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Orienting Auditory Spatial Attention Engages Frontal Eye Fields and Medial Occipital Cortex in Congenitally Blind Humans

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Abstract

What happens in vision related cortical areas when congenitally blind (CB) individuals orient attention to spatial locations? Previous neuroimaging of sighted individuals has found overlapping activation in a network of frontoparietal areas including frontal eye-fields (FEF), during both overt (with eye movement) and covert (without eye movement) shifts of spatial attention. Since voluntary eye movement planning seems irrelevant in CB, their FEF neurons should be recruited for alternative functions if their attentional role in sighted individuals is only due to eye movement planning.

Recent neuroimaging of the blind has also reported activation in medial occipital areas, normally associated with visual processing, during a diverse set of non-visual tasks, but their response to attentional shifts remains poorly understood.

Here, we used event-related fMRI to explore FEF and medial occipital areas in CB individuals and sighted controls with eyes closed (SC) performing a covert attention orienting task, using endogenous verbal cues and spatialized auditory targets. We found robust stimulus-locked FEF activation of all CB subjects, similar but stronger than in SC, suggesting that FEF plays a role in endogenous orienting of covert spatial attention even in individuals in whom voluntary eye movements are irrelevant. We also found robust activation in bilateral medial occipital cortex in CB but not in SC subjects. The response decreased below baseline following endogenous verbal cues but increased following auditory targets, suggesting that the medial occipital area in CB does not directly engage during cued orienting of attention but may be recruited for processing of spatialized auditory targets.

Six keywords not in title

fMRI; endogenous; cue; covert; reorganization; plasticity

INTRODUCTION

Human neuroimaging experiments comparing covert and overt shifts of spatial attention have implicated a common network of cortical areas in the frontal and parietal lobes during both tasks (e.g. Corbetta et al., 1998; Gitelman et al., 1999; Nobre et al., 2000; Donner et al., 2000; Beauchamp et al., 2001). This network includes the putative human homologue of monkey FEF that is known to be involved in voluntary control of eye movements (Paus, 1996; Bruce & Goldberg, 1985). The frontal eye fields have long been considered a critical

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locus for the control of spatial attention (Mesulam, 1981). Recently, Wardak et al. (2006) reported a selective loss in detecting spatial targets amongst distracters in a covert attention task following muscimol inactivation of the FEF area in monkeys, suggesting that the FEF area neurons play a functional role even in covert attention, without eye movement. Similarly, recent TMS studies in humans (O'Shea et al., 2004; Ruff et al., 2006) also imply a functional role for FEF in covert shifts of attention.

Behavioural (e.g. Rizzolatti et al., 1987; Hoffman & Subramaniam, 1995) as well as single neuron and microstimulation studies of FEF neurons in non-human primates have suggested a tight link between attention and oculomotor processes (e.g. Sheliga et al., 1995; Kustov & Robinson, 1996; Moore & Fallah, 2001). It has even been suggested that planning eye movement constitutes the neural equivalent of orienting spatial attention (Rizzolatti et al., 1987). However, a substantial literature of single unit recordings in nonhuman primates has demonstrated the existence of several distinct subpopulations of neurons within the FEF area including some that seem to code for locations of expected stimuli without any evidence of premotor saccade planning or post stimulus saccadic activity (Juan et al., 2004; Schall, 2004; Thompson et al., 2005; Kodaka et al., 1997; Muggleton et al., 2003). Convergent evidence comes from human neuroimaging experiments in which FEF activation has been consistently found during shifts of spatial attention even when great care was taken to avoid eye movements (e.g. Gitelman et al., 1999; Donner et al., 2000; Beauchamp et al., 2001; Serences et al., 2004; see Corbetta & Shulman 2002 for a review). A recent case study of a sighted human subject with a congenital inability to make eye movements due to impaired eye muscles found impaired exogenous attention but intact endogenous covert spatial attention, suggesting that the two subsystems may be dissociated (Smith et al., 2004).

Although these results suggest that FEF is a part of the control network for spatial attention independent of the oculomotor system (Posner & Peterson, 1990; Kanwisher & Wojciulik, 2000; Kastner & Ungerleider, 2000; Serences et al., 2004), the role of eye movements in covert attention remains controversial because in normally sighted subjects it is difficult to eliminate the possibility that unexecuted eye movements were still planned but then their execution was suppressed during selective attention tasks involving spatial cues (Rizzolatti et al., 1987).

Congenitally blind (CB) subjects provide a unique opportunity to find evidence relevant to this issue, since their complete visual deprivation from birth makes voluntary control of eye movements an irrelevant response to spatial cues. In a recent diffusion tensor imaging study, Shimony et al. (2006) reported evidence of atrophy of the geniculocortical tracts in all five of their CB subjects and suggest that blindness leads to a reorganization of cerebral white matter; the authors suggest that visual cortex functionality in blindness is primarily mediated by corticocortical as opposed to thalamocortical connections. Previous studies of blind subjects have found a lack of voluntary control of eye movements in cases where there was a complete absence of light perception from birth (Hall et al., 2000; Leigh & Zee, 1980). While a recent study has suggested that a limited form of fixation control was possible in some cases of CB (Després et al., 2005), three of their six blind subjects had light perception (no information was published regarding the history of light perception in the other three). In any case, without external feedback resulting from foveation of target stimuli, it seems extremely unlikely that CB individuals would develop voluntary eye movement plans in response to endogenous spatial cues, such as spoken direction words delivered in a non-spatial manner. Since FEF neurons in monkeys are not active preceding the quick phase of nystagmus (Bizzi & Schiller, 1970), any FEF activity in CB individuals should be related to shifts in covert spatial attention.

If the FEF region is normally activated by eye movement planning then the lack of such planning might be expected to lead to its reorganization, either by infiltration by adjacent cortex (e.g. Merzenich et al., 1984; Buonamano & Merzenich, 1998) or as a result of changes in the

receptive fields of its pre-existing afferent connections (Bavelier & Neville, 2002). Furthermore, while critical periods in eye movement control have not been established in humans, the studies of rats and monkeys have found that deprivation leads to significant changes in the expression of genes controlling extra-ocular muscles metabolism that are reflective of critical periods in the development of oculomotor functions (Cheng et al., 2005). This, in addition to observations that critical periods of other functions such as visual acuity and language are over by the onset of puberty in humans (Ellemberg et al., 1999, Hensch, 2004), suggests that congenital blindness spanning this period would prevent similar coordination of external stimulation and eye movements from developing. If, as a result of visual deprivation, FEF area neurons have been recruited by other neural systems for other tasks then there should be significant differences in the pattern of FEF activation between the CB and SC groups in the covert attention switching task. Alternatively, if a sub-population of FEF neurons is involved in orienting attention independent of the eye movement planning, then the response in FEF should be similar in CB and SC individuals.

