

Corollary discharge and spatial updating: when the brain is split, is space still unified?

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Abstract: How does the brain keep track of salient locations in the visual world when the eyes move? In parietal, frontal and extrastriate cortex, and in the superior colliculus, neurons update or 'remap' stimulus representations in conjunction with eye movements. This updating reflects a transfer of visual information, from neurons that encode a salient location before the saccade, to neurons that encode the location after the saccade. Copies of the oculomotor command — corollary discharge signals — must initiate this transfer.

We investigated the circuitry that supports spatial updating in the primate brain. Our central hypothesis was that the forebrain commissures provide the primary route for remapping spatial locations across visual hemifields, from one cortical hemisphere to the other. Further, we hypothesized that these commissures provide the primary route for communicating corollary discharge signals from one hemisphere to the other. We tested these hypotheses using the double-step task and subsequent physiological recording in two split-brain monkeys. In the double-step task, monkeys made sequential saccades to two briefly presented targets, T1 and T2. In the visual version of the task, the representation of T2 was updated either within the same hemifield ("visual-within"), or across hemifields ("visual-across"). In the motor version, updating of the visual stimulus was always within-hemifield. The corollary discharge signal that *initiated* the updating, however, was generated either within the same hemisphere ("motor-within") or in the opposite hemisphere ("motor-across"). We expected that, in the absence of the forebrain commissures, both visual-across and motor-across conditions would be impaired relative to their "within" controls.

In behavioral experiments, we observed striking initial impairments in the monkeys' ability to update stimuli across visual hemifields. Surprisingly, however, both animals were ultimately capable of performing the visual-across sequences of the double-step task. In subsequent physiological experiments, we found that neurons in lateral intraparietal cortex (LIP) can remap stimuli across visual hemifields, albeit with a reduction in the strength of remapping activity. These behavioral and neural findings indicate that the transfer of visual information is compromised, but by no means abolished, in the absence of the forebrain commissures. We found minimal evidence of impairment of the motor-across condition. Both monkeys readily performed the motor-across sequences of the double-step task, and LIP neurons were robustly active when within-hemifield updating was initiated by a saccade into the opposite hemifield. These results indicate that corollary discharge signals are available bilaterally. Altogether, our findings show that both visual and corollary discharge signals from opposite hemispheres can converge to update spatial representations in the absence of the forebrain commissures. These investigations provide new evidence that a unified and stable representation of visual space is supported by a redundant circuit, comprised of cortical as well as subcortical pathways, with a remarkable capacity for reorganization.

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Introduction

We perceive a visual world that is richly detailed, stable, and continuous. This perception allows us to perform a range of spatial behaviors, from reaching for a cup of coffee to navigating through a busy street. The ease with which we perform these actions gives the impression that our sensory experience is a direct — and passive — reflection of the world around us. Our perception, however, is by no means a transparent read-out of incoming sensory inputs. The active nature of perception is readily appreciated when we consider the nature of the visual signals that arrive at the periphery. We explore and analyze the world using the high-acuity center of the retina, the fovea. In order to direct the fovea toward objects of interest we make rapid eye movements, called saccades, about three times each second. About every 300 milliseconds, the brain receives a new image, yet we are oblivious to these nearly continuous displacements of the retinal scene. What we perceive is an internal representation of the visual world, which seamlessly compensates for our own movements.

How does the mind construct this stable representation of visual space from such constantly changing input? In 1866, Helmholtz observed that when he passively displaced his eye by gently pressing it, the image of the world was also displaced (Helmholtz, 1866). In contrast, when he displaced his eye by generating a voluntary eye movement, the image of the world remained still. Helmholtz proposed that our perception of the visual world is kept stable by the “effort of will” associated with making an eye movement. This “effort of will,” placed in the context of contemporary physiological studies, is a copy of the motor command that generates the saccadic eye movement. This *corollary discharge* can support the computations needed to anticipate what the visual world will look like once the eyes reach their new location. By using corollary discharge signals, the brain can update the internal representation of space, keeping it in register with the incoming retinal signals. In this way, the brain compensates for the retinal displacements caused by eye movements, producing a stable representation of objects in the visual world. This dynamic process, known as spatial updating, is the focus of the present study.

Updating involves a transfer of visual and motor signals

In the past two decades, neurophysiological studies have provided considerable insight into neural mechanisms that contribute to the phenomenon of spatial constancy. Single-unit recording studies in awake, behaving monkeys indicate that several brain areas participate in updating spatial representations when the eyes move. In parietal, frontal, and extrastriate cortex, and in the superior colliculus, neurons exhibit a surprising kind of activity, which exemplifies the important influence of action upon perception. Neurons in these areas have classical visual responses, firing when stimuli appear within the receptive field. These neurons also fire, however, when a saccade brings the receptive field onto a previously stimulated location — even though no physical stimulus ever appears within the field (Mays and Sparks, 1980; Goldberg and Bruce, 1990; Duhamel et al., 1992a; Walker et al., 1995; Umeno and Goldberg, 1997, 2001; Nakamura and Colby, 2002). This firing, called *remapping*, is a response to a memory trace of the stimulated location, which has been updated in conjunction with an eye movement. Remapping provides a dynamic internal representation of the visual world that takes our eye movements into account.

Remapping requires the communication of visual as well as motor signals. When the eyes move, the *visual* representation must be transferred from neurons that encode the stimulus location before the eye movement, to neurons that will encode the location after the eye movement (Colby and Goldberg, 1999). This transfer must be initiated by a copy of the *motor* command, the corollary discharge signal. Recent studies emphasize that these motor signals contribute vitally to visual processing and spatial behavior (Guillery and Sherman, 2002a,b; Guillery, 2003; Sommer and Wurtz, 2004b). Spatial updating is one such instance in which corollary discharge information must play a role. For example, if the eyes are going to move 10° to the right, information about the impending saccade must be available to visual areas, initiating a transient 10° shift in receptive field locations. The current experiments investigate the circuitry supporting the communication of these visual and oculomotor signals. In the following

sections, we describe the rationale for these experiments and our specific hypotheses. We then present behavioral and physiological evidence that reveals an intriguing dissociation between pathways that mediate the communication of visual as compared to corollary discharge signals are also presented.

Both visual and motor signals must be communicated between hemispheres

One of the most noteworthy aspects of remapping is that, at the time of the eye movement, neurons are responsive to locations outside their classical receptive fields. Accordingly, neurons must have access to information from throughout the visual field, even from the opposite visual hemifield. In the original experiments on remapping in the lateral intraparietal cortex (LIP), stimulus representations were updated from one visual hemifield to another (Duhamel et al., 1992a). This neural activity has a behavioral complement: both humans, and monkeys are capable of performing spatial tasks that require across-hemifield remapping (Goldberg et al., 1990; Duhamel et al., 1992b; Li and Andersen, 2001; Jeffries et al., 2003; Zivotofsky et al., 2003). Successful across-hemifield updating must require a transfer of information between neurons in opposite hemispheres, as the representation of visual stimuli is highly lateralized (Trevarthen, 1990; Medendorp et al., 2003; Merriam et al., 2003). Similarly, physiological and behavioral studies indicate that corollary discharge signals must also be transferred between hemispheres. Oculomotor signals, like visual signals, are highly lateralized. Yet neurons in area LIP exhibit updating activity regardless of saccade direction (Heiser and Colby, 2003), and updating behavior is accurate when a saccade into one hemifield initiates updating within the opposite hemisphere (Heide et al., 1995). What pathways provide the substrate for these signals to travel between hemispheres?

