Differential Activation of Multiple Current Sources of Foveal VEPs as a Function of Spatial Frequency

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Summary: The purpose of the present study was to map sensory-evoked potentials to foveally presented square-wave gratings of different spatial frequencies with a high density electrode montage. Scalp isocontour voltage and scalp current density (SCD) maps were computed to assess differences in scalp topography of the sensory-evoked responses as a function of spatial frequency. Topographic analysis showed a segregation of evoked responses to stimuli of different spatial frequencies. While low frequency patterns elicited a bilateral positive potential localized at lateral occipital sites from 60-120 msec, high frequency patterns elicited a prominent midline occipital negative potential. SCD revealed that, for any spatial frequency, two current density foci were evident: an earlier negative focus (current sink), centered at mesial-occipital areas, and a later positive focus (current source), centered at lateral-occipital regions of the scalp. The current source was much more prominent than the sink for lower spatial frequency, and vice versa. Moreover, the source was larger over the right side of the scalp, whereas the current sink shifted from the right to the left side as spatial frequency increased. The present electrophysiological findings suggest the view that: (1) visual sensory-evoked potentials elicited by low versus high spatial frequencies have different polarity and topographic localization, (2) these potentials might reflect the activation of functionally distinct, topographically segregated, neural generators differentially activated as a function of spatial frequency, and (3) these generators seem asymmetrically distributed over the left (LH) and right (RH) hemispheres.

Keywords: Spatial frequency; Isocontour voltage maps; Scalp Current Density; Multiple current sources; P_{95}; N_{85}; Magno- and Parvo-cellular Systems; Striate and extra-striate areas; Hemispheric asymmetries.

Introduction

Spatial frequency selectivity of individual neurons of the visual cortex is a generally acknowledged property of the mammalian visual system (Kulikowski et al. 1982). Neurons having a similar spatial frequency selectivity (e.g., similar receptive field organization) are grouped in independent channels, organized in columns and hyper-columns and extending vertically in the primary visual cortex (Brodman's area 17, or V1 area) of brain hemispheres (Tootell et al. 1981).

Typically, surface scalp electrodes have been used in human electrophysiological studies to measure changes in bioelectrical potentials of the visual cortex, during stimulation with different spatial frequencies (Regan 1989). Evidence has been provided that variation of spatial frequency produces strong differences in the morphology of pattern-onset visual evoked potentials. An early positive component (P1) larger and faster to low spatial frequencies has been identified and described in the literature for both gratings (Skrandies 1984; Hudnell et al. 1990; Proverbio et al. 1993, 1994, 1995b, in press) and checkerboards (Skrandies et al. 1980; Zani and Proverbio 1995a).

A preceding early negative component (N70) elicited preferentially by high spatial frequencies, has also been described by visual evoked potential studies using both gratings (Jones and Keck 1978; Parker et al. 1982; Plant et al. 1983; Reed et al. 1984; Bodis-Wollner et al. 1992; Kenevans et al. 1993; Proverbio et al. 1993; Zani and Proverbio 1994, 1995b, in press) and checkerboards (Harter and White 1970; Lesèvre and Remond 1972; Zani and Proverbio 1995a).

The amplitude and latency of this component have been shown to vary as a function of pattern luminance, spatial frequency, contrast, color, and retinal location, as well as visual field size (Lesèvre 1982).

Few of these studies have dealt with the topographic distribution of the afore-mentioned sensory components as a function of spatial frequency of stimulation. More-
over, only a few have addressed the question whether differences in VEP amplitude may result from the differentiated activity of functionally and topographically distinct neural generators or, rather, from a polarity reversal of the same electrical source. For instance, Drasdo (1980) reported a positive component C1 maximally elicited by lower spatial frequencies (bars of 17° or 12°), and an earlier negative transient C0 (N70) elicited maximally by higher spatial frequencies (bars of 4° and 2.5°). The C0 component appeared to predominate at midline and mesial-occipital electrode sites. Conversely, the C1 component predominated at the more lateral-occipital electrode sites (20% and 30% of the inion-nasion distance), with a maximum at the 30% electrode location in the right hemisphere, when lower frequencies were used, and was fairly equally distributed when higher frequencies were used. On the base of these findings, a striate (area 17) and an extrastriate (area 19) origin were proposed by this author for the C0 and C1 components, respectively.

