Dynamic Properties of the Representation of the Visual Field Midline in the Visual Areas 17 and 18 of the Ferret (Mustela putorius)

In mammals, the visual field is split along the midline, each hemisphere representing the contralateral hemifield. We determined that, in the ferret, an 8- to 10-deg-wide strip of visual field near the midline is represented in both hemispheres. Bright squares (1.5 deg) were flashed at different azimuths within the central 20 deg of the visual field. Stimuli were flashed either alone or sequentially, and the responses were analyzed with the voltage-sensitive dye (VSD) RH 795 and/or by recording local field potentials (LFPs). In both VSD and LFP experiments, each stimulus evoked a cortical response field that extended over visual areas 17 and 18 up to a surface of 1–1.5 mm² and then shrank again. Amplitude of a cortical response field that extended over visual areas 17 and 18 (LFPs). In both VSD and LFP experiments, each stimulus evoked a cortical response field that extended over visual areas 17 and 18 up to a surface of 1–1.5 mm² and then shrank again. Amplitude of the responses decreased approaching the visual midline and the latency increased. These positional differences are likely to originate from the spatiotemporal structure of the peripheral response fields (PRFs) that form a mosaic in areas 17 and 18, interrupted near the visual midline. Unexpectedly, interhemispheric connections appear not to modify these PRFs’ effects and may not contribute to the responses to discrete, flashed stimuli.

Keywords: corpus callosum, ferret, interhemispheric interactions, visual cortex, visual field

Introduction

The cerebral cortex contains orderly, discrete representations of the sensory peripheries, that is, the stimulation of neighboring points, on the peripheries, activates neighboring neurons in the related cortical areas. Two mechanisms contribute to integrating responses across the cortical sensory maps. One is the divergence/convergence in the afferent projections such that neighboring points in the sensory periphery activate overlapping cortical territories. The second are the tangential connections within the cortical maps. The cortical representations of the sensory peripheries are dynamic constructs, continuously updated by incoming inputs. The number and spatial distribution of cortical neurons activated by a peripheral stimulus (here referred to as the cortical response field [CRF]; see Discussion) change with time after stimulus onset, expanding and contracting over a time scale of 100–200 ms (Grinvald et al. 1994; Petersen and Diamond 2000; Petersen et al. 2003). This aspect of CRF dynamics is believed to reflect the tangential spread of activity along horizontal corticocortical connections (Petersen et al. 2003).

The splitting of the sensory representations between the 2 hemispheres raises special problems. The representation of the retina, in particular, is divided between the 2 hemispheres along a line corresponding to the nasotemporal decussation of ganglion cell axons at the chiasm. This line is unsharp, and therefore, a narrow strip of the visual field midline is represented in both hemispheres. Interestingly, the cortical representations of this strip are also preferentially interconnected by callosal axons (Innocenti 1986; Manger et al. 2002).

Here and in the companion paper (Makarov et al. Forthcoming), we investigate the role of interhemispheric connections in integrating the 2 hemirepresentations of the visual field. The rationale for the present study was the following. Whereas within the hemifield representations, the dynamics of the CRF should reflect conduction along the short intra-areal axons, near the visual midline they should reflect conduction along the long callosal axons. The different lengths and hence conduction delays of the 2 axonal systems should cause significant differences in the dynamics of the responses to stimuli presented along the midline versus those presented in the periphery of the visual field. However, the notion that callosal connections may fail to perfectly integrate the 2 hemifield representations conflicts with the widely accepted belief that the intrahemispheric (including intra-areal) and callosal axons are functionally equivalent, albeit specialized for different portions of the visual field (reviewed in Innocenti 1986; Kennedy et al. 1991). Furthermore, the recent evidence pointing to precise timing as an essential requirement in cortical function (e.g., Engel et al. 1997; Ikegava et al. 2004; Izhikevich et al. 2004) would suggest that the temporal properties of the response to a visual stimulus should be similar across the visual field.

