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Dynamic Circuitry for Updating Spatial Representations. II. Physiological Evidence for Interhemispheric Transfer in Area LIP of the Split-Brain Macaque

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Heiser, Laura M., Rebecca A. Berman, Richard C. Saunders, and Carol L. Colby. Dynamic circuitry for updating spatial representations. *J Neurophysiol* 94: 3249–3258, 2005. First published May 11, 2005; doi:10.1152/jn.00029.2005. With each eye movement, a new image impinges on the retina, yet we do not notice any shift in visual perception. This perceptual stability indicates that the brain must be able to update visual representations to take our eye movements into account. Neurons in the lateral intraparietal area (LIP) update visual representations when the eyes move. The circuitry that supports these updated representations remains unknown, however. In this experiment, we asked whether the forebrain commissures are necessary for updating in area LIP when stimulus representations must be updated from one visual hemifield to the other. We addressed this question by recording from LIP neurons in split-brain monkeys during two conditions: stimulus traces were updated either across or within hemifields. Our expectation was that across-hemifield updating activity in LIP would be reduced or abolished after transection of the forebrain commissures. Our principal finding is that LIP neurons can update stimulus traces from one hemifield to the other even in the absence of the forebrain commissures. This finding provides the first evidence that representations in parietal cortex can be updated without the use of direct cortico-cortical links. The second main finding is that updating activity in LIP is modified in the split-brain monkey: across-hemifield signals are reduced in magnitude and delayed in onset compared with within-hemifield signals, which indicates that the pathways for across-hemifield updating are less effective in the absence of the forebrain commissures. Together these findings reveal a dynamic circuit that contributes to updating spatial representations.

INTRODUCTION

Visual perception reflects the active processing of both sensory and motor information. Each eye movement results in a new image on the retina, and the brain must dynamically integrate these images to yield a coherent perceptual experience. Single-unit recording studies in awake behaving monkeys have shown that neurons in parietal, frontal, and extrastriate cortex, as well as the superior colliculus, update the representations of spatial locations when the eyes move (Duhamel et al. 1992a; Goldberg and Bruce 1990; Nakamura and Colby 2002; Walker et al. 1995). These neurons respond to the memory trace of a stimulus location that has been updated in conjunction with the eye movement. This updating, or *remapping*, serves to maintain a representation of visual space in eye-centered coordinates: the location of a stimulus is always coded in terms of its distance and direction from the fovea

(Goldberg and Bruce 1990). The advantage of this representation is that salient locations are encoded in the coordinates needed to guide eye movements toward targets of interest.

One of the intriguing implications of remapping is that neurons must be able to receive information from far beyond the classical receptive field, and even from the opposite hemifield. In the original demonstration of remapping in the lateral intraparietal cortex (area LIP), Duhamel and colleagues (1992a) showed that stimulus representations could be updated from one visual hemifield to the other. This observation indicates that neurons in LIP have access to visual information from the opposite hemifield.

We hypothesized that direct cortico-cortical links, the forebrain commissures, provide the substrate for updating spatial representations of stimulus locations from one hemifield to the other. In the preceding study, we tested this hypothesis using behavioral methods. We measured the performance of two split-brain monkeys on a task that requires spatial updating. The monkeys performed two contrasting conditions, one that required across-hemifield updating and another that required within-hemifield updating. We found that the split-brain monkeys were selectively impaired on the across-hemifield condition in initial testing. Contrary to our expectation, however, we discovered that this impairment was not permanent: both split-brain monkeys were ultimately capable of performing the across-hemifield condition.

This unexpected behavioral observation led us to investigate neural signals in cortex and their relation to across-hemifield updating. In the present study, we focused on the activity of single neurons in parietal cortex, an area known to be critically involved in generating updated spatial representations (Duhamel et al. 1992b; Heide et al. 1995). In the normal animal, updating activity in area LIP reflects a transfer of stimulus trace activity from neurons that encode a location before the eye movement, to neurons that encode the location after the eye movement (Colby and Goldberg, 1999; Quaia et al. 1998). In the split-brain monkeys, the direct link between parietal cortices was no longer available to mediate this transfer. This raised the possibility that the behavioral recovery was supported by subcortical pathways alone.

The aim of the present study was to determine whether neurons in LIP participate in across-hemifield updating in the absence of the forebrain commissures. We recorded from

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single LIP neurons in both split-brain and intact monkeys while they performed a single-step saccade task, which allows observation of the neural activity associated with spatial updating. We monitored LIP activity during two conditions of the single-step task, analogous to those studied in the behavioral experiments. In the across-hemifield condition, the stimulus is updated from one hemifield to the other (Fig. 1A). In contrast, in the within-hemifield condition, it is updated within the same visual hemifield (Fig. 1B). We found that in the absence of the forebrain commissures, many LIP neurons still exhibited remapping in the across-hemifield condition. The remapped signal was attenuated and delayed compared with within-hemifield remapping. In the intact animals there was no difference in activity between the two conditions. We conclude that the forebrain commissures support the most rapid and robust across-hemifield updating responses in area LIP, but are not strictly necessary.

METHODS

Subjects

Four rhesus monkeys (*Macaca mulatta*) were used in this study. Monkeys CH and EM, whose spatial behavior is described in the preceding paper, underwent a complete transection of the corpus callosum and anterior commissure (see preceding paper). Monkeys FF and OE, with commissures intact, served as controls. Animals were cared for in accordance with National Institutes of Health guidelines and all experimental protocols were approved by the University of Pittsburgh Institutional Animal Care and Use Committee.

The commissurotomy of the split-brain animals was performed at the outset of the experiment and before behavioral testing. This procedure is described in the companion paper. Briefly, the monkeys were prepared for this surgery with dexamethasone, and anesthesia

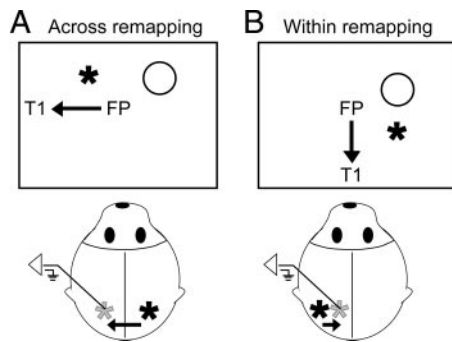


FIG. 1. Spatial configurations used to compare within- and across-hemifield remapping. Exact configuration is determined by the location of the receptive field. Hypothetical neuron under study is located in the left hemisphere (gray asterisk). *A*: across-hemifield condition. Stimulus is located in the left visual field when the eyes are at a central fixation point (FP), and so is represented by neurons in the right hemisphere (black asterisk). When the eyes reach the target (T1), however, the location where the stimulus appeared is now in the right visual field; the *stimulus trace* is thus represented by neurons in the left hemisphere, including the neuron under study (gray asterisk). Updating in this condition involves a transfer of visual information between neurons in opposite cortical hemispheres. *B*: within-hemifield condition. Stimulus appears in the right visual field when the eyes are at FP. Its retinal location is represented by neurons in the left hemisphere (black asterisk). After the saccade to T1, the location where the stimulus appeared is still in the right visual field, represented by neurons in the left hemisphere. Updating in this condition therefore involves the transfer of visual signals within the same hemisphere. We expected that in the absence of the forebrain commissures, across-hemifield remapping would be less robust than within-hemifield remapping.

