Visual Dysfunction between Migraine Events

Allison M. McKendrick,1,2 Algis J. Vingrys,1 David R. Badcock,3 and John T. Heywood4

PURPOSE. To evaluate interictal visual dysfunction in persons with migraine in terms of spatiotemporal selectivity and location within the visual pathways.

METHODS. The vision of a group of 15 persons who had experienced migraine with aura was compared with that of 15 normal age-matched control subjects. A range of thresholds was measured to evaluate precortical (background modulation, contrast thresholds for static, and moving stimuli), area V1 (orientation discrimination and motion discrimination thresholds), and higher order (global dot motion thresholds) visual processes. Testing was performed centrally and at 10° in the superior visual field. For each of the tests, the spatial and temporal parameters of the stimuli were selected to bias detection toward either parvocellular or magnocellular visual mechanisms.

RESULTS. No defects were found for parvocellular processes. Significant (P < 0.05) losses were apparent with the temporal background modulation method (16 Hz), orientation discrimination (0.5 cyc/deg), and global dot motion tasks.

CONCLUSIONS. Both cortical and precortical visual dysfunction were identified in migraine group 7 days after the headache. This loss was selective for targets with temporal modulation of approximately 16 Hz. (Invest Ophthalmol Vis Sci. 2001;42:626–633)

Migraine is a common neurologic disorder affecting between 10% and 15% of the population.1 Visual symptoms are common, with most experiencing photophobia and mild visual disturbances.2 A subgroup of persons who experience migraine with aura have more severe visual symptoms, such as positive (for example, flashes of light, stars, zig-zags) or negative (for example, central or paracentral blind spot) scotoma.2,3 Aura may also include other neurologic symptoms, such as hemiparesis or dysphasia.2,3

Visual aura is thought to arise due to a change in cortical neural function known as cortical spreading depression (CSD).4 Decreases in regional cerebral blood flow have been demonstrated in posterior areas of the cortex5,6 and appear to spread across the cortex at rates similar to those in experimental CSD.6 These physiological changes raise the possibility that changes in visual processing may be apparent even after an episode has subsided. Anomalies of cortical visual processing reported in migraineurs include heightened levels of visual discomfort and aversion when viewing patterns designed to induce visual illusions.7,8 Decreased reaction times to orientation detection and temporal order judgment tasks have also been demonstrated,9 although a recent report failed to replicate this finding.10

Visual anomalies in migraineurs may also arise from precortical dysfunction. Coleston et al.11 report anomalies using a background modulation method (BMM). This task measures the threshold luminance of a spot for its detection against either a spatially or temporally modulated background12 and is thought to be processed monocularly, because the characteristic band-pass spatial and temporal tuning curves are flat under dichoptic viewing conditions.13,14 Visual field assessment has also revealed a large number of individuals with unilateral visual field loss consistent with the possibility of a precortical loss.15–17 In a number of the studies that report precortical losses, investigators have used stimuli that are temporally modulated by either motion or flicker.11,17–20 Deficits identified with flickering stimuli are common to a number of ocular diseases, including glaucoma,21–24 and are suggestive of a disorder of the magnocellular visual pathways. Of interest is the reported association of migraine and glaucomatous neuropathy,25–28 although this finding is not universal.29

Therefore, the literature suggests that both cortical and precortical visual processing anomalies occur in migraine that may be more readily detected using flickering or moving stimuli. The purpose of this study was to systematically explore, in a single group of patients with migraine, evidence for cortical versus precortical loss, evidence for temporal processing deficits, and whether foveal or peripheral eccentricities are more affected. Addressing these questions psychophysically relies on the assumption that the tasks are measuring performance of separate neural streams at various levels of the visual pathway. The location of the proposed neural basis of the tasks used in this study has been derived from studies of single-cell neurophysiology30,31 and from observations of behavior subsequent to discrete lesions at various levels of the visual pathway32–35 or inferred from psychophysical studies.13,14,36–39

We chose to explore two groups of visual tasks, measures of low-level spatiotemporal processing and motion processing, which are summarized in Table 1. To assess spatiotemporal processing at precortical levels we used the background modulation method,12 described by Coleston et al.11 Cortical processing of pattern was assessed using an orientation discrimination task, because substantial orientation tuning of neurons is first apparent in cortical area V1.30

