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# Temporal and spatial resolution in foveal vision of multiple sclerosis patients

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**Abstract**

Deficits of spatial and temporal resolution were compared in a group of 49 definite multiple sclerosis(MS) patients showing no major evidence of previous optic neuritis attack but representative of the population of the Belgian National MS Centre as to age and the most important disease variables. Resolution in the two domains was measured foveally with forced-choice staircase psychophysical procedures using Landoldt C and double flash stimuli, respectively. The two measurements were equally sensitive to MS-induced deficits and did not exhibit cross-sensitivity. Since discrete deficits of either kind were equally prevalent and outnumbered combined deficits, this suggests a nonselective but nonuniform destruction of M and P visual pathway function in these patients. © 1998 Elsevier Science Ltd. All rights reserved.

*Keywords:* Double flash-foveal visual pathways; Landoldt acuity; Multiple sclerosis; Nonuniform nonselective damage

## 1. Introduction

Beginning at the level of the retina, two parallel channels can be distinguished both anatomically and physiologically within the primate primary visual system [1–3] and many psychophysical findings are explained by this dichotomy [4]. The processing capacity of the magnocellular channel degrades more rapidly than that of the parvocellular channel with increasing spatial frequency and conversely, the temporal processing capacity of the parvocellular channel degrades more rapidly than in the magnocellular channel [5]. Further, there exists some evidence for the involvement of cortical areas (such as the striate cortex, MT and V4) in spatial and temporal resolution [6–8]. For these reasons a discrete deficit (that is, a deficit that is not accompanied by a deficit of the other class) of a subject's temporal resolution could be the expression of selective damage to an M pathway, comprising the magnocellular channel as well as the cortical areas involved in temporal resolution. A discrete deficit of spatial resolution could be an indication of selective damage to a P pathway, including the parvocellular channel and the cortical areas involved in spatial resolution. Evidence for these selective damages can be found in a series of lesion experiments [6–11].

Temporal [12–15] and spatial [16] resolution can be disturbed in MS patients, but to our knowledge anatomical evidence for selective damage to either M or P pathways in optic neuritis (ON) and MS has not appeared in the literature. Nevertheless evidence for three types of deficit has been presented: a pattern of nonselective deficits affecting small axons to about the same degree as large axons [17,18], and two selective types of deficit affecting either only small axons [17,19] or only large axons [20,21], respectively. Most of this evidence comes from psychophysical studies either comparing chromatic and luminance sensitivity (for a review see [18,22]), studying contrast sensitivity at different (suprathreshold) spatiotemporal conditions [17,18], or comparing [20,24,23] contrast-defined (CD) and motion-defined (MD) letter reading. Recently, VEP recordings [24–26] have provided new evidence for each of these types of deficit. The electrophysiological and the behavioural experiments, however, have yielded conflicting results. Hence, little is known about the relative importance of these patterns of deficit. Two methodological factors have been deemed responsible,

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at least to some extent, for the discrepancies among the colour vision psychophysical studies and among the contrast sensitivity studies [17,18,27]. In our opinion, they may also partially account for discrepancies within the motion perception approach and within the VEP data and explain for conflicts between electrophysiological and behavioural data [24,26]. First, when two stimulus conditions are compared within a single individual in order to establish selective damage to a particular pathway, the two stimuli should be equally sensitive to myelin loss, since it is known that the spatiotemporal and contrast characteristics of stimulus conditions can affect the degree to which their processing is impaired by myelin loss. If processing of these stimuli is unequally impaired by myelin loss, then this can give rise to interpretative difficulties as pointed out in the papers of Mullen and Plant [27] and Russel et al. [18]. Secondly, conflicting conclusions regarding the selectivity of certain visual deficits may arise from the fact that results were averaged over a number of patients. Because of this, they depend both upon the relative proportions of specific deficits in the local population from which the sample was taken, as well as upon sampling errors. MS patients form a heterogeneous group with respect to their ability to process spatial [16] and temporal [14] visual information, just as they do in regard to many other clinical variables. Some factors, such as a sign or history of ON [15,21,28] and the clinical classification of MS (suspected, probable, definite) [28] have proven to be important predictors of the frequency and consistency of visual dysfunction. Differences in these clinical variables may have contributed greatly to the conflicting nature of the evidence.

To get a better idea about the prevalence of the patterns of deficits in MS, a study had to be conducted in which these methodological considerations were taken into account. This was the aim of the present paper. Because we first had found temporal and spatial resolution to be equally sensitive to demyelination we have assumed that a discrete deficit can be interpreted as an indication of discrete damage to a particular pathway. The target population was narrowly defined, and the patients' pathological and biographic characteristics were described as accurately as possible to facilitate comparisons of results of this study while a large sample size and a random selection procedure were employed to minimise sampling errors. Observations were restricted to temporal and spatial resolution in foveal vision, since subjects had to fixate a detail, at least at threshold level, smaller than 1° of visual angle [29]. Only recently has it been demonstrated [30] that both M and P pathways can be studied by foveal observations alone [31]. Deficits were detected with psychophysical threshold procedures making use of Landoldt C targets and double-flash stimuli.