To analyze how the visual field is integrated along the interhemispherically split visual midline, we first investigated the width of the bihemispheric visual field representation. We next flashed short-lasting square stimuli alone or in a sequence at different positions within the visual field and investigated the dynamics of the CRFs as function of stimulus distance from the midline using 2 complementary techniques, fast optical imaging with voltage-sensitive dyes (VSDs) and local field potentials (LFPs). We then recorded the peripheral response fields (PRFs), that is, the portions of the visual field from which responses can be obtained at a given cortical site, near the midline of the visual field, and studied their spatiotemporal structure and dynamics.

Materials and Methods

Anesthesia

Fourteen female, adult ferrets (Mustela putorius), bought from a Swedish authorized breeder, were used in this study, subdivided among different experiments as detailed below. The animals were anesthetized with intramuscular doses of ketamine hydrochloride (Ketalar 10 mg/kg) and medetomidin hydrochloride (Domitor 0.3 mg/kg), supplemented with atropine sulfate (0.15 mg/kg). After inserting a cannula into the femoral vein and a tracheal tube, the animals were placed in a...
Electrophysiology

The visual cortex was exposed in the right hemisphere (or in both; below) and protected with mineral oil. Varnish-insulated tungsten microelectrodes (0.95–1.3 MΩ, exposed tip of ~15 μm), were inserted to 300–500 μm below the pial surface. The position of the penetrations was marked on a photograph of the cortical surface taken at the beginning of the experiment. The signals amplified via WPI DAM-5A and Tektronix AM502 amplifiers were studied in 2 frequency bands at 1–100 Hz and at 10 Hz–3 kHz. Using a script within Spike 4 acquisition system (Cambridge Electronic Design Ltd, Cambridge, UK), we computed the summated LFP from the low-passed signal and the poststimulus time histograms (PSTHs) from the high-passed signal, appropriately thresholded for spike extraction. Both PSTH and LFP were computed on 15 stimulus presentations.

The VSDs

A hermetic chamber was sealed to the skull over the cortex and filled with the staining solution, that is, 1 mg of VSD (RH795; Molecular Probes/Invitrogen, Carlsbad, CA) in 1.3 ml of artificial cerebrospinal fluid (NaCl 125 mM, KCl 2.5 mM, CaCl2 2 mM, MgCl2(H2O) 1 mM, NaHCO3 2.5 mM, NaH2PO4 1.25 mM, glucose 25 mM). The solution was left on the cortex for 2 h and then removed. A photograph of the recording area was taken with a CCD camera. The recordings were represented in both hemispheres. This bihemispherically represented in both hemispheres and the role of input from the contralateral visual areas in the representation. In 2 animals, 3–4 anteroposterior rows of penetrations, crossing the 17/18 border area, 18, spaced at 1.5 mm from each other, were performed in each hemisphere; within each row, the recordings were spaced at 500 μm. The position of the zero vertical meridians (i.e., the central border of the hemifield representation) for the left and the right eye were marked on the screen. The electrophysiological signal was amplified and filtered, visualized on an oscilloscope, and played through a loudspeaker. Receptive fields were outlined by hand by moving a bright circle or bar across the screen (as in Manger et al. 2002). In 2 additional animals, recordings were performed only in the right hemisphere, and lesions of striate and extrastriate areas were performed by aspiration of the gray matter in the left hemisphere. The histological analysis of the brains confirmed the extent of the lesions. We remapped the visual field in the right hemisphere repositioning the electrodes at the locations recoded before the lesion and compared the maps before and after the lesion.