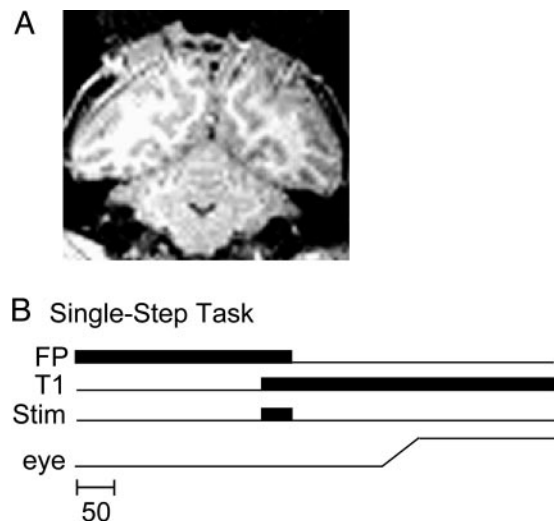


FIG. 2. Recording sites and behavioral paradigm. *A*: coronal magnetic resonance image showing the locations of the recording chambers in monkey CH. Neurons were recorded from the lateral bank of the intraparietal sulcus in both hemispheres. *B*: timing of the single-step task, as described in METHODS.

was induced with ketamine and maintained with isoflurane. Mannitol was administered throughout the surgery to minimize tissue swelling. Under sterile conditions, the callosum was transected along its full length using a small glass pipette with suction; the anterior commissure was fully transected. In the 2 wk after the surgery, analgesics were given to control postsurgical pain and antibiotics were administered daily to prevent infection.

After completion of behavioral training, monkeys were prepared for chronic physiological recording. For the split-brain animals, recording began 14–21 mo after the commissurotomy and 7–11 mo after the beginning of behavioral testing. Monkeys underwent sterile surgery under general anesthesia induced with ketamine and maintained with isoflurane. The placement of the recording chamber (1.8 cm diameter) was determined using the standard stereotaxic locations for area LIP (5 mm posterior and 12 mm lateral in Horsley–Clarke coordinates), and anatomical information from structural magnetic resonance images (MRIs). We used MRI to verify that the chambers were located over the intraparietal sulcus (Fig. 2A).

Physiological methods

During recording sessions, the monkey sat in a darkened room with its head fixed in a primate chair, facing a tangent screen. Visual stimuli were back-projected onto the tangent screen using an LCD projector. Stimulus presentation was under the control of two computers running a C-based program, CORTEX, made available by Dr. Robert Desimone at NIMH. Eye position was monitored using scleral search coils (Judge et al. 1980), with a sampling rate of 250 Hz. Further details on general procedures can be found in the preceding paper.

Neural activity was recorded using tungsten microelectrodes (FHC) introduced into the cortex through stainless steel guide tubes placed flush with the dura. The guide tubes were stabilized by a nylon grid (Crist Instruments) held rigidly in the recording chamber. The grid system permitted parallel penetrations along the bank of the intraparietal sulcus with a resolution of 1 mm. Action potentials were amplified and filtered with a band pass of 500 Hz to 5 kHz, and digitally sampled using template matching at 20 kHz. Individual neurons were isolated by means of an on-line spike-sorting system using a template-matching algorithm (Signal Processing Systems).

Behavioral paradigms

MEMORY-GUIDED SACCADE TASK. We used the memory-guided saccade task to search for neurons and assess their visual, memory, and saccade-related response properties. In this task, the monkey initially maintained its gaze on a central fixation point. After an initial delay of 300–500 ms, a stimulus flashed in the receptive field for 50 ms. After a second delay of 400–800 ms, the fixation point was extinguished, which cued the monkey to make a saccade to the location of the flashed stimulus. After the saccade, the stimulus reappeared and the monkey maintained fixation on it for an additional 300–500 ms. We used standard mapping procedures to determine the location of a neuron's receptive field (Barash et al. 1991).

SINGLE-STEP TASK. The single-step task was used to assess the neural activity associated with spatial updating (Fig. 2B). The monkey maintained fixation on a central fixation point (FP) for 300–500 ms. Two events then occurred simultaneously: a peripheral stimulus appeared outside of the neuron's receptive field and a new fixation point (T1) was illuminated. The peripheral stimulus was extinguished 50 ms later, simultaneously with the offset of FP. This was the monkey's cue to make a visually guided saccade to T1. The saccade to T1 moved the receptive field onto the location of the now-extinguished stimulus. The monkey maintained gaze on T1 for an additional 500–700 ms to receive a juice reward.

SACCADE-CONTROL TASK. This task was used to determine whether activity in the single-step task could be attributed to the generation of the saccade. The timing of the task was identical to the single-step task, except that no peripheral stimulus was presented.

STIMULUS-CONTROL TASK. The stimulus-control task was used to ensure that the stimulus location used in the single-step task was outside of the receptive field and did not drive the neuron. In this task, the monkey maintained central fixation for 300–500 ms. The peripheral stimulus was flashed for 50 ms, and the monkey was required to maintain fixation for an additional 1,200–1,500 ms.

Experimental design

We tested each neuron in two conditions of the single-step task: within-hemifield and across-hemifield. The exact geometry of the two conditions was tailored for each neuron, based on the location of the receptive field (see Fig. 1). By definition, different spatial configurations are required for remapping stimulus traces within and across hemifields. We held saccade amplitude constant and varied the saccade direction for the two conditions. Average saccade amplitude was 24.5 deg (± 5.3 SD). The standard spatial configurations were a vertical saccade for the within-hemifield condition and a horizontal saccade for the across-hemifield condition. With a vertical saccade, the representation of the stimulus remained within the same hemifield both before and after the eye movement. A horizontal ipsiversive saccade moved the representation of the stimulus from one hemifield to the other. For neurons, for which this standard configuration was not feasible, we used diagonal saccades for one or both conditions.

