Variation of visual evoked potential delay to stimulation of central, nasal, and temporal regions of the macula in optic neuritis

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Abstract

Objectives—To compare the degree of visual evoked potential (VEP) delay to stimulation of central, nasal, and temporal regions of the macula in optic neuritis, to determine whether the differential involvement of parvocellular and magnocellular fibre types suggested by other studies is governed by retinotopic factors.

Methods—VEPs were recorded to reversal of 40° checks in the central (4° radius) and the left and right surrounding regions of the visual field (as far as 10° vertical and 14° horizontal) in 30 patients recently recovered from the acute stage of optic neuritis, and in 17 age matched controls.

Results—In the control group, VEP latencies were similar to stimulation of the central and temporal regions of the macula, marginally shorter from the nasal region. In the patients with optic neuritis, VEPs were significantly more delayed from the central region, on average by about twice as much as from the nasal and temporal regions. Delays seen in some of the VEPs from the patients' fellow eyes tended to be more uniformly distributed.

Conclusions—Although the central region of the macula is where the density of parvocellular innervation is greatest, there is no reason to suppose that the VEPs to stimulation of the nasal and temporal regions (almost all P100 activity arising from within the central 10°) are mediated by fibres of another type. Consequently it is suggested that the central fibres were most affected by demyelination, not on account of their belonging to the parvocellular type but because of their particular situation in the optic nerve. Centrally located fibres may experience greater exposure to factors causing demyelination, or fibres located closer to the edge of the plaque may undergo more effective remyelination in the first few weeks after the acute episode.

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Keywords: optic neuritis; multiple sclerosis; visual evoked potential; demyelination

The natural history and pathophysiology of optic neuritis have been extensively studied using electrophysiological,^{1–7} psychophysical,^{8–22} and imaging techniques.^{23–24} This has greatly improved our understanding of the factors contributing to the acute visual impairment, which

usually recovers over a period of a few weeks, coincident with the resolution of inflammation and blood-brain barrier leakage within the optic nerve.²⁵ The period of inflammation also coincides with that during which optic nerve fibres become demyelinated, resulting in latency prolongation of the visual evoked potential (VEP). Although VEP latencies may remain abnormal for many years, there is a tendency for them to shorten over a period of 2 years or more.^{6–26} This, we have suggested, may represent an ongoing process of remyelination which, although relatively insignificant in its immediate functional consequences, might serve to protect demyelinated fibres from degeneration.

The visual pathways of primates are anatomically and physiologically differentiated into parvocellular and magnocellular subsystems. The first is mainly concerned with form and colour perception, comprising relatively small retinal ganglion cells and thinner optic nerve axons which (in the macaque monkey) account for about 80% of the projection to the lateral geniculate nucleus (LGN).²⁷ The magnocellular pathway on the other hand is particularly concerned with motion perception and arises from relatively large retinal ganglion cells which project via thicker axons to the magnocellular layers of the LGN. The two subsystems also involve different layers of the visual cortex V1.^{28–30} An issue which remains controversial is whether optic nerve fibres of the two types are differentially affected by optic neuritis. From the findings of contrast sensitivity studies and VEPs to chromatic stimuli, some have suggested predominant involvement of parvocellular fibres.^{3–7 10 12 13 20} Others, however, have noted a particular defect of visual motion sensitivity which suggests involvement of magnocellular fibres.^{15 16 19 21}

In the two decades or more during which VEPs have been widely used as a diagnostic tool for optic neuritis, many technical variations have been explored. The methods which have become generally adopted have in common the use of high contrast chequer boards or gratings to stimulate the macula. This, of course, is the region which is most extensively represented in the visual cortex, and it is generally true to say that little or no cortically generated VEP activity can be recorded to stimuli outside 10° or possibly 15° eccentricity.³¹ Even within this area, it is acknowledged that the most dependable evidence of conduction delay, characteristic of optic neuritis and presumed to reflect the extent of optic nerve demyelination, is obtained with centrally fix-

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Table 1 Clinical findings at the time of testing