Three tasks were used to assess motion processing: motion detection, motion discrimination, and a global dot motion (GDM) task. Motion detection measures the minimum contrast required to detect a moving target and assesses performance early (retina to V1); direction-selective neurons are not found at this level of the visual pathway.32 Direction-selective units are first found in cortical area V1; therefore, measuring threshold contrast to discriminate direction of motion evaluates the function of V1 or higher.32–35 A GDM task was used to selectively measure performance at higher levels of the motion pathway. The GDM task has been shown to be very sensitive to damage in the middle temporal (MT) area32–35,40; thus, abnormal GDM performance can arise from dysfunction at MT or higher or from abnormal magnocellular pathway function earlier in the visual system. A GDM deficit without a motion detection deficit indicates a cortical locus.
In an attempt to independently assess the magnocellular and parvocellular pathways, we chose stimulus parameters to bias detection toward these pathways: low spatial and higher temporal frequency for the magnocellular system\(^{36}\) and higher spatial and lower temporal frequency for the parvocellular system\(^{37}\) (Table 1). Although the main input to motion detection and discrimination is magnocellular, some parvocellular pathways provide inputs to orientation discrimination and can be assessed.\(^{42}\) Because lesions of the magnocellular and parvocellular pathways in primates affect contrast sensitivity, we included a contrast sensitivity task.\(^{36,37}\)

### METHODS

#### Subjects

We tested 15 patients who had had episodes of migraine with aura (age range, 23–35 years) as well as 15 normal control subjects (age range, 22–31) using inclusion criteria provided elsewhere.\(^{17}\) All participants had a neurologic examination and migraine with aura was diagnosed using the criteria of the International Headache Society.\(^{13}\) Visual field results for these subjects have been reported.\(^{17}\) The research was approved by the Human Research Ethics Committee of the Department of Optometry and Vision Sciences, University of Melbourne, and complied with the tenets of the Declaration of Helsinki. All subjects gave written informed consent before participating in the study.

Each subject performed four 2-hour test sessions at least 7 days after a headache event. Subjects received approximately 10 minutes of training on all tasks and were instructed to take rest breaks as required. For each task, the order of stimulus presentation and location (foveal or \(10\)° superior visual field) was randomized. All tasks were performed monocularly. We have previously reported visual field performance for this group of subjects and selected the test eye for the migraine group as the eye with the worst visual field results.\(^{17}\) For the control group the test eye was selected randomly. Informal assessment of fixational stability was performed by direct viewing, and all subjects appeared to be stable. Because lesions of the magnocellular and parvocellular pathways in primates affect contrast sensitivity, we included a contrast sensitivity task.\(^{36,37}\)