A complete data set for each neuron consisted of six types of trials: three tasks (stimulus control, saccade control, single-step) \times two conditions (within, across). We collected 12–20 trials for each trial type. The different tasks were run in separate blocks of trials and always in the same order: stimulus control, saccade control, and single-step. We collected data in this order because previous experiments have demonstrated that long-term intertrial memory responses can persist after experience with the single-step task (Umeno and Goldberg 2001). The within and across conditions were randomly interleaved for each task.

Neural analysis

SELECTING NEURONS FOR ANALYSIS. We analyzed the activity in the stimulus-control tasks to be certain that the response in the single-step task could not be attributed to the presence of the stimulus alone. We assessed this with a *t*-test ($P < 0.05$), comparing activity in a visual epoch (50–250 ms after stimulus onset) to activity in the baseline epoch (200–300 ms after attainment of fixation). We excluded neurons from further analysis if they had a significant visual response in either the within- or across-stimulus-control condition.

MEASURING REMAPPING ACTIVITY. We used a standard epoch to analyze activity in the single-step tasks: 0–200 ms relative to saccade onset. This standard epoch provides an unbiased way to compare remapping activity between the within and across conditions. This epoch is similar to that used in previous remapping studies (Kusunoki and Goldberg 2003) and captured the peak updating response present in the population. For all analyses of the strength of remapped responses, it was important that the activity observed in the single-step task could not be attributed simply to the generation of the saccade. Accordingly, we measured activity in the same 200-ms epoch of the saccade control task. Remapping was defined as the activity in the single-step task that exceeded activity in the corresponding saccade control. We used a simple subtraction to quantify the updated response: Remapping = Single-step activity – Saccade control activity.

MEASURING NEURAL LATENCY. We measured the latency of the remapped response relative to saccade onset. Neural latency can be reliably defined only if all of the activity present in the single-step task is attributable to remapping the stimulus, rather than simply to the generation of the saccade. In contrast to the analysis of the strength of the remapped responses described above, there was no method to account for saccade control activity in the analysis of neural latency. Therefore if there was any significant activity in the saccade control associated with a particular single-step condition, we excluded it from latency analyses.

Previous studies have shown that remapping can occur over a broad range of latencies (Kusunoki and Goldberg 2003; Umeno and Goldberg 1997). We used the following method to measure neural latency in individual neurons (Nakamura and Colby 2000). We looked for the onset of the neural response in a period spanning 100 ms before saccade onset to 300 ms after saccade onset. We used a sliding window to find the time when the firing rate first began to differ significantly from activity during the baseline epoch (200–300 ms after attainment of fixation). Specifically, we measured activity in successive 20-ms response windows. We used a *t*-test ($P < 0.05$) to assess whether activity in each response window differed significantly from baseline activity. If there was no significant difference, the window was shifted forward by 2 ms and the procedure was repeated until the activity in the response window was significantly greater than baseline activity. To avoid spurious results, we defined latency based on the occurrence of two consecutive windows that achieved significance. The midpoint of the first significant window was considered the onset of the neural response. If this criterion was not met within 300 ms after saccade onset, we concluded that there was no response associated with remapping the stimulus trace. We used an analogous method to determine the visual response latency in the memory-guided saccade task. The calculated latency was verified by inspection.

ANALYSIS OF NEURONAL RESPONSE PROPERTIES. Activity in the memory-guided saccade task was analyzed to determine the visual, memory, and saccade-related responses of individual neurons. The visual epoch was the 100-ms epoch beginning at the onset of the visual response. The memory epoch was 250 to 350 ms after stimulus onset; the saccade epoch was –100 to +100 ms relative to the onset of the saccade. We compared activity in each of these epochs to activity in the baseline epoch, using a *t*-test ($P < 0.05$).

RESULTS

We recorded from 306 visually responsive LIP neurons in three hemispheres of two split-brain monkeys. Of these, 223 had no significant response in either the within or across stimulus-control conditions and were included in further analysis. We recorded from 74 visually responsive LIP neurons in two hemispheres of two intact monkeys. Of these, 55 had no response in the stimulus-control conditions and were included in further analysis.

LIP neurons remap stimulus traces across hemifields in the split-brain monkey

Our primary finding is that individual neurons in LIP update visual representations both within and across hemifields in the split-brain monkey. An example neuron is shown in Fig. 3. In the within-hemifield condition, the neuron began to fire before the onset of the saccade and its activity persisted until well after the saccade was completed (Fig. 3C). In other words, this neuron exhibits a standard remapping response in the within-hemifield condition. The critical test was whether this same neuron would also respond when information had to be transferred across hemispheres. As shown in Fig. 3D, we found that

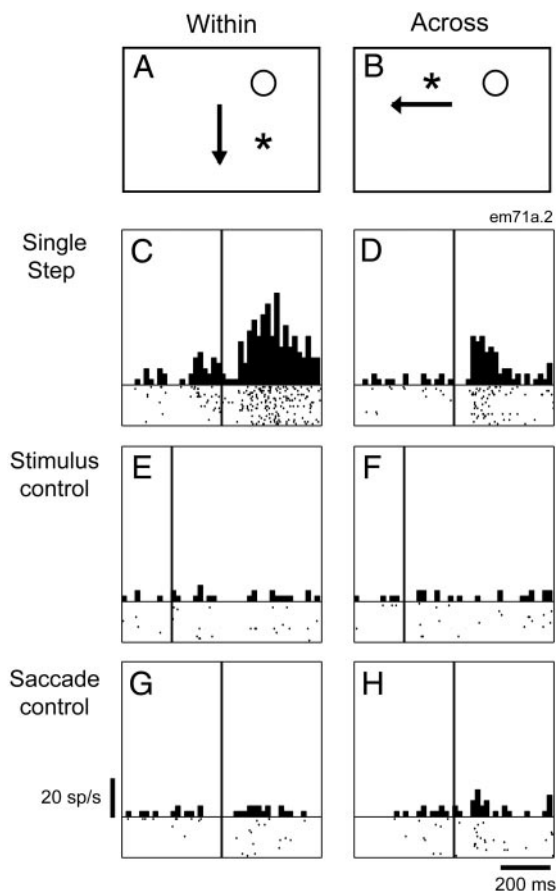


FIG. 3. Example of a neuron that remaps stimulus traces both within and across hemifields in the split-brain monkey. *A* and *B*: spatial configurations for within and across conditions. For both conditions, updating activity in the single-step task (*C*, *D*) is significantly greater than that elicited by the stimulus alone (*E*, *F*) or saccade alone (*G*, *H*). Histograms represent average firing rate; rasters show action potentials on individual trials. Data are aligned on either saccade onset (*C*, *D*, *G*, *H*) or stimulus onset (*E*, *F*).

