Representation of eye position in the human parietal cortex

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ABSTRACT

Neurons that signal eye position are thought to make a vital contribution to distinguishing real-world motion from retinal motion due to eye movements, but relatively little is known about such neurons in the human brain. Here we present data from functional magnetic resonance imaging experiments that are consistent with the existence of neurons sensitive to eye-position in darkness in the human posterior parietal cortex. We utilised the enhanced sensitivity of multi-voxel pattern analysis (MVPA) techniques, combined with a searchlight paradigm, to isolate brain regions sensitive to direction of gaze. During data acquisition, participants were cued to direct their gaze to the left or right for sustained periods as part of a block-design paradigm. Following the exclusion of saccade-related activity from the data, the multivariate analysis showed sensitivity to tonic eye position in two localised posterior parietal regions, namely the dorsal precuneus and, more weakly, the posterior aspect of the intraparietal sulcus. Sensitivity to eye position was also seen in anterior portions of the occipital cortex. The observed sensitivity of visual cortical neurons to eye position, even in the total absence of visual stimulation, is possibly a result of feedback from posterior parietal regions which receive eye position signals and explicitly encode direction of gaze.
INTRODUCTION

Signals that indicate the position of the eyes in the head are critically important in vision, allowing us to disambiguate the information inherent in the retinal image. The initial representation of the visual world is retinotopic: receptive field locations are fixed relative to the retina. When the eyes move, a retinocentric system is liable to misinterpret the resulting image movement as movement of the world. In fact, we have very stable perception of a stationary world, showing that at some stage of processing, the retinocentric framework is discarded and a geocentric, or at least a craniocentric, frame of reference is adopted. Such a framework is necessary not only for stable perception but also for effective visually guided reaching and eye movements.

Knowledge of eye position may not always be sufficient to ensure stable and veridical perception but it is believed to be an important requirement (e.g. Howard, 1993).

In the primate visual system, neurons sensitive to the position of the eye in the orbit are found in the posterior parietal cortex (PPC) (Mountcastle et al. 1975; Sakata et al. 1980). These neurons show sustained activity when the animal fixates a specific region of visual space, suggesting that they may signal the current eye position. Gaze-sensitive neurons are found in parietal area 7a (Andersen et al. 1990; Squatrito and Maioli 1996) and also in nearby lateral intraparietal cortex (LIP) (Andersen et al. 1990; Bremmer et al. 1997a) and ventral intraparietal cortex (VIP) (Bremmer et al. 1999). Eye-position information is also present in and around the parieto-occipital sulcus (Galletti et al. 1995), in the frontal eye fields (Bizzi 1968) and in sub-cortical structures including the superior colliculus (Campos et al. 2006; Van Opstal et al. 1995). The origin and maintenance of the eye position signal are incompletely understood and may be complex, but are thought to involve efference copy from such structures as the
superior colliculus, which sends a corollary discharge to the frontal and parietal eye fields when, or even before, a saccade occurs (Andersen et al. 1997; Duhamel et al. 1992; Lewis et al. 1998; Sommer and Wurtz 2002).

The encoding of eye-position or direction of gaze in humans has received relatively little attention. It is known from fMRI studies that both motor-related and visual activity can be influenced by direction of gaze (Baker et al. 1999). Deutschländer et al. (2005) examined the dependence of brain activity on eye position, but in the absence of visual stimulation. Most of the gaze-dependent activity they found was in occipital, rather than parietal, cortex. In the primary visual cortex, activity was increased in the hemisphere contralateral to the direction of gaze, while elsewhere in occipital cortex it was greater in the ipsilateral hemisphere. These influences probably reflect modulations of visual sensitivity (or spontaneous activity in the absence of stimulation) and not the eye position code itself. Parietal effects were found when fixation was contrasted with rest, but when rightward and leftward fixation were contrasted, differential activity was sparse.