Mauguière and colleagues (1985) reported that the sensory components N95 and P100 could be distinguished from each other on the basis of their scalp topography and amplitudes as a function of the physical features of pattern stimulation (spatial frequency, stimulus size, luminance, etc.). Hudnell and colleagues (1990), in a pattern-onset visual evoked potential study, reported a clear dissociation between an early positive component (P90) which decreased in amplitude with increasing grating spatial frequency, and a negative component (N110) which was small or absent with low spatial frequencies, but increased in amplitude with higher spatial frequencies. Importantly, they proposed that these components had functionally distinct generators based on their different patterns of adaptation. Similarly, Blumhardt and colleagues (1989) and Bodis-Wollner and colleagues (1992), using pattern-reversal and pattern-onset stimuli respectively, found an early negative component (N70), whose latency and amplitude increased with spatial frequency, and described it as a post-synaptic cortical potential generated by foveal neurons and localized in the striate cortex.

Most of the VEP studies reviewed above have used a small (3-5) number of recording sites placed over the posterior occipital areas of the scalp. This makes it difficult to use topographic information to evaluate the responses recorded. Indeed, some evidence has been provided for multiple underlying sources, and significant differences in the location and orientation of the best-fitting equivalent current dipole (ECD) of the visual evoked magnetic field (VEP) as a function of spatial frequency of the evoking grating (Aine et al. 1990).

The purpose of the present study was to investigate the sensory evoked responses of the brain to a representative range of low, medium and high spatial frequencies (1.5 to 12 c/deg) foveally presented to healthy humans, and to map their topographic distribution with a high density electrode montage. Visual evoked potentials to square-wave gratings were recorded from 61 electrode locations distributed over the anterior and posterior areas of the scalp. Scalp current density (SCD) topographic maps were used to assess differences in scalp topography of neural generators of sensory component(s) elicited by different spatial frequencies. Foveal stimulation was used because N70 is known to be more exquisitely sensitive to the activation of foveal than peripheral neurons (Bodis-Wollner et al. 1992).

Methods

Subjects

Nine right-handed subjects (5 males, 4 females) ranging in age from 18 to 28 years participated in this experiment. All had normal or corrected-to-normal vision, and were paid for their participation.

Stimuli and procedure

Stimulus patterns were presented on a Macintosh color-video monitor. The screen was covered by a mask that only revealed a circular field subtending 2 degrees of visual angle at the viewing distance of 114 cm. In this way, foveal stimulation was provided. Four achromatic luminance-modulated square-wave gratings of different spatial frequency (1.5, 3, 6 and 12 c/deg) were presented for 100 msec in pattern onset mode. Contrast was 80%. The inter-stimulus intervals (ISI) randomly varied between 660 and 760 msec post-stimulus. The average stimulus luminance was 5.46 fL. Each stimulus replaced a gray background of 6.65 fL. Hence, the space-averaged luminance of the grating was isoluminant with the background. The stimuli were presented in random sequences, each lasting about 3 minutes. Short rest periods of about 1 minute were given between each sequence of stimuli. In total, 100 stimuli were presented to each subject for each of the four spatial frequencies.

The subjects were comfortably seated in front of the monitor in a dimly lit, sound attenuated, and electrically shielded chamber. They were instructed to maintain eye fixation toward the center of the circular field, and to avoid ocular or body movements and blinks. To ensure that fixation was maintained, the horizontal and vertical electro-oculogram was monitored. Furthermore, during active recording, subjects' eyes were monitored by means of an infrared video-camera.

