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ABNORMALITIES IN LUMINANCE THRESHOLD, CHROMATIC AND LUMINANCE FLICKER FUSION, AND OTHER TEMPORAL MEASURES IN MULTIPLE SCLEROSIS

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Summary—1. A range of visual functions was assessed in a group of 27 patients with multiple sclerosis (MS) and in a group of matched normal controls. Luminance threshold, two-flash resolution, relative perceptual latency, luminance critical flicker frequency (CFF), and chromatic CFF were all measured foveally. Variabilities of these functions and correlations between their values were also evaluated.

2. Overall results for the MS group showed a statistically significant impairment relative to the control group. More detailed analysis was performed after division of the patient group according to history of visual involvement: subgroup A without previous optic neuropathy (ON) and subgroup B with previous ON.

3. Subgroup B showed significant impairment for luminance threshold, luminance CFF, chromatic CFF, and variability of luminance CFF. Subgroup A also had significant impairment for luminance threshold, luminance CFF, and chromatic CFF, although the effects were less pronounced than for subgroup B.

4. Significant correlations amongst parameters involved mainly luminance and chromatic CFF. Consistent with results of a previous study, it was found that the gradient of the plot of chromatic CFF against luminance CFF offered the clearest division of the subgroups.

Key words—Multiple sclerosis; optic neuropathy; chromatic and luminance CFF; luminance threshold.

INTRODUCTION

The visual system is specially vulnerable to damage in multiple sclerosis (MS) and a variety of abnormalities in visual function have been described. 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; Foster *et al.*, 1985). Evidence has been presented for selective losses in chromatic sensitivity (Fallowfield and Krauskopf, 1984; Mullen and Plant, 1986) and for nonselective losses (Foster *et al.*, 1985; for review, see Foster, 1986). There is often impairment of temporal visual function, shown by increased relative 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; Galvin *et al.*, 1977), 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), and altered temporal frequency response functions (Plant and Hess, 1985; for review, see Hess and Plant, 1986). Although measures of the temporal properties of vision are dependent indirectly on luminance threshold, the abnormalities found for such measures in MS patients cannot be attributed solely to 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, a range of visual functions was evaluated at single retinal sites in one eye each of 27 patients with clinically classified MS. Luminance threshold, relative perceptual latency, two-flash resolution, chromatic CFF, and luminance CFF were determined and the variabilities for these measurements and their interdependencies were also computed. Mea-

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surements were made at a single (eccentric) foveal site in one eye of each patient. For comparison, normal subjects were matched to the patients and tested in the same way. For the purposes of analysis, the patient group was subdivided into two subgroups: those with a history of optic neuropathy (ON); and those without such a history. Seven of the patients also participated in a separate study in which visual function was assessed at multiple retinal sites. These data have been reported in full elsewhere (Snelgar *et al.*, 1985).

SUBJECTS AND METHODS

Subjects

Twenty-seven patients participated in the study. All patients were investigated in the Neurology Unit at the North Staffordshire Royal Infirmary. Other neurological diseases were excluded, as necessary, by appropriate investigation which included computerized tomography, myelography, and cerebrospinal fluid estimation. Patients were classified according to the clinical criteria of McDonald and Halliday (1977). Electrophysiological tests and immunological data were not included as objective evidence for the presence of a demyelinating lesion in classifying patients. Normal controls, matched for age and sex to the patient group, had a similar range of visual acuities.

The patient group was divided into two subgroups. Subgroup A comprised those patients with MS without previous ON (Perkin and Rose, 1979). Subgroup B comprised those patients with previous ON, either as a consequence of an isolated lesion or in conjunction with other features of MS. The diagnosis was strictly clinical. The presence of temporal pallor of the optic disc did not of itself justify inclusion in this group. Clinical features of the two subgroups are given in Table 1. More patients in subgroup B had a longer duration of disease and more had clinically definite MS than in subgroup A. Therefore, although none of the patients in this study were severely disabled, subgroup B was representative of more advanced MS. The preponderance of clinically definite MS in subgroup B may be partly explained by the relative ease with which ON is recognized as a clinically separate lesion compared with the discrimination of brain stem from spinal cord lesions.