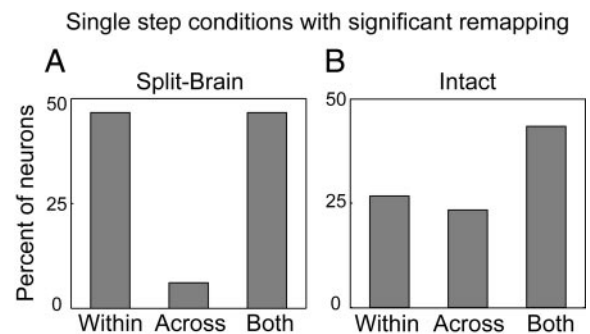


FIG. 4. Proportion of neurons with significant remapping for within-hemifield, across-hemifield, or both conditions. *A*: in the split-brain monkey, an equal proportion of neurons show significant remapping for within only and for both types of remapping, whereas a small number show significant remapping only for the across condition. *B*: in the intact monkey, most neurons have significant remapping for both conditions and nearly equal proportions have significant remapping for only one condition.

this same neuron responded robustly in the across-hemifield condition.

The control tasks demonstrate that this response cannot be attributed to visual or motor activity alone. The neuron does not respond when the stimulus is presented in the absence of the saccade (Fig. 3, *E* and *F*). Similarly, the responses in the saccade control conditions were negligible (Fig. 3, *G* and *H*). It is only when the stimulus and saccade occurred together, as they do in the single-step task, that the neuron responded. This example demonstrates our principal finding that even after the forebrain commissures are removed, LIP neurons can access visual information from the opposite hemifield.

For this neuron, the response in the saccade control task differs for the within and across conditions. For the across condition, the saccade alone elicits a small response that occurs at nearly the same latency as the updating response observed in the single-step task. For this condition, the saccade moves the outer edge of the receptive field onto the location of the initial fixation point, FP. The fixation point itself is a salient visual stimulus that can be remapped, and we attribute this postsaccadic response to remapping the location of FP. For the configurations we used, this activity was more common in the across than the within condition of the task. As discussed in the following text, we designed analysis methods to account for the disparity in activity generated in the saccade-control conditions.

We asked whether individual neurons showed statistically significant remapping in both the within and across conditions. We defined remapping as statistically significant if activity in the single-step task was greater than that observed in the saccade-control task (*t*-test, $P < 0.05$; see METHODS). In the split-brain monkeys, most neurons (80%, 179/223) showed statistically significant remapping in at least one condition of the single-step task (Fig. 4A). Almost half of the population remapped stimulus traces only within the same hemifield (46%). An example of such a neuron is shown in Fig. 5. An equal number (46%), however, remapped stimulus traces both within and across hemifields. A small number of neurons (6%) showed remapping only in the across condition. These findings indicate that many neurons update stimulus traces across hemifields even in the absence of the forebrain commissures.

In the intact monkey, more than half of the neurons in our population had significant updating activity (51%, 28/55). Of

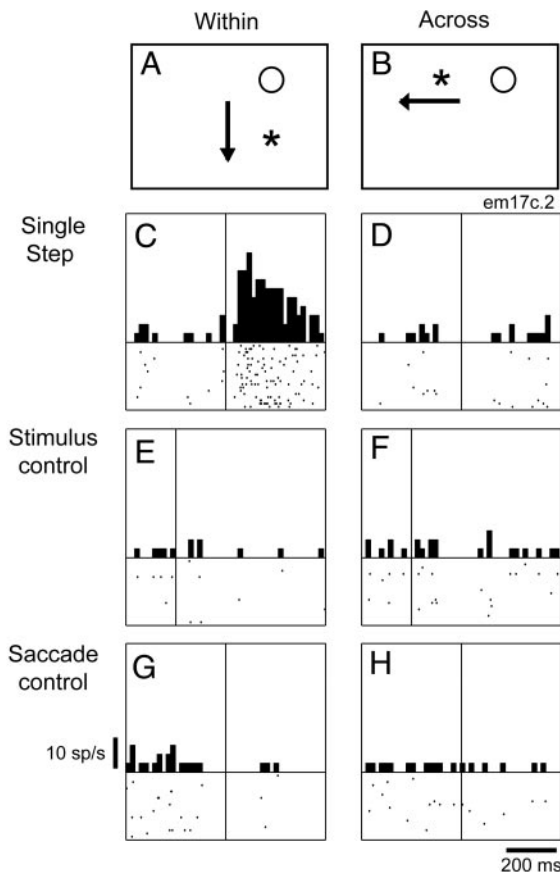


FIG. 5. Example of a neuron that remaps stimulus traces within but not across hemifields in the split-brain monkey. *A* and *B*: spatial configurations. *C* and *D*: single-step task. *E* and *F*: stimulus controls. *G* and *H*: saccade controls. Conventions as in Fig. 3.

these, many remapped for both conditions (46%, Fig. 4*B*). In contrast to our observation in the split-brain monkeys, the remaining neurons were nearly equally divided between those that remap within only (28%) and those that remap across only (25%). The distributions of neurons with remapping were significantly different for the two groups of animals (chi-square test, $\chi^2 = 16.8$, $df = 2$, $P < 0.01$). These results indicate that the reduced prevalence of across-hemifield remapping in the split-brain monkey indeed results from transection of the forebrain commissures.

