Visual fMRI Responses in Human Superior Colliculus Show a Temporal–Nasal Asymmetry That Is Absent in Lateral Geniculate and Visual Cortex

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Sylvester R, Josephs O, Driver J, Rees G. Visual fMRI responses in human superior colliculus show a temporal–nasal asymmetry that is absent in lateral geniculate and visual cortex. J Neurophysiol 97: 1495–1502, 2007. First published November 29, 2006; doi:10.1152/jn.00835.2006. Eye patching has revealed enhanced saccadic latencies or attention effects when orienting toward visual stimuli presented in the temporal versus nasal hemifields of humans. Such behavioral advantages have been tentatively proposed to reflect possible temporal–nasal differences in the retinotectal pathway to the superior colliculus, rather than in the retinogeniculate pathway or visual cortex. However, this has not been directly tested with physiological measures in humans. Here, we examined responses of the human superior colliculus (SC) to contralateral visual field stimulation, using high spatial resolution fMRI, while manipulating which hemifield was stimulated and orthogonally which eye was patched. The SC responded more strongly to visual stimulation when eye-patching made this stimulation temporal rather than nasal. In contrast, the lateral geniculate nucleus (LGN) plus retinotopic cortical areas V1–V3 did not show any temporal–nasal differences and differed from the SC in this respect. These results provide the first direct physiological demonstration in humans that SC shows temporal–nasal differences that LGN and early visual cortex apparently do not. This may represent a temporal hemifield bias in the strength of the retinotectal pathway, leading to a preference for the contralateral hemifield in the contralateral eye.

INTRODUCTION

Eye patching provides a simple way to reverse which visual hemifield (left or right) is temporal or nasal. With the right eye patched, the left hemifield becomes temporal and the right nasal, whereas the reverse holds with the left eye patched instead. Eye patching has uncovered temporal–nasal differences in several aspects of visual behavior. For instance, newborns show pronounced advantages for orienting toward visual stimuli in the temporal versus the nasal hemifield (Lewis and Maurer 1992; Rothbart et al. 1990). Although such biases are less absolute in adults, temporal hemifield advantages are still detectable with more subtle measures such as saccadic latencies (Kristjansson et al. 2004), covert orienting (Rafal et al. 1991) or choice saccades to bilateral stimuli (Posner and Cohen 1980).

It has frequently been proposed (Rafal et al. 1991) that such behavioral results may reflect a biased representation favoring the temporal hemifield in the retinotectal pathway from retina to superior colliculus (SC), which may lead to a preference for the contralateral hemifield of the contralateral eye in the SC. This might account for the pronounced temporal–hemifield advantages found in infants, whose retinotectal pathway is thought to mature before geniculostriate vision (Johnson 1990). It might also explain why these same temporal–hemifield advantages can still occur in hemianopic adult patients (Dodd et al. 2002; Rafal et al. 1990), who retain intact retinotectal pathways despite damage to the geniculostriate system.

Although retinal projections from the contralateral eye that specifically represent the temporal visual field predominate in the cat retinotectal pathway (Sterling 1973), this anatomic asymmetry may be less complete in monkeys (Hubel et al. 1975; Perry and Cowey 1984; Pollack and Hickey 1979; Williams et al. 1995; Wilson and Toyne 1970). Moreover, some temporal–nasal asymmetries for the peripheral field may arise even at the retina (Stone and Johnston 1981; Van Buren 1963) or striate cortex in monkeys (LeVay et al. 1985), although at greater eccentricities than the behavioral effects seen in man. Thus it cannot be simply assumed that only the retinotectal pathway could show temporal–nasal asymmetries in humans (just as one cannot assume that only the retinotectal pathway mediates visual orienting; Sumner et al. 2002). One physiological method for examining any asymmetries in humans is to use functional magnetic resonance imaging (fMRI) to compare visual responses elicited by temporal and nasal visual stimulation in the SC with those of the lateral geniculate nucleus (LGN) and visual cortex.

