Topography of covert visual attention in human superior colliculus

Sucharit Katyal, Samir Zughni, Clint Greene, and David Ress

University of Texas at Austin

Center for Perceptual Systems, Imaging Research Center, Section for Neurobiology, and Department of Psychology,

1 University Station, A8000

Austin, Texas

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Corresponding author:

David Ress

ress@mail.utexas.edu

University of Texas at Austin

Imaging Research Center, R9975

3925-B West Braker Lane

Austin, TX 78759
ABSTRACT

Experiments were performed to examine the topography of covert visual attention signals in human superior colliculus (SC), both across its surface and in its depth. We measured the retinotopic organization of SC to direct visual stimulation using a 90°-wedge of moving dots that slowly rotated around fixation. Subjects ($N = 5$) were cued to perform a difficult speed-discrimination task in the rotating region. To measure the retinotopy of covert attention, we used a full-field array of similarly moving dots. Subjects were cued to perform the same speed-discrimination task within a 90° wedge-shaped region, and only the cue rotated around fixation. High-resolution fMRI (1.2 mm voxels) data were acquired throughout SC. These data were then aligned to a high-resolution T1-weighted reference volume. The SC was segmented in this volume so that the surface of the SC could be computationally modeled, and to permit calculation of a depth map for laminar analysis. Retinotopic maps were obtained for both direct visual stimulation and covert attention. These maps showed a similar spatial distribution to visual stimulation maps observed in rhesus macaque, and were in registration with each other. Within the depth of SC, both visual attention and stimulation produced activity primarily in the superficial and intermediate layers, but stimulation activity extended significantly more deeply than attention.

KEYWORDS

superior colliculus; visual attention; retinotopic map; laminar profiles; fMRI; topographic registration
The superior colliculus (SC) is a midbrain structure that exhibits a variety of visual functions. It exhibits retinotopically organized responses to visual stimulation (Cynader and Berman 1972), is involved in gaze shifts and the orientation of eye movements, and its activity is known to be modulated by the deployment of covert visual attention (Cavanaugh and Wurtz 2004; Ignashchenkova et al. 2004; Muller et al. 2005; Robinson and Kertzman 1995; Schneider and Kastner 2009).

SC is a laminar structure divided into seven layers: three superficial (thickness 1.3—1.8mm), two intermediate (thickness 1.3—1.8mm) and two deep (thickness 0.7—1.3mm) (Paxinos and Mai 2004; Tardif and Clarke 2002). Superficial layers receive direct retinal input, and contain neurons that respond primarily to visual stimulation (Robinson and McGlurkin 1989). Intermediate layers contain visually responsive neurons and visuomotor neurons that discharge prior to saccades (Ma et al. 1991). Deep layers contain neurons that respond to multimodal sensory (somatosensory, auditory, visual) inputs (Sparks and Hartwich-Young 1989). Visual response is thus most prominent in the superficial layers and decreases with depth into the SC (Tiao and Blakemore 1976; Wallace et al. 1996).

Studies in rhesus monkeys have demonstrated that SC contains a retinotopic map of visual stimulation in the superficial layers (Cynader and Berman 1972). This stimulation map is aligned and functionally connected with a retinotopic motor map of eye movements in the intermediate layers (Lee et al. 1997; Robinson 1972; Schiller and Stryker 1972; Sparks 1988; Tardif et al. 2005). In each SC, the map represents the contralateral visual field. Roughly speaking, polar angle is
represented along the medio-lateral direction with neurons having receptive fields in upper visual field located medially and those having receptive fields in the lower visual field located laterally within the SC. Eccentricity is represented along the antero-posterior direction with foveal eccentricities located in anterior and peripheral eccentricities located in posterior part of SC.

Consistent with its role in facilitating gaze orientation, SC also appears to be involved in the orientation of covert attention. Electrophysiology studies in monkeys have used spatial cueing tasks to demonstrate that attention produces an enhancement in SC activity (Goldberg and Wurtz 1972; Ignashchenkova et al. 2004). Also, microstimulation studies in monkeys have shown a spatially specific enhancement of performance in visual tasks (Cavanaugh and Wurtz 2004; Muller et al. 2005), suggesting a retinotopic organization of visual attention in SC.

There have been fewer studies of SC in humans using functional magnetic resonance imaging (fMRI). SC is a difficult structure to image because of its small size and close proximity to large blood vessels. Early work using fMRI in humans demonstrated that visual stimulation signals are reliably lateralized within the SC (DuBois and Cohen 2000). Subsequently, it was shown that human SC contains a polar angle retinotopic map of the visual stimulation to the contralateral hemifield (Schneider and Kastner 2005). Schneider and colleagues recently also demonstrated the presence of visual attention signals in the SC using fMRI, though a retinotopic variation of attentional signals was not assessed. Methodological challenges in imaging the SC have recently been addressed by (Wall et al. 2009) who demonstrated a set of fMRI techniques for improving signal quality in SC. Using
some of the principles from that study another recent study has shown that saccade execution is also lateralized in the contralateral human SC (Krebs et al. 2010).

Here, we present measurements using higher resolution fMRI methods that demonstrate the presence of a retinotopic map of covert visual attention in human SC in addition to the map of visual stimulation. The data also show that the two maps are in good registration. Our high-resolution data permit analysis of laminar activity profiles in SC. The results show that both visual stimulation and attention produce activity principally in the superficial 2 mm of depth. However, attention activity is significantly more superficial than that of stimulation.

