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Orientation Discrimination and Contrast Detection Thresholds in Migraine for Cardinal and Oblique Angles

Marc S. Tibber, Antonio Guedes, and Alex J. Shepherd

PURPOSE. To determine whether orientation discrimination deficits in migraine, which have been found to depend on the spatial frequency of the stimulus, are due to precortical dysfunction or to abnormal patterns of orientation tuning at cortical loci. Further, to assess whether any cortical involvement is restricted to the striate cortex or whether higher cortical areas are also involved. Orientation-specific abnormalities would provide evidence of cortical dysfunction.

METHODS. Orientation-discrimination and contrast-detection thresholds were assessed at cardinal (0°) and oblique (45°) orientations using explicit lines defined by Gabor patches. To test for extrastriate dysfunction, participants made orientation judgments using virtual lines defined by two widely spaced circles. Migraine history, migraine triggers, and pattern sensitivity were also assessed. Twenty migraineurs (10 with visual aura, 10 without) and 20 control participants were tested.

RESULTS. Orientation-discrimination thresholds were lower for discriminations made about the cardinal axis than for discriminations made about the oblique axis, a well-documented phenomenon known as the oblique effect. Relative to the control group, the migraine group exhibited orientation-specific sensitivity losses on explicit and virtual judgments. Orientation-discrimination thresholds about the oblique axis were significantly elevated in the migraine group. In contrast, the migraine and control groups’ detection thresholds did not differ.

CONCLUSIONS. These findings reflect abnormal function of striate and extrastriate cortex in migraine. In addition, the discrimination data are consistent with wider orientation-tuning curves for orientation-sensitive cells in migraine, whereas the detection data suggest peak sensitivity does not differ between the groups. (Invest Ophthalmol Vis Sci. 2006;47:5599–5604) DOI:10.1167/iovs.06-0640

The study of visual perception in migraine stems from the observation that, in a subset of individuals with the condition, the headache is preceded or accompanied by a visual aura, which manifests as mild visual hallucinations (e.g., the classic fortification spectra). This effect has been attributed to a wave of excitation and subsequent inhibition known as a wave of excitation and subsequent inhibition known as the oblique effect (OE). Orientation-specific abnormalities would provide evidence of cortical dysfunction.

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The oblique effect (OE) was first noted by Ernst Mach, and refers to an increased sensitivity to stimuli presented at cardinal orientations (horizontal and vertical) relative to stimuli presented at oblique orientations. The OE has been demonstrated with electrophysiology, psychophysics, and functional magnetic resonance imaging (fMRI). Further, correlates of the OE have been demonstrated for a wide variety of tasks and even in a study of esthetic preference. The OE is neural in origin rather than a result of astigmatic or refractive errors, since it persists when stimuli are presented on the retina using laser interference techniques that discount the optics of the eye. Moreover, thalamic cells of the lateral geniculate nucleus (LGN) exhibit only weak orientation selectivity at best and, hence, classic explanations of the OE focus on the overrepresentation of cardinal orientations in the primary visual cortex (area V1). In addition, there is evidence of coarser and asymmetric tuning of V1 cells responsive to oblique stimuli relative to cells that are tuned to cardinal orientations. The existence of OE correlates for stimuli that rely on the processing of global form and motion, however, or on the perception of illusory lines, suggests that the OE can originate from a more diffuse locus and may involve multiple cortical areas.
We used the OE to examine the contribution of a cortical dysfunction to the orientation discrimination deficits that have been described in migraine. Two types of stimuli were used: a Gabor patch, incorporating explicitly defined lines, and a virtual line defined by a pair of widely spaced circles. The latter stimulus was included for two reasons: (1) It would not stimulate V1 receptive fields (RFs) and would thus allow an assessment of extrastriate dysfunction and (2) to test the hypothesis that elevated orientation thresholds in migraine are simply due to an increased aversion to striped patterns. For each, orientation-discrimination thresholds were tested in migraine and control participants for stimuli oriented about the cardinal and oblique meridians. Detection thresholds were also examined by using the Gabor patch, to ensure that any differences in performance between migraine and control groups were not simply a reflection of impaired contrast sensitivity or an aversion to the stimulus.