Studies of macaque SC suggest that it is anatomically and functionally divided into superficial and deep layers. Neurons in the deep layers are weakly visually responsive but are primarily involved in orienting movements of the head and eyes in response to sensory stimuli. In contrast, neurons in the superficial layers respond to a broad range of stationary and moving visual stimuli apparently regardless of stimulus orientation, size, shape, or velocity (Cynader and Berman 1972; Goldberg and Wurtz 1972) and contain an orderly map of the contralateral visual field (Cynader and Berman 1972). Most cells, apart from those at the posterior pole representing the far temporal periphery (Hubel et al. 1975), receive binocular input (Moors and Vendrik 1979) and many show some tuning for retinal disparity (Berman et al. 1975). Their main input is from the retinotectal pathway (Schiller and Malpeli 1977), but their response properties may also be influenced by the geniculo-striate pathway by corticotectal feedback projections from striate cortex (Wilson and Toyne 1970) and extrastriate cortex (Fries 1984).

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The human SC shows fMRI responses to contralateral visual field stimulation and also some degree of retinotopy (Schneider and Kastner 2005). If temporal–nasal differences largely reflect retinotectal pathway contributions as previously proposed (see above), then SC responses to monocular visual stimuli should presumably be greater for temporal versus nasal hemifields, but those of structures in the geniculostriate pathway should not. Accordingly, here we measured visual responses of the SC, LGN, and retinotopic V1–V3 using fMRI, while independently manipulating two factors: which eye viewed the stimuli and which visual field was stimulated. Because reversing the stimulated eye reverses whether the left or right hemifield is temporal or nasal, this design correspondingly manipulated whether visual stimulation contralateral to a particular brain hemisphere was temporal or nasal (see Supplementary Fig. S1A for a diagram showing hypothesized visual pathways from the retina to early visual areas). Note that any such manipulation of temporal/nasal stimulus presentation can also be understood in terms of eye preferences in any area with responses lateralized to one visual hemifield. For instance, temporal hemifield biases could reflect a preference for contralateral stimuli presented in the contralateral eye.

The SC is small and lies close to prominent blood vessels, making it difficult to image with conventional fMRI (although see Schneider and Kastner 2005). We therefore used high spatial resolution fMRI (3T with 1.5 × 1.5 × 1.5-mm voxels) giving occipital lobe and upper brain stem coverage only. To circumvent physiological noise from cardiac-cycle influences on SC images, we adapted established algorithms that correct for cardiac-induced brain stem motion (Glover et al. 2000). We then determined whether SC and other visual structures showed any temporal–nasal biases in fMRI responses to lateralized monocular stimulation.

Methods

Eight healthy right-eye-dominant subjects (mean age 30.2 yr, four male) gave written informed consent to participate in the study, which was approved by the local ethics committee. Eye dominance was assessed using the Porta sighting test (Porta 1593), which consists of an observer extending one arm, then with both eyes open aligning the thumb with a distant object. The observer then alternates closing of one or the other eye to determine which eye is viewing the object (i.e., the dominant eye). Subjects lay supine in the scanner and had one of their eyes covered with a patch attached to a wooden pole that could easily be moved to cover the other eye between runs. To ensure that no light leaked in through the edges of the patch, we first made sure that the patch completely blocked out light entering the eye it covered in each subject in the scanner environment. Before the start of each run in the study, we verified that subjects were covering the correct eye and that they could not see anything out of the patched eye. Subjects were then instructed not to move the patch until the run ended and we verified that the patch had stayed in place before moving it over to the other eye (in preparation for the next run). Visual stimuli were projected from an LCD projector (NEC LT158, refresh rate 60 Hz) onto a screen viewed by a mirror positioned within the MR head coil. All stimuli were presented using MATLAB (The MathWorks) and the COGENT 2000 toolbox (www.vislab.ucl.ac.uk/Cogent/index.html). In addition to a 0.5° central fixation cross, the visual stimuli consisted of a 13° wedge with a 3° foveal cutout, made up of alternating black and white checks (scaled linearly with eccentricity) reversing contrast at 8 Hz. This stimulation was presented either to the left or to the right of fixation, at 3 and 13° eccentricity for the innermost and outermost edge, respectively (see Supplemental Fig. S1B for a diagram). To minimize any influence of extraneous scattered light, the external scanner environment was darkened and the scanner bore and head coil were lined with nonreflective material.

