J Neurol (1982) 227: 125–133

Journal of
Neurology

Original Investigations

Subclinical Visual Field Defects in Multiple Sclerosis

Demonstration and Quantification with Automated Perimetry, and Comparison with Visually Evoked Potentials

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Summary. Fourteen patients with definite but inactive multiple sclerosis (MS) and 17 normal controls were examined with the automated perimeter octopus. Most of the patients had subclinical visual field defects, typically consisting of patchy, shallow scotomata located mostly in an area of between 15° and 30° eccentricity. In 8 patients, more than 15% of the tested visual field of at least one eye was abnormal. The severity and extent of the defects was unrelated to a history of optic neuritis. When visually evoked potentials (VEPs) of these subjects were examined using a reversing pattern, no correlation was found in the MS patients between prolonged VEP latencies and the location, depth or extent of visual field defects. Since subclinical visual field defects may be found in MS patients with normal VEP latencies, automated perimetry can be helpful in diagnosing some cases.

Key words: Multiple sclerosis – Visual fields – Visual evoked responses

Introduction

At present, recording of visually evoked potentials (VEPs) is the most widely used method for detecting subclinical damage to the visual pathways in order to establish the diagnosis of multiple sclerosis (MS). A high percentage of patients—even those in the early stages of the disease—have been shown to have abnormal VEPs [1, 6, 9, 12, 15–17, 19, 23, 24, 28]. Using only a tangent screen or conventional static perimetry some neuro-ophthalmologists [4–6, 11, 12] have been able to detect subtle visual field defects in MS patients without a history of optic neuritis. However, these examination procedures are time-consuming; the findings are either semiquantitative or confined to a few profiles through the visual field; and the examination needs much experience to obtain reliable results.

Supported in part by Geigy Jubilaeumsstiftung, Basel
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0340-5354/82/0227/0125/$01.80

The VEP examination procedure is, by contrast, fast and easy. Automated perimetry affords a standardized test of the visual field irrespective of the examiner's experience and provides quantitative results [3, 7, 8, 10]. Provided that selection of the proper scanning density and of the visual field area revealing the maximal abnormality do not unduly prolong the examination time, automated perimetry may facilitate the diagnosis of MS.

We report the visual field defects found by means of the automated perimeter octopus in a group of patients with definite MS, and compare these findings with the VEP findings in the same patients. Simple methods of quantifying examination results are presented.

Materials and Methods

Fourteen patients (11 women, 3 men) aged 18–52 years (mean, 36 years) were studied. All had MS established clinically according to the criteria of McAlpine et al. [20], but the disease was inactive at the time they were studied and they had no visual disturbances. Their corrected visual acuity was 0.6 or better, mostly in the 0.9–1.0 range. Ocular disorders not attributable to MS were excluded. Each patient was examined twice in the same week, once using the automated perimeter octopus and once by making VEP recordings.

VEPs were recorded by the method previously described [21]. A checkerboard pattern extending 24° of arc horizontally and 16° vertically, with checkers of 60 min each, was presented on a television screen; it reversed every second. VEPs were recorded by an electrode placed 5 cm above the inion in the midline, with the reference electrode placed midfrontally. Each eye was examined twice, the eye fixated for the first run at the center of the pattern, for the second at the upper border in the midline. For each run, 64 responses were recorded and averaged. The upper limits of normal for the latency of the major positive wave (P 100) were 116 ms (the mean + 3 SD for 78 healthy subjects) for center fixation, and 113 ms (the mean + 3 SD for 52 healthy subjects) for upper-border fixation.

Static examination of the visual field was performed with the automated perimeter octopus [2, 7, 26]. The target size was 3 (diameter 0.43°), stimulus presentation time 100 ms, and background luminance 1.27 cd/m^2. This perimeter determines local visual thresholds with a bracketing strategy. Each eye was tested with the combined standard programs 33 and 34, which corresponds to threshold determinations at 149 locations homogenously distributed within a central visual field area with a radius of 30°. Thus the distance between two test locations, i.e., the resolution, was 4.2°. Deviations from normal performance are determined automatically by comparison of the actual sensitivity values with age-corrected mean normal values stored in the computer memory. Since the physiologic threshold is subject to variation, only deviations of more than 4 dB from normal are printed out. The area of the blind spot was omitted from quantitations. For additional statistical calculations, the data could be transferred from the octopus to an IBM 3033 computer. The sensitivity values were integrated both for the whole visual field and for separate areas. The *t*-test was used to evaluate differences between the group with and the group without previous optic neuritis. The computer also correlated the visual field data with the VEP latencies.