Since reports of an aspecific pattern of deficit affecting both small and large axons appear to dominate the literature [17,18], we expected deficits combining spatial and temporal resolution to prevail in our sample as well. Based on existing evidence, some instances in which damage was confined to either the M or P pathway were also expected. Statistical comparisons of deficits of temporal and spatial resolution have enabled us to draw certain conclusions concerning the nature of the physiological processes underlying them.

## 2. Methods

### 2.1. Subjects

#### 2.1.1. MS-patients

An effort was made to take a random sample of 111 in and out-patients from the clientele of the Belgian National Multiple Sclerosis Centre. After the application of a series of exclusionary criteria, forty-nine subjects were selected. The criteria are listed in Table 1.

An ophtalmological examination determined whether the patients could wear their own spectacles or had to use lenses providing more suitable correction. Because the study contained a neuropsychological component patients showing any visual impairment that might interfere with this kind of testing were excluded. For this reason all subjects having a Snellen acuity less than 20/70 (criterion proposed in [32]) in both eyes after optical correction and patients with diplopia while looking straight ahead were rejected. We were aware

Table 1
List of exclusionary criteria applied to the initial sample of 111 randomly recruited MS patients.

1. Dazed or confused because of medication/alcohol or drug abuse /CNS diseases other than MS/psychiatric conditions (psychiatric diagnosis) ($N = 18$)[a].
2. Not able/willing to cooperate ($N = 16$).
3. Mental deterioration (score below 24/30 on Mini Mental State) ($N = 13$).
4. Binocular Snellen acuity after optical correction less than 20/70 ($N = 11$).
5. Interfering ophtalmological afflictions other than retinal anomalies and glaucoma ($N = 11$).
6. Diplopia ($N = 8$).
7. Presence of either an absolute or a relative central scotoma ($N = 8$).
8. Signs of disease activity other than acute ON ($N = 5$).
9. Acute ON ($N = 3$).
10. Retinal anomalies ($N = 2$).
11. No definite MS according to Poser et al. [40] ($N = 1$).
12. Glaucoma ($N = 1$).
13. Residing in a nursing home or other institutional setting ($N = 1$).

[a] Number of patients rejected because of the criterion. Several patients were eliminated because of more than one criterion.

that decreases in visual acuity can occasionally be observed in MS patients in the absence of any link to demyelination. Nevertheless, patients were excluded according to only a single assessment of Snellen acuity because, for our purposes, it was more important to exclude all patients with low vision than to include all those who might be able to perceive the neuropsychological test stimuli at least under certain conditions.

*2.1.2. Control Subjects*

After the selection of the patient group, a normal control group (NC) of 30 healthy volunteers was created. On a group level, MS patients and NC were matched as to age and education level. During a short interview, controls were screened (observation, antecedents) for ophtalmological, neurological, psychiatric and neuropsychological problems, to ascertain that they showed no major afflictions of these kinds. Controls were also checked for uncorrected refractive errors. Those who reported that their existing prescription lenses corrected sufficiently were admitted directly. Those who did not were referred to an ophthalmologist to be fitted with suitable corrective lenses.

## 3. Stimuli

### *3.1. Temporal Resolution*

Temporal resolution was evaluated by measuring double-flash thresholds (DFT). DF stimuli were generated by red light emitting diodes (LEDs). The LEDs subtended a visual angle of 26' of arc and according to the manufacturer, have a luminance of 7 cd/m$^2$. The luminance of the inner surface of the white sphere that served as background measured approximately 0.4 cd/m$^2$ with a photometer. Viewing distance was 0.39 m.

### *3.2. Spatial Resolution*

To evaluate spatial resolution, visual acuity thresholds (VAT) were determined. Landoldt Cs were used as stimuli because, like LEDs, they allow very precise measurements of retinal position. To create a high contrast test condition, stimuli were presented as black figures on a white ground. The subject's task was to report the direction of the opening in the ring. By putting the subject at a distance of 6 m from the stimuli, the gap width of the smallest possible C equalled 0.16′ of arc. According to the literature [33] this is sufficiently small. The testing chamber was illuminated at 13–16 cd/m$^2$, which is adequate for testing visual acuity [34].

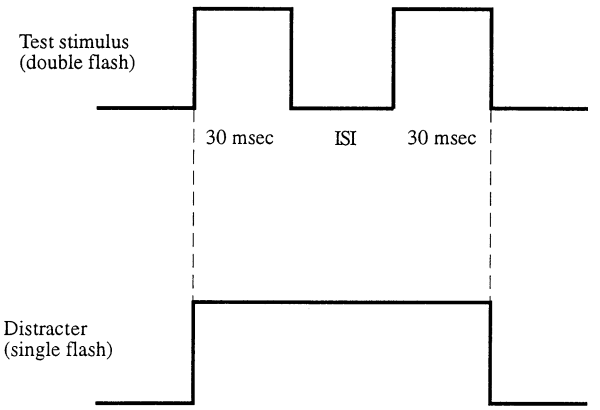


Fig. 1. Double-flash (DF) stimulus and distracter of a block up-and-down two-interval forced-choice (BUDTIF) trial.