### METHODS

#### Participants

Twenty migraineurs and 20 sex-matched control participants were recruited. All completed a questionnaire detailing characteristics of their headaches. All migraine participants fulfilled the International Headache Society’s (IHS) diagnostic criteria. Ten had migraine without visual aura (MO), and 10 had migraine with visual aura (VA). Control participants did not meet IHS criteria, and none had a history of frequent, severe headaches (Table 1).

All participants had a visual acuity of at least 20/25 for each eye (with or without optometric correction). In addition, any participant with astigmatisms in each eye that fell within 15° of the oblique angle (i.e., 30°–60° clockwise from the vertical) was excluded from the study. The presence of astigmatisms and the affected axes were assessed using the standard fan chart. No participant had taken acute medication within 48 hours of testing, and none were taking daily medication. None had experienced migraine within the 48 hours preceding the test or in the 24 hours after. Informed written consent was obtained in accordance with the Declaration of Helsinki, and ethical approval was obtained from Birkbeck College’s School of Psychology ethical committee.

#### Orientation Discrimination and Contrast Detection Thresholds

Stimuli were presented on a 22-in. calibrated CRT monitor with spatial and temporal resolutions of 1024 × 768 pixels and 100 Hz, respectively, and were created in commercial software (MatLab; The MathWorks, Natick, MA; using the PsychToolbox set of functions). Images were viewed from a distance of 1 m through a circular mask that occupied 12° of the visual field.

For all orientation-discrimination tasks observers were required to decide whether the target stimulus was oriented clockwise (CW) or anticlockwise (ACW), relative to a reference stimulus in a two-alternative, forced-choice (2-AFC) procedure (Fig. 1). Target and reference stimuli were presented sequentially for 25 ms and were separated by a 75-ms delay. Auditory feedback was given when an incorrect response was registered. A two-down, one-up staircase method was used to track the 71% threshold. Two staircases were interwoven: one presenting CW transformations of the stimulus, the other presenting ACW transformations. An initial step size of 1° was reduced to 0.1° after several reversals.

Two types of stimuli were used: (1) explicit: orientation was defined by a Gabor patch (Michelson contrast of 34%, average luminance of 21 cd/m², spatial frequency of 4 c/deg); (2) virtual: a virtual line defined by two black circles presented either side of the fixation point. Both the Gabor patch and virtual line subtended an average of 1.6°; for stimuli of this size, orientation discrimination using Gabor patches is contrast invariant. In an attempt to minimize the likelihood that observers would perform the virtual task by tracking lateral displacements of the circles, the circles’ spatial separation was randomly altered by 50%, 0%, or −50% on each presentation. The fixation point was removed whenever a stimulus was presented.

Contrast detection thresholds were calculated using Gabor patches in a two-down, one-up 2-AFC staircase procedure. Observers had to decide whether the target pattern was presented during the first or second of two intervals, both of which were preceded by an auditory cue. Auditory feedback (higher frequency) was given when an incorrect response was registered. The two intervals lasted for 25 ms and were separated by 75 ms. Two staircases were interwoven, starting from different contrast levels (23% and 45%). Stimulus contrasts were progressively reduced to track the 71% threshold. An initial step size of 2.2% was reduced to 0.22% after several reversals (Michelson contrast).

All thresholds were measured at 0° (cardinal) and 45° CW from vertical (oblique), and were presented against a gray display (21 cd/ m²). For each threshold, response times (RTs) were also recorded, to assess the possibility of a speed-accuracy tradeoff. All trial blocks were counterbalanced. Trial blocks were terminated after a minimum of 10 reversals for each staircase, and thresholds were calculated as the mean of the last 5 reversals and an average taken of both staircases.

#### Pattern Sensitivity and Visual Triggers

The viewing of certain striped patterns can cause discomfort and induce the perception of illusions, a phenomenon that is more pronounced in migraine and may correlate with performance on certain visual tasks. Pattern sensitivity was ascertained by gauging participants’ responses to a series of high-contrast, horizontal, square-wave gratings presented at 0.8, 3, 7, and 17 c/deg. Each stimulus was presented four times for 10 seconds. After each presentation, participants were asked to note whether they experienced any illusions involving (1) motion, (2) color, or (3) shape.

