

MOTION-ONSET VEPS IMPROVE THE DIAGNOSTICS OF MULTIPLE SCLEROSIS AND OPTIC NEURITIS

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Summary: In addition to standard pattern-reversal VEPs, the motion-onset VEPs were examined in 50 patients with acute unilateral retrobulbar neuritis (RN) and in 187 patients with possible or definite multiple sclerosis (MS). In MS patients (without sign or history of RN), the results of both types of VEPs correlated only partially. 26.2% of them displayed changes only in the motion-onset VEPs having the pattern-reversal VEPs completely normal. That is why we suppose that the magnocellular system (tested by motion-onset VEPs) can be affected by demyelination separately. In 28 patients with „pure“ RN (without any other sign indicating demyelination disease) the always abnormal pattern-reversal VEPs were accompanied by delayed motion-onset VEPs in only 28.6% of patients. In contrast, much higher rate - 68.2% - of delayed motion-onset VEPs was found in the 22 RN patients simultaneously suspected of MS. These results indicate that RN affects predominantly the parvocellular visual system (tested by reversal VEPs). Distinct latency changes of the motion-onset VEPs in RN patients seem to signal a linkage between RN and demyelination.

Key words: Optic neuritis; Multiple sclerosis; Pattern-reversal VEP; Motion-onset VEP

Souhrn: Diagnostický přínos zrakových evokovaných potenciálů při stimulaci pohybem u demyelinizačního a zánětlivého postižení zrakové dráhy. U 50 pacientů s akutní optickou neuritidou (ON) a u 187 pacientů s diagnózou suspektní nebo definitivní roztroušené sklerózy mozkomíšni (RSM) byly testovány zrakové evokované potenciály (ZEP) na standardní reverzační stimulaci a na začátek pohybu struktury v zorném poli. U pacientů s RSM výsledky obou typů ZEP korelovaly pouze částečně. U 26,2 % pacientů byly patologické změny zachyceny jen v „pohybových“ ZEP (reverzační ZEP byly zcela normální). Z toho vyplývá, že magnocelulární zrakový systém (testovaný „pohybovými“ ZEP) může být demyelinizací postižen samostatně. U 28 pacientů s „čistou“ ON (bez dalších příznaků naznačujících demyelinizaci) byly abnormální reverzační ZEP doprovázeny prodloužením latencí „pohybových“ ZEP pouze ve 28,6 %. Naproti tomu ve skupině pacientů s ON, u kterých i další klinické příznaky svědčily pro RSM (22 osob), byly patologické změny „pohybových“ ZEP nalezeny v plných 68,2 %. Tyto výsledky ukazují, že ON postihuje primárně parvocelulární systém zrakové dráhy (testovaný specificky „reverzačními“ ZEP). Případné změny „pohybových“ ZEP pak svědčí pro demyelinizační původ ON.

Introduction

It is well known that retrobulbar neuritis (RN) is one of the first symptoms of demyelination in many cases. For example, Rizzo and Lessel (11) in their long-term prospective study reported that multiple sclerosis (MS) would develop in about 30% of men and in 70% of women within the 10 to 15 years after the first attack of retrobulbar neuritis, which means that in each case of neuritis, demyelination should be considered. This raises the question whether the underlying cause of the RN can be diagnosed solely on the basis of the VEP tests.

The most commonly used type of VEPs - the pattern-reversal VEP can not provide this information, because both neuritis and MS lead to exactly the same VEP abnormalities - namely to a latency increase and amplitude reduction of the main positive peak (for details see e.g. 9). Thus, if we do not find in a patient with unilateral optic neuritis some abnormality also in the normal fellow eye, the eventual linkage between RN and demyelination remains unclear.

In contrast, the motion-related VEPs, as we would like to show in this study, seem to provide some more hope in this respect, since their results for the RN and MS patients differ considerably.

Subjects and methods

Within the last 4 years we compared the motion-onset VEPs with standard pattern-reversal VEPs in 187 patients with a diagnosis of either definite or possible MS and in 50 patients with acute unilateral retrobulbar neuritis. None of the MS patients had any ophthalmological disorder at the time of our examination. As to the 50 RN patients, 28 of them came with first attack of RN without any other sign indicating the eventual demyelination disease, whereas the other 22 were labeled by referring neurologists as being suspected of MS.

All recordings were performed in a sound-attenuated, electromagnetically shielded chamber with a background luminance of 1 cd/m². The subject was seated in a comfortable dental chair with a neck support to reduce muscle artefacts. A dark fixation point of 15' diameter was placed in the centre of the stimulus field and the subjects were instructed not to follow the moving or reversing pattern with their eyes.

