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Spatial Updating in Human Parietal Cortex

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Summary

Single neurons in monkey parietal cortex update visual information in conjunction with eye movements. This remapping of stimulus representations is thought to contribute to spatial constancy. We hypothesized that a similar process occurs in human parietal cortex and that we could visualize it with functional MRI. We scanned subjects during a task that involved remapping of visual signals across hemifields. We observed an initial response in the hemisphere contralateral to the visual stimulus, followed by a remapped response in the hemisphere ipsilateral to the stimulus. We ruled out the possibility that this remapped response resulted from either eye movements or visual stimuli alone. Our results demonstrate that updating of visual information occurs in human parietal cortex.

Introduction

The idea that visual perception is an active process has attracted considerable interest. Nowhere is the active nature of vision more evident than in the construction of a stable image of the world. As we move our eyes, new images are constantly presented to the brain, yet we perceive the world as remaining still. This spatial constancy suggests that the act of making an eye movement changes the brain's representation of visual information. Visual and motor signals interact to construct an internal representation that is constantly updated and spatially stable (Colby and Goldberg, 1999).

Neurons in monkey parietal cortex participate in updating visual signals. Parietal neurons have retinotopic receptive fields that move with the eyes. In the remapping paradigm, when the eyes move so that the receptive field of a neuron lands on a previously stimulated screen location, the neuron fires even though the stimulus is no longer present (Duhamel et al., 1992a). This response to the trace of the stimulus indicates that a transformation in the neural representation has occurred: neurons that initially encoded the location of the visual stimulus have transferred their information to the neurons that will represent the location of the stimulus after the eye movement. The representation of visuospatial information is thereby remapped, or updated, in conjunction with the eye movement. A corollary discharge of the eye movement command is thought to trigger remapping. Updating creates a stable representation of space by compensating for the displacement of objects on the retina.

We hypothesized that spatial updating also occurs in humans. Behavioral results in humans and nonhuman primates have shown that they have similar abilities in double-step eye movement tasks that require the use of updated visual information (Baizer and Bender, 1989; Hallett and Lightstone, 1976). Moreover, the parietal lobe is critical for task performance. Humans with parietal lobe damage are unable to perform double-step tasks (Duhamel et al., 1992b; Heide et al., 1995), and parietal neurons in monkeys are specifically active in these tasks (Goldberg et al., 1990). We thus hypothesized that updating would produce physiological activity in human parietal cortex and that we would be able to visualize it using fMRI. We were encouraged in this endeavor by a previous human fMRI study that tested subjects in a conceptually related triple-step eye movement task (Heide et al., 2001). While these authors found activation in multiple cortical sites, they suggested that parietal cortex in particular was related to the updating component of the task. For these reasons, we focused our data acquisition and analysis on parietal cortex.

We scanned subjects while they performed an eye movement task that is directly analogous to the task used to demonstrate remapping in monkeys. The sequence of events in our spatial updating task is shown in Figure 1A. At the beginning of the trial, the subject fixated a stable target (right cross). A visual stimulus appeared at the center of the screen and remained on for 2 s. The stimulus disappeared at the same time that a tone cued the subject to make a leftward saccade to a stable target (left cross). This eye movement brought the previously stimulated screen location into the right visual field. No physical stimulus was present in the right visual field at any time during the trial.

Previous studies have shown that visual stimuli activate extensive regions of contralateral visual and parietal cortex (DeYoe et al., 1996; Engel et al., 1997; Sereno et al., 1995). We hypothesized that ipsilateral parietal cortex would also become activated when an eye movement brought the stimulus location into the opposite visual field, even though the stimulus had already disappeared by the time of the eye movement. In the example shown in Figure 1A, we expected activation to shift from the right to the left hemisphere when the eyes moved, despite the fact that no physical stimulus ever appeared in the right visual field. In addition, we predicted that the remapped activation would appear later than the visually evoked activation, because the eye movement was cued 2 s after the onset of the visual stimulus (Figure 1B). Based on previous single-neuron studies in monkey (Duhamel et al., 1992a), we also expected that activation due to remapping would be smaller in amplitude than the visually evoked activation. Finally, we predicted the opposite pattern of activation when a right visual field stimulus was followed by a rightward saccade (Figures 1C and 1D).

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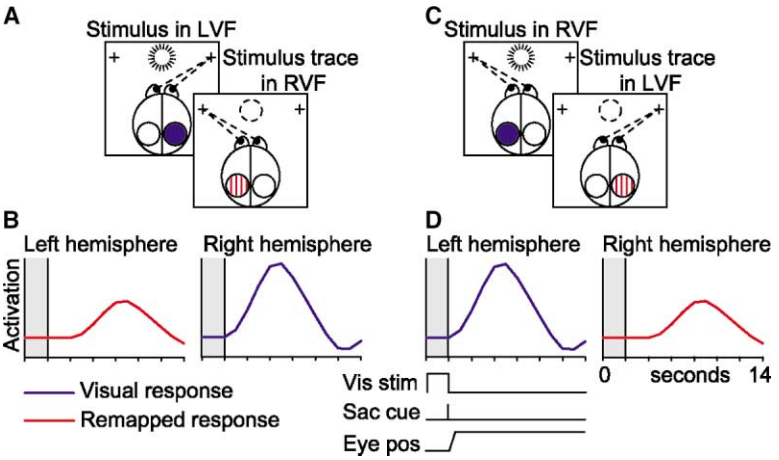

Figure 1. fMRI Paradigm and Predicted Results

(A) Sequence of events in the spatial updating condition. The stimulus appears in the left visual field at the beginning of the trial and remains on the screen for 2 s. We expected the stimulus to activate right hemisphere occipital and parietal cortex (blue circle). Simultaneously, the stimulus disappears and a tone cues the subject to make a leftward eye movement. This saccade brings the screen location of the now-extinguished stimulus (dotted circle) into the right visual field. We predicted that remapping of the stimulus trace would cause activation to shift from the right to the left hemisphere (red hatched circle).

(B) Predicted time course of activation. The shaded region indicates the time that the stimulus is on, and the vertical line at 2 s indicates the time of the auditory cue to make an eye movement. Activation in the right hemisphere, due to the stimulus, was expected to follow the standard hemodynamic time course (blue curve). Activation in the left hemisphere, due to the remapped stimulus trace, was expected to occur with a similar time course but shifted by 2 s because the cue to make an eye movement occurs 2 s after stimulus onset. We also expected the remapped response to be smaller in amplitude than the visual response.

(C and D) The spatial updating condition and predicted results on trials in which the stimulus appears in the right visual field and is followed by a rightward eye movement. Note that the expected pattern of activation is a mirror reflection of that described in (A) and (B). In this and all subsequent figures, shades of blue represent visual responses and shades of red represent remapped responses.

Results

Eye Movement Analysis

To ensure that subjects performed the updating task accurately, we tested subjects outside the scanner and measured their eye position. Three issues were addressed by this test. First, it was important that subjects be able to maintain fixation while the stimulus flashed in the periphery. We tested subjects on either 36 or 72 trials, as in the scanned experiment. We calculated the mean and standard deviation of the eye position over all trials from all subjects (Figure 2A). There was no deviation in gaze caused by the presence of the stimulus. This assured us that the physical stimulus did not enter the opposite hemifield. Second, it was crucial that subjects made an eye movement at the appropriate time in response to the auditory cue. Average saccade latency was 279 $\pm$ 85 ms relative to the auditory cue. Subjects never made a saccade prior to the auditory cue. Third, it was important that subjects be able to fixate after the eye movement for the remainder of the trial. As is shown in Figure 2A, subjects maintained gaze after the saccade.

In order to quantify these data, we divided the task into three epochs, each lasting 2 s: a "prestimulus" epoch consisted of the period prior to the onset of the visual stimulus; a "stimulus" epoch consisted of the period in which the stimulus was present, and a "postsaccade" epoch consisted of the 2 s period beginning 1 s after the auditory cue to make the saccade. Figure 3B shows that there was no difference in eye position between the prestimulus and stimulus epochs, indicating that subjects were able to maintain accurate fixation despite the presence of the peripheral stimulus. We also tested the amount of eye position jitter (the standard deviation of eye position across each epoch). While there was slightly more jitter in the stimulus epoch (Figure 3C), this difference was not significant [$t(318) = 1.54$, n.s.]. These data indicate that subjects were able to perform this simple oculomotor task with a high degree of spatial and temporal accuracy.