Neurons giving tonic responses related to eye position appear to have no systematic arrangement on the cortical surface (Squatrito and Maioli 1996). Demonstrating effects of eye position via changes in BOLD amplitude is extremely difficult if neurons with different preferences are intermingled: changing gaze might change the distribution of responses within a local population but would not change the total activity in the population and so would not show as a change in the BOLD response. In this study, we utilise the enhanced sensitivity of multi-voxel pattern analysis (MVPA) techniques, combined with a searchlight paradigm to establish brain locations sensitive to eye position changes. Such multivariate analyses have recently been utilised to explore the microarchitecture of cortical areas whose functional
properties are beyond the resolution of conventional fMRI approaches (see Haynes and Rees 2006 for review). For example, as expected in the case of eye-position neurons, cells which code the orientation of visual features are arranged at such a fine spatial scale that standard, univariate BOLD responses to differently oriented stimuli are indistinguishable. MVPA approaches have shown that it is entirely possible to determine the orientation of a stimulus based on a multivariate analysis of the fMRI data, thus demonstrating response selectivity to this feature (Kamitani and Tong 2005; Haynes and Rees 2005). Using such a multivariate paradigm, we provide evidence that there are two areas in posterior parietal cortex that show behaviour consistent with the presence of neurons that give a tonic, eye-position-dependent discharge in darkness. In addition, we confirm that modulation by eye position occurs in the occipital cortex.

METHODS

Two experiments are presented here, the aim being to determine whether pattern classification techniques could successfully distinguish between signals evoked by cells that code different eye positions, and to identify their location within the brain.

Participants and design: Eight, healthy experienced observers (4 female) participated in the experiments, two of which participated in both; mean age was 29.1 (range, 20-55). All had normal, or corrected-to-normal vision, and gave written informed consent. The stimulus comprised two small, dim points of light viewed in total darkness. These acted as fixation points. They were generated by two lasers, each consisting of a red LED and a lens that was adjusted so as to focus the beam on a rear-projection screen situated at the end of the scanner behind the subject’s head. When viewed from the supine position via a mirror these fixation points were separated horizontally by 20 degrees of visual angle. To reduce scattered light to sub-threshold
levels, an adjustable neutral density filter was placed in the projection path. The attenuation was set such that the light sources themselves were barely visible and no scattered light was visible. All sources of stray light in the room were eliminated., All participants reported that they could see nothing except the two dim spots, even after prolonged dark adaptation. This ensured that when the eyes moved, there were no changes in retinal stimulation to which BOLD activity could be attributed.

Both experiments followed a block design. The first experiment had a fixation point appearing on the right for 40s, and then on the left for 40s; this was repeated a total of three times. This gave the appearance of a single spot that moved every 40s. The task was to fixate the spot at all times making a saccade as it moved from one side to the other. The stimulus sequence was preceded by a 10s period where no spot was present, giving a total experiment time of 250s. Each participant completed ten repetitions of the experiment. The second experiment was identical to the first in every respect, except that within each block the fixation spot was turned off 2s after switching location. Thus participants would see a spot appear on the right for 2s, they would fixate the spot, attempt to maintain their current fixation for a further 38s in darkness, after which time the spot would reappear on the left for 2s, and the process repeated (see Fig. 1). During this experiment, eye movements were monitored throughout with a 60Hz infrared video camera and pupil-tracking software (Arrington, Inc.). This enabled us to check that participants were broadly maintaining the correct gaze direction. Visible red light from the infrared source was completely removed by filtering (Kodak Wratten 87c).

**Imaging:** Data were acquired at the Combined Universities Brain Imaging Centre (CUBIC) with a 3T MRI scanner (Magnetom Trio, Siemens, Erlangen, Germany) using a standard Siemens 8-channel array headcoil (Exp. 1) or a custom 8-channel occipito-parietal array coil (Stark Contrast, Erlangen, Germany; Exp. 2).
Functional images were acquired with a gradient-echo, echoplanar (EPI) sequence (TR 146 ms, TE 31 ms, voxel size 3x3x3 mm). The acquisition volume consisted of 28 oblique slices (64 x 64 matrix) covering the posterior part of the brain including occipital cortex and posterior parietal cortex, and approximately parallel with the calcarine sulcus. Functional volumes were acquired continuously during each experimental run, giving 125 timepoints per voxel. A high resolution (1mm) anatomical scan of the whole brain was also acquired.

**Data analysis:** For each subject, the raw functional data were motion-corrected using SPM5 (http://www.fil.ion.ucl.ac.uk/spm/software/spm5/). No spatial or temporal smoothing was applied, and the data for each individual was analysed separately. Each timecourse was shifted by 3 TRs (6s) to account for the haemodynamic delay.

