tasks as the monkeys with two differences. Humans were not trained but responded to verbal instructions. There were no reinforcements for "correct" responses and hence no feedback. In the color discrimination task, the humans simply attempted to release the bar upon a subjectively determined white.

**Results.** The graph in Fig. 1 shows the difference between the color of the test stimulus selected as "white" paired with red during the adaptation and the corresponding green-paired stimulus on that day for both monkey and human observers over the 6 days. For monkeys, on each day but the second day for the second monkey, differences in average test settings were in the direction consistent with human performance under conditions which produced a McCollough effect upon achromatic stripes. The human data are also graphed for comparison. In order to test for significance, t tests were performed on the individual observers, with the average data for each day used as raw scores in matched comparisons of red vs. green adaptation orientations. All tests were significant (monkey 1, t(5) = 5.64, less than 0.005; monkey 2, t(5) = 2.12, less than 0.05; Human 1, t(5) = 4.5, less than 0.005; Human 2, t(5) = 6.13, less than 0.001; all one-tailed tests). The major differences between human and monkey performance was quantitative rather than qualitative. The magnitudes of the human aftereffects appeared larger.

**Discussion.** Psychophysical investigations have repeatedly demonstrated the similarities between human and rhesus visual physiology and performance. Our data show that this similarity extends to the McCollough effect, where we have found that monkeys behave in a manner demonstrating orientation-specific chromatic aftereffects. Thus these data indicate that the neural basis of the McCollough effect may be pursued profitably by the physiological study of the monkey's visual system in order to determine the involvement of achromatic and spatially specific cortical neurons in these phenomena.

We thank Dr. Keith White, Dr. David Bender, and Dr. Werner K. Noell for their help and advice with this project.

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**Key words:** McCollough effect, color vision, visual perception, monkey

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We measured grating contrast sensitivity over a range of 1 to 25 cd/deg for vertical, horizontal, and both oblique orientations in eight "definite" multiple sclerosis patients and 11 controls, using a two-alternative forced-choice technique. Only two or eight patients did not show orientation-specific losses of contrast sensitivity. Six of eight patients had significant orientation-specific losses in one or other single eye (p < 0.05), and two of eight had significant orientation-specific differences between the left and right eyes. Some patients' orientation-specific losses were restricted to lower spatial frequencies, sparing high spatial frequencies and leaving Snellen acuity unaffected. The disorder is different from the oblique effect and from meridional amblyopia, since these affect high spatial frequencies more than lower spatial frequencies. Since there is no separate neural mechanism for oblique eye movements, these orientation-specific losses cannot be due to disordered eye movements, at least in the patients whose contrast sensitivity was depressed much more for an oblique than for the horizontal or vertical orientation. We propose that the responsible pathology is chiefly at, or central to, visual cortex. Nevertheless the disorder is puzzling because the existence of orientation-specific defects in multiple sclerosis (a disease characterized by focal demyelination) would be most easily explained in terms of some gross
physical correlate of orientation-specificity in cortical neurons, and no physiological evidence for this has yet been described.

Since Bodis-Wollner's introduction of the sine-wave grating test into clinical studies,1 it has been found that multiple sclerosis causes one of several different pathologies that can degrade visual contrast sensitivity to lower spatial frequencies while sparing sensitivity to high spatial frequencies.2 Patients with such pathologies complain of poor vision, although they may have normal Snellen acuity. We found that in a substantial proportion of multiple sclerosis patients (11 of 48), contrast sensitivity was degraded, but the loss was restricted to a narrow band of spatial frequencies centered on 10 to 20 cy/deg. In addition, a few patients (three of 48) lost contrast sensitivity for low spatial frequencies (1 to 9 cy/deg), while high spatial frequencies were spared. In the present study we searched for losses of contrast sensitivity that were specific to both spatial frequency and orientation.

Methods
Stimulus. Sine-wave grating patterns were conventionally generated on a Hewlett-Packard CRT (model 1321, P31 phosphor). The 33 cm diameter circular screen was of mean luminance 37 cd/m², had a dark surround, subtended 6.5°, and was viewed at 290 cm.