Hypothesis: Forebrain commissures are necessary for communication between hemispheres during spatial updating

The forebrain commissures — the corpus callosum and anterior commissure — provide the most obvious

path for the interhemispheric transfer of both visual and oculomotor signals during spatial updating. The corpus callosum, with roughly half a billion fibers, constitutes the most prominent route for interhemispheric communication (Lamantia and Rakic, 1990; Houzel et al., 2002), and the anterior commissure provides an immediate link between virtually all visual areas in the temporal lobes (Jouandet and Gazzaniga, 1979; Demeter et al., 1990). Of particular interest for spatial updating are the extensive callosal connections between parietal cortices in each hemisphere, and between parietal cortex and areas in the frontal lobe (Pandya and Vignolo, 1969; Hedreen and Yin, 1981; Seltzer and Pandya, 1983; Petrides and Pandya, 1984; Schwartz and Goldman-Rakic, 1984). These direct corticocortical connections could support the rapid relay of visual and oculomotor signals required to influence receptive field properties in conjunction with saccades. The importance of the forebrain commissures is further suggested by neuropsychological evidence of their functional role. Studies of split-brain humans and monkeys have demonstrated the necessity of the corpus callosum and anterior commissure for the across-hemisphere integration of visual and visuomotor processes (Gross et al., 1977; Holtzman, 1984; Gazzaniga, 1987; Eacott and Gaffan, 1989; Trevarthen, 1990; Desimone et al., 1993; Corballis, 1995). In light of this anatomical and behavioral evidence, we reasoned that the forebrain commissures are critical for interhemispheric transfer of the signals involved in spatial updating.

We hypothesized that the forebrain commissures are necessary for communicating both visual and corollary discharge signals from one hemisphere to the other. In Part I, we asked whether the forebrain commissures are required when visual representations must be updated from one hemifield to the other. In Part II, we asked whether these commissures are required when spatial updating within a single hemifield is initiated by a saccade into the opposite hemifield.

Approach

We tested these hypotheses by measuring the behavioral and neural correlates of spatial updating in two rhesus macaques whose forebrain commissures were

surgically transected. We measured spatial behavior using the double-step task, a classic method for assessing subjects' ability to localize targets after an intervening saccade (Hallett and Lightstone, 1976; Mays and Sparks, 1980; Goldberg and Bruce, 1990). The subject must make eye movements to two successively flashed targets, T1 and T2 (Fig. 1A). The critical feature of this task is that the second target (T2) disappears before the eyes leave the initial fixation point. If the subject generates the sequence based only on the retinal location of the T2, the second saccade will be incorrect (Fig. 1B). For accurate performance of the sequence, the location of T2 must be updated in conjunction with the saccade to T1 (Fig. 1C). Subsequent to behavioral testing, we asked whether neurons in parietal cortex are active when remapping requires the communication of either visual or corollary discharge signals between hemispheres.

We evaluated the integrity of spatial updating in three conditions of the double-step task, illustrated in Fig. 2. (1) In the within condition (Fig. 2A), both visual and corollary discharge signals are communicated within the same hemisphere. The second target (T2) must be updated from one location to another within the same visual hemifield. This condition therefore requires a transfer of visual information between neurons in the same cortical hemisphere. Furthermore, the initiating saccade (the saccade to the first target, T1) is directed into the same visual field in which T2 is updated. As a result, the corollary discharge signal is generated by the same hemisphere in which the transfer of visual information occurs. We compared updating in the within-condition to updating in two interhemispheric conditions. (2) In the across-hemifield condition (Fig. 2B), T2 is updated from one visual hemifield to the other. This condition is also referred to as the *visual-across* condition, to emphasize that the visual representation of T2 must be updated across hemifields. (3) In the motor-across condition (Fig. 2C), like the within condition, the representation of T2 is updated within the same visual hemifield. The critical difference is the direction of the saccade that initiates spatial updating. In the motor-across condition, the initiating saccade to T1 is directed into the opposite hemifield. The corollary discharge signal therefore must be communicated interhemispherically, from the hemisphere generating

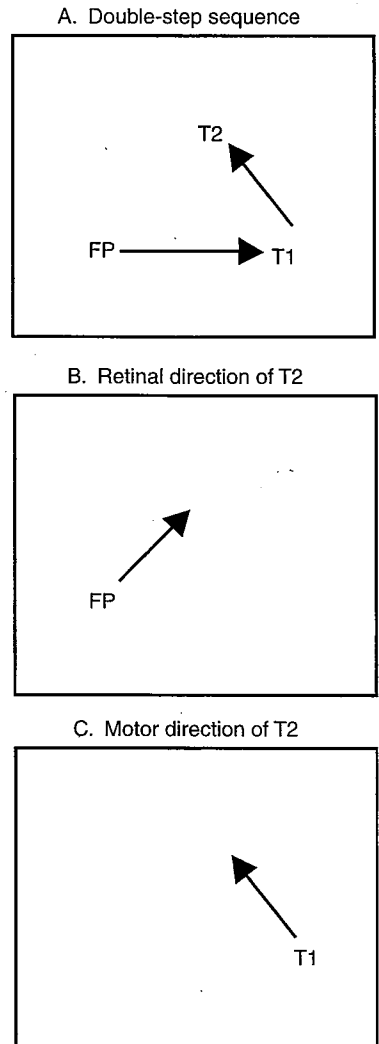


Fig. 1. Performance of the double-step saccade task requires spatial updating. (A) The double-step sequence. Subjects make two consecutive saccades, to the first target (T1) and then to the second target (T2). The second target appears very briefly, and so is visible only when the eyes are at initial fixation (FP). When the eyes are at fixation, the retinal location of T2 is up and to the right (B). If the subject generates this retinal saccade from T1, however, it will be inaccurate. For accurate completion of the sequence (C), the representation of T2 must be updated to take the saccade to T1 into account.

the saccade command, to the hemisphere in which the T2 representation is updated. This condition is referred to as *motor-across* to emphasize that spatial updating requires an interhemispheric transfer of

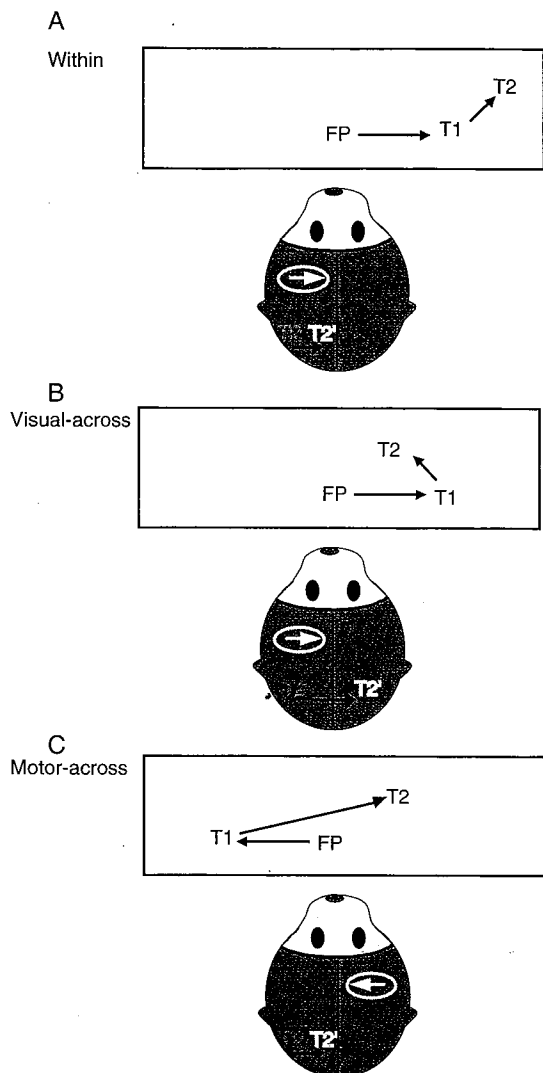


Fig. 2. Comparison of double-step conditions used to determine whether the forebrain commissures are required for interhemispheric transfer of visual and corollary discharge signals. In each condition, the monkey's task is to make a visually-guided saccade to T1, followed by a memory-guided saccade to T2. (A) In the within condition, T2 appears in the right visual field when the eyes are at FP. Its retinal location is represented by neurons in the left hemisphere (orange T2). When the eyes reach T1, T2 itself is gone, but a memory trace of T2 is still in the right visual field, encoded by neurons within the left hemisphere (yellow T2'). Updating therefore involves a transfer of visual signals between sets of neurons located within the same cortical hemisphere. The saccade that initiates this transfer — a rightward saccade — is also generated by the left hemisphere (white arrow). (B) In the visual-across condition, T2 appears in the right visual field when the eyes are at FP, but its memory trace is located in the left visual field once the eyes

oculomotor signals. We predicted that spatial updating in the split-brain monkey would be severely disrupted if not abolished in the visual-across and motor-across conditions, but not in the within-condition.

