

Rebecca A. Berman, Laura M. Heiser, Richard C. Saunders and Carol L. Colby
J Neurophysiol 94:3228-3248, 2005. First published May 11, 2005; doi:10.1152/jn.00028.2005

You might find this additional information useful...

This article cites 69 articles, 24 of which you can access free at:

<http://jn.physiology.org/cgi/content/full/94/5/3228#BIBL>

This article has been cited by 1 other HighWire hosted article:

Dynamic Circuitry for Updating Spatial Representations. III. From Neurons to Behavior

R. A. Berman, L. M. Heiser, C. A. Dunn, R. C. Saunders and C. L. Colby

J Neurophysiol, July 1, 2007; 98 (1): 105-121.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

Updated information and services including high-resolution figures, can be found at:

<http://jn.physiology.org/cgi/content/full/94/5/3228>

Additional material and information about *Journal of Neurophysiology* can be found at:

<http://www.the-aps.org/publications/jn>

This information is current as of November 29, 2007 .

Dynamic Circuitry for Updating Spatial Representations. I. Behavioral Evidence for Interhemispheric Transfer in the Split-Brain Macaque

Rebecca A. Berman,¹ Laura M. Heiser,¹ Richard C. Saunders,² and Carol L. Colby¹

¹Department of Neuroscience and Center for the Neural Basis of Cognition, University of Pittsburgh, Pittsburgh, Pennsylvania; and

²Laboratory of Neuropsychology, National Institute of Mental Health, Bethesda, Maryland

Submitted 10 January 2005; accepted in final form 4 May 2005

Berman, Rebecca A., Laura M. Heiser, Richard C. Saunders, and Carol L. Colby. Dynamic circuitry for updating spatial representations. I. Behavioral evidence for interhemispheric transfer in the split-brain macaque. *J Neurophysiol* 94: 3228–3248, 2005. First published May 11, 2005; doi:10.1152/jn.00028.2005. Internal representations of the sensory world must be constantly adjusted to take movements into account. In the visual system, spatial updating provides a mechanism for maintaining a coherent map of salient locations as the eyes move. Little is known, however, about the pathways that produce updated spatial representations. In the present study, we asked whether direct cortico-cortical links are required for spatial updating. We addressed this question by investigating whether the forebrain commissures—the direct path between the two cortical hemispheres—are necessary for updating visual representations from one hemifield to the other. We assessed spatial updating in two split-brain monkeys using the double-step task, which involves saccades to two sequentially appearing targets. Accurate performance requires that the representation of the second target be updated to take the first saccade into account. We made two central discoveries regarding the pathways that underlie spatial updating. First, we found that split-brain monkeys exhibited a selective initial impairment on double-step sequences that required updating across visual hemifields. Second, and most surprisingly, these impairments were neither universal nor permanent: the monkeys were ultimately able to perform the across-hemifield sequences and, in some cases, this ability emerged rapidly. These findings indicate that direct cortical links provide the main substrate for updating visual representations, but they are not the sole substrate. Rather, a unified and stable representation of visual space is supported by a redundant cortico-subcortical network with a striking capacity for reorganization.

INTRODUCTION

We explore the visual world by directing our gaze to locations of interest. The simple act of moving our eyes, however, introduces a complex problem. With each eye movement, the brain receives a new snapshot of the world around us. We nevertheless perceive the visual world as stable and can effortlessly localize objects despite intervening eye movements. How does the brain achieve this spatial constancy? Many mechanisms must contribute to the construction of a dynamic representation of space that can take self-generated movements into account. Of particular interest is the finding that neurons can update or “re-map” stimulus traces in conjunction with saccades (Duhamel et al. 1992a; Goldberg and Bruce 1990; Mays and Sparks 1980; Nakamura and Colby 2002; Umeno and Goldberg 1997, 2001; Walker et al. 1995). Remapping involves a transfer of visual information from neurons that

represent a stimulus location before the eyes move, to those that represent the location after the eye movement. The result is an internal representation of space that is in register with incoming retinal information—a representation that can contribute to spatial constancy. Relatively little is known about the pathways that underlie the communication of visuospatial signals necessary for updating.

The overarching aim of this research is to elucidate the neural pathways necessary for updating spatial representations when the eyes move. In this first study, we used behavioral methods to assess the necessity of direct cortico-cortical links in spatial updating. We used a simple behavioral task, the double-step saccade task, which reveals the brain’s capacity to construct a dynamic map of space that takes eye movements into account. In this task, subjects make consecutive saccades to two briefly appearing targets (Hallett and Lightstone 1976). The crucial feature of this task is that the second target is visible only when the eyes are at the initial fixation point. Consequently, there is a disparity between the initial retinal coordinates of the second target and the ultimate motor coordinates required to make a saccade to the location of this remembered target. Accurate double-step performance requires that the stimulus trace of the second target be updated in conjunction with the first saccade. Both humans and monkeys can accurately perform the double-step task (Gnadt and Andersen 1988; Goldberg and Bruce 1990; Hallett and Lightstone 1976; Mays and Sparks 1980). Furthermore, performance of the double-step task is accurate even when the second target must be updated from one visual hemifield to the other (Baizer and Bender 1989; Becker and Jurgens 1979; Dassonville et al. 1995; Goldberg et al. 1990; Jeffries et al. 2003; Li and Andersen 2001; Zivotofsky et al. 2003). This across-hemifield updating presumably requires a transfer of information between neurons in opposite hemispheres, given that the representation of visual stimuli is highly lateralized (Trevarthen 1990). We took advantage of this lateralization to investigate the role of direct cortico-cortical pathways in spatial updating.

We hypothesized that the forebrain commissures—the corpus callosum and anterior commissure—serve as the primary path for updating the representations of visual stimuli from one hemifield to the other. The corpus callosum, with roughly half a billion fibers, constitutes the most prominent route for interhemispheric communication (Houzel et al. 2002; Lamantia and Rakic 1990). The corpus callosum and anterior commissure provide extensive links between visuospatial and oculomotor

Address for reprint requests and other correspondence: C. L. Colby, 115 Mellon Institute, 4400 5th Ave, Pittsburgh, PA 15213 (E-mail: ccolby@cnbc.cmu.edu).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

areas in each hemisphere (Demeter et al. 1990; Hedreen and Yin 1981; Jouandet and Gazzaniga 1979; Pandya and Vignolo 1969; Schwartz and Goldman-Rakic 1984; Seltzer and Pandya 1983). The absence of these commissures has important functional consequences, both for neural processing and for behavior. The corpus callosum and anterior commissure contribute critically to the receptive field properties of individual neurons in striate cortex and in the ventral stream (Berlucchi and Rizzolatti 1968; Desimone et al. 1993; Gross et al. 1977). Furthermore, the commissures are necessary for integrating visual stimuli across hemifields, especially form and color information (Corballis 1995; Eacott and Gaffan 1989; Gazzaniga 1987; Gazzaniga et al. 1962; Land et al. 1983; Trevarthen 1990). Behavioral evidence from split-brain and acallosal humans indicates that information about spatial locations can be transferred between hemispheres in the absence of the corpus callosum, but only in limited circumstances and with coarse spatial resolution (Corballis 1995; Hines et al. 2002; Holtzman et al., 1981, Holtzman 1984; Reuter-Lorenz and Fendrich 1990). We asked whether stimulus traces can be accurately and precisely updated from one hemisphere to the other, when all direct links between the cortical hemispheres are severed. Our expectation at the outset of these experiments was that across-hemifield spatial updating would be abolished in the absence of the forebrain commissures.

We tested this prediction by measuring the performance of split-brain monkeys on two conditions of the double-step task. In the across-hemifield condition (Fig. 1A), updating requires a transfer of visual information between neurons in opposite hemispheres. In the within-hemifield condition (Fig. 1B), updating involves a transfer of visual information between sets of neurons within the same hemisphere. We expected that split-brain monkeys would exhibit selective impairment on the across-hemifield but not the within-hemifield condition. We found that across-hemifield updating could be profoundly impaired after transection of the commissures. Nevertheless, performance in these double-step sequences recovered substan-

tially. We carried out five sets of experiments to characterize the initial deficits and unexpected recovery of the behavior associated with across-hemifield updating in the split-brain monkey.

METHODS

Subjects

Subjects were three adult rhesus macaques, two male and one female, weighing 6.5–7.5 kg. Two monkeys, designated EM and CH, underwent a commissurotomy to remove the corpus callosum and anterior commissure. In the third monkey, FF, these commissures were intact. All experimental protocols were approved by the University of Pittsburgh Institutional Animal Care and Use Committee and were certified to be in compliance with guidelines set forth in the Public Health Service Guide for the Care and Use of Laboratory Animals.

The commissurotomy was performed at the outset of the experiment. This surgery is extremely invasive, requiring exposure of the cranial cavity, which leaves the brain vulnerable to infection. The surgery is riskier still because it requires transection of a deep structure, the anterior commissure. For these reasons, it was critical for us to take every precaution to minimize the risk of infection. Had we installed even a small cranial implant before the commissurotomy, this would have resulted in a less than sterile surgical field and compromised the chances for recovery. Accordingly, we installed an implant for behavioral testing only after the commissurotomy, when healing was complete. Details of the surgical procedure can be found in Vogels et al. (1994). The monkeys were prepared for this surgery with dexamethasone, and anesthesia was induced with ketamine and maintained with isoflurane. Mannitol was administered throughout the surgery to minimize tissue swelling. Under sterile conditions, a bone flap was made and the underlying dura turned to allow access to the corpus callosum with gentle retraction of the right hemisphere. The callosus was transected along its full length using a small glass pipette with suction. The anterior commissure was viewed through the third ventricle and then transected. After completing the transection of the forebrain commissures, the dura was returned and the bone flap sewn back into position. In the 2 wk after the surgery, analgesics were given to control postsurgical pain and antibiotics were administered daily to prevent infection.

The complete transection of the anterior commissure and corpus callosum was verified by direct vision at the time of surgery. Several months after the surgery, we used magnetic resonance (MR) imaging to confirm the absence of the commissures in coronal images spanning the entire anterior–posterior extent of cortex. Structural MR images were acquired using the 4.7-T magnet at the Pittsburgh NMR Center. Images from a normal monkey and from the split-brain monkeys are shown in Fig. 2, A–C.

After recovery, the animals were prepared for behavioral training. Under general anesthesia (induced with ketamine and maintained with isoflurane), scleral search coils were implanted for monitoring eye position (Judge et al. 1980), and head restraint bars were affixed for the purpose of holding the head stable during testing sessions (Nakamura and Colby 2000). This procedure could not be conducted until the skull was fully healed. The time between the commissurotomy and the beginning of behavioral training was 2 mo for monkey CH and 7 mo for monkey EM.

Stimuli

During behavioral sessions, the monkey sat with its head fixed in a primate chair, in a darkened room. The monkey faced a tangent screen, which subtended about 100° horizontally and 75° vertically. Visual stimuli were back-projected onto the screen using an LCD projector. Stimulus presentation was under the control of two computers running a C-based program, CORTEX, made available by R.

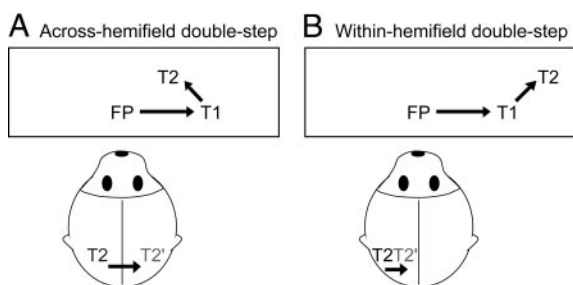


FIG. 1. Comparison of double-step saccade conditions that require the second target representation to be updated across or within visual hemifields. In each condition, the monkey's task is to make a visually guided saccade to T1, followed by a memory-guided saccade to T2. In the across-hemifield condition (A), T2 appears in the right visual field when the eyes are at the central fixation point (FP), and therefore is initially represented by neurons in the left hemisphere (black T2). When the eyes reach T1, however, the memory trace of T2 is now located in the left visual field. This location is encoded by neurons in the right hemisphere (gray T2'). Consequently, updating in this condition must involve an interhemispheric transfer of visual information. In the within-hemifield condition (B), T2 appears in the right visual field when the eyes are at FP; the memory trace of T2 is still in the right visual field when the eyes reach T1. Updating therefore involves communication between sets of neurons within the same cortical hemisphere. We expected that, in the absence of the forebrain commissures, performance of the across-hemifield condition would be selectively impaired.

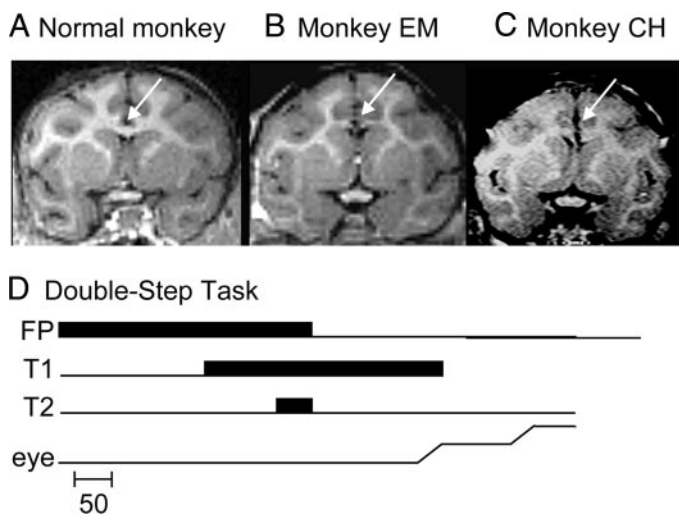


FIG. 2. Verification of commissurotomy (A–C) and timing of the double-step saccade task (D). A: coronal magnetic resonance (MR) images from a normal monkey. B and C: comparable images from split-brain monkeys EM and CH. Arrows point to the location of the corpus callosum (A) or its absence (B, C). D: events of the standard double-step task (see METHODS).

Desimone at the National Institutes of Mental Health. In the double-step task, the critical feature is that the monkeys have retinal information about the second target (T2) only when the eyes are at central fixation; once the eyes reach the first target (T1) they must rely on an updated representation of the stimulus trace to generate the second saccade. It was therefore important to demonstrate that the T2 stimulus had disappeared before the monkeys initiated the first saccade to T1. To do this, we used a photodiode to measure the phosphorescence of the briefly flashed T2 stimulus. The stimulus did not vanish instantaneously when it was turned off, but decayed to half its luminance with a time constant of 8 ms. We then calculated the luminance threshold for each monkey, using a memory-guided saccade task (Hikosaka and Wurtz 1983). By gradually dimming the flashed stimulus, we determined the luminance at which the monkey could no longer generate saccades to the location of the flashed stimulus. For all three monkeys, the stimulus fell below perceptual threshold within 40 ms of its extinction. On average, the monkeys took 152.5 ms (± 36.4 ms SD) to initiate the first saccade (S1), and minimum acceptable S1 latency was 50 ms. These observations indicate that the monkeys had access to retinal information about the T2 stimulus only when the eyes were fixated centrally; correct performance on the double-step task thus relied on updating the stimulus trace of T2.

Data collection and identification of saccades

Eye position was monitored using scleral search coils (Judge et al. 1980). Eye position was sampled at 250 Hz (monkeys EM and FF) or 100 Hz (monkey CH). Eye data were stored for off-line analysis, along with CORTEX event markers, which indicated when stimuli appeared and were extinguished.