**MATERIALS AND METHODS**

**Subjects**

Five subjects performed several two-hour-long scanning sessions: 1—2 stimulation retinotopies, 1—2 attention retinotopies. Four of the five subjects performed one lateralized stimulation, and two lateralized attention sessions.

Each session consisted of 14—18 228-s runs. The first 12-s of data was discarded to reduce transient effects. Informed consent was obtained from all subjects based on a protocol approved by the UT Austin Institutional Review Board. Three subjects (two of which had participated in the fMRI experiments) participated in separate stimulation and attention psychophysics sessions outside the scanner while their eye movements were monitored.
Stimulus protocols

Stimuli were generated using Matlab (MathWorks Inc., Natick, Massachusetts) running PsychToolbox-3 (Brainard 1997) on a Macintosh Pro computer. Stimuli were presented using a 60 Hz LCD projector onto a rear-projection screen mounted inside the scanner bore 0.5 m from the subject's eyes. The display was calibrated using a radiometer, and had a mean luminance of 109 cd/m².

Polar angle map of visual stimulation. Stimulus was a 90° wedge of moving dots (4°/s speed), eccentricity 2—10°, which was divided into 2 × 3 virtual sectors (Fig. 1A). The task of the subjects was to discriminate if dots in one of the sectors were moving at a speed faster or slower than dots in the other sectors. The wedge of moving dots was displayed for 1.5 s, followed by a 0.5-s response period. Subjects were instructed to maintain attention during the dot display period and be as accurate as possible while responding in the response period. Hence, this condition corresponds to stimulation with exogenously cued attention. The wedge was then rotated by the width of one virtual sector (30°), and the process was repeated. The entire stimulus rotated 9.5 times around fixation with a period of 24 seconds while subjects maintained fixation. Task performance of the subjects was maintained at >71% by continually adjusting the magnitude of the speed difference between dots in the faster or slower sector relative to the other dots in the wedge using a pair of randomly interleaved two-up-one-down staircases. After every two consecutive correct trials the speed difference was reduced by 8% and for every incorrect trial the difference was increased by 8%.
Before the scanning sessions, subjects practiced the task outside the scanner for 2—3 20-min training sessions until their performance stabilized. The initial speed difference was based upon their performance during these training sessions, and was typically between 1.6—2.5°/s.

During fMRI scanning sessions, subjects performed this task over the course of many ~4-min-duration runs. The discontinuity introduced between runs tends to slightly disorient subjects. We dealt with this by starting subsequent runs with a speed difference 1.5 times the mean speed difference calculated during the latter half of the previous run. This easing of difficulty permitted subjects to quickly reorient to the task strategy and their performance then tended to rapidly return to their respective thresholds after ~30—40 trials in a stereotypical fashion that repeated well from run to run.

**Polar angle map of visual attention.** Stimulus was a full field (eccentricity 2—10°) of similarly moving dots divided into $2 \times 12$ virtual sectors. A pair of orthogonal cue lines (length, 0.08°) extending from fixation directed attention of the subject to a 90° wedge-shaped region of the stimulus (Fig. 1B). The cue rotated around fixation (24-s period) and subjects performed a similar speed discrimination task in the cued aperture. To counterbalance the speed difference in the cued aperture, a speed increment or decrement was also present in one of the sectors within a 90° wedge directly opposite to the cued wedge. Subject performance was adjusted using a similar staircase procedure as described previously.
Lateralized stimulation & attention. To obtain laminar profiles, we used lateralized stimulation and attention to maximize the duty cycle of the functional response. For the lateralized stimulation condition, a 144° wedge of moving dots alternated 9.5 times between the left and right visual fields with a 24-s period. The wedge on each side was divided into $2 \times 4$ virtual sectors and task of the subjects was, once again, to discriminate if the dots in one of the sectors were moving faster or slower than dots in other sectors. Trials again had a 2-s duration, with six trials on each side. For the lateralized attention condition, there were moving-dot wedges on both left and right sides with an arrow cue below the fixation mark indicating the side to be attended. Subjects performed the same task as in the lateralized stimulation condition. In addition, during the last trial on each side, the fixation dot changed color warning the subject that attention should be switched on the next trial.

MRI methods

Imaging was performed on a 3T scanner (GE Signa Excite HD) using the GE-supplied 8-channel head coil. Eight 1.2-mm-thick quasi-axial slices (170-mm field-of-view) covered the entire SC with the prescription oriented roughly perpendicular to the local neuraxis. A set of $T_1$-weighted structural images was obtained on the same prescription at the end of the session using a 3D RF-spoiled GRASS (SPGR) sequence (15° flip angle, 0.78-mm pixels). These images were used to align the functional data to the segmented structural reference volume (see below).

MR imaging of the SC at 1.2-mm sampling requires a multi-shot acquisition. Acquisition time is limited by $T_2^*$ decay to ~60 ms. For our scanner and FOV, a single-shot acquisition requires >77 ms even at peak bandwidth. We therefore
investigated both two- and three-shot acquisitions in terms of both raw SNR and functional contrast-to-noise ratio. A low-bandwidth (62.5 kHz) three-shot acquisition worked best by both measures. Furthermore, a three-shot acquisition has a low-pass filtering effect that reduced high-frequency noise corresponding to pulse and respiration.