#### Table 1. Tasks Used to Assess Visual Function and Results for Migraine and Control Groups

<table>
<thead>
<tr>
<th>Stimulus Configuration</th>
<th>Fovea</th>
<th>Periphery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Migraine</td>
<td>Control</td>
</tr>
<tr>
<td>Precortical magnocellular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast sensitivity (% contrast)</td>
<td>3.46 ± 0.86</td>
<td>3.24 ± 0.92</td>
</tr>
<tr>
<td>16 Hz</td>
<td>t-test: (t = 0.67; df = 28; P = 0.51)</td>
<td>268.20 ± 72.88</td>
</tr>
<tr>
<td>BMM thresholds (trolands)</td>
<td>16 Hz</td>
<td>261.98 ± 77.64</td>
</tr>
<tr>
<td>Motion detection (% contrast)</td>
<td>1 unc/deg.</td>
<td>1.78/2.25/2.50</td>
</tr>
<tr>
<td>8 Hz</td>
<td>Fischer exact test: (P = 0.38)</td>
<td>3.39/0.48/5.66</td>
</tr>
<tr>
<td>Precortical parvocellular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast sensitivity (% contrast)</td>
<td>2.92/2.15/3.37</td>
<td>3.46 ± 2.42</td>
</tr>
<tr>
<td>2 Hz</td>
<td>t-test: (t = 1.00)</td>
<td>141.39 ± 50.39</td>
</tr>
<tr>
<td>BMM thresholds (trolands)</td>
<td>4 unc/deg.</td>
<td>97.49 ± 38.24</td>
</tr>
<tr>
<td>Motion detection (% contrast)</td>
<td>4 unc/deg.</td>
<td>4.05 ± 1.63</td>
</tr>
<tr>
<td>1 Hz</td>
<td>t-test: (t = 0.76; df = 28; P = 0.46)</td>
<td>12.5 ± 20.64</td>
</tr>
<tr>
<td>1 unc/deg.</td>
<td>1.38 ± 0.63</td>
<td>1.18 ± 0.61</td>
</tr>
<tr>
<td>1 Hz R-G</td>
<td>t-test: (t = -0.89; df = 28; P = 0.38)</td>
<td>Fischer exact test: (P &lt; 0.001)</td>
</tr>
<tr>
<td>Cortical magnocellular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orientation discrimination (degrees)</td>
<td>2.90 ± 1.01</td>
<td>1.85 ± 0.76</td>
</tr>
<tr>
<td>0.5 unc/deg.</td>
<td>t-test: (t = -3.21; df = 28; P = 0.003)</td>
<td>3.81/4.38/6.54</td>
</tr>
<tr>
<td>Motion discrimination (% contrast)</td>
<td>2.21 ± 0.66</td>
<td>2.00 ± 0.85</td>
</tr>
<tr>
<td>1 unc/deg.</td>
<td>t-test: (t = 0.76; df = 28; P = 0.46)</td>
<td>Fischer exact test: (P &lt; 0.001)</td>
</tr>
<tr>
<td>8 Hz</td>
<td>t-test: (t = 0.76; df = 28; P = 0.46)</td>
<td>Fischer exact test: (P &lt; 0.001)</td>
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<tr>
<td>GDM (% coherence)</td>
<td>23.1 ± 9.1</td>
<td>13.4 ± 3.6</td>
</tr>
<tr>
<td>Cortical parvocellular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orientation discrimination (degrees)</td>
<td>0.85 ± 0.43</td>
<td>0.80 ± 0.42</td>
</tr>
<tr>
<td>4 unc/deg.</td>
<td>t-test: (t = -0.34; df = 28; P = 0.74)</td>
<td>Fischer exact test: (P = 0.46)</td>
</tr>
<tr>
<td>Motion discrimination (% contrast)</td>
<td>4.24 ± 2.84</td>
<td>3.97 ± 2.91</td>
</tr>
<tr>
<td>1 unc/deg.</td>
<td>t-test: (t = 0.26; df = 28; P = 0.79)</td>
<td>Fischer exact test: (P = 0.36)</td>
</tr>
<tr>
<td>1 Hz R-G</td>
<td>t-test: (t = 0.33; df = 28; P = 0.74)</td>
<td>Fischer exact test: (P = 0.36)</td>
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</tbody>
</table>

Tasks are arranged according to the earliest part of the visual pathway known to be capable of performing the measurement (precortical or cortical) and according to the proposed neural pathway likely to dominate perception of the stimuli (magnocellular or parvocellular). Justification for such classification is detailed in the text. Results are given as the mean (±SD) for those measures that were normally distributed. Data that failed a normality test (Kolmogrov–Smirnov test: \(P < 0.05\)) are presented as the 25th quantile/median/75th quantile. MWRs, Mann–Whitney rank sum test. Significant differences have been shown in bold type.

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\* This stimulus was included in the magnocellular group because of the rapid onset and offset of presentation.

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sometime afterward. All subjects (control and migraineurs) were asked to complete a headache diary for the duration of the study, and none reported experiencing a migraine either during the tests or in close succession (<24 hours) to any of the test visits.