We designed the behavioral paradigms to incorporate controls for sensory, motor, and cognitive factors, as all training and testing were necessarily conducted after the commissurotomy to prevent infection. Once healing was complete, the animals were trained to perform the double-step task. In the first stage of training, we used vertical sequences, in which the first saccade was either straight up or straight down. Updating was therefore always within-hemifield. The monkeys were trained to perform interleaved vertical sequences at a minimum criterion of 75% correct, demonstrating a generalized understanding of the task. In the second stage of training, monkeys learned to perform a central condition in which the first saccade was horizontal (Fig. 3A, black lines). In the central sequences, T2 appeared directly above T1, so that the updated representation of T2 was available bilaterally and performance did not require interhemispheric transfer. Once the monkeys reached criterion on these sequences, we simultaneously introduced two novel test conditions: either within and visual-across (Part I) or within and motor-across (Part II). In each case, the conditions were matched in saccade amplitude and novelty, and counterbalanced for direction of the second saccade (e.g., Fig. 3A). Further, the sequences were randomly interleaved, so that the monkeys had to rely on an updated visual representation to complete each trial. This design isolated the difference of interest: accurate

reach T1. Consequently, updating in this condition involves a transfer of visual information between sets of neurons in opposite cortical hemispheres. (C) In the motor-across condition, T2 is updated within the same hemisphere, just as in panel A. The motor-across condition is distinguished by the direction of the initiating saccade. This leftward movement to T1 is generated by the opposite hemisphere (white arrow). Consequently, the corollary discharge signal from the right hemisphere must be relayed to visual areas in the left hemisphere. It was expected that performance of the visual-across and motor-across conditions, but not the within condition, would be impaired in the absence of the forebrain commissures.

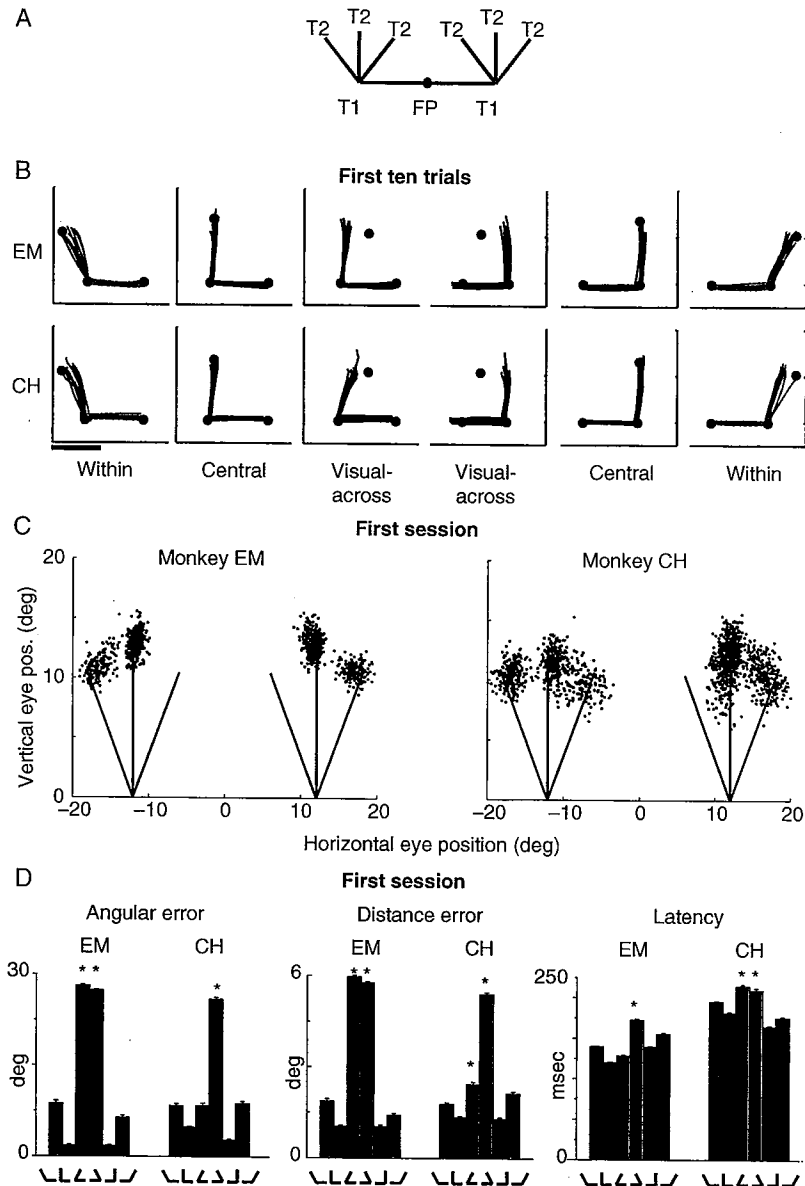


Fig. 3. Initial impairment of visual-across sequences. (A) The six randomly interleaved sequences of the double-step task: trained central sequences (black), novel within-hemifield (green) and visual-across (red) sequences. (B) Eye traces show double-step performance in the first ten trials of the first testing session, for monkey EM (top row) and monkey CH (bottom). Individual panels show the eye path for each sequence, in degrees of visual angle; scale bar represents 10° . Dots indicate the locations of the central fixation point, T1 and T2. The monkeys accurately performed the central and within conditions but demonstrated substantial impairment on the visual-across condition. (C) Second-saccade (S2) endpoints from the entire first testing session. For monkey EM (left), impairment on the visual-across condition persisted in both visual fields, throughout the first session. For monkey CH (right), performance of the visual-across sequence improved during the first session in the left but not the right visual field. (D) Quantitative measures of double-step performance in initial testing sessions. Each bar represents the mean value (\pm SE) of error or latency for one of the six sequences of the double-step task. In each panel, the first six bars are from monkey EM, second six from monkey CH. Bars are arranged according to the sequence locations (icons below). Black, central; green, within; red, across. Asterisks indicate significantly greater error or longer latency for the visual-across sequence as compared to matched central and within sequences.

double-step performance required a transfer of information either within or across hemispheres. We first asked whether spatial behavior was impaired when updating involved an interhemispheric transfer of visual information. Could these split-brain monkeys perform double-step sequences that required updating from one visual hemifield to the other?

Part I: The forebrain commissures are the primary path, though not the only path, for interhemispheric transfer of visual signals during spatial updating

Behavioral correlates of visual-across updating

We found that both monkeys exhibited a striking and selective deficit when performance of the double-step task required across-hemifield updating of the visual representation. This impairment is evident in the first ten trials of the first testing session (Fig. 3B). The monkeys were very accurate on the trained central sequences, as expected. Performance of the within condition was also accurate, even though the sequences were novel. In contrast, both monkeys made inaccurate eye movements on every trial of the first ten visual-across sequences. Saccade endpoints from the entire first session of testing demonstrate the visual-across impairment (Fig. 3C). For the central (black) and within sequences (green), endpoints are clustered near the correct T2 locations. For the visual-across sequences (red), however, most endpoints are clustered inaccurately near the central target location. These endpoint data also reveal an unanticipated finding: the beginning of recovery is already evident in the left hemifield of monkey CH.