Our aim was to determine whether pattern classification techniques could identify areas of the brain specific for coding eye position in darkness. Our approach was therefore to make no assumptions about where in the brain regions of interest (ROIs) should be located. To this end, the pattern classification analysis was based on a “searchlight” paradigm (Kriegeskorte et al. 2006), in which a 5x5x5 voxel window moved sequentially, one voxel at a time, through each dimension in the EPI volume. This provided 125 timecourses from each window for classification, for which a support vector machine (SVM) approach was utilised (LIBSVM; http://www.csie.ntu.edu.tw/~cjlin/libsvm/). The SVM is a classification algorithm based on supervised learning that utilises a training dataset to build a model that predicts whether a new dataset represents one pattern or another.

Although we eliminated all stray light, two possible confounds exist. First, when the spot moves there is inevitably a short delay before the re-fixation saccade is made and during this time, retinal stimulation, although minimal, is different from the rest of
the scan. Second, the saccade itself is expected to generate activity in various regions, including PPC (e.g. Culham et al. 2006). In order to eliminate any possible influence of these transient events on the classifier, we used a subset of timepoints from within each block. These were chosen from the centre of the block, starting 18 sec after a saccade had been made and ending prior to the next saccade (see Fig. 1). It remains possible that the selected timepoints reflect a degree of saccade planning remote to the saccade itself, but it removes all peri-saccadic activity. The chosen timepoints were averaged within each block, providing 60 independent exemplars (30 gaze left, 30 gaze right from ten experiment repetitions) for the SVM analysis. For each set of averaged timepoints, 125 voxels from the searchlight window were extracted and assembled as a feature vector, and normalised to unit length. Each vector was also labelled as representing either gazing left or gazing right.

The classification accuracy of the SVM was assessed using a leave-one-out cross-validation technique where data from one run was used for testing the classifier, and the remaining nine used for training. This was repeated ten times, using a different run for testing each time, and the 10 classification accuracies were averaged to provide an estimate of SVM performance. This measure of accuracy was assigned to the voxel coordinates at the centre of the searchlight window. The window was then shifted by one voxel and the entire process was repeated. The final result, once the window had navigated through the entire EPI volume, was a new functional volume in which voxel values correspond to classifier accuracy.

For visualisation of results in individual subjects, the SVM volume was coregistered with the subject’s anatomy. The data were viewed superimposed on the 3D anatomy and also on cortical reconstructions generated with FreeSurfer (http://surfer.nmr.mgh.harvard.edu/). To establish generalizability, the SVM volumes for
all subjects were spatially transformed to match the MNI template (using FLIRT; http://fsl.fmrib.ox.ac.uk/fsl/flirt/) and classification performance was averaged across subjects at each voxel in standard MNI space to create an average SVM volume. We also performed a second-level analysis to determine whether decoding performance was above chance between subjects using a voxelwise $t$-test, thresholded at $p<0.01$ (unc).

Finally, in order to confirm the statistical distribution of classifier accuracy scores, we carried out a permutation test; this was performed on the searchlight window containing the peak classifier performance within a subject’s SVM volume. Training set labels were randomly shuffled prior to testing to yield a classifier performance measure expected by chance. This was repeated 500 times for each subject, each time with a different shuffle, providing a distribution of classifier performance measures with a mean of 0.499 (i.e. 50% accuracy, as expected by chance) and a 95% confidence interval of 0.604 (60% classifier accuracy).

210 RESULTS

212 Experiment 1: Decoding direction of gaze in the presence of a visual fixation point.

214 GROUP RESULTS. The average SVM classification accuracy map, constructed from the MNI normalised maps of each individual from Exp. 1, is shown in Fig. 2. This reveals a number of distinct areas which show significantly above-chance classification performance between subjects for activity representing gaze to the left or right (chance performance being 50%, maps thresholded at $p<0.01$ as assessed at the group level).

Fig. 2A, which shows a series of coronal slices through the posterior portion of the head, demonstrates a network of areas that differentiate between the coding of the two eye positions extending anteriorly and dorsally from the posterior poles.
Classification performance is extensive bilaterally in medial occipital regions and extends to lateral occipital cortex (LOC). The peak in classifier accuracy (81%, Fig. 2B) is observed in a posterior occipital location centred around MNI coordinates [15 -90 -4]. Sensitivity appears to extend across the cuneus, covering the expected locations of all the early retinotopic areas, although reaching statistical significance only patchily. This sensitivity to direction of gaze comes to an abrupt halt in the proximity of the parieto-occipital sulcus (POS; Fig. 2C, arrow). In the posterior parietal cortex, a distinct classifier peak is observed in the precuneus (Fig. 2C). Gaze sensitivity here is found mainly in the right hemisphere, but the cluster does appear to cross the midline into the left hemisphere with the statistical thresholding criteria employed here.