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, except one patient with N18. All had normal colour vision as classified with The City University Colour Vision Test (TCU Test) (Birch, 1979), except one patient who showed mixed protan–deutan errors. None had nystagmus at time of testing.

Stimuli and apparatus

A specialized visual perimeter provided the stimuli. A circular, uniform background field, which appeared white, colour temperature 3060 K and luminance 160 cd/m^2, 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 appeared superimposed on the background field at one of four possible locations with 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 and half-height full bandwidth 30 nm approximately. 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

Table 1. Summary of clinical data for patients

	Subgroup A (no previous ON)	Subgroup B (previous ON)
Total cases	13	14
Classification		
Isolated ON	0	3
Suspected MS	2	0
Progressive possible	1	0
Progressive probable	1	1
Early probable	6	2
Clinically definite	3	8
Duration, years		
0–2	9	4
3–5	1	3
6–10	1	2
11–15	1	4
16–20	1	1
Mean No. of attacks	2.2 ± 0.8	2.7 ± 2.0
Mean age, years	34.2 ± 8.0	38.6 ± 8.6
Sex	2M, 11F	5M, 9F

threshold, and two-flash resolution was positioned at the eccentric location (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 eccentric site; and a pair of 20-ms pulses, one presented to the central and one to the eccentric site. The flash intensity 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. Gelatin filters controlled the spectral outputs of the channels: 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 experimeter with 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 at the perimeter screen. The flicker trains, of variable frequency and of duration 3 s, 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 the stimulus presentation with a push-button box.

Procedure

Preliminary assessments of subjects' visual acuity and colour vision were carried out using printed charts and 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. The subject sat in a chair of adjustable height with a firm headrest, and viewed the perimeter screen monocularly, 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 arc. For each patient and matched control, measurements were carried out in the same order and at the same retinal site. The general procedure used to evaluate all of the specified visual functions was as follows. First, an approximate threshold (defined below) for the function was determined by a method of limits. Next, a method of constant stimuli 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 his or her response (forced-choice) after each presentation. After each set of ten presentations the subject rested for approximately 30 s. The functions were measured 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 that 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-ms 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.

Relative perceptual latency. Latency was determined for the eccentric site relative to the central site. 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-ms 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-s duration flicker trains of red and green lights, presented in phase to give luminance flicker or in antiphase to give chromatic flicker, as described above. To minimize luminance differences between the red and green components of the chromatic flicker stimulus, heterochromatic flicker matches were first made by each subject at the site tested. (Details of methods are given by Mason *et al.*, 1982.) The intensities of the red- and green-flicker trains were set at the values obtained from 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, 1964). This gave the 50% level 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 eye tested, values were obtained for ten parameters: a threshold and a variability for each of the five visual functions. Occasionally for some functions for some subjects, measurements could not be made because of judgemental difficulties or excessive variability. The number of such failures was less than 4%.

For each parameter, a mean and standard error were calculated over each patient group and corresponding normal control group. Levels of statistical significance for differences between matched groups were calculated using correlated t-tests. Other tests used are indicated in the text. All tests were one- or two-tailed as appropriate. Correlations between parameters were also examined over each patient group and corresponding normal control group.

RESULTS

Table 2 shows, for the patient and normal groups, means for each of the ten visual parameters. Standard errors are given in parentheses. Levels of statistical significance for differences between each patient group and its corresponding control group are indicated by superscripts.

Performance by the undifferentiated MS group (subgroups A and B combined) relative to the normal control group was, as anticipated, worse than chance level ($\chi^2_{10} = 47.04$, $P < 0.001$). Specifically, there were significant increases in luminance threshold ($P < 0.01$), reductions in luminance CFF ($P < 0.001$) and in chromatic CFF ($P < 0.01$), and increases in variability of two-flash resolution ($P < 0.05$) and in variability of chromatic CFF ($P < 0.05$). There were significant correlations between thresholds and variabilities in the patient group ($\chi^2_{10} = 26.0$, $P < 0.01$) involving: luminance threshold and its variability ($P < 0.01$), two-flash resolution and its variability ($P < 0.01$), relative perceptual latency and its variability ($P < 0.01$), and luminance CFF and its variability ($P < 0.01$), although in none of these cases did the Pearson product moment correlation coefficient r exceed 0.48. Correlations between different functions are summarized later.

