision in 109 patients with possible and probable MS. They found a striking similarity between the two examinations, that is, the results of VECP and color vision were concordant in 71% of the cases. Engell et al.[5] studied VECP and color vision in 64 eyes of 33 patients of clinically definite MS whose visual acuity was normal. VECP was delayed in 84%, the Farnsworth-Munsell 100-Hue Test was abnormal in 41%, and the Ishihara Plate was misread in 31%. The cases with abnormal color vision revealed abnormal VECP except in 1 eye. They therefore concluded that VECP is the most sensitive test of them all.

Tsukamoto and Adachi-Usami[20] used the Standard Pseudoisochromatic Plates (SPP), part II, the New Color Test, the City University Color Vision Test, panel D-15, and the Ishihara Plate in 19 eyes of MS patients with chronic optic neuritis and found that the incidence of color deficiency was more frequent (89%) than was an abnormal delay of the VECP (80%) (Fig 113–2). Fujimoto and Adachi-Usami[7] later compared the cases with red-green defect and blue-yellow defect in optic neuritis in relation to VECP. Color vision was tested with SPP II and Lanthony's desaturated panel D-15 in MS patients with optic neuritis and in patients with unknown causes in which visual acuity had remained better than 5/10. The results are shown in Table 113–1. It was observed that eyes with predominant

TABLE 113–1.
Peak Latency of the P100 of Pattern Visual Evoked Cortical Potential vs. Color Vision Abnormality in Optic Neuritis (No. Eyes)*

	PVECP Latency		
Defect	Delayed	Normal	Total
Red-green			
Present	11†	2	13
Absent	6†	11	17
Total	17	13	30
Blue-yellow			
Present	8	4	12
Absent	9	9	18
Total	17	13	30

*Data from Fujimoto N, Adachi-Usame: *Acta Soc Ophthalmol Jpn* 1988; 92:1485–1488.
†$P < .01$.

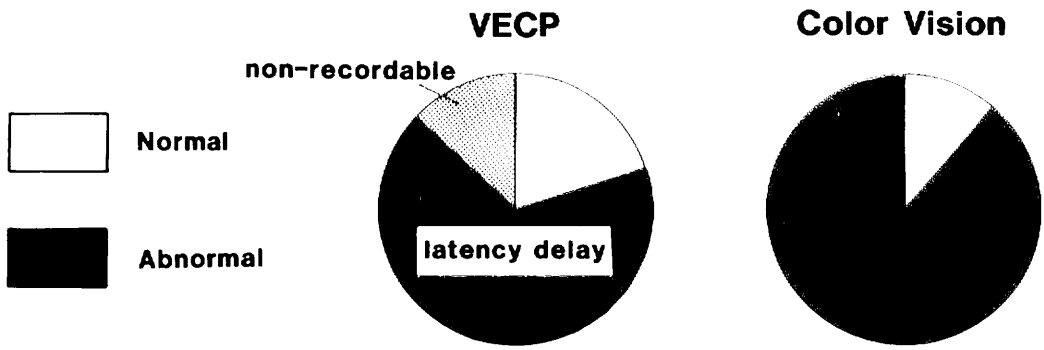

FIG 113–2.
Rates of delayed peak latency of the P100 of PVECP and abnormal color vision in 19 eyes with optic neuritis caused by definite MS. (From Tsukamoto M, Adachi-Usami E: *Acta Soc Ophthalmol Jpn* 1987; 91:613–621. Used by permission.)

red-green defects had a significantly delayed PVECP latency and a delay in recovery. In general, it seems to be true that abnormal VECP is related to abnormal color vision in MS.

Visual Field Defects

Recent advances in the procedures of visual field testing have led to the detection of visual field defects that could not be determined by the conventional methods represented by the tangent screen and Goldmann perimetry. There have been several papers that compared visual field defects and pattern VECP in MS by using these newly developed instruments. Van Dalen et al.[21] examined 29 patients with MS by means of static perimetry. An abnormal VECP was found in 32 eyes (55%), and an abnormal visual field was noted in 46 eyes (79%). In 16 eyes with a normal VECP an abnormal visual field was detected, but in only 2 eyes with a normal visual field was an abnormal VECP found. When using an Octopus automated perimeter similar results were described by several authors. Meienberg et al.,[12] using programs 33 and 34, found visual field defects in MS patients who showed normal VECP latencies and stated that no correlation was found between delayed VECP latencies and the location, depth, or extent of visual field defects. Lowitsch and Welkoborsky[10] also reported that there was no clear-cut relationship between VECP and visual field defects in spite of the high percentage of abnormal visual fields in MS.