INDIVIDUAL RESULTS. Being based on spatially normalised brains, results from the above group analysis cannot be used for accurate identification of the anatomical locations of peak classifier performance. For this, we have superimposed individual classification maps on cortical reconstructions from individual subjects. Fig. 3 shows the resulting maps from all five participants in Exp. 1, thresholded at 65% classifier accuracy. This is an arbitrary threshold chosen to optimise the display of areas sensitive to direction of gaze, yet is substantially beyond the 95th percentile of classification accuracies expected by chance alone (see Methods). Note that much higher classification performance is observed in some individuals in comparison to the group maps because the process of averaging inherently reduces the maximum effect. The central panels show posterior views of both hemispheres, while the left and right panels show medial views of posterior cortex. The maps demonstrate strong classifier performance evident in the occipital cortex as seen in the group analysis (e.g. ATS, AW). It is evident from these maps however that not all participants show such strong
selectivity of responses, participant AB in particular shows no evidence of being able to
distinguish between left and right gaze in areas around the posterior calcarine or LOC. A
similar picture is evident for participant KL, but with better classifier performance
around the calcarine.

In all participants, classifier performance is high in an area of the precuneus,
close to the border with the SPL (Fig. 3, asterisks), the only exception being the right
hemisphere of participant ATS. In some participants, the activity in the precuneus is
located more anteriorly (e.g. KL), while in others, it is situated posteriorly, closer to the
POS (e.g. AS). Thus the apparent extent of precuneus gaze sensitivity in the group
analysis (Fig. 2C) may be an artefact of averaging.

In several cases, regions of high classification performance can be seen in lateral
PPC, including parts of the IPS (Fig. 3, arrows). Sensitivity is clearly observed in the
right hemisphere of each of our participants, but with the current threshold levels, there
is scant evidence for it in the left hemisphere. Activity in the IPS is not evident in the
group analysis even in the right hemisphere, perhaps because of variability in its
position across individuals. The medial occipital sensitivity to direction of gaze near the
POS that was identified in the group analysis (Fig. 2C) is also evident in some of the
individual maps. It is particularly prominent in participant KL, where this sensitivity to
direction of gaze is also observed to extend into the fundus of the POS (confirmed from
inflated representations). In AS on the other hand, it is slightly more medial/posterior
and this is more typical of the group. This region could be V6, or possibly V3A, but this
cannot be confirmed without independently localizing these areas.

Experiment 2: Decoding direction of gaze in complete darkness
Experiment 1 revealed activity in the early visual areas. Even though the experiment was conducted in darkness, the fixation point was continuously present and this may have been enough to cause some visual drive, at least in the foveal representation. If fixation stability was asymmetric, this might result in differences that would permit eye position to be decoded based on visual activity alone. Any such visual drive might feed forward to other cortical regions, where the same might occur. The purpose of Experiment 2 was to test this possibility. Subjects were shown a fixation spot at the start of each block for 2s only; thereafter they were requested to maintain fixation broadly in the same direction in the absence of any visual stimulation. This has the advantage that any observed occipital activity cannot be explained by visual drive, but the disadvantage that fixation control is open-loop and likely to be much less stable than in Experiment 1. For this reason, eye position was measured continuously.

EYE-MOVEMENT MONITORING. Fig. 4 shows monocular eye-movement recordings averaged over the ten repetitions of the experiment for each participant. It demonstrates that participants were able to maintain their direction of gaze broadly to the left or right. Some of the position traces indicate a drift of gaze away from the original fixation at the start of a block, but its magnitude is sufficiently small that there is a clear distinction between gazing left and gazing right.

GROUP RESULTS. Fig. 5 shows the average SVM classification accuracy map for Exp. 2 in the same format as Fig. 2. This reveals a broadly similar network of areas that are sensitive to gaze direction, with the same overall bias towards the right hemisphere. Most areas showing gaze sensitivity correspond to areas identified in Experiment 1. The
most notable difference is the much weaker eye-position coding in posterior parts of the occipital cortex (Fig. 5A). Sensitivity in more anterior portions remains strong.