Both patient subgroup A, without previous ON, and subgroup B, with previous ON, showed significant overall worsening in performance relative to their normal control groups, although the magnitude of impairment was greater for subgroup B ($\chi^2_{10} = 23.08$, $P < 0.05$, for subgroup A, and $\chi^2_{10} = 34.72$, $P < 0.001$, for subgroup B).

Subgroup A, without previous ON, showed significant increase in luminance threshold (0.22 log unit, $P < 0.05$), and decrease in luminance CFF (-3.2 Hz, $P < 0.05$) and in chromatic CFF (-4.0 Hz, $P < 0.05$). There were also numerically large increases in relative perceptual latency (14 ms) corresponding to an additional delay for the central site relative to the eccentric site, variability in two-flash resolution (42%), variability in chromatic CFF (45%), and variability in relative perceptual latency (23%), although none of these was sufficiently large in relation to the spread in values to reach significance ($P > 0.05$). Both patients in subgroup A and their matched normal controls showed greater-than-chance correlations amongst parameters (for patients, $\chi^2_{25} = 58.65$, $P < 0.001$; for controls, $\chi^2_{25} = 53.88$, $P < 0.001$), with the greatest contributions in each case coming from the interdependence of chromatic and luminance CFFs (for patients, $r = 0.81$, $P < 0.001$; for controls, $r = 0.87$, $P < 0.0001$), from the interdependence of luminance flicker and its variability (for patients, $r = 0.84$, $P < 0.0001$; for controls, $r = 0.79$, $P < 0.001$),

Table 2. Means (±SEM) of visual parameter values for normal control group (27 eyes), undifferentiated MS patient group (27 eyes), patient subgroup A with no previous optic neuropathy (13 eyes), and patient subgroup B with previous optic neuropathy (14 eyes)

Visual parameter	Control group	MS Group	Subgroup A	Subgroup B
Luminance threshold, log cd/m^2	1.68 (±0.05)	1.93 (±0.08)[2]	1.83 ± (±0.10)[1]	2.02 (±0.12)[1]
Luminance threshold variability, log cd/m^2	0.18 (±0.03)	0.19 (±0.01)	0.17 (±0.02)	0.20 (±0.02)
Two-flash resolution, ms	65.8(±5.7)	61.9 (±6.0)	61.6 (±6.8)	62.1 (±9.8)
Two-flash resolution variability, ms	20.6 (±2.5)	28.3 (± 3.1)[1]	23.5 (±3.1)	32.4 (±5.0)
Perceptual latency, ms	−23.4 (±4.7)	−22.2 (± 5.0)	−13.1 (±8.6)	−30.7 (±4.7)[5]
Perceptual latency variability, ms	40.1 (±6.2)	41.1 (±6.4)	40.7 (±8.1)	41.4 (±10.2)
Chromatic CFF, Hz	18.9 (±1.0)	14.7 (±1.0)[2]	14.8 (±1.5)[1]	14.6 (±1.4)[1]
Chromatic CFF variability, Hz	2.5 (±0.3)	3.6 (±0.4)[1]	3.7 (±0.5)	3.5 (±0.7)
Luminance CFF, Hz	32.8 (±1.0)	28.0 (±1.0)[3]	30.0 (±1.2)[1]	25.8 (±1.5)[2,4]
Luminance CFF variability, Hz	2.1 (±0.2)	2.2 (±0.2)	2.1 (±0.3)	2.4 (±0.3)[1]

Levels of significance for differences between groups are indicated by the superscripts thus: MS groups vs controls: [1]$P < 0.05$, [2]$P < 0.01$, [3]$P < 0.001$; subgroup B vs subgroup A: [4]$P < 0.05$, [5]$0.1 > P > 0.05$.

and, for patients alone, from the interdependence of relative perceptual latency and its variability ($r = 0.75$, $P < 0.001$).