Data processing and statistical analyses were carried using custom-written MATLAB programs and SPSS. For all experiments, saccades were identified in MATLAB on the basis of velocity criteria. The beginning of the saccade was defined as the timepoint when velocity exceeded 50°/s. The end of the saccade was defined as the timepoint when velocity fell below 20°/s. The accuracy of saccade identification was verified on a trial-by-trial basis.

Timing of the double-step task

At the beginning of each trial, the monkey fixated a central fixation point (FP) for 300–500 ms. The first target (T1) then appeared. The

second target (T2) appeared 100 ms later and was extinguished after 50 ms. FP was extinguished simultaneously with T2 offset, cueing the monkey to initiate the double-step sequence. T1 was extinguished once the monkey attained it. If the monkey successfully reached the T2 location, this target reappeared after 100 ms. The monkey was required to refixate T2 for an additional 300–500 ms to receive a juice reward. In *expt 5*, we measured performance on a delayed version of the double-step task, which was identical to the standard task in all respects, except that the monkey had to maintain fixation during a 300- to 500-ms delay period before generating the sequence.

Spatial configuration of the double-step task

For each testing session, we measured double-step performance in three conditions (Fig. 3A). One condition, the *central* condition, was always familiar to the monkeys. The other two conditions, *within-hemifield* and *across-hemifield*, were both unfamiliar. All three conditions began with a first saccade directed either to the right or to the left. 1) In the well-trained central condition, the second saccade was vertical. This sequence did not require interhemispheric transfer of visual information. 2) In the within-hemifield condition, updating required a transfer of visual signals within the same hemisphere. 3) In the across-hemifield condition, updating required an interhemispheric transfer of visual signals. We tested these conditions in each quadrant of the visual field, testing upper and lower fields in separate sessions. In each session, then, six sequences were randomly interleaved without replacement; trials did not repeat on error.

In the standard paradigm (*expt 1*), the first and second saccades were 12° in amplitude. The within- and across-hemifield S2 trajectories were offset from the central S2 by 30° in angle. The location of T2 was at an eccentricity of 12° for the central condition, 18° for the within condition, and 6° for the across condition. Electronic eye windows were $\pm 2^\circ$ at central fixation and T1 and $\pm 2.7^\circ$ at T2. In *expts 2–4*, we tested performance on the double-step task using different target geometries, which are described in RESULTS. For these experiments, eye windows were adjusted such that the T1 and T2 eye windows were equal to about 15% and about 20% of saccade amplitude, respectively. The eye windows for T2 were less stringent than those for T1 because saccades are known to be less accurate when directed toward a remembered target compared with a visual target (Barash et al. 1991). The T2 eye windows were always constrained so as to be nonoverlapping for the three targets (within, central, across) in each quadrant.

Training on the double-step task

Our objective was to train the animals extensively on the double-step task, so that they were proficient on the task and could respond accurately even on double-step sequences they had not seen before. This approach was important for ensuring that, if deficits were present, we could attribute the deficits to impaired spatial updating rather than to a general inability to adapt to new target arrangements. It was also critical that we train the animals without using sequences that resembled either of two critical test conditions (within-hemifield or across-hemifield). Training took place in two stages. In the first stage, we used a vertical version of the double-step task. In these sequences, the first target (T1) appeared directly above or directly below central fixation. The second target (T2) appeared either in the left (LVF) or right visual field (RVF). For these vertical sequences, the location of T2 was represented by the same cortical hemisphere both when the eyes were at fixation and when the eyes reached T1. The monkeys were trained to a criterion of 75% correct for all sequences in the upper and lower visual fields. Both split-brain monkeys reached criterion after about 4 mo of training; the normal monkey reached criterion within 1 mo.

Once the animals had learned to perform the vertical double-step sequences, we moved to the second stage of training. In this second

stage, we used only one condition, the central condition (Fig. 3A, black lines). On central sequences, the first saccade was a horizontal saccade, directed 12° either to the right or to the left. The second saccade (also 12° in amplitude) was vertical, and so did not require across-hemifield updating of the T2 stimulus trace. The monkeys were trained to perform the central condition in each of the four visual quadrants. This stage of training proceeded rapidly, requiring only a single session for monkeys CH and FF to reach criterion, and two sessions for monkey EM. In further training sessions, we varied the saccade amplitude of the central sequences, to reinforce the principle of the task and ensure the monkeys' ability to adapt to changes in target geometry. The rapid acquisition of the central sequences indicated that the monkeys were proficient on the double-step task. After these two stages of training were complete and the animals were very good at the task, we began testing in *expt 1*.

Data analysis

We excluded from analysis any double-step trials in which the latency of the first saccade was <50 or >500 ms. In addition, we excluded trials in which the monkey attained T1 but directed the second saccade into the wrong vertical visual field. Trials in which the first saccade went to neither T1 nor T2 were also excluded from further analysis. Having removed anticipatory or otherwise erratic trials from analysis, we classified the trials according to error type, defined as follows. *Correct* trials were those in which the first saccade reached T1 and the second saccade reached T2. *S2 error* trials were those in which the first saccade reached T1 but the second saccade failed to reach T2. *T2-first* trials were those in which the first saccade was directed to T2, rather than to T1. The criteria for a saccade to reach a target location were implemented in off-line analysis, by measuring angular error (angular offset between the saccade trajectory and the ideal trajectory) and distance error (distance between the saccade endpoint and the target). For the first saccade, angular error had to be <10° and distance error had to be <15% of the target's amplitude (i.e., a gain of 0.85). For the second saccade, angular error had to be <12° and distance error had to be <20%.

We assessed accuracy and latency by conducting a univariate ANOVA to determine the significance of three independent factors: updating condition (central, within, or across), direction of the first saccade ("S1 direction," right or left), and vertical visual field (upper or lower). This analysis included only those trials where the monkey accurately reached T1 (i.e., correct trials and S2 error trials). ANOVAs were conducted separately for each monkey. We used post hoc analyses to determine whether specific across-hemifield sequences were significantly impaired. We corrected for all possible pairwise comparisons between the sequences (Tukey's HSD [Honestly Significantly Different], calculated at $\alpha = 0.05$ for 66 pairs), but focused on the comparison of each of the across-hemifield sequences to three matched sequences that controlled for saccade metrics and unfamiliarity. The well-trained central sequence in the same hemifield was matched for direction of the first saccade. The within-hemifield sequence in the *same* hemifield was matched for unfamiliarity and for direction of the *first* saccade. The within-hemifield sequence in the *opposite* hemifield was matched for unfamiliarity and the direction of the *second* saccade. If all three pairwise comparisons were significant, we concluded that there was an impairment in spatial updating, rather than an impairment related to saccade metrics or to encountering unfamiliar sequences. Throughout the results, we refer to individual across-hemifield sequences as being significantly impaired only if they met these criteria.

RESULTS

Experiment 1: Initial impairment of across-hemifield sequences

We began behavioral testing after the monkeys completed both stages of training on the double-step task, described in

METHODS. Monkeys were able to perform an extensive set of double-step sequences accurately, and had demonstrated an ability to generalize when presented with sequences they had not previously seen. It was crucial that the monkeys had not yet encountered the two conditions of experimental interest, the within-hemifield and across-hemifield conditions (Fig. 3A, red and green lines). On the trained central sequences, their performance reliably exceeded 75% correct (Fig. 3A, black lines). With this evidence that the animals understood the double-step task, we proceeded to test the essential question: could the split-brain monkeys perform double-step sequences that required updating from one visual hemifield to the other? We tested the monkeys' double-step performance in the upper visual field in the first session, and in the lower visual field on the subsequent day. In each session, we simultaneously introduced four test sequences, two across-hemifield and two within-hemifield conditions, in the right and left visual fields. Across- and within-hemifield sequences were equally unfamiliar and were counterbalanced for the direction of the first and second saccades. This design isolated the difference of interest: accurate double-step performance required either across-hemifield or within-hemifield spatial updating. These initial testing sessions were critical because the monkeys' performance was not confounded by experience with either test condition (within or across). As such, these sessions provide unique insight into the integrity of spatial updating in the split-brain monkey.

PERFORMANCE ON EARLY TRIALS. In each animal, first exposure to the across- and within-hemifield conditions revealed a conspicuous and selective impairment for sequences that required updating across visual hemifields. Eye traces from the upper field demonstrate the initial double-step deficit (Fig. 3B). Traces from the central condition show that the monkeys were very accurate in the execution of these well-trained sequences. The monkeys were also able to perform the within condition with considerable accuracy, despite the fact that these particular sequences were unfamiliar. In contrast, both monkeys made inaccurate movements on every trial of the first ten across-hemifield sequences. On these trials, the trajectory of the second saccade deviated substantially from the ideal trajectory, and resembled a straight vertical saccade. These data are consistent with the prediction that performance on across-hemifield sequences would be impaired in the absence of the forebrain commissures.

Eye traces from the lower field, tested on Day 2, show a similar pattern but also reveal some surprising dissimilarities (Fig. 3C). As in the upper field, both monkeys performed well on central and within conditions. Monkey EM showed a clear impairment for the across-hemifield sequences: saccade trajectories were predominantly vertical, in keeping with observations in the upper field. Monkey CH, however, was able to execute the lower-field across-hemifield sequences with considerable accuracy, even in the first ten trials. This successful performance may have emerged partly as a result of the order of testing. We tested the upper visual field first and the lower field sequences on the subsequent day. This raises the possibility that monkey CH, having learned to perform the across-hemifield sequence in the upper left quadrant on the first day (see below), was able to generalize rapidly to the lower field sequences.

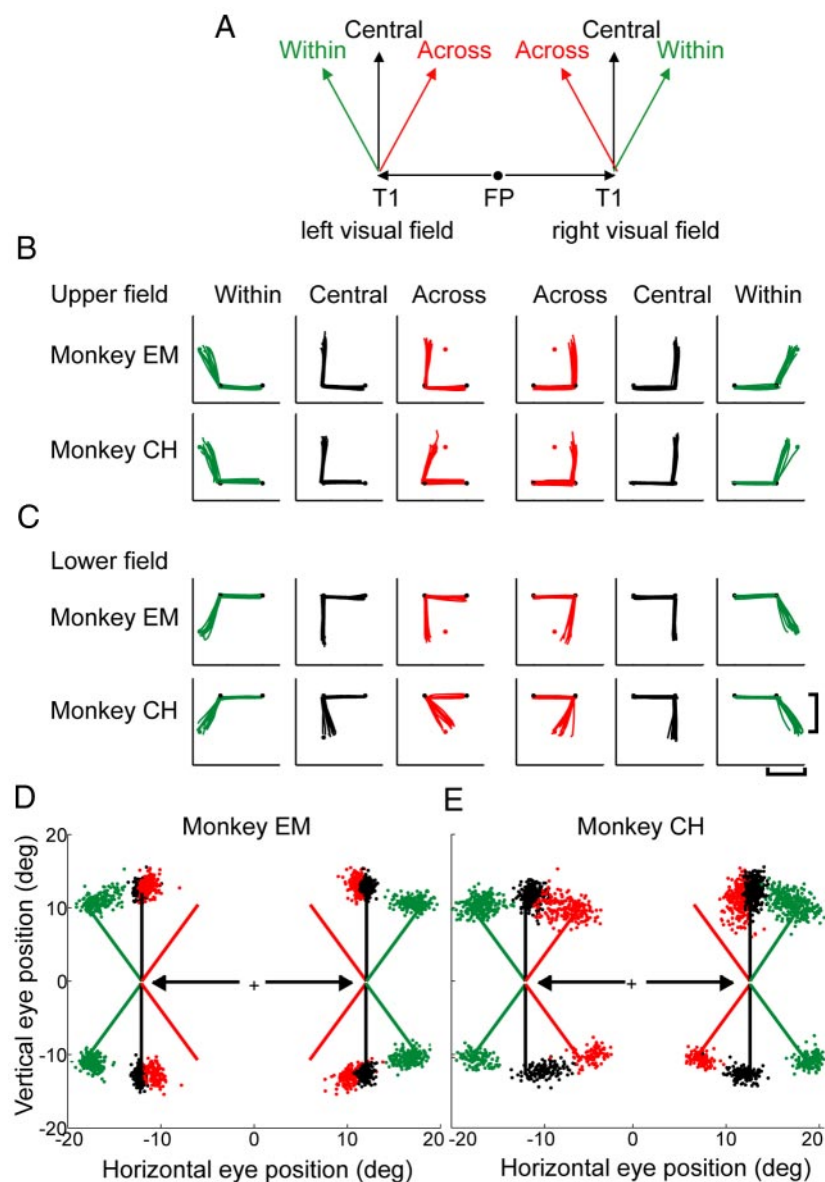


FIG. 3. Initial double-step performance of split-brain monkeys for across-hemifield compared with within-hemifield updating. *A*: standard test configuration: testing was conducted first in the upper field (shown) and then in the lower field. Horizontal arrows represent the first saccade from FP to the first target, T1. In each quadrant, the second target (T2) appeared at one of 3 locations. Central sequences (black) served as the training condition; within-hemifield (green) and across-hemifield (red) conditions were introduced simultaneously. *B* and *C*: traces show the eye path for the first 10 trials of each sequence. Dots indicate the locations of FP, T1, and T2. Brackets represent 10° . *D* and *E*: saccade endpoints from the first session of across-hemifield testing. Lines show ideal trajectories for the second saccade of each sequence. Lines and endpoints are colored according to condition, as in *A*.

DOUBLE-STEP SACCADE ENDPOINTS FROM THE FIRST SESSION. Are the eye traces from these early trials representative of the monkeys' performance throughout the entire first session of testing? For monkey EM, the impairment of the across-hemifield sequences was clearly present throughout the first session (Fig. 3*D*). In both the upper and lower visual fields, the endpoints for the across-hemifield sequences (red) were clustered far from the correct endpoint. By comparison, endpoints for the central sequences (black) and within sequences (green) were clustered near the correct T2 locations. For monkey CH, the endpoint data were more variable (Fig. 3*E*). In the upper right field, impairment on the across-hemifield sequence continued throughout the session. Endpoints for this sequence resembled those for monkey EM. In the upper left quadrant, however, many endpoints for the across-hemifield sequence were clustered near the correct T2 location. This reflects the fact that performance improved as the monkey gained experience in the first session (about 200 trials of this sequence). In the lower field, monkey CH performed both across-hemifield

sequences with considerable accuracy throughout the session (Day 2 of testing).

The data in Fig. 3 show two contrasting results: in the absence of the forebrain commissures, the performance on across-hemifield sequences was impaired in most cases, but was surprisingly accurate in a few cases. These results are borne out in quantitative analysis, described below. We characterized the monkeys' initial performance using three analytic approaches. First, we classified the trials according to error type. Second, we quantified saccadic accuracy and latency and subjected these measures to statistical analyses. Finally, we investigated the precision of the monkeys' across-hemifield performance.

FEWER CORRECT TRIALS FOR ACROSS-HEMIFIELD UPDATING IN THE FIRST SESSION. In the first analysis, we determined the percentage of trials belonging to each of three categories: 1) correct; 2) S2 errors, in which the monkey made an accurate saccade to T1 but not to T2; and 3) T2-first errors, in which the monkey's first saccade went directly to T2 (Fig. 4). For both

monkeys, percentage correct (filled columns) typically was high for the central (black) and within-hemifield conditions (green). The percentage correct for the across-hemifield condition (red) varied by monkey and visual quadrant. For monkey EM, percentage correct was 0, regardless of visual quadrant. For monkey CH, it ranged from 0% (upper RVF) to 80% (lower RVF).