An extensive search of the neuroimaging literature revealed no specific information pertaining to the function of FEF in CB. While evoked potential (ERP) studies in CB found changes in the amplitude and distribution of signal potential over frontal cortex (e.g. Lehtokoski et al., 1998; Röder et al., 1999a; Kujala et al., 2000), the technique lacks the spatial resolution to localize changes within specific frontal structures such as FEF.

In contrast to the lack of FEF studies in the blind, there is rapidly growing evidence for a functional role for the visual cortex in early blind individuals (see Kujala et al., 2000, Burton 2003, and Pascual-Leone et al., 2005 for reviews). Broadly localized occipital cortex responses to various auditory stimuli have been demonstrated using electrophysiological methods in the blind in tasks such as detecting a deviant frequency (Kujala et al., 1995, 2000), amplitude of a target tone from competing distracters (Liotti et al., 1998), and azimuthal location of target sounds (Leclerc et al., 2000). Neuroimaging experiments have further localized the occipital response in both striate as well as extra-striate visual cortex. Sadato et al. (1996, 1998, 2002) have demonstrated activation of primary and secondary visual areas during Braille reading and other tactile discrimination tasks in early-blind persons. Disruption of Braille reading performance, either temporarily induced by transcranial magnetic stimulation (TMS) over the occipital area (Cohen et al., 1997), or permanently caused by a stroke leading to bilateral occipital damage (Hamilton et al., 2000), strongly suggests that occipital activation plays a functional role in blind subjects. Activation of early visual areas has also been demonstrated using auditory tasks such as auditory verb generation (Burton et al. 2002, Amedi et al. 2004), semantic judgment (Burton 2003, Noppeney et al. 2003), sentence processing (Röder et al., 2002), and verbal memory (Amedi et al., 2003). More relevantly, recent neuroimaging investigations of auditory localization in early blind subjects have also reported activation the dorsal and lateral occipital cortex using spatialized sounds that were created with binaural head-related transfer functions and delivered via headphones (Weeks et al., 2000), as well as using free-field sounds (Gougoux et al., 2005).

It is worth emphasizing that most studies of the blind have found occipital involvement mainly in actively attended versions of the task but not during passive control tasks with very similar auditory or tactile stimuli (see Kujala et al., 2000 for a review). For example, in a recent study in our lab using an oddball detection paradigm with simultaneous auditory and tactile input streams, we found that the BOLD responses in the early visual cortices of blind subjects were significantly larger when they attended to the auditory targets as compared to the same auditory stimuli when the subjects were attending to tactile targets (Weaver & Stevens, 2007). Recently, Ruff et al. (2006) demonstrated that TMS over the right human FEF can modulate functional activity in early visual cortex (including V1) with perceptual consequences. Taken together, these findings suggest that attentional modulation may play a role in activating the early visual

areas in the blind. Therefore, a secondary goal of this study was to explore the nature of any BOLD response in the medial occipital area of the blind group to spatialized auditory stimuli following cues that orient attention.

We scanned both CB and SC subjects while they performed an auditory spatial discrimination task based on a covert auditory attention switching paradigm (Posner, 1980; McDonald & Ward, 1999). Discrimination of sound locations, unlike mere detection of sounds, is effective in producing reliable response-time validity effects (Spence & Driver, 1994; McDonald & Ward, 1999). We used endogenous verbal cues and non-directional manual responses to further minimize any need for eye movement planning during the task.

METHODS

Subjects

Nine CB (ages 36–57, mean 52 yrs; 6 M, 3 F) and ten SC (ages 28–53, mean 46 yrs; 5 M, 5F) individuals participated. Eight blind subjects reported having no light perception since birth; one subject (22TS) reported formless diffuse perception to bright light; four subjects had prosthetic eyes (see Table 1 for individual details). All ten SC subjects and six CB were right handed; two of the CB subjects were left handed and one ambidextrous. The education levels of both groups were matched (CB: 17 ± 3 yrs; SC 17 ± 3 yrs). Audiometric intensity thresholds were assessed for all subjects and all had normal hearing in both ears. All subjects provided informed written consent and were paid for their participation. All procedures were approved by the Institutional Review Board at Oregon Health & Science University.

Data Acquisition

Covert attention switching to auditory targets task—We scanned subjects as they performed a cued auditory spatial discrimination task. Subjects heard verbal cues (the words “left”, “right”, or “centre”) indicating the side where a target was most likely to occur, and responded to the subsequent target sounds (Fig. 1a). On each trial a target was presented at one of five virtual locations (0° , $\pm 10^\circ$, $\pm 60^\circ$) along the azimuthal plane (Fig 1A). The “left” and “right” cues, were each randomly presented on 40% of trials, followed by a target sound at one of four locations (“peripheral”: $\pm 60^\circ$ and “nasal”: $\pm 10^\circ$) on either side of the mid-plane. The target was “valid” (on the cued side) in 80% and “invalid” in 20% of the (left/right) trials. Subjects were instructed to direct their attention to the cued side, while keeping their eyes closed and still, and press a button with their right index finger if the target occurred at the peripheral (“go”) but not the nasal (“no-go”) sounds. Peripheral and nasal targets were randomly intermixed in 50% of the left/right trials each. The “centre” cue was presented on 20% of the trials randomly intermixed with the (80%) left/right trials, and was always followed (100% valid) by the central target (at 0°). Subjects were instructed to press a button on all central targets. Trials with RT > 1500 ms or < 150 ms were considered error trials.

All auditory stimuli were presented binaurally at 73–78 dB SPL through Koss ESP-950 electrostatic speakers fitted into sound attenuating ear protectors. Cue words were amplitude normalized and compressed to 300 ms in order to standardize them without losing clarity. We created spatialized target sounds using head related transfer functions (Algazi et al., 2001, Bushara et al., 1999; Weeks et al., 2000). Target sounds were 2000 Hz and 4000 Hz tones, mix-pasted with Gaussian noise, enveloped at 2 ms and separated by 10 ms of silence. The resulting sound was normalized and convolved with a standard head related transfer function (non-individualized, large-pinna KEMAR parameter set) to create the spatial sounds of 200 ms duration (Fig. 1a). The stimulus onset asynchrony between the cue and the target was 2.2 s or 4.4 s (randomized, 50% each), and the inter-trial interval randomized between 2.2 s (50% trials), 4.4 s, and 8.8 s (25% each). Two EPI runs of 100 trials each were acquired per subject

yielding 940 scan volumes. Subjects were briefly trained on the task outside the scanner; we confirmed that they were able to distinguish the sound locations by having them point to the perceived locations.