The group-level analysis identifies two distinct peaks in classification performance. The first, and overall, peak in classifier performance (81%) is located at the most anterior aspect of the occipital lobe on the superior (dorsal) side of the calcarine sulcus and close to the junction with the POS (Fig. 5B, [8 -65 16]). Sensitivity is observed along the entire length of the POS, and in contrast to the first experiment, is observed to extend into the parietal lobe. Note, however, that with more stringent statistical thresholding criteria, this becomes restricted to the occipital lobe. The second cluster is found in the precuneus (the medial wall of the posterior parietal cortex; Fig. 5C) with a peak in classification performance in a very similar location to that observed in Exp. 1, although here we observe a symmetrical spread of sensitivity into both hemispheres.

INDIVIDUAL RESULTS. Individual SVM maps in Exp. 2 show considerable variation in peak classification accuracies between participants. For this reason different threshold criteria have been used to illustrate the more salient areas of sensitivity, although we emphasise that the thresholds are always greater than the 95th percentile identified in the permutation tests. The maps in Fig. 6 clearly illustrate the absence of sensitivity in the posterior occipital regions, although participant PK does have more extensive occipital sensitivity comparable to that observed in Exp. 1.

The group data presented in Fig. 5 suggests that areas of the anterior cuneus, close to the POS show the highest sensitivity for coding of direction of gaze. This localisation is supported by examination of the individual SVM maps presented in Fig. 6. While sensitivity isn’t always confined to the area close to the POS (e.g. more
posterior in participant DV), all participants demonstrate greater than chance classification performance in this occipital region of the brain. In most cases, this sensitivity does not extend into and beyond the POS.

Exp. 1 identified a region of the precuneus having high sensitivity to direction of gaze, which was also evidenced in Exp. 2 and the group analysis presented in Fig. 5. This is confirmed in the individual maps, where classifier performance is high in the majority of participants, although it is clearly more extensive in some compared to others (Fig. 6, asterisks). In addition, Fig. 6 (arrows) highlights areas of lateral PPC and IPS that have greater than chance classification accuracies for direction of gaze. These areas were not evident in the group analysis of Fig. 5, possibly due to the variation in the location and magnitude of sensitivity. However, similar to Exp. 1, sensitivity appears to be confined to the right hemisphere.

DISCUSSION

Using a multivariate fMRI paradigm, in which eye position (direction of gaze) was varied in darkness, we have provided evidence that eye position is represented in several different posterior cortical brain regions, with good reproducibility between two experiments. Activity associated with saccades and alerting responses between fixation blocks was excluded. Our data are restricted to two eye positions, left and right, and further experimentation will be needed to establish whether a comprehensive map of eye position exists in some or all of the position-sensitive areas identified. Although we discuss the results in terms of encoding physical eye position in the orbit, this correlates with other attributes. It is possible that what is represented is eye position relative to the body rather than the head. More fundamentally, it could be that the line of sight in
external space is represented, or even that perceptual awareness of an external location in space is represented. In our experiment, all are correlated and cannot be distinguished. In Experiment 2, a possible confound arises from the slow drift of eye position that can be seen in Fig. 4. If the drift is in opposite directions for right and left gaze then it is possible that direction of eye drift, not eye position, is what is being decoded. This is unlikely because the pattern of results in Experiment 2 is similar to that in Experiment 1, in which fixation can be assumed to be good. However, as a check, we analysed the eye position traces from Experiment 2 for direction of drift. For each participant, we isolated the eye-position signal within each block, calculated the first temporal derivative of the signal and summed it over all blocks with the same gaze direction. The rationale is that blocks exhibiting drift in a consistent direction should have a non-zero summed derivative (positive or negative, depending on drift direction). The results showed numerical drifts that were small and inconsistent across participants. Only 1 of 5 participants showed clearly opposite drifts in right and left blocks.

As a check that participants were in fact able to maintain good fixation in Experiment 1, we partially repeated the experiment, scanning three of the original participants and conducting three scan runs for each. The conditions were identical to Experiment 1 except that eye position was recorded. The resulting eye traces are shown in Figure 7. Fixation is very stable for all three participants.