To determine the physiological properties of the visual field midline, in 7 experiments, we studied, in the right hemisphere, the CRFs either with VSD or by reconstructing the distribution of LFPs recorded at different cortical locations. We used triplets of monocularly presented stimuli whose positions were systematically shifted across experiments within the visual field representation. Triplet consisted of a center (test) stimulus and of 2 additional (conditioning) stimuli falling on its right or on its left, at 4°-deg center-to-center separation. Each stimulus was presented alone, and then the center stimulus was preceded by presentation of the stimulus to its left (i.e., more peripherally in the same hemifield) or to its right (i.e., more central in the same hemifield) at 100-ms interstimulus interval. The position of the screen was adjusted so to place the stimuli near the visual midline, and their precise location was verified by mapping the visual field representation at the end of the experiment (as in Manger et al. 2002).

To study the CRFs, that is, the portion of the visual field from which responses can be obtained at a single electrode site, in 3 experiments, we recorded the responses to stimuli flashed at different locations in the visual field. A center (test) stimulus (same size, duration, etc., as above) was either presented alone or preceded by conditioning stimuli with the same characteristics but placed at 2°, 4°, 6°, or 8° above, below, on the right, or on the left of the test stimulus. The conditioning stimulus was presented 8, 25, 50, 100, or 200 ms before the onset of the test stimulus. We also recorded the response to the conditioning stimulus alone.

Results

Bihemispheric Representation of the Visual Midline in the Ferret

A total of 110 recordings were performed, evenly distributed between 2 animals and hemispheres, and the minimal response fields for each eye were mapped at each location (Fig. 1). A binocular, 8- to 10-deg-wide vertical strip of the visual field is represented in both hemispheres. This bihemispherically represented strip of visual field is narrower than the callosally
connected portion of the retinotopic maps in areas 17 and 18. This reaches as far as 20 deg of visual field, based on the retinotopic location of cell bodies of callosally projecting neurons and of callosal terminals. However, a fraction of neurons with receptive field centers beyond 10 deg from the zero meridian falls in acallosal zones. This fraction increases with eccentricity, from 10% at 10-deg azimuth to 100% at 50 deg (see Fig. 10 in Manger et al. 2002). In 2 experiments (data not shown), the minimal response fields near the vertical meridian were mapped before lesion of the contralateral areas 17–19 and then remapped after the lesion. All the receptive fields that were mapped before the lesion could also be mapped after the lesion. Therefore, we postulated that the corpus callosum (CC) might not provide a strong “driving” input to the contralateral hemisphere in the intact animal, although it does in the split chiasm preparation (Berlucchi and Rizzolatti 1968; Lepore and Guillemot 1982).

**Properties of Responses Elicited from the Midline of the Visual Field**

The position of the stimuli was systematically shifted across experiments (Fig. 2). Based on the results above, we expected stimuli falling in the peripheral 10–11 deg of the visual field to be processed in the contralateral hemisphere and those falling in the central 10 deg to be processed in both hemispheres with the medialmost stimuli, processed perhaps prevalently in the hemisphere contralateral to the recordings.

**CRFs Visualized with VSD**

The dynamics of the VSD/CRFs are shown in Supplementary Figure 1 and in Figure 3. The responses begin about 40–50 ms after the stimulus onset as an irregularly elongated spot of activity about 1 mm in its maximal diameter, oriented perpendicular to the 17/18 border. They progressively expand during the subsequent 40–50 ms to reach their maximal diameter of about 1.5 mm perpendicular to the 17/18 border and 1.1 mm parallel to it. They maintain the same diameter for about 40 ms to shrink again to their initial location in the next 80 ms and have disappeared at about 250–300 ms after stimulus onset. Comparison of the responses elicited from the central (right) and peripheral (left) stimuli (Supplementary Fig. 1) showed that the CRFs activated by the 2 stimuli overlap extensively, particularly at the peak of activation. However, the response to the first stimulus is centered slightly posterior to

