

Contribution of Head Movement to Gaze Command Coding in Monkey Frontal Cortex and Superior Colliculus

Julio C. Martinez-Trujillo, Eliana M. Klier, Hongying Wang, and J. Douglas Crawford

Centre for Vision Research and, Departments of Psychology, Biology and Kinesiology and Health Sciences, York University, Toronto, Ontario M3J 1P3, Canada

Submitted 4 April 2003; accepted in final form 17 June 2003

Martinez-Trujillo, Julio C., Eliana M. Klier, Hongying Wang, and J. Douglas Crawford. Contribution of head movement to gaze command coding in monkey frontal cortex and superior colliculus. *J Neurophysiol* 90: 2770–2776, 2003; 10.1152/jn.00330.2003. Most of what we know about the neural control of gaze comes from experiments in head-fixed animals, but several “head-free” studies have suggested that fixing the head dramatically alters the apparent gaze command. We directly investigated this issue by quantitatively comparing head-fixed and head-free gaze trajectories evoked by electrically stimulating 52 sites in the superior colliculus (SC) of two monkeys and 23 sites in the supplementary eye fields (SEF) of two other monkeys. We found that head movements made a significant contribution to gaze shifts evoked from both neural structures. In the majority of the stimulated sites, average gaze amplitude was significantly larger and individual gaze trajectories were significantly less convergent in space with the head free to move. Our results are consistent with the hypothesis that head-fixed stimulation only reveals the oculomotor component of the gaze shift, not the true, planned goal of the movement. One implication of this finding is that when comparing stimulation data against popular gaze control models, freeing the head shifts the apparent coding of gaze away from a “spatial code” toward a simpler visual model in the SC and toward an eye-centered or fixed-vector model representation in the SEF.

INTRODUCTION

The majority of the literature concerning gaze control arises from experiments in head-fixed (i.e., head immobilized) animals. For example, numerous studies have employed electrical microstimulation of the brain to determine the motor output of gaze-control centers. One of these studies quantified the magnitude and position-dependence of these movements to assess the nature of gaze coding in the stimulated sites (Russo and Bruce 1996). Other studies have microstimulated the same brain structures in head “free” (i.e., unimmobilized) animals and have reported that the procedure elicited gaze shifts composed of both eye and head movements (Freedman et al. 1996; Guillaume and Pelisson 2001; Klier et al. 2001; Martinez-Trujillo et al. 2003; Pelisson et al. 1989; Roucoux et al. 1980). This raises the question, does freeing the head fundamentally change the nature of the evoked gaze shifts?

Anecdotal evidence suggested that it does, at least during stimulation of sites in the posterior portion of the superior colliculus (SC). For example, Pare et al. (1994) and Pare and

Guitton (1998) in the cat and Freedman et al. (1996) in the monkey have shown examples of gaze trajectories evoked from posterior SC sites with the head both fixed and free, where the gaze shifts evoked with the head free were longer and less convergent as a function of initial gaze position. Moreover, these examples suggested that the eye-in-head (Eh) component of the head-free movements looks very much like the oculomotor gaze shift made with the head fixed. However, no one has made a quantitative comparison of head-fixed versus head-free gaze shifts evoked from a broad population of SC sites.

Similar to these SC studies, we have recently shown that electrical stimulation of the supplementary eye-fields (SEF), located in medial frontal cortex, produces gaze shifts that include a considerable head contribution (Martinez-Trujillo et al. 2003). The spatial code used to specify gaze commands in the SEF has been a subject of considerable controversy. Stimulation studies of the SEF in the head-fixed monkey apparently suggested the existence of eye-centered (Russo and Bruce 1996), head-centered (Tehovnik et al. 1998), and multiple (Schlag and Schlag-Rey 1987) coding strategies in this area. Given that the SEF also codes coordinated eye and head movements like the SC, one wonders how much of this controversy might simply be due to the use of a head-fixed preparation.

The goal of the current investigation was to quantitatively compare the traditional measures of spatial gaze coding—gaze amplitude, direction, and position-dependency—in movements evoked by electrical microstimulation of SC and SEF brain sites with the head both fixed and free. Our aim was not to compare the SC and SEF, but rather to examine both to obtain basic principles that might pertain to gaze control in general. Our results suggest that the findings of previous head-fixed stimulation studies of the SC, SEF, and probably other gaze-related structures need to be re-interpreted.

METHODS

A total of four monkeys participated in the study: two *Macaca fascicularis* in the SC experiments and two *Macaca mulatta* in the SEF experiments. The differences between the two species are not relevant to the purposes of the current study since the required comparisons are made between head-fixed and head-free data *within* the same species and not *across* species. As stated above, we have included an analysis of both structures to highlight general principles.