## 4. Apparatus

As in the study of Galvin et al. [14] temporal perimeter was used to present the DF stimuli. Because this study dealt with DFT at foveal retinal sites, only the central LED of the perimeter was used. Landoldt Cs were generated at VGA resolution on a monochrome, 14 in. computer monitor driven by an Intel-based 486PC. Viewing distance was kept constant by the use of a form-fitting device to hold the patient's head stable.

## 5. Procedures

### *5.1. Threshold Determinations*

Testing was always monocular and each subject was tested in both eyes. Thresholds were measured by means of staircase psychophysical procedures with forced choice incorporated into the procedure. For DFT, a block up-and-down, two-interval forced-choice (BUDTIF) procedure initially described by Campbell and Lasky [35] was used. Each trial consisted of two intervals (stimuli): a single flash, used as a distracter, and a DF comprising two 30 ms flashes separated by a dark interstimulus interval (ISI) of variable length and adjustable in steps of 5 ms. The duration of the distracter in any given trial was equal to that of the corresponding DF, including the ISI (Fig. 1). The order of presentation was randomised and the patients' task was to identify whether the first or second interval contained the DF.

A block of four trials was given at a particular stimulus level. During the procedure the DF appeared equally often in each interval. The DF threshold stimulus is defined by the 75% correct-criterion. A proportion of correct responses exceeding this criterion resulted in a decrease in the ISI by 5 ms on the next

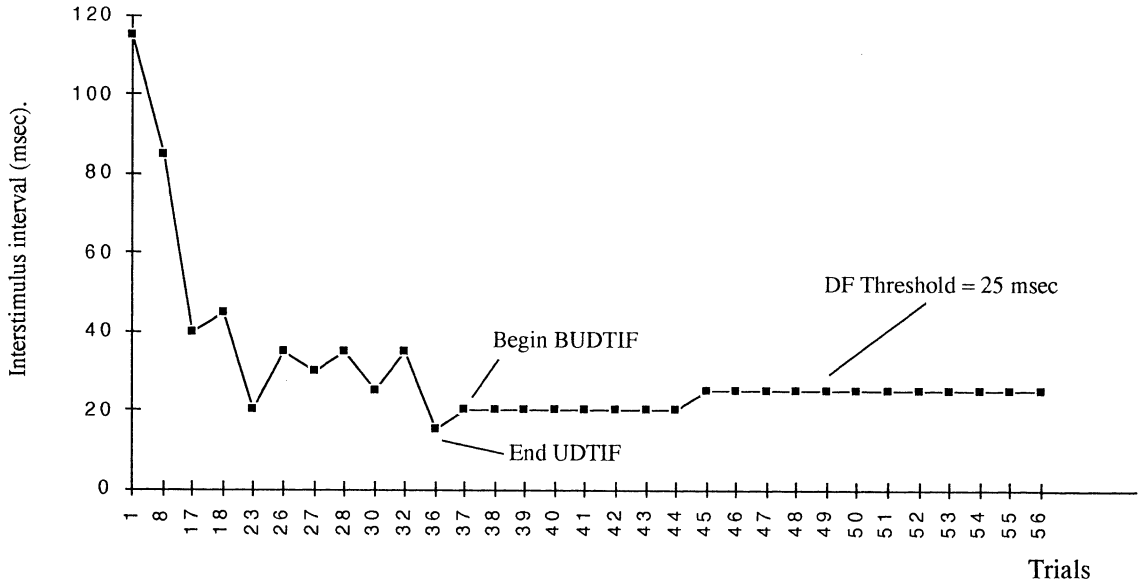


Fig. 2. Double-flash threshold (DFT) determination for foveal vision in a normal control (NC) subject (subject nr.15, left eye).

trial block. If the proportion of correct responses was less than criterion, ISI was increased by 5 ms on the next block, and if it equalled the criterion, the same ISI was retained for the next trial block. Regardless of results, only five trial blocks were presented in any given BUDTIF session. Threshold was determined as the median stimulus value of trial blocks that were presented more than once.

When duplicate blocks did not occur, it was concluded that random drift had placed the stimulus too far below threshold to be bridged within five steps, and that the rule of good placement of observations [36] had not been met. The procedure was repeated another day.