Each subject was scanned for four runs, alternating the unpatched eye on each successive run (verified by the experimenter), in a manner that was counterbalanced across subjects. In each run the wedge stimulus was presented eight times for 21 s, with a 15-s rest period between presentations and with these presentations alternating between left and right hemifields. Subjects, who were all experienced psychophysical observers, were instructed to maintain fixation and this was confirmed by on-line monitoring of video output from a long-range infrared eyetracker (ASL 504LRO Eye Tracking System, Applied Science Laboratories, Bedford, MA).

Imaging and analysis

A 3T Siemens Allegro system acquired T2*-weighted blood oxygenation level–dependent (BOLD) contrast image volumes, using an interleaved sequence every 3.0 s. Each volume consisted of 30 contiguous 1.5-mm-thick slices, positioned on a per subject basis in parallel to the calcarine sulcus to give coverage of the occipital lobe and upper brain stem with an in-plane resolution of 1.5 × 1.5 mm (Haynes et al. 2005). The interleaved sequence limited signal interaction between spatially adjacent slices. In total, four scanning runs, each consisting of 125 image volumes, were acquired per subject. During scanning, pulse oximetry data were recorded continuously from the right index finger to allow analysis in relation to the cardiac cycle (see following text).

Imaging data were analyzed using SPM2 (www.fil.ion.ucl.ac.uk/spm). After discarding the first five image volumes from each run to allow for T1 equilibration effects, image volumes were realigned, manually coregistered to each subject’s structural scan, and smoothed with an isotropic 2-mm Gaussian kernel (Turner et al. 1998). Automated coregistration with SPM was not used because it would lead to inaccuracies in registration of the echoplanar (EPI) and anatomical images, attributed to limited brain coverage and minor distortions in EPI images resulting from the high resolution sequence. Coregistration was therefore performed carefully by hand, allowing exact coregistration of the calcarine sulcus and superior colliculus on the EPI scans to each subject’s structural scan.

Activated voxels in each experimental condition were identified using a statistical model containing boxcar waveforms representing each of the four experimental conditions, convolved with a canonical hemodynamic response function and mean-corrected (Turner et al. 1998). Six head-motion parameters defined by the realignment procedure plus 12 parameters related to the cardiac cycle derived from pulse oximetry data (Glover et al. 2000; Josephs et al. 1997) were added to the model as 18 separate regressors of no interest. Multiple linear regression was then used to generate parameter estimates for each regressor at every voxel. Data were scaled to the global mean of the time series and high-pass filtered (cutoff: 0.0083 Hz) to remove low-frequency signal drifts.

The cardiac noise correction was implemented at the level of modeling the measured signal and not at the level of image reconstruction, i.e., image data were not modified. The underlying model we used assumed that cardiac effects on a voxel’s signal depend on the phase of the image slice acquisition within the cardiac cycle (Josephs et al. 1997). Sine and cosine series (≤third order) were used to describe the phase effect on a single reference slice (passing through SC), creating six regressors. The phase for the adjacent slice (acquired 0.5 TR later) was also used to create a second set of six sine and cosine series, thus taking into account the increased temporal difference between adjacent slices in our interleaved slice acquisition. As shown in Josephs et al. (1997), the model is best adapted to the slice of reference. However, the large coherent component in the
cardiac noise (arising from only small variations in heart rate) can be adequately corrected by a single set of regressors and functions for removal of physiological noise throughout the image. This precluded the need for regressors related to the cardiac cycle to be generated for each slice (or the need for any slice timing correction). Although this method is less sensitive to incoherent noise components from throughout the image (because these will be modeled in areas only where the regressors match the cardiac activity; i.e., the reference slice), the influence of these components is minor (Josephs et al. 1997). Because adjacent slices were acquired 1.5 s apart, using two models (one for the slice closest to the SC and one for the slice spatially adjacent to this) captured noise related to the cardiac cycle more effectively. This approach proved to be very effective in accounting for (and thereby eliminating) variance related to the cardiac cycle, particularly in the region of the upper brain stem (see Fig. 1 for an illustrative subject).