We found that the two monkeys exhibited distinct behavior, not only in terms of the percentage correct for across-hemifield trials, but also in terms of the kinds of errors committed. For monkey EM, all of the error trials were S2 errors (open columns). For monkey CH, error trials also included T2-first errors (hatched columns). These T2-first errors occurred almost exclusively for the across-hemifield sequences. The differences in error types indicate that the monkeys may have used different strategies in response to the across-hemifield condition.

ACROSS-HEMIFIELD IMPAIRMENT OF SACCADE ACCURACY IN THE FIRST SESSION. In the second analysis, we quantified saccade accuracy and latency to evaluate the monkeys' performance in the first testing sessions. We quantified accuracy of the second saccade by measuring the distance between the endpoint of the monkey's saccade and the target. We found that distance error was significantly increased for the across-hemifield condition, in most but not all cases (Fig. 5, *A* and *B*). Analysis of variance showed that, on average, the across-hemifield condition elicited greater error than the within-hemifield or central conditions (main effect of updating condition, both monkeys $P < 0.0001$). The across-hemifield impairment varied by quadrant, which was evident in a significant interaction among updating condition, direction of the first saccade (S1), and vertical visual

field (both monkeys, $P < 0.0001$). Our primary interest was to determine whether individual across-hemifield sequences were significantly impaired, relative to central and within-hemifield sequences that controlled for saccade metrics and unfamiliarity. Accordingly, we conducted post hoc pairwise comparisons, focusing on the contrast between each across-hemifield sequence and three matched sequences, the central and within sequences in the same quadrant, and the within sequence in the opposite hemifield (see METHODS). If the across-hemifield sequence was significantly impaired relative to all three matched sequences, we concluded that there was a deficit in updating, rather than an impairment related to encountering an unfamiliar sequence, or related to the metrics of the first or second saccade.

In monkey EM, accuracy was significantly impaired for all four across-hemifield sequences (increased S2 error, Fig. 5, *A* and *B*). In monkey CH, accuracy was impaired for two of the across-hemifield sequences, both in the upper visual field (Fig. 5*A*). We conclude that double-step performance in these initial sessions was generally, although not always, less accurate for across-hemifield sequences compared with matched central and within sequences.

Previous studies indicate no differences between the accuracy of across-hemifield and within-hemifield double-step performance in the normal animal (Baizer and Bender 1989; Becker and Jurgens 1979; Dassonville et al. 1995; Goldberg et al. 1990; Jeffries et al. 2003; Li and Andersen 2001; Zivotofsky et al. 2003). We confirmed this using exactly the same paradigm used for the split-brain monkeys. In contrast to the across-hemifield impairment in saccade accuracy in the split-brain monkeys, we found no selective differences in the normal animal (Fig. 5, *A* and *B*). This observation is consistent with previous findings, and demonstrates that the impairments observed in the split-brain animals are indeed attributable to the absence of the forebrain commissures.

MODERATE ACROSS-HEMIFIELD IMPAIRMENT OF SACCADE LATENCY IN THE FIRST SESSION. We hypothesized that saccade initiation would be slower for across-hemifield conditions for transfer of visual information, given the absence of the most direct interhemispheric path. We anticipated that this slowing would be most evident in the initiation of the second saccade of the double-step task. We expected the latency of the first saccade, which was visually guided, to be unaffected. We found, however, that latencies of *both* the first and the second saccades were prolonged for the across-hemifield compared with the within and central conditions (main effect of updating, all $P < 0.0001$).

The latency of both the first and second saccades depended significantly on the interaction between updating condition, S1 direction, and vertical field (S1 latency: $P < 0.0001$ for monkey EM, $P < 0.05$ for monkey CH; S2 latency: $P < 0.0001$ for both monkeys; Fig. 5, *C–F*). As with the accuracy data, we asked whether the latencies of individual across-hemifield sequences were significantly increased relative to the three matched central and within sequences. For each monkey, latencies for the *first* saccade were significantly prolonged in one of four quadrants (Fig. 5, *C* and *D*). Latencies for the *second* saccade were significantly prolonged in three of four quadrants (Fig. 5, *E* and *F*). In the normal monkey, by contrast, first saccade latencies in the across-hemifield condition were not prolonged in any quadrant. Second saccade latencies in the across-hemifield condition were slowed significantly in one

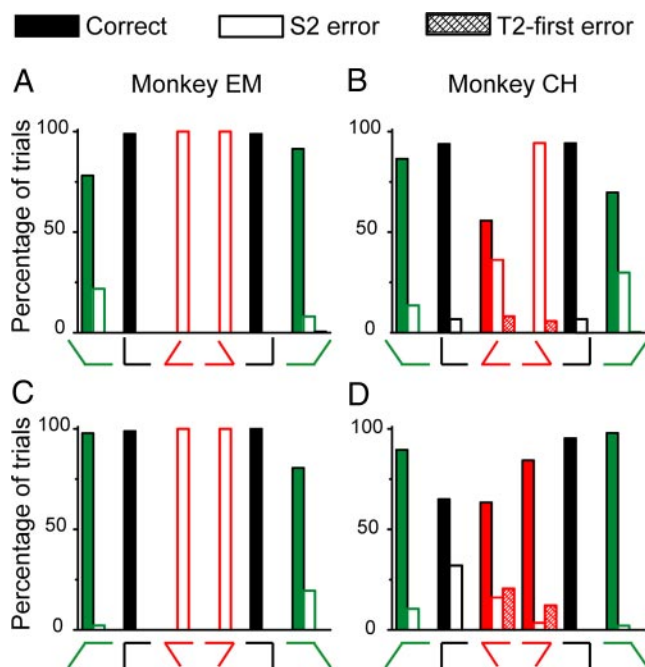


FIG. 4. Percentage of correct and incorrect trials for double-step performance in the first session of testing, for upper (*A*, *B*) and lower field (*C*, *D*). Each panel shows percentages from 6 sequences; icons along the *x*-axis. Color coding as in Fig. 3. Solid bars represent the percentage of correct trials. Open bars indicate incorrect trials in which the first saccade went to T1 but the second saccade did not reach T2. Hatched bars indicate incorrect trials when the monkey made the first saccade directly to T2 (monkey CH, across-hemifield sequences only).

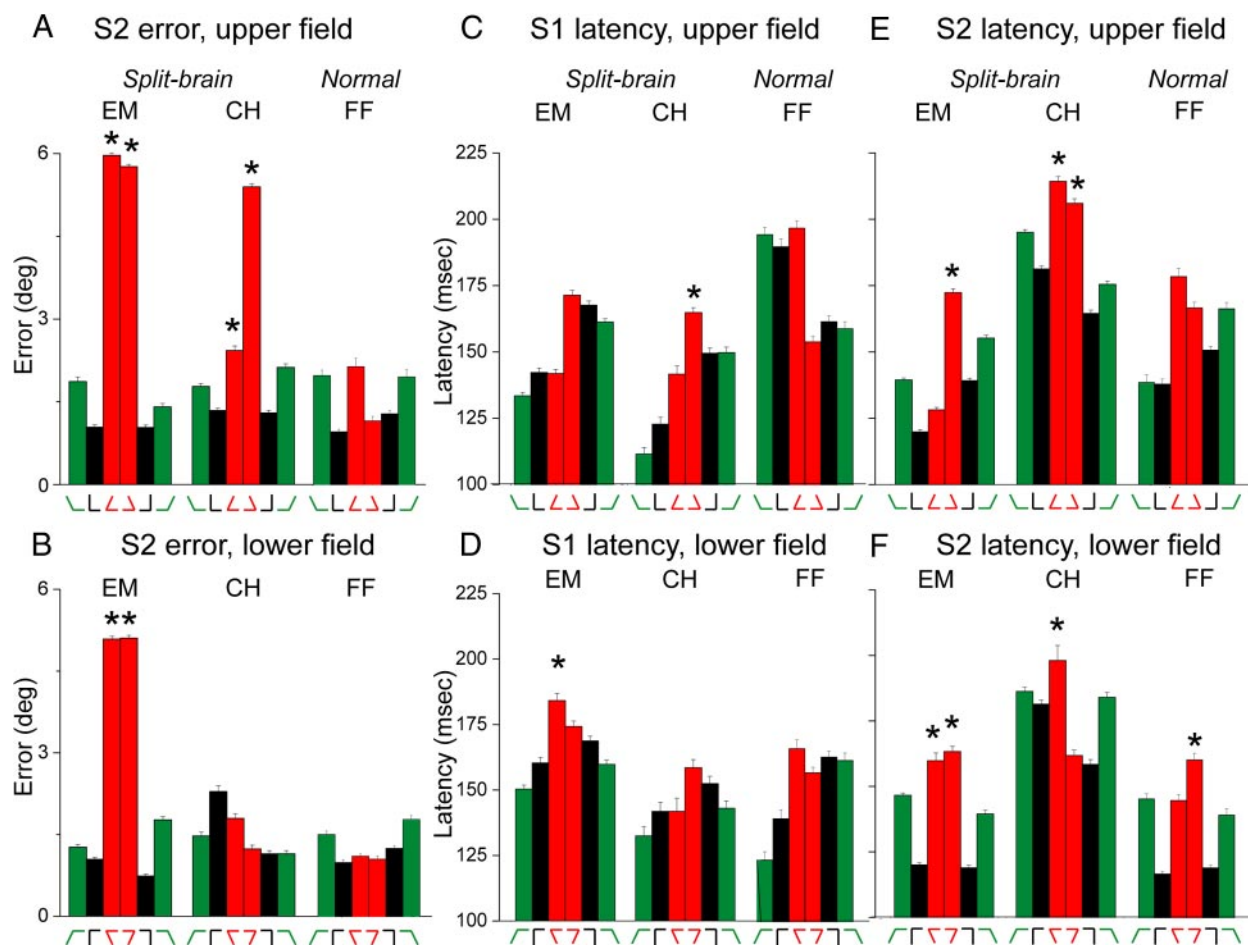


FIG. 5. Accuracy and latency of double-step performance in initial testing sessions for the split-brain monkeys (EM, CH) and normal monkey (FF). In each panel, each set of 6 columns represents data (mean \pm SE) from one monkey (EM, CH, FF). Icons indicate the sequence; color coding as in previous figures. *A* and *B*: distance error. *C* and *D*: latency for the first saccade (S1). *E* and *F*: latency for the second saccade (S2). Asterisks denote across-hemifield sequences in which error or latency was significantly increased, compared with the matched central sequence and to both matched within-hemifield sequences.

quadrant (lower right) and this trend was apparent in another quadrant (upper left). This slowing is compatible with the notion of longer transmission times for interhemispheric communication in the intact brain (Zaidel and Iacoboni 2003). The slowed across-hemifield latencies are nonetheless more prominent in the split-brain monkeys, indicating that updating may be less efficient in the absence of direct fibers linking the cortical hemispheres. In summary, quantitative analysis showed that performance in the split-brain monkey was significantly impaired when the double-step sequence required the representation of T2 to be updated from one visual hemifield to the other. The across-hemifield impairment was evident in moderate increases in latency and in more prominent increases in distance error.

PRECISION OF ACROSS-HEMIFIELD PERFORMANCE IN THE FIRST SESSION. What kinds of spatial representations did the split-brain monkeys use to perform the across-hemifield sequences? This question was particularly intriguing given the variability we observed in across-hemifield performance, both between the two animals and among quadrants in each individual animal. One way to get a sense of the underlying spatial representations is to assess the precision of saccade performance. In this last analysis, we focused specifically on the question of how

precisely the split-brain monkeys generated the second saccade in across-hemifield sequences. Measures of precision capture the consistency of the second saccade trajectory, regardless of whether the saccade was directed toward the correct location. For example, second saccades in the across-hemifield condition might be inaccurate but *precise*, suggesting that the monkey made use of a consistent (albeit wrong) representation of T2. We measured precision on a trial-by-trial basis, taking advantage of the slight variability in landing points of the first saccade (Sommer and Wurtz 2004b). This approach tells us how well the monkey adjusted the second saccade trajectory to take the first saccade into account. In other words, if the monkey has a precise representation of the second target location, then the trajectory of the second saccade will vary slightly according to the exact endpoint of the first saccade. For each trial, we determined the direction of the ideal second saccade, which the monkey would make if it were adjusting precisely for the first saccade. We then compared this ideal direction to the direction of the observed second saccade.

We were interested in two questions. First, when the monkey was wrong, was it always wrong in the same way, i.e., directing the second saccade to the same inaccurate location? Second, when the monkey was right, was it really updating the

second target according to where the first saccade landed, or was it inclined to use a more rote, automated strategy? We find an answer to the first question by looking at the quadrants where the accuracy impairment was most profound, for example, in the upper right quadrant for both monkeys (Fig. 6, *B* and *F*). Both animals performed this across-hemifield sequence inaccurately, but precisely: there is a highly significant relationship between the direction of the observed saccade and that of the ideal saccade. This precision can also be appreciated in Fig. 3*D*, which shows that the S2 endpoints are clustered

closely together for these across-hemifield sequences. We observed an exception to precision in the lower right quadrant for monkey EM, where observed S2 direction was not significantly related to the ideal direction (Fig. 6*D*). This indicates a more variable representation of T2. With regard to the second question—what happens when the monkey is accurate—the clearest example comes from the lower visual field of monkey CH, where performance was relatively accurate from the start on Day 2. Here, precision is relatively poor (Fig. 6, *G* and *H*). The absence of a strong correlation between observed and ideal directions may indicate that the monkey's representation of T2 was changing over time and becoming more accurate. Alternatively, it may indicate that the monkey was performing these across-hemifield sequences without genuinely updating the T2 representation to account for the first saccade. We later address this second possibility more fully (*expt 3*). The basic points here are that the monkeys were typically precise even when they were inaccurate and that directional precision tended to be worst when accuracy was best.

RULING OUT OTHER SOURCES OF ERROR. We considered the possibility that the initial across-hemifield impairment in the split-brain monkey resulted from inaccuracy of the first saccade. We minimized the variability in first saccade accuracy by making that saccade visually guided. Furthermore, the accuracy and latency measures described above were computed only from those trials where the monkey's first saccade fell within two degrees of T1. The ANOVA revealed main effects of updating condition on the accuracy of S1 ($P < 0.0001$, both monkeys), but the differences were exceedingly small. Average error was increased by no more than 0.17° for the across-hemifield condition relative to the central and within conditions. This observation confirms that conditional differences in the first saccade were slight and could not account for those observed in the second saccade.

We also considered the possibility that the split-brain monkeys' performance on the across-hemifield condition reflected a sensorimotor or mnemonic impairment, rather than an impairment in spatial updating. We tested these possibilities by having the monkeys perform single memory-guided saccades (MGS) to the T2 locations used in the double-step task, either directly from the central fixation point or directly from the first target (T1) locations. These single-saccade tasks measure the monkeys' ability to encode and remember the T2 locations relative to the initial position of the eyes and relative to the position of the eyes at T1. We evaluated the accuracy and latency of these single memory-guided saccades to determine whether impairment in the double-step task reflected a deficit in these sensorimotor or memory processes.