Functional images were obtained on a prescription co-aligned with the above structural images. A 6.4-ms windowed-sinc pulse was used to provide a sharp slice-select resolution. We used a three-shot outward-spiral acquisition (Glover 1999; Glover and Lai 1998) to obtain an inplane pixel size of 1.2 mm. Echo time, $T_E = 40$ ms, was longer than typically used in cortex (30 ms), because we measured a correspondingly longer $T_2^*$ in SC tissue (~60 ms) than typically observed in cortical gray matter (~45 ms). Acquisition bandwidth was limited to 62.5 kHz to reduce peak gradient current that causes unwanted heating on our scanner. We chose $T_R = 1$ s, so with three shots, a volume was acquired every 3 s.

The multiple shots were combined together after correction by subtracting the initial value and linear trend of the phase. Registration of the functional and structural images was generally very good, so $k$-space calibration of the gradients was unnecessary. Image reconstruction was done by gridding with a Kaiser-Bessel kernel using 2:1 oversampling. $T_E$ was incremented by 2-ms on the first frame to estimate a field map from the first two volumes acquired, and this map was used for linear correction of off-resonance image artifacts (Glover and Law 2001). Concomitant field effects arising during the readout gradients were also corrected by adding a time varying phase in the image reconstruction (King et al. 1999).
Reconstructed images had a SNR of ~20. Temporal power spectra in SC voxels typically showed little of the structure associated with physiological noise; the use of a 3-shot acquisition had a strong filtering effect on the comparatively high-frequency effects of cardiac pulse and respiration.

The anatomical images collected in each session were used to align the functional data to a structural 3D reference volume, which was acquired for each subject in a separate session. The structural reference volume was T₁-weighted with good gray-white contrast, and was acquired using a 3D, inversion-prepared, SPGR sequence (min. $T_E$ and $T_R$, $T_I = 450$ ms, $15^\circ$ flip angle, isometric voxel size of 0.6 or 0.7 mm, 2 excitations, ~28-min duration).

**Image Analysis**

Analysis of the fMRI data was done using the mrVista software package (available for download at [http://white.stanford.edu/mrvista.php](http://white.stanford.edu/mrvista.php)) as well as tools developed upon the mrVista framework in our lab. We estimated in-scan motion using a robust scheme (Nestares and Heeger 2000) applied to a temporally smoothed (3—5-frame boxcar) version of the fMRI time-series data. Between-run motion was corrected using the same intensity-based scheme, this time applied to the temporal average intensity of the entire scan. The last run of the session was used as the reference. After motion correction, the many runs recorded during each session were averaged together to improve SNR.

The intensity of the averaged data was spatially normalized to reduce the effects of coil inhomogeneity. The normalization used a homomorphic method, that is, dividing by a low-pass filtered version of the temporally averaged volume image.
intensities with an additive robust correction for estimated noise. A sinusoid at the
stimulus repetition frequency was then fit to the normalized time series at each
voxel, and from this fit we derived volume maps of response amplitude, coherence,
and phase. The coherence value is equivalent to the correlation coefficient of the
time-series data with its best-fit sinusoid.

We segmented the tissue of the midbrain, brainstem, and portions of the
thalamus (Fig. 2A) using a combination of automatic and manual methods provided
by the ITK-SNAP application (Yushkevich et al. 2006). The CSF-tissue interface of
the SC was then interpolated from the segmentation using isodensity surface
tesselation, and this initial surface was refined to reduce aliasing artifacts (Figs. 2B,
D) using a deformable-surface algorithm (Xu et al. 2006). This surface provided
vertices and outward normal vectors used as a reference for the laminar
calculations described below as well as a means to visualize the functional data.

A distance map was calculated between the SC tissue voxels and the vertices of
the SC surface. We used these distances to measure laminar position (i.e., depth, s)
in the reference volume. Functional data were then aligned and resampled to the
reference volume (Nestares and Heeger 2000). Thus, each volume voxel was now
associated with a complex response (amplitude, phase, and coherence) and a
laminar coordinate.

Laminar profile analysis. We used these complex response and laminar coordinate
associations to calculate laminar profiles of functional activity. Because SC has a
variable thickness across its lateral-medial extent, we defined three 3-mm-diam
regions-of-interest (ROIs) to cover activated regions on lateral, central, and medial
portions of each SC. The active portion of the SC was first obtained based on the lateralized stimulation condition as described below. In each of the three ROIs for every subject, we obtained the complex amplitude as a function of depth for all runs averaged together. In order to correct for hemodynamic delay, phase normalization was performed for each run by dividing the complex amplitude of the profile with the mean phase within the respective ROI restricted to the collicular surface where the data was strongest and most reliable. A boxcar-smoothing kernel (0.6- or 0.7-mm width) was convolved with the average complex amplitude data as a function of depth; the magnitude of this convolution was the laminar profile. Laminar profiles for attention and stimulation were normalized to unity for ease of comparison. Profiles obtained without correction for the hemodynamic delay were qualitatively similar but less reliable.

We used bootstrapping to obtain confidence intervals on the laminar amplitude profiles in each subject and all subjects combined. For each ROI, we calculated the complex amplitudes for each run to create an ensemble (typically 36 for each subject) of complex amplitude datasets. We then formed averages by resampling this ensemble with replacement over 5000 iterations, and calculated the laminar profile anew for each resampled average.