FEF localization task—The location of the FEF ROIs was established in an initial experiment in which only the SC subjects (all ten) participated. Subjects performed saccades to visually presented targets, to the auditory targets presented at $\pm 60^\circ$ (also used in the auditory spatial discrimination task), and to corresponding verbal cues (“left” and “right”). The stimulus conditions were presented in a fixed-block design. The visual stimuli were projected on a screen seen via a mirror attached to the head coil. At the start of every visual block an “eyes open” command was delivered via the headphones. A central fixation cross was followed after 2.2 s by a 0.6° circular dot presented in pseudo-random order at one of 8 locations 7.1° from the centre. Subjects were asked to move their eyes to the dot as soon as it appeared and back when the cross re-appeared. At the end of the visual block an “eyes closed” command was presented visually on the screen that then darkened during the auditory and verbal blocks. The verbal block presented a central sound followed pseudo-randomly after 2.2 s with one of the cue words “left” or “right”. The auditory block presented a central sound followed after 2.2 s with one of the two peripheral (60° left and right) target sounds. Subjects were instructed to move their eyes, while keeping them closed, towards the indicated side and back to the centre upon hearing the central sound. There were 8 trials per block and a fixation baseline of 8.8 s between each block. The three conditions were presented 5 times each, yielding 120 eye movement and 60 resting scan volumes (40 with eyes closed and 20 with eyes open).

All MRI data were acquired on a whole-body 3 Tesla Siemens Trio scanner with a standard 2-channel head coil at the Advanced Imaging Research Center at Oregon Health & Science University. The functional scans used echo-planar imaging (20 axial slices, 5 mm thick, no gap, TR 2200 ms, inter-scan interval 600 ms, TE 48 ms, FA 90° , matrix 64×64 , FOV 240 mm). A clustered volume acquisition sequence (Edmister et al., 1999) was used to remove interference of scanner noise on the stimuli, which were presented during the 600 ms silent period in each TR (Fig. 1a). A high-resolution T1-weighted 3D MPRAGE (144 axial slices, 1 mm thick, TR 2300 ms, TE 4.38 ms, FA 12° , matrix 256×256 , FOV 240 mm) was acquired for anatomical localization of activations.

fMRI Analysis

The Brain Voyager QX (Brain Innovation, Maastricht) software package was used to analyze the scan data. Motion correction was performed by Siemens system software, which uses a six parameter rigid body transformation of each acquisition to realign with the first acquisition of the run. The scans were pre-processed with slice-time correction, linear trends were removed, and then high-pass filtered at 4 cycles/time course. Each subject’s data was then z-normalized, interpolated into 1 mm^3 isovoxels, coregistered to the corresponding high-resolution anatomical scan, and transformed into standard stereotaxic coordinates of Talairach and Tournoux (1988).

The FEF regions of interest (ROI) were defined using the independent run of fixed block eye movement task on the ten sighted controls. Each of the five stimulus blocks (visual saccades, verbal saccades, auditory saccades, resting baseline with eyes open, resting baseline with eyes closed) was modelled by a boxcar function convolved with a standard hemodynamic response gamma function (see Boynton et al., 1996; we used delta 2.5 s, tau 1.25 s). The resultant regression vector was cross-correlated with the BOLD time series, yielding scalar beta weights corresponding to the relative changes in signal strength associated with that particular stimulus. Between-subject parametric maps were calculated using a random effects model, allowing a generalization of the results to the population level. The correction for multiple comparisons

was made by rejecting spatial clusters smaller than 50 contiguous isovoxels (Forman et al., 1995) with a voxel-wise false discovery rate (FDR) threshold of 0.05 (Genovese et al., 2002).

The covert attention switching task used an event related design with inter-stimulus and inter-trial intervals randomized to allow us to trace the time-course of regional BOLD response during the course of individual trials aligned with the presentation of the cue and target stimuli. We used a GLM approach with three predictors defined for cue stimuli (“left”, “right”, “centre”) and five predictors for the target stimuli (“valid go”, “valid no-go”, “invalid-go”, “invalid-no-go”, “centre”). In order to separately analyze the trials with SOA of 2.2 s from those with SOA of 4.4 s, the three cue predictors were further split into six based on the two SOAs. The model hemodynamic response function was convolved with the occurrence of the individual events corresponding to each cue and target condition. Event related averages for each condition were computed by averaging the responses of the significant voxels within the FEF ROIs across trials of the conditions of interest.

The field of view for one of the sighted subjects (02JA) did not fully cover the ventral part of the occipital cortex and hence was dropped in the group analysis for the occipital region of interest and corresponding event related analysis.

RESULTS

During the covert attention switching task, behavioural responses to valid (correctly cued) targets were significantly faster (Fig. 1b) and more accurate (Fig. 1c) compared to invalidly cued targets. A repeated measures ANOVA with cue-type [valid, invalid, centre] as within-subject and group as between-subject factor showed a main effect of cue-type for both reaction times [$F(2,16) = 33.3$, $p < .001$] and accuracy [$F(2,16) = 37.3$, $p < .001$]. Pair-wise comparisons for reaction times showed centre < valid < invalid [$p < 0.01$ after adjustment for multiple comparisons] but accuracy comparisons were significant only for centre targets (centre > valid; centre > invalid; $p < 0.01$). There was no significant difference in accuracy between valid and invalid targets.

The performance difference between the two groups was not significant for reaction times [cue-type x group interaction: ($F(2, 16) = .17$; $p > 0.8$)] nor for accuracy [cue-type x group interaction: ($F(2, 16) = 2.2$; $p = 0.14$)]. There were also no significant differences between responses to left and right cues [$F(1, 16) = 0.01$, $p > 0.9$], or between 2.2 and 4.4 s SOA trials [$F(1, 12) = 0.63$, $p > 0.4$]. Overall, these results suggest that there was no trade-off between speed and accuracy and show a robust cue validity advantage in reaction times suggesting that subjects were indeed covertly orienting to the cued hemi-space (Posner, 1980).