Patient	Age	Sex	VA	RAPD	Disc	Colour vision
1	51	F	6/9	N/A	N/A	N/A
2	35	F	6/5	—	—	N/A
3	27	M	6/6	—	Pale	N/A
4	35	M	6/5	—	—	N/A
5	24	M	6/5	—	Pale	10/10
6	31	F	6/6	+	Pale	10/10
7	37	M	6/5	—	Pale	10/10
8	27	F	6/9	—	Pale	N/A
9	25	M	6/12	+	Pale	9/10
10	30	F	6/6	—	—	10/10
11	32	F	6/5	N/A	N/A	N/A
12	34	M	6/9	+	Pale	10/10
13	44	F	6/5	—	—	6/10
14	32	M	6/9	+	Pale	1/10
15	38	F	6/6	+	—	6/10
16	31	M	6/4	—	—	4/10
17	32	M	6/6	—	Pale	10/10
18	39	F	6/5	+	Pale	10/10
19	37	M	6/6	+	Pale	9/10
20	29	F	6/5	+	Pale	6/10
21	40	F	6/6	—	Pale	6/10
22	30	F	6/5	+	—	10/10
23	30	F	6/6	+	Pale	6/10
24	36	M	6/5	—	Pale	10/10
25	32	M	6/9	+	—	5/10
26	37	F	6/9	—	—	6/10
27	29	M	6/6	+	Pale	10/10
28	34	F	6/5	—	Pale	7/10
29	30	F	6/4	+	Pale	10/10
30	28	M	6/5	+	Pale	2/10

VA=Visual acuity; RAPD=relative afferent pupillary defect; N/A=not assessed.

ated stimuli the total subtense of which is usually no more than 10° . One reason for this is that the P100 component, by which the VEP latency is usually defined, can sometimes be confused with a later, P135 peak when relatively large visual field areas are stimulated. Another possibility, however, is that the P100 delay may actually be greater for foveal stimuli. One of the findings which led to the adoption of reversing chequer boards was that VEPs to diffuse flashes, more effective for stimulating the peripheral retina, tend to be less delayed than VEPs to high contrast checks which are optimal for foveal receptors.¹ Other studies³ have shown a relation between the delay of the “steady state” VEP and the spatial frequency of the sine wave gratings used, which might be explained by the fact that high spatial frequencies preferentially stimulate central retinal receptors.

In the present study VEPs were recorded to stimulation of central, nasal, and temporal regions of the macula in a group of patients recently recovered from the acute stage of optic neuritis. It was reasoned that by use of a uniform, high contrast chequerboard, functionally similar ganglion cells would be activated, predominantly of the parvocellular type. Previous experience³¹ suggested that the latencies of the responses from the three areas are normally similar, and that the scalp distribution of the P100 is in each case consistent with origin in the primary sensory cortex, V1. By this method, therefore, it was proposed to examine the retinotopic variation of conduction delay in optic neuritis, to see whether this might explain the differential involvement of parvocellular and magnocellular fibres suggested by other studies.

Patients and methods

Thirty patients presenting to the National Hospital for Neurology and Neurosurgery or Moorfields Eye Hospital were tested between 75 and 170 days after the onset of symptoms (mean 94 (SD 16) days, table 1). There were 17 men and 13 women aged 25–51 years (mean 33.0 (SD 5.7) years). The right eye was affected in 10 patients and the left eye in 20. The diagnosis of optic neuritis was made on clinical grounds; all patients had experienced a rapid visual acuity reduction of more than two lines on the Snellen chart, usually accompanied by a colour vision defect, relative afferent pupillary defect, and/or retro-orbital pain. All had made a good functional recovery at the time of testing (visual acuity of 6/12 or better, most 6/6 or better) although 13/24 had a persistent colour vision deficit. Two patients had a history of optic neuritis in the affected eye and seven in the fellow eye. Five patients had no evidence of neurological disease outside the visual pathway whereas 25 had symptoms, signs, or MRI evidence of disseminated disease, consistent with the early stages of multiple sclerosis (in three patients MRI was not performed). The control group initially comprised 18 volunteers with no significant history of neurological or ocular disease, 12 men and six women aged 17–44 years (mean 30.6 (SD 7.6) years).

A reversing chequerboard pattern was presented on a computer monitor screen in a dark room with the subject sitting in a reclining chair at a distance of 88 cm. The screen subtended 28° horizontally by 20° vertically, and was divided into three areas: a circular region of 4° radius centred on the fixation point (“central region”) and the remainder of the screen divided into left and right halves along

Figure 1 Stimulus screen areas used to stimulate the central, nasal, and temporal regions of the macula, and recording montage. Electrodes 1–5 were in a lateral chain, separation 5 cm. Electrode 3 was 5 cm above theinion and electrode 6 was 2.5 cm above theinion. The reference electrode was at Fz.