Visual performance can be substantially affected by pupil size: larger pupils increase the retinal illuminance and alter the level of aberration. Because differences in pupil size and responsiveness have been documented in migraineurs, all testing was conducted with dilated pupils (0.5% Tropicamide; Alcon, French’s Forest, New South Wales, Australia). Testing began 25 minutes after the first drop, and drops were administered at 40-minute intervals to ensure a stable pupil size. Pupil size during a session did not differ in any subject, and no significant difference was found between the migraine and control groups (7.84 ± 0.23 mm versus 7.78 ± 0.15 mm; analysis of variance [ANOVA]; P > 0.05) in the dilated pupil size. Dilated pupils result in a decreased retinal image contrast at higher spatial frequencies. Because we used stimuli of low or moderate spatial frequency (0.5 or 4 cyc/deg), and because no difference in pupil size was present between our two groups, we assumed the effect of dilation would be similar in each group. None of our migraine subjects reported photophobia after dilation, because they were all between migraine episodes. However, because we did not formally assess photosensitivity, we cannot rule out the existence of such effects in our subjects.

Stimuli
Stimuli were presented on a gamma-corrected color TV monitor (HM-4731-D; Hitachi, Tokyo, Japan) driven by a graphics card (VSG 2/3; Cambridge Research Systems, Kent, UK) housed in an IBM-compatible computer. At maximal output, the guns of the monitor had 1931 Commission Internationale de l’Eclairage (CIE) x, y, and Y coordinates of 0.603, 0.355, and 9.7 candelas (cd)/m² for the red gun; 0.289, 0.594, and 37.3 cd/m² for the green gun; and 0.151, 0.071, and 5.8 cd/m² for the blue gun, respectively. The white point was set at the 50% output level for each of the guns, giving x, y, and Y coordinates of 0.302, 0.316, and 26.4 cd/m², respectively. For the background modulation stimuli only (described later) the VSG 2/3 digital signal processor (DSP) was used. These stimuli were achromatic with a mean luminance of 75 cd/m². For our testing, we chose spatiotemporal frequencies that would bias detection to magnocellular processes (see Introduction).

Contrast Sensitivity
Detection thresholds were measured using 3.5° Gabor patches (sine wave carrier, windowed in a gaussian envelope) of the following spatiotemporal frequencies: 0.5 cyc/deg, 16 Hz and 4 cyc/deg, 2 Hz. In all cases the temporal modulation was achieved with drift to maintain consistency with background modulation methods, and because losses have been identified in migraineurs by using drifting stimuli. The luminance of any given pixel (x, y) within the Gabor stimulus was described by

\[
a \sin(2\pi a x + \theta) \cdot \exp \left( -\frac{x^2}{2\sigma_x^2} - \frac{y^2}{2\sigma_y^2} \right) \]

where a is the amplitude of the sine wave, \( \sigma_x \) and \( \sigma_y \) are the space constants in the x and y planes (both equal to 1.167°), and \( \omega \) determines the period of the sine wave. Stimuli were ramped on and off in a symmetrical raised-cosine temporal envelope with a stimulus duration of 1 second. A two-interval forced-choice (2-IFC) procedure was used, with one interval displaying the stimulus and the other a uniform field of mean luminance. Subjects were required to choose the interval containing the stimulus.

Background Modulation Methods
Detection thresholds were measured for a 3.5° luminance spot, which drifted (15 deg/sec) over a spatially or temporally modulated (90% contrast) background. Our stimulus parameters were selected to replicate those used by Coleston et al. who reported anomalies in migraineurs using the background modulation methods (BMM). Figure 1 is a schematic of the luminance spot drifting perpendicularly at 15 deg/sec over a background sine wave grating of variable spatial frequency.

Orientation Discrimination
Vertically oriented Gabor patches (equation 1, \( \sigma_x \) and \( \sigma_y \), both equal to 1.167°) of 0.5 cyc/deg and 4 cyc/deg and 90° contrast were presented for 500 msec within a temporal square-wave envelope to measure orientation discrimination. This spatial profile was the same as that used to assess contrast thresholds (described earlier). A 2-IFC procedure presented a vertical patch in one interval and a tilted patch (clockwise from vertical) in the other. The subject’s task was to choose the tilted patch; the degree of tilt was varied from trial to trial.