Inclusion of the cardiac regressors should influence the summary statistics but not the parameter estimates (provided that the cardiac cycle was not correlated with the visual stimuli). This was confirmed empirically with data from representative subjects where the parameter estimates of activation in SC voxels were minimally altered by applying the cardiac regressors. However, for the purposes of identification of activated voxels in the spatially local region of the SC, incorporation of the cardiac regressors was useful. Including the cardiac correction removed uncorrelated noise and led to an increase in the $t$-value for the peak activation in the SC cluster of both subjects (12 and 21%, respectively). Practically, this allowed the use of a standard threshold ($P < 0.05$, uncorrected) when identifying the SC in all subjects.

**Localization of cortical and subcortical visual areas of interest**

To identify the boundaries of primary visual cortex (V1) and extrastriate retinotopic cortical areas V2 and V3, standard retinotopic mapping procedures were used (Serenko et al. 1995). Checkerboard patterns covering either the horizontal or vertical meridian were alternated with rest periods for 16 epochs of 26 s over a scanning run lasting 165 volumes (using a standard 3 mm voxel sequence; note that only this localizer for determining the borders of cortical areas used a 3-mm resolution and the main experimental findings in SC, LGN, and V1–V3 all come from the $1.5 \times 1.5 \times 1.5$-mm sequence described above). Mask volumes for each region of interest (left and right V1, V2d, V2v, V3d, V3v) were obtained by delineating the borders between visual areas using activation patterns from the meridian localizers. We followed standard definitions of V1 together with segmentation and cortical flattening in MrGray (Teo et al. 1997; Wandell et al. 2000).

The locations of the SC and LGN in each subject were identified using an anatomical and radiological brain atlas (Duvernoy 1999) to find anatomical landmarks on each subject’s high-resolution structural scan. Next, functional data coregistered to the structural scan were used to locate visually responsive voxels within the previously defined anatomical boundaries, using a contrast of contralateral greater than ipsilateral visual stimulation. This method of localization was previously used successfully to investigate human LGN responses with high-resolution fMRI (Haynes et al. 2005). The LGN and superior colliculi plus their response to ipsilateral and contralateral visual field stimulation are shown for two illustrative subjects in Figs. 2 and 3. These figures are primarily intended to illustrate the selection of the voxels used in the experimental analysis. The signal-to-noise ratio in the SC varied widely across subjects, so localization of the SC using the underlying structural anatomy in combination with the functional localizers was technically a crucial aspect of this study.

To extract activity from cortical visual structures, we created mask volumes for each region of interest (left and right V1, V2d, V2v, V3d, and V3v) from the retinotopic maps. Regression parameters resulting from analysis of the imaging time series for the main experiment were then extracted for all voxels activated by visual stimulation of the contralateral hemifield in each region of interest (at a conventional statistical threshold of $P < 0.001$, uncorrected). These were then averaged across subjects, yielding a plot of percentage signal change in each area for each experimental condition averaged across subjects (Fig. 4). Responses reported for the LGN and SC are taken from the average of contiguous visually responsive voxels within the anatomically defined boundaries. For the SC the average cluster size for contiguous visually responsive voxels in each subject was 10 voxels ($SE \pm 1$), whereas in the LGN it was 45 voxels ($SE \pm 7$).

### RESULTS

The main findings are presented in Fig. 4. Across the group of eight subjects, all visual areas studied showed robust and statistically significant responses to contralateral visual field stimulation, as expected. The responses of subcortical structures LGN and SC to contralateral visual field stimulation were numerically lower than for retinotopic cortical areas, consistent with previous work (Kastner et al. 2004). However, when independently examining responses to temporal or nasal monocular stimulation, a strong difference was immediately apparent when comparing SC with all other visual structures (Fig. 4). Critically, the SC showed significantly increased responses to...
The data show significant differences in response to temporal versus nasal stimulation for the human retinotectal pathway (SC), but not in the geniculostriate pathway (LGN, plus V1–V3; cf. Lie 2004). However, it is conceivable that some local temporal–nasal differences within visual cortex might have been obscured by the procedure we used to select voxels. Voxels in each region of interest were selected on the basis of their response to contralateral visual stimulation across all runs (see Methods). This could in theory bias voxel selection toward voxels responding equally to contralateral stimulation in the right and left eyes, which may have excluded any voxels that showed strong eye biases. To investigate this, we therefore repeated the analyses described above but now using independent selection of voxels responding to contralateral monocular stimulation of either eye (i.e., rather than selection being biased on responding to contralateral stimulation in right and left eyes, now the selection was based on right or left eye). Reassuringly, our results were unchanged. Critically, the SC remained the only structure showing a significantly greater response to temporal versus nasal hemifield stimulation (see Supplemental Fig. S3 for full details).