Subgroup B, with previous ON, showed significant increase in luminance threshold (0.28 log unit, $P < 0.05$), decrease in luminance CFF (−6.7 Hz, $P < 0.01$) and in chromatic CFF (−4.4 Hz, $P < 0.05$), and increase in variability of luminance CFF (31%, $P < 0.05$). There was also a numerically large decrease in relative perceptual latency (−11 ms) corresponding to an additional delay for the eccentric site relative to the central site (contrast with subgroup A), and increases in variability of chromatic CFF (40%) and in variability of two-flash resolution (32%), none of which was sufficiently large to reach significance ($0.1 > P > 0.05$). Although the normal controls for subgroup B showed significant correlation between chromatic and luminance CFF ($r = 0.70$, $P < 0.01$), patients did not ($r = 0.35$, $P > 0.1$).

Comparison of subgroup B with subgroup A revealed only one significant difference: a reduced luminance CFF for subgroup B ($z = 2.21$, $P < 0.05$).

The loss in correlation of chromatic and luminance CFFs for patients in subgroup B is evident from Fig. 1, which shows chromatic CFF plotted against luminance CFF in the manner of Foster *et al.* (1980) and Mason *et al.* (1982). The straight lines in each graph in Fig. 1 are unweighted least-squares regression lines. For the full normal-control group [Fig. 1(a)], the gradient (±SEM) of the regression line was 0.76 (±0.16); for the undifferentiated patient group [Fig. 1(b)], 0.54 (±0.16); for subgroup A

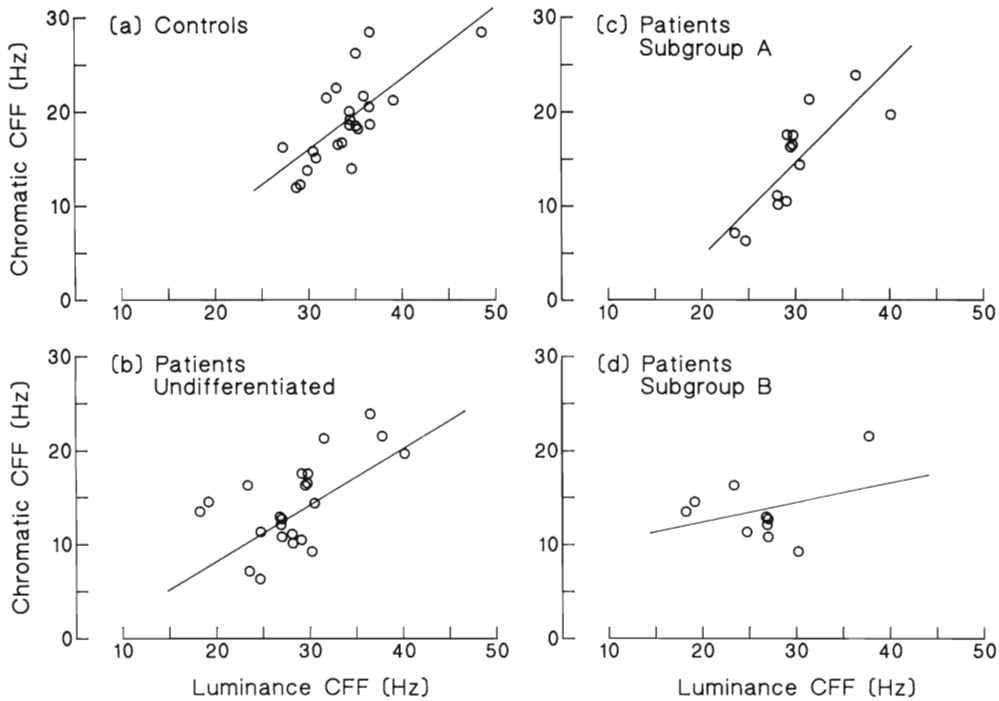

Fig. 1. (a)–(d) Chromatic CFF plotted against luminance CFF. The straight lines are least-squares linear fits to the data. (a) Normal control subjects, correlation coefficient $r = 0.72$, gradient $= 0.76 \pm 0.16$; (b) undifferentiated MS patients, correlation coefficient $r = 0.60$, gradient $= 0.54 \pm 0.16$; (c) subgroup A: MS patients without previous optic neuropathy, correlation coefficient $r = 0.81$, gradient $= 1.01 \pm 0.23$; (d) subgroup B, patients with previous optic neuropathy, correlation coefficient $r = 0.35$, gradient $= 0.22 \pm 0.21$.