BUDTIF was always preceded by a preparatory phase. Our aim was to develop a one-session DFT determination with clinical utility. In such a procedure a preparatory phase is essential. It enhances the efficiency of the subsequent BUDTIF by bringing its first stimulus nearer to threshold. It also acquaints the subject with the perhaps unfamiliar requirements of the forced-choice technique, which demands a response even when the subject does not perceive a difference between test stimulus and distracter. The preparatory phase was an up-and-down, two-interval forced-choice technique (UDTIF). The initial ISI value was always set at 120 ms, the step size was 5 ms, as in BUDTIF, but the stimulus level was adapted after each trial. At the outset, a high proportion of correct responses would be made because the initial stimulus was set far above threshold. This initial stage was followed by a phase in which an increasing number of errors were committed as the ISI approached threshold. The near-threshold stimuli subsequently presented to the subject included many in which it was not possible to discriminate between DF and distracter. After nine reversals, the preparatory phase was stopped and the BUDTIF was started. Fig. 2 shows an example of a DFT determination procedure.

Visual acuity thresholds (VAT) were measured using an up-and-down, four-alternative forced-choice (UDFAF) procedure. On each trial, a Landoldt C appeared on the computer screen in one of four possible orientations. During the procedure, each orientation appeared on the screen equally often and in a random order. After a correct answer (i.e. a correct report of the position of the gap by the subject) the gap width of the next C was decreased to 10/12 of the one preceding. A wrong answer resulted in an increase of the gap width by 20%. UDFAF was discontinued after the ninth reversal in response correctness. The minimum angle of resolution (MAR) is defined by the (geometric) mean of the last five response reversals.

The gap width of the first C of the UDFAF was always fixed at 48 computer screen pixels or 17.28 mm. At a viewing distance of 6 m, this corresponds to a visual angle of 9.9′ of arc which is well above threshold [37]. Fig. 3 shows an example of a VAT determination.

Threshold determination procedures were carried out within the framework of a broader experiment in which a comprehensive battery of thirty-three neuropsychological tests was also administered. To minimise fatigue, testing was conducted in three sessions, one of which was reserved for psychophysical measurements only. In this session, spatial and temporal resolutions alternated as the first parameter to be tested. The order of the three sessions was randomised.

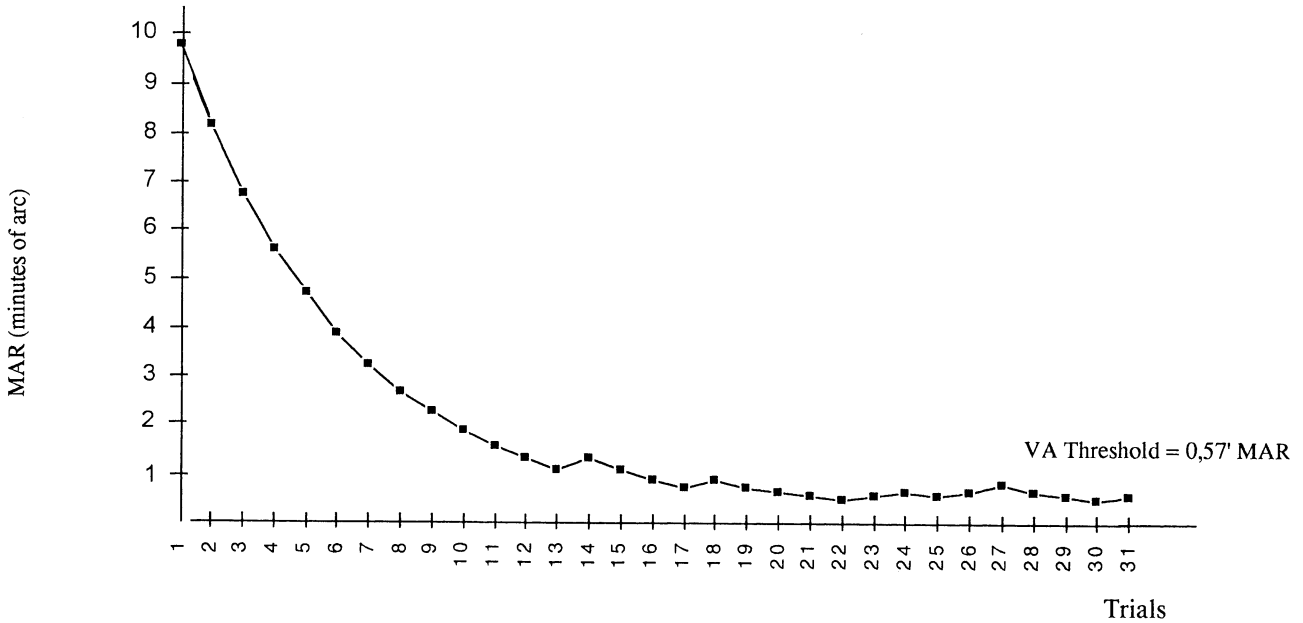


Fig. 3. Visual acuity threshold (VAT) determination for foveal vision in a normal control (NC) subject (subject nr.15, left eye).