We assessed the monkeys' initial double-step performance by analyzing the accuracy and latency of the second saccade for the entire first session of testing (~200 trials per condition, per monkey). We quantified accuracy using two measures: (1) angular error, the angular offset between the actual and target trajectory, and (2) distance error, the distance between the saccade endpoint and T2. Saccadic latency was computed as the time between the end of the first saccade and the beginning of the second saccade. We conducted two-way ANOVAs, separately for each monkey, to determine whether accuracy and latency measures depended significantly

on updating condition (central, within, or visual-across) or direction of the first saccade (right or left). Of greatest interest was the prospect that individual sequences of the visual-across condition were significantly impaired. Accordingly, we used post hoc analyses to compare performance of each visual-across sequence to that of three matched control sequences: the central sequence in the same visual field (matched for the first saccade), the within sequence in the same visual field (matched for novelty and the first saccade), and the within sequence in the opposite visual field (matched for novelty and the second saccade). If performance of the visual-across sequence was significantly worse than each of the matched controls, we concluded that the impairment reflected a deficit in spatial updating. We found significant impairment for each of the individual visual-across sequences, manifest in increased error, increased reaction time, or both (Fig. 3D; Tukey's HSD, $p < 0.05$). These data indicate a deficit in the split-brain monkeys' ability to update spatial locations across visual hemifields.

Three supporting lines of evidence demonstrate that this visual-across impairment is specific to disrupted updating in the absence of the forebrain commissures. First, humans and monkeys with the commissures intact can perform these sequences accurately (Li and Andersen, 2001; Jeffries et al., 2003; Zivotosky et al., 2003). Second, we found that the split-brain monkeys were not selectively impaired on single memory-guided saccades to the visual-across T2 locations. Thus, the visual-across impairment could not be attributed to any sensory, mnemonic, or motor deficits. Third, we determined that the monkeys could readily perform comparable double-step sequences when T2 was placed directly on the midline, and therefore was represented bilaterally. The monkeys' success in this midline paradigm demonstrates that the initial visual-across deficit did not reflect a general difficulty in reversing the direction of the second eye movement. These data support the conclusion that across-hemifield spatial updating is disrupted in the absence of the forebrain commissures.

Despite this initial deficit, both monkeys were able to learn to perform the visual-across sequences. Improvement occurred quite rapidly in some cases, as demonstrated by the first-session endpoints of

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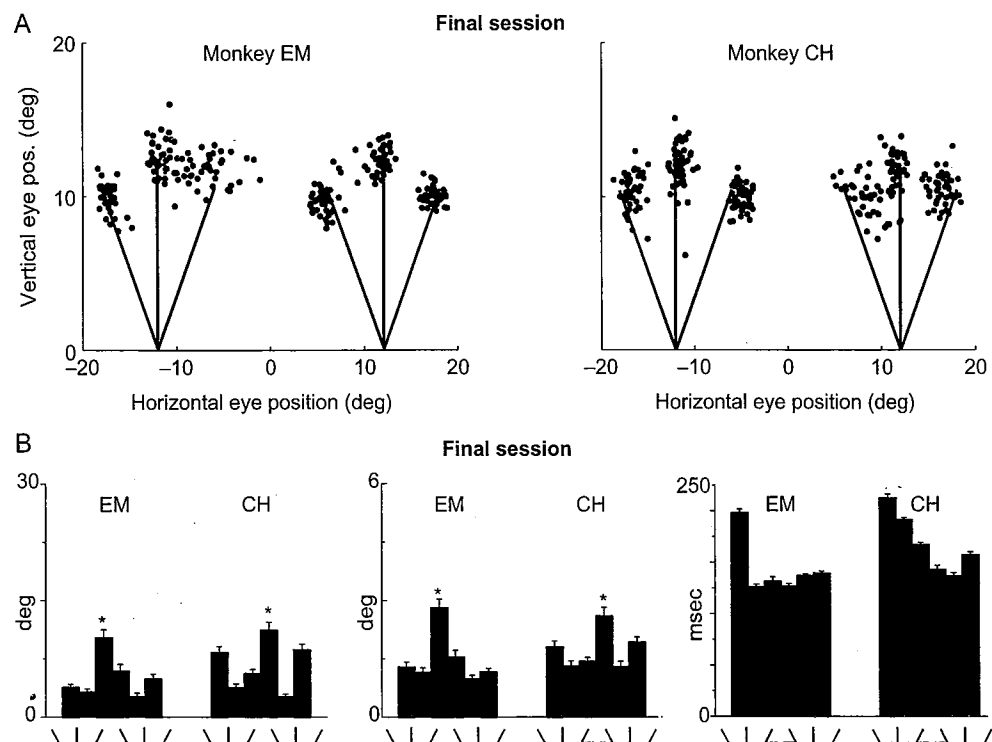


Fig. 4. Visual-across sequences can be learned. S2 endpoints (A) and quantitative data (B) show improved performance for visual-across sequences following multiple testing sessions (64 sessions for monkey EM, 27 sessions for monkey CH).

monkey CH (Fig. 4A). In the left visual field, many endpoints are clustered near the correct T2 location. These reflect the monkey's accurate performance, which emerged during the first 75 trials of this sequence. After multiple sessions of testing, performance of both visual-across sequences was relatively accurate for both monkeys (Fig. 4B). These findings indicate that, although the forebrain commissures serve as the primary route for interhemispheric updating, they are not the sole route.

Physiology of visual-across updating

The monkeys' ultimate success in performing the visual-across sequences implies the existence of neurons that update visual representations across hemispheres, even in the absence of the forebrain commissures. In the second stage of the experiment, we used single-unit recording to ask whether such

neurons are found in the lateral intraparietal area (LIP). We considered two possibilities. One is that across-hemifield updating in the split-brain animal is accomplished using circuitry entirely outside of parietal cortex. If this were the case, we would expect to observe no remapping activity in area LIP. Alternatively, neurons in parietal cortex might still be an integral component of the circuitry for the interhemispheric transfer of visual signals. In this case, we would expect LIP neurons to exhibit remapping activity for visual-across conditions. This second possibility seemed more probable in the light of evidence that parietal cortex is necessary for accurate spatial behavior in the double-step task (Duhamel et al., 1992b; Heide et al., 1995; Li and Andersen, 2001).

We tested these possibilities by recording from area LIP in these same monkeys during the single-step task. This task reveals the neural activity associated with updating a visual location when the eyes move

(Duhamel et al., 1992a). In each trial, the monkey makes a single saccade, bringing the neuron's receptive field onto a location where a stimulus has recently appeared (Fig. 5A). Critically, no physical stimulus ever appears in the receptive field. Rather, the neuron can be driven only by a memory trace of the stimulus, which has been updated in conjunction with the eye movement. We recorded from single neurons in LIP during two conditions of the single-step task, within and visual-across.

We found robust neural activity in area LIP for within-hemifield updating. The neuron shown in Fig. 5 exhibited a strong burst of activity even before the onset of the eye movement and continued to fire after completion of the saccade. Remarkably, this same neuron also fired for visual-across updating, though this activity began later and was less robust than within-hemifield activity. This neuron did not respond in any of corresponding control conditions. It did not fire when the stimulus was presented alone while the animal fixated centrally (Figs. 5G, H), nor when the animal generated the saccade alone, with no stimulus presented (Figs. 5J, K). The activity observed during the single-step task can be attributed only to remapping the memory trace of the flashed stimulus. These data demonstrate that neurons in area LIP can still participate in across-hemifield updating, despite the absence of the primary link between the cortical hemispheres.

At the population level, as in the single-unit example, remapping signals were present but reduced for the visual-across condition. We assessed the updating activity of 223 visually-responsive LIP neurons during a standard epoch (0–200 ms, beginning at saccade onset). None of the neurons responded in the stimulus-alone task, though some neurons exhibited a response in the saccade-alone task, likely due to remapping of the central fixation point. We adjusted for this activity by computing the average firing rate in the identical epoch of the saccade-alone control, and subtracting it from the average activity in the single-step task. This adjusted firing rate was computed identically for all conditions and represents the activity attributed to updating of the memory trace. We used this adjusted firing rate to ask two questions. First, is updating activity equally strong for visual-across and within conditions? We found that the magnitude of remapping was

significantly greater for the within as compared to the visual-across condition (Fig. 6A). Second, do the two conditions differ in the timecourse of neural activity? The latency of remapping was significantly delayed for visual-across as compared to within-conditions (Fig. 6B). These data show that visual representations can be updated from one hemisphere to the other in the absence of direct cortico-cortical links. The forebrain commissures, then, are not the sole mediators of across-hemifield updating. Nevertheless, the diminished strength and delayed latency of visual-across remapping provide clear evidence that the forebrain commissures are the predominant pathway for updating visual representations across hemispheres.