Neither split-brain monkey showed a selective impairment for attaining the across-hemifield T2 location in the MGS task, regardless of whether the eyes began at central fixation or at T1. Their accurate performance is apparent in the eye traces from the monkeys' first ten trials of the MGS task (Fig. 7). Analysis of variance revealed small but significant accuracy and latency differences by updating condition. These conditional differences, however, were opposite to those observed in the double-step task: overall error and latency values were increased for the within compared with the across conditions (Fig. 7). These differences likely reflect the tendency for performance in the MGS task to decline for more peripheral

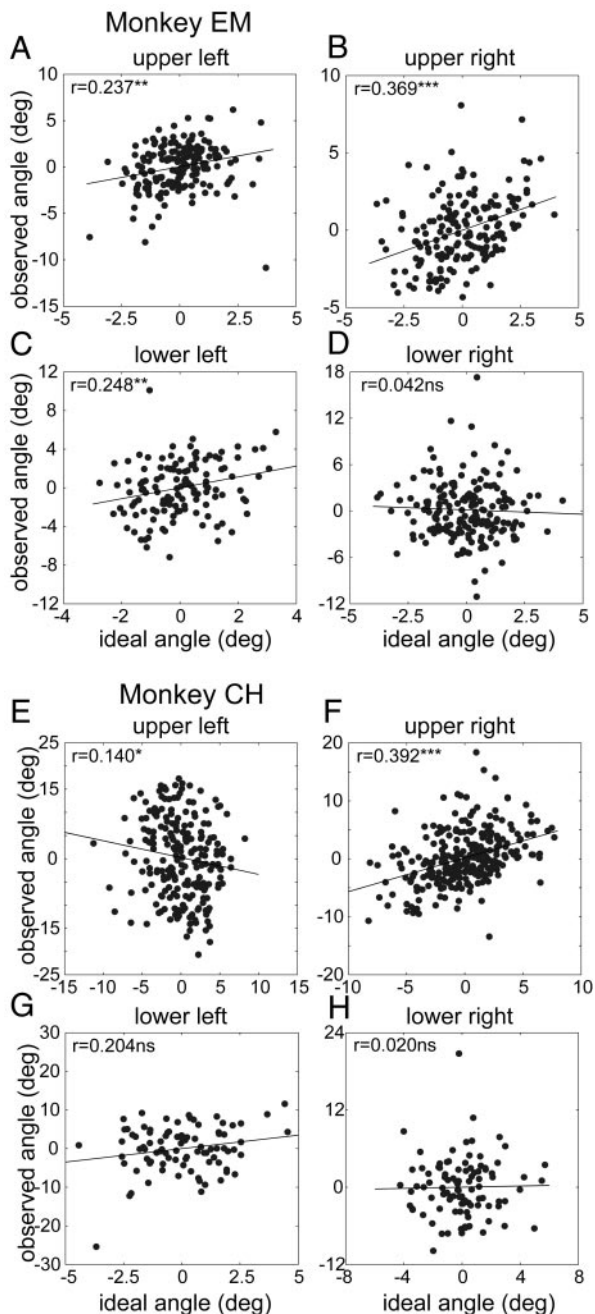


FIG. 6. Precision of across-hemifield performance in the split-brain monkeys, for each visual quadrant. In each panel, the observed angle of the second saccade (y-axis) is plotted against the ideal angle (x-axis) for individual trials. Regression lines show the slope and r values give correlation coefficients. Asterisks indicate that the strength of the relationship is significant: * $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$; ns, not significant.

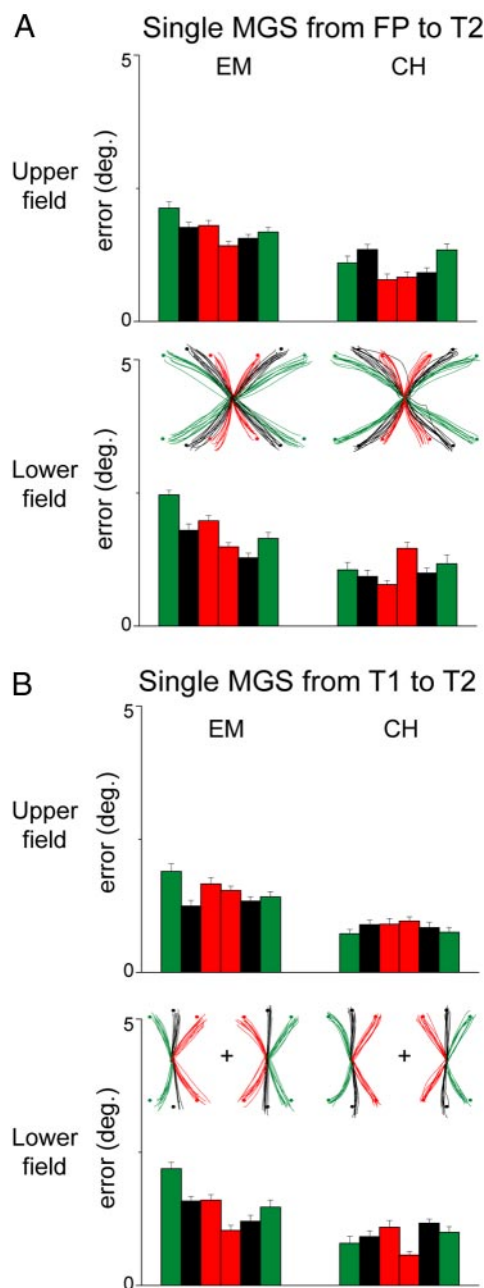


FIG. 7. Accuracy measures show no across-hemifield impairment for single memory-guided saccades (MGS) to T2 from fixation (FP; *A*) or from the first target (T1; *B*). Conditions are arranged according to the corresponding double-step conditions. *Eye traces* (between the upper and lower field panels) show performance on the first 10 trials of testing the single MGS.

targets (Barash et al. 1991; Bell et al. 2000; Gnadt et al. 1991; Kalesnyka and Hallett 1994). We conclude that the across-hemifield impairment in the double-step task cannot be attributed to a deficit in encoding, remembering, or generating eye movements to the across-hemifield T2 locations.

Experiment 1: Changes in across-hemifield performance over time

There were two exceptions to the initial impairment of the across-hemifield sequences. First, monkey CH was effectively unimpaired in the lower visual field. Second, we found that

performance on the across-hemifield sequences improved with experience for sequences that showed initial impairment. We continued to test the monkeys on the standard sequences until performance was stable, which ranged from seven sessions (monkey CH, lower field) to 65 sessions (monkey EM). In this section, we characterize the evolution of across-hemifield performance over multiple sessions.

CHANGES IN ACCURACY. We found that performance in the double-step task changed considerably over time. We first obtained an estimate of the number of trials required to reach criterion for correct performance in each across-hemifield sequence. As we saw in the initial testing session, improvement in the across-hemifield sequences was heterogeneous, varying by monkey and by quadrant (Table 1). We then plotted the mean accuracy and latency of double-step performance in each testing session (Figs. 8–10). We focus on those quadrants where across-hemifield accuracy was impaired beyond the first testing session (monkey EM, all quadrants; monkey CH, upper right quadrant). In these five quadrants, distance error was greater for the across-hemifield sequences compared with the central and within sequences (Fig. 8, *A–D* and *F*). After nearly ten sessions, monkey EM's performance on the across-hemifield sequences became even more inaccurate. At this stage, the monkey often made erratic saccades into the periphery, rather than attempting a second eye movement toward the target location. This deterioration was especially notable in the lower left quadrant (Fig. 8*C*). We found that the increased error co-occurred with a decrease in precision on across-hemifield sequences; the correspondence between ideal and observed direction of the second saccade fell to nonsignificant levels. This decline in accuracy and precision may indicate that the animal was no longer making a reasonable effort to perform the across-hemifield sequences. Alternatively, it could reflect a strategic shift, whereby the monkey began to "sample" the visual space in an effort to find sequences that were rewarded.

When improvement occurred for monkey EM, it did so in rapid, discrete steps. This is evident in the first across-hemifield sequence to improve (lower right quadrant; Fig. 8*D*). Between sessions 14 and 15, distance error decreased suddenly from 13 to 2°. Rapid decreases in error also occurred in the other three quadrants (Fig. 8, *A–C*). The onset of this improvement in accuracy was different for the four quadrants, but was accompanied by increases in directional precision for the across-hemifield condition (not shown). In other words, once the monkey learned to perform the across-hemifield sequences, performance appeared to be guided by an updated spatial

TABLE 1. Number of trials to criterion for across-hemifield sequences

	Monkey EM		Monkey CH	
	Left	Right	Left	Right
Upper field	2471 (44)	1667 (20)	70 (1)	918 (27)
Lower field	2710 (49)	1336 (15)	10 (1)	10 (1)

Number in parentheses indicates the session in which criterion was met. To reach criterion, average distance error had to be $<3.5^\circ$, for three consecutive groups of ten trials. For sequences that reached criterion during the first session of testing (<200 trials), the listed number indicates the first of these three groups. The listed number otherwise indicates the total number of trials performed, up to and including the session in which criterion was met.

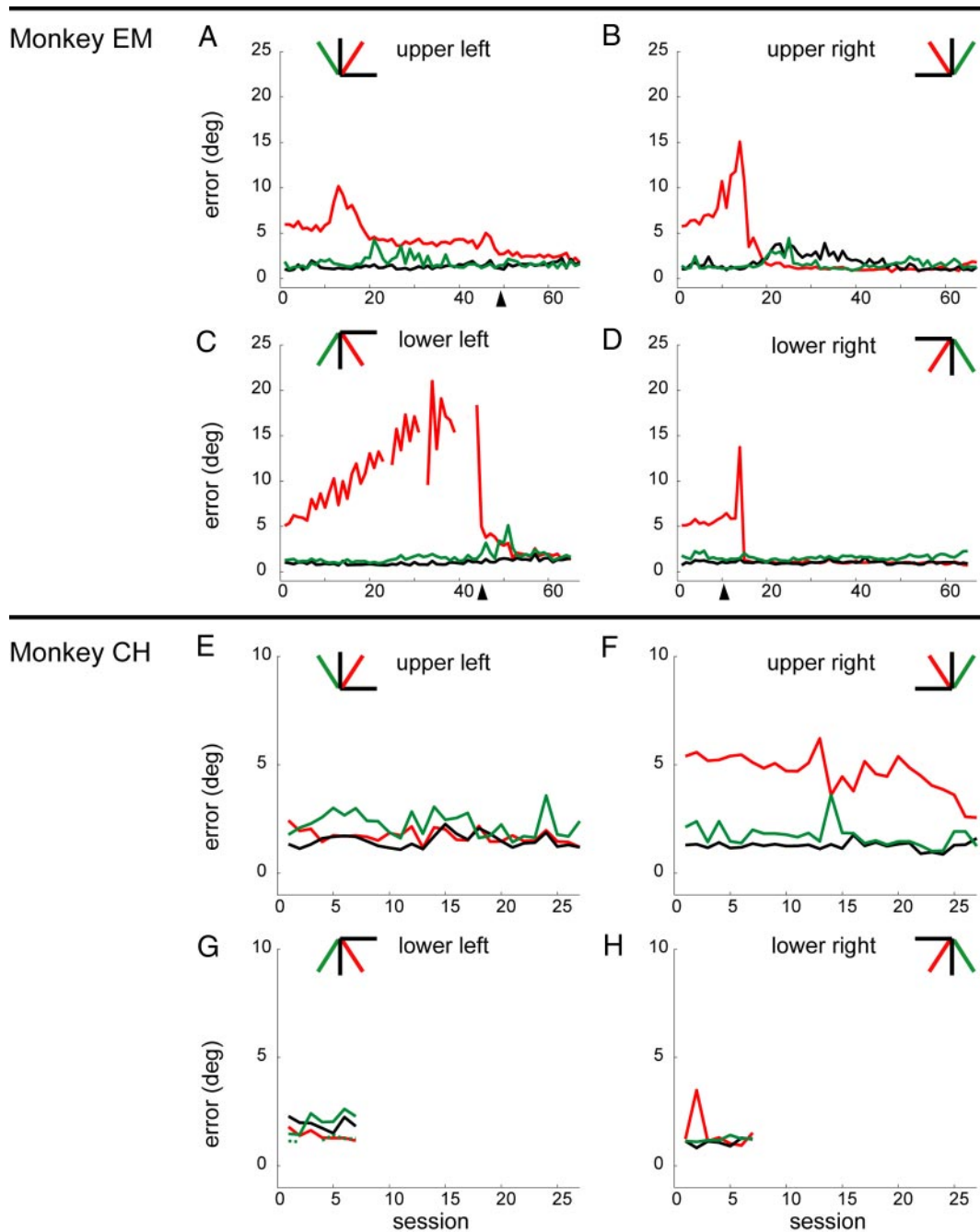


FIG. 8. Accuracy for double-step performance over multiple sessions, for monkey EM (A–D) and monkey CH (E–H). Each panel shows average distance error (y-axis) for the 3 conditions in each quadrant of the visual field, as performance evolved over testing sessions (x-axis). Testing continued until across-hemifield performance was stable, which ranged from 7 sessions (monkey CH, lower field) to 65 (monkey EM). For monkey EM, small black arrows indicate the time of events, described in the text, which influenced across-hemifield performance: A, consistent visual feedback; C, increase in size of electronic window; D, beginning of *expt 2*.

representation. For monkey CH, accuracy of the across-hemifield condition improved or was unimpaired in three of four quadrants during the first session of testing. In the remaining quadrant, the accuracy of across-hemifield trials improved slowly and discontinuously (Fig. 8F).

CHANGES IN LATENCY PARALLEL CHANGES IN ACCURACY. For both monkeys, saccadic latencies changed over the course of the testing sessions (Figs. 9 and 10). With few exceptions, changes in saccade latency co-occurred with changes in accuracy. For example, when monkey EM exhibited more erratic

across-hemifield performance, this was evident in increased error as well as increased latencies (lower left quadrant, C in Figs. 8–10). Likewise, when across-hemifield error decreased, it did so in parallel with decreases in S1 latency (monkey CH in Figs. 8F and 9F) and/or decreases in S2 latency (monkey EM in Figs. 8D and 10D). We assessed the strength of these relationships by conducting regression analyses on average accuracy and latency for the across-hemifield sequences from all testing sessions. We found a highly significant relationship between distance error and both S1 latency and S2 latency, for