Another possible reason for the pattern of results we found could be the (standard) procedure of averaging across populations of voxels within each area, if the distribution of temporal/nasal preferences across those voxels within such areas was distributed bimodally. Indeed, monocular structures such as the...
Temporal–nasal asymmetry in human superior colliculus

Figure 4. Group-average responses (n = 8) of human primary visual cortex (V1), extrastriate retinotopic cortical areas V2 and V3, LGN, and SC to monocular hemifield visual stimuli presented in the nasal or temporal visual field. BOLD contrast responses to identical monocular hemifield checkerboard stimuli, presented in the temporal or nasal visual field (manipulated by eye-patching), for V1–V3, LGN, and SC, averaged across all subjects and both hemispheres (A), or separately for the right (B) or left (C) hemispheres. See Methods for full details of data analysis procedure. Percentage signal change averaged across 8 subjects are plotted for each visual area (error bars ± 1 SE). Nasal stimulation is plotted in black and temporal stimulation in white. Only the SC showed a significantly increased response to contralateral temporal compared with nasal visual stimulation. This was the case both when averaged across subjects and hemispheres (t(7) = 3.84, P = 0.006) and for responses of the SC averaged across subjects within each hemisphere [right SC: t(6) = 2.45, P = 0.044; left SC: t(7) = 2.58, P = 0.036]. There were no significant differences in the responses evoked for temporal compared with nasal stimuli in V1–V3 and LGN, neither averaged across hemispheres nor when considering either hemisphere alone, and these areas differed reliably from the SC in this respect (interaction with area; see Results). Asterisk (*) symbol denotes statistical significance (P < 0.05, 2-tailed).

LGN might at sufficiently high spatial resolution in theory show such a bimodal distribution reflecting eye preference for laterized stimulation (although note that previous studies of LGN with identical resolution thus far showed a unimodal distribution of ocular preferences; see Haynes et al. 2005, their Supplemental Fig. 1). To systematically examine this possibility we further investigated the responses of individual voxels in LGN and V1–V3. Visually responsive voxels were defined by responses to contralateral minus ipsilateral stimulation (at P < 0.001 for V1–V3 and P < 0.01 for LGN, both uncorrected). We extracted the parameter estimates for each voxel for contralateral hemifield stimulation when the stimulus was presented temporally or nasally. We then subtracted the parameter estimate for nasal hemifield stimulation from the parameter estimate for temporal hemifield stimulation. This gave a value that provides a measure of the extent to which each voxel shows any preference to favor stimulation of either the temporal or nasal hemifield (positive values denote a numerical temporal preference; negative values denote a nasal preference). Frequency histograms of these voxelwise preferences confirmed that all such distributions were exclusively unimodal for all geniculostriate visual areas (i.e., LGN, V1, V2, V3) in all subjects (see Fig. 5). Moreover, these distributions all had a peak frequency very close to zero preference, consistent with the lack of any temporal–nasal effect in Fig. 4. However, a similar frequency histogram of the voxelwise preferences in SC in all subjects showed a distribution that was systematically skewed toward temporal preference and thus a positive mean (see Fig. 5). This is consistent with the significant temporal–nasal difference in SC responses demonstrated in Fig. 4.

Taken together, these data demonstrate directly for the first time that the human SC responds more strongly to temporal than to nasal contralateral visual stimulation. In contrast, no such difference was evident in the LGN or cortical areas V1–V3, which differed significantly from the SC in this respect.

Discussion

Our results show that human SC responses, but not those of the LGN, V1, V2, or V3, were significantly greater for monocular visual stimuli presented in the temporal hemifield than in the nasal hemifield. This provides strong and direct evidence for a biased representation favoring the temporal hemifield within the human SC (although whether this arises solely from retinotectal or also reflects some corticotectal influences on the SC is not yet established). This bias may provide a neural substrate for temporal–nasal asymmetries observed in prior purely behavioral studies that had sought to examine putatively collicular-related aspects of visual behavior (e.g., saccades and orienting; Posner 1980).

