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Updating Visual Space during Motion in Depth

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Summary

Whether we are riding in a car or walking, our internal map of the environment must be continuously updated to maintain spatial constancy. Using a memory eye movement task, we examined whether nonhuman primates can keep track of changes in the distance of nearby objects when moved toward or away from them. We report that memory-guided eye movements take into account the change in distance traveled, illustrating that monkeys can update retinal disparity information in order to reconstruct three-dimensional visual space during motion in depth. This ability was compromised after destruction of the vestibular labyrinths, suggesting that the extraretinal signals needed for updating can arise from vestibular information signaling self-motion through space.

Introduction

In our daily lives, we continuously interact with our environment in a manner that requires us to keep track of object location relative to ourselves. It is thus important that the brain not only constructs and stores internal representations of the physical world, but also that it continuously updates this stored spatial representation as we move. For example, human subjects and nonhuman primates can accurately direct their eyes to remembered targets that are no longer in view, even after gaze has deviated away from its initial position at the time of visual target presentation. This process of keeping track of the eccentricity and direction of objects around us, even in the absence of new visual information, is often referred to as "visuospatial updating" and has been studied extensively during eye movements (Hallett and Lightstone, 1976; McKenzie and Lisberger, 1986; Pelisson et al., 1989; Schlag et al., 1990; Ohtsuka, 1994; Zivotofsky et al., 1996; Herter and Guitton, 1998; Blohm et al., 2003, 2005; Mays and Sparks, 1980; Sparks and Mays, 1983).

Accurate saccades to world-fixed targets can also be elicited after intervening rotations and lateral displacements of the head and/or body that change the relative orientation of gaze with respect to the object of interest (Baker et al., 2003; Bloomberg et al., 1988; Israel et al., 1999; Klier et al., 2005; Li et al., 2005; Medendorp et al., 2002). Thus, visuospatial updating has been thought to require extraretinal signals, e.g., efference copies of the motor command, as well as vestibular or proprioceptive signals, although the specific contributions of such extraretinal information remain unknown.

Updating spatial direction, however, is only one aspect of maintaining a stored representation of the external world; updating relative depth and distance constitutes another important requirement for spatial constancy. For example, whenever we experience self-motion during walking, running, riding a bike, or driving a car, not only the eccentricity and direction but also the object's distance from ourselves must also be continuously adjusted using extraretinal information related to body displacement through space. Despite the many studies that have characterized the ability to update target direction, it remains unknown whether humans and monkeys can update egocentric distance. Unlike updating for spatial direction, which is thought to involve "remapping" of a retinotopic map of visual space (Goldberg and Bruce, 1990; Duhamel et al., 1992; Colby et al., 1993), updating of object distance would require changes in retinal disparity representations (Cumming and DeAngelis, 2001). Little is currently known about this process.

To test whether spatial memory accounts for changes in traveled distance, we trained three monkeys to make memory-guided eye movements in response to previously flashed targets after being passively moved toward or away from them. The use of passive motions ruled out motor efference as a source of the updating information, thus allowing for an examination of sensory vestibular information as potential extraretinal cues for spatial constancy. By comparing these memory-guided eye movements made during motion trials with the eye movements made in randomly interleaved stationary control trials, we found that monkeys compensated for the traveled distance by incorporating extraretinal depth motion information, likely arising from vestibular information signaling self-motion through space. The latter hypothesis was directly confirmed by showing that this ability was compromised after destruction of the vestibular labyrinths. These results demonstrate not only that monkeys can update retinal disparity information but also that intact vestibular motion cues are critical in reconstructing three-dimensional visual space during motion in depth.

Results

Basic Observations

Monkeys were trained to perform memory-guided eye movements in response to targets flashed at different distances, as illustrated in Figures 1 and 2. Each memory-guided eye movement trial was initiated with the fixation of a far, head-fixed, central LED, while a near, world-fixed, eccentric target was briefly flashed (Figure 1). Following a variable delay period, the central fixation LED was turned off and the monkey made an eye movement toward the remembered location of the flashed target. This movement consisted of a saccade, followed by a slower change in vergence angle (Figure

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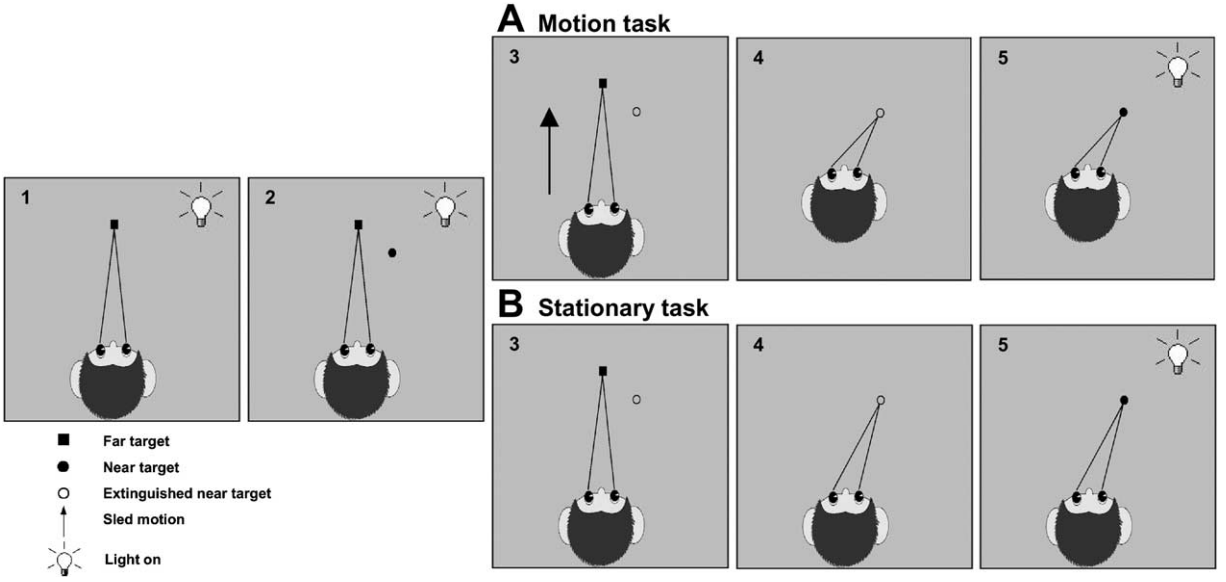