Eye-position neurons in IPS

Perhaps the most expected result, though certainly not the strongest, is the encoding of eye position in and around the right intraparietal sulcus (IPS). This result is evident in several subjects in both experiments, but not clear in the group analysis of either experiment, presumably because of variability in its location among individuals. If
reliable, it is consistent with the presence in this region of neurons that give a tonic
response to a particular eye position in darkness, different neurons preferring different
gaze directions, such as those found in area 7a of primate posterior parietal cortex
(Andersen et al. 1990; Mountcastle et al. 1975; Sakata et al. 1980). Area 7a is located in
the inferior parietal lobule, on the lateral surface of the brain adjacent to the
lateral/inferior lip of the IPS. In our data, the gaze-sensitivity is not in the corresponding
anatomical location but instead is located around the IPS itself, some 2-3 cm distant
from the corresponding location in macaques. Several fMRI studies have reported
saccade-related activity (particularly saccade planning) in and around the human IPS,
including the area lateral and ventral to the IPS that corresponds to area 7a in macaques,
in the sulcus itself, and more dorsally, in the superior parietal lobule (e.g. Colby 1998;
Konen et al. 2004; Müri et al. 1996; see Culham et al. 2006 for review). Anticipating
that saccade-related activity might be found in proximity to tonic gaze responses, we
excluded from our analysis the timepoints preceding and following each re-fixation, so
as to be sure that our results isolate tonic activity during fixation. Finding eye-position
and saccade-related activity in similar locations is perhaps not surprising: it makes
intuitive sense that an area involved in planning saccades would require information
about current eye position in order to generate effective plans.

We also conducted a standard univariate analysis of our data. A statistical
contrast between left and right gaze positions revealed no differential activity in any part
of the acquisition volume in either a random-effects or a fixed-effects group analysis
(p<0.05 FWE). This suggests that neurons with different preferences are intermixed on
the scale of MRI voxels, requiring multivariate pattern analysis to reveal their presence;
certainly multivariate analysis is much more sensitive. This is perhaps surprising
because the human IPS contains several areas that have retinotopic maps of attended
space, as revealed by either covert attentional shifts or saccades (Schluppeck et al. 2005; Sereno et al. 2001; Silver et al. 2005). However, the lack of spatial organization of eye position neurons (as far as we are able to detect), even to the extent of a contralateral preference, is in line with physiological data from macaque area 7a. For example, Squatrito and Maioli (1996) say “[eye position] neurones very close to each other in space often showed disparate … ramp orientations” and “our experiments did not reveal any ordered arrangement of the preferred eye positions in the cortex” (p. 393).

The gaze-related activity we see in the IPS is confined to the right hemisphere. This may reflect genuine laterality, although caution is required in case we simply missed the corresponding decoding ability in the left hemisphere through sensitivity limitations (e.g. Fig. 3, AB shows some left hemisphere sensitivity). According to Konen et al. (2004), the right IPS is more heavily involved than the left in saccade-related activity but we know of no evidence of this in the case of tonic gaze responses. However, if gaze information in IPS is functionally tied to saccade planning then it would make sense for the two to be co-localized and that might include being co-lateralized.

**Medial parietal eye-position neurons**

We have also provided evidence that eye position is encoded in the precuneus (the medial portion of the human posterior parietal cortex). In contrast to the IPS, this result is highly robust, being seen in the group analysis in both experiments and in almost all individual hemispheres, both left and right. The position of this region varies somewhat in the anterior-posterior dimension but is always in the dorsal part, close to the SPL. Eye position neurons do not appear to have been reported in the precuneus of the macaque. However, this region of the macaque brain has been much less extensively
studied than lateral parietal cortex. Moreover, there is evidence that macaque precuneus is strongly connected with lateral parietal regions (Leichnetz 2001) and that it is concerned with spatially guided behaviour (Salamon et al. 2003). Equally little is known of the human precuneus. It has been characterized in cytoarchitectonic terms (Schepersjans et al. 2008) and a recent fMRI study (Marguilles et al. 2009) shows that it can be divided into three zones based on connectivity at rest. The same zones could be discerned with fMRI in macaques, suggesting a common overall organization. In a review of precuneus function, Cavanna & Trimble (2006) conclude that the region “works in concert with lateral posterior parietal cortex in elaborating information about egocentric and allocentric spatial relations for body movement control.” It is likely that much of medial and lateral posterior parietal cortex uses eye position information in one way or another, in both macaques and humans. Although the primate evidence for “pure” eye position neurons concerns lateral parietal cortex, it could be that such neurons also exist in the macaque precuneus but have not been found (or even sought).

