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Multiple sclerosis: abnormalities in luminance, chromatic, and temporal function at multiple retinal sites

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Abstract. Visual function was assessed in a group of patients with multiple sclerosis (MS) and in a group of matched normal controls. In these patients the disease was relatively mild. For each subject, measures of a range of psychophysical visual functions were carried out at multiple sites in each eye. Previous reports have only included some of these functions. Here, luminance threshold, two-flash resolution, perceptual latency, luminance critical flicker frequency (CFF), and chromatic CFF were all measured. Variabilities of these functions and correlation between chromatic and luminance CFFs were also evaluated. For both the MS group and the normal control group, the correlations between pairs of visual parameters were not overall significantly greater than chance level. The MS group did give a significantly reduced value relative to the normal group for luminance CFF and for the gradient of the plot of chromatic CFF against luminance CFF. This group was then subdivided according to history of visual involvement. The subgroup with previous visual symptoms had significant impairment for luminance threshold, variability of luminance threshold, luminance CFF, variability of two-flash resolution, and for the gradient of the plot of chromatic CFF against luminance CFF. The subgroup without previous visual symptoms showed no significant impairment for any individual parameter, although the gradient of the plot of chromatic CFF against luminance CFF was lower than normal.

Introduction

Multiple sclerosis (MS) frequently gives rise to abnormalities in a variety of visual functions (Perkin and Rose, 1979; Regan, 1981). Luminance threshold and variability of luminance threshold have been shown to be abnormal in certain patients after retrobulbar neuritis (Harms, 1976), and in patients with MS (Patterson et al., 1980). There is often an impairment of temporal visual function, shown by increased perceptual latencies (Heron et al., 1974; Regan et al., 1976), increased interval for the resolution of a double light flash (Galvin et al., 1976a, b, 1977), and decreased critical flicker frequencies (CFFs) for luminance stimuli (Titcombe and Willison, 1961; Daley et al., 1979; Mason et al., 1982), and for chromatic stimuli (Mason et al., 1982). Although measures of the temporal properties of vision are dependent

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indirectly on luminance threshold (see Discussion), the abnormalities found for such measures in MS patients are not necessarily a simple consequence of raised luminance thresholds (Patterson et al., 1981).

The various studies of visual function referred to above were made on separate and heterogeneous groups of patients. In the present investigation, all the above visual functions were measured at multiple sites in each eye in a single group of patients with 'relatively mild' MS. Of the seven patients tested, five had probable, one possible, and one definite MS. Luminance threshold, perceptual latency, two-flash resolution, chromatic CFF, and luminance CFF were determined and the variabilities for these measurements were also computed. Measurements were made at four parafoveal sites in one eye of each patient. In all, twenty-eight sites were thus tested. For comparison, normal subjects were matched to the patients and tested in the same way. For analysis purposes three patient subgroups were considered: the whole group; those with a history of optic neuropathy; and those without such a history.

Subjects and methods

Subjects

Seven patients with MS took part in the study. All were female. Patients were classified according to the criteria of McDonald and Halliday (1977). Clinical details are given in Table 1. Only two patients had suffered more than one relapse and only one patient (No. 3, Table 1) had active progressive demyelination. Three patients had clinical evidence of past optic neuritis (ON). None of the patients had advanced disease, and as a whole they were representative of relatively benign MS (McAlpine et al., 1965). For purposes of analysis the whole group of patients were considered first as an undifferentiated MS group, and second as two subgroups: subgroup A comprised the first four patients (Table 1) with no previous visual symptoms and with a mean duration (± SEM) of disease of 2.1 (± 1.0) years; subgroup B comprised the remaining three patients (Table 1) with previous episodes of ON and a mean duration of disease of 6.0 (± 2.1) years. Seven healthy subjects, matched individually for age and sex with the patient group, acted as normal controls. All subjects were unaware of the purpose of the experiment and were unpractised in psychophysical procedures. Informed consent was obtained from each patient and normal subject. None had visual acuity worse than Snellen 6/9 and Near Vision N12. All had normal colour vision as classified with The City University Colour Vision Test (TCU Test) (Birch, 1979). None had nystagmus.