Motion Detection and Discrimination
Motion thresholds were measured using Gabor patches of the same extent and luminance profile as given by equation 1. We used both isoluminant red–green (R-G) and achromatic targets of 1 cyc/deg, 1 Hz and 1 cyc/deg, 8 Hz and 4 cyc/deg, 1 Hz and 4 cyc/deg, 8 Hz. Our drift rate of 8 Hz is based on Metha et al. who were unable to measure thresholds for faster isoluminant stimuli beyond 6° eccentricity; however, later we will discuss limitations caused by choosing this rate. Isointensities were determined from the subjective point of minimum drift, a method of adjustment. A 2-IFC procedure presented a stationary Gabor patch in one interval and a drifting Gabor patch in the other, for the motion-detection task. Subjects were required to choose the drifting patch. Target contrast was varied from trial to trial. The motion discrimination task presented a Gabor patch drifting to the left in one interval and to the right in the other, with subjects being required to choose the interval containing the rightward drift.

Global Dot Motion
Motion-coherence thresholds were tested using a random-dot stimulus in which a percentage of dots (signal) move in a common direction.
while the remaining dots (noise) move in random directions. The signal dots are randomly varied between successive frames, which means that, at low signal dot levels, the probability that the same dot will carry the global motion signal over successive frames is small. This ensures that the local motion cue cannot be used over successive frames (tracking of a single dot) to establish the global motion percept. The stimuli consisted of an eight-frame global dot motion (GDM) sequence with frame duration being 50 msec. The spatial step size (0.3°) produced a stimulus speed of 6 deg/sec, which is within the optimal range for MT cells.48 At any time, a total of 100 dots (0.2°, density of 0.88 dots/deg²) were shown within a circular viewing aperture of 12°. Each dot had a luminance of 26 cd/m² and was seen on a 17-cd/m² background. A 2-IFC procedure comprised the control interval, with dots moving in random directions, and the test interval, which had a variable number of signal dots (coherence ratio percentage), moving upward. Subjects were required to identify the interval with the upward signal.

### Threshold Procedure

Thresholds for all tasks were established using 2-IFC procedures in the fovea and at 10° in the superior visual field. With the exception of the orientation discrimination task a three-up, one-down staircase was used to establish threshold.49 The two intervals were separated by 500 msec, and thresholds (79% correct) were estimated as the geometric mean of the last six (of nine) reversals using a 0.1-log-unit step (contrast detection, motion detection/discrimination, background modulation method) or one-dot step (motion coherence task) size.

A method of constant stimuli (MOCS) containing seven levels of tilt (clockwise from vertical) was presented randomly twenty times at each level to establish orientation thresholds. Hit rates from the MOCS were fit with a Weibull function,

\[ P_c(\theta) = 1 - (1 - \gamma) e^{-(\theta/a)^b} \]  

where \( \theta \) is the angle of tilt, \( P_c \) is the proportion correct when the angle is \( \theta \), \( \gamma \) is the correction for guessing (equal to 0.5), \( a \) is the threshold angle (81.6% level), and \( b \) is an index of the steepness of the psychometric function. Fitting was achieved by minimizing the \( \chi^2 \) statistic using a Marquardt-Levenberg algorithm, weighted by the variance at each of the seven levels. The thresholds (81.6%) returned from these fits were used for comparative purposes.

### Analysis

Experimental results were analyzed in terms of between-group differences (Table 1) and individual departures from age-matched norms (Table 2). When the group data had gaussian characteristics (Kolmogrov-Smirnov test, \( P > 0.05 \)) with equal variance, comparisons were performed using a two-tailed Student’s t-test. In other cases a Mann-Whitney rank sum test was used. To maintain an \( \alpha \) of 0.05 in the presence of multiple comparisons, a Bonferroni adjustment procedure was applied, and \( P < 0.004 \) was adopted as the significance level for each test.

To analyze individual migraine subject performance, we used the control subject data to determine a reference interval51 that encompassed the values obtained from the majority of the normal subjects. Migraine subjects with performance outside the reference interval were identified. For those tests in which the control data had gaussian characteristics we chose a parametric approach where a 95% reference interval was chosen and calculated as the mean ± 1.96 SD. For those tasks where the control data failed a formal test of non-normality (Kolmogrov-Smirnov test, \( P > 0.05 \)), the reference interval was chosen using an empiric percentile approach.51 In this case, the limits of the reference interval were defined by the 7th and 93rd quantiles, which, given our sample size of 15, meant that performance equal to or worse than the worst normal or better than or equal to the best normal fell outside our reference interval. It should be noted that performance outside the reference interval does not necessarily imply abnormality, because with small samples there is considerable uncertainty associated with the limits of the reference interval.\(^{51,52}\)