ERP recording

Visual-evoked potentials to pattern-onset stimuli were recorded from 61 scalp sites using tin electrodes.
Figure 1. Schematic representation of a human scalp in back view with the posterior electrode montage. Additional electrodes to the 10-20 International System were located half the distance between parietal and posterior-temporal sites (Pl, Pr), between posterior-temporal and occipital sites (O1, O2) and 10% the nasion-inion distance below occipital sites (In3, In2, In4). (NC = Non-cephalic lead).

mounted in an elastic cap (Electro-cap, Inc.). The electrodes were located according to the International 10-20 system. Additional electrodes were located at non-standard intermediate locations. Figure 1 shows a back view of an idealised scalp with the electrode locations indicated by black dots. As can be seen, electrodes were located at central, parietal, posterior-temporal, and occipital standard and non-standard scalp sites of the International 10-20 System. Additional anterior electrodes were located at standard and non-standard frontal scalp sites (Fp3, Fp4, Fpz, F1, F2, F3, F4, F5, F6, F7, F8) and half the distance between frontal and central scalp sites (FC1, FC2, FC3, FC4, FC5, FC6, FC7, FC8). Two extra-electrodes were used to record from a balanced non-cephalic sternovertebral lead. All scalp sites were referenced to an electrode on the right ear, but they were subsequently re-referenced off-line to the average of the left and right ears. Blinks and vertical eye movements were monitored with an electrode below the right eye (monopolar lead). Horizontal eye movements were recorded from electrodes placed at the outer canthi of the eyes (bipolar lead) and amplified with a band pass of 0.01-100 Hz. The EEG signals were amplified with a band pass of 0.1-100 Hz. Electrode impedance was kept below 5 KOhms. EEG and EOG epochs were digitized for 200 msec prior to, and 1400 msec after stimulus onset at a rate of 250 Hz, and were aligned to the mean amplitude of the 100 msec prestimulus baseline. Trials containing artifacts due to ocular move-

ments, blinks or amplifier saturation were excluded from the averaged ERP waveforms. Separate average waveforms were computed for each spatial frequency.

Data analysis

Since at posterior infero-occipital and occipital sites positive and negative potentials coexisted in the same latency range, quantification of amplitude and latency of sensory evoked components was accomplished by measuring mean amplitude values across a 70-120 msec latency window and the latency at peak amplitude, respectively. All measures were performed automatically by a computer program and the same criteria were used for all the electrodes and subjects.

To map the scalp distribution of sensory components we used the spherical spline interpolation algorithm developed by Ferrin et al. (1989). Both scalp isocountour voltage and current density (SCD) maps were computed. The voltage or current density values were radially projected on the two-dimensional surface of an idealized spherical head.

Results

Figure 2 shows the primary sensory components
elicited by the different spatial frequencies at the electrodes located over the occipital, temporal and occipital-parietal areas. As can be seen, at these locations low spatial frequencies (1.5 and 3 c/deg) elicited an early positive deflection that was widely distributed over occipital scalp and peaked at about 95 msec (P95). The amplitude of this positivity was larger at lateral occipital (OL and OR) and posterior temporal (T5 and T6) electrode sites, and reached its maximum amplitude at the right-sided lateral occipital site (OR). The amplitude of this response decreased significantly as the spatial frequency of the stimuli increased (6 and 12 c/deg). This was especially pronounced at left and midline scalp sites. The high spatial frequency gratings (6 and 12 c/deg) also elicited an earlier negative deflection peaking at about 85 msec (N85) at midline and mesial occipital locations (INZ, OZ, O1, O2). This negativity reached its maximum amplitude at midline locations, and tended to spread toward the left mesial occipital location.

Topographical maps.

To investigate the distribution and localization of the early VEP components obtained, isocontour voltage maps of brain potentials recorded between 70 and 120 msec latency post-stimulus were computed as a function of spatial frequency. Figure 3 shows a back view of the latter maps. In the upper part are maps to stimuli of low spatial frequency (1.5 and 3 c/deg), and in the lower part to stimuli of high spatial frequency (6 and 12 c/deg). Bright colours refer to the positive current sources, while dark colors refer to negative sinks. As clearly visible, the maps confirmed that the positive source was focused at the right lateral occipital location, and greatest to low frequency gratings. From the maps also appear that for all spatial frequencies this positivity sensibly decreased going from occipital-temporal sites to central-parietal-temporal ones.