Stimuli and apparatus

A modified visual perimeter provided the stimuli. A circular background field which appeared white, colour temperature 3060 K and luminance 160 cd.m^{-2},

Table 1. Summary of clinical data for patients

Patient	Age	ON	MS	Duration of disease (years)	No. attacks	Classification
1	28	—	Spinal	1	2	Early Probable
2	30	—	Spinal Brain Stem Cerebellar	5	3	Early Probable
3	47	—	Spinal	2	Progressive from onset	Progressive Probable
4	48	—	Spinal Cerebellar	0.5	3	Progressive Possible
5	34	+	Spinal Sensory	10 (ON)	2	Early Probable
6	37	+	Spinal	3 (ON)	2	Early Probable
7	42	+	Spinal	5 (ON + S)	2	Clinically Definite

and which subtended 20 deg of visual angle at the subject's eye, was present for all experiments.

Test stimuli were circular, 10-min-arc angular subtense, and were presented superimposed on the background field at one of four locations of eccentricity 2.5° and azimuth 45° to the horizontal. For perceptual latency measurements, stimuli were also presented at the centre of the background field.

Test stimuli were separately produced by two systems. For all measurements except those of CFF, two light-emitting diodes (LEDs) were used. These were both red (Monsanto MV5752) with peak emission wavelength 630 nm. Intensities and time courses of the LEDs were controlled by suitable electronics. One LED, used in perceptual latency measurements only, was positioned at the centre of the perimeter screen. The other LED, used in measurements of perceptual latency, luminance threshold, and two-flash resolution was positioned at one of the four eccentric locations (see above). Stimuli produced by the LEDs were of three different types: a single light pulse of 20-ms duration; a pair of 20-ms pulses presented to the same parafoveal site; and a pair of 20-ms pulses, one presented to the fovea and one to a parafoveal site. The flash intensty, and the onset delay of the pairs of flashes, were each controlled by the experimenter.

For measurements of CFF, a tungsten-halogen lamp was used to provide the test stimuli. Fibre-optic guides took light from this lamp to form two light channels. A gelatin filter controlled spectral output of each channel: in one channel a red long-pass filter gave maximum intensity, in situ, at 640 nm with half-height cut-on wavelength at 607 nm; in the other channel a green bandpass filter gave maximum intensity, in situ, at 540 nm with half-height full bandwidth of 62 nm. Intensity of light in each channel could be

varied independently by the experimenter with rotary neutral-density wedges. A rotating sector, controlled by suitable electronics, interrupted these channels to produce red- and green-flicker (square-wave) trains of the same frequency. The flicker trains were combined with a fibre-optic Y-guide, and made spatially uniform with a small glass diffusing plate. The flicker trains, of variable frequency and of duration 3 sec, could be presented either in antiphase or in phase. The antiphase condition gave alternating spatially coincident red and green lights, the intensities of which were adjusted at each site tested to equalize their luminances (see Procedure). This stimulus was used to measure chromatic CFF. The stimulus size used (10 min arc) although small was sufficient to involve the pathways subserving chromatic function (Foster, 1981). The in-phase condition of the flicker trains was used to measure luminance CFF, the intensities of the red and green lights being identical to those used for the chromatic flicker stimulus. Thus the two types of flicker stimulus were equated for time-averaged spectral content and time-averaged luminance.

In all experiments, subjects controlled the start of a stimulus presentation with a push-button box.

Procedure

Preliminary assessments of subjects' visual acuity and colour vision were carried out using printed charts and the TCU Test.