FEF Localization

Previous studies by Paus (1996), Luna et al (1998), and Sweeney et al. (1996) have located peak FEF activity from the depths up to the lip of the precentral sulcus (PreCS) at the posterior-most aspect of the superior frontal sulcus (SFS). We combined functional and anatomical considerations by selecting voxels that were significantly activated in the SC group performing the saccade task as well as were located within a narrow range along the PreCS near its intersection with the SFS to localize the two FEF ROIs (one for each hemisphere). Fig. 2b illustrates the resulting FEF ROI in coronal and axial slice views (green voxels in the left column).

Active voxels were located using the contrast [(visual saccades) > (eyes open resting baseline) + (verbal saccades) > (eyes closed resting baseline) + (auditory saccades) > (eyes closed resting baseline)]. When analyzed separately, the significant voxels for all three types of saccades were highly similar near the anatomical FEF; conjunction analysis resulted in a region substantially

similar to the FEF ROI we have used in rest of this paper. These voxels were then further anatomically restricted to within a narrow range along the PreCS near its intersection with the SFS to define the left and right FEF ROIs (in Talairach coordinates, this restricted the ROI voxels to be within the range $[-40 < x < -18]$ for left FEF, $[20 < x < 41]$ for right FEF, and $[-17 < y < -5]$ and $[40 < z < 61]$ for both; the two FEF ROIs are shown as green voxels in the left column of Fig. 2b).

All nine CB subjects showed a robust BOLD response in both left and right FEF ROIs during the covert attention switching task (we used the GLM contrast [left + right + centre] cues > baseline). CB group maps of significantly activated voxels ($FDR < 0.05$) are shown in Fig. 2a, right column of Fig. 2b, and individual maps in Fig. 3a (voxels activated during the covert attention switching task are shown in red/yellow). The voxels significantly activated during the covert attention task clearly overlap with the FEF ROI (green area overlaps with underlying red/yellow voxels in the right column of Fig. 2B). When the location of active voxels produced by the overall GLM analysis of the CB group for the covert attention task was compared with the active voxels from the SC performing the visual saccade task, we found a significant overlap within the FEF region (see Table 2 for Talairach coordinates of the centre of gravity and voxel counts of the activation). 74% of the voxels activated within the left FEF ROI and 67% of the voxels within the right FEF ROI overlapped with those activated by the SC during the saccade task.

The FEF activation volume in all ten SC subjects similarly showed a significant overlap between the saccade and the covert attention tasks (see middle column of Fig. 2b and Fig. 3b). The voxels significantly activated during the covert attention task clearly overlap with the FEF ROI (green area overlaps with underlying red/yellow voxels in the middle column of Fig. 2b). The covert attention switching activated 94% of the voxels in the left FEF and 65% in the right FEF that had been activated by the saccade tasks (see Table 2).

Activation among all nine CB and all ten SC subjects during the covert attention switching task was consistently located laterally along the PreCS from its medial intersection with the SFS and, in some cases, slightly anterior along SFS (Fig. 3a, b). Vertically, activation extended from the lip to the depth of the PreCS (Fig. 3c).

Event Related Activity

Cue-aligned responses were evaluated by constructing the average event-related BOLD responses in the FEF ROIs (see Methods) and a repeated measures analysis of variance between group (SC, CB) and for cue type (left, right, and centre), hemisphere (left, right) and at the two highest signal peaks in the time course (scan time), which occurred at the third and fourth acquisition following the cue (Fig. 4). Note that since the SOA between the cue and target stimuli was not large enough to completely separate cue from target induced responses, cue-aligned activity may contain target induced response; similarly target-aligned activity may contain cue-related response. Probability estimates were corrected for deviations from sphericity of the variance matrix using the Greenhouse-Geisser method wherever appropriate.

Bilateral FEF areas showed a clear cue-locked pattern that was similar in both the blind and sighted groups (Fig. 4). A repeated measures ANOVA with group as between-subject factor and hemisphere, cue-type [left, right, centre], and scan-time [scans 3 & 4 post-cue] as within-subject factors found no reliable effect of group [$F(1,17) = 0.42$, $p > 0.5$], nor of hemisphere [$F(1,17) < 0.01$, $p = 0.97$], while the main effect of cue-type [$F(2, 34) = 12.04$, $p = 0.002$], scan-time [$F(1,17) = 19.1$, $p < 0.001$] were significant. Post-hoc pair-wise comparisons between the FEF response to left, right, and centre cues showed left > right > centre [left > right, $p < 0.001$; right > centre, $p < 0.05$]. The group x hemisphere interaction was significant [$F(1,17) = 4.95$, $p = 0.04$], which appeared to be a result of the greater response in the left FEF

of the CB group to the invalidly cued targets, and relatively symmetric responses across all cue conditions in the SC group. There was also a significant cue-type $\times$ scan-time interaction [$F(2, 34) = 4.65, p = 0.02$] which was a result of the invalid cues resulting in a consistently later peak than the valid and centre cues (Fig. 4). Also the hemisphere $\times$ cue-type $\times$ Time interaction was significant [$F(2,34)=5.67, p = 0.015$]. No other interactions were significant.

We then compared target-related responses for valid, invalid and centre conditions by aligning trials to the target onset (averaging after aligning the SOA 2.2 and 4.4 targets). The FEF response to invalidly cued targets was strongest and that of central targets weakest in both groups (Fig. 5). Again, a repeated measures ANOVA was conducted with group as a between-subject factor and hemisphere, target-type [valid, invalid, centre], and scan-time [scans 2 & 3 post-target] as within-subject factors. The overall target-aligned FEF responses of the CB group were stronger than those of SC (Fig. 5) indicated by a reliable main effect of group [$F(1, 17) = 9.64, p = 0.006$]. Also, there were reliable main effects of target-type [$F(2, 34) = 22.7, p < 0.001$] and scan-time [$F(1, 17) = 18.98, p < 0.001$], but not for hemisphere [$F(1, 17) = 1.14, p = 0.3$]. Post-hoc pairwise comparisons between the FEF response to valid, invalid, and central targets revealed invalid $>$ valid ($p < 0.001$) and valid $>$ centre ($p < 0.03$).

There was also a significant interaction between group and target-type [$F(2, 34) = 4.4, p < 0.03$]. We followed up the group by target-type interaction with paired T-tests, comparing peak FEF signal responses (Fig. 5; TR = 2) in CB and SC for the three types of “go” targets (valid, invalid, centre), collapsing across hemispheres. We found that the FEF responses to invalid targets were stronger in the CB group than in the SC group ($p < 0.01$) but FEF responses to targets did not differ significantly between the groups on valid trials. The responses to central targets showed a tendency to be stronger in CB compared to SC (Fig. 4) although this failed to reach the significance threshold ($p = 0.08$). No other interactions were significant.