Conversely, the maps showed that the current sink was centered at the mesial-occipital sites and greatest to high frequency gratings. It also showed a tendency to spread toward the left mesial occipital site as spatial frequency increased. As a whole, then, the voltage maps indicated that the electrode sites over the occipital, occipital-parietal, and temporal sites showed the most relevant activation in response to low and high spatial frequency gratings.

The afore-mentioned pattern of results was strongly supported by the SCD maps (see figure 4), calculated on
Table I. F-values, degrees of freedom (df), and significance levels in the ANOVAs performed on the mean area amplitude values and the peak latency values. F = spatial frequency; E = electrode site; H = hemisphere. Significance levels were corrected using Greenhouse-Geisser epsilon adjustment to control for variance inhomogeneity.

<table>
<thead>
<tr>
<th>ANOVA</th>
<th>FACTORS</th>
<th>F value</th>
<th>df</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Amplitude</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-way</td>
<td>F</td>
<td>4.55</td>
<td>3.24</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>6</td>
<td>7.56</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>3-way</td>
<td>F</td>
<td>4.6</td>
<td>3.24</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>11.95</td>
<td>1.8</td>
<td>&lt;0.009</td>
</tr>
<tr>
<td></td>
<td>E x H</td>
<td>10.6</td>
<td>2.16</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>2-way</td>
<td>O1-O2</td>
<td>F</td>
<td>6.9</td>
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</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td>Peak Latency</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-way</td>
<td>O1-O2</td>
<td>F x H</td>
<td>4.3</td>
<td>&lt;0.01</td>
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<tr>
<td>(P&lt;0.05 - for 1.5 &amp; 3 - vs. N&lt;0.05 - for 6 &amp;12 c/deg)</td>
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<td></td>
<td></td>
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<tr>
<td>2-way</td>
<td>O1-O2</td>
<td>F</td>
<td>17.56</td>
<td>&lt;0.0000</td>
</tr>
<tr>
<td>(P&lt;0.05)</td>
<td></td>
<td>F x H</td>
<td>2.9</td>
<td>&lt;0.056</td>
</tr>
<tr>
<td>2-way</td>
<td>OL-OR</td>
<td>F</td>
<td>3.42</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>(P&lt;0.05)</td>
<td></td>
<td>H</td>
<td>12.9</td>
<td>&lt;0.007</td>
</tr>
</tbody>
</table>

the multi-channel data for the early rising phase (time window: 60-70 msec post-stimulus latency) of sensory components in the attempt to identify their possible early neural generators avoiding later effects of volume conduction. These maps showed a positive current source density centered over the lateral-occipital brain areas of each hemisphere, asymmetrically prevailing over the right hemisphere, and decreasing systematically as spatial frequency increased. At the same time, a negative current density was evident focused at mesial-occipital locations. This negativity progressively shifted, and prevailed, over the left side of the brain (O1) as spatial frequency increased.

Overall then, the SCD maps indicated a small sink facing a larger source at posterior occipital scalp sites suggesting the superposition of the activities of two generators (one oriented radially and the other tangentially to the surface). A close examination of the maps reveals that the SCD sink corresponds to an asymmetry of the potentials. These data suggest that the brain generators active in this case cannot be described by a single equivalent current dipole.

Statistical analysis.

For control of statistical significance for differences noted in the maps as a function of spatial frequency and hemisphere, separate two and three-way ANOVAs were performed on mean area amplitude values of VEPs recorded at the homologous posterior scalp sites where the maps suggested to be localized the maximum activation. The same was done for peak-latency values. Significance levels were corrected using a Greenhouse-Geisser ε-adjustment procedure to control for variance inhomogeneity.

A two-way ANOVA was performed on amplitude values of the mean area, from 70 to 120 msec post-stimulus. Factors were spatial frequency (1.5, 3, 6, 12 c/deg) and occipital electrode sites (O1, O2, OL, OR, IN3, IN4, OZ, INZ). A main effect of electrode site resulted from the fact that the early negativity was larger at OZ and INZ electrode sites, whereas the early positivity was larger at lateral occipital sites (see Table I for results and significance levels).