### 5.2. Data Analysis

Statistical analyses were performed with the Statistical Analysis System software package [38] and dealt with the individual eyes independently. Average thresholds of MS and NC groups were compared using one-tailed t-tests. To determine the frequency of spatial and temporal resolution deficits, the closest approximation of the ninety-fifth percentile of the NC-eye scores was used as the cut-off for determining the value which was to be considered a failing score for the MS patients. For each task, the true frequency of visual deficits was defined in the MS patients as the percentage of MS eyes classified as 'failing' on the task minus the per cent of NC eyes misclassified as impaired. These true frequency rates were used as an estimate of the prevalence of spatial and temporal resolution deficits. To establish the relationship between these two parameters, a two-way dichotomous classification of eyes was carried out for the MS group. The two dichotomies were based on whether or not their respective tests, the DF and the acuity test, had passed or failed. Frequencies and proportions of the resulting contingency table were analysed to determine the occurrence of discrete and combined deficits. A $\varphi$ correlation coefficient was calculated and a $\chi^2$ test was used to test significance of association.

As stated earlier, the right and left eyes of each patient were tested and tabulated (Table 2) independently. Clearly, this can present some statistical difficulties since there is an obvious relationship between the two eyes in the same individual. To avoid this issue, the t-test and $\chi^2$ tests were carried out for right and left eyes independently.

## 6. Results

### 6.1. Control Data

There were 19 females and 11 males in the control group, ranging in age from 27–73 years with a mean of 48 years and 10 months.

Average DFT ($N = 60$) of the eyes of 30 NC subjects was found to be 29.1 ms (S.D. = 12.2 ms.). Average VAT of the NC group was defined by the Landoldt C with a 3.28 pixel gap width. At a viewing distance of 6 m this corresponds to a MAR of 0.67′ (S.D. = 0.23′) and a decimal acuity of 1.47.

### 6.2. MS Patients

There were 36 female and 13 male patients whose age ranged from 29–73 years and whose mean age of 47 years and 4 months was comparable to that of the control group. Mean disease duration (i.e. time interval between diagnosis and testing) was 12 years (S.D. = 8.3, range 1–40). Type of MS was primary progressive (PP) in 27%, secondary progressive (SP) in 51% and relapsing remitting (RR) in 22% of the patients. Mean Kurtzke score was 5.93 (S.D. = 1.99; range from 2.0–9.0). Only six of them were still engaged in professional activity. Twenty-nine of the patients had experienced one or more previous attacks of unilateral ON. Among

Table 2
Contingency table of spatial and temporal resolution deficits in MS patients.

| | Temporal Resolution | | |
|---|---|---|---|
| Spatial Resolution | Double-flash threshold below the 95th normal control percentile Normal Temporal Resolution | Double-flash threshold above the 95th normal control percentile Temporal Resolution Deficit | Marginal Frequencies Of Rows |
| Visual acuity threshold below the 95th normal control percentile Normal Spatial Resolution | 47 (48.0%) | 22 (22.4%) | 69 (70.4%) |
| Visual acuity threshold above the 95th normal control percentile Spatial Resolution Deficit | 18 (18.4%) | 11 (11.2%) | 29 (29.6%) |
| Marginal Frequencies Of Columns | 65 (66.4%) | 33 (33.6%) | Total of Observations 98 (100%) |

The observed frequencies and proportions resulted from a two way classification of individual eyes ($N = 98$, 49 patients) of the MS group. Whether or not an abnormal DFT was exhibited was the determinant for the column while its VAT determined row position. An abnormal threshold was defined as a threshold above the 95th percentile of scores in the NC-eye group.

patients having had such an attack, the interval between the last attack and testing ranged from 3 months to 35 years.

*6.2.1. Representativeness of the patients' sample of the clinic population studied*

The clinical characteristics of the MS group were compared to those of the subjects of a study [39] on 1800 hospitalised, definite [40] MS patients admitted at the Belgian National MS Centre from 1970–1992. Subjects in the Gonsette et al. study were comparable to ours with regard to major disease variables such as age at onset (mean 31.7 years, S.D. = 10.1 years), disease duration (i.e. interval between onset of symptoms and registration) (mean 17.18 years, S.D. = 10.3 years), type of MS (PP 27.5%, SP 57%, RR 15%) and proportion of ON as initial MS symptom (19.7%). The distribution of initial symptoms reported in the study of Gonsette et al. appeared to be about the same as in McAlpine's review of the literature [41]. In comparison, our sample contained a higher proportion of females than the Gonsette et al. study, but the distribution of ages was comparable in the two studies.

*6.2.2. Effects of MS with regard to temporal and spatial resolution*

For the MS group ($N = 98$, 49 subjects) average DFT was 40.45 ms (S.D. = 18.11) and average VAT was 0.96′ (S.D. = 0.59′). Differences between MS patients and NC ($N = 60$ eyes, 30 subjects) were highly significant for both DFT ($t = 3.233$; $P = 0.001$ (one tailed)) and VAT ($t = 3.003$; $P = 0.002$ (one tailed)). The distributions of DFT and of VAT in both experimental groups are shown in Fig. 4A and B, respectively.

DFT and VAT averaged 38 and 42% higher, respectively, in the MS group compared to NC. Ranges of threshold were also wider in the MS group, suggesting that MS patients constitute a heterogeneous group with regard to both spatial and temporal resolution.

