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

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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 cortical spreading depression, which traverses cortical areas associated with vision. In addition, there is anecdotal evidence that visual perception is altered between attacks, such as reports that certain visual patterns may induce feelings of discomfort or trigger a migraine. Several studies have demonstrated visual abnormalities in migraine during the interictal phase by using psychophysical, transcranial magnetic stimulation (TMS), and electrophysiological methods, which are thought to reflect both precortical and cortical dysfunction (reviewed in Refs. 8–10). For example, abnormal processing of color, flicker, shape, and motion have all been implicated in migraine.

One difficulty in this area is in the selection of tasks and displays for which performance can be unambiguously attributed to processing at a particular stage or pathway within the visual system. Orientation discrimination should be able to address cortical abnormality in migraine, as narrow orientation tuning first appears in the primary visual cortex. Indeed, several studies have examined orientation discriminations in migraine, although results are somewhat contradictory. Wilkin and Croatto, using Gabor patches presented at 9 cycles/degree, reported consistent but statistically insignificant elevations in orientation-discrimination thresholds in a subset of migraineurs with visual aura compared with a control group. Using a similar task, however, McKendrick et al. reported that impaired orientation discrimination in migraine was a function of the spatial frequency of the stimuli used. Finally, impaired performance was found on a global form-perception task that requires the integration of local orientation information to be able to discriminate two patterns.19 With the exception of the latter task, however, which did not test performance at specific orientations, all the studies to date have used stimuli presented at a single orientation only: all were vertical or near vertical. Elevated thresholds, if determined at a single orientation, can reflect anomalous function at retinal, geniculate or cortical sites. Orientation-specific losses, in contrast, would indicate dysfunction at cortical rather than precortical sites.

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 ophthalmic 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 counterclockwise (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 cyc/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 cyc/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.

<table>
<thead>
<tr>
<th>Table 1. Participant Details</th>
<th>Observers (n)</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>
<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>
<td>15.1 ± 9</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>
<td>15.9 ± 9</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>
<td>14.4 ± 9</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) = 0.23, P = 0.8).
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-
tween the groups for the cardinal orientation, there is no evidence of a speed-accuracy tradeoff.

Mixed ANOVAs were performed to compare the migraine subgroups (VA and MO). No significant differences involving group emerged for either the discrimination thresholds or the RTs (each F < 0.8 and P > 0.3). Thus, the presence or absence of visual aura symptoms did not affect task performance.

**Virtual Lines.** The results obtained with the virtual line stimuli were similar to those obtained with the Gabor patches (Fig. 2B). Oblique thresholds were elevated relative to cardinal in both groups (significant main effect of orientation: F(1,38) = 142.5, P < 0.001), and the increase in oblique thresholds was significantly greater in the migraine group than it was in the control group (interaction between group and orientation: F(1,38) = 4.46, P = 0.041). The difference between migraine and control group thresholds carried through to a main effect of group (F(1,38) = 4.26, P = 0.046). When the RT data were analyzed, no significant effects were found (each F < 1.5 and P > 0.2; Fig. 4).

Mixed ANOVAs were performed to compare the migraine subgroups (VA and MO). No significant differences involving group emerged for either the discrimination thresholds or the RTs (each F < 2.5 and P > 0.15).

**Contrast Detection Thresholds**

No significant effects were found with respect to orientation or group (each F < 0.5, P > 0.5; Fig. 5). Similarly, an analysis of the RTs highlighted no significant effects involving orientation or group (each F < 2 and P > 0.25). Finally, mixed ANOVAs were performed to compare the migraine subgroups’ (VA and MO) detection thresholds and RTs. There were no significant differences between the migraine subgroups (each F < 0.5 and P > 0.5).

**Pattern Sensitivity and Visual Triggers**

Pattern sensitivity was gauged by recording the number and type of illusions seen in high-contrast, square-wave gratings (see the Methods section). One participant in the migraine group failed to complete this test because the gratings led to nausea. Scores for each illusion type (color, motion, and shape) were consistently higher in the migraine group for each of the four patterns. A general illusion index (GII) was generated by first counting the frequency with which color, motion, and shape were seen for each pattern (minimum, 0 of 4 presentations; maximum, 4). These were then averaged across the four spatial frequencies and summed to give the GII. The GII was larger for the migraine group than for the control group (3.18 compared to 2.1) although, in contrast to a previous report,7 this difference did not reach statistical significance (t(37) = 1.29, P = 0.13, one-tailed test). This result probably reflects the smaller sample size used here.

Sensitivity to visually triggered headaches and migraines was assessed by questionnaire (see the Methods section). An overall visual-trigger score was calculated by summing responses to each trigger for each participant. The result was significantly larger in the migraine group than in the control group (1.25 compared with 0.1; t(38) = 3.19, P = 0.003). Thus, individuals with migraine are more susceptible to visually triggered headaches.

To explore the intercorrelations between these measures and the experimental data, a principal components analysis was conducted (see Harle et al.44; Table 2 below). Two main components of interest were extracted (with eigenvalues > 1) with a rotated solution (varimax rotation). The discrimination thresholds contributed to the first component as did migraine frequency. Individuals who experienced frequent migraine had higher discrimination thresholds. In contrast, detection thresholds formed part of the second component, which was also negatively correlated with the GII, a measure of pattern sensitivity. Thus, individuals who were most sensitive at detecting

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**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 -0.08</td>
<td>-0.16</td>
<td></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>-0.01</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>

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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 migraine 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 that a target presented at 0.5 cyc/deg preferentially activates the magnocellular pathway, and several psychophysical and perimetric studies have demonstrated that this path-way may be impaired in migraine.17,20,25,31 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 pre cortical 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.30,38 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,30,38 or plasticity53) 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.24 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;129:1833–1843.