A separate three-way ANOVA (i.e., spatial frequency, hemisphere, and electrode site) was performed
Table II. Mean area amplitude values of pattern-onset potentials to foveal gratings of different spatial frequencies recorded between 70 and 120 ms at midline and lateralized electrode sites of the occipital scalp. Note that the values are grand-averaged across the subjects. Standard error values are reported below each mean.

<table>
<thead>
<tr>
<th>SPATIAL FREQUENCY (c/deg)</th>
<th>LEFT SITES</th>
<th></th>
<th>MIDLINE SITES</th>
<th></th>
<th>RIGHT SITES</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>O1</td>
<td>OL</td>
<td>IN3</td>
<td>OZ</td>
<td>INZ</td>
<td>O2</td>
</tr>
<tr>
<td>1.5</td>
<td>1.04</td>
<td>1.18</td>
<td>0.97</td>
<td>0.78</td>
<td>0.8</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>(0.56)</td>
<td>(0.44)</td>
<td>(0.26)</td>
<td>(0.63)</td>
<td>(0.4)</td>
<td>(0.59)</td>
</tr>
<tr>
<td>3</td>
<td>0.37</td>
<td>0.98</td>
<td>0.6</td>
<td>-0.1</td>
<td>-0.03</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td>(0.89)</td>
<td>(0.62)</td>
<td>(0.39)</td>
<td>(1.05)</td>
<td>(0.81)</td>
<td>(0.98)</td>
</tr>
<tr>
<td>6</td>
<td>-0.23</td>
<td>0.34</td>
<td>0.1</td>
<td>-0.62</td>
<td>-0.58</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>(0.71)</td>
<td>(0.46)</td>
<td>(0.28)</td>
<td>(0.78)</td>
<td>(0.52)</td>
<td>(0.75)</td>
</tr>
<tr>
<td>12</td>
<td>-0.23</td>
<td>0.44</td>
<td>0.1</td>
<td>-0.5</td>
<td>-0.54</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>(0.71)</td>
<td>(0.48)</td>
<td>(0.30)</td>
<td>(0.71)</td>
<td>(0.53)</td>
<td>(0.66)</td>
</tr>
</tbody>
</table>

with the lateralized electrode locations only (O1, O2, OL, OR, IN3, and IN4) for considering hemispheric asymmetries. The interaction of Hemisphere x Electrode indicated that the negativity (N95) was significantly larger over the left-sided mesial-occipital location, whereas the positivity (P95) was larger over the right-sided lateral-occipital location. Overall, this pattern of results can be clearly appreciated in table 2 where the mean amplitude values for the most relevant posterior occipital electrode sites are reported. No matter the electrode location, the ANOVA revealed a main significant effect of spatial frequency on the mean amplitude values. As the spatial frequency increased, the positivity (P95) decreased significantly. Post-hoc comparisons (t test, p<0.01) revealed that the positivity elicited by low spatial frequencies was significantly larger than the positivity elicited by high spatial frequencies. Conversely, as indicated by the significant effects of the spatial frequency factor, N95 recorded at O1 and O2 was significantly larger to high (6 and 12 c/deg) than low spatial frequencies.

A two-way ANOVA, with spatial frequency and hemisphere as factors, carried out on the peak latency values of the very first sensory response elicited by low (P95) versus high (N95) spatial frequencies at O1 and O2 sites, independently of their polarity, yielded a significant interaction of spatial frequency x hemisphere (see table 1). The peak latency of the potentials elicited by higher spatial frequencies (6 and 12 c/deg) showed to be significantly earlier (86 msec) than that elicited by low spatial frequencies (95 msec) over the left hemisphere (t test: p < 0.01).

Latency mean values can be seen in figure 5.

Figure 5. Mean latency values (msec) for brain potentials elicited by low versus high spatial frequency gratings at the left (LH) and right (RH) mesial-occipital locations.