Measurements at a given retinal site were made in two sessions, each lasting approximately one hour. Measurements were made on one eye only of each subject. Thus for the four sites tested each subject attended eight sessions in all. The subject sat in a chair of adjustable height with a firm headrest, and monocularly viewed the perimeter screen, at a distance of 1.7 m, through an adjustable eyepiece. Spectacles were worn if appropriate, and the eye not under test was lightly occluded. An artificial pupil was not used. Fixation was aided by a central fixation target in the form of an annulus, of diameter 35 min of arc. For each patient and matched control, measurements were carried out in the same order at each site. The same general procedure was used to evaluate all of the specified visual functions, as follows. First, an approximate threshold (defined below) for the function was determined by a method of limits (Engen, 1971). Next, a method of constant stimuli (Engen, 1971) was applied. Thus, ten consecutive stimulus settings (equally spaced on the appropriate scale) were selected, centred about the approximate threshold, and this set of stimuli then presented to the subject, five times in all, according to a randomized-block design, which minimized order and carry-over effects. On any stimulus presentation, the experimenter cued the subject, who then fixated the centre of the fixation target and pressed the button which controlled stimulus onset. The subject indicated her response (force-choiced) after each presentation. After each set of ten presentations the subject rested for approximately 30 seconds. The particular functions measured were as follows.

Luminance threshold. The intensity of the single eccentric LED stimulus was varied in 0.1-log-unit steps. Subjects reported whether or not they saw the stimulus flash. Threshold was defined as the intensity of the flash which was seen on 50% of occasions.

Two-flash resolution. The intensity of the single eccentric LED stimulus was set at 3.68 log cd.m^{-2}. Onset delay was varied in 10-msec steps. Subjects reported whether they saw two flashes or one. Threshold was defined as the onset delay at which two flashes were seen on 50% of occasions.

Perceptual latency. Latency was determined for each of the four parafoveal sites relative to the fovea. Intensities of the LED stimuli were set at 4.10 log cd.m^{-2} for the central stimulus and 3.68 log cd.m^{-2} for the eccentric stimulus. Onset delay was varied in 20-msec steps, with positive values corresponding to the central flash preceding the eccentric flash. Subjects reported which flash appeared first. Threshold was defined as the onset delay at which the central flash was seen to precede the eccentric flash on 50% of occasions.

Critical flicker frequency. CFFs were determined with 3-sec-duration flicker trains of red and green lights, presented in phase to give luminance flicker or in antiphase to give chromatic flicker, as explained above. To minimize luminance differences between the red- and green-components of the chromatic CFF stimulus, heterochromatic flicker matches were first made by each subject at each site tested. (Details of methods are given by Mason et al., 1982.) The intensities of the red- and green-flicker trains were equated to 2.12 log cd.m^{-2} by the heterochromatic flicker matches. For both CFF measurements, flicker frequency was varied in 1-Hz steps. Subjects reported whether or not they saw flicker. Threshold was defined as the frequency at which flicker was seen on 50% of occasions.

Data analysis

Raw data were analyzed by computer-based probit analysis (Finney, 1952). This gave the 50% seeing point corresponding to stimulus threshold for the given visual function, and a standard deviation that may be interpreted as the variability of that threshold (Patterson et al., 1980). Thus, for each of the four sites tested in each subject, values could be obtained for ten parameters: a threshold and a variability for each of the five visual functions. (Occasionally for some sites in some subjects, measurements could not be made because of judgemental difficulties or excessive variability).

Further analysis was carried out on the parameters to establish any differences between the various patient and normal groups. First for each subject the interquadrant variation (the difference between the maximum and minimum values) was calculated for each parameter. Uncorrelated and correlated t-tests were performed on the interquadrant variations for levels of significance

of differences between each patient group and the normals for each parameter. Next correlation coefficients were calculated on the results from the four sites for each subject for each possible pair of parameters; a χ^2 test was performed to test the significance of the level of correlation for each subject and each group of subjects. These two analyses were to assess the presence or otherwise of 'islands of demyelination' (Regan et al., 1976) at which parameters might be similarly affected.

For each parameter, a mean and standard error were then calculated over all sites and eyes in each patient group and normal group. Significance levels of differences between groups were calculated using t-tests. The t-tests were one- or two-tailed as appropriate; thus, for perceptual latency a two-tailed t-test was used, and one-tailed t-tests for all other parameters. Additionally, for the flicker fusion data, least-squares regression lines were fitted for chromatic CFF plotted against luminance CFF, for each patient group and the normals, and correlation coefficients were calculated.