Parietal Voxels Respond to Visual Stimuli and Updated Stimulus Traces

We found evidence for remapping in the form of strong and consistent activation in the ipsilateral parietal lobe during the spatial updating task. We used anatomical criteria to define the borders of regions of interest (ROIs)

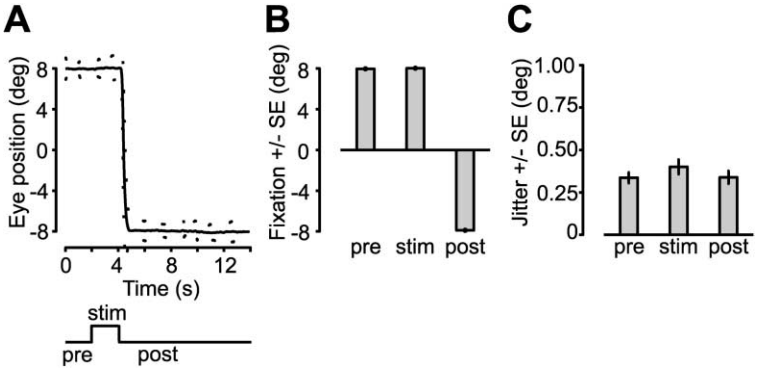

Figure 2. Eye Position

(A) Horizontal eye position over time averaged across all 450 trials from eight subjects. The dotted line indicates $\pm$1 SD. Traces from leftward eye movement were flipped and averaged with traces from rightward eye movements.

(B) Mean eye position during each epoch averaged across all trials and subjects.

(C) Mean jitter from the fixation point during each epoch averaged across all trials and subjects. Error bars indicate 1 SEM in (B) and (C).

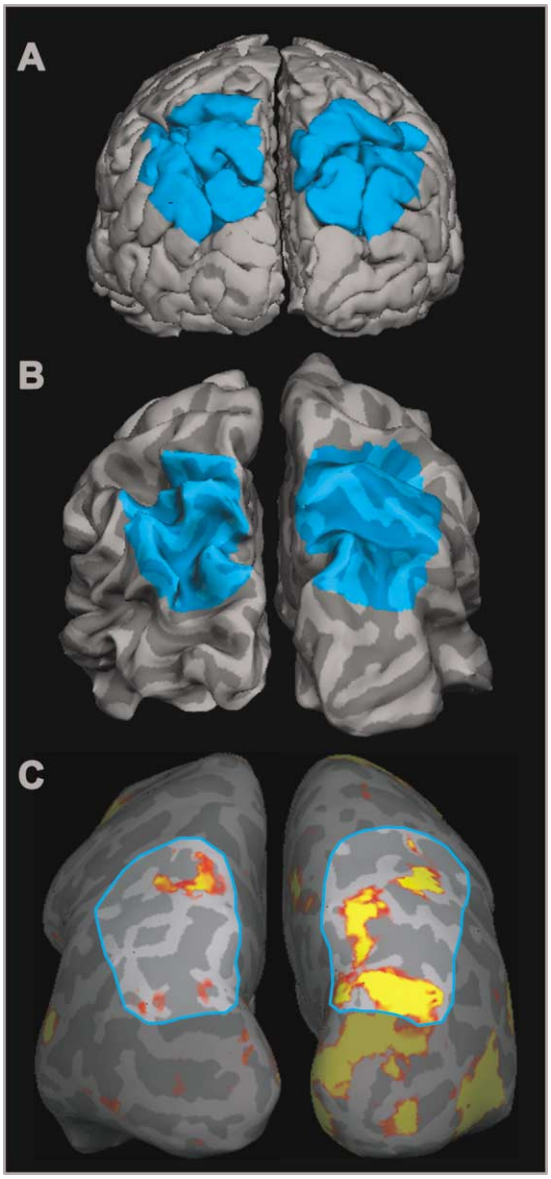

Figure 3. Region of Interest in Parietal Cortex

(A) Posterior view of both hemispheres of a single subject rendered at the outermost layer of gray matter. The regions of interest are shown in blue.

(B) Partially unfolded view of the same two hemispheres. Blue shading indicates the location of the ROI. Shades of gray indicate the curvature of the cortical surface: dark gray indicates concave areas, and light gray indicates convex areas.

(C) Activation from a single subject on updating trials in which a left visual field stimulus was followed by a leftward saccade. This condition elicited activation in contralateral (right) hemisphere occipital and parietal areas, as expected. Activation was also observed in the ipsilateral (left) parietal lobe, indicating that the visually evoked activation was remapped in conjunction with the eye movement.

that included the intraparietal sulcus and adjacent gyral cortex (Figures 3A and 3B; see Experimental Procedures). Within this ROI, we selected voxels for inclusion in our analysis if there was a significant response in at least one of the six types of trials: trials of the stimulus-only condition in which the stimulus appeared in the (1) contralateral or (2) ipsilateral visual field; trials of the saccade-only condition in which subjects made (3) contraversive or (4) ipsiversive saccades; and trials of the spatial updating condition in which the stimulus location was remapped to the (5) contralateral or (6) ipsilateral visual field. A large population of task-related voxels was identified in each of the 16 hemispheres tested. Figure 3C shows activation in a single subject on trials of the spatial updating condition in which the stimulus appeared in the left visual field and was followed by a leftward saccade. The left visual field stimulus resulted in strong visual responses in the right hemisphere. The leftward eye movement brought the stimulus location into the right visual field, resulting in remapped responses in left parietal cortex.

We illustrate our main results with data from a single subject that showed responses typical of the group (Figure 4). In a given hemisphere, we measured visual responses on trials of the spatial updating condition in which the stimulus appeared in the contralateral visual field and was then followed by a contraversive saccade. In the example illustrated in Figure 4A, visual responses (blue) were measured in the left hemisphere (left panel) on trials in which the stimulus appeared in the right visual field and was followed by a rightward saccade. The visual stimulus elicited a large, biphasic response: the signal first rose to a peak of $\sim$1% above baseline at 6 s after the onset of the stimulus. The response then quickly dipped to $\sim$0.5% below baseline at around 10 s poststimulus. The shape and magnitude of the visual response correspond well with previous reports of BOLD activation evoked by contralateral visual stimuli (Boynton et al., 1996).

The updating task was designed so that this initial visual response would be followed about 2 s later by a remapped response in the opposite hemisphere. We measured remapped responses on trials of the spatial updating condition in which an ipsilateral stimulus was followed by an ipsiversive saccade. In the example illustrated in Figure 4, remapped responses (red) were measured in the left hemisphere (left panel) on trials in which the stimulus appeared in the left visual field and was followed by a leftward saccade. Remapped responses differed from visual responses in several respects. In this example, the remapped responses had later rise times than the visual responses, as expected. The remapped responses shown here also had lower peak amplitudes and slower returns to baseline. The BOLD-image raster plots indicate that these remapped responses were both present and robust throughout the course of the scanning session (Figures 4B and 4C).

A similar pattern of activation was present in all 16 hemispheres (Figure 5). We observed strong visual responses to stimuli in the contralateral hemifield in every hemisphere. We also observed consistent remapped responses. The response curves in Figure 5 are the average of all task-related voxels in each hemisphere. We used a partial F test to assess the significance of both response types for each voxel independently (see Experimental Procedures). We converted the F values to Z scores and represented the distribution of Z scores in each hemisphere in a boxplot (Figure 6). Z scores associated with the visual responses (blue boxes) exceeded the significance threshold ($p < 0.05$; horizontal

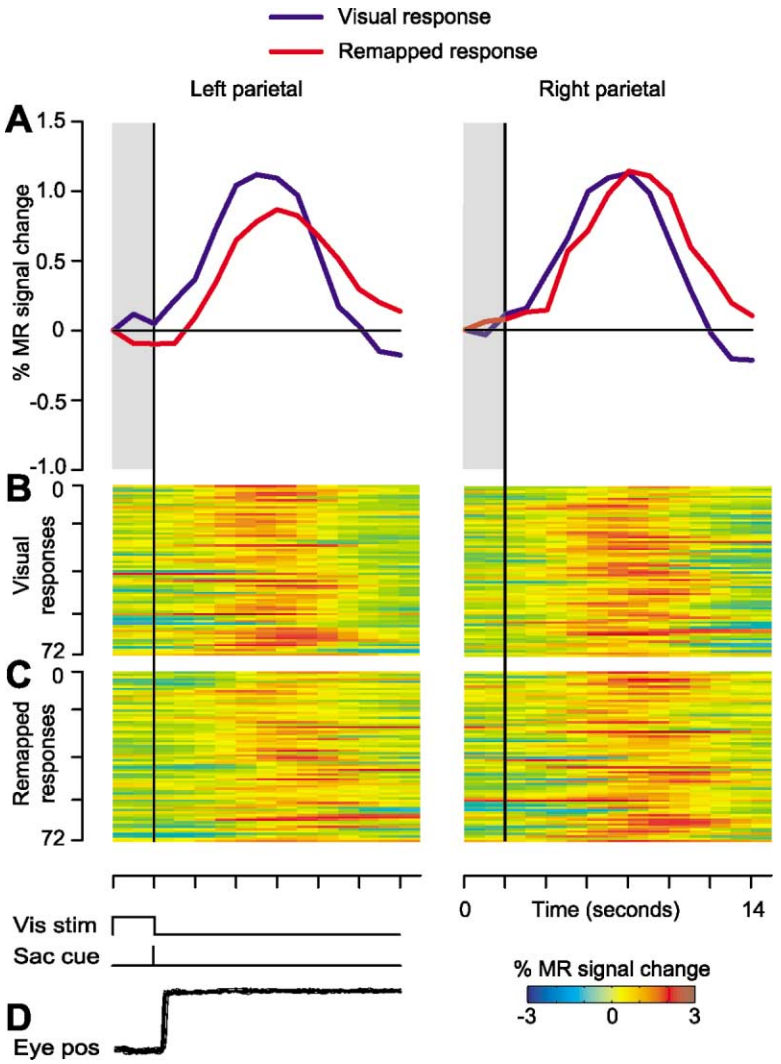

Figure 4. Visual and Remapped Responses from Each Hemisphere of a Single Subject

(A) Time course of activation evoked by the visual and remapped responses from parietal cortex. The MR time course over the 15 s task epoch represents the average of 72 trials from 49 voxels in the left hemisphere and 33 voxels in the right hemisphere. The shaded gray bar indicates when the stimulus was present, and the vertical line at 2 s shows the time of the auditory cue to make a saccade. The remapped response (red line) occurs later and is smaller than the visual response (blue line).