Across-hemifield remapping and LIP neuron response properties

Why do some neurons remap stimulus traces for only the within or only the across condition whereas others remap for both conditions? We considered the possibility that the presence of memory or motor activity might be related to a neuron's ability to update stimulus traces across hemifields. To address this possibility, we analyzed each neuron's activity in the memory-guided saccade task to determine the presence of memory or motor signals; neurons were selected for analysis based on their visual response in this task, so all carried visual signals. We asked whether across-hemifield remapping was more prevalent for any particular class of neurons (visual neurons, visual-memory neurons, etc). For each class, we determined the proportion of cells with significant remapping

TABLE 1. Visual, memory, and saccade-related characteristics of neurons

	Within Only	Across Only	Within and Across	Total
Vis	15 (75%)	2 (10%)	3 (15%)	20
Vis-Mem	3 (75%)	1 (25%)	0 (0%)	4
Vis-Sac	18 (60%)	5 (17%)	7 (23%)	30
Vis-Mem-Sac	51 (43%)	2 (2%)	64 (55%)	117

Values indicate number of neurons. Values in parentheses indicate percentages of neurons in each class with significant remapping for within, across, or both conditions. Vis, visual activity; Mem, memory activity; Sac, saccade-related activity.

within and across hemifields (Table 1). Within-hemifield remapping was more common than across-hemifield remapping for three of the four neuron classes (visual only, visual-memory, and visual-saccade). For neurons with visual, memory, and saccade-related activity, we observed a tendency for across-hemifield remapping to be more common. Nonetheless, across-hemifield remapping was observed in all four cell classes and did not depend on the presence of either memory and saccade-related activity.

Strength of across-hemifield remapping is attenuated in split-brain animals

How does the magnitude of the remapping signal compare for the within- and across-hemifield conditions? We found that the magnitude of the remapped response was significantly greater for within-hemifield compared with across-hemifield updating (Wilcoxon matched-pairs test, $P < 0.0001$; Fig. 6*A*). This finding confirms that in the absence of the forebrain commissures, the ability to remap stimulus traces across hemifields is compromised. As expected, we found no difference in the strength of remapping when the commissures are intact (Fig. 6*B*). In the intact monkeys, there is no difference in the strength of remapping for the two conditions (Wilcoxon paired-sample test, $P > 0.30$). This finding demonstrates that normally there is no cost associated with updating stimulus traces from one hemifield to the other. This result is in agreement with observations that there is normally no difference in the magnitude of remapping within and across hemifields (Heiser and Colby 2003).

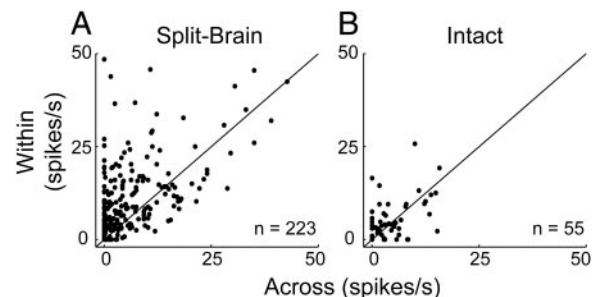


FIG. 6. Magnitude of updating activity for within and across conditions. Each point represents data from a single neuron. Magnitude of updating activity is calculated as the difference between activity in the single-step and saccade control tasks. *A*: in the split-brain monkey, activity is significantly greater for within- than for across-hemifield remapping. *B*: in the intact monkey, there is no difference in the magnitude of within- and across-hemifield remapping.

To further quantify the results from the split-brain and intact monkeys, we computed a Within–Across Remapping Index (WA Index) for each neuron. With this index, we can assess how robustly neurons remap stimulus traces across hemifields versus within a single hemifield. The WA Index normalizes remapping activity observed in the single-step tasks to the total activity observed in the single-step and saccade control tasks

$$\text{WA Index} = \frac{(SS_w - SAC_w) - (SS_a - SAC_a)}{(SS_w + SAC_w) + (SS_a + SAC_a)}$$

In this formula, SS_w and SS_a represent the firing rates measured in the within and across conditions of the single-step task and SAC_w and SAC_a represent the firing rates measured in the corresponding saccade control conditions. Positive values indicate that activity was stronger for within-hemifield compared with across-hemifield updating, whereas negative values indicate that activity was stronger for across-hemifield updating. A value of 0 indicates no difference in the magnitude of remapping within and across hemifields.

We found that the distribution of WA Indices from the split-brain monkeys (Fig. 7A) is significantly skewed toward positive values (one-tailed t -test, $P < 0.0001$), indicating stronger remapping for the within-hemifield condition. This finding was statistically significant in both split-brain monkeys (one-tailed t -test, $P < 0.0001$). In contrast, the distribution of WA Indices in the intact animal is not significantly shifted (one-tailed t -test, $P > 0.60$, power > 0.95 ; Fig. 7B). This result provides further evidence that, in the intact monkey, there is no difference in the magnitude of the signal associated with these two conditions. We next asked whether there is any difference in the distributions from the two groups of animals. The average WA Index value from each group of monkeys was significantly different (split-brain: mean = 0.11, SE = 0.012; intact: mean = 0.019, SE = 0.018; Kolmogorov–Smirnov [KS] test, $P < 0.001$). Together these findings indicate that the signal associated with across-hemifield updating is reduced in the absence of the forebrain commissures.

Remapping across hemifields occurs later in split-brain animals

We asked whether the time course of across-hemifield remapping was affected by disconnecting the cerebral hemispheres. In the previous sections, we analyzed spike counts in a fixed epoch. Here we were interested in the time at which an appreciable change in updating activity first occurs. For each

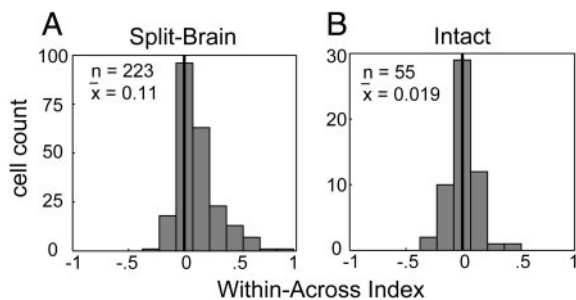


FIG. 7. Strength of remapping for within and across conditions. A: split-brain monkey. Distribution is significantly skewed toward positive values. B: intact monkey. Distribution is not significantly different from 0. Distributions are significantly different from one another.