[Fig. 1(c)], 1.01 (± 0.23); and for subgroup B [Fig. 1(d)], 0.22 (± 0.21). The difference in gradients for subgroup A and its matched control group was not significant ($z = 1.35$, $P > 0.05$), but the difference was significant for subgroup B ($z = 2.32$, $P < 0.02$). The difference in gradients for subgroup A and subgroup B [Fig. 1(c) and (d)] was also significant ($z = 2.56$, $p < 0.01$). Omission of possible outlier points in Fig. 1 did not alter the qualitative nature of these results.

DISCUSSION

In contrast to the findings of an earlier study (Snelgar *et al.*, 1985) involving the same tests but on a small group of patients with MS, the present results show clear losses in visual performance both in patients with previous ON (subgroup B) and in patients without previous ON (subgroup A). The severity of visual impairment was, however, different for these two subgroups, and not all functions were affected in the same way.

Luminance threshold

Raised luminance thresholds have been reported by Burde and Gallin (1975) and by Harms (1976) in the affected eyes of patients with previous retrobulbar neuritis (RBN). Both subgroup A and subgroup B showed significant elevations in threshold relative to their matched normal control groups, and although subgroup B, with previous ON, showed a slightly greater effect the difference was not significant. On the basis of impaired luminance sensitivity alone, the two subgroups were indistinguishable.

Because of the spectral composition of the test flash used in the present threshold measurements, it is likely (Foster *et al.*, 1985) that the stimulus was not strictly selective for luminance function and that pathways subserving chromatic function were also involved in the response. It has been shown, however, that for foveal sites loss in sensitivity due to demyelination is, on average, equal for chromatic and luminance function (Foster *et al.*, 1985), a result which is consistent with available data on the size spectra of macular fibres (Potts *et al.*, 1972; Ogden, 1984) and the greater vulnerability of small-diameter fibres to artificially induced demyelination (Tremain and Ikeda, 1983). It should also be noted that patients' colour matching performance, as assessed with The

City University Colour Vision Test, was not abnormal overall.

Neither patient subgroup showed an increase in variability of luminance threshold. This result is not necessarily inconsistent with earlier findings by Patterson *et al.* (1980) who demonstrated abnormal variability in a group of patients with subclinical ON and classified as having probable or definite MS. Patterson *et al.* (1980) deliberately selected patients on the basis of initially varying thresholds, and introduced greater background luminance levels than those used here. As noted already, abnormal variabilities in other visual functions were observed in the present study.

Two-flash resolution

The two-flash paradigm, although offering an apparently direct measure of temporal resolution, is technically complicated and may involve masking effects and other artifacts (summarized by Snelgar *et al.*, 1985) not directly related to temporal visual function. Galvin *et al.* (1977) reported that patients with advanced definite MS and previous visual involvement did show significantly poorer two-flash resolution than patients with less advanced MS with or without visual involvement. The present result showing that two-flash resolution was not significantly worse for any of the patient groups may have been a consequence of the relatively less advanced state of their disease. It should be noted, however, that two-flash resolution involves the transient behaviour of the visual pathway (compare Roufs, 1973), whereas critical flicker frequency, which was significantly affected in all patient groups, involves its steady-state behaviour. It would be expected from data from animal models of demyelinating disease (McDonald and Sears, 1970; Rasminsky and Sears, 1972; Low and McLeod, 1977) that conduction block in partly demyelinated pathways would be more likely to occur under conditions of repeated stimulation, as occurs with steady-state flicker stimuli. Although not significant, there were large (30–40%) increases in variability in two-flash resolution in the patient groups.

Relative perceptual latency

Animal models of demyelinating disease (Rasminsky and Sears, 1972) and previous clinical studies have shown increased transmission times for affected pathways. In particular, abnormalities in perceptual latency for an extrafoveal site of one eye relative to the fovea of the other eye have been demonstrated in patients with previous RBN and in some patients with spinal MS (Heron *et al.*, 1974; Regan *et al.*, 1976; Galvin *et al.*, 1976a), and abnormalities in delays between sites in the same eye have also been deduced (Regan *et al.*, 1976). As with all these measurements, the demonstration of abnormal relative perceptual latencies depends on the presence of differential impairment in nerve transmission.