Part II: The forebrain commissures are not the primary path for interhemispheric transfer of motor signals

Behavioral correlates of motor-across updating

Our findings indicate that the forebrain commissures indeed serve as the primary route for transferring visual signals between the cortical hemispheres at the time of an eye movement. Are these same commissures also the primary route for relaying information about the impending eye movement, in order to initiate visuospatial updating? We addressed this question by testing the monkeys on a configuration that allowed us to compare performance of the within condition to the motor-across condition (Fig. 7A). In the motor-across condition, the representation of T2 is updated in the same hemifield, and thus the transfer of visual information is within-hemisphere. The corollary discharge signal that initiates the updating, however, is thought to arise in the opposite hemisphere. The conditions of interest, motor-across and within, were introduced after the monkey reached criterion of 75% correct on the central training sequences. We asked whether the monkeys were impaired selectively on the motor-across sequences.

We found that performance of the motor-across sequences was relatively unimpaired, as shown by the eye traces from the first ten trials (Fig. 7B). Both monkeys performed this sequence effortlessly, with one exception. Monkey EM made large errors in the

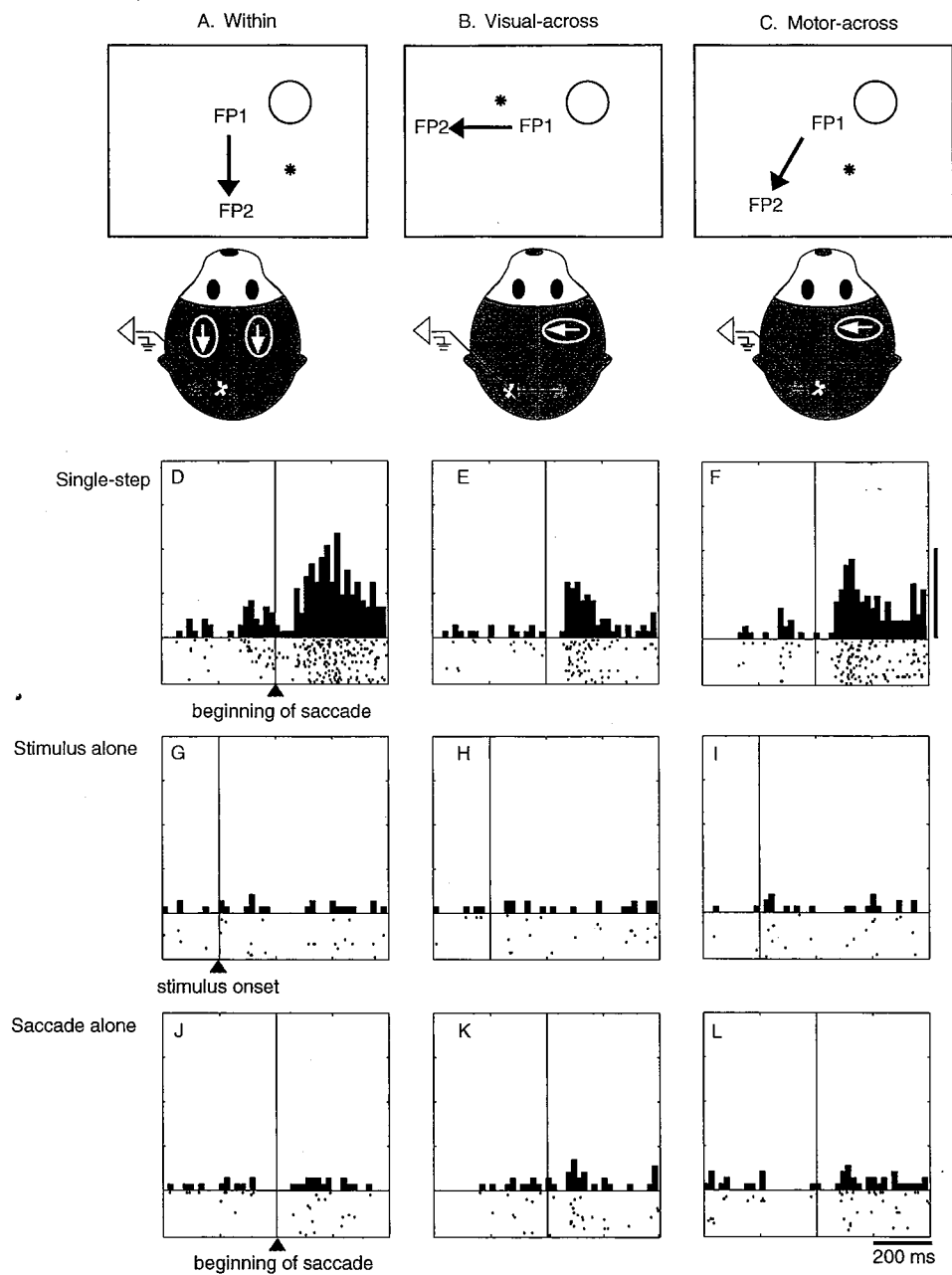


Fig. 5. Activity of a single neuron in the single-step and corresponding control tasks. Top panels show the spatial configurations for the within (A), visual-across (B), and motor-across (C) conditions. Spatial configurations are determined by the neuron's receptive field, located in the upper right quadrant; the neuron under study was located in the left hemisphere. Cartoons illustrate the presumed communication of signals required for spatial updating in each condition. The neuron fired briskly for all three conditions of the single-step task (D-F). The corresponding control conditions show that activity was minimal when the stimulus appeared alone (G-I) and when the saccade was generated in the absence of the stimulus (J-L). In each panel, the histogram shows summed activity in 18 ms bins. Rasters represent individual trials; each tic mark is a single action potential. The vertical bar to the right of F indicates a firing rate of 40 spikes per second.

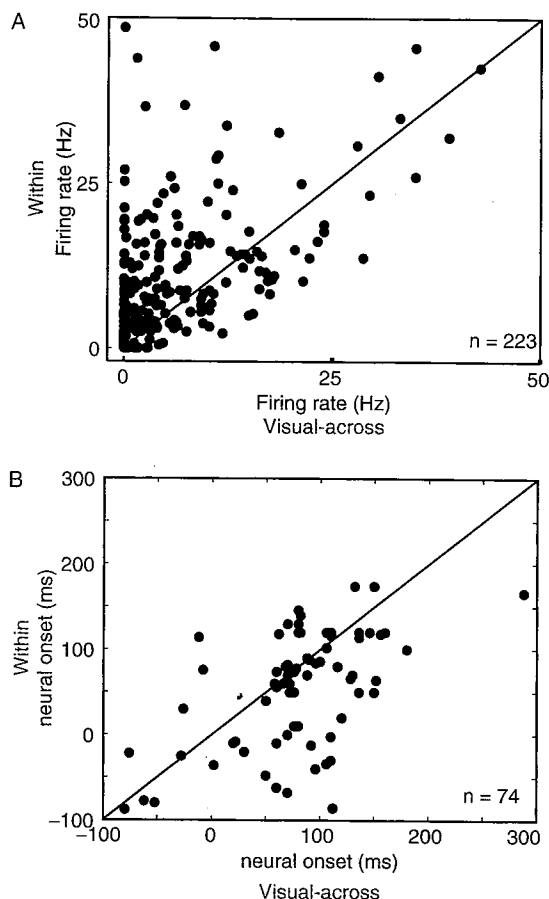


Fig. 6. Firing rate and neural latency for visual-across as compared to the within condition. Each point represents a single cell. (A) LIP neurons fire more strongly for updating within-hemifields as compared to across-hemifields. For each neuron, mean firing rate in the visual-across condition (x-axis) is plotted against mean firing rate in the within condition (y-axis). Firing rate was computed for each neuron using a 200 ms epoch, which began at saccade onset; mean firing rate during the single-step task was adjusted by subtracting mean firing rate during the same saccade-aligned epoch of the saccade-alone control task. Points falling along the unity line indicate that both single-step conditions elicited the same magnitude of remapping activity. Most points fall above the line, indicating that neurons fired more strongly for within-hemifield as compared to visual-across updating. (B) LIP neurons exhibit earlier remapping for the within as compared to the visual-across condition. For this analysis, we included only those neurons that met the following two criteria: first, the latency was definable for both the within and visual-across conditions; second, there was no significant activity in either control condition. Most points fall below the line, indicating that the onset of remapping activity occurred later for the visual-across condition.