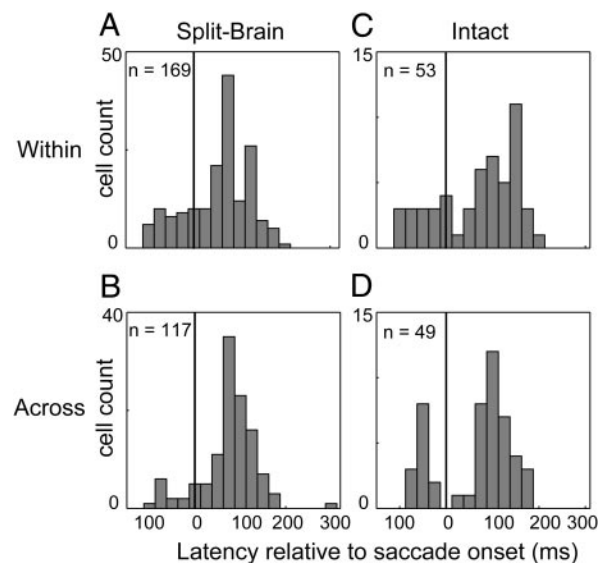


FIG. 8. Comparison of the latency of remapping within and across hemifields. Latency is defined relative to saccade onset (vertical line). A and B: in the split-brain monkey, remapping occurs significantly earlier for within-hemifield updating. C and D: in the intact monkey, there is no difference in the latency for remapping within and across hemifields.

neuron, we defined the latency of the neural response in the two remapping conditions relative to the beginning of the saccade. We asked two questions about the latency of updating, first analyzing the entire population and then analyzing individual neurons. We used different but overlapping subsets of neurons in these analyses, as described below.

The first question focused on signals present in the population as a whole: are average neural latencies comparable for the within and across condition? To address this question, we performed an unmatched analysis, including all neurons with a valid latency in either the within or across condition. In the split-brain monkeys (Fig. 8, A and B), remapping occurred earlier for within-hemifield updating ($n = 169$, mean = 54.50 ms, SE = 5.34 ms) than for across-hemifield updating ($n = 117$, mean = 76.39 ms, SE = 5.70 ms; Wilcoxon rank-sum test, $P < 0.01$). No such difference was present in the intact monkey (Fig. 8, C and D). Here, remapping latencies averaged 67.55 ms (± 11.72 ms SE) for the within condition and 65.84 ms (± 11.12 ms SE) for the across condition (Wilcoxon rank-sum test, $P > 0.05$). These findings indicate that the forebrain commissures provide the main pathway for the rapid transfer of visual information from one hemisphere to the other.

Second, is there any difference in neural latency if we consider individual neurons that have valid latencies for both conditions? In this analysis, we included only those cells where the latency was definable for both conditions (split-brain: $n = 74$; intact: $n = 37$). For each neuron, we compared the latency of within-hemifield remapping to that of across-hemifield remapping (Fig. 9A). Points that fall along the unity line represent neurons with remapping activity that began at the same time for the two conditions. For the split-brain monkeys, most points fall below the line, indicating that remapping across visual hemifields is delayed relative to remapping within the same hemifield (Wilcoxon sign-rank test, $P < 0.01$). In the intact monkey, the points are equally distributed above and below the line (Fig. 9B; Wilcoxon sign-rank test, $P > 0.60$).

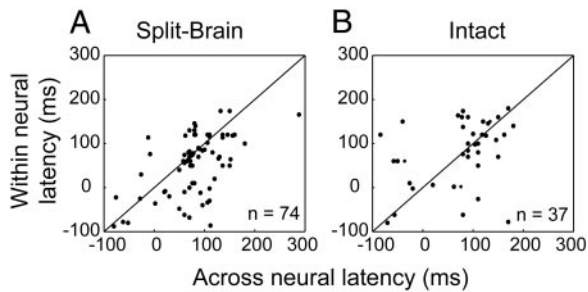


FIG. 9. Response latencies for within- and across-hemifield remapping. Latency is defined relative to the onset of the saccade; each dot represents the latency observed in the within condition plotted against latency observed in the across condition. Across-hemifield remapping was significantly delayed as compared with within-hemifield remapping in the split-brain monkey (A) but not in the intact monkey (B).

We conclude that there is normally no difference in the time at which neural signals associated with remapping within and across hemifields become available. In the absence of the forebrain commissures, however, across-hemifield remapping is delayed.

The earliest remapping signals are absent in the split-brain monkey

In both conditions, and in both groups of animals, we observed considerable variability in the latency of remapping. These results are similar to previous studies, in which a wide range of latencies were observed (Umeno and Goldberg 1997). Some neurons respond in the single-step task at a time that precedes the expected visual latency of the neuron (Duhamel et al. 1992a; Goldberg and Bruce 1990; Nakamura and Colby 2002; Umeno and Goldberg 1997; Walker et al. 1995). These predictive signals provide an updated representation that is available well before reafferent visual signals are available.

Remapping is considered predictive in nature if the onset of the response in the single-step task is earlier than the visual latency observed in the memory-guided saccade task. We found that the average visual latency for LIP neurons was 98.65 ms, as measured in the memory-guided saccade task. On average, then, remapping latencies that are shorter than this can be considered predictive. For some predictive neurons, the response in the single-step task begins even before the onset of the saccade. For these neurons, the location of the receptive field shifts even before the eyes begin to move. Neurons with *presaccadic* latencies are a subset of those with *predictive* latencies.

We asked whether neurons in the split-brain monkey could exhibit predictive remapping. In particular, we tested whether the proportions of predictive and presaccadic latencies would be similar between the within and across conditions. We addressed this issue by analyzing the entire population of neurons with valid latencies. We observed a nearly equal proportion of predictive responses for within- and across-hemifield updating in the split-brain monkey [within 63% (107/169), across 58% (68/117)]. We observed a similar proportion of predictive responses in the intact monkey [within 62% (33/53), across 61% (30/49)]. These data show that even if the primary route for the interhemispheric transfer of information is abolished, signals related to spatial updating are still transferred between hemispheres rapidly.

What about the frequency of *presaccadic* latencies? Is there any difference in the frequency of neurons showing the earliest predictive latencies? In contrast to our findings on the overall frequency of predictive neurons, we found that presaccadic responses were twice as common for within-hemifield remapping in the split-brain monkey [within 22% (38/169), across 11% (13/117)]. In contrast, in the intact monkey, presaccadic latencies occurred with nearly equal frequency for the two conditions [within 25% (13/53), across 27% (13/49)]. Similar proportions of predictive and presaccadic neurons were observed in the subset of neurons used in the paired analysis (see Fig. 9). Although across-hemifield remapping can occur quite rapidly in the split-brain animal, fewer neurons exhibit presaccadic latencies for this condition than for the within-hemifield condition. This implies that the absence of the forebrain commissures reduces the very earliest signals when across-hemifield remapping is required.