Figure 1. Task Outline

Schematic description of the motion (A) and stationary (B) memory tasks. Intervals 1 and 2 (similar for both tasks) included fixation of the head-fixed, far, central target in an illuminated room while a world-fixed, near, peripheral target flashed briefly (200 ms). Then (interval 3), the room lights were turned off while the monkey maintained fixation on the central target for an additional 750–1750 ms. Motion trials (A) differed from stationary trials (B) in that the animal was moved toward or away from the target array during this time (sled motion, interval 3). The offset of the central target was the cue for the memory-guided eye movement (interval 4). The peripheral target and the room lights were relit after eye position stayed within memory behavioral windows (see Experimental Procedures) for 1 s. A corrective eye movement (interval 5) defined the successful completion of the trial, and a juice reward was delivered.

2). Because memory-guided eye movements tend to underestimate the required change in vergence for near targets (Li et al., 2005; Medendorp et al., 2003), a corrective eye movement brought the eyes closer to the target when it was turned back on at the end of each trial.

In "motion" trials, the monkey was passively moved 5 cm forward or backward (17→12 cm, 17→22 cm, 27→22 cm, and 27→32 cm) during the delay period while maintaining fixation on the head-fixed central target in an otherwise totally dark room (Figure 2A; see Experimental Procedures). Interleaved with these motion trials were stationary runs, which were performed at the corresponding initial (Figure 2B) and final (Figure 2C) motion task positions. For stationary trials, the required change in vergence was specified exclusively by visual cues (retinal disparity, blur). In contrast, the motion trials changed the relative distance of the target and thus dissociated the required change in vergence angle from the retinal disparity of the flash. If solely visual cues were used to specify flash location in short-term spatial memory, then vergence angle in the motion trials should change similarly as in the initial position stationary trials (memory vergence in Figure 2A should be the same as in Figure 2B; bottom traces).

Alternatively, if the distance traveled was continuously monitored using extraretinal motion cues, then the stored relative distance of the flash should be updated, such that the vergence angle change for motion trials should be similar to that for final position stationary trials (memory vergence in Figure 2A should be the same as in Figure 2C; bottom traces). As shown in Figure 2A, the vergence eye movement at the end of the memory period (shaded area) was more similar to that of the final position rather than the initial position stationary task, suggesting that the distance traveled by the animal was taken into account when programming the memory eye movement.

Figure 3 illustrates memory vergence responses for the 17→12 cm motion task (green traces), superimposed on the corresponding data for the initial (blue traces) and final (red traces) position stationary task. Responses are shown separately for all four (up, down, left, and right) targets in all three animals (M1, M2, and M3). Data for each individual run have been aligned at memory saccade onset (time = 0 ms), such that the displayed traces compare mean (±SEM) vergence responses throughout the remaining duration of the memory period (lasting ~1000 ms after the initial saccade, which brought the eyes within the specified memory behavioral windows; see Experimental Procedures). Although the temporal aspects of vergence responses differed among animals (and vergence often continued to increase throughout the memory period; see also Li et al., 2005), motion task vergence changes were always different than those of the initial position stationary trials and in most cases more similar to those of the final position stationary trials (Figure 3, compare green with blue and red traces).

Similar observations were made for all distance/motion combinations (17→12 cm, 17→22 cm, 27→22 cm, and 27→32 cm). To quantify these effects, we

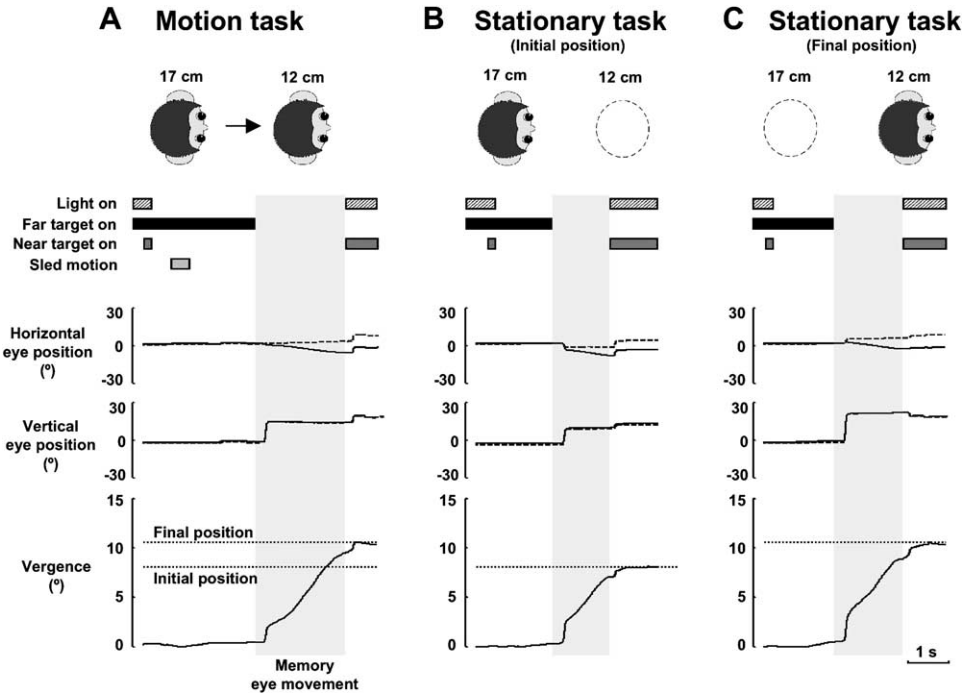

Figure 2. Examples of Individual Motion and Stationary Trials

The animal made memory-guided eye movements to an upward target flashed at a distance of 17 cm (A and B) or 12 cm (C). During the delay period in (A), the animal was moved 5 cm forward. From top to bottom, horizontal and vertical positions of the right and left eyes (solid and dashed lines, respectively), as well as vergence angle, have been illustrated. For the vergence plot in (A), dotted lines illustrate the visually guided vergence angle from the initial and final position stationary trials in (B) and (C). The time period corresponding to the memory eye movement (interval 4, which was variable from trial to trial) is highlighted in gray. Data from animal M2.