Centroids of the laminar profiles were calculated to quantify comparisons of depth between the attention and stimulation conditions using:

\[ c = \frac{1}{A} \int_{s_{\min}}^{s_{\max}} sA(s)ds, \]
where $A(s)$ is the amplitude as a function of depth and $\hat{A}$ is the average amplitude.

The integration limits $s_{\text{min}}$ and $s_{\text{max}}$ were set to 0 and 4 mm, respectively, as that is roughly the thickness of human SC. The centroid calculation was also bootstrapped across the ensemble of runs to obtain confidence intervals.

Retinotopy analysis. For the retinotopic mapping data, we performed a laminar segmentation process to enable depth averaging that improves the quality of data. Small (1.6-mm-diam) disks of tissue were associated with each vertex of the surface model along the entire superficial SC surface, and each disk was then extended both inward and outward from the SC tissue using the local surface normals to form an individual laminar neighborhood (Ress et al. 2007). For each point on the SC surface, we used these associations to average the time series over a particular depth range. Coherence analysis was performed on this depth-averaged time series to obtain amplitude, phase and coherence values. For visualization we used the phase values of the functional data, with time-series depth averaged over a range of 0—1.8 mm, overlaid upon the SC surface (Fig. 3).

We used the depth-averaged lateralized stimulation data to define ROIs in each individual subject for the analysis of the retinotopic maps and the laminar profiles described above. ROIs were defined by choosing a contiguous region consisting of the most responsive portion of the collicular surface. Specifically, ROIs were defined for each subject by adjusting the coherence threshold for each subject within the range 0.30—0.50, so that a similar surface area was included, ~23 mm$^2$. These ROI boundaries are marked using black dotted lines in Fig. 3.
To test the registration of the visual stimulation and attention maps, we performed correlation analyses within the ROIs described above between phase values obtained for the attention retinotopies against those obtained for the visual stimulation retinotopies. Phase values for each session were corrected by subtracting an estimate of the hemodynamic delay. This was obtained by calculating the mean phase of data obtained in the ROIs of both colliculi in the complex plane, and then subtracting $\pi$. Delay values were small, in the range of 1.5—4 s. Mean hemodynamic delay, averaged across all subjects for both attention and stimulation conditions, was 2.9 s; the color pinwheel in Fig. 3 has been rotated accordingly.

We also obtained rough boundaries of the entire superficial extent of the SC using manual inspection of the high-resolution $T_1$-weighted volume anatomy. These boundaries are marked in Fig. 3 by red dashed lines.

We again used bootstrapping to obtain confidence intervals on the correlations for each subject and all subjects combined. For each attention session, we calculated a run-by-run ensemble of depth-averaged complex amplitude datasets. We then performed our correlation analysis with the retinotopy data for 5000 averages of the attention-condition runs, each average obtained by resampling the ensemble with replacement. The $p$ values corresponded to the fraction of the correlations yielding a fit with slope $\leq 0$.

In order to verify our retinotopic mapping procedures, we also obtained ROIs located in dorsal early visual areas V2d and V3d in three of the five subjects. We used standard phase-encoded retinotopic-mapping methods (DeYoe et al. 1996; Engel et al. 1997; Sereno et al. 1995) to initially define these regions, and then
restricted our analysis only to that portion of the each ROI that intersected with our slice prescription. Our experiments produced widespread activation in these early visual areas for both stimulation and attention conditions (Fig. 2C). We also verified registration between stimulation and attention maps in these visual cortex ROIs.

In order to evaluate the quality of the retinotopic phase progression, we calculated the orientation of the retinotopic phase spatial gradient for each of the stimulation and attention maps using a method similar to a previously described approach (Silver et al. 2005). Horizontal and vertical components of the gradient were calculated with depth-averaged phase values for each pixel on flattened maps of cortex. The horizontal component was the mean difference between the sine of the phases of the three adjacent pixels on the right and the sine of phases of the three adjacent pixels on the left, and similarly for the vertical component. Orientation of each pixel was calculated as the inverse tangent of the ratio of the vertical to the horizontal phases. Orientation of each map was calculated as the mean orientation of pixels within the retinotopy ROIs described above. Orientations of the stimulation and attention maps for each subject are marked below individual colliculi with dark blue arrows (Fig. 3A). The two brown arrows show 95% confidence intervals of the phase gradient calculated using bootstrapping procedures similar to those described previously. We also used the horizontal and vertical vector components to calculate the statistical significance of each phase gradient. For each bootstrapped repetition, we formed the dot product of the vector with the mean vector. The $p$-value was then fraction of the dot product magnitudes <0.
Eye Movements

For each of three subjects we ran six 216-min runs each of the stimulation and attention stimuli while eye movement data was collected using the ASL Eye-Trac 6000 (Applied Science Laboratory, Bedford, MA) eye tracking system outside the scanner. Time series of horizontal and vertical gaze coordinates as well as the pupil diameter were acquired at a sampling rate of 60 Hz. In order to examine eye movements we projected each eye-position measurement onto a unit vector in the direction of the target or cue region, yielding a large ensemble of measurements (~12,000, after taking valid pupil and corneal reflection recognition into account). The mean of this measurement quantifies the bias of eye position in the target direction, which can be compared to the mean eccentricity of the target region. We repeated this comparison for saccade vectors extracted from the eye-position data to also test for bias in saccadic eye movements.