*6.2.3. Spatial and temporal resolution deficits in MS: frequencies and relationship*

The true frequency rate of spatial resolution deficits was 24.5% and that for temporal resolution deficits was about the same (28.67%). Bilateral spatial resolution deficits were found in 14.6% of the subjects. Bilateral temporal resolution deficits were found in 16.3% of the cases. Thus in our MS group the two kinds of deficits were equally prevalent.

Frequencies and proportions in Table 2 provide a detailed picture of the degree of interaction between the occurrence of spatial and temporal resolution deficits in MS patients. These figures suggest that there is no discernable relationship between these two kinds of deficits. The φ correlation was as low as 0.058. A test for association proved to be negative ($\chi^2_{(1)} = 0.329$, $P = 0.566$).

The same analysis was conducted on the group of MS patients ($N = 58$ eyes) with a history of ON. Results shown in Table 3 demonstrate that frequencies and proportions remained comparable to those of Table 2.

*6.2.4. Left and right eyes*

Spatial resolution in the right and left eyes of individual patients were significantly correlated (Pearson $r = 0.52$, $P = 0.0002$). The same held true for temporal resolution (Pearson $r = 0.52$, $P = 0.0001$). Since these dependencies might have artificially enhanced the significance of group effects and of the correlation shown in Table 2, analyses were repeated for left and right eyes independently, but the results did not alter any of our conclusions. The group effects found for VAT and DFT remained significant for both left ($t = 3.30$ and