computed the total change in vergence at the end of the memory period (50 ms before the peripheral target was turned back on; see Experimental Procedures). Considering all data from the three animals, vergence changes for motion trials were significantly different from the respective initial position stationary trials [factorial ANOVA, $F(4196, 1) = 44.9$, $p << 0.001$]. In contrast, vergence angle changes for motion trials were indistinguishable from those for final position stationary trials [factorial ANOVA, $F(3882, 1) = 0.8$, $p >> 0.05$].

To further illustrate these results, the mean (±SEM) changes in vergence at the end of the memory period for motion trials have been plotted versus the corresponding changes for either the initial position or final position stationary trials in Figures 4A and 4B, respectively. Data points for motion trials fell tightly along the unity slope (dotted) line only when plotted as a function of the vergence eye movements made from the respective final position stationary trials (Figure 4B). In contrast, when motion task vergence was plotted versus the corresponding initial position stationary task vergence, data points fell either above or below the unity slope line, for forward and backward displacements, respectively. When considering data from all three monkeys (M1: circles; M2: triangles; and M3: squares), correlations were higher for final position (Figure 4B: R^2 = 0.96; slope = 0.95, 95% confidence intervals: 0.89, 1.00) than initial position (Figure 4A: R^2 = 0.60; slope = 1.27, 95% confidence intervals: 1.03, 1.54).

Extrapolation to Novel Conditions with No Visual Feedback

Because animals were extensively tested with these tasks in the presence of visual feedback (the peripheral target was turned back on during interval 5, see Figures 1 and 2), it is possible that this ability simply reflected learned correlations between each condition. Thus, to verify that these results reflect an online sensorimotor transformation, rather than an arbitrary stimulus-response mapping, data were also collected in additional blocks that included novel (oblique) targets and novel (3 cm) displacements. These novel motion trials included 15→10 cm, 15→12 cm, 15→18 cm, and 15→20 cm displacements, randomly interleaved within the corresponding stationary runs. Importantly, these tasks were performed in the absence of visual feedback (i.e., the peripheral target was not turned back on at the end of the trial; thus, the animal never experienced the error in foveating the target).

Mean (±SEM) memory vergence responses for the novel 3 cm displacements (15→12 cm and 15→18 cm) have been plotted, along with data from the corresponding initial and final stationary conditions in Figure 5A. Vergence eye movements during the 15→12 cm (green traces) and 15→18 cm (cyan traces) motion trials were different from each other and from the 15 cm stationary trials (blue traces). Furthermore, the memory vergence changes for the 15→12 cm and 15→18 cm displacements were closer to those for the respective

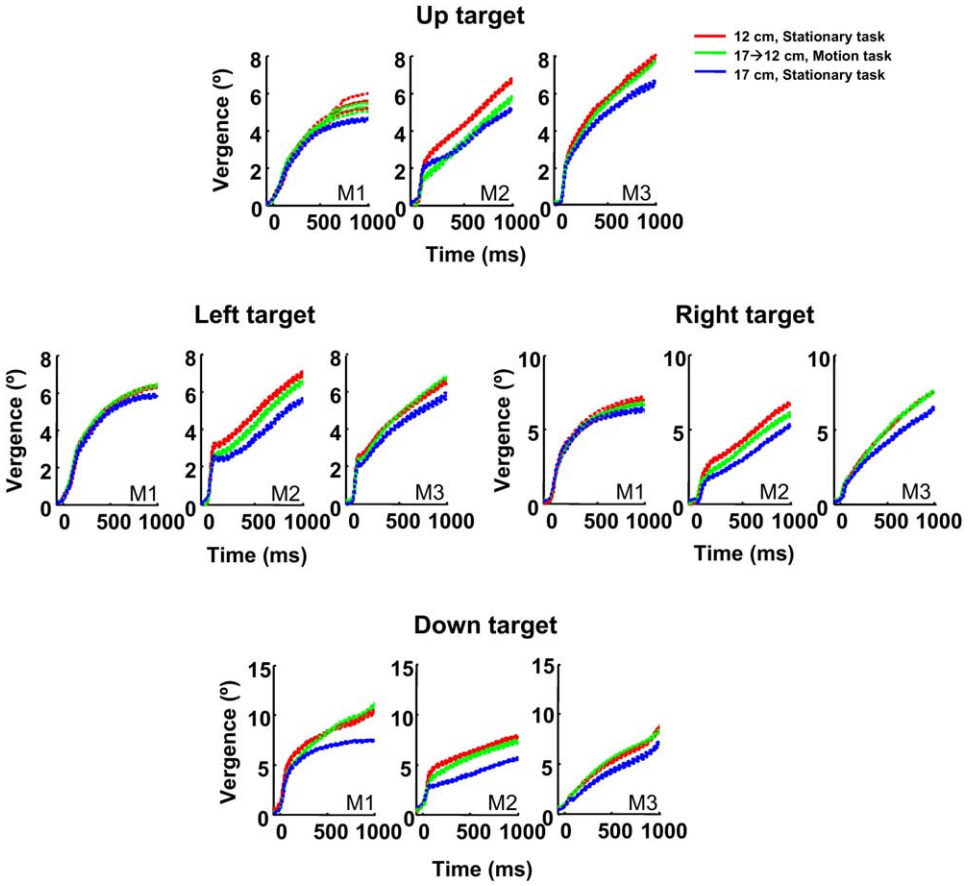

Figure 3. Examples of Mean Responses

Data illustrate mean ± SEM (solid and dotted lines, respectively) of the memory vergence elicited for each of the four flashed targets (up, down, left, and right) for the 17→12 cm motion task (green traces), as well as the corresponding initial (17 cm, blue traces) and final (12 cm, red traces) stationary trials. Data are shown separately for each animal (M1, M2, or M3). To compute the averages, individual runs were aligned at saccade onset (time = 0). Notice that vergence often continued to increase throughout the memory period, a characteristic of open-loop memory vergence (Li et al., 2005).

final position stationary trials (12 cm, red traces; and 18 cm, magenta traces) than those for the initial position stationary task (15 cm, blue traces).