Occipital Activation

Our secondary region of interest was the early visual processing area located in the medial occipital cortex. Voxels in this area were significantly activated bilaterally using the targets contrast (targets $>$ baseline) in the CB group (Fig. 6a) but not in SC (Fig. 6b). We defined an occipital ROI for event related analysis by choosing the maximally activated voxel near the calcarine sulcus ($x = 2; y = -81; z = 5$) and including all significantly activated voxels ($FDR < 0.05$ and cluster size > 50) within 20 isovoxels from the centre of activation in all 3 dimensions (Fig. 6 shows the occipital ROI with a dotted boundary; 5179 isovoxels were included around the centre of gravity [$x = 2; y = -81; z = 5$]).

The BOLD response in the occipital ROI of CB subjects showed a somewhat different pattern of response to that found in FEF. Most notably, when CB occipital responses to trials where the target arrived 2TRs after the cue are averaged, the signal time-course in the medial occipital areas decreased below the pre-cue baseline until the arrival of the target, at which point there was a sharp increase (Fig. 7a; compare the blue line with circles for targets delivered after 1 TR after the cue with the green line with triangles for targets delivered after 2 TRs). One-sample T tests confirmed that the average normalized responses (in trials with an SOA of 2TRs) aligned to cue delivery in the occipital ROI was significantly smaller than baseline 2TRs after the cue [$t(8) = -3.5, p < 0.01$] and significantly larger 4TRs after the cue [$t(8) = 8.4, p < 0.001$].

The occipital response started rising later as well as peaked later than the corresponding FEF response (Fig. 7b; e.g. compare the FEF response at scan 5, shown in red line with crosses, with that of the occipital region, shown in green line with triangles). Paired-sample T tests confirmed that average normalized responses aligned to cue delivery in the occipital ROI was significantly smaller than FEF response 2TRs after the cue [$t(8) = -4.0, p = 0.004$] but larger than FEF response 5TRs after the cue [$t(8) = 8.0, p < 0.001$].

When aligned to target delivery (i.e. combining the TR1 and TR2 targets), the occipital response in CB group showed clear differences between invalid, valid and central targets (Fig. 7c) and were significantly stronger than the corresponding response in the SC group (compare Fig 6a with 6b, and Fig. 7c with 7d; ANOVA with group as between-subject, and target-type and scan-time [scans 3 & 4 post-target] as within-subject factors for occipital responses showed a main effect of target-type [$F(4, 68) = 3.7, p < 0.01$], group [$F(1, 17) = 4.9, p = 0.04$], and scan-time [$F(1, 17) = 6.5, p = 0.02$], but the target-type $\times$ group interaction was not significant [$F(4, 68) = 2.1, p > 0.1$]). No other interactions were significant.

DISCUSSION

FEF Activation

Both left and right hemisphere FEF areas were significantly activated in a stimulus-aligned manner in all SC and CB individuals during the covert auditory spatial orienting task. Consistent with the cueing effects present in the behavioural data (response times for invalid, valid, and central targets were ordered invalid > valid > centre), FEF activity was greatest on invalidly cued trials and least on central targets (invalid > valid > centre). The overall temporal profile of the FEF response of the CB group in the FEF areas was generally similar to that of SC with the exception that the peak CB response to invalid targets was stronger than the corresponding response in the SC group (Fig. 5). Additionally, the trend towards a response to centre cues in the blind but not the sighted subjects also is consistent with the possibility of reorganization of the FEF area in the blind due to lack of input from visual modality.

Neuroimaging studies of FEF activity in normally sighted individuals are usually confounded by the possibility that such activity represents planned eye movements that are not executed, perhaps due to active inhibition of the planned movement. Thus it is significant that we found robust and stimulus-aligned FEF activity in congenitally blind subjects during covert orienting (similar to corresponding activity in sighted controls) suggesting the possibility that FEF activity during covert orienting is independent of planned eye movements.

The responses we observed in sighted controls are consistent with previous neuroimaging studies that have consistently found FEF activation in visuospatial attention tasks regardless of eye movement involvement (e.g. Corbetta et al., 1998; Gitelman et al., 1999; Nobre et al., 2000; Donner et al., 2000; Beauchamp et al., 2001; Astafiev et al., 2003). For example, Serences et al. (2004) reported event-related FEF activity when subjects shifted attention between two objects overlapping at the same central visual fixation. Recent studies using transcranial magnetic stimulation (TMS) have implicated a functional role in spatial attention for the FEF area (e.g. Muggleton et al., 2003; O'Shea et al., 2004; Smith et al., 2005) and the temporal profile of TMS interference has been interpreted as demonstrating an early role for human FEF in visual target discrimination that is independent of saccade programming (O'Shea et al., 2004). Our finding adds to this extensive literature on FEF activation in normally sighted individuals by demonstrating that FEF is clearly responsive to auditory stimuli cued by words and responded to with non-directional (i.e. non-oculomotor) go/no-go button presses.

The lack of target-dependent laterality effects between left and right FEF regions is consistent with several recent studies of preparatory spatial attention signals in FEF that found weak evidence of location selectivity during tasks that force subjects to switch attention between locations (e.g. Corbetta et al., 2005 and Yantis et al., 2002). In their FEF inactivation study in monkeys, Wardak et al. (2006) also suggest a bilateral role in directional shifts of covert attention instead of a simple contralateral deficit (unlike saccades subsequent to inactivation which showed a clear contralateral pattern). Furthermore, fMRI may lack the spatial and temporal sensitivity to detect fine grained laterality effects because rapid interactions at the level of cortical columns between hemispheres may be necessary to balance orienting signals

in dorsal frontoparietal areas (Stanton et al., 1989; Goldman-Rakic, 1988; McGuire et al., 1991).

Response patterns in the FEF regions to left and right cues were similar across all subjects. Responses to “left” cues were strongest in both left and right FEFs in both CB and SC groups. It is not clear why the response to the left cue is slightly stronger than to the right. However, since we used only right finger responses, we cannot rule out a response laterality bias effect.