Table 2 Control P100 latency and amplitude values in 17 normal subjects

Macular region	Left eye			Right eye		
	Central	Nasal	Temporal	Central	Nasal	Temporal
Latency (ms):						
Mean	95.8	92.4	93.3	95.4	90.5	94.4
SD	4.9	4.1	4.4	4.4	4.1	3.1
Amplitude (μ V):						
Mean	6.9	3.9	3.4	7.0	3.6	4.0
SD	2.7	2.0	1.6	2.9	1.7	2.1

the vertical meridian, termed “nasal” or “temporal” according to which region of the macula was stimulated (fig 1).³¹ The checks in each region reversed in rotation at intervals of 303 ms, and the responses were averaged concurrently in separate stores. The individual checks each subtended 40', their luminances being 2 cd/m² for the dark and 88 cd/m² for the light checks. The frame rate of the monitor was 100 Hz and the raster scan was vertical, taking 10 ms to refresh the screen moving from left to right. As the reversal of the checks and the beginning of the recording epoch were both time locked to the frame rate, check reversal on the far left of the screen consistently preceded that on the far right by 10 ms, hence it was necessary to apply a correction factor to the VEP latencies. It was calculated from the data of Blumhardt *et al*³² that there would be little or no contribution to the P100 from regions of greater eccentricity than 10°, and that for the nasal and temporal regions (excluding the central 4°) most P100 activity would arise from between 4° and 7°. VEP latencies were therefore measured from the time of check

reversal at the centre of the screen for the central region and 5.5° to the left or right of centre for the nasal and temporal regions. This involved a correction factor of +2 ms for the left and -2 ms for the right visual field areas, compared with the central region.

Six recording electrodes were attached to the scalp with paste, their contact impedances reduced to less than 5 kOhm by skin preparation. Five electrodes were located in a lateral chain across the occiput, 5 and 10 cm to either side of a midline electrode 5 cm above the inion (fig 1). The sixth electrode was on the midline, 2.5 cm above the inion, and the reference electrode was at Fz. The EEG was amplified with corner frequencies of 0.16 Hz and 1 kHz, and digitised at 2 kHz for 250 ms after each stimulus. Responses to 100 stimuli were averaged, three repetitions were made for the left and right eyes alternately and the repetitions were subsequently averaged together if judged to be satisfactorily consistent. For the central macular region the P100 was usually maximal at the electrode 2.5 cm above the inion; hence in each case its amplitude and latency were measured there, its amplitude from the preceding N75 peak. When two positive peaks were present between the latencies of 80 and 150 ms, if the later one was larger at lateral electrodes than at the midline it was judged to be a P135³² and the amplitude and latency of P100 were measured from the earlier peak. When the P100 itself seemed to be bifid, such that no single latency value could be considered definitive, this patient was excluded

Figure 2 Visual evoked potentials of the left eye, mean waveforms of the control group and the patients with left optic neuritis, electrodes numbered as in fig 1. Asterisks mark the measured P100 peaks, at the midline electrode 2.5 cm above the inion for the central region and in the derived 5 cm ipsilateral-contralateral waveforms for the nasal and temporal regions.

Figure 3 Visual evoked potentials of the right eye, mean waveforms of the control group and the patients with left optic neuritis.

from parametric analysis. For the nasal and temporal VEPs, the P100 and associated N75 and N145 peaks were usually maximal at the electrode 5 cm ipsilateral to the stimulated field area, whereas a complex of similar latency and morphology but opposite polarity (P75, N105, P135) was present on the contralateral side.³³ To maximise the recorded amplitude, the waveform at the electrode 5 cm lateral to the midline, contralateral to the stimulated field, was digitally subtracted from the 5 cm ipsilateral waveform. In the resultant derivation the P100 was always distinguishable from the P135, which appeared with negative polarity, although in some patients the P100 was again judged to be bifid and their data excluded from parametric analysis.

On the same day as the VEP study, visual fields were assessed by means of a Humphrey automatic visual field analyzer using the manufacturer's central 30–2 threshold procedure (Automatic field analyzer, Allergan 1992). Wide angle lenses were used to correct refractive errors where necessary. Analysis was made of two concentric zones of the visual field: the first consisted of four targets within 5° of the fixation point, the threshold values of which

were averaged together; the second zone comprised the surrounding visual field area between 5° and 10° eccentricity, divided into nasal and temporal areas (four targets each) according to which side of the macula was concerned.

The Shapiro-Wilks test was used to ensure that latency values conformed to a gaussian distribution. Latency values were compared between stimulated regions using ANOVA and paired *t* tests. Visual field data were analyzed using the Wilcoxon test.