To determine sensitivity to visually triggered headaches (in the control group) or migraines (in the migraine group), all participants were asked to note whether certain visual stimuli (1) commonly, (2) occasionally, or (3) never triggered an attack. Commonly was scored as 2, occasionally as 1, and never as 0, for the following visual stimuli: flickering lights, certain visual patterns (e.g., stripes or lattices), and alternate light and shade.

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**Table 1. Participant Details**

<table>
<thead>
<tr>
<th>Observers</th>
<th>Female:Male Ratio</th>
<th>Age Range (y)</th>
<th>Age (y)</th>
<th>Migraine Frequency</th>
<th>Migraine Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>20</td>
<td>5.7:1</td>
<td>20–50</td>
<td>31 ± 9</td>
<td>—</td>
</tr>
<tr>
<td>Migraine</td>
<td>20</td>
<td>5.7:1</td>
<td>21–46</td>
<td>30.6 ± 8</td>
<td>11.7 ± 14</td>
</tr>
<tr>
<td>MO</td>
<td>10</td>
<td>9:1</td>
<td>21–46</td>
<td>30.1 ± 9</td>
<td>16.1 ± 19</td>
</tr>
<tr>
<td>VA</td>
<td>10</td>
<td>4:1</td>
<td>23–43</td>
<td>31.1 ± 7</td>
<td>7.3 ± 7</td>
</tr>
</tbody>
</table>

Participant age, migraine frequency, and duration (number of years experienced) are presented in the form of group means ± SD. None of the groups (VA, MO, and control) differed significantly with respect to age (one-way ANOVA: F(2,37) = 0.05, P = 0.955).
RESULTS

Four Main Trends Emerged from the Analyses:

1. All oblique discrimination thresholds were elevated relative to cardinal thresholds, reflecting the OE (Fig. 2).
2. Oblique thresholds were elevated in the migraine group relative to the control group for both explicit (Fig. 2A) and virtual (Fig. 2B) line stimuli.
3. Detection thresholds did not differ between the migraine and control groups (Fig. 3).
4. Response times did not differ systematically between groups or between tasks (Fig. 4).

All threshold data were normally distributed (Kolmogorov-Smirnov tests). Therefore, statistical analyses were undertaken with a mixed ANOVA with one between-factor (group: either migraine versus control or VA versus MO) and one within-factor (orientation: cardinal versus oblique).

Orientation-Discrimination Thresholds

Gabor Patches. In both groups, the oblique threshold was elevated relative to the cardinal, reflecting the OE (significant main effect of orientation: F(1,38) = 91.79, P < 0.001). In addition, the increase in oblique thresholds was greater in the migraine group than it was in the control group (significant interaction between group and orientation: F(1,38) = 5.01, P = 0.031). This did not carry through to a main effect of group, however (F(1,38) = 2.93, P = 0.095; Fig. 2A).

The reaction times (RTs) for the different orientations were indistinguishable (Fig. 4), with the exception of the control data for the cardinal condition which was reduced (interaction between group and orientation: F(1,38) = 6.101, P = 0.018) and carried through to a main effect of orientation (F(1,38) = 8.033, P = 0.007). As discrimination thresholds did not differ be-

![FIGURE 1. The stimuli and sequence of events. Two stimuli were used: (A) a Gabor patch occupying 1.6° of the visual field (mean luminance, 21 cd/m²; Michelson contrast, 34%; spatial frequency, 4 cyc/deg) and (B) a virtual stimulus comprising two widely spaced circles (average separation, 1.6°). For the orientation-discrimination tasks the reference (ref.) and target stimuli were presented sequentially for 25 ms and separated by a 75-ms delay. To determine contrast detection thresholds the same Gabor patch shown in (A) was used. Contrast varied with performance.](image)

![FIGURE 2. Orientation-discrimination thresholds for (A) Gabor patches and (B) virtual line stimuli for stimuli oriented about the cardinal and oblique meridians in the migraine and control groups. *P < 0.05.](image)
Contrast-detection thresholds for Gabor patches oriented about the cardinal and oblique meridians for the migraine and control groups.