Most intriguing was the responses to centre stimuli which showed a tendency to differ between the sighted and blind subjects. As expected, the sighted group showed essentially no response to the completely predictable central stimuli requiring minimal attention. The unexpected response to centre stimuli shown by some of the CB subjects may reflect an enhanced sensitivity in monitoring central locations for auditory cues to avoid objects as they move around in their daily life, a role normally played by foveal vision in the sighted. However, because the centre condition was included as a baseline condition, and therefore no validity manipulation used, the meaning of the response in CB subjects is difficult to gauge. Nevertheless, previous studies of blind individuals have found evidence of changes in the perceptual organization peripheral and central space (Zwiers et al., 2001; Röder et al., 1999b), which is consistent with the apparent increased response to centre cues in the CB subjects. Additionally, Voss and colleagues (2004) have demonstrated that although blind individuals do not show greater acuity than sighted individuals in minimal audible angle discrimination in frontal fields, they do show significantly better minimal auditory depth perception for sounds presented directly in front of them at different distances compared to sighted. While speculative, the centre cue response in our blind subjects may reflect a similar alteration in the ability to focus auditory spatial attention. This may be analogous to the BOLD response in FEF reported by Serences et al. (2004) to shifts in attention between visual objects presented at the same foveal location, which also suggested FEF was responding to a shift in attention rather than eye movement planning.

While the robust and time-locked FEF activation in congenitally blind subjects suggests that FEF activity during covert orienting is independent of oculomotor planning, we now consider several alternative explanations. An alternative interpretation might be that FEF activity continues to reflect a voluntary plan to direct eye movements to auditory locations, even in CB individuals, but that atrophy of effectors further downstream from FEF prevents the plan from resulting in actual eye movements in CB individuals as they shift attention to spatial locations of sounds. However, there is scant evidence that CB individuals can control their eye movements voluntarily to endogenous commands (Leigh & Zee, 1980; Hall et al., 2000). Previous studies have only found weak evidence of a residual ability to learn a limited form of fixation control after receiving training using auditory feedback, especially in blind individuals that still retained some residual light sensitivity (Hall & Ciuffreda, 2002; Després et al., 2005). This is a very different form of ocular control that may be dependent on external visual stimulation. It is important to note that eight of our nine CB subjects had no light perception and had no recollection of any during their lifetime (the one exception, 22TS, reported only a diffuse and formless sensation to strong light), and consequently have had no opportunity to calibrate their (voluntary or involuntary) eye movements to external targets. During a follow-up session with six of our subjects outside the scanner, we attempted to induce eye movements to centrally delivered verbal commands but found that the subjects had trouble following this instruction and would typically “scrunch up” their whole face by contracting their facial muscles when asked to simply move their eyes towards the left or right. Unlike sighted controls, none of the CB subjects seemed to show any obvious reflexive eye movement upon hearing unexpected spatialized sounds (e.g. when an unexpected knock is heard on the door). In light of their lifelong lack of external visual feedback, we find it extremely unlikely that our CB subjects would engage in voluntary planning of eye movements in response to non-spatially delivered verbal endogenous cues (see Röder et al., 2000 for a similar discussion).

Another explanation for FEF activity in CB could be that it reflects a different underlying function than in SC, even though the fMRI activation looks similar in both groups. CB individuals tend to orient their head in response to auditory events; it is possible that blindness causes changes in the weighting of afferent information to, as well as in efferent signals out of, the FEF area neurons. Thus, auditory stimuli may still generate similar signals to FEF in CB and SC individuals, but whereas FEF processing in normally sighted individuals leads to preparation of eye movements towards the stimulus location, in CB it leads to motor preparation for head orienting. This would suggest that planning occurs in a head oriented reference frame. Microstimulation of some FEF area neurons can elicit head movements in monkeys (e.g. Chen, 2006), and in a recent fMRI study in humans, Petit & Beauchamp (2003) found overlapping FEF activation during both eye and head movements. In non-human primates, the FEF area has been shown to be reciprocally connected to the caudal auditory belt cortex thought to be involved in auditory spatial processing (Romanski et al., 1999; Romanski, 2004), and neurons in and around FEF have been found to respond to actively localized sounds irrespective of accompanying saccades (Vaadia et al., 1986). Importantly, FEF neurons did not respond to mere passive listening of these sounds; attentive localization was required (Vaadia et al., 1986). The significantly stronger FEF response to invalid targets compared to valid ones we found is consistent with a role in reorienting attention following unexpected auditory stimuli, although it is possible that the stronger BOLD response corresponds simply to a longer time-on-task.

Another alternative explanation for the FEF activation arises from the head-centred reference frame used in sound localization. Since even the sighted controls had their eyes closed, the common FEF activation may simply reflect the possibility that both groups used a head-centred (craniotopic) reference frame for sound localization and the eye-centred reference frame was equally irrelevant to both groups on this task. However, Russo & Bruce (1994) have demonstrated that FEF neurons in monkeys use a retinotopic reference frame preceding aurally guided saccades, even in the dark. Both visual and auditory target representations, although initially obtained in different coordinate systems, appear to converge to a common movement vector representation in the FEF after transformation of auditory targeting information from its original craniotopic framework into a retinotopic one; they suggest that this transformation may take place in the frontal lobe as auditory receptive fields of aurally responsive cells with in and adjacent to FEF partially compensate for shifts in the direction of gaze (Russo & Bruce, 1989, 1994). While this evidence is about presaccadic neurons as opposed to neurons involved in purely covert attention, other experiments in crossmodal covert attention seem to suggest the existence of a supramodal endogenous attention system that operates with common abstract spatial reference (e.g. see Spence, Pavani, & Driver, 2000). Alternative models of multidirectional integration using predictive recurrent networks (e.g. Avillac et al., 2005) eschew a common spatial code but still predict the dominant frame of reference for FEF neurons to be retinotopic. These findings, coupled with the significant overlap of active voxels in both the saccade and covert attention task in the SC group, seem to contradict the notion that a craniotopic reference frame was used by SC individuals. The question remains open for CB individuals; it is possible that they used a craniotopic reference frame.

Several recent studies in monkeys have demonstrated that the FEF area contains distinct types of neurons with functions ranging from input selection to saccade planning (Wardak et al., 2006; Juan et al, 2004; Schall, 2004; Thompson et al., 2005). Juan et al. (2004) have interpreted these patterns of activity as consistent with the hypotheses that covert shifts of attention can occur without saccade preparation and that FEF contributes to covert (as well as overt) orienting. Demonstrating that covert orienting and saccade production seem to be separate processes that are mediated by separate populations of FEF neurons, Thompson et al. (2005) have proposed that spatially selective activity in visually selective FEF neurons corresponds to covert attention via modulation of ongoing visual processing.