Our intention was to achieve a qualitative assessment of patterns of dysfunction rather than a precise quantitative value.
RESULTS

The results of the group comparisons for all stimulus conditions appear in Table 1. Significant differences between groups are denoted in bold font and include the BMM task (16-Hz, periphery), the orientation discrimination task (0.5 cyc/deg, fovea), and the GDM task (fovea and periphery). Table 1 presents 26 test conditions, and the results for some of these tasks are presented graphically in Figures 2 (BMM), 3 (orientation), and 4 (GDM). Individual data are presented in all three figures, along with group means (± SEM) in Figures 3 and 4: Subjects experiencing migraines are shown by the filled symbols and control subjects by the open symbols.

For the BMM task (Fig. 2) with the 16-Hz background, two migraineurs were unable to see the spot foveally, even at the brightest spot luminance (Fig. 2, gray symbols). This increased to nine subjects with peripheral viewing (significant difference between the number of subjects in each group who could perform the task, Fischer exact test: $P < 0.001$).

Analysis of individual performance is shown in Table 2 for foveal and peripheral viewing, respectively, where subjects whose performance fell outside the control reference limits have been identified. In this analysis we also included the orientation discrimination task in these tables, because the mode of presentation (0.5 cyc/deg, 500-msec square wave) makes it plausible that this stimulus is also processed by magnocellular pathways. Because we did not find any significant losses for parvocellular tasks (isoluminant R-G, high spatial, processed by magnocellular channels. We have also included the orientation discrimination task in these tables, because the mode of presentation (0.5 cyc/deg, 500-msec square wave) makes it plausible that this stimulus is also processed by magnocellular pathways. Because we did not find any significant losses for parvocellular tasks (isoluminant R-G, high spatial,
low temporal frequencies), these have not been included in Table 2.

The analysis presented in Table 2 is designed to present a qualitative, rather than a strictly quantitative, assessment of patterns of deficit. Indeed, our sample size is too small to quantify precisely the relative risk of cortical versus precortical dysfunction in migraine. Inspection of Table 2 reveals, however, the following trends. There were very few subjects whose performance fell within the control reference limit for all tasks. However, because multiple tests were being performed, the probability of finding a significant observation on one test was relatively high. It is therefore important to explore common patterns of deficit. With foveal viewing, difficulty performing the GDM task is common, sometimes in isolation, but more often in the presence of difficulties with tasks processed earlier in the visual pathways. In the peripheral visual field, there is little evidence for cortical dysfunction in isolation, suggesting that limitations in cortical processing are likely to arise due to abnormalities at lower levels.

**DISCUSSION**

Our data show that vision is not normal 7 days or more after a headache in those who experience migraine with aura. Deficits were measured both foveally and peripherally, using tasks presumed to assess precortical (BMM) and cortical (orientation discrimination, GDM) function. Because deficits were identified using stimuli of low spatial and moderate temporal frequencies, it is more likely that these represent processing abnormalities of the magnocellular pathways than of the parvocellular pathways.36

Several aspects of the data require further explanation. Given the deficits for the 16-Hz BMM task and the GDM task, it may be expected that reduced contrast sensitivity would be measured for the 16-Hz stimulus, along with abnormalities in motion detection and discrimination, but this was not the case. Furthermore, our assumption of magnocellular dysfunction would suggest that motion detection for isoluminant stimuli should be normal and should be disrupted for achromatic stimuli. However, contrast sensitivity, motion detection, and motion discrimination measures were all normal.

In the case of the motion tasks, the highest temporal frequency chosen was 8 Hz, to ensure thresholds could be obtained with isoluminant targets. We subsequently determined that visual field deficits to flickering stimuli were present in several subjects only for temporal frequencies greater than 8 Hz.17 Therefore, it is possible that deficits may have been uncovered had we chosen a 16-Hz, rather than an 8-Hz, stimulus. Such frequency tuning is not entirely consistent with a magnocellular defect. Another possibility is that local magnocellular losses exist and the larger stimulus extent of the GDM and BMM tasks (12° and 8°, respectively) meant that they spanned these areas of visual field, which was not the case for the localized Gabor stimuli used with the other tasks (3.5° extent). Alternatively, it is possible that the luminance-pedestal involved in the BMM and temporal modulation perimetry tasks have conferred an advantage to these tests for the detection of migrainous visual dysfunction. Although the mechanism by which this acts is not clear, losses have been reported by Eisner and Samples,24 who used similar stimuli in patients with glaucoma.