Psychophysical test procedure. A trial consisted of the following sequence: (1) the screen was dark for 0.5 sec; (2) the screen returned to a mean luminance of 37 cd/m² for 400 msec (first test interval); (3) the screen was dark for 2 sec; (4) the screen returned to a mean luminance of 37 cd/m² for 400 msec (second test interval); (5) the screen was dark until the subject pressed a response button, whereupon the screen returned to a mean luminance of 37 cd/m² (blank screen). A grating was displayed on the screen throughout either the first or the second test interval. During the other test interval the screen was blank, and subjects were told this. Whether the grating was in the first or second interval was electronically randomized. Subjects were instructed to judge whether the grating was in the first or second interval and to guess if they were uncertain. No feedback was provided. Ten trials were run for each contrast. Contrast was varied in 1 dB steps. Contrast for 75% correct (i.e., threshold) was obtained from regression lines plotted on probability paper. Short rests were allowed on request, and these were frequent. A complete test required at least four sessions of 1.5 hr. Our chief findings were confirmed by bringing subjects back for further testing.

Patients and controls. We tested eight "clinically definite"3 patients and 11 control subjects. Control subjects were not rejected for spherical refractive error or astigmatism, but refractive errors were corrected during testing. All subjects were examined for nystagmus and pupillary abnormalities. The patient of Fig. 1 showed internuclear ophthalmoplegia on rightward gaze, so that if he looked to the right, the environment seemed to jiggle and he might have double vision. On the other hand, no nystagmus was evident when he was gazing straight ahead as in the conditions of our experiment. The patient of Fig. 2 showed bilateral internuclear ophthalmoplegia on sideways gaze. On the other hand, no nystagmus was evident when she was gazing straight ahead as in the conditions of our experiment. None of the six other patients tested showed nystagmus when gazing straight ahead.

The standard deviations (S.D.s) shown by vertical bars in Fig. 1 are for controls and were obtained as follows. The ratios of thresholds in the left and right eyes were calculated separately for each orientation and spatial frequency for each
Fig. 2. A, Contrast threshold of left eye vs. spatial frequency for four orientations of the test grating. B, Ratios between contrast thresholds for vertical and horizontal gratings vs. spatial frequencies.

Open circles, Multiple sclerosis patient; filled circles, control subjects (lines show mean and SD for 22 eyes). This patient’s Snellen acuity was 20/60 for the left eye shown. Disability status 7. Bilateral internuclear ophthalmoplegia. Kurtzke11 pyramidal 4, cerebellar 2, brainstem 3, sensory 3, bowel and bladder 3, others 0.

individual control. These left-to-right ratios were then averaged over subjects, and the S.D.s based on the variation between subjects were calculated.

Results

Control subjects: contrast sensitivities for different orientations. We confirmed our previous report2 that intersubject variability of contrast threshold is substantial in control subjects. For example, at 5 cy/deg, contrast threshold had an S.D. of about 2:1. Intersubject variability was lowest at 1 cy/deg.

Patients: orientation-specific differences between the left and right eyes. Fig. 1 shows an orientation-specific difference of contrast sensitivity between left and right eyes. At high spatial frequencies and also at low spatial frequencies this patient had similar contrast sensitivities for all orientations. Near 10 cy/deg, however, the right eye was about 20 times less sensitive than the left eye. This difference was restricted to the horizontal and the 10:30 o’clock orientations; the two eyes had similar sensitivities for vertical and 1:30 o’clock orientations. Snellen acuities in the two eyes were not very different (20/30 L, 20/20 R), as would be expected from Fig. 1 where contrast sensitivities at 25 cy/deg are shown to be similar in the two eyes for all four orientations. When this patient was retested 2 months later, the orientation-specific differences of Fig. 1 were still evident.

A second patient lost sensitivity for the two obliques at 5 cy/deg, while sensitivity to the horizontal orientation was unaffected. At high spatial frequencies, sensitivities for obliques and horizontal orientations were similar, consistent with the similarity of Snellen acuities in left and right eyes (20/30 R, 20/30 L).