first few motor-across trials in the right visual field. The monkey nevertheless learned this sequence rapidly, as is evident in the saccade endpoints from the entire session (Fig. 7C). Endpoints for the motor-across condition are clustered near the correct T2 location for all sequences, indicating that both animals were readily capable of performing the motor-across sequences as well as the within sequences.

The monkeys' overall success in performing the motor-across condition is evident in the measures of saccadic accuracy and latency (Fig. 7D). ANOVAs revealed a significant effect of updating condition for both monkeys, for both measures of accuracy (all $p < 0.001$). The pattern of conditional differences, however, did not reflect an overall impairment of the motor-across sequence. Rather, overall error values were increased for the within condition relative to both the central and motor-across conditions. We conducted post hoc analyses as for the visual-across experiments, asking whether the accuracy of each motor-across sequence was significantly worse than the accuracy of the matched central and within sequences. There was significant impairment for only one of the motor-across sequences (Fig. 7D). This was the sequence in the right field, which monkey EM had initially performed incorrectly (Fig. 7B). The remaining motor-across sequences were not significantly less accurate than their matched counterparts.

We considered the possibility that, despite the monkeys' accurate performance, the reaction times for the second saccade might still be slowed for the motor-across condition as compared to the within condition. It was found that latencies for the motor-across sequences were either equivalent to, or faster than, those of the controls; none were significantly prolonged relative to matched central and within sequences ($p > 0.05$, Tukey's HSD). This finding, in concert with the accuracy data, indicates that performance of the motor-across double-step task is only minimally disrupted in the absence of the forebrain commissures.

Why was overall performance better for the motor-across sequences than the visual-across sequences? The most parsimonious explanation is that the transfer of motor signals, unlike that of visual signals, is not typically accomplished via the

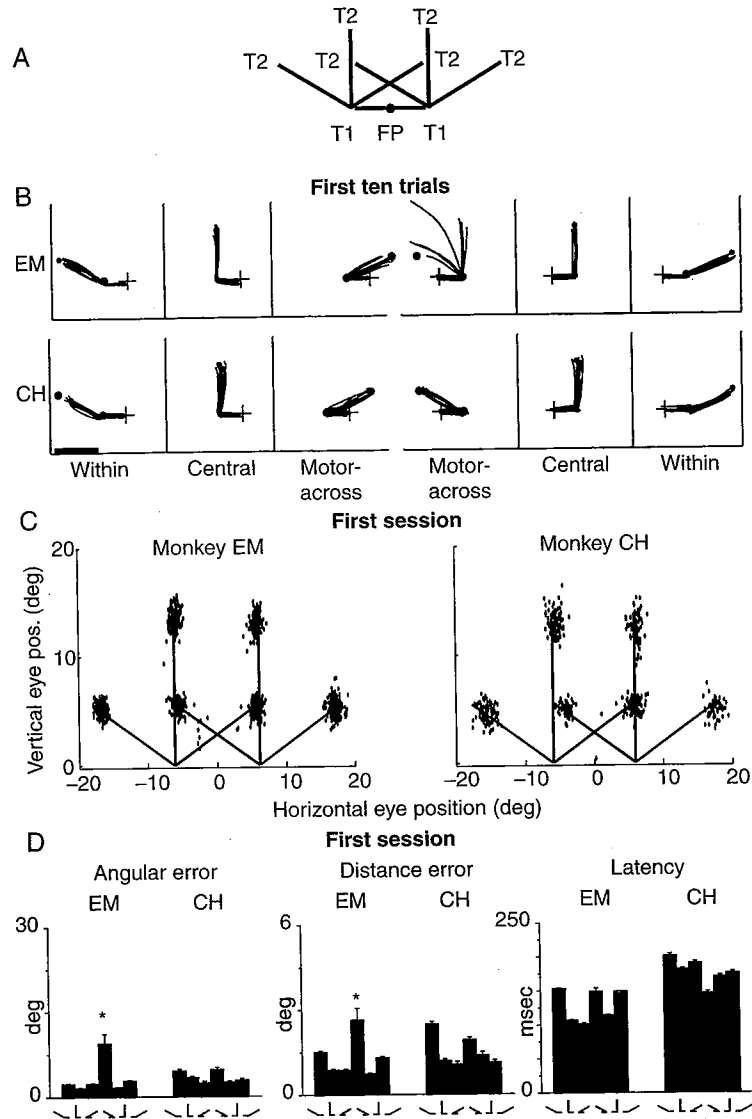


Fig. 7. Initial performance of visual-across sequences. (A) The six randomly interleaved sequences of the double-step task: trained central sequences (black), novel within (green) and motor-across (blue) sequences. (B) Eye traces show that performance of motor-across sequences was relatively unimpaired as compared to within sequences. Individual panels show the eye path, in degrees of visual angle, for the first ten trials of each sequence; conventions as in Fig. 3. Monkey EM made initial errors in the motor-across condition in the right visual field, but began to adjust the trajectory toward the target as the trials progressed. (C) Second-saccade endpoints from the entire first testing session for the motor-across condition. (D) Quantitative measures of double-step performance in the initial motor-across testing session. Each bar represents the mean value (\pm SE) of error or latency for one of the six sequences of the double-step task. In each panel, the first six bars are from monkey EM, second six from monkey CH. Bars are arranged according to the sequence locations (icons below). Black, central; green, within; blue, motor-across. Asterisks indicate significantly greater error or longer latency for the motor-across sequence as compared to matched central and within sequences.

forebrain commissures. Before reaching this conclusion, however, we needed to rule out an alternative explanation, which emerged from the use of different configurations for the motor-across and visual-across testing. The motor-across sequence may have been easier due to the different spatial location of T2 or the metrics of the first saccade. We addressed this

possibility by employing a new spatial configuration, in which the motor-across and visual-across sequences were directed to the identical T2 location. The sequences were also matched for the amplitude of the first saccade, and were interleaved randomly with the central sequences in the same session (Fig. 8A). We conducted this experiment in monkey EM,