Two further two-way ANOVAs with hemisphere and spatial frequency as factors were carried out to compare P1 peak latency to low versus high spatial frequencies separately at mesial (O1 and O2) and lateral occipital (OL and OR) locations. At mesial locations, P1 latency increased significantly as spatial frequency increased (94, 92, 100, 119 msec respectively for 1.5, 3, 6, and 12 c/deg). Furthermore, P1 to low spatial frequency tended to be faster over the right (RH) than left hemisphere (LH), as suggested by the interaction of Spatial frequency x Hemisphere (see table 1). Similarly, at lateral occipital locations P1 latency increased with spatial frequency increasing (90, 93, 99, 105 respectively), and showed to be significantly earlier over the RH (90 msec) than the LH (103 msec) (see table 1 for these results), and to low than high spatial frequencies (t test: p<0.05).
Discussion

The present electrophysiological findings indicate that foveal pattern-onset stimuli of low versus high spatial frequencies preferentially elicit sensory responses that have different activity patterns at the scalp electrodes over the primary and secondary visual areas. They also indicate that early sensory potentials elicited by low versus high spatial frequencies are characterized by a different intra-hemispheric neurotopographic distribution, and a strong hemispheric asymmetry.

Overall these findings suggest the hypothesis that they might originate from functionally and anatomically distinct neural sources.

Functional dissociation of response generators to low versus high spatial frequencies

The data from the present study clearly indicate that the early cortical electrophysiological response to pattern-onset gratings of different spatial frequency is characterized by positive ($P_{95}$) and negative ($N_{85}$) early components over the posterior scalp area. The amplitude and latency of these components are differentially affected by spatial frequency of stimulation. On the one hand, $P_{95}$ amplitude decreased while $N_{85}$ amplitude increased with increasing spatial frequency. The finding that a positive peak decreases while a negative peak increases with increasing spatial frequency is fully in agreement with those of previous studies (Reed et al. 1984; Previc 1988; Bodis-Wollner et al. 1992; Zani and Proverbio 1994, 1995a, 1995b, in press). On the other hand, $P_{95}$ peak latency increased as spatial frequency increased. That the amplitude and, especially, the latency of the two components were inversely affected by spatial frequency seems to rule out the possibility that they may merely reflect the activity of a same electrical source inverting in polarity. Rather, our data strongly suggest that they might result from the activity of functionally distinct neural sources that are differentially activated by different spatial frequencies. Overall, then, these results seem to provide evidence for the hypothesized functional dissociation between low-frequency and high frequency response generators (Drasdo 1980; Blumhardt et al. 1989; Hudnell et al. 1990; Aine et al. 1990; Bodis-Wollner et al. 1992).

A series of studies using visual evoked potentials to achromatic gratings, colored gratings, and colored stimuli, have shown an analogous dissociation between a positive and a negative early sensory component, characterized by different functional properties and described as having different neural generators. Kulikowski and colleagues (1989) reported an early negative component elicited by the onset of colored gratings as opposed to an early positive component elicited by achromatic luminance-modulated gratings. Paulus and Plendl (1988) showed a greater $P_{100}$ to white unpatterned stimuli clearly lateralized to occipital peripheral sites, as opposed to a color-evoked $N_{87}$ localized at the central occipital locations. They also suggested that $N_{87}$ reflected the activity of afferent geniculate P-cells and argued in favour of a striate cortex generator.

That the early negative mesial-occipital component described both in the previous literature and the present study was elicited by bright color patterns and high spatial frequencies, as opposed to the early positive lateral-occipital component elicited by achromatic patterns and low spatial frequencies, suggests the intriguing possibility that these two components may reflect the activity of the two geniculo-cortical Parvocellular and Magnocellular systems described by Livingstone and Hubel (1988). More in particular, the fact that $P_{95}$, albeit reduced in amplitude for higher frequencies, was elicited by gratings of both low and high frequencies, suggests that this component may manifest both magnocellular and parvocellular processing. Conversely, the fact that $N_{85}$ was mostly elicited by gratings of high spatial frequency, could mean that the latter component mostly reflects the output of the parvocellular pathway. This conclusion is shared by other studies (Previc 1988; Blumhardt et al. 1989; Hudnell et al. 1990; Zani and Proverbio 1994, 1995a, 1995b, in press).