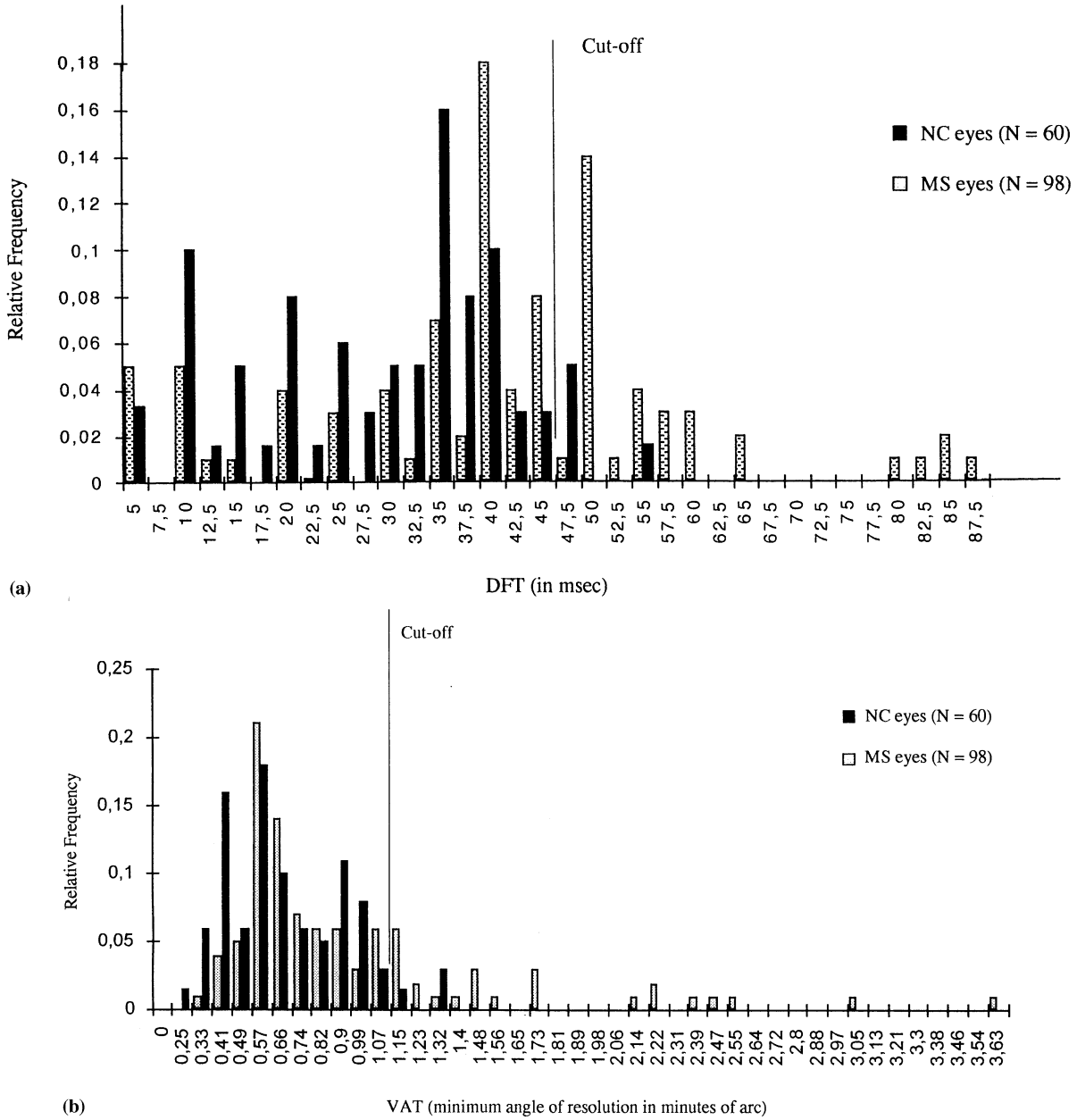


Fig. 4. (a)Distribution of double-flash thresholds (DFT) in the eyes of normal controls (NC) and of MS patients. Cut-off is the closest approximation of the ninety-fifth percentile of scores in the NC-eye group. (b)Distribution of Visual Acuity Thresholds (VAT) in the eyes of normal controls (NC) and of MS patients. Cut-off is the closest approximation of the 95th percentile of scores in the NC-eye group.

3.07 respectively, $P = 0.001$ for the two t-values) and right eyes ($t = 2.64$ and 2.65 respectively, $P = 0.005$ for the two t-values).

Correlation between spatial and temporal resolution deficits did not reach significance either for the left ($\varphi = 0.012$, $\chi^2_{(1)} = 0.007$, $P = 0.933$) or right eyes ($\varphi = 0.095$, $\chi^2_{(1)} = 0.433$, $P = 0.50$) as considered separately. Frequency patterns and attendant contingency tables were similar to Table 2. It was concluded that the correlations between the patients' left and right eyes with respect to spatial and temporal resolution did not pose a difficulty in this study.

## 7. Discussion

Within the group of MS patients examined, the prevalence and average severity of deficits in temporal resolution were comparable to those observed for spatial resolution. Discrete deficits outnumbered combined deficits and the two measurements did not correlate at all.

An attempt was made to enhance the efficiency and accuracy of DFT determination as a measure of the temporal resolution capacities of MS patients by using a staircase psychophysical procedure with an incorpo-

Table 3
Contingency table of spatial and temporal resolution deficits in the group of MS patients with a history of ON ($N = 58$, 29 subjects).

| | Temporal Resolution | | |
|---|---|---|---|
| Spatial Resolution | Double-flash threshold below the 95th normal control percentile Normal Temporal Resolution | Double-flash threshold above the 95th normal control percentile Temporal Resolution Deficit | Marginal Frequencies Of Rows |
| Visual acuity threshold below the 95th normal control percentile Normal Spatial Resolution | 29 (50%) | 17 (29%) | 46 (79%) |
| Visual acuity threshold above the 95th normal control percentile Spatial Resolution Deficit | 8 (14%) | 4 (7%) | 12 (21%) |
| Marginal Frequencies Of Columns | 37 (64%) | 21 (36%) | Total of Observations 58 (100%) |

rated forced-choice technique. The psychophysical method [14] previously used to measure DFT, the method of ascending and descending limits, is notoriously inefficient and inaccurate for normal individuals, and we can only surmise that this is even more true for neurologically impaired patients [42]. Because of fatigue and concentration difficulties in MS patients as well as the possible occurrence of Uhthoff's syndrome, the duration of our procedure was limited. This may have had a negative impact on the reliability of the method. Uhthoff's syndrome is a somewhat bizarre syndrome consisting of a reduction of visual acuity or an enlargement of a pre-existing scotoma after physical activity showing that at least occasionally the optic neuropathy of multiple sclerosis seems to be influenced by exercise. However, we argue that the validity of the procedure we used was satisfactory for the purpose of this study for the following reasons. (1) The difference between the mean DFT in our NC group and in the normal controls of Galvin et al. [14] was as small as the step size (5 ms) used in the procedures of the two experiments, and thus we conclude that these results were comparable; (2) The MS effect we had expected emerged quite clearly, and it is possible that the sizes of the observed effects would have been even greater had we not excluded subjects with bilaterally low vision and/ or central scotoma; (3) In a preparatory study of the DFT of normal subjects, the Pearson test retest correlation was 0.89.

The average VAT in our NC group was better than the 1.3 decimal acuity assumed to be the normal average [34] although still poorer than the average MAR of 0.42′ found by Jacobs [37]. The latter is close to optimal visual acuity which is situated at 0.4′ or 2.5 decimal acuity [33]. By the same token it means that the experimental conditions under which we had measured acuity were acceptable. Besides the high contrast of our stimuli, either the absence of a possible crowding effect or the selection of subjects with well-corrected vision may in part account for the high levels of visual acuity in the present paper.

The high proportion (48%) of MS patients showing neither spatial nor temporal resolution deficits may be explained by the ophtalmological selection criteria that we employed during the recruitment of our subjects and by the limited fashion in which sensitivity for visual stimuli was assessed, employing only a single high temporal frequency and a single spatial frequency. In a more comprehensive approach Collins et al. [28] compared five different visual measurements and found 73% (non ON condition) to 92% (ON condition) cases having at least one abnormal visual score. Further, the fact that observations were restricted to foveal vision might also account for the relatively low sensitivity shown by the tests presented in this paper. In another experiment [43] the greater sensitivity of peripheral temporal resolution and standard pattern-reversal VEPs to MS as compared to that of foveal temporal resolution is clearly demonstrated.