(B) BOLD-image raster plots of the visual responses from the same hemispheres for 72 successive trials. Activation on individual trials is plotted along the *y* axis, with percent signal change represented in pseudocolor plotted over time (*x* axis).

(C) BOLD-image raster plots of the remapped responses for 72 successive trials.

(D) Eye position recorded in 36 trials of the same task performed outside the scanner.

dotted line) in virtually every individual task-related voxel in every hemisphere. A smaller proportion of voxels had a significant remapped response (red boxes). In two hemispheres, the median Z score for the remapped responses fell below the statistical threshold of $p = 0.05$. We excluded these two hemispheres from subsequent analyses.

The data shown in Figures 4 and 5 indicate that the remapped responses were typically smaller than the visual responses. To compare response amplitudes directly, we calculated the amplitude of both response types by taking the difference between the minimum and the maximum of the response curve (Figure 7). We then subtracted the remapped response amplitudes from the visual response amplitudes. Large values indicate an amplitude difference between response types; a value of zero indicates no difference. The 95% confidence interval of the median was greater than zero in 8 out of 14 hemispheres, indicating that there was a significant amplitude difference in just over half of the hemispheres (Figure 7A, filled dots). A t test on the median values from each hemisphere revealed that the difference, while small, was significant across the population [$t(13) = 3.96$, $p < 0.01$].

We interpret the existence of remapped responses as evidence of a spatial updating signal in human parietal cortex. In the following sections, we rule out two alternate explanations for these results. First, we show that the remapped responses are not due to the ipsiversive eye movements per se. Second, we demonstrate that remapped responses cannot be attributed to the retinal impact of the stimulus in the ipsilateral visual field.

Saccades Alone Do Not Account for the Remapped Responses

One possible explanation of the present results is that saccades by themselves activate ipsilateral parietal cortex. To rule out this possibility, we tested all subjects on a saccade-only condition that was identical to the spatial updating condition in terms of oculomotor requirements. However, in the saccade-only condition, no stimulus appeared before the eye movement. Remapped responses were larger than the responses to ipsiversive saccades in this control condition (Figure

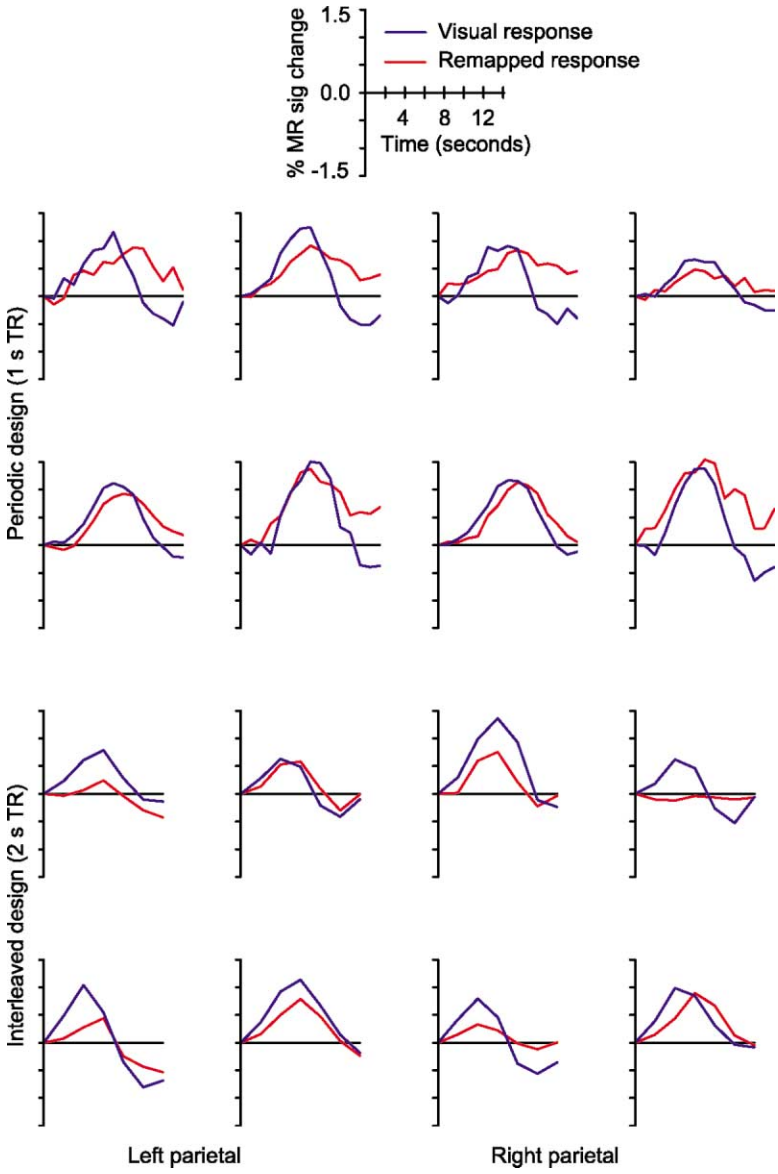

Figure 5. Visual and Remapped Responses from All 16 Hemispheres

Time course of activation evoked by the visual and remapped responses averaged over all task-related voxels in each of 16 hemispheres. Same format as in Figure 3.

7B). This difference was significant across the population of 14 hemispheres [$t(13) = 5.44$, $p < 0.001$]. A within-hemisphere analysis revealed that this difference was also significant in 11 out of the 14 individual hemispheres (Figure 7B, filled circles).

Ipsilateral Stimuli Alone Do Not Account for the Remapped Responses

A second possible explanation of the present results is that visual stimuli activate ipsilateral parietal cortex directly. To rule out this possibility, we tested all subjects on a stimulus-only condition that was identical to the spatial updating condition in terms of retinal input but that did not require an eye movement. Remapped responses were larger than responses to ipsilateral stimuli (Figure 7C). This difference was significant across the population of 14 hemispheres [$t(13) = 5.44$, $p < 0.001$]. A within-hemisphere analysis revealed that this difference was also significant in 11 out of the 14 hemispheres (Figure 7C, filled circles).

Remapped Responses Occur Later than the Visual Responses

The timing of the remapped responses also indicates that they were not caused directly by the ipsilateral stimuli. The time series plots in Figures 3 and 4 show that the remapped responses occur later than the visual responses, which would not have been the case if they had been elicited by the stimulus itself. We used Fourier analysis to estimate the temporal shift between the visual and remapped responses in the eight hemispheres that were tested using a periodic design (Figure 8). We first applied a Fast Fourier Transform (FFT) to the time series from each voxel. We then plotted the phase and magnitude of the FFT at the task frequency (1/15 s) in polar coordinates (Figures 8A and 8B). Each voxel is