Table 2. Rotated Component Matrix

<table>
<thead>
<tr>
<th>Component</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabor discrimination, cardinal</td>
<td>0.92</td>
<td>0.07</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td>Gabor discrimination, oblique</td>
<td>0.86</td>
<td>-0.19</td>
<td>-0.08</td>
<td>-0.16</td>
</tr>
<tr>
<td>Virtual discrimination, cardinal</td>
<td>0.9</td>
<td>0.03</td>
<td>-0.21</td>
<td>0.21</td>
</tr>
<tr>
<td>Virtual discrimination, oblique</td>
<td>0.86</td>
<td>-0.35</td>
<td>0.14</td>
<td>0.04</td>
</tr>
<tr>
<td>Detection, cardinal</td>
<td>-0.15</td>
<td>0.64</td>
<td>0.57</td>
<td>0.13</td>
</tr>
<tr>
<td>Detection, oblique</td>
<td>-0.01</td>
<td>0.85</td>
<td>0.03</td>
<td>-0.1</td>
</tr>
<tr>
<td>Duration since last attack</td>
<td>0.04</td>
<td>0.07</td>
<td>0.94</td>
<td>0.05</td>
</tr>
<tr>
<td>Years experienced (n)</td>
<td>-0.11</td>
<td>-0.32</td>
<td>-0.44</td>
<td>0.71</td>
</tr>
<tr>
<td>Frequency (migraines/year)</td>
<td>0.63</td>
<td>0.28</td>
<td>-0.6</td>
<td>0.03</td>
</tr>
<tr>
<td>General illusion index</td>
<td>-0.14</td>
<td>-0.8</td>
<td>-0.03</td>
<td>0.06</td>
</tr>
<tr>
<td>Visual trigger score</td>
<td>-0.15</td>
<td>-0.05</td>
<td>-0.31</td>
<td>-0.88</td>
</tr>
</tbody>
</table>

A principal components analysis was undertaken to examine the pattern of intercorrelations between the data. The correlations between each variable and the component with which it correlates most highly are shown in bold. Component 1 (a discrimination component) accounted for 32.5% of the variance in the original variables, whereas component 2 (a sensitivity component) accounted for 19.4%, component 3 accounted for 17.6%, and component 4 accounted for 12.6%.
the target experienced a greater number of illusions while viewing high-contrast gratings.

Component 3 is somewhat less interesting. The two strongest loadings simply reflect an association between migraine frequency and the time elapsed since the last attack. Cardinal detection thresholds also load moderately, which indicates that the less frequent the migraine, and hence the more distant the last migraine attack, the worse the threshold performance. This pattern has been reported previously and is consistent with a build-up of cortical changes that culminate in a migraine episode. Finally, the visual trigger score and the number of years that migraine has been experienced contribute to component 4. The opposite loadings suggest that individuals who have experienced migraine for many years are less likely to have an OE triggered by a visual stimulus.

Some of the data reported herein have been published previously in abstract form.45

DISCUSSION

An OE was clearly discernible in both the migraine and control groups’ orientation-discrimination thresholds. Individuals were approximately three times more sensitive to differences in orientation involving cardinal stimuli than they were to identical stimuli presented at oblique angles. Further, migraine participants exhibited an orientation-specific deficit relative to the control group, with elevated discrimination thresholds for oblique angles only. This was evident for both explicitly defined and virtual stimuli. In contrast, detection thresholds did not differ between migraine and control groups at either of the orientations tested. The performance of the migraine subgroups did not differ significantly on any of the tasks.

The precise origin of the OE continues to be debated. However, it is clearly neural in origin and is unlikely to originate from precortical sites (see the Introduction). Evidence from electrophysiological, psychophysical, and fMRI studies instead point to an early cortical locus for the OE when lines or gratings are used (e.g., within area V1).22,29,36,37 The existence of OE correlates for more complex tasks, however, suggests the OE could involve multiple cortical regions.51,52 Here, orientation-specific deficits in migraine occurred for discriminations when both explicitly defined and virtual lines were used. The role of V1 cells in the perception of illusory contours remains controversial46–48; however, the spatial separation of the circle end-points used to define the virtual stimulus (1.6° on average) is too large for any V1 receptive field.53 The present results therefore point to the existence of a cortical abnormality in migraine that affects striate and extrastriate regions of the visual system (see Refs. 19,49,50). It is unclear, however, whether the extrastriate dysfunction reflects feed-forward effects from abnormalities in area V1, or whether visual processing is affected in both striate and extrastriate regions as a result of a shared ontogenetic history.