Results

CONTROL GROUP

The P100 was present with a single main peak to stimulation of all visual field regions in 17/18 control subjects (one subject had ill defined potentials to central stimulation and was excluded from analysis). The P100 amplitude measured on average approximately 7 µV for the central region and 3.3–4.0 µV for the nasal and temporal regions (table 2, figs 2 and 3). Latencies were on average 95–96 ms for the central, 93–95 ms for the temporal, and 90–93 ms for the nasal macula. Analysis of variance (ANOVA) showed a significant main effect of macular region on both amplitude (left eye $F(2,32)=30.795$, $p<0.0001$; right eye $F(2,32)=28.396$, $p<0.0001$), and latency (left eye $F(2,32)=5.146$, $p=0.012$; right eye $F(2,32)=15.371$, $p<0.0001$). In Bonferroni corrected paired *t* tests the responses of the central region were significantly larger than the other regions ($p<0.0001$) and longer in latency than the nasal region ($p<0.01$). The temporal

Table 3 VEP classification of 30 patients

Macular region	Affected eye			Fellow eye		
	Central	Nasal	Temporal	Central	Nasal	Temporal
Normal	1	7	8	20	19	21
Delayed	27	20	17	9	6	5
Bifid	1	3	3	1	3	4
Absent	1	0	2	0	2	0

Table 4 P100 latency values of the affected eye (ms, excluding bifid and absent waveforms) in 15 patients with left optic neuritis (ON) and eight patients with right ON

	Macular region					
	Left ON			Right ON		
	Central	Nasal	Temporal	Central	Nasal	Temporal
Mean	127.8	108.0	111.3	124.5	116.7	109.6
SD	11.5	11.3	13.4	12.6	14.9	9.4
Difference from control group:						
Mean	32.0	15.6	18.0	29.1	26.2	15.2

response was longer in latency than the nasal response for the right eye only ($p < 0.001$). In interocular comparison, the VEPs to stimulation of the temporal macula were significantly

longer in latency than those from the nasal macula of the other eye (right regions $p < 0.001$, left regions $p < 0.05$) whereas temporal/temporal, nasal/nasal, and central/central comparisons were all non-significant; VEP latencies were therefore clearly shortest for the nasal macula and not significantly different for the central and temporal regions of either eye. Normal latency ranges (mean ± 2.5 SD) were computed separately for the central, nasal, and temporal responses. Upper limits of normality were defined as the longer of the values obtained from the two eyes: central region 108 ms, temporal region 105 ms, nasal region 103 ms.

Figure 4 Visual evoked potentials of the left eye in patient 10 and of the left and right eyes in patient 22, both with left optic neuritis. The responses of the previously affected right eye of patient 22 are prolonged in latency, but the difference between the three macular regions is less marked than for the recently affected left eye, or for the left eye of patient 10 in whom the VEP latency from the nasal macula is within normal limits.

Figure 5 Mean (SD) VEP latencies to stimulation of three macular regions of the affected (filled) and the fellow (unfilled) eyes in 15 patients with no history or evidence of optic neuritis in the fellow eye.

PATIENTS WITH OPTIC NEURITIS

Visual acuity on the Snellen chart was converted to an ordinal scale in which 6/6 corresponded to 10, 6/9 to 9 etc. The mean acuity in the patient group was 10.2 (SD 1.0) compared with 10.7 (SD 1.2) for the controls, indicating only marginal residual visual acuity impairment. A relative afferent pupillary defect was present in 14/28 patients who had ocular examination, optic disc pallor was present in 19/28 and colour vision impairment (one or more mistakes on the standard pseudoisochromatic plates part II) in 13/24. On visual field analysis, two patients (Nos 9 and 14) had central scotomata in the affected eye and one (No 28) had homonymous scotomata in the inferior left hemifield. The most common visual field defects, seen in 11 affected eyes and eight fellow eyes, were small scotomata outside 20° eccentricity, hence of no direct relevance to the VEP findings.

When compared with the limits of the control group, VEP latencies were abnormally prolonged in the affected eye of 27/30 cases (90%) for the central, 20/30 (67%) for the nasal, and 17/30 (57%) for the temporal regions (table 3). In χ^2 tests, the incidence of latency prolongation was significantly greater for the central compared with the temporal region ($p < 0.01$). In the fellow eye the corresponding values were 9/30 (central), 6/30 (nasal), and 5/30 (temporal), the differences being non-significant. Including those with absent or bifid P100, the overall incidence of abnormality in the affected eye was 97% (central), 77% (nasal), and 73% (temporal); corresponding values for the fellow eye were naturally lower, and also more uniform (33%, 37%, and 30% respectively).