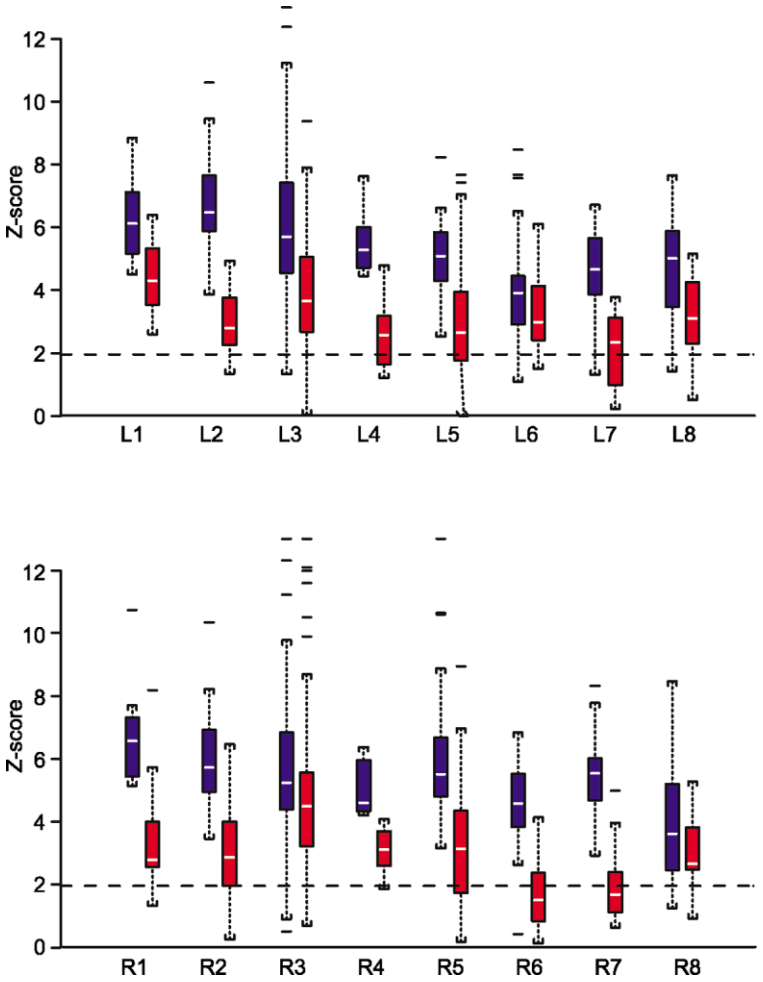

Figure 6. Significance of the Visual and Remapped Responses

Boxplots of Z scores representing the significance of visual and remapped responses for left (L1–L8) and right (R1–R8) hemispheres. For each box, the white horizontal line indicates the median Z score for the hemisphere. The top and bottom of the box indicate the first and third quartile. The vertical lines ("whiskers") above and below the box indicate the upper and lower range of the data for that hemisphere, and the floating horizontal bars indicate outliers. The response in a given hemisphere was significant if the median exceeded the statistical threshold ($p = 0.05$; indicated by dotted horizontal line). All 16 hemispheres had a significant visual response, with the first quartile of voxels falling well above the significance threshold (blue boxes). In each hemisphere, the remapped response was associated with smaller Z scores (red boxes). The median remapped response was not significant in two hemispheres.

plotted twice: once for the signal elicited by the visual stimulus, and again for the signal elicited by the updated stimulus trace. The polar plot of voxels from the left hemisphere of a single subject reveals a clear segregation in phase based on response type (Figure 8A). The visual responses cluster in quadrant II, while the remapped responses cluster in quadrant III, indicating a phase shift across the population of voxels. A similar pattern was observed when voxels from all eight hemispheres were pooled together (Figure 8B).

This Fourier analysis shows that voxels in parietal cortex exhibit a remapped response that occurs later

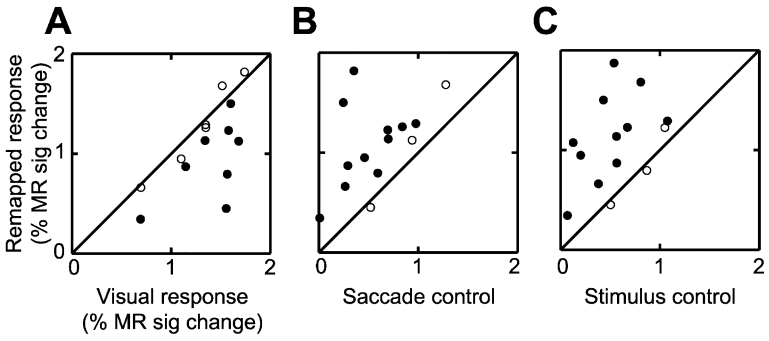

Figure 7. Comparison of Remapped Responses with Control Conditions

(A) Amplitude of the remapped responses (*y* axis) compared with responses to contralateral stimuli (*x* axis) for the 14 hemispheres that had significant remapped responses. Each dot represents the median response amplitude from a single hemisphere. Filled dots indicate that the 95% confidence limits of the median response for a single hemisphere did not intersect the unity line, indicating a significant effect across the population of voxels in that hemisphere. Contralateral stimuli elicited a larger MR response than the updated trace of the stimulus in 8 out of 14 hemispheres. A t test on the medians confirmed that the visual responses were consistently larger than the remapped responses across hemispheres [$t(13) = 3.96$, $p < 0.01$].

(B) The remapped responses were significantly larger than the responses elicited by ipsiversive eye movements in the saccade alone control condition in 11 out 14 hemispheres. This difference was significant across the group of 14 hemispheres [$t(13) = 5.44$, $p < 0.001$].

(C) The remapped response was significantly larger than the response in the stimulus alone control condition in 11 out of 14 hemispheres. This difference was significant across the group of 14 hemispheres [$t(13) = 5.44$, $p < 0.001$]. All amplitude values represent the maximum percent MR signal change minus the minimum.

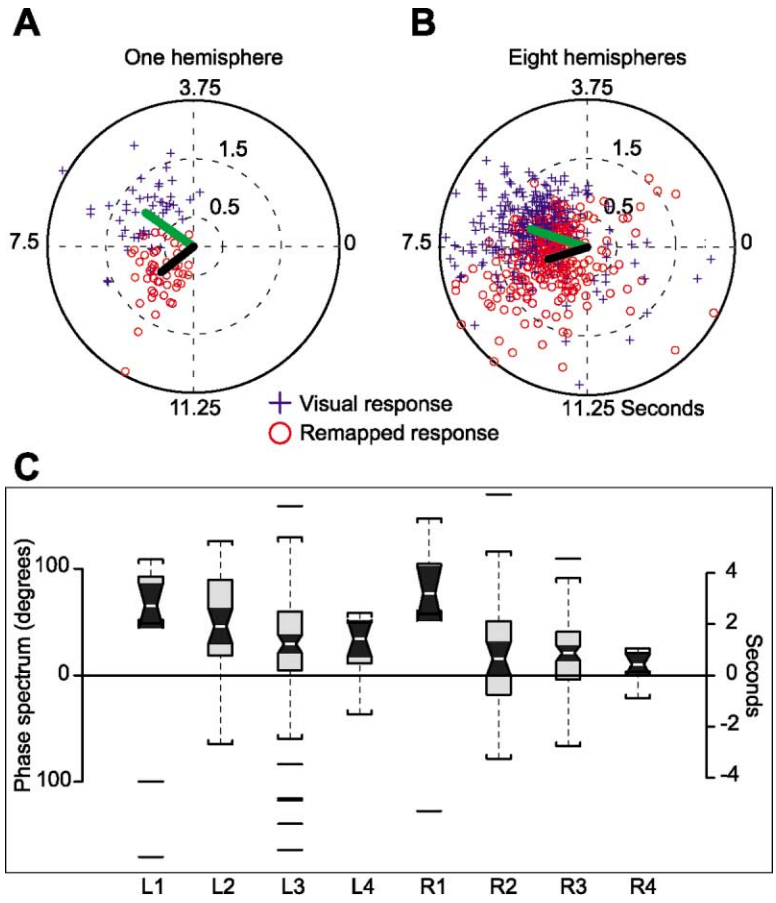

Figure 8. Fourier Analysis of Visual and Remapped Responses

(A) The magnitude (ρ) and phase (θ) of the FFT at the task frequency are plotted in polar coordinates for a single subject. The vertical and horizontal dotted lines indicate 0, 3.75, 7.5, and 11.25 s. Each voxel is plotted twice: once for the visual response (blue, +), and again for the remapped response (red, ○). The average vectors for the two response types are shown as green and black solid lines. The magnitudes of the visual responses were normalized to 1; the dotted circles represent magnitude values proportional to the average magnitude of the visual responses. Remapped responses tended to have later phases and smaller magnitudes than the visual responses.

(B) Phase and magnitude of all voxels from all eight hemispheres scanned using a periodic design.

(C) Boxplot of phase spectra representing the difference in time between the visual and remapped responses for eight hemispheres. Phase is represented on the *y* axis in both degrees (left) and seconds (right). For each box, the white horizontal lines indicate the median phase. The notched black region around the median indicates the 95% confidence limits for the median. The bottom of the lower gray portion of the box indicates the first quartile; the top of the upper gray portion of the box indicates the third quartile. The vertical lines ("whiskers") above and below the box indicate the upper and lower range of the data for that hemisphere, and the floating horizontal bars indicate outlier voxels. The notched black region is above the zero line in each hemisphere, indicating a significant phase shift between the visual and remapped responses across the population of voxels.

than the visual response in the same voxels. To test the significance of this observation, we calculated the phase spectrum of the visual and remapped responses. The distribution of phase spectra across all voxels and hemispheres is summarized in a boxplot in Figure 8C. Large phase spectrum values indicate a large difference in the time of the responses. We calculated a 95% confidence interval of the median phase spectra value in each hemisphere. In each case, the 95% confidence interval was greater than zero, indicating a significance phase shift between the two signals.