For both types of VEPs the same pattern-square-wave black and white checkerboard with an element size of 40', contrast of 90% and luminance of 17 cd/m² was back-projected via a moving mirror onto the circular stimulus field subtending 35°. Mirror movement was produced by an optical scanner (General Scanning Inc., USA) controlled by square-wave or ramp signals. For pattern-reversal VEP a rate of 2 rev/s was used. For motion-onset VEPs the pattern moved rightward with a velocity of 5 deg/s for 200 ms and was presented stationary during 1.5 s long interstimulus interval. In each patient the monocular VEPs from both eyes were recorded in the bipolar O_z-C_z lead (optimal for pattern-reversal VEP recording) and in three unipolar leads with the electrodes placed at O_z and 5 cm to the right and to the left from this point - O_R and O_L electrodes are more convenient for motion-onset VEP recording, since the maximum of this type of VEP is usually located over the right or

left occipital area (5,6). Linked earlobes served as reference. After amplification (Tektronix AM 502) in the 0.1 - 100 Hz band, 100 epochs of 400 ms duration were averaged on a PC with a sampling rate of 500 Hz.

In pattern-reversal VEP we estimated the latency of the main positive P100 peak, which is very probably related only to activity of the parvocellular visual pathway (8). In motion-onset VEPs we were interested in parameters of the dominant negative peak (with a mean peak latency of about 160 ms), because, on the basis of another study (8), it reflects selectively the function of the magnocellular pathway.

Results

We have found that in the group of MS patients the results of pattern-reversal and motion-onset VEPs correlate only partially. This can be seen in Fig. 1 where the latencies of the reversal VEPs are plotted against the latencies of the motion-onset VEPs for all the eyes investigated. In the left bottom and the right top parts, there are the eyes in which the results of both types of VEPs correlated, showing either normal or abnormally delayed individual latencies. More important, however, are the findings of abnormal pattern-reversal VEPs accompanied by normal motion-onset VEPs in the eyes falling into the right bottom part as well as the reversed situation depicted in the left top part of the figure that shows the eyes in which only the latencies of the motion-onset VEPs are pathologically increased.

Table I gives an overview of the incidence of abnormal and normal findings of pattern-reversal and motion-onset VEPs in the MS patients. In 26.2% of our patients the diagnosis of MS could be made only on the basis of motion-onset VEP - a concrete example of such a case is given in Fig. 2. Whilst the pattern-reversal VEPs are normal in both eyes, the motion-onset VEP displays clear abnormality in the left eye.

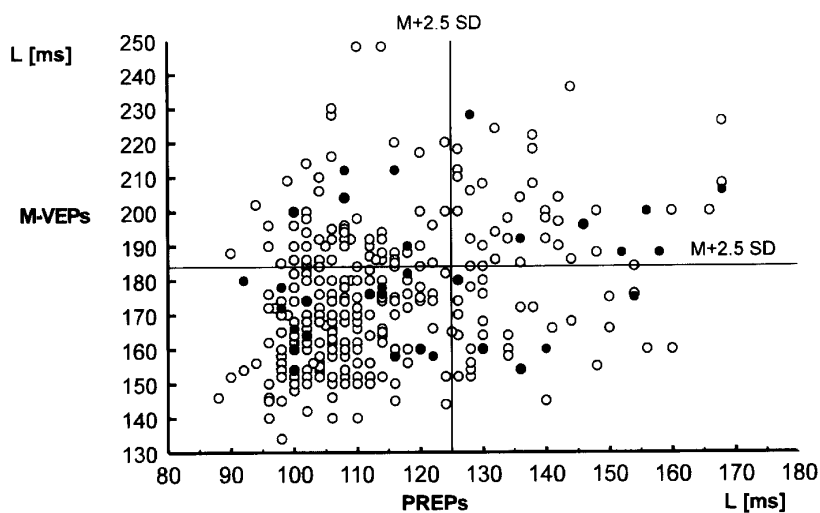


Fig. 1: Distribution of pattern-reversal VEP (PREP) versus motion-onset VEPs (M-VEP) latencies from the 374 eyes of the whole group of patients suspected of MS (o) and with definite MS (•). The lines indicate the upper limits (mean + 2.5 standard deviation [SD]) of the values of the control group.