These observations were quantified by measuring the vergence changes at the end of the memory period (see Experimental Procedures). The end memory vergence differed significantly between motion and interleaved stationary trials at corresponding initial positions [factorial ANOVA, forward motion: $F(275,1) = 89$, $p << 0.001$; backward motion: $F(297,1) = 29$, $p << 0.001$]. In contrast, end memory vergence was more similar between motion and final position stationary trials [factorial ANOVA, forward motion: $F(280,1) = 1.7$, $p = 0.18$; backward motion: $F(279,1) = 3.6$, $p = 0.06$]. Thus, the ability to accordingly adjust memory vergence angle during forward and backward motions was also present for totally novel conditions in the absence of visual feedback, suggesting a trial-by-trial sensorimotor transformation.

Once data for these novel motion conditions were collected in the absence of visual feedback, we repeated these experiments with the memory target turned back on at the end of the trial. These additional blocks were done to directly compare whether visual feedback altered the relative vergence difference between motion and stationary trials. Adding visual feedback changed the magnitude and time course of memory vergence responses, but not the relative difference between motion and stationary trials. As illustrated in Figure 5B, which plots the same conditions as those shown in Figure 5A albeit now in the presence of visual feedback, the relative differences between motion and stationary trials remained similar to those observed without visual feedback.

Figure 6 summarizes the results for the novel motion trials (15→10 cm, 15→12 cm, 15→18 cm, and 15→20 cm) with and without visual feedback. The mean (±SEM) vergence changes at the end of the memory period for these 3 cm and 5 cm motion trials have been plotted versus the corresponding vergence changes for the initial and final position stationary trials in Figures 6A and 6B, separately for data without and with visual feedback (gray circles versus black triangles) and forward/backward motions (filled versus open symbols). The correlations of memory vergence changes for motion trials were stronger when compared to final than

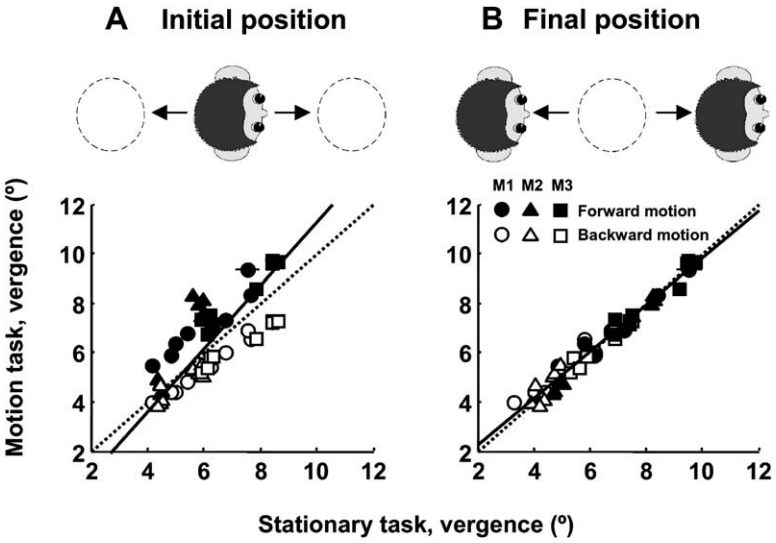

Figure 4. Updating Accuracy during Motion in Depth

Vergence angles for motion trials (ordinate) have been compared with the respective values from stationary trials (abscissa) at the corresponding initial (A) or final (B) positions. In the absence of updating, data in (A) (but not in [B]) should fall along the unity slope (dotted) line. With perfect updating, data in (B) (but not in [A]) should fall along the unity slope line. Data shown are means (±SEM), plotted separately for each target and distance (total of 4 targets × 4 distance/motion combinations) and each of the three animals (M1, M2, and M3). Solid symbols are used for the forward motion (17→12 cm and 27→22 cm), whereas open symbols are used for backward motion (17→22 cm and 27→32 cm). Solid lines illustrate linear regressions.

initial position trials (no visual feedback: $R^2 = 0.93$ versus $R^2 = 0.59$, respectively; visual feedback: $R^2 = 0.94$ versus $R^2 = 0.31$, respectively).

Mean vergence changes (averaged across all targets) have also been plotted versus the respective displacement amplitude, separately for the trials without visual feedback and the follow-up blocks in the presence of visual feedback in Figure 6C (gray circles versus black triangles). There was a significant displacement amplitude effect either with or without visual feedback (ANCOVA, no visual feedback: $F = 153$, $p << 0.001$; visual feedback: $F = 356$, $p << 0.001$).

Finally, to further quantify that updating accuracy was independent of visual feedback, percent differences in memory vergence for motion and final position stationary trials (expressed relative to stationary task vergence) have been plotted as a function of time in Figure 6D. As illustrated in the figure, open and solid symbols superimpose. This means that, although absolute vergence changes were largest (thus, the memory eye movement error was also smallest) in the presence of visual feedback, this occurred for both the motion and stationary tasks in parallel such that their relative difference remained unchanged. Statistical comparisons indeed confirmed that the percent vergence difference was independent of visual feedback (ANCOVA, $F = 0.02$, $p >> 0.05$) and did not change as a function of time (ANCOVA, $F = 1.5$, $p >> 0.05$). These data illustrate that, even for novel displacements and conditions, a trained animal can adjust vergence angle ap-