Functional MRI of human superior colliculus

In nonhuman primates, earlier single-cell recording showed that individual neurons in the superficial layers of the SC are highly responsive to visual stimuli and receive afferent inputs from the retina (Schiller and Malpeli 1977), striate cortex (Wilson and Toyne 1970), extrastriate cortex (Fries 1984), and frontal eye fields (Fries 1984; Kuypers and Lawrence 1967). Within the superficial layers of each SC there is a systematic map of the contralateral visual field (Cynader and Berman 1972; Goldberg and Wurtz 1972). The central visual field is represented anteriorly, whereas the periphery is represented posteriorly. The upper fields are represented medially and the lower fields laterally. The central 10° of the visual field is expanded to represent >30% of the surface of the colliculus. The projection of the contralateral hemiretina includes the entire colliculus, whereas the projection of the ipsilateral hemiretina is represented only in the anterior portion of the colliculus, leaving a monocular representation of the temporal hemifield at the posterior pole (Hubel et al. 1975).

As far as can be ascertained, human SC seems to follow a similar anatomical pattern (Hilbig et al. 1999; Laemle 1981; Tardif et al. 2005). However, it has been difficult to study human SC responses using neuroimaging techniques until recently because of the small size of the SC, plus its deep location near vascular structures that increase local physiological noise (Guimaraes et al. 1998). Previous attempts to image the superficial layers of the SC used either cardiac triggering of
responded to temporal compared with nasal stimulation (see also Fig. 4). Positive values denote a temporal preference; negative values denote a nasal preference. For averaging across subjects, there were no systematic preferences in the overall responses of either left or right LGN or V1 for stimulation of the contralateral hemifield in the contralateral eye (V1, 54%; LGN, 34%). This contrasts with our findings in SC, where 90% of voxels showing eye biases preferred stimulation of the contralateral hemifield in the contralateral eye (equivalent to the temporal hemifield). This suggests that the differential effect of temporal and nasal visual stimulation we found in SC but not in LGN or V1, might arise from the responses of monocular neurons within SC. However, the same pattern of results could arise if neurons within voxels showing eye preference were weakly binocular with responses favoring the contralateral eye.

Of note, there did not seem to be any consistent clustering of such voxels preferring stimulation of one eye within SC (Supplemental Fig. S4). However, caution is appropriate before concluding that human SC shows no monocular structure, resulting from the small size of the SC and comparatively coarse fMRI spatial resolution. In monkey, the SC largely constitutes binocularly responsive neurons (as discussed above), although there is a monocular region at the posterior pole (which represents the far temporal periphery, i.e., >25°). We found no consistent evidence for a posterior region showing monocular preference within the human SC here (Supplemental Fig. S4). However, the lateral extent of temporal visual field stimulation in the fMRI scanner was limited by the head coil to 20°. We may therefore have been unlikely to have stimulated this putative monocular region representing very eccentric visual locations. It is conceivable, although unlikely, that either extraocular (King et al. 1996) or intraocular (Faubert et al. 1999) light scatter might have led to inadvertent stimulation of visual field locations outside the central 20° eccentricity of our visual stimulus. As is standard practice, we took precautions against this arising, including darkening the external scanner environment plus lining the scanner bore and head coil with nonreflective material. Nevertheless, if such inadvertent scattered peripheral stimulation had taken place, it is in

FIG. 5. Distributions of nasal and temporal field preferences in visually responsive voxels in V1–V3, LGN, and SC. A–E: frequency histograms across subjects plot the number of voxels in each visual area (V1–V3, LGN, and SC) as a function of their numerical preference for monocular temporal vs. nasal contralateral stimulation. Preference of each voxel was derived by subtracting the response estimate arising from contralateral nasal stimulation from the response estimate arising from contralateral temporal hemifield stimulation (see RESULTS). Positive values denote a temporal preference; negative values denote a nasal preference. For averaging across subjects, the absolute number of voxels was normalized by dividing by the total number of voxels in each visual area in each subject. Vertical dotted lines represent the mean; dashed lines represent ±95% CI. In areas V1–V3 and LGN (A–D), it is apparent that all distributions are unimodal (rather than bimodal), suggesting that voxels in each area formed a single population with a mean response to temporal vs. nasal stimulation centered on zero (see also Fig. 4). However, in the SC (E), the distribution was positively skewed and the mean was >0, suggesting that the SC preferentially responded to temporal compared with nasal stimulation (see also Fig. 4).