Although alternative explanations cannot be completely ruled out, the convergence of our results with these findings non-human primates suggests that a sub-population of neurons within FEF may be involved in the control of endogenous attention in a manner that is *independent* of eye movement planning. Importantly, our results do not preclude the possibility of a tight linkage between supramodal attention control networks and a separate eye movement planning network, both located within the FEF region. Indeed, a strong link between the attention control and eye movement networks could explain the behavioural findings of a strong connection between attention and oculomotor planning (e.g. Hoffman & Subramaniam, 1995) without necessarily positing that the two are one and the same (Rizzolatti et al., 1987). Our findings are consistent with models of visuospatial attention that have posited a *supramodal* role for FEF as a part of a frontoparietal network of areas involved in the control of endogenous attention (Posner & Peterson, 1990; Kanwisher & Wojciulik, 2000; Kastner & Ungerleider, 2000; Corbetta & Shulman, 2002).

Occipital Activation

The medial occipital area of the CB group, including the calcarine sulcus, was robustly engaged by our cued auditory task in a pattern that was time-locked to the delivery of the auditory spatialized targets rather than the verbal endogenous cues; the BOLD response clearly differed between the various types of targets (Fig. 7c). The occipital activation is partially consistent with previous neuroimaging results that have found activation in the visual cortices in the blind during a variety of non-visual tasks in both tactile and auditory modalities (for reviews, see Burton, 2003 and Pascual-Leone et al., 2005).

Previous studies of *sound localization* have found only weak evidence for engagement of medial occipital areas. A PET study of auditory localization in congenitally blind by Weeks et al. (2000) used spatialized sounds created using binaural head-related transfer functions and found activation in the association (but not early visual) areas of the right occipital cortex of the blind. More recently, Gougoux et al. (2005) used free-field sounds and reported activation of early visual cortex under monaural but not under binaural conditions.

In contrast to those studies, we found that the bilateral medial occipital area, including the calcarine sulcus, was clearly recruited during our cued location discrimination task in the blind. Indeed, we found activation using binaural sounds in both dorsal association areas as well as in medial occipital areas in both hemispheres (Fig. 6). The discrepancy may be due to the fact that, unlike the simple, non-cued localization tasks used by both these previous studies, we provided endogenous directional cues before presenting the target sounds whose location needed to be discriminated, sometimes at unexpected locations ("invalid" targets).

Previous studies have also found that medial occipital areas are engaged by semantic processing of verbal stimuli (e.g., Amedi et al., 2003; Burton, 2003). In the current study, however, calcarine areas showed initial decreases to verbal stimuli that cued the stimulus location. The intriguing pattern shown by the occipital hemodynamic response - a decrease from the baseline following the verbal cue followed by an increase with the arrival of the target sound (Fig. 7a) as well as the significant lag when compared to the corresponding FEF response (Fig. 7b) - suggests that the endogenous attention cue may not directly engage the medial occipital region in CB individuals but that discriminating the subsequent target's location does engage it. Previous studies in sighted individuals have shown that endogenous cues demanding attention to an auditory stream for an expected auditory target engage auditory cortical areas in the temporal cortex (Shomstein & Yantis, 2004). Studies of switching attention between auditory and visual stimuli have reported that when attention is switched away from one sensory modality (e.g., visual) to another (e.g., auditory), there is a corresponding increase in the sensory cortical areas corresponding to the newly attended modality, and a decrease in signal in sensory cortical areas corresponding to the now unattended stimuli (Woodruff et al., 1996;

O'Leary et al., 1997; Shomstein & Yantis, 2004). Drawing on these switching effects, one possible explanation for the cue-related decrease in the medial occipital region of the CB subjects is that the endogenous verbal cue induced a shift to auditory areas in anticipation of the auditory target, causing a decrease in medial occipital areas during the cue phase of the auditory task. The robust response to the subsequent auditory target in medial occipital areas may reflect its recruitment for subsequent processing of the target and the associated behavioural response. This would suggest that medial occipital areas are not directly involved in orienting attention, but rather have been recruited into networks that are involved in functions associated with target-based processing (Pascual-Leone & Hamilton, 2001). However, dissociating these effects will require further studies which provide a clearer dissociation of cue, target, and response related effects. Ruff et al. (2006) recently demonstrated in sighted individuals that TMS over the right FEF modulates functional activity in visual cortex in a fashion that differs between the central and peripheral visual fields. That demonstration of the influence of FEF on visual cortical fields raises the possibility that in the blind FEF may continue to influence functional properties of medial occipital areas, which have demonstrably altered functions in the blind.

It is not yet clear whether cross-modal recruitment of early visual areas in the blind is due to latent pathways that participate in multimodal perception in sighted subjects that become unmasked in the blind or whether there is direct input from other sensory modalities into primary visual cortical areas (Falchier et al., 2002; Pascual-Leone et al., 2005). Multimodal areas of the dorsal extrastriate association cortex have been shown to have cortical connections to both primary auditory and visual areas (Falchier et al., 2002; Felleman & Van Essen, 1991) and may provide a route for auditory stimuli to reach visual areas such as V1 (see Sadato et al., 2002 for a similar argument for tactile stimuli). It has recently been shown that TMS of (normally sighted) human FEF seems to causally modulate functional activity in early retinotopic visual cortex (including V1) in a systematic fashion that has corresponding perceptual consequences (Ruff et al., 2006).

Conclusion

Our finding of robust activity in FEF in the congenitally blind suggests that it is actively engaged during endogenous auditory spatial orienting in the blind despite the irrelevance of voluntary eye movements. We also found activity in the medial occipital areas, but only the blind, consistent with an auditory role in the congenitally blind of cortex that is normally visual.

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Figure 1.

(a) During the covert attention switching task, oral cue words and virtually spatialized auditory targets (see Methods for details) were delivered via headphones in the scanner. The scan was clustered with a 600 ms silent gap during which all the auditory stimuli were presented. (b) Response times and (c) Accuracy (% correct responses) for different conditions (C: centre cue and target; VL: valid left cue, left target; VR: valid right cue, right target; IVL: invalid left cue, right target; IVR: invalid right cue, left target). Responses to valid targets were significantly faster and more accurate than to invalid ones. Error bars indicate $\pm$ SEM.

Figure 2.