SCD maps obtained in the present study showed a topographical segregation between the multiple foci differentially activated by low versus high spatial frequencies, suggesting that the two components might have anatomically distinct cortical sources. The positive bilateral potential maximally elicited by low spatial frequency patterns showed a bilateral high-density focus centered at lateral-occipital sites, with a strong asymmetry in favour of the right-sided site. Conversely, the density focus of the early negative potential elicited preferentially by high spatial frequencies was centered at mesial-occipital sites. The negative current source of the latter component appears clearly lateralized to the right hemisphere for the lowest spatial frequency (1.5 c/deg) and toward the left hemisphere for the highest spatial frequency (12 c/deg). Indeed, there is a close similarity between the present high-density VEP results and the visual evoked magnetic field (VEF) findings by Aine's and colleagues (1990). They found separate multiple sources, topographically segregated. These sources were differentially activated as a function of spatial frequency, analogously to the ones found in the present study.

If the notion is accepted that foveal visual stimulation would mostly elicit a radial dipole near the occipital pole, then, the positions of $N_{85}$, closer to midline, and $P_{95}$, closer to the lateral-occipital sites, seem roughly to correspond to a projection of the former component to area 17
(striate area), and the second component to areas 18 and 19 (extra-striate areas). These results are similar to those of previous studies reporting an extra-striate source for the first positive P1 peak of pattern-onset VEPs to large check sizes (Lesèvre and Joseph 1979; Drasdo 1980; Maier et al. 1987; Van Dijk and Spekreijse 1989; Ossenblok and Spekreijse 1991; Ossenblok et al. 1994), and a striate source for the foveal N70 of human VEPs (Drasdo 1980; Blumhardt et al. 1989; Bodis-Wollner 1992), and the N50 intracortically recorded in the alert monkey (Schoeder et al. 1991), a simian equivalent of the human N70, in response to higher frequency gratings.

Support for the hypothesis of an origin of these components in the proposed cortical areas seems to derive also from neurophysiological evidence. First, evidence has been provided that the striate area is activated by both Magnocellular and Parvocellular afferents, whereas the extra-striate area is activated mostly by Magnocellular afferents (Lennie 1980; Mitzdorf 1986; Merigan and Maunsell 1993). Second, the activity of neural cells of these areas of visual cortex (striate and extra-striate areas) is characterized by being differently sensitive to spatial frequency, probably because of the well-known differences in the size of their receptive fields, being larger for extra-striate than for striate neural cells (Desimone and Schein 1987).

**Hemispheric asymmetries**

Hemispheric differences in latency and amplitude of P95 and N95 components as a function of spatial frequency have been found in the present study. P95 was larger to low spatial frequencies over the right hemisphere, whereas N95 was larger to high spatial frequencies over the left hemisphere. Again, while for high spatial frequencies N95 was faster than P95 over the LH, P95 was faster to low than high spatial frequencies over the RH. Then, on the one hand, these data clearly indicate that the LH responds more efficiently, with larger amplitude and shorter latencies, to high spatial frequencies, whereas, on the other hand, the RH responds with larger amplitude and shorter latencies to low spatial frequencies. Overall, these findings appear to be consistent with current neuropsychological models of hemispheric asymmetries in spatial frequency processing (Sergent 1982; Sergent and Hellige 1986; Hellige 1993).

In this regard, notwithstanding gratings used in this study were composed by square-wave bars, which implies that higher harmonics overlapped to the fundamental spatial frequency of the various stimuli, thus not allowing a clean disentangling of hemispheric asymmetries for low versus high spatial frequencies, it seems very probable that the present findings might reflect a true hard-wired hemispheric asymmetry for spatial frequency processing. This view is supported by similar results of a hemispheric asymmetry in VEPs amplitude as a function of spatial frequency obtained with lateraled sinusoidal gratings in a split-brain patient (Proverbio et al. 1995).