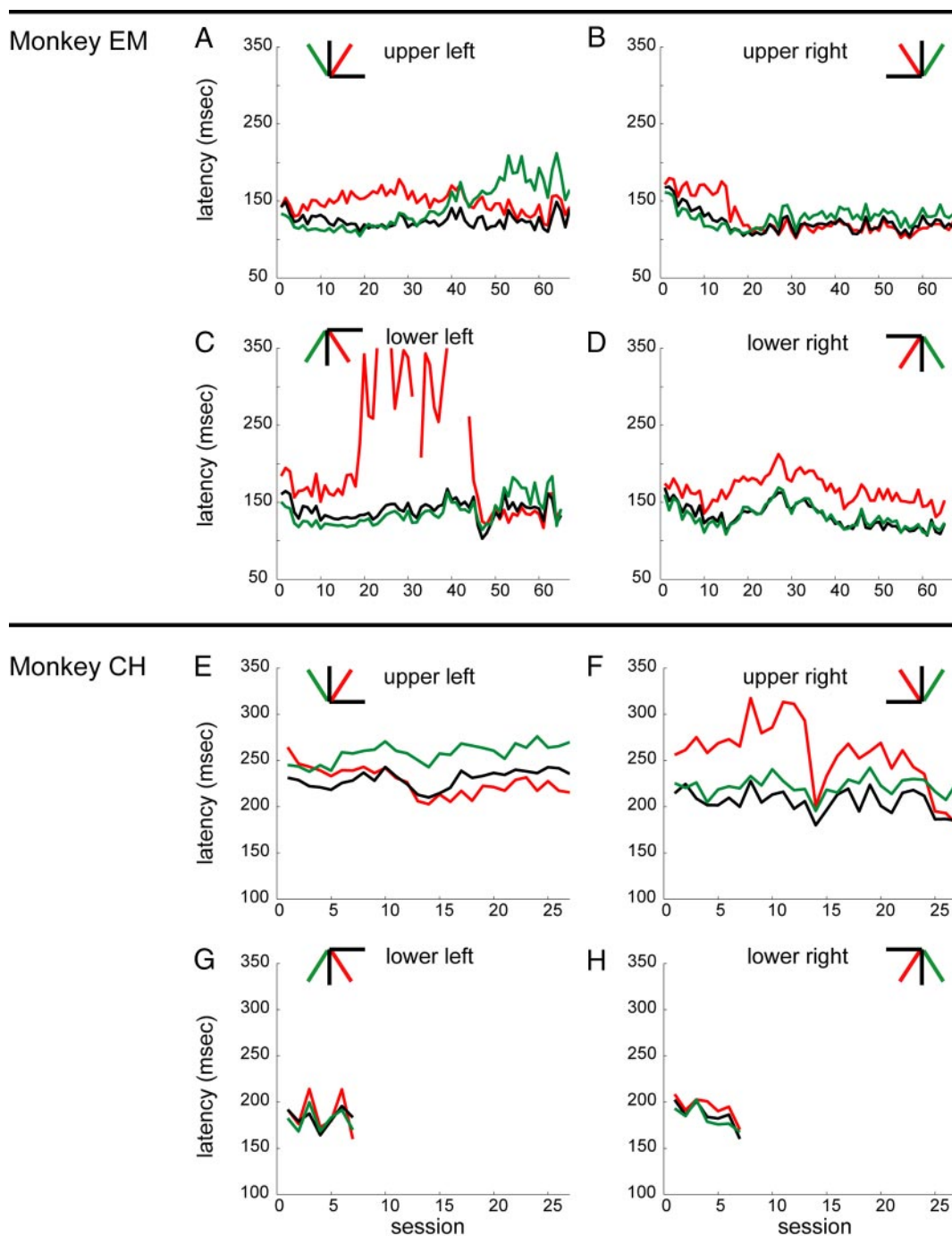


FIG. 9. Latency for the first saccade in double-step performance over multiple sessions, for monkey EM (A–D) and monkey CH (E–H). Conventions as in Fig. 8.

all cases except the lower field sequences in monkey CH (all significant at $P < 0.001$). This adds further support to the central observation that improvement on the across-hemifield sequences was marked by concomitant decreases in error and latency.

FACTORS CONTRIBUTING TO IMPROVED PERFORMANCE. What elicited the improvement in across-hemifield performance? Two factors likely influenced performance: specific experimental manipulations and visual feedback. For monkey EM, across-hemifield performance improved in most quadrants only after *expt 2* (below), in which the across-hemifield T2 location

was placed closer to, and then directly onto, the vertical midline. We began *expt 2* in session 10, while we continued to test the standard sequences from *expt 1* in a separate block during the same session. At this point, we observed an initial *increase* in error on the standard sequences. Subsequently, successful performance at the midline seemed to extend gradually to a recovery of across-hemifield performance on the standard sequences.

Visual feedback was also likely important for improvement on across-hemifield sequences. Whenever the monkey performed a trial correctly, the T2 target reappeared and the

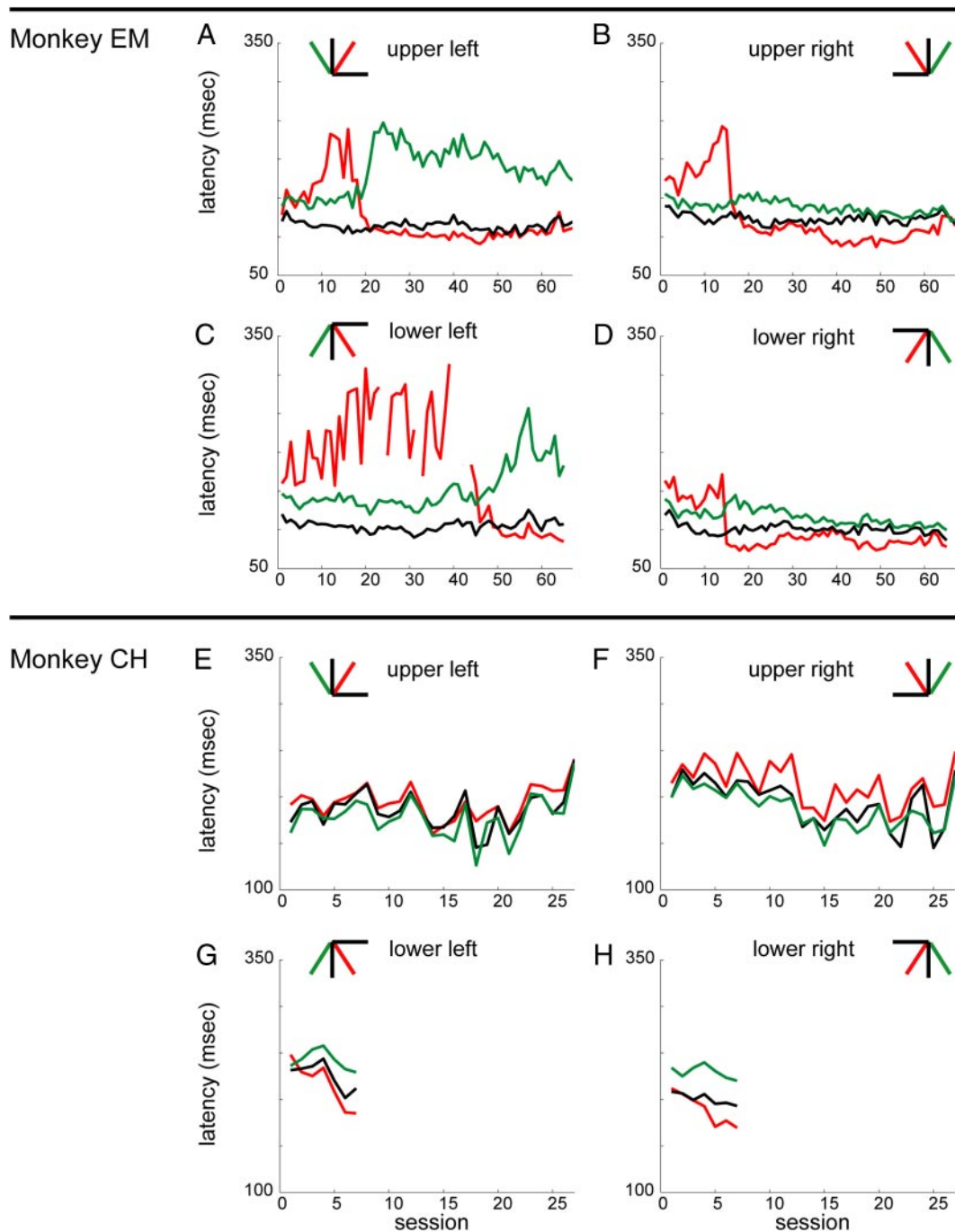


FIG. 10. Latency for the second saccade in double-step performance over multiple sessions, for monkey EM (A–D) and monkey CH (E–H). Conventions as in Fig. 8.

monkey refixated its location. The presence of visual feedback likely accounted for the discrete and rapid decreases in error. Typically, the monkey spontaneously initiated a change in behavior that allowed it to perform some trials correctly, but there was one exception to this self-initiated improvement. In the lower left quadrant, monkey EM was unable to perform the across-hemifield sequences even after 40 sessions, and performance had actually deteriorated (Fig. 8C). The monkey's performance on this sequence was so erratic in several sessions that no valid trials were available for analysis (breaks in line). In session 45, we expanded the size of the electronic eye

window at T2, to determine whether the across-hemifield sequence could be learned under any circumstance. As a result, the monkey received visual feedback even for very inaccurate saccades. The monkey's subsequent performance shows a rapid improvement. Visual feedback therefore appears to be sufficient to instigate accurate behavior. It is not, however, strictly necessary. In the upper left quadrant, monkey EM did not receive consistent visual feedback for the across-hemifield sequence until session 49, but accuracy improved substantially at session 15 (Fig. 8A). Accuracy improved still further after session 49, when performance was consistently reinforced. In

sum, visual feedback appears to play a central role in eliciting accurate behavior on across-hemifield sequences.

ACROSS-HEMIFIELD PERFORMANCE AFTER MULTIPLE SESSIONS. Data from the final testing sessions show appreciable improvement in the performance of across-hemifield sequences (Fig. 11). We were specifically interested in whether the monkeys continued to be impaired on individual sequences of the across-hemifield condition in this final testing session. We used our standard post hoc procedure used in *expt 1* to assess

whether each across-hemifield sequence was significantly impaired relative to the matched central and within sequences. In initial testing, the across-hemifield accuracy was significantly worse in six quadrants (all four in monkey EM, and two in monkey CH; Fig. 5). In final testing, this impairment was significant in only two quadrants (one in each monkey). Monkey EM continued to show increased across-hemifield errors in the upper left quadrant, monkey CH in the upper right quadrant (Fig. 11C). The magnitude of this impairment, however, is far

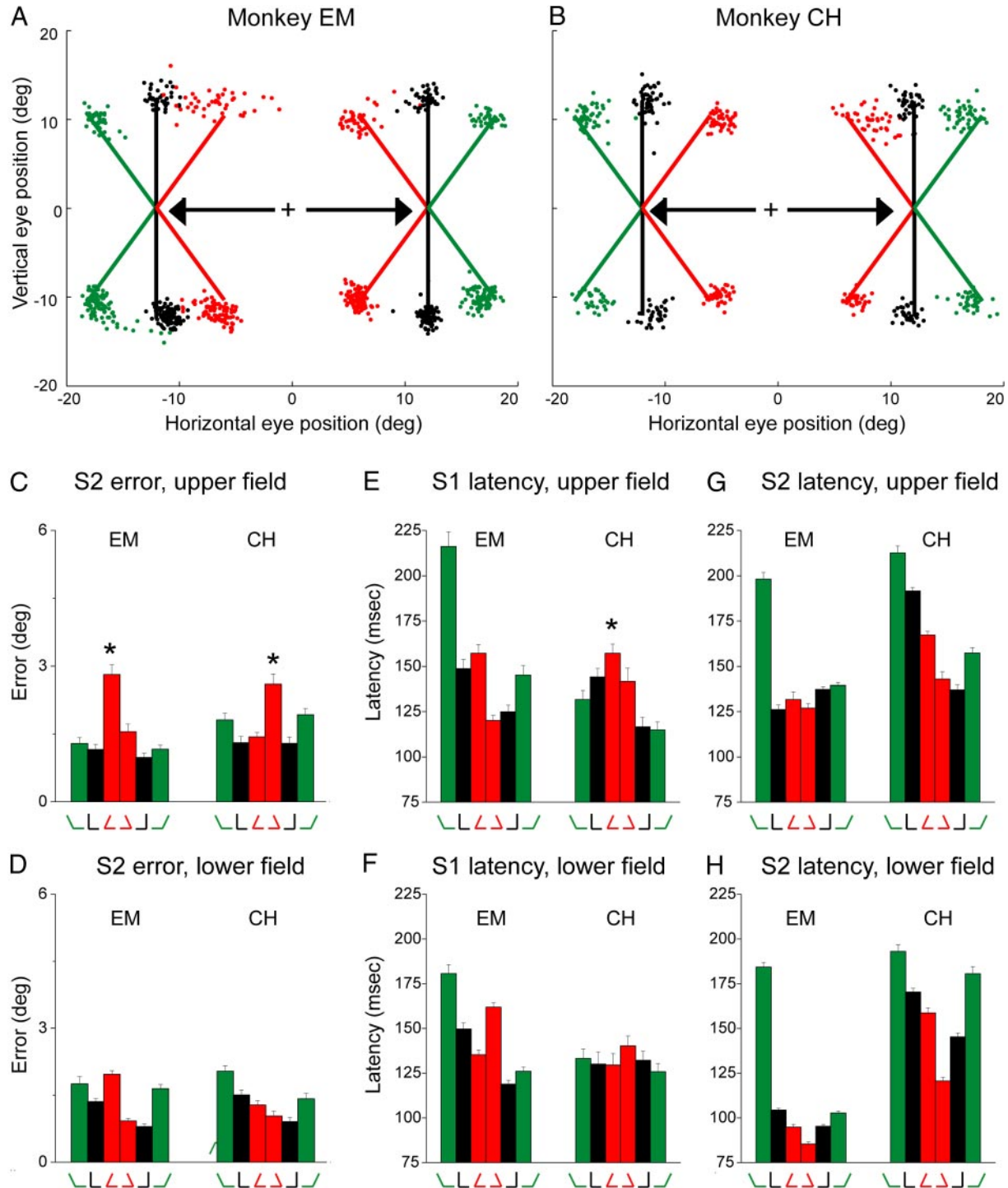


FIG. 11. Performance of the split-brain monkeys on standard double-step sequences in final testing sessions. *A* and *B*: saccade endpoints for monkey EM (*A*) and monkey CH (*B*); conventions as in Fig. 3. *C–H*: accuracy and latency of double-step performance; conventions as in Fig. 4.

less than that observed in the first session of testing (Fig. 5A, same scale).

Finally, we investigated the monkeys' saccade latencies for the learned across-hemifield sequences. We considered the possibility that accurate performance on the across-hemifield sequence might require slow, deliberate eye movements. In the final behavioral testing session, however, we found that latency in the across-hemifield sequence was significantly slowed only for the first saccade and only in one quadrant in monkey CH (Fig. 11E, upper left quadrant). In all other cases, initiation of the across-hemifield sequence was equivalent to, or even faster than, the matched central and within sequences. These data indicate that the monkeys did not have to perform the double-step task more slowly to complete the across-hemifield sequences successfully.

In sum, we made five observations regarding the monkeys' performance on the across-hemifield condition over time. 1) Improvement in the across-hemifield condition took place over a range of timescales, varying by monkey and by visual quadrant. 2) When improvement began, errors on across-hemifield sequences typically decreased in rapid steps. 3) Saccade latencies changed abruptly as across-hemifield sequences were learned, often in parallel with changes in accuracy. 4) Visual feedback was sufficient, although not necessary, to elicit improved performance on across-hemifield sequences. 5) Both monkeys showed minimal impairment of across-hemifield sequences in the final testing session, although significant inaccuracies persisted in one quadrant for each monkey.

Experiment 2: Ipsilateral representation of space and saccade reversal.

The initial impairment in across-hemifield performance prompted us to investigate two issues, which we addressed simultaneously in *expt 2*. Our main objective was to determine whether ipsilateral representations were available for updating in the split-brain animals. In investigating this issue, we were also able to address and rule out an alternative explanation for the across-hemifield impairment.

In our consideration of ipsilateral representations, we focused on the lateral intraparietal area (LIP). Area LIP is an important site for the construction of updated spatial representations (Colby and Goldberg 1999; Duhamel et al. 1992b; Heide et al. 1995; Quaia et al. 1998). Physiological studies of area LIP in the normal monkey generally indicate a strong contralateral bias in spatial representation. When ipsilateral responses are found, they are rarely elicited by stimuli more than a few degrees beyond the vertical meridian (Barash 1991; Ben Hamed et al. 2001; but see Platt and Glimcher 1998). In the standard paradigm we used in initial testing, we intentionally placed the across-hemifield T2 at a location that was unlikely to be encompassed by receptive fields extending into the ipsilateral field (six degrees from the midline). It was nevertheless important for us to consider the possibility that ipsilateral representations could contribute to performance in the across-hemifield condition. If so, a single hemisphere would have access to visual representations of the across-hemifield T2 location, both before and after the first eye movement.