	Definite MS		Suspected MS		All patients with MS	
	(n=15)		(n=172)		(n=187)	
	N	%	N	%	N	%
Abnormal PREPs and M-onset VEPs	8	53.3	43	25.0	51	27.3
Abnormal PREPs, normal M-onset VEPs	1	6.7	17	9.8	18	9.6
Normal PREPs, abnormal M-onset VEPs	3	20.0	46	26.7	49	26.2
Normal PREPs and M-onset VEPs	3	20.0	66	38.3	69	36.9
Total abnormal PREPs	9	60.0	60	34.9	69	36.9
Total abnormal M-onset VEPs	11	73.3	89	51.7	100	53.5
Total abnormal findings	12	80.0	106	61.6	118	63.1

Tab. I. Incidence of abnormal and normal findings of pattern-reversal VEPs (PREPs) and motion-onset (M-onset) VEPs in patients with MS

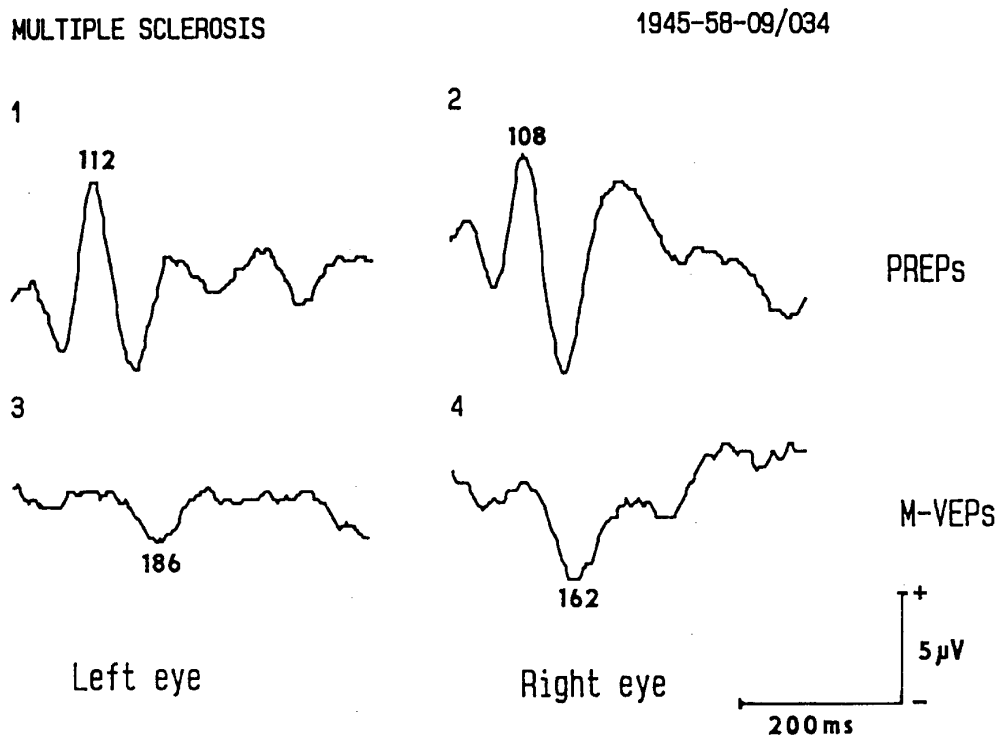


Fig. 2.: Concrete example of pattern-reversal VEP (PREP) and motion-onset VEP (M-VEPs) findings in a patient with definite MS (confirmed by MRI). Note that the only abnormality found is a delayed motion-onset VEP latency upon the stimulation of the left eye.

Fig. 3 shows the pattern-reversal and motion-onset VEPs latencies comparison for patients with acute unilateral RN. In part A there are the results from 28 patients with „pure“ RN (i.e. without other symptoms pointing to MS) and in part B there are the findings from the 22 RN patients who were simultaneously suspected of MS.

In the „pure“ RN patients both types of VEPs were entirely normal in all nonaffected eyes. In eyes with RN the pattern-reversal VEPs were always abnormal - either exceeding the upper limit of the norm (125 ms) or showing the abnormally large interocular difference (more than 10 ms). The delayed motion-onset VEP latencies were found only in 28.6% of the eyes with RN.

In contrast, as many as 68.2% of the patients who were referred as suspected of MS, exhibited pathologically prolonged motion-onset VEPs in eyes with RN that accompanied the always abnormal pattern-reversal VEPs. Moreover, delayed latencies of pattern-reversal and/or motion-

onset VEPs were found in 59.1% of the apparently normal fellow eyes.

Discussion

Within the last 22 years a high incidence of delayed pattern-reversal VEP in multiple sclerosis patients has been reported by many authors (for overview see e.g. 9) and so the pattern-reversal VEP has become the investigation of choice for electrophysiological diagnosis of demyelination disease. The abnormal changes of this type of VEP have been found not only in the patients in whom the demyelination was accompanied by clinical symptoms of optic neuritis, but also in those who did not have any history or clinical findings suggesting involvement of the visual system (11).