(a) Group activation map of the blind subjects during covert attention switching trials superimposed on a 3D surface; white arrows indicate FEFs. (b) Coronal ($y = -11$) and axial ($z = 49$) views of FEF ROI (green areas in the left column), sighted (middle column), and blind (right column) group maps. Voxels activated by the covert attention switching task are shown in red/yellow with the green FEF areas superimposed to show overlap. All maps were created with whole brain random effects GLM and used cues > baseline contrast at $FDR < 0.05$ and a cluster minimum of 50 voxels; the legend bar shows the corresponding $t(64)$ values for the CB case, $p < 0.0039$; for the SC group the corresponding $t(72)$ ranged from 2.67 to 6.00, $p < 0.0095$.

Figure 3.

Individual axial (z= 53) activation maps in and around the FEF region of all subjects performing the covert attention switching task. All (a) blind and (b) sighted subjects showed consistent activation around the intersection of superior frontal and precentral sulci bilaterally. (c) Axial slices detail of one blind subject (08JS_CB) shows activation aligned closely with precentral sulcus as it descends from its top (z = 57) to bottom (z = 47). All maps were generated using a cue > baseline contrast at FDR < 0.05 and a cluster minimum of 50 voxels; the legend color bar shows the corresponding t-values.

Figure 4.

Event related response of the FEF region aligned to cue delivery, showing percent change over baseline in BOLD signal averaged across all voxels in: (a) left FEF in blind, (b) right FEF in blind, (c) left FEF in sighted, (d) right FEF in sighted. The cue was delivered at scan 0; target followed after 2 scans (only trials where targets arrived after 2 TRs or 4.4 seconds are shown here for visual clarity; targets after 1 TR resulted in similar patterns - see Fig. 5 for the combined analysis of all targets). The baseline was computed by averaging the three scans before and including 0 separately for every cue epoch (both valid and invalid targets were combined). Responses to “centre” cue (and centre targets) shown with black lines and circles, to “left” cue shown with blue lines and triangles, and to “right” cue shown with red lines with squares. Responses to left and right cues are similar in both groups, but the responses to central cues (black lines with crosses) tend to differ between SC and CB. Error bars indicate $\pm$ SEM.

Figure 5.

Event related response of the FEF region aligned to target delivery, showing percent change over baseline in signal averaged across all voxels for responses aligned to targets classified according to whether they followed central/valid/invalid cues and whether they were go/nogo; (a) left FEF in blind, (b) right FEF in blind, (c) left FEF in sighted, (d) right FEF in sighted. The target was delivered at scan labelled 0. The baseline was computed by averaging the three scans previous to and including scan 0 for every target epoch (the baseline thus incorporates the first part of the response to delivery of the preceding cue). Blue lines with triangles show “invalid go”, green lines with squares show “valid go”, red lines with filled circles show “valid nogo”, pink lines with diamonds show “invalid nogo” targets, and black lines with unfilled circles show responses to “centre” targets. Responses to most targets are similar in both groups, with response to invalid-go targets being the strongest; the exception is the response to central targets for which the blind response tended to be stronger than sighted. Error bars indicate $\pm$ SEM.

Figure 6.

Group contrast maps showing Targets > Baseline ($p(\text{FDR}) < 0.05$, minimum cluster size > 50) along the medial occipital wall and calcarine sulcus of **a)** congenitally blind and sighted (**b**) subjects during covert attention switching trials with sagittal view (at $x = 2$) shown on the left and coronal view (at $y = -81$) on the right side. Voxels activate during the covert attention switching task are shown in red/yellow with the occipital ROI shown with a dotted outline. The white cross hairs are centred on the peak voxel ($x = 2$; $y = -81$; $z = 5$) on the lower bank of the calcarine sulcus.

Figure 7.

Average event-related response from the medial occipital ROI (see Fig. 6) showing percent change over baseline. **(a)** The occipital responses aligned to cues for CB group are shown separately for targets that followed the cue by a delay of 1 TR (blue lines) or 2 TRs (green lines). Cue delivery is at scan 0. **(b)** The average response of the occipital region to targets after 2TRs, (green line), is compared to the corresponding response in the FEF region, shown (red line). The occipital response shows an initial decrease followed by a sharp rise after target delivery. The cue delivery is at scan 0 and the target at scan 2. **(c–d)** Occipital responses to targets are shown for the CB group in **(c)** and SC group in **(d)**. The event-related response under different target conditions. Blue lines with triangles show “invalid go”, green lines with squares show “valid go”, red lines with filled circles show “valid no-go”, pink lines with diamonds show “invalid no-go” targets, and black lines with unfilled circles show responses to “centre” targets. The target was delivered at scan labelled 0. CB responses to both cues and targets were significantly stronger than SC responses and clearly differ for different kind of targets. Error bars indicate $\pm$ SEM.

Table 1

Details of the blind subjects used in the study.

Subject	Sex	Age (yrs)	Edu. (yrs)	Cause of Blindness	Age of Onset	Prosthetic Eyeballs?	Light Perception	Handedness
03CDC	F	55	15	Retinopathy of Prematurity	Birth	N	None	R
05KK	F	56	23	Retinopathy of Prematurity	Birth	Y	None	R
07PM	M	59	18	Retinopathy of Prematurity	Birth	N	None	R
08IS	F	49	14	Retinopathy of Prematurity	Birth	Y	None	R
13KM	F	53	19	Retinopathy of Prematurity	Birth	Y	None	L
14MW	F	50	17	Anophthalmia	Birth	Y	None	R
16TA	M	57	14	Underdeveloped optic nerve	Birth	N	None	R
20MM	F	55	17	Retinopathy of Prematurity	Birth	N	None	Both
22TS	M	36	13	Retinopathy of Prematurity	Birth	N	Formless, of strong light	L

FEF locations and voxel overlaps. Centre of gravity of active voxels, voxel count, and percentage overlap of the functional cluster of significantly active voxels during the covert attention task. The FEF ranges (shown in brackets) were derived using SC subjects performing a saccade task (see Methods). The percent overlap indicates significant voxels within the FEF region that were common to the covert attention and saccade tasks.

Table 2

	Left Hemisphere			# voxels (% overlap)			Right Hemisphere			# voxels (% overlap)
	X	Y	Z	X	Y		X	Y	X	
FEF ROI										
SC	[-40 -18]	[-17 -5]	[40 61]	[20 41]	[-17 -5]		[40 61]			1691 (65%)
CB	-28	-11	51	31	-10		49			1137 (67%)
	-28	-12	51	32	-10		50			