Occipital sensitivity to eye position

Our multivariate analysis reveals extensive sensitivity to eye position in occipital cortex. In Experiment 1, the location and extent of this sensitivity suggests that it includes all the early retinotopic areas and also lateral occipital cortex. In medial occipital cortex (broadly corresponding to V1-V3) sensitivity appears to be greater near the occipital pole, where the central visual field is represented, than in more anterior portions representing the far periphery. However, in Experiment 2, sensitivity is much reduced in the central visual field representation. This suggests that it may be an artefact of visual stimulation by the fixation spot, which was present continuously in Experiment 1. Sensitivity to eye position in anterior parts of retinotopic cortex is still strong in
Experiment 2, suggesting that this is unrelated to the fixation point (which in any case can only stimulate the fovea and parafovea, even allowing for a degree of fixation instability).

Our results are consistent with the notion that the well-established visual areas in medial occipital cortex contain many neurons that have receptive fields defined in retinal space but response gain that is strongly modulated by gaze direction (or, equivalently, real-world stimulus location), akin to those found in various primate visual areas (Bremmer et al. 1997b; Galletti and Battaglini 1989; Galletti et al. 1991; Rosenbluth and Allman 2002; Trotter and Celebrini 1999). However, since our study was conducted in darkness, our results do not address gaze-dependence of response gain but instead suggest that occipital visual neurons show gaze-dependent changes in resting discharge (baseline responses). A few previous human fMRI studies also suggest such an interpretation. Deutschländer et al. (2005) found gaze-dependent baseline changes in occipital cortex that occurred in darkness and therefore reflect baseline changes. In addition, the gaze-related changes shown by DeSouza et al. (2002) in V4 and MT+ appeared to concern baseline activity levels more than response magnitude. Finally, evidence from multivariate analysis for modulation of visual responses by gaze direction in early visual areas has recently been reported in abstract form (Merriam et al. 2008).

If we assume that much of the eye position sensitivity in the parafoveal representation seen in Experiment 1 is an artefact of visual stimulation, we are left with the conclusion that sensitivity is much stronger in peripheral than central parts of the visual field representation. This is very clear in Figs. 5B and 5C. If eye position sensitivity in occipital cortex reflects modulatory influences from parietal and/or frontal regions, then this modulation may be stronger in peripheral parts of the visual field.
The eye position sensitivity we report in occipital cortex includes a small region on the posterior bank of the parieto-occipital sulcus (POS), near the dorsal surface of the brain, that is thought to be the human homologue of macaque visual area V6 and/or V6A (Galletti et al. 1991; Galletti et al. 1996). In macaques, these areas are found in the anterior bank and fundus of the POS. Many neurons in V6 and V6A are sensitive to direction of gaze, and V6A contains non-visual cells that are affected by gaze in total darkness (Galletti et al. 1995; Galletti et al. 1996). It has been suggested that V6A explicitly encodes eye position (Nakamura et al. 1999). Gaze-dependent neurons in V6/V6A show no contralateral or up-down organization of gaze preference; instead gaze preferences appear to be randomly intermingled (Galletti et al. 1995). This leads to the expectation that their human equivalents would not be detectable with standard fMRI but would require multivariate analysis to reveal them. This is our experience: we found no differential activity in the vicinity of POS in a standard univariate contrast of left- and right-gaze blocks.

In humans, V6A has not been identified but V6 has been identified on the basis of both retinotopic mapping (Pitzalis et al. 2006) and sensitivity to optic flow (Cardin and Smith 2010; Pitzalis et al. 2010). It is located slightly more posteriorly than in macaques, in the posterior bank of the POS. In our hands (Cardin and Smith 2010), the mean Talairach co-ordinates of human V6 are [14 -77 30] (right), and [11 -79 30] (left). This corresponds well to the location of the POS gaze-sensitive region in the present study (which peaks at MNI: 10 -86 34 in Experiment 1) and on this basis we conclude that our occipital eye-position-sensitive region probably includes V6. Since gaze sensitivity is apparently more developed in macaque V6A than V6, it is plausible that it could include both regions.
Functional relationship of gaze-sensitive brain regions

We have observed sensitivity to tonic eye position in several different brain regions. Our data do not directly address the relationships among these areas, but a plausible speculation is that the medial and lateral parietal gaze-sensitive regions are primary in the sense that they code eye position explicitly, while the occipital visual areas including V6/V6A utilize this information to modulate their activity in a way appropriate to visual function. As stated in the Introduction, eye-position information has been found in several cortical and sub-cortical regions, but the origin and inter-relation of these signals remains unclear. Further experiments will be needed to elaborate the connectivity of the eye-position-sensitive brain regions we have described.