Results

There was found to be no significant difference between patient and normal groups for interquadrant variations. The χ^2 tests on the extent of correlation between pairs of parameters gave non-significant levels for all patients, and all normals but one, the latter associated with a significance level of $p < 0.05$.

Table 2 shows, for the patient and normal groups, means for each of the ten visual parameters after averaging over retinal sites and eyes. Standard errors are given in parentheses. Levels of significance for differences between groups are indicated by superscripts.

The undifferentiated MS group gave one result only which was significantly different from that of the normal group: a marginally reduced mean luminance CFF. More substantial differences became evident when the MS group was differentiated into the two subgroups with and without histories of visual disturbance.

Subgroup A, without previous visual involvement, gave no results indicating significant impairment in visual function. Variability of perceptual latency was, however, lower than that for the normal subjects. Subgroup B, with previous visual involvement, gave results indicating significant impairment for four of the parameters. Luminance threshold, variability of luminance threshold, variability of temporal resolution, and luminance CFF for subgroup B were all significantly worse than those for the normal group, and, additionally, were all significantly different from those for subgroup A (Table 2).

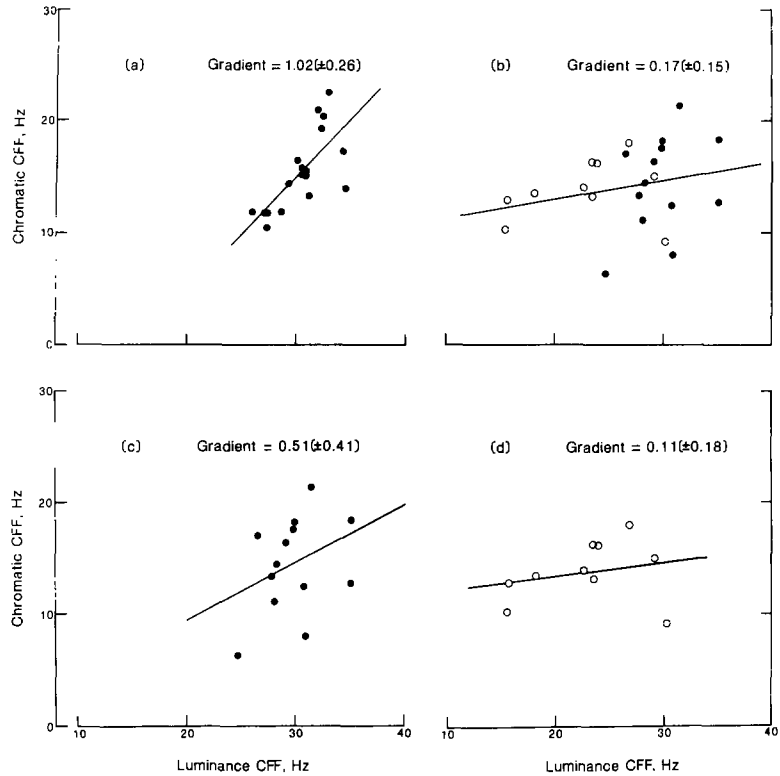
More detailed analysis of the data concerning CFFs is given in Figures 1(a)–(d); chromatic CFF is plotted against luminance CFF, in the manner of Foster et al. (1980) and Mason et al. (1982), for the normal group and each of the patient groups. The straight lines in the figures are least-squares

Table 2. Means (± SEM) of visual parameter values for normal group and patient subgroups. Levels of significance for differences between groups are indicated by the superscripts thus:

	MS Group v. Normals	Subgroup B v. Normals	Subgroup B v. Subgroup A
1	$p < 0.05$	–	–
2	–	$p > 0.05$	$p < 0.05$
3	–	$p < 0.05$	$p < 0.005$
4	–	$p < 0.005$	$p < 0.005$