Discussion

We found that visual information is updated in human parietal cortex when the eyes move. Stimulus evoked activation in one hemisphere is remapped to the opposite hemisphere. This activation is a response to the trace of the stimulus at a particular spatial location. The stimulus had already disappeared by the time the eye movement was cued, so it could not be a direct visual response. This response to the stimulus trace indicates that neurons in human parietal cortex maintain a representation of space that is dynamically updated in conjunction with eye movements.

We were able to rule out several alternative explanations for our findings. First, remapped responses were not due to the ipsiversive eye movements per se. Some neurons in monkey LIP fire when a saccade is made toward the visual receptive field, which is almost always located in contralateral space (Colby et al., 1996). As expected from these single-unit data, human parietal cortex is also activated by saccades to contralateral targets (Sereno et al., 2001). While these and other studies suggest that parietal cortex should not be activated by ipsiversive eye movements, it was important to consider the possibility. The saccade-only condition was thus crucial in demonstrating that the remapped responses we observed were not due to a motor response associated with the saccade itself.

Second, remapped responses were not due to direct visual stimulation. Neurons in monkey area LIP have large, contralateral receptive fields that increase in size with eccentricity from the fovea (Barash et al., 1991; Ben Hamed et al., 2001). Some LIP neurons have receptive fields near the fovea, and a subset of these neurons have receptive fields that extend across the vertical meridian. The representation of the ipsilateral visual field is not extensive in LIP, but some cells do respond to stimuli located as far as 5° in the ipsilateral visual field. Human

imaging studies have reported both positive and negative activations in early visual areas in response to ipsilateral, contrast-modulated checkerboard stimuli (Tootell et al., 1998), and it is possible that these ipsilateral responses might extend into parietal cortex. Nonetheless, ipsilateral responses were not observed in our stimulus-only condition. Moreover, the stimuli in our experiment were located far from the fovea (~8°) along the horizontal meridian, decreasing the likelihood of activating receptive fields in ipsilateral cortex. Finally, the remapped responses were time locked to the eye movement, not the onset of the visual stimulus. If the remapped responses were in fact retinal in origin, they would have been concurrent with the visual responses.

The third alternate explanation that we considered was whether the remapped responses might be related to the auditory stimulus that was the instruction cue to initiate a saccade. A small number of cells in monkey LIP respond to auditory stimuli if the monkey has been trained to make saccades to a spatial location cued by an auditory stimulus (Grunewald et al., 1999; Linden et al., 1999; Mazzoni et al., 1996). In our experiment, a tone cued subjects to initiate an eye movement, but the saccade itself was directed toward a stable visual target. While it is possible that the tone activated parietal cortex, it was not the source of the responses we observed. The saccade-only condition also involved making eye movements in response to the same auditory stimuli, yet we did not observe the same pattern of activation in that condition. Furthermore, the auditory stimulus was presented binaurally, so we would not have observed the temporal shift between the visual and remapped responses had the auditory stimulus itself driven the activation in parietal cortex.

Cognitive Factors and Spatial Updating

We considered the degree to which the remapped responses might be related to cognitive factors, such as anticipation, attention, and memory. Half of the subjects were scanned using a randomized interleaved design that prevented the subjects from predicting which condition would be tested on upcoming trials, and from anticipating when the next trial would occur. This experimental design helped ensure that additional variables, such as anticipation, were equally present in the both the experimental and control conditions.

Spatial updating and attention are fundamentally similar phenomena at the neuronal level. The spatial response properties of LIP neurons change when the eyes move, and can do so in advance of the eye movement (Duhamel et al., 1992a). This predictive remapping follows the same time course as the behaviorally measured attention shift that occurs prior to eye movements (Hikosaka et al., 1996; Kowler et al., 1995). Remapping of receptive fields may thus be a neural instantiation of an attention shift. However, as shown by single-unit recording studies, an attention shift by itself is not sufficient to induce remapping (Colby, 1996; Duhamel et al., 1992a). The attention shift that occurs prior to the saccade must by followed by an actual eye movement, or remapping does not occur. This is evident in our experiment because remapped responses did not occur in the stimulus-only condition, which had the same attention demands, but did not require an actual eye movement.

We also considered the relationship between spatial working memory and the parietal activation we observed. At the beginning of the trial, the stimulus activates a set of neurons that maintain a representation of the stimulus location. At the time of the eye movement, those neurons transfer their information to a second set of neurons that represent the new retinotopic location of the stimulus. This updating involves memory since the neurons are responding to a stimulus that is no longer physically present. Many previous imaging studies have reported frontal, parietal, and extrastriate activation in tasks that involve the active maintenance of spatial information (Berman and Colby, 2002; Courtney et al., 1998; Heide et al., 2001; Sereno et al., 2001; Sweeney et al., 1996). Two studies in particular have demonstrated the importance of memory-related activation in parietal cortex during eye movements. Heide et al. (2001) found preferential activation in parietal cortex when subjects performed memorized sequences of eye movements, and Sereno et al. (2001) demonstrated a spatial map in parietal cortex when subjects made memory-guided saccades to retinotopic targets. These studies indicate that memory traces exist in human parietal cortex, in accord with the present findings.

Comparison with Single-Unit Physiology

In the present study, an eye movement brings a previously stimulated screen location into the opposite visual field. In single-unit studies in monkeys, the eye movement brings the spatial location of the vanished stimulus into the receptive field of the neuron being recorded. Both cases are demonstrations of a spatially specific response in the absence of direct visual stimulation.

The results from our study suggest functional similarities between monkey and human parietal cortex. The physiological response properties of spatial updating were comparable in two important ways. First, in our study, both the visual and remapped responses occurred at about the same time relative to the hypothesized arrival of visual information in cortex. In the updating condition, the visual stimulus appeared 2 s prior to the cue to make an eye movement. The remapped response was therefore shifted in time relative to the visual response, reflecting the period between the onset of the visual stimulus and the cue to make an eye movement. In monkeys, neurons exhibit a remapped response that occurs coincident with or even before the eye movement (Duhamel et al., 1992a; Nakamura and Colby, 2002; Umeno and Goldberg, 1997). We found that some voxels responded earlier than the time predicted by the cue to make the eye movement. Early neuronal activity may reflect a predictive response that allows the brain to represent the updated location before the end of the saccade.

Second, we found that the remapped response was smaller in magnitude than the visual response. This finding is consistent with physiological studies in monkeys in which cells have remapped responses that are on average half as large as the responses to stimuli in the receptive field (Duhamel et al., 1992a). These similarities

suggest that the mechanisms governing remapping may be similar in humans and monkeys.

Functional Areas in Human and Monkey Parietal Cortex

Monkey parietal cortex contains multiple functionally and anatomically defined areas (Colby and Duhamel, 1991). Whether human parietal cortex is divided into a similar set of regions is unknown (for review, see Culham and Kanwisher, 2001). Two interrelated issues regarding parietal organization are currently under debate. The first issue is the degree of functional specialization within parietal cortex. Some studies have reported overlapping regions of parietal activation in tasks with very different cognitive and behavioral requirements, emphasizing the generality of function in human parietal cortex (Wojciulik and Kanwisher, 1999). Other studies have identified multiple, functionally specialized zones within the parietal lobe. For example, a large region in inferior parietal cortex is activated by tasks involving language processing and abstract numerical calculation, while other regions in superior parietal cortex are activated by eye movements, attention, and manual grasping (Corbetta and Shulman, 2002; Simon et al., 2002). Conjunction paradigms (Price and Friston, 1997) have been a successful strategy for identifying functionally specialized cortical zones in the midst of diffuse patterns of activation. In parietal cortex, Bremmer et al. (2001) measured responses to auditory, visual, and somatosensory motion. Large regions are activated by each of these types of stimuli, but only a circumscribed region responds to all three. Similarly, large regions in parietal cortex respond to objects presented in either the visual or tactile modalities, but only a small region is activated by both (Grefkes et al., 2002).

A second important issue regarding parietal cortex relates to the correspondence between areas in monkeys and humans. Numerous distinct areas have been identified along the intraparietal sulcus in monkeys in anatomical and physiological studies (Andersen et al., 1990; Colby and Duhamel, 1991; Colby et al., 1988; Maunsell and van Essen, 1983). Several authors have now used fMRI to identify functionally similar regions in parietal cortex of humans and monkeys, and some of these areas are found in the same relative positions in both species. For instance, the parietal motion area in humans, identified by Bremmer et al. (2001), is restricted to the ventral portion of the IPS. They concluded that this region is the human equivalent of the ventral intraparietal area (VIP) in monkeys, an area defined by its location and by its responses to visual and somatosensory motion stimuli (Colby et al., 1993; Duhamel et al., 1998). Likewise, the bimodal object identification region identified in humans by Grefkes and colleagues (Grefkes et al., 2002) is located anteriorly in the sulcus. Its location and response properties thus correspond well with those of the anterior intraparietal area (AIP) described in the monkey (Sakata et al., 1995).