On the other hand, a good correlation between VECP delay and visual field defects was reported by Younge (program 11),[23] Wildberger (program 31),[22] and Fujimoto and Adachi-Usami (programs 31, 33)[6] (Fig 113–3). In any case, it is clear that central visual

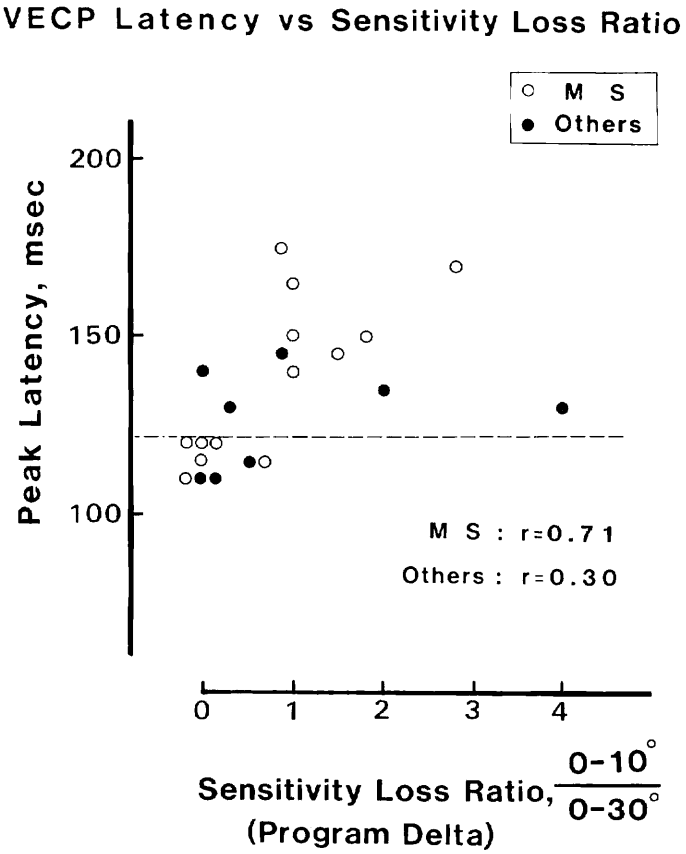

FIG 113–3.
Peak latency of the P100 of PVECP vs. the visual field sensitivity loss ratio of an Octopus perimeter in optic neuritis caused by MS and other conditions. The sensitivity loss ratio was calculated by program Delta, i.e., the ratio of the mean loss at each test location at an eccentricity of within 10 degrees over that of 30 degrees. The ratio was significantly correlated to the VECP latency in MS. The *broken line* indicates the upper limit of normal VECP peak latency. (From Fujimoto N, Adachi-Usami E: *Doc Ophthalmol* 1988; 69:263–269. Used by permission.)

field depressions within 5 degrees of the fovea are responsible for delayed VECPs in most cases.

IS THE DELAYED PATTERN VISUAL EVOKED CORTICAL POTENTIAL SPECIFIC IN MULTIPLE SCLEROSIS?

Normal Subjects

The peak latency of P100 is delayed by many factors, even in normal subjects, including both stimulus and recording conditions: lower mean luminance and contrast, smaller or larger check sizes, defocused pattern, monocular viewing as compared with binocular viewing, upper visual field stimulation, and anterior scalp electrode position. In addition, gender and age could also influence latency (see Chapter 53). Among the various factors, the effect of mean luminance is rather prominent. We[2] found that a 1-log-unit decrease in pattern luminance resulted in a 15- to 18-ms increase in the P100 latency. This value is in accordance with the results of Halliday et al.[8] Of course, luminance is reduced by smaller pupil size and opacity of the crystalline lens and vitreous body, which are the characteristic signs of senescence of the eye. As a whole, the recording conditions should be maintained as constant as possible for evaluating the VECP delay in MS. In other words, the pupil size should be kept constant with an artificial pupil after its dilation, refractive errors should be fully corrected with appropriate lenses, a fixation point must be set, and the opacity of the crystalline lens and vitreous body in addition to the fundus appearance should be checked. A reliable protocol can thus be established for examination facilities.

Other Diseases Besides Multiple Sclerosis With Delayed Visual Evoked Cortical Potential

Increased VECP latencies are also found in optic nerve diseases caused by ischemia, compression by tumors, sarcoidosis, degenerations resulting from systemic diseases such as hereditary ataxia, spastic paraplegia, etc., as well as toxic agents. In addition, the deficiency of neurotransmitters such as dopamine in Parkinsonism may increase the VECP latency.[4] Murayama and Adachi-Usami[14] found a VECP delay in a specific type of Parkinsonism—juvenile Parkinsonism—for which L-dopa is dramatically effective. However, most of the aforementioned cases can be differentially diagnosed according to other clinical data. We believe that VECP is essentially useful for determining abnormal changes in the optic nerve.

UNDERLYING MECHANISM OF DELAYED PATTERN VISUAL EVOKED CORTICAL POTENTIAL IN MULTIPLE SCLEROSIS

The VECP is not a single unit response of the neurons but a mass response originating from the visual pathway between the central retina and the visual cortex. One should therefore be careful before concluding that a delay in response means a delay in conduction velocity in the optic pathway. McDonald and Sears[11] made experimental demyelinating lesions in the spinal cord of the cat and measured conduction velocity. They showed that large areas of myelin loss in central nerve fibers produced a conduction block throughout the demyelinated zone, whereas normal conduction at an unreduced velocity persisted in the still myelinated portions of the nerve to the lesion. They also found a reduced high-frequency response in the demyelinated fibers. It can therefore be presumed that demyelination is one of the factors responsible for delayed VECPs. Pathological changes like the demyelination of nerve fibers found in MS can presumably be explained in such a way. However, the delayed responses observed in other diseases as well as a variance in stimulus conditions probably occur for other reasons. Axonal degeneration and loss from edema might also cause an increase in VECP latency. Moreover, it is suggested that the thicker neurons that transmit impulses faster are the ones mainly involved. A lowered luminance caused by miosis, defocusing, and fewer stimulated cell numbers might result in less stimulation of the faster neurons. Further experimental studies will be required.

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