The sample of patients used in this study appeared to be representative of the clinical population as a whole. Consequently, and because of the equal prevalence and average severity of the two kinds of deficit, we concluded that in this population, spatial and temporal resolution in foveal vision were equally sensitive to demyelination. As a result, and because these two measures probably reflect the integrity of different visual pathways, discrete resolution deficits were used to address the issue of selective damage to M and P systems. Surprisingly, we found discrete deficits in many cases. Because the proportion of these discrete deficits exceeded that of the combined deficits in our sample, we concluded that a uniform loss of visual function was not the most common pattern of visual deficit. A series of colour studies however, has reported that achromatic and chromatic impairments most commonly coincided in MS or ON patients [17–19,22,44–46]. As pointed out in the introduction, a possible explanation for the

existence of unequal degrees of impairment to the two visual subsystems might be the relatively low proportion (29/49 = 59%) of patients in our sample who had suffered from a previous attack of ON [15,21,28]. However we found that for the group of patients with a history of ON, frequencies and proportions of deficits remained comparable to those of the entire sample of the MS patients we studied. This indicates that in our MS group it was unlikely that the low proportion of ON patients accounted for the low number of combined deficits. Moreover, it has been observed that spatial and temporal resolution can return to normal after ON [15,47]. By excluding patients with low vision and central scotoma, our sample might have contained many such cases of recovered ON. Another reason for the high incidence of discrete visual deficits in our study as compared to the colour studies might have to do with the nature of the measurements we used. The P and M pathway functions that were tested in our study are probably very different from chromatic and luminance sensitivity. For instance, Patterson et al. [48] showed that in MS, abnormal temporal resolution is not a simple functional consequence of altered luminance thresholds.

Obviously, the finding that discrete temporal resolution deficits were just as prevalent as their spatial counterparts could have been predicted from the equal prevalence of temporal and spatial resolution deficits. It nevertheless suggests that when evaluated with the particular foveal tasks discussed in this paper, M and P pathways are equally likely to suffer independent demyelination. This is consistent with the conclusion that a lack of anatomical selectivity exists with respect to demyelinating lesions in MS, which is also suggested by Herbst et al. [24]. Only recently has new evidence appeared for a specific compromising of M pathway fibres and/or connections to them [20,21,24,25,49]. Previously, few authors had found the existing evidence for this possibility convincing [18] since, in contrast to the situation where thick fibres were concerned, there were rather more reports in the literature [17,19,50] of individual cases of ON and MS exhibiting a pattern of specific deficits of thin fibres. Some of the methodological issues probably responsible for discrepancies between these findings were discussed in the introduction.

The complete absence of correlation that was found between the incidences of spatial and temporal resolution disorders at the fovea indicates that the physiological processes underlying these particular kinds of functional disorders, those involving foveal fibres of the respective M and P systems, were not related. Why these pathological processes should operate independently remains unclear, although a number of possibilities can be suggested which are not mutually exclusive of one another. One such reason might be the existence of two specific categories of affliction, each having a preference for a particular type of fibre. As our study dealt with localised deficits, another basis for these observations could be the random propagation of lesions within circumscribed regions of specialised visual pathways, restricting most lesions to a single type of deficit. This hypothesis seems to be especially relevant for lesions to the postchiasmatic visual pathways in which some general segregation of large and small axons can be found. It also seems relevant to the pathology of MS (see also [24]) in which demyelination has been observed at different levels along the visual pathways including optic nerves, tracts, radiations, striate and extrastriate cortical regions [51,52]. Because of the significant correlations that were found between the two eyes in our group of MS patients for both temporal and spatial resolution, neither does our experiment exclude the possibility of cortical loci for many deficits. Most probably temporal and spatial resolution deficits, as reported here, reflect damage to both pre and postchiasmatic pathways. In the pre-chiasmatic pathway however, there is no segregation between small and large axons and considering only the second hypothesis, it is hard to imagine how prechiasmatic lesions could cause discrete deficits. Perhaps the large number of axons serving foveal vision in the optic nerve can account for the mild consequences of a lesion affecting a portion of these axons.

## 8. Summary

In summary, the data presented here suggest that the visual tests in this report are valid measures for a large population of MS patients and that the tests are not only equally sensitive to demyelination in either of the two visual pathways vulnerable to this condition in MS, but that they also provide complementary information about the integrity of those pathways. In this respect, we agree with Marx et al. [53] who argued that a battery of visual tests should incorporate spatial as well as temporal stimuli to detect dysfunction in multiple sclerosis. Together the simple tests we employed were likely to reveal visual problems in as many as 50% of the cases in a hospital population of MS patients who are not clinically considered to be visually handicapped by their disease.

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