The location of the lateral intraparietal area (LIP) in humans is a matter of much current interest. Parietal cortex is activated when subjects make saccadic and smooth pursuit eye movements (Berman et al., 1999; Corbetta et al., 1998; Luna et al., 1998; Petit and Haxby, 1999). It is also strongly activated when subjects make saccades to remembered targets (Sweeney et al., 1996). A recent study found two foci of activation near the intraparietal sulcus that encode remembered saccade targets in retinotopic coordinates (Sereno et al., 2001). One of these regions is located near the middle part of the intraparietal sulcus, at the junction of the superior and inferior branches. The other region is located posteriorly at the base of the sulcus. While further studies are needed to establish the complete set of parietal areas in humans and nonhuman primates (Press et al., 2001; Van Essen et al., 2001), the emerging picture is one of a similar anatomical and physiological organization across species.

The goal of the present study was to demonstrate and characterize updating of visual information in human cortex. Our approach differs considerably from that of the localization studies described above. We asked whether voxels in the intraparietal sulcus exhibit response properties that are similar to those of single neurons recorded in parietal cortex in behaving primates. We did this without restricting our analysis by means of a conjunction paradigm. Rather, we began with a large anatomically defined ROI and included voxels that responded in any one of our task conditions (visual, saccade, or spatial updating). Once we identified task-related voxels, we performed a series of analyses on the entire population. This approach allowed us to demonstrate the existence of physiological responses to remapping in humans. The cortical region analyzed in this study likely includes both the anterior and posterior maps described by Sereno et al. (2001). This region presumably includes both the human homolog of area LIP and additional extrastriate and parietal visual areas as well. Further studies will be needed to identify the specific regions in which remapping is localized and their correspondence to parietal areas in the monkey.

Experimental Procedures

Stimuli and Task Conditions

Subjects were scanned during three experimental conditions. (1) In the spatial updating condition, subjects fixated one of two stable crosses located at $+8^\circ$ and -8°. A flickering stimulus appeared at the center of the display screen. The stimulus was a white spot, the size and flicker frequency of which changed randomly (ranging from 0° to 2°, and 6 to 10 Hz). The stimulus fell in either the right or left visual hemifield ($\pm 8^\circ$) and remained on the screen for 2 s. At the time of stimulus offset, a binaurally presented tone cued the subject to make a saccade to the fixation cross located on the opposite side of the screen. This eye movement caused the screen location where the stimulus had appeared to enter the opposite visual hemifield. There were two types of trials in the spatial updating condition: trials in which the stimulus appeared in the right visual field and was followed by a rightward saccade, and trials in which the stimulus appeared in the left visual field and was followed by a leftward saccade.

(2) In the stimulus-only condition, the subject maintained fixation on either the right or left cross, and the stimulus appeared for 2 s at the center of the screen. There were two types of trials in the stimulus-only condition: trials in which the stimulus appeared in the right visual field, and trials in which the stimulus appeared in the left visual field.

(3) In the saccade-only condition, the subject made saccades to stable crosses when prompted by a binaurally presented auditory cue, but no visual stimulus appeared on the screen. There were two types of trials in the saccade-only condition: trials in which subjects

made a rightward saccade, and trials in which subjects made a leftward saccade.

Visual and auditory stimuli were presented using CORTEX software (http://www.cortex.salk.edu/) running on a PC. Visual stimuli were back projected onto a Lucite screen using a 3-panel LCD projector. Auditory stimuli were presented using pneumatic headphones.

Experimental Design

The particular ordering and spacing of trials in fMRI experiments is known to have a profound impact on both the nature of the evoked MR response and the analysis methods used to analyze the data (Aguirre and D'Esposito, 2000). There are costs and benefits associated with different design options. We used two different experimental designs to enhance our ability to detect remapped response, to control cognitive factors, and to estimate the fine temporal aspects of the responses.

Theoretical work indicates that randomization of both trial order and interstimulus interval enhances the ability to estimate the shape of the MR response (Birn et al., 2002; Liu et al., 2001). We tested half of the subjects ($n = 4$) using a randomized design in which three conditions occurred in an interleaved fashion. On a given trial, subjects either viewed a peripheral stimulus while maintaining fixation (stimulus-only condition), or made an eye movement in the absence of a stimulus (saccade-only condition), or made an eye movement after the stimulus disappeared (updating condition). We randomized both the trial order and the interstimulus interval within the ordering constraints of the task (e.g., subjects never performed two successive eye movements in the same direction). Within each 480 s run, subjects performed an average of eight trials of each condition and the interstimulus interval varied from 6 to 15 s. The interleaved design ensured that cognitive factors and motor preparation were held constant across the different conditions. This design also ensured that variables such as slow drifts in the MR signal and head motion were evenly distributed across task conditions. Our analysis allowed us to calculate an impulse-response function for each condition independently even though the MR responses overlapped in time.

It was also critical for our study to be able to detect small temporal differences between the visual and remapped responses. In periodic designs, the power of the signal is concentrated around the fundamental frequency of the task, rather than across the entire spectrum, as in randomized designs (Aguirre and D'Esposito, 2000). This type of design allows the use of Fourier analysis to estimate the time of the MR signal evoked by each response type (Saad et al., 2001; Sereno et al., 1995). Accordingly, we tested the other four subjects using a fixed interval, periodic design. Within each 551 s run, subjects fixated during the first 11 s. They then performed 36 trials. One trial occurred every 15 s. This task frequency confers optimal sensitivity for detecting brief events (Bandettini and Cox, 2000). In two control runs, subjects viewed a peripheral stimulus while maintaining fixation (stimulus-only condition). In another two control runs, subjects made eye movements in the absence of a stimulus (saccade-only condition). In an additional two to four runs, subjects made an eye movement after the stimulus disappeared (updating condition).

MR Data Collection

Eight right-handed subjects, ages 23–30, participated. All subjects had been scanned previously for other studies and were highly experienced in performing oculomotor tasks in an MR environment. The protocol for this study was approved by the IRB at the University of Pittsburgh and informed consent was obtained from all subjects. MR images were collected on a GE Signa 3 Tesla scanner. A high-resolution SPGR anatomical sequence was collected at the beginning of each scanning session (TR, 24 ms; flip angle, 30°; number of slices, 124; in-plane voxel dimensions, 0.98 × 0.98 mm; slice thickness, 1.0–1.5 mm depending on head size).

We used two different pulse sequences to collect BOLD-sensitive images. For subjects scanned using the interleaved design, we collected images using an echo-planer pulse sequence developed by GE (EPI-RT) with a 2000 ms time to repetition (TR) and a 30 ms echo time (TE). Twenty oblique slices (3.125 × 3.125 × 3.0 mm, with a 1 mm gap) covered the entire parietal lobe, as well as superior portions of the occipital lobe, and posterior portions of the frontal lobes. In each run, we collected 240 images per slice. Subjects were scanned for six to eight runs each, resulting in at least 28,800 images per subject. For subjects scanned using the periodic design, we used a locally developed spiral scanning sequence to achieve higher temporal resolution (TR = 1 s; TE = 18 ms). Eighteen oblique slices (3.125 × 3.125 × 3.0 mm, with no gap) were positioned to cover the entire parietal lobe. In each run, we collected 551 images per slice. Subjects were scanned for six to eight runs each, resulting in at least 59,508 images per subject. Subjects lay quietly in the dark for 1–2 min between runs and were instructed to keep their eyes closed.

Analysis of fMRI Data

Our approach to data analysis for both experiments involved three stages: (1) preprocessing and noise reduction; (2) voxel selection; and (3) response parameter estimation.

Preprocessing and Noise Reduction

The data were preprocessed using locally developed FIASCO software (Eddy et al., 1996) (available at http://www.stat.cmu.edu/~fiasco). Preprocessing steps included a correction for fluctuations in mean intensity; motion correction of the raw, complex-valued K space data; image reconstruction; linear detrending; and outlier correction using a Windsor filter. Outliers were defined as data points farther than ten times the interquartile range from the median. The image data were not spatially smoothed.

Voxel Selection: ROI Definition and Response Detection

The goal of this second stage of data analysis was to identify voxels that were candidates for exhibiting remapping activity. We used two criteria to select voxels. First, we applied anatomical criteria to define a region of interest in parietal cortex in each hemisphere. Second, we applied a functional criterion by selecting voxels that showed a significant response in at least one of the six conditions (contra- or ipsilateral visual stimuli, saccades, or spatial updating). Voxels that fulfilled these criteria were considered to be task related.