Patients: orientation-specific loss that was the same in both eyes. Several patients experienced orientation-specific losses that were similar in both eyes. In all, three of eight patients showed significant (p < 0.05) orientation-specific loss that was restricted to lower spatial frequencies. One patient’s orientation-specific loss was present at all frequencies.

Fig. 2, A, shows orientation-specific loss for a patient’s left eye. Sensitivity to both obliques and horizontal orientations was degraded, while visual sensitivity to the vertical orientation was spared. This orientation-specific loss was restricted to spatial frequencies near 7 cy/deg; at low and at high spatial frequencies visual sensitivity to all orientations was similar. Fig. 2, B, compares control means and S.D.s with the patient’s data of Fig. 2, A, and confirms that there was no significant difference in sensitivity to horizontal and vertical gratings for control subjects but that the patient showed a difference near 7 cy/deg. Similar levels of significance were obtained when the patient’s relative sensitivities to vertical and oblique orientations were separately plotted.

Discussion. We previously reported that some multiple sclerosis patients experience orientation-specific losses of contrast sensitivity even in the presence of normal Snellen acuity.4 This preliminary evidence was obtained by the method of limits. The present study verifies and extends this finding by means of a considerably more rigorous
and thorough psychophysical method. We note that an independent study in Bodis-Wollner's laboratory,\(^5\) using the quite different technique of evoked potential recording, has demonstrated orientation-specific delays in multiple sclerosis.

We previously found that 20 of 48 multiple sclerosis patients had lost contrast sensitivity, whereas Snellen acuity was spared.\(^2\) Since we tested with vertical gratings only, we may have failed to detect visual damage in some patients whose contrast losses were restricted to oblique or horizontal orientations. Again, some patients who did not show evoked potential delays to checkerboard pattern stimulation\(^6\) \(^7\) may have been missed because only one orientation of the pattern was used.

For the following two reasons our finding cannot be attributed to either the oblique effect or meridional amblyopia. (1) Orientation-specific differences between left and right eyes can be as large as 20:1. This is much larger than differences associated with the oblique effect or with meridional amblyopia.\(^4\) (2) In meridional amblyopia and the oblique effect, contrast sensitivity losses are restricted to high spatial frequencies, with comparative sparing at lower spatial frequencies.\(^8\) \(^9\) We find, however, that multiple sclerosis can produce the converse effect, where contrast losses are restricted to lower spatial frequencies and high spatial frequencies are comparatively spared (e.g., Figs. 1 and 2).

Eye movement abnormality is one possible explanation for our findings. In order to explore this possibility we took advantage of the finding that neural mechanisms exist that control horizontal and vertical eye movements, but there is no separate mechanism for obliques.\(^10\) A loss for horizontal plus obliques that spared the vertical (Fig. 2) could not be explained in terms of disordered vertical and/or horizontal eye movement mechanisms. Again, Fig. 1 could not be explained entirely in terms of disordered horizontal and/or vertical mechanisms. A separate argument is that it is difficult to see how disordered eye movements could produce a loss of sensitivity restricted to a middle-spatial-frequency band. We therefore argue that disordered eye movements could not provide a complete explanation for our findings.

Finally, we turn to the possible site of the orientation-specific pathology. We attribute the disorder to cortical neurons for the following two reasons. (1) Orientation-specific neurons are not found peripheral to cortex in cat and monkey. (2) Grating adaptation transfers interocularly in man. Nevertheless, our finding of orientation-specificity is puzzling. Multiple sclerosis is associated with focal plaques of demyelination, and thus orientation-specific losses are more straightforwardly explained if we assume that, in area 17 or 18, cortical neurons exist whose orientation specificity has some gross physical or biochemical correlate (e.g., cortical location or axon diameter). Alternatively, we might assume that interconnections exist between cortical neurons tuned to the same orientation. There is as yet no physiological evidence to support these two speculations. An alternative possibility is that the responsible pathology is central to area 18, but at present comparatively little is known of the relevant neurophysiology.