RESULTS

Behavioral performance. All subjects were able to successfully maintain accuracy at >71% during each run. For the stimulation and attention retinotopies, average performance was 81% and 82% respectively. Discrimination thresholds were somewhat better for the attention retinotopy condition (1.0°/s) than the stimulation retinotopy (1.2°/s); this difference was significant (negligible p) in three of the five subjects. Performance was slightly better for lateralized stimulation and attention conditions, 85% and 82% respectively, with discrimination thresholds of 1.2 and 1.1°/s, respectively and not significantly different for all four subjects (p > 0.4).
lower thresholds for the attention condition suggests that some subjects were able to perform the purely attentional task more effectively than the stimulation (with attention) task, probably because the latter task does not elicit full usage of covert attentional resources.

In order to quantify the retinotopic maps we calculated phase gradients (see Materials and Method), indicated by dark arrows under each individual colliculus in Fig. 3 along with their bootstrapped 95% confidence range indicated by the two brown arrows. The phase gradients were statistically significant ($p < 0.05$) in 8/10 individual colliculi (subjects 1, 3 and 4 bilateral, subject 2 and 5 left) and were between 93—95% confidence for the other two colliculi. Retinotopic phase gradients were also highly significant ($p \sim 0$) in the group data. In 5/10 colliculi, there was a reliable anterior-posterior tilt to the retinotopic maps, from antero-medial through postero-lateral (subject 4 bilateral, subjects 1, 5 right, subject 2 left). However, the phase progression right colliculus of subject 2 seems to be reliably oriented in an anterior-posterior direction.

**Polar angle map of visual stimulation.** For all subjects, visual stimulation was reliably lateralized, i.e., phases corresponding to the left visual field were observed in the right colliculus and those corresponding to the right visual field in the left colliculus (Fig. 3A). Amplitudes of the MR signal were typically between 0.1—0.2%, except for subject 4, who was an unusually strong responder (Table 1). On visual inspection, 8/10 colliculi were seen to have a nearly complete polar angle retinotopic map of visual stimulation (subjects 3—5 bilateral, subjects 1—2 right). The top half of the contralateral visual field was represented medially (blue in the left colliculus and
cyan/green in the right colliculus) and the bottom half was represented laterally (pink/magenta in the left and yellow in the right colliculus). There was an over-representation of phases corresponding to the horizontal visual field in the colliculi as compared to the vertical visual field, with a particular paucity of phases near the lower vertical meridian.

Polar angle maps of visual attention. As in the visual stimulation condition, phases corresponding to visual attention were also reliably lateralized in all subjects (Fig. 3B). Amplitudes of the attention signals were smaller than the stimulation signals, typically between 0.05—0.13% (Table 1). On visual inspection, phase progressions in 7/10 colliculi gave the appearance of retinotopic maps with a medial-to-lateral organization of phases corresponding to the upper and lower contralateral visual fields respectively, similar to the stimulation maps (subjects 1, 4, and 5 bilateral; subject 3 left). In 4/10 colliculi, the phase-gradient calculations indicated a reliable ($p < 0.05$) medial-to-lateral organization of attention signals (subjects 3—4 bilateral). When the phase gradient data was analyzed across all subjects, it was highly significant ($p \sim 0$) for both left and right colliculi.

If SC indeed contains retinotopic maps of stimulation and attention, they should be in spatial registration. Testing this registration provides another measure of the validity and reliability of the observed spatial distributions. In order to quantify registration, we performed correlations between the visual stimulation and attention polar-angle phase data within the same depth-averaged regions. Statistical significance of these correlations was assessed non-parametrically using bootstrapping (see Methods above). Correlations for individual colliculi ($R^2 = 0.55$—
0.95) were significant ($p < 0.05$) in 6/10 colliculi (Table 1). Correlations with both colliculi analyzed together were large (typically $R^2 = 0.72—0.97$) and significant ($p \sim 0$) for all subjects indicating strong and reliable lateralization of the SC responses.

Figure 4A shows correlation results for a representative single subject (left: $R^2 = 0.78$, $p = 0.02$; right: $R^2 = 0.26$, $p = 0.22$; together: $R^2 = 0.89$, $p \sim 0$). For all subjects combined (Fig. 4B), correlations were strong (left: $R^2 = 0.32$; right, $R^2 = 0.56$, together: $R^2 = 0.80$) and highly significant for both individual and combined colliculi ($p \sim 0$).

To confirm the efficacy of our high-resolution fMRI mapping methods for both stimulation and attention, we performed our analyses in the early visual cortex of three subjects during the same sessions. Based on previous work (Brefczynski and DeYoe 1999), we expected that both visual stimulation and attention would produce retinotopically specific activation in these brain regions, and the two maps would be in good registration. Slice prescription in three of the five subjects covered the dorsal aspect of early visual cortex. Accordingly, for each of the three subjects we analyzed fMRI response data in four visual areas: left and right dorsal V2 and V3. Strong and significant correlations between the stimulation and attention polar angle phase data were observed in nine of the twelve individual subject ROIs (Table 2) as well as for the combined ROI data (left: $R^2 \sim 0.42$, $p < 0$; right: $R^2 \sim 0.56$, $p < 0$) (Fig. 4C).

Slopes of the fits between attention and stimulation were less than unity in three of the colliculi that showed significant correlations between stimulation and
attention, as well as the group-averaged data (Table 1). Slopes of the fits were also less than unity in the visual cortex group data.