Visual Parameter	Normal Group	MS Group	Subgroup A	Subgroup B
Luminance threshold, log cd.m^{-2}	1.716(± 0.044)	1.835(± 0.077)	1.655(± 0.078)	2.075(± 0.118)[4]
Luminance threshold variability, log cd.m^{-2}	0.167(± 0.020)	0.225(± 0.039)	0.130(± 0.013)	0.351(± 0.076)[4]
Two-flash resolution, msec	61.5(± 3.3)	56.7(± 3.3)	59.1(± 4.0)	53.0(± 5.8)
Two-flash resolution variability, msec	24.2(± 2.0)	26.6(± 2.3)	22.1(± 2.3)	33.9(± 3.8)[3]
Perceptual latency, msec	−36.4(± 5.8)	−26.0(± 4.1)	−33.2(± 4.3)	−16.4(± 6.8)[2]
Perceptual latency variability, msec	47.7(± 7.5)	34.2(± 5.0)	25.3(± 4.5)	46.0(± 9.1)[2]
Chromatic CFF, Hz	15.5(± 0.8)	14.1(± 0.8)	14.4(± 1.2)	13.9(± 0.9)
Chromatic CFF variability, Hz	2.8(± 0.4)	3.5(± 0.4)	3.8(± 0.6)	3.2(± 0.5)
Luminance CFF, IIz	28.8(± 0.7)	26.4(± 0.9)[1]	28.5(± 1.0)	23.5(± 1.4)[4]
Luminance CFF variability, Hz	1.7(± 0.1)	1.8(± 0.2)	1.9(± 0.3)	1.7(± 0.2)

regression lines. For the normal group (Figure 1(a)) the correlation coefficient is 0.71. For the patient groups (Figures 1(b)–(d)) the correlation coefficients are lower: 0.24, 0.35, and 0.22 for the undifferentiated MS group, subgroup A, and subgroup B, respectively. Nonetheless, there is an evident difference



Figures 1(a)–(d). Chromatic CFF plotted against luminance CFF. The straight lines are least-squares linear fits to the data. (a) shows the CFF plot for normal control subjects; (b) the CFF plot for all MS patients, open circles indicating eyes previously classified as abnormal; (c) the CFF plot for patients without a history of visual disturbance (subgroup A); (d) the CFF plot for patients with a history of visual disturbance (subgroup B).

between the gradient for the normal group and the gradient for each of the patient groups: 1.02 for the normal group versus 0.17, 0.51, and 0.11 for the undifferentiated MS group, subgroup A, and subgroup B, respectively. This difference reached significance for the undifferentiated MS group and for subgroup B (each $p < 0.005$).

Discussion

The results of the analyses of interquadrant variation and the extent of correlation between pairs of parameters for each subject suggest that there were no 'islands of demyelination' at which all or most parameters were similarly affected. This is in agreement with findings by Regan et al. (1976), Galvin et al. (1976a), and Patterson et al. (1981). There are differences, however, between patients and normals when the individual parameters are considered, as described below.

The results shown in Table 2 suggest that the demonstration of abnormalities in visual function depends critically on the apparent location of demyelination and duration of the disease. Subgroup A, without a history of visual disturbance and with a short mean duration of the disease, gave no significant loss in function in any of the visual parameters evaluated. For subgroup B, with a history of visual disturbance and with a longer mean duration of the disease, there were fundamental changes in performance. Possible reasons for the different results obtained from each subgroup are suggested in the Conclusions section. First, results for individual parameters are discussed.

Luminance threshold. Abnormally raised luminance thresholds have been shown in patients with previous retrobulbar neuritis (RBN) (Burde and Gallin, 1975; Harms, 1976) and, in the present study, luminance thresholds for patients with a history of visual disturbance, subgroup B, were significantly elevated. Patterson et al. (1980) found raised luminance thresholds at high background luminance levels (eg 3.0 log cd.m^{-2}) in MS patients who had suffered no previous visual symptoms in the eye tested, although all had subclinical optic neuropathy as evidenced by visual field defects. In the present study, the group of patients without a history of visual disturbance, subgroup A, did not show abnormal luminance thresholds, but the background luminance level (2.2 log cd.m^{-2}), used for all subjects, was lower than that at which Patterson et al. (1980) obtained abnormal thresholds. Additionally, the patients in the latter study (three clinically definite and two probable cases) had more advanced MS than those of the present subgroup A.