Results

The characteristic visual field defects found in our patients are exemplified on the left side of Fig. 1. Typically, they had several small scotoma, which tended to concentrate at the periphery of the tested area. The profiles in the lower half of Fig. 1 indicate the depths of the defects. A comparison of the single profiles on the left

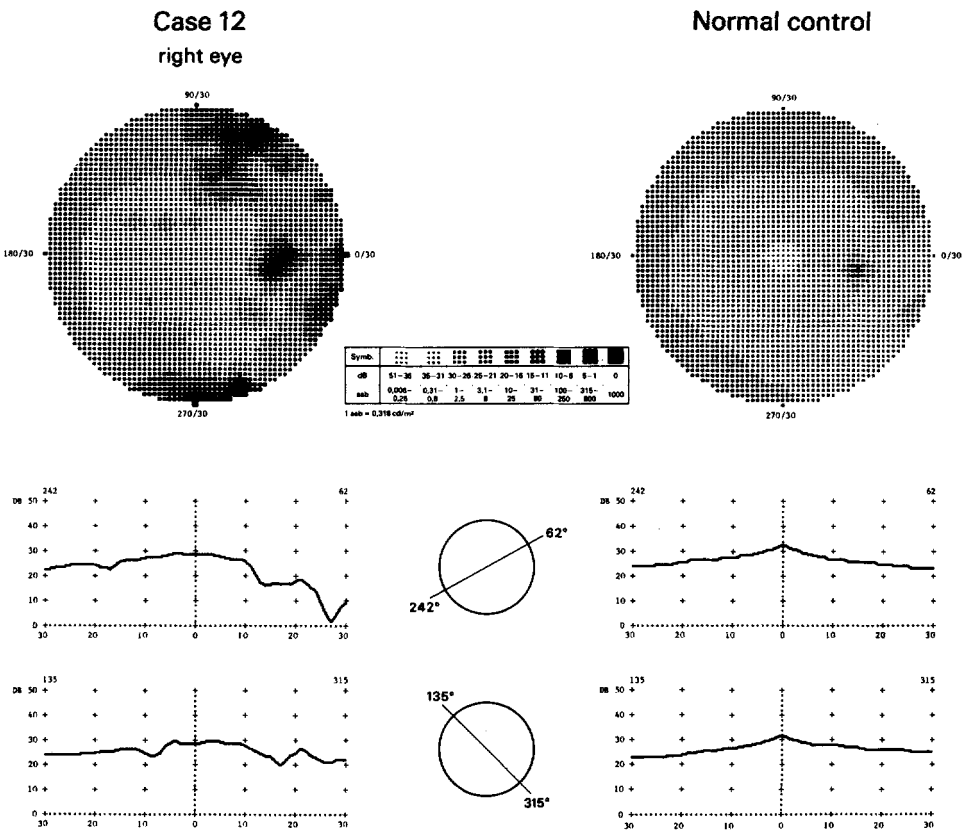

Fig. 1. *(Left)* Visual field (radius 30°) from the right eye of a patient, showing several scotomata, especially in the periphery; *(right)* visual field from a normal subject of the same age

side of Fig. 1 with the gray printout representing a conflation of the data from programs 33 and 34 makes it apparent that several defects are inevitably missed by examinations employing only one or two profiles.

Some of the data from our 14 patients are presented in Table 1. Eleven had a history of optic neuritis, which was bilateral in three instances. In all, 14 eyes (7 right and 7 left) had neuritis and 14 did not. The VEP latencies did not differ significantly between these two groups, for either center or upper-border fixation.

The VEP latencies of two patients who had documented neuritis 3 and 5 years before were normal for the formerly afflicted eyes (Fig. 2). There was no significant correlation between the severity or location of the visual field defects detected by the octopus and the eye previously afflicted or not afflicted, regardless of whether the whole field or only the macular area was analyzed, or whether only the inner or outer 15°, or only the upper or lower halves were considered. There was also no significant correlation between defects in any of these areas and the VEP latencies.