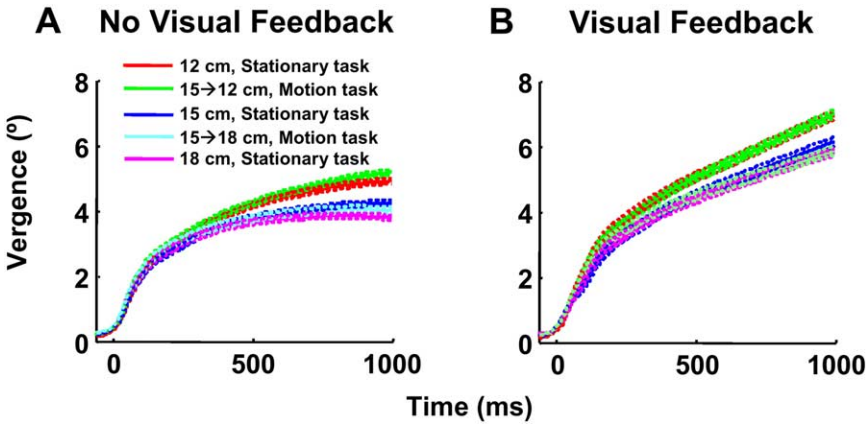

Figure 5. Generalization to Novel Motion Tasks

Mean ± SEM (solid and dotted lines, respectively) of the memory vergence for the 15→12 cm and 15→18 cm motion tasks (green and cyan lines), along with the respective stationary position data (initial position, blue lines; final position, red and magenta lines), obtained during initial experiments in the absence of visual feedback (A) and in subsequent blocks with visual feedback (B). Data represent means for all four oblique flashed targets. To compute the averages, individual runs were aligned at saccade onset (time = 0). Note that in (A), the evoked vergence scaled according to the intervened motion, even though the animal never experienced these movements in the presence of visual feedback. Data from animal M1.

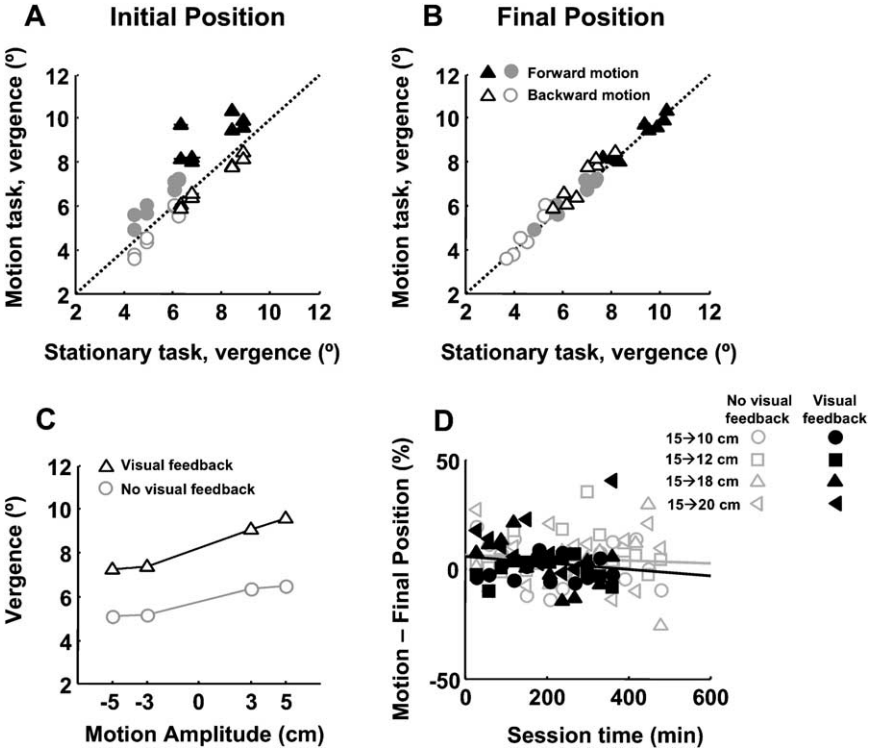

Figure 6. Generalization to Novel Motion Tasks

(A and B) Mean (±SEM) vergence angles for motion trials (ordinate) plotted versus the corresponding values from stationary trials (abscissa) at the same initial (A) or final (B) position. Solid symbols are used for forward motions (15→12 cm and 15→10 cm), whereas open symbols are used for backward motions (15→18 cm and 15→20 cm). Gray circles indicate data first collected in the absence of visual feedback. Black triangles indicate data subsequently collected in the presence of visual feedback (target was turned on at trial end). Dotted lines are unity slope lines. (C) Mean (±SEM) memory vergence as a function of motion amplitude in the absence (gray circles) or in the presence (black triangles) of visual feedback. (D) The percent vergence differences between motion and final position stationary trials (expressed relative to stationary task vergence) have been plotted as a function of time. Different symbols are used for the four different motions (15→10 cm, 15→12 cm, 15→18 cm, and 15→20 cm) averaged across all targets. Open gray and filled black symbols correspond to data without and with visual feedback, respectively. Gray and solid lines illustrate the corresponding linear regressions. Data from animal M1.

propriately to compensate for the imposed movement. Thus, to program the eye movement, the brain clearly did not rely solely on retinal disparity information at the time of the flash, but took into account the intervening motion.

Origin of Extraretinal Information for Spatial Updating in Depth

Unlike active movements, extraretinal information in our experiments can arise neither from self-generated cues nor from an efference copy of the motor command. Thus, the passive head and body displacements used here leave the vestibular system as the most likely sensory source for motion-related information. To directly test the hypothesis that extraretinal signals necessary for updating vergence eye movements during these depth motion tasks arise from the activation of otolith afferents, we tested two of the trained animals (M1 and M3) with the original task (17→12 cm, 17→22 cm, 27→22 cm, and 27→32 cm) one week after bilateral destruction of both vestibular labyrinths (cf. Angelaki et al., 2000; Newlands et al., 2002).