Our final point is that the orientation-specific differences between the left and right eyes that we observed in some patients implies pathology affecting input to binocularly driven cortical neurons or (if we assume that they contribute to grating detection) pathology affecting monocularly driven cortical cells. Orientation-specific losses that are similar in both eyes are (if we discount coincidence) consistent with pathology affecting binocularly-driven neurons centrally to the point of binocular convergence.

We thank the patients and control for their cooperation over many hours of testing. We are indebted to Dr. David B. King for kindly referring patients. We thank Dr. D. H. Hubel for pointing out the possible effect of abnormal eye movements early in this study and Dr. T. Bahill for his comments on oblique eye movements. We thank Drs. I. Bodis-Wallner, M. Cynader, A. M. Halliday, and S. G. Waxman for criticizing an earlier draft of the manuscript.

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Key words: multiple sclerosis, visual acuity, contrast, spatial frequency, Snellen test

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Eye movements of the blind. R. JOHN LEIGH AND DAVID S. ZEE.

We investigated a group of patients who were blind because of disease affecting the anterior visual pathways. All subjects showed an inability to maintain steady eye position, with a consequent jerk nystagmus. Blindness from birth was associated with an impaired vestibulo-ocular reflex and inability to voluntarily initiate saccades, although quick phases of nystagmus were maintained. Acquired blindness was associated with relatively preserved vestibulo-ocular responses and the ability to initiate voluntary saccades and smoothly track self-moved targets. Certain features of the eye movements of the blind are similar to those due to cerebellar dysfunction.

Certain aspects of oculomotor control have been better characterized by studying the eye movements of normal individuals made during darkness (the "open loop" condition). We wondered how chronic deprivation of visual feedback due to blindness might affect the neural guidance of oculomotor movements. Bartels' noted that the blind invariably show oculomotor abnormalities and that those who had lost vision at an early age lacked the ability to voluntarily direct their eyes. Ohm² noted both pendular and jerk nystagmus, which he ascribed to a vestibular imbalance. We have attempted to assess how visual feedback influences the development and maintenance of function of each of the specific oculomotor subsystems (saccadic, pursuit, and vestibular).

Subjects and methods. We observed the eye movements of 18 blind subjects, 18 through 61 years of age, who were either employed or undergoing training at a vocational center for the blind. Seven subjects had no light perception (four since birth), and none had visual acuity better than 20/200. Loss of vision was due to a variety of abnormalities of the anterior visual pathways, including retrolental fibroplasia, glaucoma, trauma, and congenital rubella. We supplemented our clinical observations with motion pictures. We had only limited success with electro-oculography (EOG), since the ocular diseases from which most subjects suffered usually attenuated the corneoretinal potential. When EOG was possible, an approximate calibration was obtained with ±45° used for extremes of lateral gaze.

Results. All subjects showed a continuous nystagmus, with slow and quick phases usually in the horizontal plane. While they attempted to maintain their eyes in the primary position, the nystagmus would typically be of high frequency (up to 5 Hz), and in many subjects it would, over the course of 20 or 30 sec, reverse direction. In one subject with partial visual loss since an early age, the nystagmus was rapid and downbeating; in another with partial visual loss due to retrolental fibroplasia, a primary torsional component was present. In several subjects with total blindness since an early age, slower vertical oscillations appeared to be superimposed upon a predominantly horizontal nystagmus. In all subjects, attempts to hold eccentric horizontal or vertical eye position caused the nystagmus to become more prominent and "gaze paretic" in type, with exponential drifts back to some null position interrupted by corrective saccades (Fig. 1, A).

Rotational stimuli produced convincing vestibulo-ocular responses in eight subjects, five of whom had some residual vision, two of whom had lost all but light perception during their teens, and one who had been completely blind for 20 years (Fig. 1, C). Subjects who had been totally blind since birth appeared to have either an absent or markedly reduced vestibulo-ocular response, although they described normal sensations of self-rotation. Voluntary saccades were preserved in those subjects who either had partial preservation...