Irrespective of whether the OE originates in the striate cortex alone, or whether extrastriate regions are also implicated, it is clear that an orientation-specific deficit in migraine reflects a cortical abnormality. Indistinguishable contrast detection thresholds for migraine and control groups reinforce this conclusion by ruling out the possibility that differential performance was due to impaired contrast sensitivity as a result of damage or dysfunction at a precortical locus. In addition, poorer performance by the migraine group cannot be explained by a general aversion to high-contrast patterns with a repetitive component, as performance was equally impaired on the virtual stimulus task.

An orientation-specific deficit in migraine, which only affects oblique judgments, is consistent with previous studies in which migraineurs exhibited no significant impairments in orientation discrimination when vertical stimuli were presented at both 9 cyc/deg24 and 4 cyc/deg.25 However, a reduced sensitivity in migraine was reported when stimuli were presented at 0.5 cyc/deg.25 One explanation of this apparent discrepancy is that it reflects two distinct abnormalities that are differentially highlighted as a function of stimulus spatial frequency. McKendrick et al.50,52,53 and Coleston et al.41 suggested that a target presented at 0.5 cyc/deg preferentially activates the magnocellular pathway, and several psychophysical and perimetric studies have demonstrated that this pathway may be impaired in migraine.17,20,25,51 Thus, orientation-specific abnormalities for high-spatial-frequency stimuli may reflect cortical dysfunction, whereas orientation-independent sensitivity losses found only when using very low spatial frequencies may originate from abnormalities in precortical pathways.

What might be the mechanisms of this cortical dysfunction in migraine? One possibility is that it reflects abnormal patterns of orientation tuning in the visual cortex. The response of an orientation-selective cell in the cortex is largely defined by the shape of its orientation-tuning curve.52 Several psychophysical studies have attempted to account for the OE itself with models of broader or asymmetric tuning of V1 cells to oblique stimuli.50,58 Indeed, a broader tuning of orientation-selective cells in migraine may account for the pattern of results reported herein—specifically, that detection thresholds are normal despite elevated discrimination thresholds. Although detection of a stimulus presented near threshold relies on the overall level of activation in a population of cells sensitive to the properties of that stimulus, suprathreshold discriminations rely at least in part on the differential level of activity induced by the two stimuli to be compared and hence the tuning width of the sensitive cell populations. Thus, a broader tuning of V1 cells would predict impaired orientation discrimination in conjunction with normal (or even reduced) detection thresholds in migraine. This was indeed the pattern observed here. One potential limitation of this explanation, however, is that it cannot easily account for the fact that orientation discriminations were impaired only for oblique stimuli in migraine, as the tuning of cells responsive to both cardinal and oblique meridians are dependent on similar processes. However, it is possible that existing differences between cell populations tuned to cardinal and oblique angles (e.g. differences in population size, 22,36,37 natural tuning characteristics,50,58 or plasticity55) differentially predispose the oblique population to physiologically relevant dysfunction.

The present study could be extended to address orientation-tuning in migraine directly by using a simultaneous masking paradigm adapted from Saarinen and Levi.54 The relative increase in the orientation-detection threshold is determined as a function of a range of mask orientations to generate a precise tuning curve. This technique could be used to ascertain whether a difference in the width of tuning curves is indeed restricted to oblique orientations and confirm whether tuning curve peaks do not differ between migraine and control groups. Such a study may also help refine general models of hyperexcitability, which could be interpreted as a shift of the orientation tuning curve along the ordinate axis, raising the peak and increasing the level of neural noise; or, as elevated postactivation excitation, which would increase the height of the tuning curve peak and increase the signal-to-noise ratio. Alternatively, a change in the width of the tuning curve without a change in the peak could reflect an abnormal pooling of the excitatory and/or inhibitory inputs that underlie orientation specificity. While the data reported herein are consistent with wider orientation tuning in migraine, this hypothesis should be tested directly.
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50. Shepherd A. Local and global motion after-effects are both enhanced in migraine, and the underlying mechanisms differ across cortical areas. *Brain.* 2006;129:1833–1845.