Conclusion

In summary, we present evidence consistent with the previously reported existence of sensitivity to gaze direction in human early visual areas, using multivariate analysis. We address the possible origins of the signals that modulate visual cortex by demonstrating similar sensitivity, in total darkness, in two posterior parietal regions. The more prominent is in bilateral medial PPC (precuneus), with weaker sensitivity in lateral PPC, in and around the right intraparietal sulcus.

REFERENCES


Figure Legends

Fig. 1. Schematic of the timecourse of the experiment and the extraction of data for the SVM. Participants directed their gaze to the left or right during 40s blocks. Of the 20 volumes collected during each block, only 13 volumes (timepoints 7 to 19) were utilised for pattern classification in order to exclude saccade-related activity. These timepoints were averaged to create a single entry in the feature matrix; the process was repeated for each voxel within the 5x5x5 voxel window to make up the remaining features of the classifier feature matrix. The schematic provides one illustration of data extraction from a ‘gaze right’ block, but the feature matrix comprised data from all sixty blocks (6 blocks, 10 runs), together with associated labels to indicate gaze left or right. All timepoints were shifted by 3 TRs (6s) in order to account for the haemodynamic delay and this is incorporated in the schematic, thus the acquisition of timepoint 7 started 18s after the onset of rightward gaze. The lower panels of the figure indicate the onset and duration of the laser fixation points in Exp.1 and Exp. 2.

Fig. 2. Group SVM classification accuracy map averaged across five participants from Exp. 1, and superimposed on a template brain in the standard MNI coordinate space. Panel A shows a series of coronal slices through the posterior portion of the head (neurological convention), while the side panels show selected sagittal views. The maps have been thresholded at $p<0.01$ as determined from a second-level group analysis. Panel B shows the location of overall peak classifier accuracy, which occurs in the posterior aspect of the medial occipital lobe. Panel C shows how the medial occipital sensitivity extends anteriorly but ends at the POS (arrow). Panel C additionally
Fig. 3. Individual classification maps superimposed on cortical reconstructions for all five participants from Exp. 1, thresholded at 65% classifier accuracy. The side panels show medial views of the occipital and parietal regions, while the central panels show posterior views of both hemispheres. Only three of the five participants show the strong occipital sensitivity to direction of gaze, but the precuneus sensitivity is present in all subjects (indicated by an asterisk). All subjects show right hemisphere intraparietal sulcus sensitivity to direction of gaze (arrows). Some degree of lateral occipital sensitivity is also evident.

Fig. 4. Average eye-movement recordings for all participants in Exp. 2. The blue traces represent an average of recordings across ten repetitions of the experiment, the grey areas representing ±1 SD of the mean. Time (in seconds) is represented on the abscissa, while horizontal eye-movement is represented on the ordinate. Peak-to-peak amplitudes represent approximately 20 degrees of visual angle. Example images as recorded with the infrared video camera for gazing left/right are shown for two subjects in the lower right panel.

Fig. 5. Group SVM classification accuracy map averaged across five participants from Exp. 2, and superimposed on a template brain (see Fig. 2 for details). Panel A shows a similar pattern of sensitivity to gaze direction to Fig. 2, but with reduced sensitivity near the occipital pole. Panel B shows the location of overall peak classifier accuracy, now shifted to an anterior location in the medial occipital lobe (c.f. Exp. 1, Fig. 2). Panel C
shows a distinct peak of greater-than-chance classifier performance in the medial precuneus, similar to that observed in Exp. 1 (Fig. 2).

Fig. 6. Individual classification maps superimposed on cortical reconstructions for all five participants from Exp. 2. Classifier accuracy thresholds are as indicated. The side panels show medial views of the occipital and parietal regions, while the central panels show posterior views of both hemispheres. Asterisks indicate the location of precuneus sensitivity to direction of gaze, evident in all participants although varying in magnitude and location, and all bar one show IPS sensitivity to direction of gaze (arrows), confined to the right hemisphere.

Fig. 7. Average eye-movement recordings, in the format of Fig. 4, for all participants in a supplementary experiment to check eye stability in Experiment 1. The blue traces represent an average of recordings across three repetitions of the experiment and the grey areas represent ±1 SD of the mean.
20 TRs 125 voxels

13 TRs (7:19)

Averaged TRs

10 repetitions of the experimental paradigm

Gaze Gaze Gaze Gaze Gaze Gaze

Right Left Right Left Right Left

40s fixation point duration

Exp. 1

2s fixation point duration

Exp. 2