---

**Figure 1.** Hand-mapped multiunit receptive fields recorded from the 2 hemispheres in experiment 0906. Receptive fields are numbered according to penetrations (different numbers for the different hemispheres). The same numbers refer to right eye and left eye receptive fields, with the dominant receptive field occasionally denoted with “D.” The zero meridians are defined as the line running through the ipsilateral periphery of the most nasal receptive fields (as in Manger et al. 2002). This is different from the vertical meridian, which by definition is the midline of the visual field and therefore runs half way between the zero meridians of the 2 hemispheres. Notice that the zero meridians of the 2 hemispheres are separated by 8–10 deg of visual angle; the strip of visual field between them provides a conservative estimate of the overlap of the visual field representations in the 2 hemispheres of the ferret. Notice also that the region of overlapping representation in the 2 hemispheres is callosally connected (see Fig. 10 in Manger et al. 2002).
that for the second stimulus. Therefore, the stimulus closest to the midline activated posterior area 18 and the adjacent area 17, and the other stimulus activated anterior area 18 and perhaps area 19, in agreement with the known topographical organization of the 2 areas (Manger et al. 2002). In most experiments, the expansion of the CRF was greater parallel than perpendicular to the 17/18 border, and so was the speed of expansion, with across-experiment variability (range of 8 measures 8.7–133 μm/ms).

The CRFs to the test stimulus were depressed by a preceding conditioning stimulus. In the example shown in Figure 3, the response to the center stimulus began at about 50 ms after stimulus onset (at 200 ms) and continued for about 200 ms (up to 440–460 ms). When preceded by the conditioning stimulus, the 2 CRF initially merge (at 260 ms), but then the CRF to the center stimulus is powerfully depressed. The depression might actually improve spatial and temporal resolution of the response because the CRF elicited by the center stimulus shrinks and its duration is decreased to about 100 ms. The depressive effects

Figure 2. Position of stimuli in the combined cortical imaging and VSDs mapping experiments. Three stimuli were flashed at different azimuths, separately or in a sequence (see text). Stimuli in the left hemifield were aimed at the hemisphere of recording (contralateral hemisphere) and those in the right hemifield at the other hemisphere (ipsilateral hemisphere). Stimuli near the midline of the visual field presumably reached both hemispheres (compare with Fig. 1). Stimulus width is 1.5 deg, and center-to-center stimulus separation is 4 deg.

Figure 3. Example of CRF dynamic evoked by the center stimulus and inhibition of CRFs to the center (cent) stimulus by the conditioning right and left stimuli. Notice that the response to the center stimulus alone which was flashed at 200 ms begins between 240 and 260 ms (preceding activity is either residual motion artifact due to heartbeat or spontaneous activity) and lasts until 460 ms. When preceded by the right or left stimuli (flashed at 100 ms), the response begins to fade at 300 ms and is terminated at 380 ms. The occurrence of stimuli (50 ms) is denoted by continuous lines.
were qualitatively similar in the 2 experiments in which the stimuli spanned the greatest azimuth (0915 and 0820; Fig. 2) and were also similar when comparing the effects of the most peripheral stimulus ("left" stimulus in 0820) with that of the most central stimulus ("right" stimulus in 0915; Fig. 2).

Because in the experiment 0915 the right (central) stimulus evoked a very weak CRF, the findings indicate that the magnitude of the depressive effect is independent of that of the CRF recorded at the same location. The depressive effect might originate from the activity of neurons far away, that is, in the contralateral hemisphere.

VSD/CRF and microelectrode recording sites are superposed in Supplementary Figure 2, and the VSD signal, LFPs, and PSTH of multunit responses are shown for each microelectrode location. The 3 types of response are usually elicited by the same stimulus, but the VSD response can be seen at cortical locations lacking PSTH response and, occasionally, the LFP response (Supplementary Fig. 2). LFP responses can be observed in the absence of PSTH responses (Supplementary Fig. 2), suggesting differential sensitivity of the 3 methods, with the VSD being slightly more sensitive than the LFP. The VSD response consists of a single upward signal (normalized as explained in Materials and Methods) lasting about 200–300 ms, depending on location, and essentially damping the oscillatory component of the LFP (described below). The peak of the PSTH precedes that of the LFP by 10.1 ± 3.1 ms \((P < 0.01)\) and the peak of the LFP precedes that of the VSD by 23.4 ± 7.0 ms \((P < 0.01)\) \((t\)-tests). CRFs Visualized with LFPs

The results of the VSD experiments conducted with the VSD RH 795 appeared not to be amenable to a more detailed quantitative spatiotemporal analysis. Instead, this was possible with the LFP responses.