Abnormal variability in luminance threshold was noted by Harms (1976) in patients recovering from RBN. Patterson et al. (1980) quantified this variability in a selected group of patients. These authors showed that threshold variability in normal subjects remained substantially constant with increasing background luminance, whereas, for MS patients, variability increased rapidly. Patterson et al. (1980) suggested that either ephaptic transmission (Rasminsky, 1978), or intermittent conduction block (Rasminsky and Sears, 1972), could be the underlying cause of this variability. In the present study, threshold variability was significantly greater than normal for subgroup B with a history of visual disturbance. Subgroup A without a history of visual disturbance gave no abnormal threshold variability. These results are consistent with the fact that there was no evidence of subclinical optic neuropathy in the latter group, unlike that of Patterson et al. (1980) where, additionally, patients were selected specifically for the purpose of studying abnormally variable luminance thresholds.

Two-flash resolution. Two-flash resolution has been used to indicate abnormal temporal resolution in MS patients with previous RBN (Galvin et al., 1976a, b) and in MS patients without previous RBN (Galvin et al., 1977). The paradigm is in fact complicated, and factors such as total luminance, total

duration and spatial frequency of the stimuli have been shown to influence performance (Kietzman and Sutton, 1968; Boynton, 1972; Corfield et al., 1978). Abnormal two-flash resolution found previously in MS patients has, however, been shown not to depend simply on raised luminance thresholds (Patterson et al., 1981). In the present study, abnormal two-flash resolution was not apparent in our patients. It may be relevant in this context that Galvin et al. (1977) reported that patients with advanced definite MS and previous visual involvement showed significantly poorer foveal two-flash resolution than did patients with less advanced MS with or without visual involvement. The majority of the patients tested in the present study had relatively mild MS, and none had advanced MS.

Subgroup B, with a history of visual disturbance, did show a significant increase in the variability of two-flash resolution. This result may be analogous to the finding by Patterson et al. (1980) that significantly increased variability in luminance threshold occurred at all non-zero background luminance levels, yet a significant increase in luminance threshold itself occurred only at the highest background luminance level. Thus, for the present two-flash resolution data, it might be suggested that the background level although too low to elicit abnormal two-flash resolution was sufficient to elicit abnormal variability in that function.

Perceptual latency. Abnormalities in perceptual latency for an extrafoveal site of one eye relative to the fovea of the other have been shown in patients who had experienced a previous attack of RBN and in some patients with spinal MS (Heron et al., 1974; Regan et al., 1976; Galvin et al., 1976a). Moreover Regan et al. (1976) derived the perceptual delay between the fovea and a parafoveal site for single eyes of patients with spinal MS, and showed that there was often an abnormal delay between sites in the same eye. As Regan et al. (1976) pointed out, a delay between two sites in the same eye could occur either if demyelination was patchy or of a different degree at different sites. In the present study, perceptual latency was measured for each of the four parafoveal sites relative to the fovea of the same eye. Mean perceptual latency for the group of patients with a history of previous visual disturbance, subgroup B, was greater than the normal value. Although the difference did not reach significance ($p < 0.1$) delays introduced in fibres transmitting signals from the fovea may have been greater than those for fibres transmitting signals from the parafoveal sites in subgroup B. Subgroup A did not show an abnormal mean perceptual latency.

Latency variability was not worse than normal for any of the patient groups. For those patients without a history of visual disturbance, subgroup A, latency variability was, in fact, smaller than for both subgroup B and the normal group. The latter two groups did not differ significantly from each other. The reason for the low latency variability in subgroup A is not immediately apparent.

Critical flicker fusion. Patients with MS have been reported as having abnormally lowered CFFs both for luminance flicker (Titcombe and Willison, 1961; Daley et al., 1979; Mason et al., 1982) and for chromatic flicker (Mason et al., 1982). All these studies measured foveal CFF. The value of CFF has been shown to depend on the intensity of the stimuli (de Lange, 1958; Roufs, 1972) yet the abnormal results given by MS patients are not a simple consequence of abnormal luminance thresholds (Patterson et al., 1981). Mason et al. (1982) found that luminance CFF was reduced more than chromatic CFF in patients with MS, and that luminance CFF and chromatic CFF were highly correlated both in normal and in patient groups. The underlying linearity of the plot of chromatic CFF against luminance CFF was, however, characterized by a lower gradient for the MS group.