Eye movements. It is possible that the retinotopic maps were affected by subjects moving their eyes towards the stimulus aperture. To ensure that the subjects were able to maintain fixation as instructed, we tracked eyes of three subjects in separate sessions outside the scanner. The gaze coordinate components along the polar angle of the stimulus for all subjects were very small, with a mean value 0.06° and –0.01° of visual angle for attention and stimulation conditions respectively. Though the attention projections were significant (p<0.05) due to the large number of samples (~12000), they were still minute compared to the 5° mean eccentricity of the stimulus. We also tested bias by analyzing the component of saccades along the stimulus or cue region; the mean values were small, <0.1° and statistically indistinguishable from zero, except for one subject in the stimulation condition (mean ~0.3°, p<0.01). Thus, subjects’ eye position did vary from the fixation mark, but their eye movement errors were random, without significant bias toward the target aperture.

Laminar Profiles of Stimulation and Attention. In order to evaluate laminar activity profiles of stimulation and attention, we chose three ROIs for each colliculus: lateral, central and medial (Fig. 5A). Laminar profiles for the left colliculus of subject 4 (Fig. 5B) show the typical character of the data, which reached a peak near the superficial surface of the colliculus and decreased with increasing depth. We did not see significant left-right or subject-to-subject differences in the profiles, so we obtained profiles averaged across both colliculi in all subjects (Fig. 5C) to improve our
statistical power. Stimulation and attention laminar profiles were normalized to unity to facilitate visual comparison between the profiles. The activity was distinctly superficial for both stimulation and attention conditions, generally evident only for $d < 2$ mm, with much less activity for $2 < d < 4$ mm. The medial and central profiles were ~32% thinner than the lateral profile, which is consistent with the anatomy of SC (Paxinos and Mai 2004; Tardif and Clarke 2002). Laminar profiles for the lateral and central ROIs showed that activity in the stimulation condition extended deeper into the colliculus than the attention condition. This difference of depths as measured by the centroid of distribution over a depth of 0-3.5 mm was significant for both the lateral and central ROIs (centroid differences: lateral, 0.31 mm, $p = 0.0002$; central, 0.22 mm, $p = 0.016$; medial, 0.09 mm, $p = 0.20$). For both conditions, the superficial activity extended outside of the SC ($d < 0$), probably because of the presence of superficial blood vessels. Since the depth of the colliculus is variable, we also calculated centroids over depth ranges of 0—3 and 0—4 mm and found that the differences in centroids for the lateral and central ROIs had similar absolute values that remained significant (centroid differences, 0—3 mm: lateral, 0.30 mm, $p \sim 0$; central, 0.15 mm, $p = 0.027$; medial, 0.05 mm, $p = 0.26$; centroid differences, 0—4 mm: lateral, 0.34 mm, $p = 0.0014$; central, 0.24 mm, $p = 0.04$; medial, 0.14 mm, $p = 0.15$).

At a coherence threshold of 0.30, ~40% of the colliculus showed activity corresponding to the lateralized stimulation condition, which had a maximum eccentricity of 10°. This is roughly consistent with monkey stimulation maps that
have shown that a third of the colliculus is represented for the central 10° of the visual field (Cynader and Berman 1972).

**DISCUSSION**

We observed a topographic representation of signals corresponding to visual stimulation in the SC of 8/10 colliculi using fMRI, and in the group data, thus confirming the presence of retinotopic maps of polar angle in human SC. The orientation of these maps was roughly consistent with the visual stimulation and eye movement maps obtained in monkeys (Cynader and Berman 1972; Robinson 1972) as well as those obtained in a previous fMRI study in humans (Schneider and Kastner 2005).

In at least 4/10 individual colliculi, and in the group data, covert visual attention signals were also topographically organized, indicating the presence of polar angle retinotopic maps of visual attention in human SC. Visual inspection gave the appearance of similar patterns of phase progression between the attention and stimulation maps (Fig. 3).

Phase correlations in the individual colliculi between the polar angle stimulation and attention conditions supported the presence of a retinotopic map of visual attention in SC (Fig. 4). We obtained good correlations in 7/10 individual colliculi, though the individual slopes were typically less than unity (Table 1). The correlations obtained for both colliculi together were strong and had near-unity slope, demonstrating that visual stimulation and attention signals were similarly lateralized.
Likewise, in early visual cortices, fMRI has previously demonstrated the presence of a retinotopic map of covert attention that is in registration with the retinotopic map of visual stimulation (Brefczynski and DeYoe 1999). Here, we verified that observation using high-resolution fMRI in areas V2d and V3d (Fig. 4c).

The intermediate layers of human SC contain neurons that are believed to respond retinotopically to eye movements. Since, eye movements were not tracked during our scanning sessions, it is possible that the stimulation and attention maps may have been partly confounded by subjects’ eye movements. However, we did track eye movements in separate sessions outside the scanner and showed that the subjects were able to successfully maintain fixation while performing the visual stimulation and attention tasks.

Typically, the amplitudes of responses were slightly higher for the stimulation than the attention condition (Table 1). Data quality in SC for the attention condition was slightly worse than stimulation, which is why we combined two attention runs for three of the five subjects. The noise levels in the phase data are not surprising, given the very small amplitudes of signals observed in this study.