Figure 4 shows location and dynamics of LFP/CRF to stimuli flashed at different azimuths in the same experiment shown in Supplementary Figure 1. LFPs typically consist of a first negative peak lasting about 100–120 ms, followed by a longer positivity lasting 150–200 ms. At some locations, the negative potential consists of 2 incompletely separated peaks corresponding to "on" and "off" stimulus components. Plotting together the responses to the same stimuli obtained at different locations shows that the negative peak of the response CRFs begins at 25–30 ms after stimulus onset and expands in the subsequent 20–30 ms to cover a territory 1–1.5 mm². It shrinks in the subsequent 80 ms and is replaced by the positive component of the LFP lasting up to 300 ms after stimulus onset. The amplitude of the response is largest near the CRF center and decreases toward its periphery. The topography of the CRF is compatible with the retinotopic organization of areas 17 and 18 (Manger et al. 2002) and with the VSD findings. The stimulus, which lies more peripheral in the contralateral visual hemisphere, activates area 18 anteriorly, whereas the more centrally located stimulus activates area 18 posteriorly, extending into area 17.

To clarify how the CRFs change with stimulus position, amplitude and latency of the negative LFP peak evoked by each stimulus were averaged across their CRFs in areas 17 and 18. The values obtained were subdivided in 5 stimulus azimuth bins from 0 deg, corresponding to the estimated border of the region of bitemporal representation, to 16–20 deg in the contralateral hemifield. The mean amplitudes and latencies across experiments at each azimuth were entered in Figure 5. The amplitude of the negative peak of the response drops by 50% from stimulus locations at 12- and 16- to 20-deg azimuth to those at 0 deg. The latency of the response peak increases from 46.7 to 60.3 ms over the same azimuth span. LFPs to stimuli within the central 0-8 deg of visual field have significantly longer latencies than those for stimuli at 12–20 deg \((t\)-test; \(P < 0.003)\). The significance of latency differences between the LFPs to right and left stimuli in the individual experiments tends to increase approaching the visual field midline \((t\)-test; \(P < 0.2\) for experiment 0909, \(P < 0.08\) for 0904, and \(P < 0.04\) for 0915).

The interaction between the peripheral (conditioning) stimuli caused depression of the negative component of the LFP response to the center (test) stimulus at 112 and facilitation at 42 microelectrode locations. An example of depressive interaction on the LFP/CRFs is shown in Supplementary Figure 3. When the center stimulus is preceded by the conditioning stimuli, the response is strongly depressed at 50 ms after stimulus onset and is completely replaced by the positive LFP component already at 70 ms.

Figure 5 shows a weak tendency to a decreased depression with test stimuli approaching the visual field midline. However, the differences in the magnitude of the depression caused by conditioning stimuli central or peripheral to the test stimulus in the 2 experiments in which they spanned the greatest azimuth (0915 and 0820; Fig. 2) were far from statistical significance \((P < 0.16; t\)-test, \(n = 40)\). Equally nonsignificant were differences in the depression elicited by the left stimulus in the experiment 0820 (the most peripheral stimulus across experiments) and by the right stimulus in 0915 (the most central stimulus across experiments; \(P < 0.36; t\)-test, \(n = 40)\). Finally, in the experiment 0915, the central and peripheral stimuli significantly differ for latency and amplitude of the LFP but not in their interaction with the test stimulus \((P < 0.11; t\)-test, \(n = 40)\). (These results also imply that the size of the depressive effect is independent from that of the negative (excitatory) phase of the LFP. Indeed, no significant correlation was found between the 2 across the entire set of the present data. We then investigated if proportionality existed between the size of the depressive interactions and the latency of the LFP, but none was found. There was also no significant correlation between the latency of the LFP and its amplitude. To explore further, the relations between latency/laterality of the LFP responses and magnitude of the depressive interaction, the results were divided in 2 groups according to whether the latency of LFP to the central stimulus was larger or smaller than that to the peripheral stimulus. This resulted in 2 groups of locations with highly significant latency differences (52.3 and 62.9 ms), but there were no significant differences in the magnitude of the interaction with the response to the test stimulus, nor with the size of the LFPs. Together, the results described seem to confirm that the suppressive effects are triggered from far away neurons as confirmed in Makarov et al. Forthcoming.)