The time course of across-hemifield remapping is altered in split-brain monkeys

We next considered the time course of signals carried by the population of neurons in area LIP during within and across-hemifield remapping. We did so by calculating the WA Index over time on the entire population of neurons, in both split-brain and normal animals (Fig. 10). We determined the time at which signals associated with within- and across-hemifield remapping first began to differ. This is represented by the time at which the index first began to diverge significantly from zero. In the absence of the forebrain commissures, the WA Index first reached significance 110 ms before the onset of the saccade and remained significant throughout the duration of the test period (500 ms after saccade onset). The index reached its maximum 190 ms after saccade onset. These data show that, well before the initiation of the saccade, there is a difference in the neural signal associated with updating stimulus traces within as compared to across hemifields. This difference persists for many hundreds of milliseconds after the saccade is completed. In contrast, in the intact animal, the WA Index remains near 0 throughout the duration of the analysis epoch.

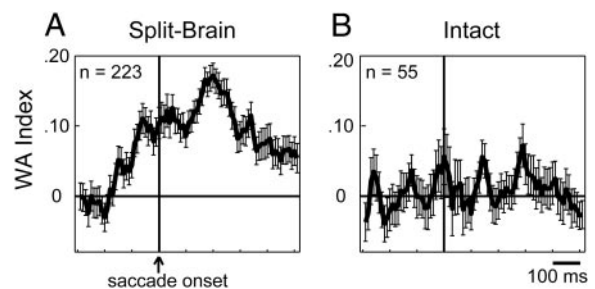


FIG. 10. Analysis of the time course of remapping within and across hemifields. Each plot shows the Within–Across Index computed as a function of time. Positive values indicate that remapping is more robust for the within than the across condition. Values near zero (horizontal line) indicate that remapping is equal for the 2 conditions. Index is computed in 50-ms epochs, beginning 300 ms before the onset of the saccade. Epoch is moved up by 10 ms, and the index is recomputed. This procedure is repeated for all timepoints until 500 ms after the onset of the saccade. Error bars represent SE. A: split-brain monkey. Within–Across Index becomes significantly positive beginning 110 ms before the onset of the saccade and remains significant throughout the duration of the analysis epoch. B: intact monkey. Within–Across Index remains near zero throughout the test period.

Remapping across hemifields is independent of receptive field location

We asked whether the strength or latency of across-hemifield remapping might be related to the location of the receptive field (RF). We were specifically interested in the possibility that neurons with receptive fields near the midline were more likely to remap across hemifields. This interest was prompted by physiological findings in the normal monkey, which indicate that some LIP neurons have receptive fields that can extend up to five degrees into the ipsilateral visual field (Ben Hamed et al. 2001; but see Platt and Glimcher 1998). We asked two questions regarding the relationship between RF location and the properties of across-hemifield remapping in the split-brain animal. First, is the strength of across-hemifield remapping related to the RF location? We addressed this question by comparing the WA Index for each neuron to its horizontal distance from the vertical meridian (Fig. 11). Linear regression revealed that there was no significant relationship between RF location and ability to remap stimulus traces across hemifields ($P > 0.3$). The strength of across-hemifield remapping, compared with within-hemifield remapping, is independent of RF eccentricity. We conclude that neurons in LIP have equal access to stimuli in the opposite hemifield, whether they have proximal or peripheral receptive fields.

Second, is the latency of remapping related to the RF location? Specifically, do neurons with central RFs have earlier access to information about stimulus traces remapped across hemifields? In Fig. 12, we plot neural latency against distance from the midline for each neuron. There was no significant relationship between remapping latency and receptive field eccentricity (linear regression, within $P > 0.20$, across $P > 0.50$). From this, we can infer that there is no difference in the time required to compute the updated location of a visual stimulus, regardless of how far across the vertical meridian the signal must be transferred.

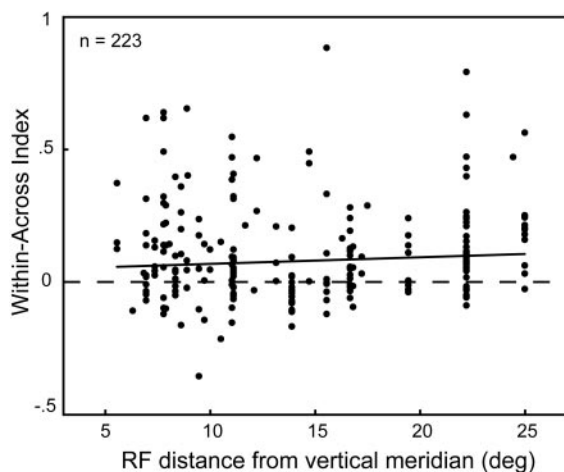


FIG. 11. Relationship between strength of remapping and receptive field location in the split-brain monkey. For each neuron, the distance of the receptive field from the vertical meridian was estimated using the memory-guided saccade task. A Within-Across Index of zero (horizontal line) indicates equivalent remapping in each condition of the task. There was no significant relationship between receptive field location and Within-Across Index (linear regression, $P > 0.3$).

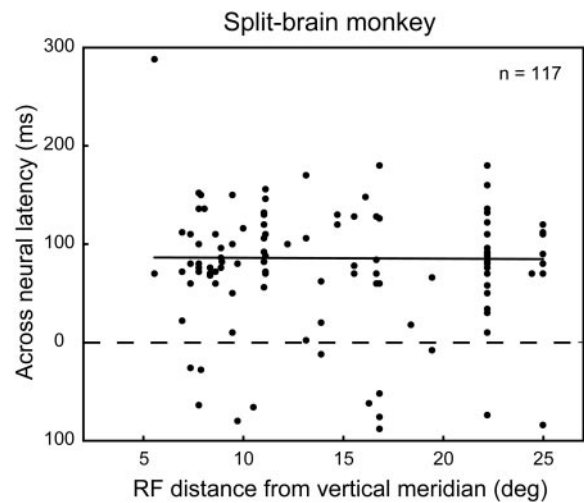


FIG. 12. Relationship between across-hemifield remapping latency and receptive field location in the split-brain monkey. Distance of the receptive field from the midline is plotted against neural latency (relative to saccade onset). There was no relationship between neural latency and receptive field eccentricity (linear regression, $P > 0.5$).