Interestingly, evidence has been provided of gross asymmetries in the contributions of the hemispheres to VEPs generated in the striate cortex (Celesia 1985; Kuroiwa et al. 1987). More recently, with a multi-channel electrophysiological study Brandeis et al. (1992) showed a clear pattern of hemispheric asymmetry in P1 amplitude for low (1.76 c/deg) versus high (6.24 c/deg) spatial frequency gratings. Specifically, P1 was larger over the right occipital locations, and to low spatial frequency gratings than to diffuse white light flashes, whereas the sensory component revealed more negative to high spatial frequency gratings than to flashes over the left occipital locations. Moreover, the event-related potential (ERP) study by Zani and Proverbio (1995a) showed a hemispheric asymmetry in the amplitude of an early negative component (N115) evoked by full-field high frequency checkerboards (3, 4.5 and 6 c/deg). This component, which was almost negligible for low frequency patterns (0.5, 0.75, and 1.5 c/deg), reached larger amplitudes at mesial-occipital scalp locations (O1 and O2) for high frequency checks, and showed its maximum at the left-sided mesial location. Conversely, an early positive component (P30 or P1) showed a higher amplitude to low frequency patterns at the lateral occipital electrode locations (O1 and OR), with a maximum at the right-sided lateral location.

SCD maps of the present investigation lend strong support to the findings quoted above. Thanks to their localized representation of surface currents, they clearly indicate that the current density focus located at mesial-occipital scalp sites for the negative response increases and shifts from the right to the left side of the occipital pole as spatial frequency increases. Conversely, the current density focus for the positive evoked response, much larger with lower spatial frequencies, is clearly lateralized toward the right-sided lateral occipital site, located at the borderer between the lateral occipital pole, and the posterior temporo-parietal regions.

A last point has to be discussed. One might find surprising the hemispheric asymmetry pattern found for the sensory-evoked responses since in the present study stimulus input was provided bilaterally within the foveal field. However, the findings of some experimental studies using lateraled extra-foveal presentation of gratings are consistent with our results. For instance, Bodis-Wollner and colleagues (1992), as well as Zani and Proverbio (1994, in press) have found that N70 was largest to higher frequency gratings, and ipsilaterally to the side of stimulation, on each of the two hemispheres. Nonetheless, it
also showed a neat left-sided asymmetry at mesial-occipital locations. On the other hand, both Brandeis and colleagues (1992) and Zani and Proverbio (1994, 1995b, in press) have found a P1, larger to lower frequency gratings, and contralaterally to the stimulation hemifield, but having a maximum amplitude at the right lateral-occipital site. Furthermore, and most importantly, some recent data obtained in a study randomly presenting different spatial frequency gratings in a 2° left or right hemi-foveal sector (Proverbio et al. 1996) confirmed that, while the N70 was always larger at ipsilateral mesial-occipital sites and increased with spatial frequency, it was larger over the right hemisphere for low frequency, and over the left hemisphere for high frequency gratings. This study also confirmed that, conversely, the P1 was as a whole larger at the lateral-occipital site over the right hemisphere, notwithstanding it was larger contralaterally to the hemisector of presentation and decreased with the increase of spatial frequency.

Conclusions

The present findings showed a topographical and functional spatial-frequency dependent segregation of foveal evoked responses to gratings. In agreement with previous literature, isocontour voltage maps showed that low frequency patterns elicited a bilateral positive source localized at lateral-occipital sites, whereas high frequency patterns mostly elicited a mesial negative (N70) source. SCD maps indicated that multiple foci were evident for any spatial frequency suggesting the view of distinct neural sources differentially activated by spatial frequency of stimulation. The topographic locations of these foci suggested the assumption of an extra-striate magnocellular source for the positive component, and a striate parvocellular source for the negative component. In addition, the differential variation in their current density over the two hemispheres as a function of spatial frequency also indicated the presence of hemispheric asymmetries in the distribution of these sources.

References