Various laboratories tried more or less successfully to increase the sensitivity of reversal VEP examination in MS

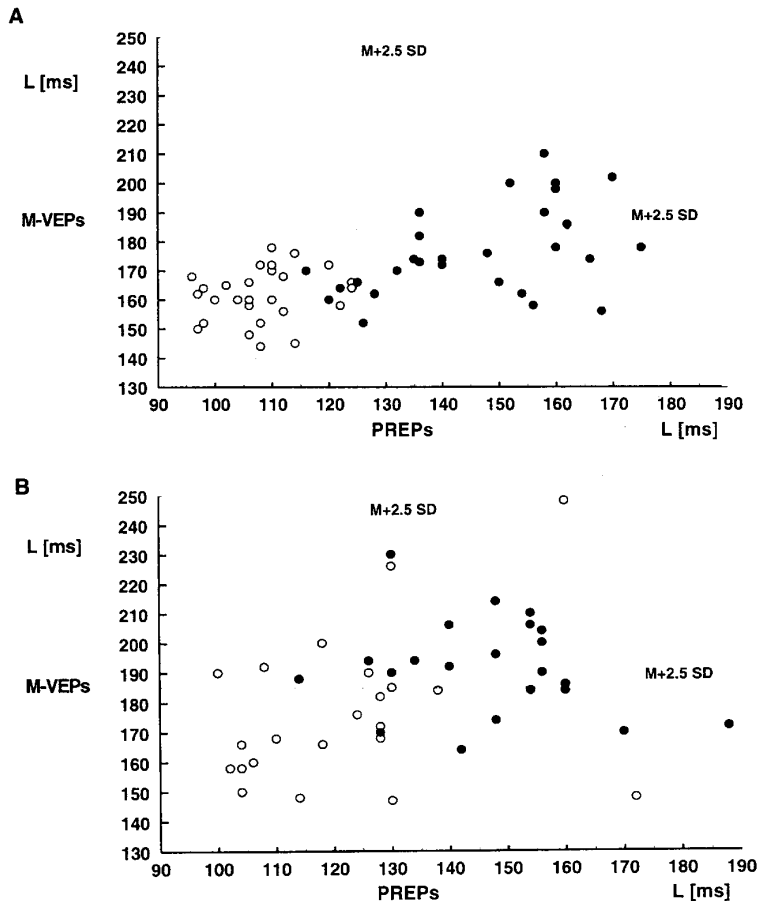


Fig. 3.: Distribution of pattern-reversal VEP (PREP) versus motion-onset VEPs (M-VEP) latencies from the normal eyes (o) as well as eyes affected by RN (•) in patients with unilateral RN. The lines represent the upper limits (mean + 2.5 standard deviation [SD]) of the normal values. A part shows the findings for patients with „pure“ RN (without any other sign pointing to demyelination), B displays those who were simultaneously suspected of MS.

patients by additional performance of foveal or hemifield stimulation (4,2,3,1). Besides the pattern-reversal stimulation, also pattern-onset or pattern-offset stimuli have been reported to improve abnormality detection in demyelination (10, 13).

In our present study, which substantially extends the results of our first study on this topic (7) we wanted to contribute to all the attempts to improve the VEP diagnostic possibilities in MS by introducing a stimulation so far in the clinical practice relatively unknown - onset of pattern movement. Recently (8) we have presented an evidence that the main negative peak of the motion-onset VEP reflects selectively the activity of the magnocellular subdivision of the visual system, which means that this type of the VEP can give information different from that obtained by all the pattern-related VEPs (the pattern-reversal VEP inclusive).

Our above presented results show that in those MS patients who had no sign of optic neuritis at the time of our investigation the delayed motion-onset VEPs can occur without simultaneous increase of the pattern-reversal VEP latency (and vice versa). For this reason we suggest that the two relatively independent visual pathways - the parvo- and the magnocellular ones might be affected separately by demyelination. Rather high incidence (26.2%) of cases in which only the abnormal motion-onset VEPs were found in patients suspected of MS or having the diagnosis of definite MS (confirmed in 2 patients by positive MRI findings) indicates that the additional use of the motion-onset stimulation increases the sensitivity of the VEP examination in this disease.

Since a reduced visual acuity dominates in the clinical picture of optic neuritis, we can hypothesize that the parvocellular pathway (transmitting the information about the form) is always affected by the neuritis. That is why the changes of the pattern-reversal VEP can be predicted in these patients and indeed, all our patients with RN displayed prolonged latencies of the P100 peak. In contrast, the rate of prolonged motion-onset VEPs latencies did not reach that of the pattern-reversal VEPs, which indicates that the magnocellular pathway is less affected. This is especially true for the „pure“ RN patients (without any other sign pointing to MS) because in this group the delayed motion-onset VEPs occurred only in 28.6% of the eyes with RN. However, much higher percentage of abnormal motion-onset VEPs (68.2%) was found in the group of RN patients simultaneously suspected of MS. This fits well with our suggestion that distinct changes of motion-onset VEPs when found in RN patients point to the demyelination origin of neuritis.

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