The facilitatory interactions between stimuli appear to relate to the size of the LFP response to the center stimulus. Indeed, while the large responses are invariably depressed, some of the small ones are facilitated (data not shown).

PRF Near the Vertical Visual Field Midline

The fact that amplitude and latency of the responses differed in the central versus more peripheral portions of the visual field
could be due either to properties of the callosal connections or to the spatiotemporal structure of the PRFs (i.e., the portion of the visual field from which responses can be obtained at a single microelectrode position) in the callosally connected region near the 17/18 border. The latter was investigated by recording the responses to 1.5-deg square stimuli, flashed in a random sequence for 50 ms, in 2-deg steps along the 4 arms of a cross extending as far as 8 deg from a stimulus centrally located in the PRF. Responses (PSTHs or LFPs) were recorded at 15 locations, in the right hemisphere, within the central 10 deg of the visual field, in 3 ferrets.

At any given cortical location, amplitude and latency of the LFP response varied with stimulus eccentricity (Figs 6 and 7). The amplitude of the response negativity was maximal near the center of the PRF and progressively decreased away from it, usually disappearing at 8 deg, whereas the positivity could have a broader span. The amplitude of the LFP also depended on depth in the cortex, being maximal near the layer where, as a rule, recordings were performed (Fig. 7). The latency of the negative peak increased with eccentricity from 46.3 ms near the PRF center to 53–60 ms at 8 deg in the periphery. There were small (6 ms on average) nonsystematic variations of response latency with depth in the cortex.

To determine if stimuli interacted differently depending on timing and position within the PRFs in 5 experiments (12 locations; right hemisphere), we studied how conditioning
stimuli flashed at 2-, 4-, 6-, or 8-deg separation central or peripheral to a center stimulus modified the response to the latter. The center stimulus was, as above, placed in the center of the PRF, within the 10-deg portion of the visual field with bihemispheric representation. The interval between conditioning and test stimuli was of 8, 25, 50, 100, or 200 ms. The conditioning stimuli either enhanced or depressed the response to the test stimulus depending both on the angular and temporal separation between the stimuli. The strongest and clearest interactions were seen with 2- to 4-deg separation between stimuli and attenuated with larger stimulus separations (Fig. 7). The facilitatory effects dominated at interstimulus time intervals of 8 ms (55% of cases), whereas with time intervals of 25–200 ms depressive effects predominated (84% of cases). No consistent differences related to whether conditioning stimuli were central or peripheral to the test stimuli could be demonstrated.

Discussion

Mapping Visual Responses with VSDs and LFPs

The CRF and the PRF responses we recorded are closely related, respectively, to the "point image" introduced by McIlwain’s (1975) retinocollicular studies and to the traditional receptive fields of visual electrophysiology. However, because they are based on the analysis of VSD and LFP signals instead of single units, they achieve a lower level of spatial resolution and higher sensitivity. These properties help in understanding if some features of the responses recorded near the midline of the visual field might be due to callosal connectivity.