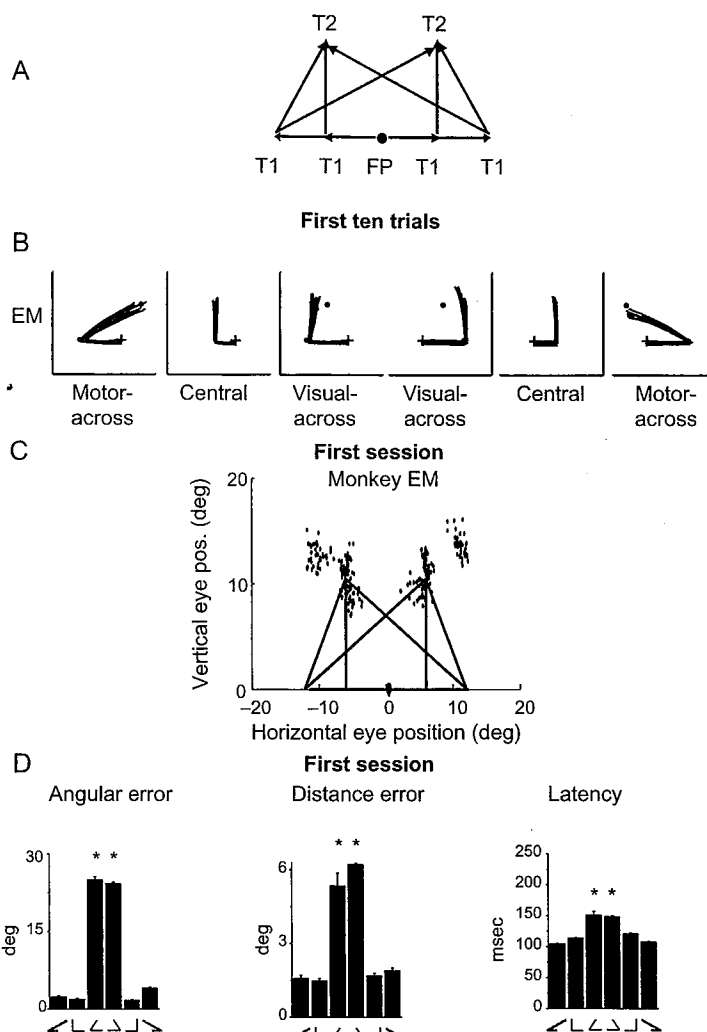


Fig. 8. Performance of visual-across sequences is impaired when tested directly against motor-across sequences. (A) The six randomly interleaved sequences of the double-step task: trained central sequences (black), novel visual-across (red) and motor-across (blue) sequences. (B) Eye traces show that performance of motor-across sequences was unimpaired as compared to visual-across sequences. Individual panels show the eye path, in degrees of visual angle, for the first ten trials of each sequence; conventions as in Fig. 3. (C) Second-saccade endpoints from the entire testing session that directly compared visual-across and motor-across conditions. (D) Quantitative measures of double-step performance. Asterisks indicate significantly greater error or longer latency for the visual-across sequence as compared to matched central and motor-across sequences.

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The monkey was able to perform the double-step task accurately for the motor-across but not the visual-across sequences. This dissociation is evident in the first ten trials, in the saccade endpoint data from the entire testing session (Fig. 8B), and in the measures of accuracy and latency (Fig. 8D). We compared the accuracy of individual sequences using the standard post hoc procedure, except that each visual-across sequence was now compared to its matched central and *motor-across* (rather than within) sequences. We found that both angular and distance error were significantly greater for the visual-across condition, for both visual fields. This indicates that the split-brain monkey could accurately reach the location of the second target when updating was within-hemifield, even though the saccade that initiated updating was directed into the opposite hemifield. By contrast, the very same target location was not attained when updating was across-hemifield. The relative lack of impairment for motor-across sequences suggests that the forebrain commissures are not the primary path for relaying information about an upcoming saccade to cortical areas representing visual locations.

Physiology of motor-across updating

Finally, we asked whether LIP neurons are active when updating requires the interhemispheric transfer of corollary discharge signals. In our behavioral experiments, we found that the monkeys were effectively unimpaired when performing the motor-across condition of the double-step task. We therefore expected that LIP neurons would exhibit robust updating activity in the motor-across condition of the single-step task.

We observed significant updating activity in the motor-across condition of the single-step task. An example neuron is shown in Fig. 5. We previously described this neuron's activity in the within (Fig. 5D) and visual-across conditions (Fig. 5E), noting that it exhibited remapping in both conditions, though activity was reduced in the visual-across condition. This same neuron had strong and significant activity in the motor-across condition (Fig. 5F).

We assessed the strength of remapping in the motor-across condition in a population of 116 LIP neurons (Fig. 9). We first compared the within and motor-across conditions were compared (Fig. 9A), plotting the average firing rates against one another and asking whether activity was greater for the within condition (y-axis) than the motor-across condition (x-axis). Most points fall near the unity line, representing equivalent firing for the two conditions. We nevertheless found a significant diminution of activity in the motor-across condition (average of 12.3 Hz, compared to 13.8 Hz in the within condition, adjusted firing rates, $p < 0.05$, paired t -test). The small difference in firing rate between these conditions (1.5 Hz on average) indicates a slight yet systematic reduction in remapping activity for the motor-across as compared to the within condition. We next asked whether activity in the motor-across condition differed significantly from that in the visual-across condition (Fig. 9B). We found that neural activity was significantly stronger for the motor-across condition (12.3 Hz, compared to 8.4 Hz in the visual-across condition; $p < 0.0001$, paired t -test). This difference is apparent in Fig. 9B, in which a majority of points fall above the unity line, indicating stronger remapping in the motor-across condition.

These observations indicate that LIP neurons in the split-brain monkey exhibit robust remapping when corollary discharge signals must be relayed between hemispheres: activity in the motor-across condition was only slightly diminished relative to the within condition. Direct comparison of the two interhemispheric conditions — motor-across and visual-across — demonstrated that remapping signals in LIP were significantly stronger in the motor-across condition. We concluded that the interhemispheric transfer of corollary discharge signals, unlike that of visual signals, is relatively unaffected by the absence of the forebrain commissures.

Subcortical and cortical areas contribute to remapping

Transfer of visual signals

Our behavioral and physiological findings indicate that the across-hemispheric updating of visual

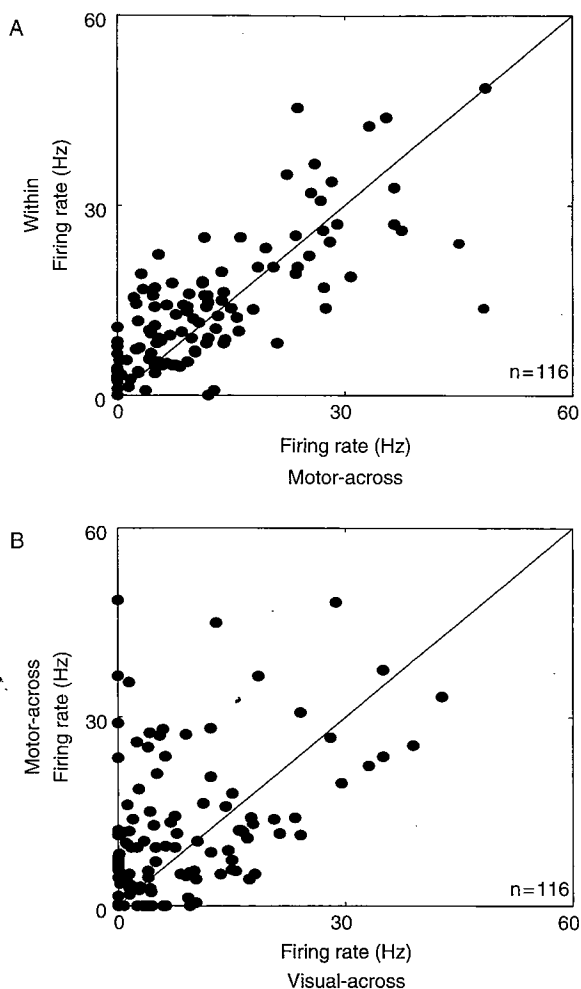


Fig. 9. Remapping activity in the single-step task, for the motor-across condition as compared to the within condition (A) and visual-across condition (B). When average remapping activity in the motor-across condition (x-axis) is plotted against activity in the within condition (y-axis), the distribution of points is primarily centered on the unity line. More points fall above the line, indicating slightly higher firing rates for the within condition (mean = 13.8 Hz for within, 12.3 Hz for motor-across, $p < 0.05$). In B, when remapping activity in the motor-across condition (y-axis) is compared to that of the visual-across condition (x-axis) most points fall above the unity line (mean = 12.3 Hz for motor-across, 8.4 Hz for visual-across, $p < 0.0001$). These data show that, on average, the motor-across condition elicited remapping activity that was slightly diminished in magnitude compared to that of the within condition, and substantially greater than that of the visual-across condition.

representations is compromised in the absence of the forebrain commissures. In behavioral experiments, we found that split-brain monkeys exhibited an initial impairment in performance of double-step sequences that required updating across visual hemifields. In physiological experiments, we found that remapping activity in LIP was less robust when visual information had to be transferred across hemifields as compared to within. These deficits indicate that the forebrain commissures provide a principle, direct route for visual information to be updated from one hemisphere to the other. Despite these clear deficits, however, remapping was not abolished as was expected. Instead, we observed an ultimate recovery of function in spatial behavior, as measured by the double-step task. This behavioral success was paralleled by our discovery in subsequent recording studies that parietal neurons exhibited significant remapping when across-hemisphere transfer of visual information was required. Additional pathways must be recruited to transmit information from one hemisphere to the other.