Comparison printouts (Fig. 3) provided a basis for some rough calculations. The 'disturbed area' (calculated as a percentage of the whole test field in Table 1) provides an estimate of their horizontal extension, and the mean loss per abnormal

Table 1. Summary results of VEP and octopus perimetry testing in 14 multiple sclerosis patients

Case	Age/ Sex	Eye	History of optic neuritis	VEP latencies		Octopus results		
				Center fixation	Upper-border fixation	Mean loss per test point (dB)	Disturbed area (%)	Mean loss per abnormal test point (dB)
1	28/F	R	+	94[a]	92[b]	10.3	79	13.4
		L	–	92[a]	93[b]	4.4	45	9.7
2	37/F	R	+	120	123	0.15[c]	2.7	5.5
		L	–	98[a]	108[b]	0.05[c]	0.7	5.0
3	31/F	R	+	100[a]	99[b]	0.6	10	6.7
		L	+	120	117	1.1	17	6.8
4	35/F	R	–	127	128	0[c]	0	0
		L	+	124	128	0.3[c]	5.5	6.6
5	49/F	R	+	129	129	2.7	35	7.8
		L	–	109[a]	109[b]	0.8	10	7.0
6	18/F	R	–	183	143	2.5	30	8.4
		L	–	124	125	0.6	10	6.0
7	39/F	R	+	125	120	1.7	19	9.5
		L	–	90[a]	90[b]	1.8	12	13.8
8	48/M	R	–	129	131	0.1[c]	2	5.7
		L	+	148	153	0.1[c]	1.5	6.0
9	20/F	R	–	146	146	0.1	1.5	8.0
		L	+	137	127	0	0	0
10	24/M	R	+	136	136	0	0	0
		L	+	153	162	0.7	10	7.5
11	31/F	R	–	138	144	8.2	66	12.2
		L	+	128	135	3.4	39	8.7
12	36/F	R	–	117	117	3.6	36	9.3
		L	–	127	125	1.2	18	6.6
13	51/F	R	+	157	157	1.7	16	9.9
		L	+	151	144	0.2	3	8.0
14	52/M	R	–	134	140	0.3	5	6.9
		L	–	180	180	0.05	0.7	5.0

[a] Values within normal limits, where upper limit (mean + 3 SD) is 116 ms
[b] Values within normal limits, where upper limit (mean + 3 SD) is 113 ms
[c] Values within normal limits, where upper limit (mean + 3 SD from 17 age-matched controls) is 0.5 dB

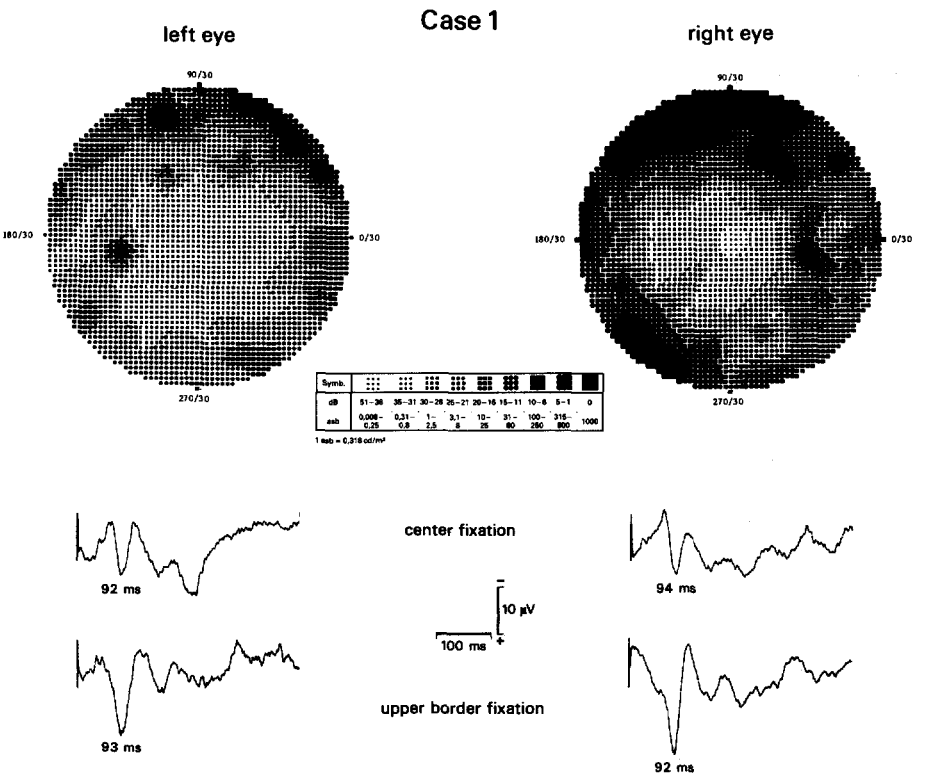

Fig. 2. Visual fields of case 1. The right eye had a history of optic neuritis 3 years previously. The left eye, also showing a markedly disturbed visual field, had no history of optic neuritis. The VEPs from both eyes were normal

test point (Table 1) gives some indication of their vertical extension, i.e., their depth. Both of these factors varied considerably from patient to patient and often from eye to eye in a single patient. Two eyes in which there was a history of optic neuritis had completely normal visual fields. In 8 of the 14 patients, the 'disturbed area' was greater than 15% of the visual field in at least one eye. The defects tended to range from shallow to moderately deep, with absolute defects being extremely rare (Table 2).