We observed slopes less than unity in some of the phase correlations between the attention and stimulation conditions in SC and visual cortex. Taken literally, this would indicate a more compact distribution of attention phases compared to stimulation, possibly because of a weaker response along the vertical meridian for attention as compared to simulation. However, we note that for individual colliculi, the slope increases with the $R^2$ value — more strongly correlated data have slopes closer to unity. This suggests that the observation of slopes < 1 may be an artifact
caused, for example, by small misalignments between the attention and stimulation runs, or by additional noise in the attention data causing phase wrapping.

The present study has also demonstrated a novel collection of MRI methods that improve the reliability and utility of functional data in subcortical structures. An interleaved (3-shot) spiral sequence provided a useful means of physiological noise suppression. We used a reference volume segmented at the tissue-CSF boundary of the midbrain, including the SC, facilitating the averaging of data over multiple sessions. Moreover, we formed accurate surface models at the tissue-CSF boundary, allowing us to average the fMRI activity over depth. Altogether, these averaging techniques considerably improved contrast-to-noise ratios, enabling the higher spatial resolution used in this study. The methods also permitted analysis of laminar variations in BOLD activity, which will be greatly useful for the study of the structurally heterogeneous subdivisions evident in sub-cortical brain regions.

Our laminar profiles showed that in both the stimulation and attention conditions, activity reached a peak near the superficial surface of the SC, and then gradually decreased with increasing depth. Activity was greatest at depths <2 mm, corresponding most likely to the superficial and intermediate layers of the SC. This is consistent with the decrease in the number of visually responsive neurons and the increase in their visual receptive field sizes as one proceeds inward from the superficial layers (Tiao and Blakemore 1976; Wallace et al. 1996).

Alternatively, it is possible that because oxygenated blood is delivered and recovered superficially, laminar profiles of BOLD activity may not have a one-to-one spatial correspondence to local neural activity; activity in deeper regions may
simply be less hemodynamically evident than superficial activity. A similar tendency for hemodynamic activity to peak near the superficial tissue surface has been previously observed in cortical gray matter (Harel et al. 2006; Lu et al. 2004; Ress et al. 2007).

Irrespective of the explanation of the superficial nature of the laminar profiles, we observed that the centroids of activity in the stimulation condition were significantly deeper than the attention condition, and produced significantly more activity in the deeper layers of the SC (Fig. 5).

Evidence from electrophysiology studies has suggested that there is an enhancement of activity in the superficial and intermediate layers due to attention (Cavanaugh and Wurtz 2004; Goldberg and Wurtz 1972; Ignashchenkova et al. 2004). The laminar activity observed in our profiles is consistent with these studies. However, previous studies have not suggested that stimulation related signals might be present deeper in the colliculus than attentional signals.

In our experiments the attention condition involved endogenous attention only while the stimulation condition involved stimulation combined with endogenous attention. Based upon the differences between the conditions, there are at least three possible explanations for our observation of deeper activity during the stimulation condition.

First, visually responsive neurons in the deeper layers may respond more strongly to visual stimulation than to covert endogenous attention. As mentioned previously, the population of visually responsive neurons decreases monotonically with depth. Our results suggest that endogenous attentional signals may be present
in the superficial layer visual neurons containing direct retinal inputs, but less so in
the deeper layer visual neurons that are typically multimodal in their
characteristics. The relative contribution of intermediate layer visuomotor neurons
to the response is difficult to assess from our data because of its limited spatial
resolution.

Second, the reduction of deeper response in the attention condition could be
due to suppressive effects. Previous studies have reported that active fixation causes
increased activity in rostral portions of the SC that represent the fovea, and a
suppression of activity in the deeper layer neurons of the SC (Bell et al. 2003; Munoz
and Wurtz 1993). Our experiments required subjects to continuously fixate
throughout each experimental run, and were not designed to quantify the
magnitude of such fixation-evoked signals.

Third, it is possible that the laminar effects were driven by differences in the
stimulus associated with the endogenous cue. However, the size of the cue was very
small (0.08°) as compared to the extent of the stimulus (2—10°). Considering the
over-representation of near foveal eccentricities from the monkey maps in SC
(Cynader and Berman 1972; Robinson 1972), the cue and the stimulus should be
substantially separated. Hence, the differences in profiles between the stimulation
and attention conditions were probably not an artifact of the cue manipulations.

All in all, our results provide further details about the presence and nature of
visual attention in human SC, buttressing a long history of research. Wurtz and
colleagues observed that spatially specific ablation of SC in monkeys increased
saccadic latencies while accuracy remained consistent (Wurtz and Goldberg 1972)
and that neural responses in the SC corresponding to a spot of light are enhanced if monkeys use that spot as the target for a saccade (Goldberg and Wurtz 1972). A recent fMRI study (Schneider and Kastner 2009) also reported attention-related signals in the SC, though it did not examine their spatial organization. Our observation of reliable and strong lateralization of cue-evoked responses is consistent with these results. Monkey microstimulation studies eliciting a spatially specific enhancement of performance in visual tasks indicated a spatiotopic organization of visual attention in the SC (Cavanaugh and Wurtz 2004; Muller et al. 2005). Our results have extended this work by demonstrating that the organization of cue-evoked attentional activity conforms to a retinotopic map. In monkeys, the retinotopic maps of visual stimulation and eye movement are known to be in alignment (Cynader and Berman 1972; Robinson 1972) and functionally connected with each other (Lee et al. 1997). Here, we have shown that in humans, covert attention signals are aligned with visual stimulation, indicating the presence of visual stimulation and attention maps aligned with the eye-movement maps.