The initial impairment we observed on across-hemifield sequences indicates that the split-brain monkeys could not easily make use of ipsilateral representations to guide accurate performance. This observation is compatible with several interpretations. It might simply confirm the idea that stimuli located six degrees from the midline are not represented bilaterally, in either the normal or the split-brain animal. Or, these ipsilateral representations may be absent in the split-brain animal. This possibility is consistent with evidence from ventral stream areas, where ipsilateral representations disappear after transection of the forebrain commissures (Gross et al. 1977). We also considered, however, two alternative explanations. The first was that ipsilateral representations may be present in the split-brain animal, but only for locations closer than six degrees to the vertical meridian. The second was that the across-hemifield deficit was not actually related to updating, but reflected a more general inability to perform sequences that required a reversal in saccade direction (e.g., rightward S1, leftward S2).

We tested these possibilities by measuring the monkeys' performance on the double-step task in three different spatial configurations. The first configuration was the standard across-hemifield paradigm used in *expt 1*. We refer to this configuration as the six-degree paradigm to emphasize the eccentricity of the across-hemifield T2. In the second configuration, the across-hemifield T2 was located three degrees from the midline ("three-degree" paradigm). In the third configuration, T2 was located directly on the midline ("zero-degree" paradigm). This last configuration does not require across-hemifield updating because each cortical hemisphere contains a representation of the vertical meridian. Even so, we use the term "across-hemifield" to underscore the parametric comparison of the three configurations. For each paradigm, we continued to test all three updating conditions (central, within-hemifield, and across-hemifield), and saccade amplitudes were equivalent for each condition. For the three- and zero-degree paradigms, we first trained the monkeys on the new central condition, which differed from the original only in the location of T2 (Fig. 12A, black lines). Then we simultaneously introduced the new within and across conditions. We began by testing the three-degree paradigm and tested the zero-degree paradigm in the following day's session.

To determine whether performance improved when T2 was placed nearer to the midline, it was critical that the monkeys continued to show impairment in the standard six-degree paradigm. We found that performance on the standard across-hemifield sequences remained impaired throughout this experiment (example data, Fig. 12A).

We first asked whether this across-hemifield impairment could be mitigated by placing the second target closer to the vertical midline. When T2 was located three degrees from the midline, performance on the across-hemifield sequences did not improve. On the contrary, performance worsened in all quadrants. The deterioration in performance may reflect a response to the unfamiliarity of this sequence, which exacerbated the existing across-hemifield impairment. This degraded performance indicates that the monkey was unable to use ipsilateral representations to perform the double-step task.

We next asked whether the monkeys could perform the across-hemifield sequences if T2 were placed directly on the midline. We expected the monkeys to perform these sequences

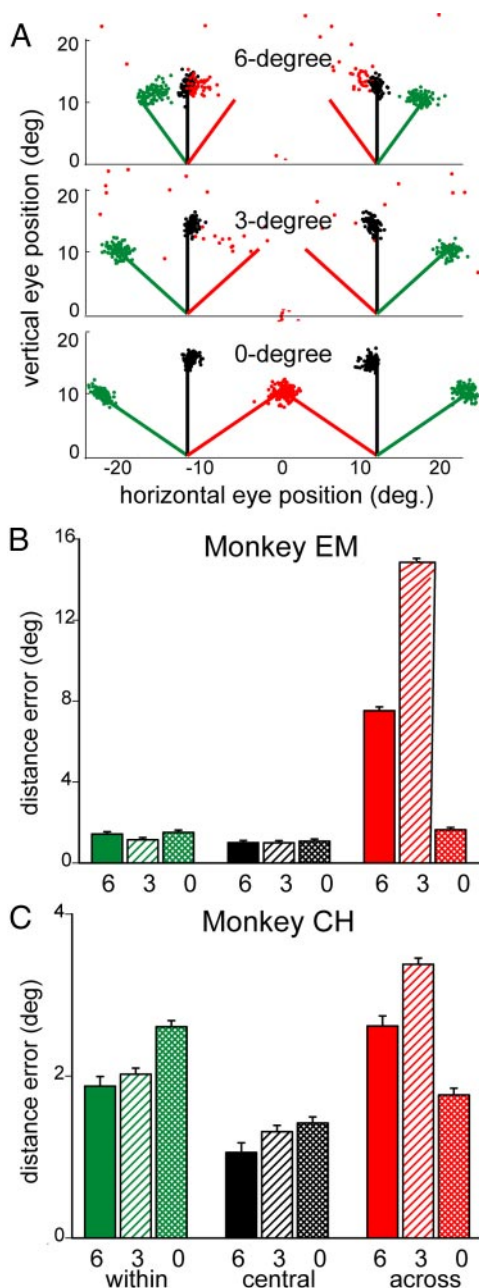


FIG. 12. Across-hemifield impairment persisted when T2 was located 3 degrees from the midline but was abolished when T2 was on the midline. A: example endpoint data from the upper field, monkey EM; conventions as in Fig. 3. B and C: average distance error, grouped by condition (within = green, central = black, across = red). Bars show average error from all 4 quadrants for each paradigm (6-, 3-, 0-degree).

without difficulty because each hemisphere would have access to the updated representation of T2. If, however, the monkeys were simply impaired in generating sequences that require a reversal of saccade direction, performance would remain inaccurate. We found that performance on the midline sequences was very accurate (Fig. 12A). These data indicate that the initial across-hemifield impairment did not arise from a difficulty in reversing saccade directions.

We assessed the relationship between T2 location and across-hemifield performance using a four-factor ANOVA [updating condition, S1 direction, vertical visual field, and

paradigm (6°, 3°, or 0°)]. Of greatest interest was the significant interaction between updating condition and paradigm (both monkeys, $P < 0.0001$). Post hoc analyses confirmed that across-hemifield accuracy improved significantly for the midline configuration compared with the three- and six-degree paradigms, for both monkeys (Fig. 12, B and C; $P < 0.05$, Bonferroni correction). In contrast, the accuracy of within sequences was either unchanged or decreased for the midline compared with the three- and six-degree configurations. This decline in within-hemifield performance likely occurred because the T2 locations were farther in the periphery (21° and 24°).

The data from *expt 2* indicate that stimuli presented three degrees from the midline cannot be updated across visual hemifields in the absence of the forebrain commissures. Locations along the midline, however, are updated readily. The monkeys' ability to perform the midline sequence also rules out the possibility that the across-hemifield impairment reflects a simpler deficit in generating a second saccade in the opposite direction opposite to that of the first saccade.

Experiment 3: Across-hemifield performance is under sensory control

What kind of information do the monkeys use to perform the across-hemifield sequences correctly? One possibility is that the monkeys learned to apply a motor rule, such as "if the first saccade is leftward and the second saccade is unknown, then direct the second saccade up and to the right." In this scenario, the monkeys would not be using sensory information about the actual target location. This possibility was consistent with our precision analysis of initial across-hemifield performance. In the precision analysis, we had observed the least precision for the across-hemifield sequences that were performed most accurately, making it possible that successful performance (as initially observed in monkey CH) was not genuinely based on updating T2 in conjunction with the first saccade. We explicitly tested this possibility in both monkeys when their performance on the across-hemifield sequences had reached asymptote in at least two quadrants. In this experiment, we introduced a small shift of the T2 locations (Fig. 13A). The shift, or *phi*, varied unpredictably from trial to trial and was small enough to allow the monkeys to perform the trials correctly without taking sensory information into account. In other words, the monkeys would continue to receive reward if they executed the same "learned" saccade to the original T2, even on offset trials. If the monkeys were using a motor rule, we expected that the trajectory of S2 would not change systematically with the location of T2. If, however, the monkeys used sensory information about the precise location of T2, even on across-hemifield sequences, then the trajectory of S2 would vary according to the position of T2.

Both monkeys generated the double-step sequences according to the actual location of the second target. This spatial precision was observed not only for the within-hemifield condition, as expected, but also for the across-hemifield condition. As seen in Fig. 13A, endpoints for the standard within-hemifield and across-hemifield conditions (green or red) are flanked by endpoints for the *phi* conditions (pink and cyan). Likewise, the average data from both monkeys demonstrate that the second saccade endpoints varied according to T2 location (Fig. 13, B and C). We assessed the significance of this relationship

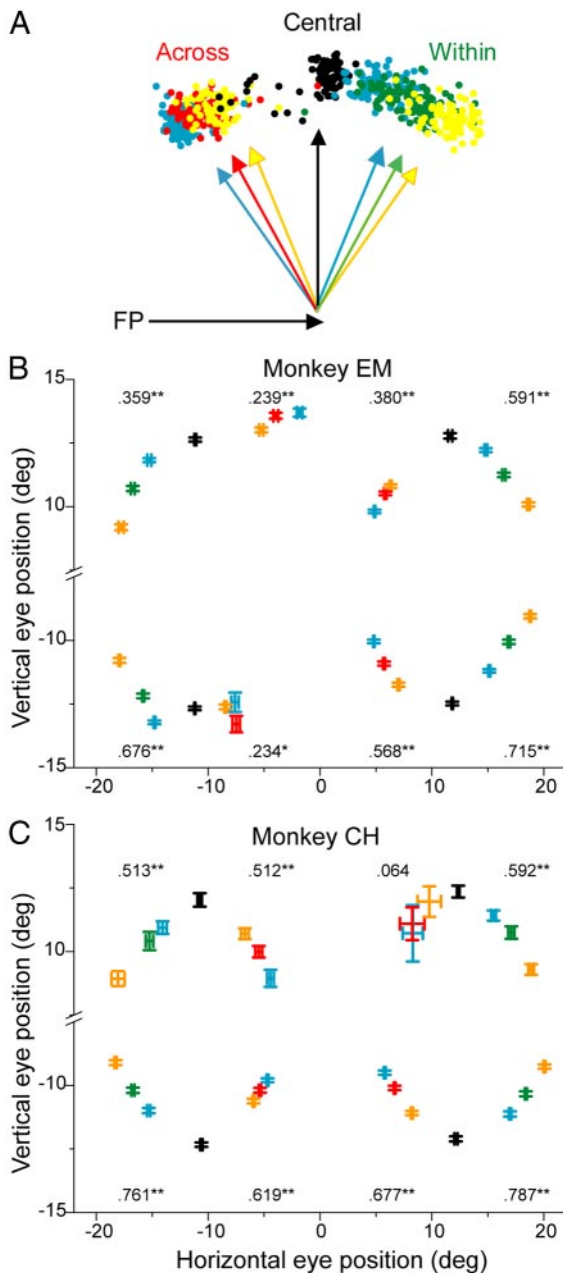


FIG. 13. Spatial updating is under sensory control, even for the across-hemifield condition. *A*: testing configuration and example data from Monkey EM. For each standard within (green) and across (red) sequence, the T2 location was unpredictably displaced by 5 angular degrees either toward (cyan) or away from (yellow) the vertical meridian. *B* and *C*: crosshairs show mean endpoint (\pm SE) of the second saccade for each sequence, for each monkey; color coding as in *A*. R^2 values, shown either above or below each set of sequences, indicate the strength of the relationship between the direction of the monkey's saccade and the ideal direction; all but one were significant at either $**P < 0.0001$ or $*P < 0.05$.

by conducting a regression analysis, asking whether the angular trajectory of the ideal saccade was predicted by the angular trajectory of the monkey's saccade. Like the precision analysis we conducted on the data from *expt 1*, this approach also tells us how well the monkey took the first saccade into account on a trial-by-trial basis. We conducted the regression separately on the data from each standard sequence with its associated shifted sequences. We found highly significant R^2 values ($P <$

0.0001) for all but two across-hemifield sequences, where performance remained impaired: the lower left quadrant for monkey EM ($P < 0.05$) and the upper right quadrant for monkey CH ($P = 0.06$). We also observed significant displacement even for across-hemifield sequences that were not fully learned (monkey EM, upper left quadrant). We conclude that the monkeys were not ultimately using a motor rule or another automated approach to perform the across-hemifield sequences, but were in fact basing their behavior on the sensory location of T2 and updating this representation in conjunction with the first saccade.

We have shown that the monkeys were able to learn the across-hemifield sequences and execute them under sensory control. We next considered that the performance on these across-hemifield sequences might be particularly susceptible to increases in task difficulty. The following two experiments address this possibility by asking whether across-hemifield performance is robust in response to novel target geometries (*expt 4*) and increased mnemonic load (*expt 5*).

Experiment 4: New spatial configurations disrupt across-hemifield performance

In *expt 4* we asked whether the monkeys' success on the standard across-hemifield sequences would generalize to a novel configuration of the double-step task. This possibility was of particular interest given the variability we observed in initial across-hemifield performance. We reasoned that the monkeys might be least able to generalize in quadrants where across-hemifield performance had improved most slowly. We tested the monkeys' ability to generalize by changing the amplitude of both saccades and altering the angular displacement of the second saccade. In this new configuration, the amplitudes of the first and second saccades were 8 and 15°, respectively, and angular displacement was 45°; in the standard sequences, saccade amplitudes were both 12°, with a displacement of 30°. Once again we simultaneously introduced the new within- and across-hemifield sequences, after brief training to criterion on the new central sequences. Data from the standard configuration were obtained at the end of each session.

Both monkeys were able to perform all the new sequences, although with more inaccuracy than that for the standard sequences. Our specific interest was the interaction between updating condition and novelty: did the new configuration disrupt performance on the across-hemifield condition more than the within-hemifield condition? We conducted a multivariate ANOVA with four factors (updating condition, S1 direction, vertical visual field, and novelty). We observed a highly significant interaction between updating condition and novelty (both monkeys, $P < 0.0001$), and indeed, the difference between old and new configurations was significant for the across but not the within condition ($P < 0.05$, Tukey's HSD). On average, then, the monkeys were subject to reimpairment when introduced to novel spatial geometries.