Mean (±SEM) memory vergence responses from M1 before and after the vestibular lesion for the 27→22 cm and 27→32 cm motion tasks, along with the corresponding stationary task controls, have been plotted in Figures 7A and 7B. In sharp contrast to the labyrinthine-intact animal, where vergence changes in the motion task followed those of the final position stationary task (Figure 7A, green trace is superimposed on the red trace; similarly, the cyan trace is closer to the magenta), motion task vergence changes in the lesioned animal were indistinguishable from those of the initial position stationary task (Figure 7B, green and cyan traces are superimposed on the blue trace).

Quantitative analyses confirmed these observations. After lesion, memory and vergence changes for motion trials were significantly different from the respective final position stationary trials [factorial ANOVA, forward motion: $F(185,1) = 48.7$, $p << 0.001$; backward motion: $F(146,1) = 46.4$, $p << 0.001$]. In contrast, vergence angle changes for motion trials were statistically indistinguishable from those for initial position stationary trials [factorial ANOVA, forward motion: $F(217,1) = 0.6$, $p >> 0.05$; backward motion: $F(178,1) = 0.2$, $p >> 0.05$]. Similar results were also found in animal M3. Thus, in contrast to the labyrinthine-intact animal's ability to adjust the amplitude of the evoked vergence eye movement

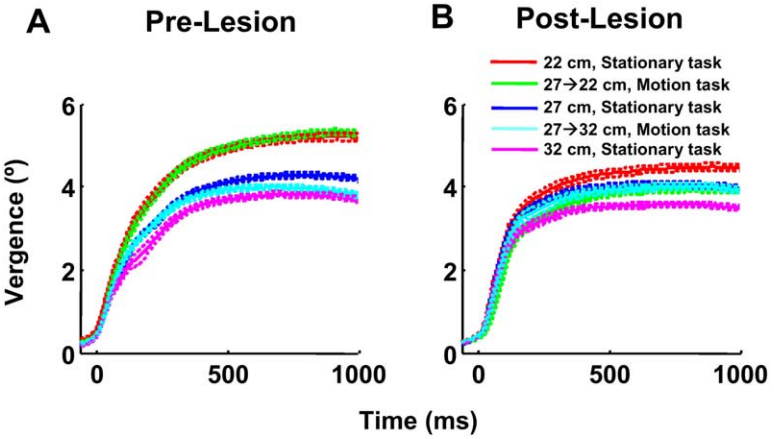

Figure 7. Role of Intact Vestibular Cues for Spatial Updating during Motion in Depth

Mean (±SEM) of the memory vergence for the 27→22 cm and 27→32 cm motion tasks (green and cyan lines), as well as the corresponding initial (27 cm, blue lines) and final (22 cm and 32 cm, red and magenta lines, respectively) stationary trials. Data are plotted separately before ([A], prelesion) and one week after bilateral labyrinthectomy ([B], postlesion). Data represent means for all four targets. To compute the averages, individual runs were aligned at saccade onset (time = 0). Data from animal M1.

according to the direction and amplitude of the intervened motion, the lesioned animal only used retinal disparity to plan and execute memory eye movements during both the stationary and motion tasks.

Data for all distance/motion combinations (17→12 cm, 17→22 cm, 27→22 cm, and 27→32 cm) before and after the lesion have been summarized for both animals (M1: circles; M3: squares) in Figures 8A and 8B. In this plot, percent differences in memory vergence for motion and final position stationary trials (expressed relative to the stationary task vergence) have been illustrated as a function of the corresponding percent vergence differences for motion and initial position stationary trials. For perfect depth updating, data should fall along the horizontal dotted line. In contrast, if there were no updating and retinal disparity alone specified the vergence eye movement, data should fall along the vertical dotted line. As illustrated in Figure 8, prelesion and postlesion data differed, with prelesion data falling along the horizontal line (Figure 8A) and postlesion data falling along the vertical line (Figure 8B).

Quantitative analyses confirmed that the labyrinthine lesion had a significant effect for both forward [repeated measures MANOVA, M1: $F(2,6) = 8.5$, $p = 0.018$; M3: $F(2,6) = 12.7$, $p = 0.007$] and backward [M1: $F(2,6) = 12.8$, $p = 0.007$; M3: $F(2,6) = 68.4$, $p << 0.001$] motion tasks. The corresponding means (±SEM) for the respective percent differences have been summarized in Table 1. Although only the Motion – Final Position (but not the Motion – Initial Position) percent differences were statistically indistinguishable from zero in the intact animals (as expected for accurate updating; Figure 8A), the reverse was true in the lesioned animals (Figure 8B; see Table 1). Therefore, labyrinthine lesions eliminated the animals' ability to adjust vergence according to the interleaved motion, suggesting that intact vestibular signals are critical for providing the necessary motion cues for spatial updating during motion in depth.

Discussion

By comparing the vergence eye movements made during a motion task with those in stationary control experiments, we have shown that monkeys can compensate for the traveled distance in depth using extraretinal motion-related information. For the passive displacements

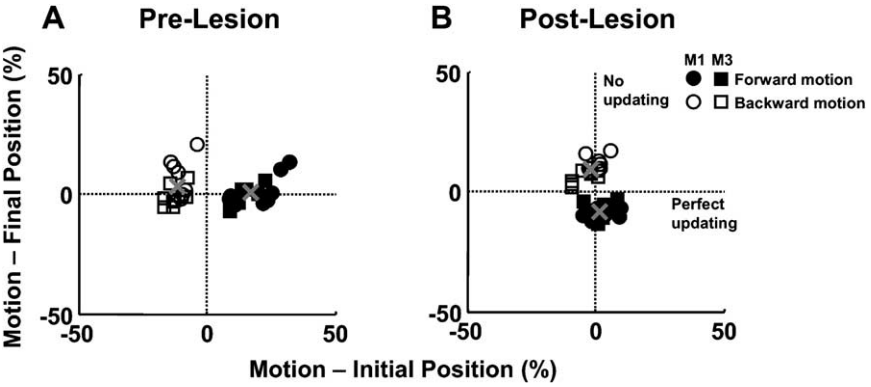

Figure 8. Loss of Updating Accuracy during Motion in Depth after Labyrinthine Lesion

Percent vergence differences between motion and final or initial position stationary trials, plotted relative to each other before (A, prelesion) and one week after bilateral labyrinthectomy (B, postlesion). With (without) updating, data should fall along the horizontal (vertical) dotted line. Results are plotted separately for each of the four targets and four distance/motion combinations. Solid circles indicate forward motion (17→12 cm and 27→22 cm); open circles indicate backward motion (17→22 cm and 27→32 cm). X, mean values, computed separately for forward and backward motions. Data from animals M1 (circles) and M3 (squares).