DISCUSSION

The physiological observations reported here reveal that a dynamic neural circuit mediates visuospatial updating in the primate brain. Our principal finding is that across-hemifield remapping of stimulus traces occurs even in the absence of the forebrain commissures. A substantial proportion of LIP neurons in the split-brain monkey showed significant and robust activity when spatial representations of stimulus locations were updated from one hemifield to the other. This indicates that the forebrain commissures are not required for the transfer of visual information between hemispheres: alternative pathways can suffice. Our second main finding is that across-hemifield updating activity is reduced in the absence of the forebrain commissures. Specifically, we found that across-hemifield remapping was less prevalent than within-hemifield remapping in area LIP of the split-brain monkey. When these across-hemifield signals were present, they were diminished in magnitude and delayed in onset. Notably, we found that the very earliest remapped responses were all but absent when spatial representations had to be updated across hemifields. These results indicate that direct cortical links are an important substrate for the neural signals associated with spatial updating in area LIP but they are not the sole substrate.

Circuitry for across-hemifield remapping in the absence of the forebrain commissures

Our observation of across-hemifield remapping in LIP of the split-brain monkey indicates that alternative pathways can support interhemispheric updating when direct cortico-cortical connections are absent. Three of our physiological findings provide insight into the limitations and capacities of this alternative system. First, as noted above, the signals associated with across-hemifield updating were modified in the split-brain monkey: across-hemifield responses were smaller and appeared later compared with within-hemifield responses. These modifications indicate that less direct pathways, which presumably make use of subcortical structures, mediate across-hemi-

field remapping in the absence of the more direct cortico-cortical route. Second, we found that across-hemifield remapping was observed regardless of the eccentricity of the neurons' receptive fields. This finding demonstrates that the pathways supporting across-hemifield updating in the split-brain monkey are not biased toward representing limited spatial locations, such as those nearest the vertical meridian. Rather, these pathways can support spatial updating throughout the visual field. This is in keeping with evidence that LIP neurons in the normal animal have access to visual representations from throughout the visual field (Heiser and Colby, 2003). Third, we found that across-hemifield remapping in LIP was present in all classes of visual neurons, as defined in the memory-guided saccade task. In other words, updated representations were observed whether the neurons carried only visual signals, or visual signals in combination with memory and/or saccade activity. Across-hemifield remapping was most prevalent in neurons with all three signals—visual, memory, and saccade-related activity. Whereas activity related to across-hemifield updating was observed most commonly in this subset of LIP neurons, it was nevertheless present throughout the population of neurons studied in the split-brain monkeys.

Correspondence with behavioral results

How do these physiological findings relate to the behavioral results from these split-brain animals? In the preceding paper, we describe a series of behavioral experiments that tested whether the forebrain commissures are necessary for the performance of a spatial task that requires across-hemifield updating. We measured the performance of the split-brain monkeys on the double-step saccade task, which entails sequential saccades to two successively appearing targets. Accurate performance requires that the representation of the second target be updated to take the first saccade into account. We tested two conditions of the double-step task, comparable to those tested physiologically in the present study. Within-hemifield sequences required that the second target be updated within the same visual hemifield, whereas across-hemifield sequences required that this target be updated from one hemifield to the other.

Our behavioral experiments demonstrated that the split-brain monkeys were initially impaired on across-hemifield compared with within-hemifield sequences of the double-step task. Unexpectedly, this impairment was not permanent or universal, and both split-brain monkeys were ultimately able to perform across-hemifield sequences. This recovery of function is consistent with our physiological finding that neurons in area LIP can respond to stimulus traces that have been updated across hemifields. Our behavioral experiments also demonstrated that, despite substantial recovery, performance on across-hemifield sequences remained somewhat compromised. In particular, we found that the across-hemifield impairment could be reinstated when we changed the spatial geometry of the double-step targets. This behavioral marker of impairment is consistent with our physiological observation that remapping in area LIP is less robust for across-hemifield compared with within-hemifield conditions. These parallel behavioral and physiological findings suggest that updating activity in area LIP may be used to guide behavior.

At the time of physiological recording in area LIP, the split-brain monkeys had been extensively tested on the double-step task. At this time, performance on the across-hemifield sequences had recovered substantially, although not completely. Is the behavioral recovery a prerequisite for the presence of across-hemifield updating activity in area LIP? Previous experiments in the normal monkey have shown that remapping in the single-step task does not depend on earlier training on the double-step task (Duhamel et al. 1992a; Walker et al. 1995). In keeping with these findings, we observed significant updating activity in the single-step task in the intact monkeys, who had not been previously trained on the double-step task. We can conclude that, in general, training on the double-step task is not required for updating activity to exist in area LIP. For the split-brain monkeys, however, experience with the across-hemifield double-step task may have been important for activating pathways that also subserve the updating activity we observed in area LIP. Further studies will be required to elucidate the relationship between activity in area LIP and spatial behavior.

Forebrain commissures and the neural correlates of visual function

What are the physiological consequences of transecting the forebrain commissures? Several previous investigations have addressed this question, focusing on neural activity in the ventral stream where activity is predominantly related to form and color representations (Ungerleider and Mishkin 1982). These studies have demonstrated that the corpus callosum and anterior commissure are important for transmitting the neural signals required to make across-hemifield associations between complex visual stimuli (Hasegawa et al. 1998; Tomita et al. 1999). These commissures are also necessary for conferring the ipsilateral receptive field properties of neurons in the inferotemporal cortex and area V4 (Desimone et al. 1993; Gross et al. 1977). Much less is known regarding the contribution of these commissures to neural activity in dorsal stream areas. Our findings provide new evidence that activity in area LIP is disrupted but not abolished when both the corpus callosum and anterior commissure have been transected. In the split-brain monkey, single neurons in area LIP exhibit diminished and delayed across-hemifield remapping but nonetheless have access to visual representations that originate in the opposite hemisphere. Our physiological findings also expand on behavioral studies from split-brain and acallosal human patients. These investigations have suggested that coarse spatial information can be transferred between hemispheres for the purpose of making perceptual judgments (Holtzman 1984). Location information may also be available to guide attention across hemifields (Holtzman et al. 1981; but see also Hines et al. 2002; Reuter-Lorenz and Fendrich 1990). We have now shown that stimulus traces can be updated from one hemifield to the other in the absence of the forebrain commissures. This attests to a significant resilience in the pathways that adjust spatial representations in conjunction with eye movements.

In summary, the goal of this experiment was to gain insight into the neural circuitry underlying spatial updating. Our essential finding is that, even in the absence of the forebrain commissures, neurons in the lateral intraparietal area can update stimulus traces across hemifields. This indicates that

alternative, subcortical pathways must be available to subserve this function. Additionally, we found that across-hemifield remapping is attenuated compared with within-hemifield updating. These physiological findings parallel our behavioral results described in the preceding paper. Taken together, these data demonstrate a previously unrealized redundancy in the neural circuitry for stable spatial representations.

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