The present data, although obtained at parafoveal sites, are broadly in agreement with those described above. Luminance and chromatic CFFs for the undifferentiated MS group were reduced relative to the normal group (Table 2), but only for luminance CFF was this difference significant. When patient subgroups are considered, it is apparent that the reduction in luminance CFF for the undifferentiated MS group resulted from the large reduction in luminance CFF for subgroup B with previous visual involvement; subgroup A showed no significant difference from the normal group. This finding is consistent with the results of Titcombe and Willison (1961) and Mason et al. (1982, see their Figure 2a): those eyes that had previous visual involvement gave most reduction in luminance CFF. Daley et al. (1979), however, reported no differential effect of previous visual disturbance.

The change in interdependence of chromatic and luminance CFFs shown in Figure 1 for the normal and patient groups is of the same form as that reported by Mason et al. (1982). Thus in the present study the gradient for the normal group was 1.02 and for the undifferentiated patient group 0.17; Mason et al. (1982) obtained values of 1.06 and 0.56 respectively, the latter with a differently constituted group of patients. As expected, the two patient subgroups in the present study gave different gradients (0.51 for subgroup A, and 0.11 for subgroup B) although this difference did not reach significance.

The reduction for MS patients in the gradient of the regression line fitted to chromatic and luminance CFF data had been interpreted by Mason et al. (1982) in terms of the impairment of high temporal frequency function in affected nerve fibres. Luminance CFF, which in normal subjects is typically more than 10 Hz higher than chromatic CFF, is assumed to be preferentially reduced by such an impairment. This suggestion is supported by the data on mean values shown in Table 2.

There were no significant differences in CFF variabilities between any of the groups in this study, but, for each group, the variability of chromatic CFF was larger than that of luminance CFF.

Conclusions

As already noted, correlations over retinal sites of the means and variabilities of the visual functions investigated in the MS group in this study were not significantly different from chance level. In other words, the retinal distribution of abnormal values for one visual parameter did not, in general, coincide with the retinal distribution of abnormal values for another parameter.

MS subgroup B, comprising patients with a past history of visual disturbance, gave abnormal values for 40% of the parameters evaluated, and, on the whole, these results confirm and extend those of previous studies cited earlier. In particular, luminance threshold, variability of luminance threshold, variability of two-flash resolution, and luminance CFF were all affected. Subgroup A, comprising patients without a history of visual disturbance, gave essentially normal values for all parameters. The undifferentiated MS group gave one abnormal result, for luminance CFF; this, however, was attributable to the large reduction in luminance CFF for subgroup B.

It is possible that the relationship between the two types of CFF (expressed by the gradient of the regression line for the plot of chromatic CFF against luminance CFF, Figure 1) may be a more sensitive indicator of demyelination in the optic nerve and tract than any of the measures taken separately. Both the full MS group and subgroup B gave significantly reduced gradients. Additionally, the gradient for subgroup A was lower than that for the normal group, although this difference was not significant.

The absence of abnormal values for individual parameters for subgroup A need not be characteristic of patients without a history of visual disturbance. Duration of disease for the two subgroups in the present study was different (see Methods). In two of the four patients, symptoms had been present for less than one year. It is well known that the incidence of visual involvement increases as the disease progresses (Perkin and Rose, 1979). The apparent 'normality' in subgroup A may be an expression of the relatively mild, early, or benign nature of the disease in those patients. None had 'clinically definite' MS. It is clear, from comparison of the present results with those of our previous studies in which patients with more advanced MS participated, that the severity of the disease must be taken into account when assessing the significance of the presence or absence of abnormalities in visual function (see Galvin et al., 1977). Future studies of visual function, measured early in the disease and sequentially, are indicated for a clearer understanding of the natural history of demyelination, its temporal profile, and its pathophysiology.

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