We drew anatomically defined regions-of-interest (ROIs) on the high-resolution structural scans from each hemisphere using tools included in the FreeSurfer software package (Dale et al., 1999; Fischl et al., 1999). ROIs included the entire extent of the intraparietal sulcus. The ROI extended anteriorly to the segment of the sulcus that joins the postcentral sulcus, and extended posteriorly toward the occipital lobe, stopping at the "T" junction formed by the IPS and the transverse occipital sulcus (Figures 3A and 3B). The ROI extended outside the sulcus to include the adjacent gyral surface, as well as both medial and lateral side branches. ROIs were then resampled to the resolution of the functional data. This method allowed us to define the ROIs using the detailed anatomical information from the structural scans without resampling or distorting the functional data in any way.

We used multiple regression to detect voxels that showed significant responses to any task condition. Multiple regression was performed using software from the AFNI analysis package (Cox, 1996) (http://afni.nimh.nih.gov/afni). The detailed methods for this procedure have been described elsewhere (Ward, 1998). In short, the regression model included a separate regressor to model the signal at each time point in a 14 s window following the start of each trial. Activation maps were created by using a partial F test that compared the variance accounted for by the regressor associated with each condition to the full model fit to the data. Activation maps were thresholded using a false discovery rate procedure that controls the rate of false positives while obviating the need for explicit correction for multiple comparisons (Genovese et al., 2002).

Response Parameter Estimation

Once we identified a population of task-related voxels in each hemisphere, we carried out several analyses aimed at describing the properties of the visual and remapped responses. Raw time series data were analyzed using custom software written in Matlab (MathWorks, Inc.) and in the "S" programming language implemented in S-Plus (MathSoft, Inc.).

We created BOLD-image raster plots (Duann et al., 2002) in order to display the variability of responses across trials (Figures 4B and 4C). Each line in the raster plot represents the response in a single trial, averaged over all task-related voxels in the ROI. Data were then converted to units of percent signal change by dividing by the mean. Each time point of the 15 s hemodynamic response was smoothed with a 2 s wide moving window. Data were not smoothed across trials. The time course data for each trial were represented as a series of horizontal bars, stacked sequentially in trial order, and pseudocolor coded for activation level. Conventional time series plots were created by averaging across the trials represented in the BOLD-image plots using the unsmoothed data (Figures 4A and 5).

We used the F values from the multiple regression analysis described above to determine the significance of the visual and remapped responses. We converted the F values to Z scores and then displayed the Z score values for each hemisphere using standard boxplots (Figure 6). The population response in a given hemisphere was considered significant if the median Z score exceeded a threshold of $p = 0.05$ (horizontal dotted line, Figure 6). We chose to use the median of the population because it is both interpretable and robust to outliers.

In order to compare the size of the remapped responses to the size of the other response types, we first calculated the minimum and maximum percent signal change in each voxel for each condition. We then created a single amplitude measure by calculating the difference between the minimum and maximum values. We compared the amplitudes of the remapped responses to the amplitudes of the visual responses, to the responses in the saccade-only condition, and to the responses in the stimulus-only condition (Figure 7). Comparisons were made for the same saccade direction and for the same stimulus location. We performed two analyses to determine the significance of the comparisons. In the first, within-hemisphere analysis, we subtracted the amplitudes elicited by the control conditions from the amplitudes elicited by the remapped responses. We then calculated the median and a 95% confidence interval of the median of these difference values. Within-hemisphere population comparisons were considered significant if the 95% confidence interval of the median did not intersect zero. In the second, cross-hemisphere analysis, the median amplitudes of the remapped responses in each hemisphere were plotted against the median amplitudes of the visual responses (Figure 7A), ipsiversive saccade responses (Figure 7B), and ipsiversive stimulus responses (Figure 7C). We used conventional t tests to test the significance of the comparisons across the population of hemispheres.

It was critical to measure the latency of the visual and remapped responses from the same population of voxels because response latency is known to vary considerably from voxel to voxel in the brain (Saad et al., 2001). Temporal variability appears to be substantial even within a given visual area. This variability likely arises from differences in vascular physiology rather than from neuronal sources, and highlights the importance of making within-voxel comparisons. To measure the latency of the response, we took the FFT of the time series from each voxel. We then extracted the phase at the fundamental frequency of the task (one trial every 15 s) from the unsmoothed periodogram. To illustrate the differences in phase between the two conditions, we made scatter plots of all voxels in the ROI in polar coordinates, simultaneously representing both the phase (θ) and the magnitude (ρ) of the response (Figures 8A and 8B). The phase spectrum is a good estimate of the phase difference between two time series (Brockwell and Davis, 1991). We calculated the phase spectrum of the two signals and performed a t test, comparing the phase spectra values of the population of voxels in each hemisphere to zero phase.

Eye Movement Recording

We monitored eye position with a video-based eye tracking system (ISCAN, Boston, MA) and analyzed the data using ILAB software (Gitelman, 2003) (http://groups.yahoo.com/group/ilab/). We used the saccade finder utilities in ILAB to detect saccades and calculate their latencies. A saccade was registered if eye velocity exceeded 40°/s and the eyes moved more than 1.5°. We recorded saccade latency by calculating the time when the eyes reached 15% of their maximal velocity.

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References

Aguirre, G.K., and D'Esposito, M. (2000). Experimental design for brain fMRI. In Functional MRI, C.T.W. Moonen, and P. A. Bandettini, eds. (Berlin: Springer), pp. 369–381.

Andersen, R.A., Asanuma, C., Essick, G., and Siegel, R.M. (1990). Corticocortical connections of anatomically and physiologically defined subdivisions within the inferior parietal lobule. J. Comp. Neurol. *296*, 65–113.

Baizer, J.S., and Bender, D.B. (1989). Comparison of saccadic eye movements in humans and macaques to single-step and double-step target movements. Vision Res. *29*, 485–495.

Bandettini, P.A., and Cox, R.W. (2000). Event-related fMRI contrast when using constant interstimulus interval: theory and experiment. Magn. Reson. Med. *43*, 540–548.

Barash, S., Bracewell, R.M., Fogassi, L., Gnadt, J.W., and Andersen, R.A. (1991). Saccade-related activity in the lateral intraparietal area. II. Spatial properties. J. Neurophysiol. *66*, 1109–1124.

Ben Hamed, S., Duhamel, J.R., Bremmer, F., and Graf, W. (2001). Representation of the visual field in the lateral intraparietal area of macaque monkeys: a quantitative receptive field analysis. Exp. Brain Res. *140*, 127–144.

Berman, R.A., and Colby, C.L. (2002). Spatial working memory in human extrastriate cortex. Physiol. Behav. *77*, 621–627.

Berman, R.A., Colby, C.L., Genovese, C.R., Voyvodic, J.T., Luna, B., Thulborn, K.R., and Sweeney, J.A. (1999). Cortical networks subserving pursuit and saccadic eye movements in humans: an FMRI study. Hum. Brain Mapp. *8*, 209–225.

Birn, R.M., Cox, R.W., and Bandettini, P.A. (2002). Detection versus estimation in event-related fMRI: choosing the optimal stimulus timing. Neuroimage *15*, 252–264.

Boynton, G.M., Engel, S.A., Glover, G.H., and Heeger, D.J. (1996). Linear systems analysis of functional magnetic resonance imaging in human V1. J. Neurosci. *16*, 4207–4221.

Bremmer, F., Schlack, A., Shah, N.J., Zafiris, O., Kubischik, M., Hoffmann, K., Zilles, K., and Fink, G.R. (2001). Polymodal motion processing in posterior parietal and premotor cortex: a human fMRI study strongly implies equivalencies between humans and monkeys. Neuron *29*, 287–296.

Brockwell, P.J., and Davis, R.A. (1991). Time Series: Theory and Methods, Second Edition (New York: Springer-Verlag).

Colby, C.L. (1996). A neurophysiological distinction between attention and intention. In Attention and Performance XVI: Information Integration in Perception and Communication, T. Inui, and J.L. McClelland, eds. (Cambridge, MA: The MIT Press), pp. 157–177.

Colby, C.L., and Duhamel, J.R. (1991). Heterogeneity of extrastriate visual areas and multiple parietal areas inthe macaque monkey. Neuropsychologia *29*, 517–537.

Colby, C.L., and Goldberg, M.E. (1999). Space and attention in parietal cortex. Annu. Rev. Neurosci. *22*, 319–349.

Colby, C.L., Duhamel, J.R., and Goldberg, M.E. (1993). Ventral intraparietal area of the macaque: anatomic location and visual response properties. J. Neurophysiol. *69*, 902–914.

Colby, C.L., Gattass, R., Olson, C.R., and Gross, C.G. (1988). Topographical organization of cortical afferents to extrastriate visual area

PO in the macaque: a dual tracer study. J. Comp. Neurol. *269*, 392–413.

Colby, C.L., Duhamel, J.R., and Goldberg, M.E. (1996). Visual, presaccadic, and cognitive activation of single neurons in monkey lateral intraparietal area. J. Neurophysiol. *76*, 2841–2852.

Corbetta, M., and Shulman, G.L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nat. Rev. Neurosci. *3*, 201–215.