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turn conceivable that the high sensitivity of the superior colliculus to contrast (Schneider and Kastner 2005) might have led to elevated SC responses associated with the putative monocular region of the SC. Further research with even higher spatial resolutions and visual stimulation at much greater (or more restricted) eccentricities may therefore be necessary to definitively resolve this remaining issue.

Possible neural substrate for behavioral temporal–hemifield advantages is confirmed in the collicular pathway

The retinotectal pathway is phylogenetically ancient and predates the geniculostrate system (see Karten 1989). It might have evolved to augment rapid orienting of the eyes and head to salient peripheral stimuli. In species where the eyes are positioned on or toward the side of the head, such a temporal–hemifield advantage in the retinotectal pathway could convey a survival advantage by reducing the time required to orient to objects appearing in the periphery of vision. Our data provide the first direct evidence that human SC responses are greater for stimuli presented in the temporal versus nasal visual field. The SC is considered intimately involved in orienting to salient stimuli through target selection (Ignashchenkova et al. 2004; McPeek and Keller 2004) and related shifts of visual attention (Muller et al. 2005). Increased responses in the human SC for temporal hemifield stimuli, as observed here, might thus explain temporal–hemifield advantages previously observed in human visual orienting behavior (e.g., Kristjansson et al. 2004; Posner and Cohen 1984; Rafal et al. 1990). Indeed, such behavioral asymmetries were previously tentatively attributed to the retinotectal pathway. However, hitherto such proposals were all based on indirect speculation that temporal–nasal asymmetries might arise within the colliculus but not for the geniculate–striate pathway. Here, for the first time, we confirm these asymmetries directly in the human brain. It remains uncertain whether the temporal–nasal asymmetries shown behaviorally, and now with fMRI, are merely a relic of evolution or continue to convey useful advantages in primates.

This study (and indeed any noninvasive imaging study of any stimulus property in humans) cannot distinguish whether any bias in fMRI responses evoked by a particular stimulus arises from an increased number of neurons responding to that stimulus or to a larger gain associated with neuronal responses to one particular stimulus. There are established anatomical asymmetries in temporal versus nasal hemifields in the retina (Stone and Johnston 1981; Van Buren 1963) and striate cortex in monkeys (LeVay et al. 1985), but only for retinal eccentricities of well beyond 15°. In the central 15° of the visual field, where temporal hemifield behavioral advantages occur (see Rafal et al. 1991), and where we stimulated here, there is no evidence for any anatomical asymmetry in the temporal versus nasal projection from the retina to the SC (Williams et al. 1995) it is still possible that the SC might be fed by differently distributed populations of retinal ganglion cells when compared with LGN and V1. Although our findings do not distinguish between a structural or functional explanation for the bias toward the temporal hemifield seen in the SC, importantly they accord with the temporal–nasal behavioral asymmetry found in humans (Rafal et al. 1991).

BOLD contrast fMRI activity more closely correlates with local field potentials than with axonal spiking (Logothetis et al. 2001) and thus at a population level that cannot clearly distinguish between the effect of feedforward and feedback influences on a region. The temporal–hemifield biases we observed in SC responses could therefore in principle reflect either retinotectal or corticotectal influences. However, we found no differences in BOLD signal from V1 or other retinotectal cortical areas here when comparing temporal and nasal hemifield stimulation. This lack of temporal–nasal asymmetry in cortical structures may argue against the notion that the temporal biases we observed in SC originate from the corticotectal pathway (see also, e.g., Fries 1984). However, our data cannot exclude the influence of corticotectal feedback on the SC. This might be examined in the future by imaging the SC in patients with cortical lesions.

In conclusion, we have provided direct evidence for a bias in the visual response of the human SC that favors the temporal over the nasal contralateral hemifield. No such bias was apparent in the geniculostrate pathway (LGN, V1–V3), which differed significantly from the SC in this respect. The collicular preference for the temporal–hemifield shown here may thus provide a neural substrate for analogous temporal–hemifield advantages in visual behavior.

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