We further asked whether there was evidence of generalization on the across-hemifield condition in any quadrant. When we examined across-hemifield performance in each quadrant, we found a variable pattern of results, not unlike the pattern observed in initial behavioral testing. Monkey EM was consistently worse on new compared with old across-hemifield sequences in all quadrants (Fig. 14A, all red triangles above

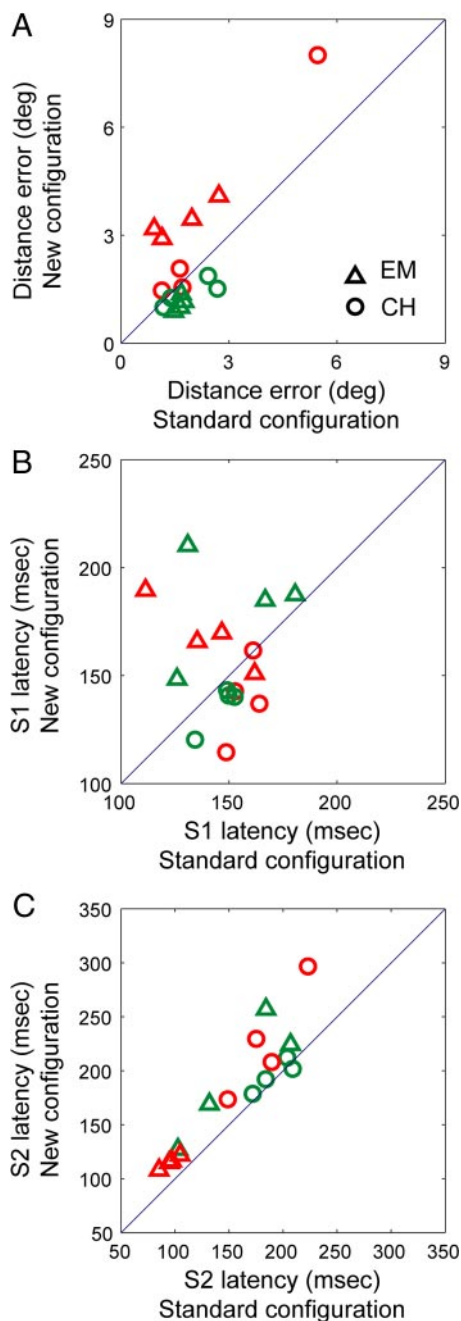


FIG. 14. Introduction of new spatial geometries was more deleterious for across-hemifield than for within-hemifield updating. Average error (A) and latency (B, C) for the new configuration (y-axis) compared with the standard configuration (x-axis). Each symbol represents average performance from one quadrant, for either the across (red) or within (green) condition.

unity line). Monkey CH showed a selective impairment on the new across-hemifield sequences in some quadrants but not all, and in some cases distance error increased only slightly (Fig. 14A, red circles above unity line). This monkey's ability to generalize in some quadrants is consistent with our observations from initial testing: we found that Monkey CH was able to learn the across-hemifield sequence in the upper left quadrant on Day 1, and subsequently performed the across-hemifield sequences well in the lower field on Day 2 of testing.

With respect to saccade latencies, we found that introduction of the new configuration led to similar changes in first-saccade

latencies for the within-hemifield and across-hemifield conditions. Monkey EM initiated the new sequences more slowly (Fig. 14B, triangles above the line), whereas monkey CH initiated them more quickly (Fig. 14B, circles below the line). Neither monkey exhibited a specific first-saccade slowing on the new across-hemifield condition. For the second saccade, the effect of novelty differed for the two animals. Monkey EM was uniformly slower to initiate the second saccade, both for within and for across sequences (Fig. 14C, triangles above the line). Monkey CH, however, showed a selective slowing on the across-hemifield condition when the new configuration was introduced (Fig. 14C, more red than green circles above the line). These accuracy and latency data indicate that, overall, generalization to new sequences is less robust for the across-hemifield condition. The data from each monkey on performance of the new sequences parallel across-hemifield performance in initial testing sessions. Specifically, they indicate that monkey CH was more adept at generalizing to new across-hemifield sequences than was monkey EM.

Experiment 5: Across-hemifield updating is intact in a delayed double-step task

Performance in the double-step task depends on remapping an evanescent trace of a briefly appearing stimulus. We were interested in the possibility that the stimulus trace for the across-hemifield condition might fade more quickly in the absence of the forebrain commissures. Our interest in this issue was motivated by the variable across-hemifield performance of Monkey CH in initial testing. We noted that the monkey was most impaired on the across-hemifield condition in the upper right quadrant, where latencies of the first saccade were also slowest (Fig. 5C). This led us to ask whether the monkey's success in the other quadrants depended on being able to generate the first saccade rapidly, so as arrive at T1 in time to access a rapidly vanishing memory trace of the stimulus.

We reasoned that performance on the across-hemifield condition might deteriorate in all quadrants if the monkey had to hold the T2 stimulus trace in mind during a delay period. We tested this by introducing a delay (300–500 ms) between the time of T2 appearance and the monkey's cue to initiate the double-step sequence. This experiment was conducted in monkey CH at a time when its performance had recovered. We used a training procedure similar to the original one that preceded *expt 1*. The monkey first learned to perform a vertical version of the delay task and was then trained on the central condition of the horizontal version of the task. Finally, we introduced the across-hemifield and within-hemifield sequences simultaneously, to determine whether the monkey's performance was affected by the imposed delay.

We found that performance of the across-hemifield sequences was not selectively impaired in the delay paradigm. The scatterplots of saccade endpoints show that performance was less accurate for all three conditions in the delayed version, compared with the standard version of the double-step task (Fig. 15A; compare with Fig. 11). Across-hemifield performance was not selectively worse, however, relative to performance on the central or within conditions, except in one quadrant (upper right; Fig. 15B). The monkey had shown persistent impairment for this sequence in the standard version

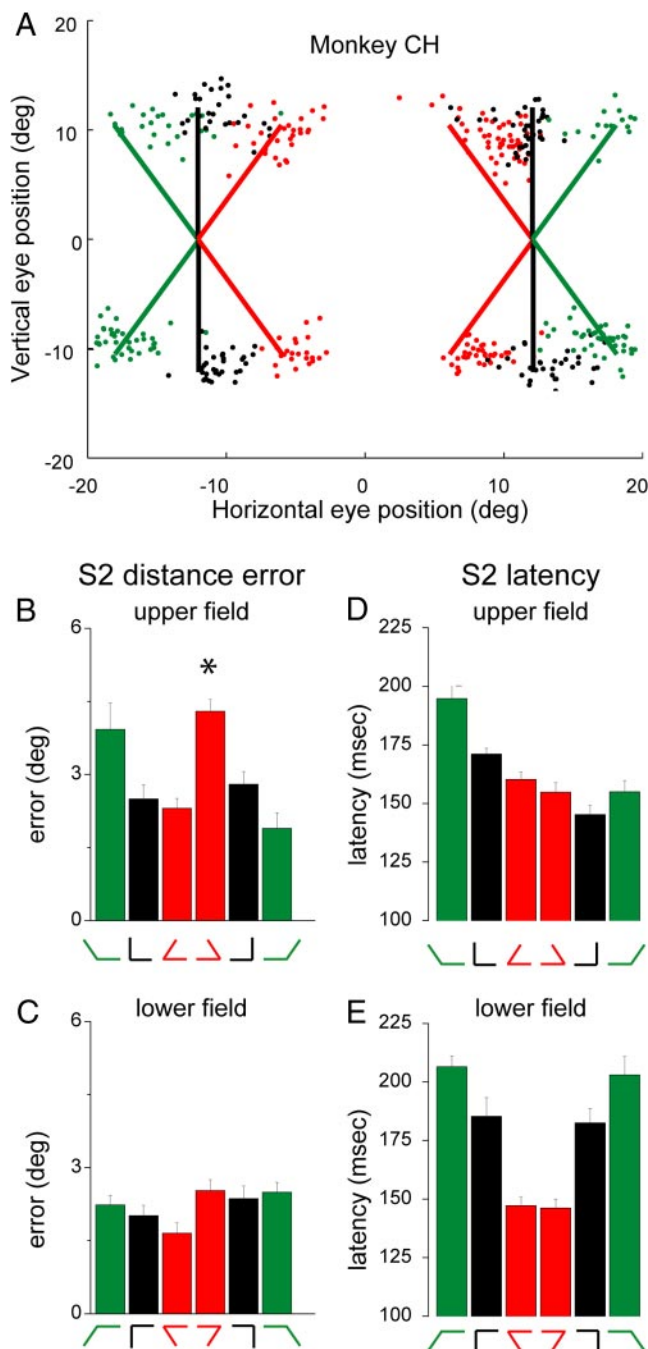


FIG. 15. Performance of the across-hemifield condition was not significantly impaired in the delayed double-step task. *A*: endpoints of the second saccade; conventions as in Fig. 3. *B–E*: measures of accuracy and latency; conventions as in Fig. 4.

of the double-step task. Therefore the increased error in the delay task cannot be attributed to the additional mnemonic requirements of this paradigm. Latencies for both the first and second saccades were also not significantly prolonged for the across-hemifield sequences (Fig. 15, *D* and *E*; shown for S2 only). We conclude that the remembered T2 representation is robust for the across-hemifield sequences and that the circuitry supporting across-hemifield updating in the split-brain monkey is not disrupted by increased working memory demands.

SUMMARY

These experiments provide five main findings regarding spatial updating in the split-brain monkey. First, our standard paradigm revealed an initial impairment and ultimate improvement of performance on double-step sequences that required across-hemifield updating. Second, we found that the initial impairment was not mitigated by placing the across-hemifield target nearer to the midline. Third, once performance on across-hemifield sequences began to improve, the monkeys were able to generate the sequences under sensory control, taking into account small shifts in target position. Fourth, recovery of the across-hemifield sequences did not generalize readily to new spatial configurations; rather, the monkeys required experience with specific across-hemifield sequences for performance to improve. Finally, an increase in working memory load did not selectively disrupt double-step sequences that required across-hemifield updating.

DISCUSSION

The construction of a continuously accurate spatial map requires that visual representations be updated in conjunction with saccades. The neural circuits by which this updating is accomplished remain unknown. In the present study, we investigated the mechanisms for updating a representation from one visual field to the other. Specifically, we asked whether performance of the double-step task was impaired in the split-brain monkey when updating required the transfer of visual signals from one hemisphere to the other. Two central findings emerge from these behavioral experiments.

The first is that spatial updating typically relies on communication by direct cortico-cortical links. In a series of experiments, we showed that across-hemifield updating is compromised in the absence of the forebrain commissures. The split-brain monkeys were initially impaired on double-step sequences that required updating of the second target representation from one visual hemifield to the other (*expt 1*). This impairment was most evident in increased distance error and, to a lesser extent, in increased saccade latencies for the across-hemifield sequences. The task design allowed us to attribute these deficits to a disruption of spatial updating and not to confusion caused by unfamiliar sequences: the across-hemifield sequences were selectively impaired relative to equally unfamiliar within-hemifield sequences. We also ruled out three alternatives for the initial impairment in split-brain monkeys. It cannot be attributed to: 1) inaccuracy of the first saccade; 2) basic sensory, memory, or eye movement deficits; or 3) a deficit in generating sequences that require a reversal in saccade direction. Further, we found that the impairment persisted even when the target of the second saccade was placed very near to the midline (*expt 2*). This indicates that ipsilateral visual representations were unable to support updating. This finding is compatible with physiological studies, which demonstrate that ipsilateral visual representations in the ventral stream depend on the corpus callosum and anterior commissure (Gross et al. 1977). Finally, we found that in some cases, the across-hemifield impairment was reinstated when we introduced new sets of targets (*expt 4*). This indicates that alternate interhemispheric routes may be used on an as-needed basis between restricted portions of the visual field. These results are consistent with reports of experience-dependent plasticity and

recovery in both the auditory and visual systems (Huxlin and Pasternak 2004; Karni and Sagi 1991; Recanzone et al. 1993; Rudolph and Pasternak 1999). Taken together, our behavioral findings clearly demonstrate that across-hemifield updating is compromised in the absence of direct cortico-cortical pathways.

The second main finding is that direct cortico-cortical links are ultimately not required for accurate spatial updating. In the absence of the forebrain commissures, the impairment of across-hemifield performance was not universal or permanent. One of the split-brain monkeys exhibited rapid improvement on one of the across-hemifield sequences during the first day of testing in the upper visual field. On the subsequent day, we found that this same monkey was effectively unimpaired in the lower visual field. This may reflect a successful generalization. Both monkeys were ultimately able to perform the across-hemifield double-step sequences even in quadrants where impairment was initially profound. We found that improvement of the individual across-hemifield sequences occurred over different time courses. There is no obvious explanation for these differences, which we observed both between monkeys and among quadrants within each individual monkey. The differences may reflect several factors, including the ability to generalize to new across-hemifield sequences, complex variations in strategy, and biases in the representation of visual space (Ellison and Walsh 2000; Maunsell and Van Essen 1987; Previc 1990). The critical result is that both monkeys were ultimately successful in performing double-step sequences that required updating of the second target representation from one hemifield to the other. Two further experiments showed that this successful across-hemifield performance was precise and robust in the split-brain monkey. We found that across-hemifield updating was under sensory control (*expt 3*) and was unaffected by increased working memory demands (*expt 5*). These important and unexpected findings demonstrate that spatial representations can be updated across visual hemifields in the absence of the forebrain commissures.

Role of the forebrain commissures in visuospatial behavior

Our findings build on previous investigations of visual processing in split-brain individuals. Earlier neuropsychological and physiological studies have shown that, in the absence of the forebrain commissures, interhemispheric transfer is clearly disrupted for color and form information, including visual associative memory (Corballis 1995; Eacott and Gaffan 1989; Hasegawa et al. 1998; Land et al. 1983; Tomita et al. 1999; Trevarthen 1990). What has been less clear is the extent to which *spatial* representations can be transferred interhemispherically when both the corpus callosum and anterior commissure are severed. Studies of human split-brain patients have shown that spatial information can be transferred in the absence of the corpus callosum, but with limited resolution and for limited purposes. These patients are capable of comparing locations of stimuli presented in opposite hemifields, but only at a coarse spatial resolution (Holtzman 1984). Further, a stimulus presented in one visual hemifield may be able to guide *attention* in the opposite hemifield (Holtzman et al. 1981; but see Hines et al. 2002; Reuter-Lorenz and Fendrich 1990), yet this stimulus cannot be used for explicit identification of locations in the opposite hemifield (Holtzman et al. 1981).

These findings suggest that subcortical–cortical interactions can subserve interhemispheric transfer of limited spatial information, although it is also important to note that the preserved functions in these split-brain patients may be mediated either subcortically or by the intact anterior commissures. Our results provide new evidence that the representations of stimulus traces can be transferred between hemispheres in the absence of all direct cortico-cortical links, and that these updated representations can be used to guide subsequent eye movements with fine spatial resolution.

Pathways for spatial updating

Our results demonstrate that spatial updating is a robust phenomenon, supported by a redundant circuitry that includes not only cortical but also subcortical structures. The present study has focused on the substrate for transferring visual representations in conjunction with saccades and complements recent research that delineates a subcortical–cortical pathway for communicating a corollary discharge signal. Corollary discharge—a copy of the command to move the eyes—must be used to initiate the updating of stimulus representations in visual areas (Goldberg et al. 1990). Recent physiological and inactivation studies indicate that corollary discharge information is conveyed from superior colliculus to the frontal eye field by the mediodorsal thalamus (Sommer and Wurtz 2004a,b). Inactivation of this pathway disrupts the communication of information about the impending saccade, causing a deficit in performance on the double-step task (Sommer and Wurtz 2004b). These investigators found a significant yet partial deficit, indicating that alternate pathways and/or mechanisms may also contribute to the ability to monitor ongoing eye movements. The anatomical basis of corollary discharge signals is a subject of current interest (Bellebaum et al. 2005; Guillery 2003; Sommer and Wurtz 2002, 2003, 2004a,b; White et al. 2004). These signals may arise from many brain structures, both cortical and subcortical. A full understanding of the circuitry for spatial updating will need to account for the pathways by which this motor information modifies visual representations, particularly those in higher-order areas such as parietal cortex.