Corbetta, M., Akbudak, E., Conturo, T.E., Snyder, A.Z., Ollinger, J.M., Drury, H.A., Linenweber, M.R., Petersen, S.E., Raichle, M.E., Van Essen, D.C., et al. (1998). A common network of functional areas for attention and eye movements. Neuron *21*, 761–773.

Courtney, S.M., Petit, L., Maisog, J.M., Ungerleider, L.G., and Haxby, J.V. (1998). An area specialized for spatial working memory in human frontal cortex. Science *279*, 1347–1351.

Cox, R.W. (1996). AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput. Biomed. Res. *29*, 162–173.

Culham, J.C., and Kanwisher, N.G. (2001). Neuroimaging of cognitive functions in human parietal cortex. Curr. Opin. Neurobiol. *11*, 157–163.

Dale, A.M., Fischl, B., and Sereno, M.I. (1999). Cortical surface-based analysis. I. Segmentation and surface reconstruction. Neuroimage *9*, 179–194.

DeYoe, E.A., Carman, G.J., Bandettini, P., Glickman, S., Wieser, J., Cox, R., Miller, D., and Neitz, J. (1996). Mapping striate and extrastriate visual areas in human cerebral cortex. Proc. Natl. Acad. Sci. USA *93*, 2382–2386.

Duann, J.R., Jung, T.P., Kuo, W.J., Yeh, T.C., Makeig, S., Hsieh, J.C., and Sejnowski, T.J. (2002). Single-trial variability in event-related BOLD signals. Neuroimage *15*, 823–835.

Duhamel, J.R., Colby, C.L., and Goldberg, M.E. (1992a). The updating of the representation of visual space in parietal cortex by intended eye movements. Science *255*, 90–92.

Duhamel, J.R., Goldberg, M.E., Fitzgibbon, E.J., Sirigu, A., and Grafman, J. (1992b). Saccadic dysmetria in a patient with a right frontoparietal lesion. The importance of corollary discharge for accurate spatial behaviour. Brain *115*, 1387–1402.

Duhamel, J.R., Colby, C.L., and Goldberg, M.E. (1998). Ventral intraparietal area of the macaque: congruent visual and somatic response properties. J. Neurophysiol. *79*, 126–136.

Eddy, W.F., Fitzgerald, M., and Noll, D.C. (1996). Improved image registration by using Fourier interpolation. Magn. Reson. Med. *36*, 923–931.

Engel, S.A., Glover, G.H., and Wandell, B.A. (1997). Retinotopic organization in human visual cortex and the spatial precision of functional MRI. Cereb. Cortex *7*, 181–192.

Fischl, B., Sereno, M.I., and Dale, A.M. (1999). Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system. Neuroimage *9*, 195–207.

Genovese, C.R., Lazar, N.A., and Nichols, T. (2002). Thresholding of statistical maps in functional neuroimaging using the false discovery rate. Neuroimage *15*, 870–878.

Gitelman, D. (2003). ILAB: a program for postexperimental eye movement analysis. Behav. Res. Methods Instrum. Comput. *34*, 605–612.

Goldberg, M.E., Colby, C.L., and Duhamel, J.R. (1990). Representation of visuomotor space in the parietal lobe of the monkey. Cold Spring Harb. Symp. Quant. Biol. *55*, 729–739.

Grefkes, C., Weiss, P.H., Zilles, K., and Fink, G.R. (2002). Crossmodal processing of object features in human anterior intraparietal cortex. An fMRI study implies equivalencies between humans and monkeys. Neuron *35*, 173–184.

Grunewald, A., Linden, J.F., and Andersen, R.A. (1999). Responses to auditory stimuli in macaque lateral intraparietal area. I. Effects of training. J. Neurophysiol. *82*, 330–342.

Hallett, P.E., and Lightstone, A.D. (1976). Saccadic eye movements to flashed targets. Vision Res. *16*, 107–114.

Heide, W., Blankenburg, M., Zimmermann, E., and Kompf, D. (1995). Cortical control of double-step saccades: implications for spatial orientation. Ann. Neurol. *38*, 739–748.

Heide, W., Binkofski, F., Seitz, R.J., Posse, S., Nitschke, M.F., Freund, H.J., and Kompf, D. (2001). Activation of frontoparietal cortices during memorized triple-step sequences of saccadic eye movements: an fMRI study. Eur. J. Neurosci. *13*, 1177–1189.

Hikosaka, O., Miyauchi, S., Takeichi, H., and Shimojo, S. (1996). Multimodal spatial attention visualized by motion illusion. In Attention and Performance XVI: Information Integration in Perception and Communication, T. Inui, and J.L. McClelland, eds. (Cambridge, MA: The MIT Press), pp. 237–262.

Kowler, E., Anderson, E., Dosher, B., and Blaser, E. (1995). The role of attention in the programming of saccades. Vision Res. *35*, 1897–1916.

Linden, J.F., Grunewald, A., and Andersen, R.A. (1999). Responses to auditory stimuli in macaque lateral intraparietal area. II. Behavioral modulation. J. Neurophysiol. *82*, 343–358.

Liu, T.T., Frank, L.R., Wong, E.C., and Buxton, R.B. (2001). Detection power, estimation efficiency, and predictability in event-related fMRI. Neuroimage *13*, 759–773.

Luna, B., Thulborn, K.R., Strojwas, M.H., McCurtain, B.J., Berman, R.A., Genovese, C.R., and Sweeney, J.A. (1998). Dorsal cortical regions subserving visually guided saccades in humans: an fMRI study. Cereb. Cortex *8*, 40–47.

Maunsell, J.H., and van Essen, D.C. (1983). The connections of the middle temporal visual area (MT) and their relationship to a cortical hierarchy in the macaque monkey. J. Neurosci. *3*, 2563–2586.

Mazzoni, P., Bracewell, R.M., Barash, S., and Andersen, R.A. (1996). Spatially tuned auditory responses in area LIP of macaques performing delayed memory saccades to acoustic targets. J. Neurophysiol. *75*, 1233–1241.

Nakamura, K., and Colby, C.L. (2002). Updating of the visual representation in monkey striate and extrastriate cortex during saccades. Proc. Natl. Acad. Sci. USA *99*, 4026–4031.

Petit, L., and Haxby, J.V. (1999). Functional anatomy of pursuit eye movements in humans as revealed by fMRI. J. Neurophysiol. *82*, 463–471.

Press, W.A., Brewer, A.A., Dougherty, R.F., Wade, A.R., and Wandell, B.A. (2001). Visual areas and spatial summation in human visual cortex. Vision Res. *41*, 1321–1332.

Price, C.J., and Friston, K.J. (1997). Cognitive conjunctions: a new experimental design for fMRI. Neuroimage *5*, 261–270.

Saad, Z.S., Ropella, K.M., Cox, R.W., and DeYoe, E.A. (2001). Analysis and use of FMRI response delays. Hum. Brain Mapp. *13*, 74–93.

Sakata, H., Taira, M., Murata, A., and Mine, S. (1995). Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. Cereb. Cortex *5*, 429–438.

Sereno, M.I., Dale, A.M., Reppas, J.B., Kwong, K.K., Belliveau, J.W., Brady, T.J., Rosen, B.R., and Tootell, R.B. (1995). Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. Science *268*, 889–893.

Sereno, M.I., Pitzalis, S., and Martinez, A. (2001). Mapping of contralateral space in retinotopic coordinates by a parietal cortical area in humans. Science *294*, 1350–1354.

Simon, O., Mangin, J.F., Cohen, L., Le Bihan, D., and Dehaene, S. (2002). Topographical layout of hand, eye, calculation, and language-related areas in the human parietal lobe. Neuron *33*, 475–487.

Sweeney, J.A., Mintun, M.A., Kwee, S., Wiseman, M.B., Brown, D.L., Rosenberg, D.R., and Carl, J.R. (1996). Positron emission tomography study of voluntary saccadic eye movements and spatial working memory. J. Neurophysiol. *75*, 454–468.

Tootell, R.B., Mendola, J.D., Hadjikhani, N.K., Liu, A.K., and Dale, A.M. (1998). The representation of the ipsilateral visual field in human cerebral cortex. Proc. Natl. Acad. Sci. USA *95*, 818–824.

Umeno, M.M., and Goldberg, M.E. (1997). Spatial processing in the monkey frontal eye field. I. Predictive visual responses. J. Neurophysiol. *78*, 1373–1383.

Van Essen, D.C., Lewis, J.W., Drury, H.A., Hadjikhani, N., Tootell, R.B., Bakircioglu, M., and Miller, M.I. (2001). Mapping visual cortex in monkeys and humans using surface-based atlases. Vision Res. *41*, 1359–1378.

Ward, B.D. (1998). Deconvolution analysis of fMRI time series data. Documentation for the AFNI software package. http://afni.nimh.nih.gov/afni/docps/3dDeconvolve.ps.

Wojciulik, E., and Kanwisher, N. (1999). The generality of parietal involvement in visual attention. Neuron *23*, 747–764.