Table 1. Accuracy in Memory-Guided Eye Movements before and after Labyrinthine Lesion

	Motion – Initial Position	Motion – Final Position
Animal 1		
Forward Motion Task		
Prelesion	19.94 ± 1.15 ($p << 0.001$)	1.44 ± 0.83 ($p = 0.557$)
Postlesion	2.06 ± 0.68 ($p = 0.319$)	–9.30 ± 0.22 ($p << 0.001$)
Backward Motion Task		
Prelesion	–10.41 ± 0.39 ($p << 0.001$)	6.85 ± 1.03 ($p = 0.052$)
Postlesion	0.38 ± 0.39 ($p = 0.739$)	12.03 ± 0.37 ($p << 0.001$)
Animal 3		
Forward Motion Task		
Prelesion	14.37 ± 0.62 ($p << 0.001$)	–0.60 ± 0.49 ($p = 0.623$)
Postlesion	1.66 ± 0.60 ($p = 0.092$)	–7.64 ± 0.43 ($p << 0.001$)
Backward Motion Task		
Prelesion	–12.77 ± 0.43 ($p << 0.001$)	–1.17 ± 0.55 ($p = 0.614$)
Postlesion	–4.17 ± 0.58 ($p = 0.040$)	6.10 ± 0.32 ($p << 0.001$)

Values illustrate means (±SEM) of the percent differences in vergence angle at the end of the memory period between motion and initial (first column) or final (second column) position stationary trials. The p values show whether the differences are statistically significantly different from zero.

used here, the main neural signal that contributed to spatial updating would likely be of vestibular origin. We have directly confirmed this hypothesis by showing that trained animals lost their ability to accordingly adjust memory vergence angle after destruction of the vestibular labyrinths. There is evidence from human studies that otolith-driven linear displacement information can be stored in spatial memory and used to reproduce the traveled path (Israel and Berthoz, 1989; Israel et al., 1993; Berthoz et al., 1995). Here, we have shown that such extraretinal spatial information can also be used to update three-dimensional space during motion in depth.

Most investigations of visual spatial function and visuospatial updating have so far focused on issues related to two-dimensional visual stimuli and conjugate eye movements. Yet, representation of the three-dimensional world requires retinal disparity information to provide a measure of the object's depth from the plane of fixation (Cumming and DeAngelis, 2001; Poggio, 1995). The absolute egocentric distance can then be computed when retinal disparity information is combined with an estimate of fixation distance, for which the most important cue is vergence angle (Cumming and DeAngelis, 2001). Indeed, there is growing evidence that retinal disparity information modulates the activity of neurons in both parietal and frontal visuomotor areas, with cells being characterized by three-dimensional receptive fields (Ferraina et al., 2000, 2002; Fukushima et al., 2002; Gnadt and Beyer, 1998; Gnadt and Mays, 1995). At present it remains unclear whether the three-dimensional tuning curves of visuomotor neurons reflect absolute depth with respect to the body (egocentric distance) or depth with respect to the plane of fixation (Genovesio and Ferraina, 2004; Gnadt and Mays, 1995).

The exact representations of visual space within the brain remain under active investigation, with accumulating evidence suggesting that the direction and eccentricity of objects are stored within a retinal reference frame, i.e., with respect to the current location of the eyes (Andersen et al., 1985; Colby and Goldberg, 1999; Duhamel et al., 1992). It is generally believed that visuospatial updating takes place through either a vector substraction (Goldberg and Bruce, 1990; Duhamel et al., 1992; Quaia et al., 1998) or reference frame multiplication (Klier et al., 2005; Medendorp et al., 2002) of the memorized retinal location of the flash and the intervening eye-in-space rotation. For example, lateral intraparietal (LIP) neurons have been shown to be active whenever the next conjugate eye movement would move the eyes into the cell's frontoparallel response field (Colby et al., 1993; Duhamel et al., 1992; Gnadt and Andersen, 1988). Given that the large majority of LIP neurons have three-dimensional receptive fields (Gnadt and Mays, 1995), the process of visuospatial remapping may operate not just in the frontoparallel plane but also in depth. The results of these experiments suggest that to update either retinal (disparity)-derived depth or distance-related information, the brain has to integrate self-motion-related information that arises from the vestibular system. A neural basis for such integration might be found in either parietal or frontal visuomotor neurons with three-dimensional receptive fields (Gnadt and Mays, 1995).

Experimental Procedures

Animals

Three rhesus monkeys (M1, M2, and M3) chronically implanted with a head ring and scleral eye coils in both eyes (details for these procedures can be found in Angelaki, 1998; Angelaki et al., 2000) were used to study spatial memory updating during passive head and body motion in depth. All surgical procedures and animal handling were in accordance with institutional and National Institutes of Health guidelines.

Data Acquisition

Binocular eye movements were measured using a three-field magnetic coil system (CNC Engineering, Seattle, WA). Eye movements were calibrated monocularly, using a daily fixation task with positive eye position corresponding to upward and rightward directions. Data were filtered (six-pole Bessel; DC, 200 Hz), digitized at 833.3 Hz with 16-bit resolution, and stored for offline analyses. A custom-written script in the Spike2 software controlled stimulus presentation and data acquisition hardware (CED Power 1041; Cambridge Electronic Design, Cambridge, UK). Motion stimuli were delivered using a linear sled (Neurokinetics, Pittsburgh, PA).