Role of parietal cortex in spatial updating

Parietal cortex plays a central role in spatial updating (Colby and Goldberg 1999; Duhamel et al. 1992a; Gottlieb et al. 1998; Medendorp et al. 2003; Merriam et al. 2003; Pierrot-Deseilligny et al. 2004; Pisella and Mattingley 2004; Quaia et al. 1998; Van Donkelaar and Muri 2002). Neuropsychological studies have shown that accurate performance of the double-step task depends on parietal but not frontal cortex (Duhamel et al. 1992b; Heide et al. 1995). Patients with parietal damage can accurately generate double-step sequences when both saccades are visually guided, but are impaired when the second saccade is memory guided and requires spatial updating of the second target location. The importance of parietal cortex in performance of the double-step task has also been demonstrated in monkeys. Inactivation of area LIP impairs performance on the double-step task, as evidenced by decreased accuracy and increased latencies for the second eye movement (Li and Andersen 2001). These findings provide converging

evidence for the proposal that parietal cortex is the site where the computations for remapping are carried out. In the normal animal, updating activity in area LIP is thought to reflect a direct transfer of stimulus trace activity from neurons that encode a stimulus location before the eye movement, (Colby and Goldberg, 1999) to neurons that encode the location after the eye movement. In the split-brain monkeys, the direct link between the parietal cortices is severed, yet our behavioral results indicate that a stimulus trace that is initially encoded in one hemisphere can still be accurately updated to the opposite hemisphere. This raises the possibility that parietal cortex is no longer engaged in across-hemifield updating; the transformations may be accomplished entirely by subcortical pathways. In the accompanying paper, we describe physiological experiments that test whether LIP neurons participate in across-hemifield updating in the split-brain monkey.

These investigations shed new light on the circuitry that contributes to our perceptual experience of the visual world. Like visual representations themselves, the pathways that support spatial updating are not static but dynamic. Direct cortical links are not the only substrate for producing updated spatial representations. Instead, updating is subserved by a flexible network of cortical and subcortical structures, in which motor signals act on visual information to create a stable representation of the world around us.

ACKNOWLEDGMENTS

We thank K. McCracken and Dr. Kevin Hitchens for technical assistance, and our colleagues at the Center for the Neural Basis of Cognition for constructive comments.

Present addresses: R. Berman, Laboratory of Sensorimotor Research, National Eye Institute, National Institutes of Health, Bethesda, MD 20892; L. Heiser, Life Sciences Division, Lawrence Berkeley National Lab, Berkeley, CA 94720.

GRANTS

This work was supported by National Institutes of Health Grant EY-12032, technical support was provided by core grant EY-08908, and collection of MR images was supported by P41RR-03631. Support was also provided by National Science Foundation Fellowship to R. A. Berman, and National Aeronautics and Space Administration Fellowship to L. M. Heiser.

REFERENCES

- Baizer JS and Bender DB.** Comparison of saccadic eye movements in humans and macaques to single-step and double-step target movements. *Vision Res* 29: 485–495, 1989.
- Barash S, Bracewell RM, Fogassi L, Gnadt JW, and Andersen RA.** Saccade-related activity in the lateral intraparietal area. II. Spatial properties. *J Neurophysiol* 66: 1109–1124, 1991.
- Becker W and Jürgens R.** An analysis of the saccadic system by means of double step stimuli. *Vision Res* 19: 967–983, 1979.
- Bell AH, Everling S, and Munoz DP.** Influence of stimulus eccentricity and direction on characteristics of pro- and antisaccades in non-human primates. *J Neurophysiol* 84: 2595–2604, 2000.
- Bellebaum C, Daum I, Koch B, Schwarz M, and Hoffmann KP.** The role of the human thalamus in processing corollary discharge. *Brain* 2005 [epub ahead of print].
- Ben Hamed S, Duhamel JR, Bremmer F, and Graf W.** Representation of the visual field in the lateral intraparietal area of macaque monkeys: a quantitative receptive field analysis. *Exp Brain Res* 140: 127–144, 2001.
- Berlucchi G and Rizzolatti G.** Binocularly driven neurons in visual cortex of split-chiasm cats. *Science* 159: 308–310, 1968.
- Colby CL and Goldberg ME.** Space and attention in parietal cortex. *Annu Rev Neurosci* 22: 319–349, 1999.
- Corballis MC.** Visual integration in the split brain. *Neuropsychologia* 33: 937–959, 1995.
- Dassonville P, Schlag J, and Schlag-Reg M.** The use of egocentric and exocentric location cues in saccadic programming. *Vision Res* 35: 2191–2199, 1995.
- Demeter S, Rosene DL, and Van Hoesen GW.** Fields of origin and pathways of the interhemispheric commissures in the temporal lobe of macaques. *J Comp Neurol* 302: 29–53, 1990.
- Desimone R, Moran J, Schein SJ, and Mishkin M.** A role for the corpus callosum in visual area V4 of the macaque. *Vis Neurosci* 10: 159–171, 1993.
- Duhamel JR, Colby CL, and Goldberg ME.** The updating of the representation of visual space in parietal cortex by intended eye movements. *Science* 255: 90–92, 1992a.
- Duhamel JR, Goldberg ME, Fitzgibbon EJ, Sirigu A, and Grafman J.** Saccadic dysmetria in a patient with a right frontoparietal lesion. The importance of corollary discharge for accurate spatial behaviour. *Brain* 115: 1387–1402, 1992b.
- Eacott MJ and Gaffan D.** Interhemispheric transfer of visual learning in monkeys with intact optic chiasm. *Exp Brain Res* 74: 348–352, 1989.
- Ellison A and Walsh V.** Visual field asymmetries in attention and learning. *Spat Vis* 14: 3–9, 2000.
- Gazzaniga MS.** Perceptual and attentional processes following callosal section in humans. *Neuropsychologia* 25: 119–133, 1987.
- Gazzaniga MS, Bogen JE, and Sperry RW.** Some functional effects of sectioning the cerebral commissures in man. *Proc Natl Acad Sci USA* 15: 1765–1769, 1962.
- Gnadt JW and Andersen RA.** Memory related motor planning activity in posterior parietal cortex of macaque. *Exp Brain Res* 70: 216–220, 1988.
- Gnadt JW, Bracewell RM, and Andersen RA.** Sensorimotor transformation during eye movements to remembered visual targets. *Vision Res* 31: 693–715, 1991.
- Goldberg ME and Bruce CJ.** Primate frontal eye fields. III. Maintenance of a spatially accurate saccade signal. *J Neurophysiol* 64: 489–508, 1990.
- Goldberg ME, Colby CL, and Duhamel J-R.** Representation of visuomotor space in the parietal lobe of the monkey. *Cold Spring Harb Symp Quant Biol* 55: 729–739, 1990.
- Gottlieb JP, Kusunoki M, and Goldberg ME.** The representation of visual salience in monkey parietal cortex. *Nature* 391: 481–484, 1998.
- Gross CG, Bender DB, and Mishkin M.** Contributions of the corpus callosum and the anterior commissure to visual activation of inferior temporal neurons. *Brain Res* 131: 227–239, 1977.
- Guillery RW.** Branching thalamic afferents link action and perception. *J Neurophysiol* 90: 539–548, 2003.
- Hallett PE and Lightstone AD.** Saccadic eye movements to flashed targets. *Vision Res* 16: 107–114, 1976.
- Hasegawa I, Fukushima T, Ihara T, and Miyashita Y.** Callosal window between prefrontal cortices: cognitive interaction to retrieve long-term memory. *Science* 281: 814–818, 1998.
- Hedreen JC and Yin TC.** Homotopic and heterotopic callosal afferents of caudal inferior parietal lobule in *Macaca mulatta*. *J Comp Neurol* 197: 605–621, 1981.
- Heide W, Blankenburg M, Zimmermann E, and Kompf D.** Cortical control of double-step saccades: implications for spatial orientation. *Ann Neurol* 38: 739–748, 1995.
- Hikosaka O and Wurtz RH.** Visual and oculomotor functions of monkey substantia nigra pars reticulata. III. Memory-contingent visual and saccade responses. *J Neurophysiol* 49: 1268–1284, 1983.
- Hines RF, Paul LK, and Brown WS.** Spatial attention in agenesis of the corpus callosum: shifting attention between visual fields. *Neuropsychologia* 40: 1804–1814, 2002.
- Holtzman JD.** Interactions between cortical and subcortical visual areas: evidence from human commissurotomy patients. *Vision Res* 24: 801–813, 1984.
- Holtzman JD, Sidtis JJ, Volpe BT, and Gazzaniga MS.** Dissociation of spatial information for stimulus localization and the control of attention. *Brain* 104: 861–872, 1981.
- Houzel JC, Carvalho ML, and Lent R.** Interhemispheric connections between primary visual areas: beyond the midline rule. *Braz J Med Biol Res* 35: 1441–1453, 2002.
- Huxlin KR and Pasternak K.** Training-induced recovery of visual motion perception after extrastriate cortical damage in the adult cat. *Cereb Cortex* 14: 81–90, 2004.
- Jeffries SM, Kusunoki M, Krishna SB, Cohen IS, and Goldberg ME.** Localization errors in a double-step saccade task are qualitatively explained by peri-saccade response patterns in LIP. *Soc Neurosci Abstr* 386.13, 2003.

- Jouandet ML and Gazzaniga MS.** Cortical field of origin of the anterior commissure of the rhesus monkey. *Exp Neurol* 66: 381–397, 1979.
- Judge SJ, Richmond BJ, and Chu FC.** Implantation of magnetic search coils for measurement of eye position: an improved method. *Vision Res* 20: 535–538, 1980.
- Kalesnykas RP and Hallett PE.** Retinal eccentricity and the latency of eye saccades. *Vision Res* 34: 517–531, 1994.
- Karni A and Sagi D.** Where practice makes perfect in texture discrimination: evidence for primary visual cortex plasticity. *Proc Natl Acad Sci USA* 88: 4966–4970, 1991.
- Lamantia AS and Rakic P.** Cytological and quantitative characteristics of four cerebral commissures in the rhesus monkey. *J Comp Neurol* 291: 520–527, 1990.
- Land EH, Hubel DH, Livingstone MS, Perry SH, and Burns MM.** Colour-generating interactions across the corpus callosum. *Nature* 303: 616–618, 1983.
- Li CS and Andersen RA.** Inactivation of macaque lateral intraparietal area delays initiation of the second saccade predominantly from contralesional eye positions in a double-saccade task. *Exp Brain Res* 137: 45–57, 2001.
- Maunsell JH and Van Essen DC.** Topographic organization of the middle temporal visual area in the macaque monkey: representational biases and the relationship to callosal connections and myeloarchitectonic boundaries. *J Comp Neurol* 266: 535–555, 1987.
- Mays LE and Sparks DL.** Dissociation of visual and saccade-related responses in superior colliculus neurons. *J Neurophysiol* 43: 207–232, 1980.
- Medendorp WP, Goltz HC, Vilis T, and Crawford JD.** Gaze-centered updating of visual space in human parietal cortex. *J Neurosci* 23: 6209–6214, 2003.
- Merriam EP, Genovese CR, and Colby CL.** Spatial updating in human parietal cortex. *Neuron* 39: 361–373, 2003.
- Nakamura K and Colby CL.** Visual, saccade-related, and cognitive activation of single neurons in monkey extrastriate area V3A. *J Neurophysiol* 84: 677–692, 2000.
- Nakamura K and Colby CL.** Updating of the visual representation in monkey striate and extrastriate cortex during saccades. *Proc Natl Acad Sci USA* 99: 4026–4031, 2002.
- Pandya DN and Vignolo LA.** Interhemispheric projections of the parietal lobe in the rhesus monkey. *Brain Res* 15: 49–65, 1969.
- Pierrot-Deseilligny C, Milea D, and Muri RM.** Eye movement control by the cerebral cortex. *Curr Opin Neurol* 17: 17–25, 2004.
- Pisella L and Mattingley JB.** The contribution of spatial remapping impairments to unilateral visual neglect. *Neurosci Biobehav Rev* 28: 181–200, 2004.
- Platt ML and Glimcher PW.** Response fields of intraparietal neurons quantified with multiple saccadic targets. *Exp Brain Res* 121: 65–75, 1998.
- Previc FH.** Functional specialization in the lower and upper visual fields in humans: its ecological origins and neurophysiological implications. *Behav Brain Sci* 13: 519–575, 1990.
- Quaia C, Optican LM, and Goldberg ME.** The maintenance of spatial accuracy by the perisaccadic remapping of visual receptive fields. *Neural Networks* 11: 1229–1240, 1998.
- Recanzone GH, Schreiner CE, and Merzenich MM.** Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys. *J Neurosci* 13: 87–103, 1993.
- Reuter-Lorenz PA and Fendrich R.** Orienting attention across the vertical meridian: evidence from callosotomy patients. *J Cogn Neurosci* 2: 232–238, 1990.
- Rudolph K and Pasternak T.** Transient and permanent deficits in motion perception after lesions of cortical areas MT and MST in the macaque monkey. *Cereb Cortex* 9: 90–100, 1999.
- Schwartz ML and Goldman-Rakic PS.** Callosal and intrahemispheric connectivity of the prefrontal association cortex in rhesus monkey: relation between intraparietal and principal sulcal cortex. *J Comp Neurol* 226: 403–420, 1984.
- Seltzer B and Pandya DN.** The distribution of posterior parietal fibers in the corpus callosum of the rhesus monkey. *Exp Brain Res* 49: 147–150, 1983.
- Sommer MA and Wurtz RH.** A pathway in primate brain for internal monitoring of movements. *Science* 296: 1480–1482, 2002.
- Sommer MA and Wurtz RH.** The frontal eye field sends predictively remapped visual signals to the colliculus. *J Vision* 3:146a, 2003.
- Sommer MA and Wurtz RH.** What the brain stem tells the frontal cortex. I. Oculomotor signals sent from superior colliculus to frontal eye field via mediodorsal thalamus. *J Neurophysiol* 91: 1381–1402, 2004a.
- Sommer MA and Wurtz RH.** What the brain stem tells the frontal cortex. II. Role of the SC-MD-FEF pathway in corollary discharge. *J Neurophysiol* 91: 1403–1423, 2004b.
- Tomita H, Ohbayashi M, Nakahara K, Hasegawa I, and Miyashita Y.** Top-down signal from prefrontal cortex in executive control of memory retrieval. *Nature* 401:699–703, 1999.
- Trevarthen C.** Integrative functions of the cerebral commissures. In: *Handbook of Neuropsychology*, edited by Boller FG and Grafman J. Amsterdam: Elsevier, 1990, vol. 4, p. 49–83.
- Umeno MM and Goldberg ME.** Spatial processing in the monkey frontal eye field. I. Predictive visual responses. *J Neurophysiol* 78: 1373–1383, 1997.
- Umeno MM and Goldberg ME.** Spatial processing in the monkey frontal eye field. II. Memory responses. *J Neurophysiol* 86: 2344–2352, 2001.
- van Donkelaar P and Muri R.** Craniotopic updating of visual space across saccades in the human posterior parietal cortex. *Proc R Soc Lond B Biol Sci* 269: 735–739, 2002.
- Vogels R, Saunders RC, and Orban GA.** Hemispheric lateralization in rhesus monkeys can be task-dependent. *Neuropsychologia* 32: 425–438, 1994.
- Walker MF, Fitzgibbon EJ, and Goldberg ME.** Neurons in the monkey superior colliculus predict the visual result of impending saccadic eye movements. *J Neurophysiol* 73: 1988–2003, 1995.
- White RL III and Snyder LH.** Delay period microstimulation in frontal eye fields updates spatial memories. *Soc Neurosci Abstr* 527: 9, 2004.
- Zaidel E and Iacoboni M.** Introduction: Poffenberger's simple reaction time paradigm for measuring interhemispheric transfer time. In: *The Parallel Brain: The Cognitive Neuroscience of the Corpus Callosum*, edited by Zaidel E and Iacoboni M. Cambridge, MA: MIT Press, 2003, p. 1–7.
- Zivotofsky AZ, Tzur R, Caspi A, and Gordon CR.** Evidence for co-processing of orthogonal compared to co-linear saccades. *Soc Neurosci Abstr* 441: 6, 2003.