Seven patients were excluded from parametric analysis on account of absent or bifid responses to stimulation of at least one region

Table 5 Mean (SD) of P100 latencies (ms) from the affected and fellow eyes in 15 patients without clinical or VEP evidence of fellow eye involvement

	Affected eye	Fellow eye	Difference
Central macula	126.8 (10.5)	98.2 (5.1)	28.6 (11.0)
Nasal macula	110.8 (13.1)	93.2 (5.2)	17.6 (14.1)
Temporal macula	106.6 (8.7)	95.6 (6.2)	11.0 (8.2)
Central v nasal			$p < 0.05$
Central v temporal			$p < 0.01$
Nasal v temporal			NS

of either eye. This included the two patients with central scotomata in the affected eye, one of whom (No 14) had no measurable P100 from the central or the temporal region, the other (No 9) a bifid P100 from the temporal region. In the other five patients (Nos 3, 6, 16, 23, 27) there were no suggestive features in the ocular or visual field examination which correlated with absence or bifidity of the P100.

In the remaining 23 patients, responses of the affected eye were parametrically compared with the control data for the corresponding eye (table 4). The P100 from the central region was delayed on average by 32.0 ms (left optic neuritis) or 29.1 ms (right optic neuritis), the P100 from the nasal region by 15.6 or 26.2 ms, and the temporal region by 18.0 or 15.2 ms, all intergroup differences being highly ($p < 0.001$) significant. Corresponding values for the fellow eye were naturally lower and also more uniform; considering only those patients whose fellow eye VEPs were above the upper limit of normal latency for one or more regions, and combining the data from left and right eyes, the mean delay was 19.4 ms for the central, 18.3 ms for the nasal, and 13.1 ms for the temporal maculae. Group mean VEP waveforms of the control subjects and the 20 patients with left optic neuritis are illustrated for the left eyes in fig 2 and the right eyes in fig 3. Despite the smoothing caused by the scatter of latency values, the tendency for VEPs from the central region to be more delayed than the temporal or nasal VEPs in the patient group is clear. The same tendency is apparent in the example patients (fig 4), one of whom illustrates the more uniform latency values obtained from the fellow eye VEPs which were also abnormally delayed in this patient.

A paired comparison was made between the affected and fellow eye VEPs in 15 patients, excluding all those with absent or bifid responses and those with evidence (clinical history or VEP delay) of previous optic neuritis in the fellow eye (table 5, fig 5). The central VEPs were delayed on average by 28.6 ms, the nasal by 17.6 ms, and the temporal by 11.0 ms. In ANOVA the effect of visual field region on the affected fellow eye latency difference was significant ($F(2,28) = 9.504$, $p < 0.001$), and Bonferroni corrected t tests confirmed that the central response delay was significantly greater than the temporal ($p < 0.01$) or nasal ($p < 0.05$) responses. The difference between nasal and temporal regions was not significant. Concentric zone analysis of the visual field data was performed in the same 15 patients (table 6). The mean difference in thresholds was largest

Table 6 Visual field sensitivity in 15 patients without clinical or VEP evidence of fellow eye involvement (concentric analysis of central 5° and temporal and nasal 5–10°)

Macular region	Central	Nasal	Temporal
Affected eye:			
Mean	29.2	27.6	28.9
SD	2.9	4.5	3.3
Fellow eye:			
Mean	31.0	29.7	29.7
SD	1.9	1.2	1.5
Wilcoxon test	$p < 0.01$	NS	NS

for the nasal macula (about 7%) and smallest for the temporal (about 3%), but the interocular difference was significant only for the central region (about 6%, $p < 0.01$, Wilcoxon test).