Here the eccentric site was close to the comparison central site (2.5° visual angle) and both patient subgroups showed numerically rather small differences in relative perceptual latencies with respect to their matched control groups: 14 ms for subgroup A and 11 ms for subgroup B. The differences were, however, in opposite directions, with the eccentric site showing the greater delay for subgroup A and the central site showing the greater delay for subgroup B. Although not significantly different from their normal control values, the difference between the two subgroups did approach significance (Table 2). This may have been a consequence of the different visual histories of the two subgroups and the different durations of their disease (Table 1). Variability of relative perceptual latency was not significantly worse than normal control values for any of the patient groups.

Critical flicker fusion

A reduction in critical flicker frequency in patients with demyelination of the optic nerve and tract is compatible with a variety of experimental data from animal models showing intermittent conduction block, failure to transmit rapid trains of impulses, and increased refractory period, both in acute demyelination (McDonald and Sears, 1970; Rasminsky and Sears, 1972) and in chronic demyelinating disorders (Low and McLeod, 1977). Reductions in CFF for luminance flicker (Titcombe and Willison, 1961; Daley *et al.*, 1979; Mason *et al.*, 1982) and for chromatic flicker (Mason *et al.*, 1982) have both been observed for foveal stimulation in patients with MS. Abnormalities in modulation thresholds for flicker have also been reported (Plant and Hess, 1985; Hess and Plant, 1986).

One finding by Mason *et al.* (1982) was that luminance and chromatic CFFs were correlated with each other over different subjects, both in normal controls and in patients. Importantly, the underlying linear dependence of chromatic CFF on luminance CFF was characterized by a

lower gradient for the patient group relative to the normal control group.

In the present study, both subgroup A, without previous ON, and subgroup B, with previous ON, showed significant reductions in chromatic and luminance CFFs relative to their normal control groups (Table 2). Although mean chromatic CFFs for subgroup A and subgroup B were about equal, mean luminance CFF for subgroup B was significantly lower than that for subgroup A. The latter reduction was consistent with results of Titcombe and Willison (1961) and Mason *et al.* (1982) showing that eyes that had previous visual involvement gave most reduction in (luminance) CFF.

The differences between subgroups A and B were most clearly evident, however, in the plots of chromatic CFF against luminance CFF (Fig. 1c, 1d). The gradient for the underlying linear interdependence was 1.01 for subgroup A and 0.22 for subgroup B, and the difference was highly significant. A reduction of the gradient of the regression line has been explained generally (Mason *et al.*, 1982) in terms of the blocking of high-frequency trains of impulses in affected nerve fibres. Because luminance CFF is normally greater than chromatic CFF it was assumed that it would be preferentially reduced by such blocking; and the greater the severity of demyelination, the greater the reduction in gradient. The effect was apparently sufficiently large for subgroup B that it led to the clustering of data points and loss in correlation shown in Fig. 1(d). The grouping of data points for affected eyes offers the possibility of classification by chromatic and luminance CFF plots using linear discriminant analysis, although larger populations of patients would be required to establish more precise boundaries.

In summary, the present study of a range of visual functions in patients with MS has shown that subclinical visual impairment was present in patients who had no visual symptoms and who had no clinical evidence of previous ON; in particular, luminance threshold and luminance CFF were both significantly affected. It is well known that the incidence of visual involvement in MS increases as the disease progresses (Galvin *et al.*, 1977; Perkin and Rose, 1979), and the marginal increase in luminance threshold and significant reduction in luminance CFF for subgroup B with previous ON relative to subgroup A without previous ON were consistent with this general finding. It was, however, in the interdependence of chromatic and luminance CFFs that the two subgroups were most clearly distinguished. As noted elsewhere (Snelgar *et al.*, 1985), it is possible that the relationship between the two types of CFF may offer a more sensitive indicator of demyelination in the optic nerve and tract than any of the other measures taken separately.

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