The VSD/CRF dynamics in the ferret visual areas are similar to those reported in other sensory systems and/or species. The responses, started at about 40 ms after stimulus onset, reached their maximal expansion 40–50 ms later, to return to baseline in the following 150 ms. Similar dynamics were reported for the monkey area 17 (Grinvald et al. 1994; Slovin et al. 2002), for the visual areas of the ferret (Roland et al. 2006), and for the barrel field of the rat (Petersen et al. 2003). In both monkeys and ferrets, the activity spread faster parallel than perpendicular to the 17/18 border. Because the retinotopic magnification factor in the ferret is larger parallel than perpendicular to the 17/18 border (Manger et al. 2002), the CRF expansion might actually be radially symmetric in visual field coordinates.
We noticed 3 differences between the VSD and LFP responses. First, the LFP peaked about 20 ms before the VSD. This latency difference might in part be due to delays between the responses in layer 4, where the LFP was recorded, and the summed depolarization of the distal portion of the apical dendrites, which probably constitutes the main component of the VSD (Grinvald et al. 1994). Also, the VSD responses did not show a sign reversal corresponding to the negative-positive components of the LFP (as in Grinvald et al. 1994; but see Derdikman et al. 2003). Finally, the VSD signal spread horizontally further than the LFP signal, at least with the number of stimulus repetitions used in the present experiments, which was chosen to minimize volume conduction artifacts.

The CRF expansion appears to be due to activity spreading along the tangential collaterals of layers 2 and 3 pyramidal neurons (Grinvald et al. 1994; Petersen et al. 2003). However, we found that at a given cortical site the responses from the periphery of the PRF can be delayed by about 20 or more milliseconds, compared with the center, a finding resembling the center-periphery receptive field delays in the response of V1 neurons in the monkey (Rossi et al. 2001). Therefore, center-periphery delays in the PRFs can contribute to the different responses latencies within the CRF. The relative contribution of local connections, feedback cortical connections (Angelucci et al. 2002) or subcortical mechanisms, will have to be dissected by ad hoc experiments.

**Some Properties of the Cortical Representation of the Visual Midline**

Microelectrode recordings showed that a central 8- to 10-deg-wide strip of the retina is represented in both hemispheres in the ferret. This strip includes the central vertical meridian of the binocular visual field; therefore, 4–5 deg of the ipsilateral visual field, between the zero meridian (here defined as in Manger et al. 2002) and the central vertical meridian, are represented in each hemisphere. This is less than what was obtained by imaging the intrinsic optical signal (about 10 deg; White et al. 1999). Mapping the minimal response fields might have underestimated the degree of overlap, whereas imaging might have overestimated it, by showing subthreshold activity relayed across the CC. From retrograde transport studies, the nasotemporal overlap of the receptive field centers of ganglion cells, in the ferret retina, was estimated to be about 5 deg (Morgan et al. 1987).

In preliminary experiments (data not shown), lesions of the corresponding contralateral visual areas did not modify the ipsilateral visual field representation along the 17/18 border (as in the cat; Leicester 1968; but see Payne 1990). Also, inactivation of the contralateral hemisphere depressed but did not eliminate the responses of neurons in areas 17 and 18 (Payne et al. 1991). In contrast, callosal transection eliminated the representation of the ipsilateral visual field in area postero medical lateral suprasylvian of the cat (Marzi et al. 1982).

The visual midline showed some unexpected properties. The amplitude of the LFP responses progressively decreased approaching the zero meridian within the central 10–15 deg of the visual field, whereas the latency progressively increased. The latency difference of about 14 ms between the responses elicited from near the zero meridian and those evoked by more peripheral stimuli is compatible with the conduction delays along callosal axons (Innocenti 1986). This is how comparable delays were interpreted in man (Rugg et al. 1984; Saron and Davidson 1989; Brown et al. 1998) because the response to ipsilateral stimuli is lost in callosal or callosotomized subjects (Rugg et al. 1985; Brown et al. 1998). However, those responses were recorded from lateral occipital or parietal electrodes, and therefore, they may not reflect the activation of the primary visual areas. As mentioned above, the contribution...
of callosal connections to the responses in these areas might be stronger than in the primary areas.