Visuospatial Tasks

Animals were trained to perform memory-guided eye movements (Figure 1) from a central far target (a head-fixed LED located 1 m away; fixation target) to one of eight briefly flashed peripheral targets, placed symmetrically around the point straight ahead at 45° radial directions and mounted on a vertical panel that was secured to the floor (world-fixed). The eccentricity of the cardinal targets ranged from 6° to 15° for distances of 32 cm and 12 cm, respectively. The distance of the monkey from the target array, both prior to the initiation of each run and during the delay period, could be manipulated using the motion platform.

Monkeys performed randomly interleaved motion and stationary tasks within the same block of trials. The general outline of the tasks is illustrated in Figure 1. All trials began with the onset of the fixation target in a dimly illuminated room (interval 1). During continued fixation for at least 500 ms, one of the closer, world-fixed LEDs flashed for 200 ms (interval 2). Then, during a variable delay period lasting 750–1750 ms (interval 3), animals either remained stationary (stationary task) or were moved (motion tasks) while maintaining fixation on the central, head-fixed target. The room lights were turned off immediately after the flash, leaving the animal in complete darkness (other than the head-fixed fixation target) during this period. Thus, no visual cues were available to the light-adapted animal to indicate the direction and amplitude of the interleaved movement. Turning off the fixation target provided the cue for the monkey to look at the remembered location of the previously flashed target (interval 4). At the end of the trial, the peripheral target and room lights were turned on again (interval 5), allowing the monkeys to make a corrective eye movement (if necessary) to the relit target.

For the motion task (Figure 1A), animals were passively moved toward or away from the target array during the delay period (Figure 1B, interval 3) such that the spatial location of the memory eye movement goal differed from the location of the flash. The motion lasted 0.5 s (with a peak acceleration of 2.5 m/s^2) and was completed before the central fixation target was turned off. Because animals were required to continue fixating the central, head-fixed LED (in an otherwise totally dark room) during motion, they suppressed the vestibule-ocular reflex. For the stationary task (Figure 1B), monkeys made memory-guided eye movements while stationary in space (using the same targets and initial/final positions as in motion trials). Because the required memory eye movement was toward the location of the flash and no updating was required, these stationary trials served as controls to evaluate the updating capacity for the respective motion trials. While retinal disparity information alone is sufficient to specify the memory eye movement during stationary trials, extraretinal motion cues would be necessary to update the memorized spatial target location during motion trials.

Behavioral Monitoring

Eye movement performance was monitored online using behavioral windows for both version and vergence, computed online from left (L) and right (R) eye positions, as (R + L)/2 and L − R, respectively. Fixation windows were ±2° for version and ±0.75° for vergence. For the memory period, behavioral windows were large (±8° in version and ±4° in vergence). To allow for an often slowly changing vergence following a saccade from a far to a near target (Maxwell and King, 1992; Zee et al., 1992), version and vergence eye positions had to stay within the required behavioral limits for 1 s, before the peripheral target was turned back on (thus, the duration of interval 4 was variable from trial to trial; Figure 2, highlighted area in gray). If either the version or vergence eye position fell outside the specified behavioral windows at any time during the task, the trial was aborted and the data were discarded.

Experimental Protocols

Monkeys were trained to perform these tasks in the presence of visual feedback (interval 5) for several months, using the four cardinal targets and 5 cm movement amplitude, resulting in the following distance/motion combinations: 17→12 cm, 17→22 cm, 27→22 cm, and 27→32 cm. Once trained, behavior was also tested to other novel target, distance, and motion combinations. Specifically, on separate experimental blocks, we tested the ability to generalize this task to the four oblique peripheral targets during interleaved motion/stationary trials using the following distance/motion combinations: 15→10 cm, 15→12 cm, 15→18 cm, and 15→20 cm. To verify that a trial-by-trial sensorimotor transformation (rather than an arbitrary stimulus-response mapping) was performed during these spatial memory tasks, data for this task were first collected in the absence of visual feedback (without the reillumination of the target, interval 5).

Finally, to demonstrate directly whether vestibular signals were important for these tasks, the vestibular labyrinths were lesioned bilaterally in two of the monkeys (for details of these procedures, see Angelaki et al., 2000; Newlands et al., 2002). The animals were allowed to recover from the acute balance and acute oculomotor symptoms for a period of 6 days (Angelaki et al., 2000; Newlands et al., 2002), before again being subjected to water deprivation in order to perform the memory eye movement tasks. The role of the vestibular system in the animal's accuracy in performing these tasks was evaluated by directly comparing memory vergence eye movements made before and after the peripheral vestibular lesion.

For this, data from several blocks of interleaved 17→12 cm, 17→22 cm, 27→22 cm, and 27→32 cm motion/stationary tasks were collected during the week prior to the operation, using a slight modification of the task outlined in Figure 1. Specifically because we wanted to investigate how accurate these eye movements were before and after labyrinthectomy, and in order to avoid excluding runs in which memory performance was poor, no behavioral window was imposed for the memory period during these prelesion and postlesion blocks. Thus, all runs in which the monkeys successfully ignored the flash and refixated the memory target after it was relit were rewarded and saved for offline analysis. The animals were retested with an identical task 1 week after the operation.

Data Analyses

Offline a semiautomatic procedure was used to identify saccades when eye velocity exceeded (or fell below) 25°/sec (for details, see Li et al., 2005). For each experimental run, two sets of values were computed by averaging eye position over 20 ms time intervals: (1) The initial fixation was computed 50 ms before the head-fixed target was turned off; (2) the memory eye position was computed 50 ms before the reillumination of the memory target (i.e., 950 ms after the eyes were within the specified memory windows; see above). The changes in horizontal version (direction) or vergence (depth) of eye position following the memory-guided eye movement were then calculated as the difference between memory and initial fixation positions. For the novel condition experiment without visual feedback, these values were manually determined during visual inspection of each trial. Relationships between independent variables (e.g., Figure 4) were quantified using linear regressions, obtained by minimizing the perpendicular offset of the data to the line (using a nonlinear least-squares algorithm based on the interior-reflective Newton method). The 95% confidence intervals were computed using bootstrapping with replacement. Other comparisons between variables were made using analysis of variance (ANOVA), multivariate analysis of variance (MANOVA), or analysis of covariance (ANCOVA).

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