Discussion

A uniform, high contrast chequerboard was used to stimulate separate regions of the macula in normal subjects and in patients who had recently recovered from the acute stage of optic neuritis. Although the central macula contains a higher proportion of smaller retinal ganglion cells the axons of which conduct at slower velocities,^{34–38} this was not apparent comparing VEP latencies from the central and temporal regions, suggesting that the stimuli tended to activate receptors of a similar type within the central 10° (vertical) to 14° (horizontal) of the visual field. The slightly shorter latencies of the VEPs from the nasal region might be explained by anatomical factors, as the nasal and temporal axons respectively take direct and curvilinear courses to the optic disc.³⁹ The scalp distribution of the temporal and nasal responses, the P100 being recorded over the side of the occiput ipsilateral to the stimulated field while a complex of inverse polarity was recorded on the contralateral side, was consistent with origin in the primary visual cortex (V1) on the mesial surface of the hemisphere. The distribution of the central response, maximal on the midline adjacent to the occipital pole, was also consistent with an origin in V1. It was therefore concluded that the three responses were mediated by functionally similar receptor and fibre types, probably representing the parvocellular projection to V1. The larger amplitude of the central responses, despite the smaller area of retina stimulated, is consistent with the greater density of retinal ganglion cells in the foveal region and the consequently greater cortical “amplification factor”. We were unable to confirm the amplitude asymmetry between left and right hemispheric responses reported by others,^{40–41} using conventional hemifield stimuli.

In the patient group the incidence of VEP abnormalities in the recently affected eyes (combining latency prolongation, absence, and bifidity) tended to be greater for the central compared with the nasal or temporal macular regions. The incidence of prolonged latencies was significantly greater for the central compared with the temporal region. Excluding all patients with clinical or electrophysiological evidence of optic neuritis in the fellow eye, and comparing the affected eye with the fellow, the mean VEP delay to stimulation of the central region was significantly greater than that from the nasal or temporal regions, on average by a factor of 2. The visual field data for the same subgroup of patients showed a decrease in sensitivity which was significant only for targets within the central 5° radius of the affected eye, although the magnitude of the decrease was similar for the surrounding nasal macula.

In the acute stage of optic neuritis the visual deficit often consists of a dense central scotoma

with annular preservation of peripheral vision, or a relative scotoma causing reduced visual acuity and impaired colour vision. The use of kinetic perimetry or conventional automated visual field testing accounts for differing descriptions of the hallmark scotoma. In the first case the characteristic defect is a central scotoma, whereas in the second a wide variety of field defects has been reported.^{17–18–22} The use of stimuli different from those utilised in conventional automated perimetry shows visual field depression with a slight central preponderance.^{14–20}

Therefore, although there was little evidence for preferential loss of central fibres in visual field testing, the VEP abnormalities unequivocally supported the previously gained impression of a greater degree of conduction delay from the central region of the macula. Although temporal dispersion in the affected axons might contribute to a reduction of VEP amplitude, it seems reasonable to suppose that the prolonged P100 latencies reflect a more extensive loss of myelin from axons deriving from the central region. As the stimulus characteristics (subtense, brightness, and contrast of the checks) were identical in the three visual field areas, and the evidence of the control group suggested that all three responses were probably mediated by fibres of similar conduction velocity projecting to V1, it seems that the greater delay of the VEPs to central stimulation cannot be due to the distinction itself between parvocellular and magnocellular fibres, but may rather be a consequence of the particular situation of central fibres in the optic nerve. In addition to the gradation of fibre diameter, anatomical studies show that the centrally originating fibres are more densely packed than those projecting from other retinal regions.^{34–39–42} Although the anatomical identity of the “papillomacular bundle” is ill defined,³⁸ it is possible that the greater vulnerability of these fibres to demyelination and other forms of pathology such as that associated with toxic optic neuropathy,³⁸ may be due to their greater density or to other factors associated with their glial cell or vascular environment.

Alternatively, it may be relevant to consider the influence of early remyelination. The pathophysiological processes underlying optic neuritis are inflammation, increased permeability of the blood-nerve barrier, oedema, and demyelination, causing acute blockage of conduction in a proportion of optic nerve axons. The resolution of inflammation within a few weeks leads to partial or complete restoration of conduction and a consequent improvement of vision.^{25–43–44} At this time the demyelination process is also likely to have ceased.⁴⁵ Remyelination by oligodendrocytes starts at the edges of plaques within a month of the onset of symptoms,⁴⁶ and is likely to have been active in the patients of the present study who were recorded as close as possible to 3 months. The lesser degree of VEP delay to more peripheral stimulation might therefore reflect a more complete process of remyelination of fibres situated around the edges of the plaque. The finding of a more uniform VEP delay

across the three macular regions of the fellow eye, presumably tested at longer intervals after the (mostly asymptomatic or undocumented) occurrence of demyelination, could reflect an ongoing process of remyelination²⁶ which eventually embraces the centrally located fibres also. Further studies might examine this hypothesis by comparing the responses to stimulation of different macular regions during the acute phase, although this is likely to be hampered by the poorer signal to noise ratio of VEPs in patients whose visual acuity is significantly impaired.

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