The findings of this study agree with several other previous studies of vision in migraine that have found abnormalities by using either cortical or precortical tasks, often with flickering or moving targets. However, there are several differences between our findings and those reported in the literature. A number of previous studies have reported hypersensitivities in migraineurs that have been attributed to interruptions in cortical inhibition.8,9,53 We were unable to find any evidence for hypersensitivity in our migraine group, although our experiments were not designed specifically to consider these issues. Subjects were not required to rate their level of discomfort, nor were reaction times studied. As a consequence, we cannot rule out the possibility of heightened aversive responses in our migraine group resulting in losses of concentration and elevated thresholds. Visual discomfort in migraineurs has been demonstrated previously for foveal viewing using stimuli of 3 to 4 c/deg.8 Our measures for stimuli of 4 c/deg were all normal, at both foveal and peripheral locations. Therefore, we think it unlikely that cortical hypersensitivity to illusory stimuli was a significant factor in the visual dysfunction measured in this study. However, because hypersensitivity was not assessed directly, its influence remains unknown. Moreover, because hypersensitivity may change over time, we cannot rule out its existence closer to the headache event.

Contrast sensitivity deficits in migraineurs have been reported previously.54 Khalil and Legg report decreased contrast sensitivity in patients with a history of migraine with aura of 30 years or more, but normal performance in those with a history of migraine with aura of 10 years or less. The patients tested in this study were substantially younger, with the longest history of migraine being 25 years. If decreasing contrast sensitivity is related to migraine chronicity, it is possible that our younger subject group had not experienced sufficient migraine events for a deficit to be manifest. To investigate this issue further, we explored the relationship between the migraine characteristics of our subjects (frequency, number of lifetime attacks, duration after migraine) but were unable to find a significant relationship to any of the visual measures in this study (Spearman rank order correlation $P > 0.05$). However, this negative result should be viewed cautiously, because correlating migraine characteristics with visual dysfunction was not the purpose of our study, and the sample size was inadequate to yield a high statistical power.

The mechanism of migrainous visual dysfunction remains unclear. Current evidence supports a neural basis for the aura component of the headache, known as CSD.4 CSD results in a decrease in regional cerebral blood flow5,4 that spreads from the occipital cortex. Changes in metabolism have also been documented in persons with migraine.55,56 Although there is no evidence for ischemia as a result of CSD in uncomplicated migraine,6,6 and no obvious long-term effects of CSD induced in animal models,57 it is possible that changes in the local cellular environment may result in subtle functional changes in neural performance.

The existence of precortical dysfunction in migraineurs may seem contradictory to the cortical nature of the aura and headache. Of possible relevance to our findings is the association between migraine and glaucoma.25-26 It has been proposed that in some individuals, migraine and glaucoma may have shared vascular causative factors.58,59 Indeed, it has been demonstrated that both migraineurs and patients with glaucoma have a tendency toward abnormalities of peripheral microcirculation, as measured using nailfold capillaroscopy.59-61 Therefore, the precortical deficits measured in our migraine group may have resulted from changes in ocular vasoregulation, resulting either in functional abnormalities that are directly due to hypoperfusion or in changes to the local cellular environment that effect neural function.

Finally, any mechanism proposed to explain migrainous visual dysfunction must account for the prolonged nature of the deficits after a migraine episode. All our subjects were tested at least 7 days after headache. Furthermore, we have previously demonstrated that migrainous visual field loss can...
take up to 35 days to subside.\textsuperscript{17} Our evidence for prolonged visual anomalies in a considerable proportion of persons who experience migraine with aura suggests that the commonly held view that migraine is a benign event of cortical centers should be reassessed.

Acknowledgments

Andrew Metha provided the software for the motion detection and discrimination tasks and Mark Edwards the software for the GDM task.

References

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