Our data suggest that in MS patients definite abnormality is more frequently revealed by VEPs than by testing of visual fields with the octopus programs employed in this study. However, octopus testing can reveal unequivocally abnormal visual fields in patients whose VEP latencies are normal (Fig. 2). Comparing the results of the octopus examinations of the visual fields of our patients with the results obtained when the octopus was used to examine age-matched healthy controls (Table 2) provides an indication of the reliability of the normal values used in the octopus program.

In general, most of the visual field defects in our patients were in the periphery of the test field (Fig. 4), and/or there was more loss of sensitivity peripherally, with the center almost entirely spared. The results from the right eyes and the left eyes

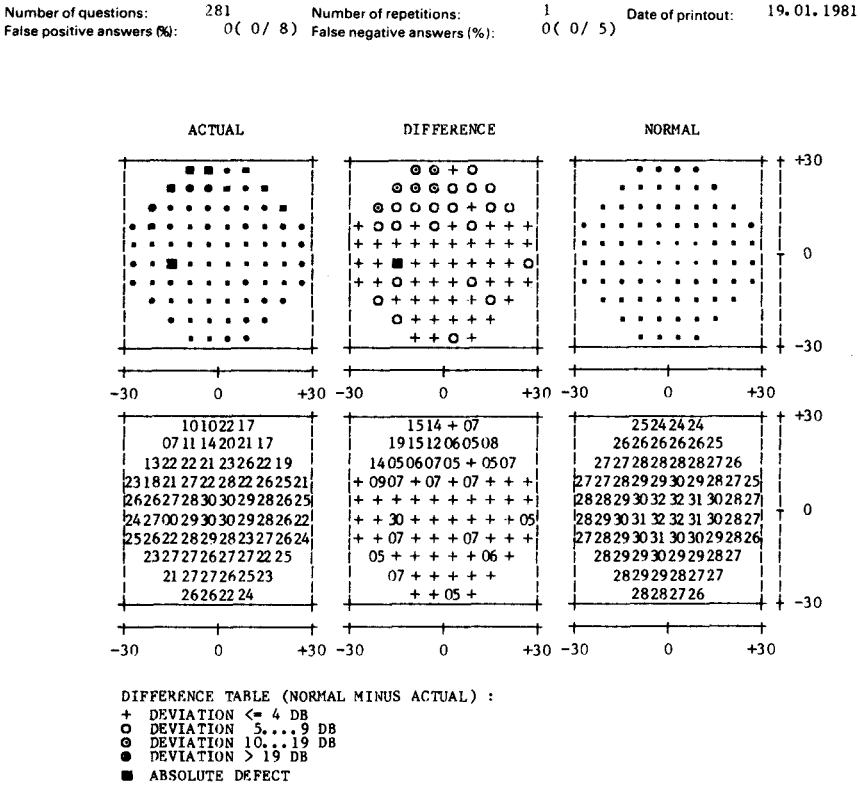

Fig. 3. Comparison printout from the examination of the left eye of case 11 using program 34. Normal values are obtained from age-matched data stored in the octopus computer. The black square in the table of differences corresponds to the blind spot; this area was omitted from quantitative analysis

Deviation from normal[a] (dB)	Percent of all points tested	
	Patients ($n = 14$)	Normal controls ($n = 17$)
≤4 dB	83.05	98.98
5–9 dB	10.61	0.94
10–19 dB	5.14	0.08
> 19 dB	0.62	0.00
Absolute defect	0.57	0.00

[a] See corresponding symbols in Fig. 3

Table 2. Deviations of the measurements of the patients and the normal controls from the age-matched normal values stored in the octopus computer and used for the comparison printouts

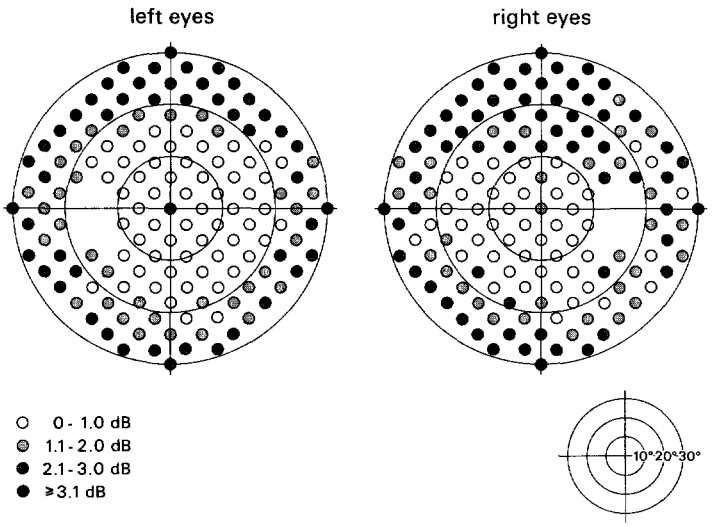

Fig. 4. Main locations where visual field defects occurred in 14 patients with MS, and mean loss per test point. The blank area corresponds to the blind spot