Perceptual peculiarities across the visual midline were tentatively ascribed to less effective interhemispheric than intrahemispheric processing. Cognitive (Kanizsa type) contours are less effectively completed across than within the hemispheres (Pillow and Rubin 2002). Waves of interocular rivalry are delayed by about 173 ms, when crossing the visual midline (Wilson et al. 2001). More relevant to the present work, visual stimuli flashed sequentially at the corners of a square centered on the visual midline are perceived as apparent motion along the vertical rather than along the horizontal (cross-hemispheric) direction. Although this could be interpreted as due to the conduction latency introduced by callosal connections in the horizontal direction, similar results were obtained in callosal-split patients (Ramachandran et al. 1986; see also Gazzaniga 1987; Naikar and Corballis 1996). Our interpretation is that they may be due to the longer response latencies near the midline.

Increased processing latency to stimuli presented near the visual field midline was reported in man (Carrasco et al. 2003). These findings were explained as due to the increasing proportion of magnocellular ganglion cells in the retinal periphery demonstrated by Azzopardi et al. (1999) in primates. A similar explanation may apply to the ferret, but we propose an alternative/complementary possibility. Retrograde fillings in the ferret showed a substantial drop of ganglion cell density near the line of nasotemporal decussation (Morgan et al. 1987). Therefore, the contribution of retinogeniculate PRF center-to-periphery gradients to the responses probably increases approaching the zero meridian. As the responses become progressively dominated by the peripheral portion of the PRFs, their latency can be expected to increase and their magnitude to decrease. Indeed, we observed increased latency and decreased amplitude of the responses with increasing distance of the stimulus from the PRF center.

The interpretations above suggest that callosal connectivity, rather than causing peculiar neurophysiological and perceptual phenomena along the visual field midline, may just fail to modify features of the cortical response caused by the properties of retino-geniculo-cortical input. Possibly, the discrete, short-lasting stimuli used here are not processed by interhemispheric interactions. This unexpected conclusion was confirmed in the companion paper that showed lack of callosal transfer for similar stimuli (Makarov et al. Forthcoming).

The depressive interactions between spatially and temporally contiguous stimuli might partially compensate for the functional heterogeneity of the visual field because they seem to be relatively independent from central-peripheral gradients and interstimulus delays (Figs 5 and 7). Depressive/inhibitory interactions between neighboring stimuli with high contrast (as those used here) falling in the same hemifield have been well documented (e.g., Toth et al. 1996; Chen et al. 2001). Callosal connections can mediate comparable inhibitory interactions between hemifields/hemispheres (Innocenti 1986; Hughes and Peters 1990; Payne et al. 1991; Desimone et al. 1993; Makarov et al. Forthcoming).

**Supplementary Material**

Supplementary Figures 1-3 can be found at: http://www.cercor.oxfordjournals.org/.

**Funding**

European Community research (contract APEREST); the Swedish Research Council (contract K2002-33X-12594-05B to G.M.I.); a Wenner-Gren Foundation fellowship and the Science Promotion, Culture, Sports, Science and Technology of Japan (Grants-in-Aid for Scientific Research C18591912) to H.N.

**Notes**

The authors are grateful to Professors Akitoshi Hanazawa and Per Roland, for their help in setting up the VSD laboratory and the analysis software, and to Sonata Valentiniene for her histological work and laboratory assistance. M.C. and F.K. were Erasmus Program students. **Conflict of Interest.** None declared.

Address correspondence to Prof. Giorgio M. Innocenti, Department of Neuroscience, Karolinska Institutet, Retzius väg 8, S-17177, Stockholm. Email: Giorgio.Innocenti@ki.se.

**References**


Makarov VA, Schmidt K, Castellanos NP, Lopez-Aguado I, Innocenti GM. Forthcoming. Stimulus-dependent interaction between the visual areas of the two hemispheres of the ferret (Mustela putorius). Cereb Cortex.