It is possible that the observed retinotopic maps correspond to the subjects’ intention to make eye movements. According to the visuomotor or ‘premotor’ theory of attention, visuo-spatial attention is mediated by the same substrates that control eye movements or other orienting responses (Moore et al. 2003; Moore and Fallah 2001; Rizzolatti et al. 1987; Rizzolatti et al. 1994). Indeed, Kustov and Robinson (Kustov and Robinson 1996) demonstrated such a link between attention and ensuing eye-movement SC of monkeys. They cued monkeys’ attention using a task similar to Posner’s cuing paradigm (Posner 1980) and then evoked saccades by
microstimulating the SC. They observed that the direction of saccades systematically shifted towards the cued location. In addition, Ignashchenkova et al. (2004) observed that the visuomotor neurons that exhibit transient baseline enhancement following a cue are the same neurons previously implicated in the intention to make eye movements.

However, it is also possible that the activity observed in this study may be specifically associated with sustained attention signals in the superficial layer visual-input neurons. A recent study in SC also suggests that SC exhibits sustained attention signals (Schneider and Kastner 2009). The design of that experiment, like our current experiments, involves an attentional target that moves regularly in the visual field. Thus, spatial attention needs to be shifted continually, so that the observed fMRI signals, which are temporally blurred by the sluggish hemodynamic response, could correspond to a sequence of transient eye-movement-like signals combined with subsequent sustained responses associated with the performance of the visual task, similar to the ones observed in early visual cortex (Kastner et al. 1999; Silver et al. 2007). Further experiments will be necessary to determine the transient and sustained nature of attentional signals in the SC.

In summary, we have demonstrated reliable lateralization and, in some subjects, retinotopic organization of visual attention signals in human SC. The attention-evoked activity specifically boosts responses in the superficial and intermediate layers of SC. Thus, attentional signals seem to be both in retinotopic and laminar registration with the neural substrates for eye movement generation. Our findings are in support of a visuomotor basis for visual attention, in accordance
with the notion that attention mediated signals are present in the same neural substrates that control eye movements or other orienting responses.

ACKNOWLEDGEMENTS

We thank Alex Huk for many helpful suggestions and conversations, and Bas Rokers for his assistance with the stimulus development. Our analysis software originally comes from the VISTA lab at Stanford University, and we are particularly grateful to the efforts of David Heeger (now at NYU), Brian Wandell, and Robert Dougherty in its development. We thank Gary Glover for providing the spiral acquisition fMRI pulse sequence. We are also grateful to the valuable suggestions made by the anonymous reviewers regarding this paper.
REFERENCES


**FIGURE LEGENDS**

**Figure 1.** Experimental stimuli. A) In the visual stimulation experiment, a 90° wedge of moving black-and-white dots on a gray background rotated slowly around fixation. The wedge was divided into an array of 6 virtual sectors (gray lines) to enable the subject to perform a speed discrimination task in a random sector. B) In the visual attention experiment, the stimulus was a full field of similar moving-dots with constant spatial distribution. Subjects were cued by thin black lines near fixation (emphasis added in figure) to perform a similar speed-discrimination task within a 90° wedge.

**Figure 2.** Segmentation and surface modeling. A) The midbrain, brainstem, and portions of the thalamus were segmented from high-resolution MRI anatomy volumes. B) A surface was created at the edge of segmented region. C) Sinusoidal-fit phase data viewed on an inplane slice. D) A rotated and enlarged view of the brainstem surface model was used to visualize phase data on the SC.

**Figure 3.** Retinotopic maps. fMRI phase maps in five subjects that encode visual polar angle; left column shows maps of stimulation, right column of attention. The color wheel shown near top relates the overlaid phases to their visual field positions. Black arrows under each colliculus depict the direction of phase gradient from upper to lower visual field. Brown arrows indicate 95% confidence intervals of
the phase gradients. Labels at the bottom right of each map show the coherence threshold used for displaying that map.

**Figure 4.** Phase correlations for right (squares) and left (circles) SC and visual cortex (VC). A) Phase values obtained for SC in the attention experiment plotted against phase values obtained in the stimulation experiment for subject 3. Slope of the fits are indicated on the graph. B) Similar plot for five subjects combined. C) Phase comparisons in visual cortex for areas V2d and V3d combined for three subjects.

**Figure 5.** Laminar profiles. A) Outlines of lateral, central and medial ROIs for subject 4. B) Laminar profiles for subject 4, left colliculus. Thick lines are the mean profiles (stimulation in blue; attention in maroon) and the thin dotted lines indicate 68% confidence intervals. C) Laminar profiles averaged for all subjects over both colliculi showing centroid differences between the attention and stimulation profiles.
**Table 1.** Stimulation and attention amplitudes (percent modulation) for each colliculus in each subject. Correlations and slopes of attention vs. stimulation for left, right and both colliculi in each subject and all subjects combined.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Stimulation amplitude (%)</th>
<th>Attention amplitude (%)</th>
<th>Attention-stimulation correlation, $R^2$</th>
<th>Attention-stimulation slope</th>
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Significance: * $p < 0.05$, ** $p < 0.005$, *** $p < 0.0005$.

**Table 2.** Correlations of attention vs. stimulation for four dorsal visual cortex ROIs.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Correlation $R^2$ and p-values for ROIs</th>
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<td>*0.68</td>
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