confirm each other. The quantitative differences in loss of sensitivity between the mean for the right eyes and the mean for the left eyes cannot be explained by the presence or absence of a previous optic neuritis, since the same number of eyes in each group had a positive history.

Discussion

The automated perimeter octopus was able to detect subclinical visual field defects in a relatively high proportion of the MS patients in our study. Typically, the defects were patchy relative scotomata, located mostly between 15° and 30° of eccentricity. With the spatial resolution used (4.2°), the macular and perimacular areas appeared to be notably unaffected. This, in combination with the comparative shallowness of most defects, serves to explain why none of the patients had visual disturbances at the time we examined them, even though the disturbed area was remarkably large in some cases. The depth, extent, and general location of the scotomata in our group of patients are identical to the findings of Frisén and Hoyt [11] and of Patterson and Heron [22], who made visual field examinations with a tangent screen 2 m from the patient. About 90% of the 41 MS patients tested by Patterson and Heron were found to have visual field defects, including 9 of 12 who had no history of visual field symptoms. In our patients, no significant difference in the extent of visual field defects was detected between eyes with or without a history of optic neuritis. This makes clear that one can never safely use an eye that has not been clinically affected as a 'normal control', as has been recommended [4, 5].

The lower incidence of subclinical visual field defects found in MS patients [6] is presumably due to the examination techniques employed. When only one or two static profiles are made through a visual field area, it is possible to miss several small defects that would be caught when using the same number of test points

distributed over the whole test area in a regular square grid. This has been demonstrated by Fankhauser and Bébié [8] and is evident from Fig. 1. The chance of detecting a scotoma of a given size obviously depends upon the density of the test point grid employed. Using octopus perimetry with a program having a spatial resolution of only 15°, Wurtz et al. [27] observed the same kind of defects as those observed by us, when they studied the affected and unaffected eyes in a group of patients in the acute stage of unilateral optic neuritis. Only a few patients were found to have minimal defects after they had recovered clinically.

The diagnostic value of VEP latencies in the early stages of MS is based on the high percentage of cases in which the VEP latencies are prolonged even when there is no history of visual disturbances. We hoped to correlate the patients' visual field defects with their VEP latencies, but we were unable to find any correlation in our patients between VEP latencies and either the location or the severity of the visual field defects. Frisén and Hoyt [11] were able to correlate the patchy, arcuate scotomata of MS patients with slit-like defects due to subclinical axon loss in the retinal nerve fiber layer. Feinsod and Hoyt [9], comparing early flash-evoked visual responses with the defects in the retinal nerve fiber layer of a group of patients with MS, hypothesized that axon loss was reflected in VEP amplitude reductions, whereas demyelination was reflected in increased latency. However, with the VEP method we used, it is not possible to obtain accurate measurements of amplitude [21, 24]. Moreover, with the pattern size we used, almost the whole potential is generated by a central retinal area about 10°–12° in radius [1, 14, 25], which is the area where the fewest visual field defects are found. For these reasons, and possibly also because visual field examinations and VEPs actually test different functions of the visual system, the lack of correlation between the results we obtained by these two methods is not surprising. This very lack of correlation suggests the need for complementary use of both methods together in diagnosing MS. As with the VEP abnormalities, so also with the visual field defects described above: they are characteristic of the disease but not specific to it. Therefore careful interpretation, taking all available clinical information into account, is mandatory. In a clinical routine, a VEP examination should still be done first, since the recording process is simple, takes less time, and depends less on the patient's cooperation. A complete visual field examination of both eyes with the octopus programs used in this study takes 50–60 min. However, if VEPs are equivocal or even normal and there is still a clinical reason to suspect MS, then octopus perimetry may be helpful—particularly in view of the possibility that VEPs in MS patients may in time normalize [1, 13, 19], as in our cases 1 and 3.

Acknowledgment. The authors are grateful to Professors F. Fankhauser and H. Bébié for their helpful advice. We also wish to acknowledge the editorial assistance of Mr. Don Shevlin.

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Received November 24, 1981