What brain structures participate in across-hemifield updating in the absence of the forebrain commissures? The superior colliculus (SC) likely plays an important role. Neurons in the intermediate layer of the SC demonstrate remapping activity (Walker et al., 1995). In the normal monkey, this activity is thought to be a reflection of signals generated in parietal cortex, which is considered to be critical for spatial updating (Duhamel et al., 1992b; Heide et al., 1995; Quaia et al., 1998; Li and Andersen, 2001). In the split-brain monkey, the updated visual representation may still be constructed in LIP, by use of a more circuitous route, and imposed on the SC. Alternatively, remapping activity in LIP may reflect processes that originate in the SC.

The SC, via the intertectal commissures, is an obvious candidate for supporting interhemispheric visual transfer in the absence of the forebrain commissures (Moschovakis et al., 1988; Munoz and Istvan, 1998; Olivier et al., 1998). Yet it is one among many structures that may participate in across-hemifield remapping. The pulvinar nucleus of the thalamus is another such structure. The pulvinar is thought to contribute to visual, oculomotor, and attentional functions (Robinson, 1993), and has been implicated as a conduit for interhemispheric transfer in the

absence of the forebrain commissures (Corballis, 1995). Remapping has not yet been investigated in the pulvinar, but it is interconnected with areas that exhibit remapping (Hardy and Lynch, 1992; Lynch et al., 1994). Furthermore, its visual responses can be modulated by extraretinal signals — possibly corollary discharge signals — related to saccades (Robinson and Petersen, 1985). These findings demonstrate that the functional properties of the pulvinar are consistent with contributing to spatial updating.

The connectivity of the pulvinar suggests two main ways in which it could transmit information for remapping. First, the pulvinar may act as an ascending link between superior colliculus and cortex (Benevento and Fallon, 1975; Hardy and Lynch, 1992; Clower et al., 2001; Stepniewska et al., 2000). This ascending route has long been considered as a second visual pathway for visual sensory signals to reach the cortex (Diamond and Hall, 1969), and physiological studies have emphasized the notion that it conveys cognitive signals, particularly those related to visual attention (Robinson, 1993; Bender and Youakim, 2001; Wurtz et al., this volume). Second, the pulvinar may provide a transthalamic link between cortical areas involved in remapping. This compelling possibility emerges from studies indicating that much of the pulvinar receives its driving input from cortical rather than subcortical structures (Bender, 1983; Feig and Harting, 1998; Guillery et al., 2001; Van Horn and Sherman, 2004). This connectivity has led to the proposal that the pulvinar is a higher-order thalamic nucleus: it does not simply relay information from subthalamic regions to the cortex, but rather, is primarily involved in transmitting and modifying complex signals between cortical areas (Guillery, 1995; Guillery and Sherman, 2002a). It is intriguing to consider how these cortico-thalamocortical paths may contribute to spatial updating, both in the normal and in the split brain.

Our discussion of the circuitry for transferring visual signals in the split-brain monkey has focused on the superior colliculus and pulvinar, but this is by no means an exhaustive consideration of possible pathways. In all likelihood, a broad network of regions, both cortical and subcortical, must work together to carry out interhemispheric remapping of

visual representations when the predominant pathways — the forebrain commissures — are absent.

Transfer of motor signals

In contrast to our observations on transfer of visual signals, our behavioral and physiological findings indicate that transection of the forebrain commissures has only a minimal effect on the communication of the corollary discharge signals that initiate spatial updating. Both monkeys easily performed the condition of the double-step task that required an interhemispheric transfer of this oculomotor information. Likewise, neurons in area LIP had strong remapping activity in this condition.

How are corollary discharge signals readily transmitted between the two hemispheres in the absence of the forebrain commissures? Studies in split-brain humans have suggested that the disconnected hemispheres are capable of generating eye movements in both directions (Holtzman, 1984; Hughes et al., 1992). This claim is further supported by the observation that hemispherectomy patients can make bidirectional saccades (Sharpe et al., 1979). Hughes et al. postulated that, in split-brain subjects, there is either an ipsilateral representation of oculomotor commands at the cortical level, or a subcortical transfer of information. If ipsilateral saccade representations are present in the cortex of the split-brain monkey, they provide a ready explanation for the relative ease of updating observed in our experiments. In effect, updating in this condition would be accomplished easily because the transfer of corollary discharge signals is intrahemispheric. Physiological studies provide scant evidence, however, that the cortical eye fields represent ipsiversive saccades.

A growing body of evidence favors a role for subcortical pathways in relaying the corollary discharge signals required for spatial updating. One of the most promising is the ascending path from the superior colliculus to the frontal eye field (FEF). Anatomical and microstimulation studies have shown that neurons in the intermediate layer of the SC project to the FEF via the mediodorsal thalamus (Lynch et al., 1994; Sommer and Wurtz, 1998). These projections are predominantly ipsilateral. In other words, information about a rightward saccade is

represented in the left hemisphere, at the level of SC and at the level of cortex.

Of direct relevance to our results, stimulation studies have recently identified a *crossed* pathway from the SC to the FEF. In a population of FEF neurons receiving input from the SC, roughly 20% of the cells received projections from the contralateral SC (M. Sommer, personal communication). This crossed ascending path could serve to transmit a corollary discharge signal interhemispherically, in both the normal and the split-brain monkey. In other words, a copy of the command to make a rightward saccade — generated in the left SC — could be sent to the right FEF. This corollary discharge command could then act upon visual representations in the right cortical hemisphere, potentially in area LIP. An alternate possibility is that the corollary discharge signal generated in one SC could cross at the level of the intertectal commissures, then travel via the uncrossed ascending tectocortical pathway. Either route could support the accurate updating observed in the present study. The anatomical basis of corollary discharge signals is an active area of research (Guillery and Sherman, 2002b; Guillery, 2003; Sommer and Wurtz, 2002, 2004a,b). These signals may arise from many brain structures, both cortical and subcortical. Our findings indicate that information about our impending eye movements is readily available to modify visual representations in each of the cortical hemispheres.

Conclusion

The phenomenon of remapping, in which visual representations are updated in conjunction with saccades, demonstrates the influence of motor signals on perceptual processing. When a command is issued to move the eyes, a corollary discharge of this command is sent to visual areas, inducing a transfer of visual information from neurons that represent a salient location before the saccade, to those that will represent the location after the saccade. We have used behavioral and physiological methods to investigate the circuitry underlying the transfer of these visual and motor signals between hemispheres.

The central implication of our findings is that direct cortico-cortical paths — the forebrain

commissures — are differentially involved in the communication of visual as compared to motor signals in spatial updating. These commissures are likely the primary conduit for the transfer of visual signals from one hemisphere to the other. They are not, however, strictly necessary. Our findings indicate that subcortical pathways play an important role in the recovery of function, and are sufficient to support across-hemifield updating when the direct cortico-cortical paths have been removed. In contrast, the forebrain commissures do not appear to be the primary route for the transfer of motor signals in spatial updating. It appears that subcortico-cortical circuits can readily communicate corollary discharge signals to visual areas in both cortical hemispheres. Together, these conclusions emphasize the idea that spatial updating is subserved by a network of cortical and subcortical structures, in which motor signals can act upon visual information to create a stable representation of the external world.

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