Address for reprint requests and other correspondence: J. C. Martinez-Trujillo, Centre for Vision Research, York Univ., 4700 Keele St., Toronto, Ontario M3J 1P3, Canada (E-mail: trujillo@yorku.ca).

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.

All animals were surgically prepared for three-dimensional (3-D) eye and head movement recordings as described previously (Crawford et al. 1999; Klier et al. 2001; Martinez-Trujillo et al. 2003). These protocols were in accordance with Canadian Council on Animal Care guidelines and preapproved by the York University Animal Care Committee.

Each monkey wore a primate jacket and sat in a modified Crist Instruments primate chair such that its head and neck were free to move as desired. The upper body (to the shoulders) was prevented from rotating in the yaw direction (i.e., movement around an earth-vertical axis) by the use of plastic molding and restraints that attached to the primate jacket to the chair. The same experimental setup was used for all four animals.

During each experimental session, one or several penetrations were made using platinum/iridium glass-covered microelectrodes (FHC, 0.5–3M Ω) and an hydraulic microdrive (Narishigi model MO-99S) positioned on the top of a recording chamber. For the SEF experiments, direct penetrations with the electrode were made in an area located between 23–30 mm anterior and 3–7 mm lateral, in stereotaxic coordinates, on both sides of the midline. The electrode was advanced until the action potentials of single neurons were isolated on an oscilloscope. Subsequently, microstimulation trains were delivered. The site was classified as a SEF site when contralateral eye movements were consistently evoked from different initial eye positions. The anatomical reconstruction of the SEF stimulation sites in the two animals can be found elsewhere (Martinez-Trujillo et al. 2003). For the SC experiments, the identification of the recording sites was made following a procedure reported elsewhere (Klier et al. 2001).

For the SEF recordings, each animal was required to direct its gaze to a spatial location where an LED was previously flashed for an interval of 500 ms. If the animal maintained its gaze at that location for a period of 2,000 ms, a reward (drop of juice) was given. Microstimulations with pulse trains (50 μ A, 300 Hz) of 200 ms were delivered during intervals when no stimulus was present and gaze was stationary (approximately 50 stimulation trains per site). These stimulation parameters have been shown to evoke kinematically normal gaze shifts in the SEF (Martinez-Trujillo et al. 2003). In one animal, the data were recorded using a sampling frequency of 100 Hz and in the other using a sampling frequency of 1,000 Hz.

For the SC recordings, the monkeys were required to move their eyes and heads freely and naturally, and they were encouraged to use their entire eye/head motor ranges through the presentation of novel sounds. A previous study reported data from these same SC experiments, in both dark and dim light conditions (Klier et al. 2001). The current results reflect data collected in the dark (as in the SEF experiments). Penetrations were made with tungsten epoxilite insulated microelectrodes (FHC) positioned through a guide tube using an hydraulic microdrive (see SEF) on the top of the recorded chamber. Microstimulations with pulse trains (50 μ A, 500 Hz, 200 ms) were delivered during periods of stationary gaze to SC sites on both sides of the midline (approximately 30–60 stimulation trains per site). These stimulation parameters have been shown to evoke kinematically normal head-free gaze shifts in the SC (Freedman et al. 1996). The data were recorded using a sampling frequency of 500 Hz.

Coil signals from the eye and the head were converted into 3-D gaze (eye-in-space) and head [head-in-space (Hs)] position quaternions that were then used to obtain Eh quaternions (Tweed et al. 1990). In an off-line analysis, gaze quaternions were plotted as a function of time, and those representing eye positions at the beginning and end of each stimulation-evoked gaze shift were manually selected by the experimenter. A given gaze shift was considered to be evoked by the stimulation when it occurred with a consistent latency and velocity profile during the 200-ms stimulation interval. These selected position quaternions were then converted into 3-D vectors scaled by their angle of rotation for statistical analysis (Crawford and Guitton 1997).

For the data analysis shown in Figs. 2 and 3, the characteristic vector (CV) for each site was computed through a multiple linear

regression procedure relating the stimulus induced displacement of gaze as a function of initial gaze position. The CV represents the theoretical trajectory that would be evoked by stimulating the site with the animal looking straight ahead. All the trajectories and the CV were rotated and aligned with the horizontal meridian. For each individual trajectory, measurements of initial positions (IPs) and final positions (FPs) in both the abscissa and the ordinate were taken. A convergence index for the movements' direction (CId) was computed by determining the slope of the regression line relating the IP and the gaze displacement (FP-IP) along the ordinate. A convergence index for the movements' amplitude (CIa) was computed by determining the slope of the regression line relating the IP and the FP-IP along the abscissa (see Klier et al. 2001; Russo and Bruce 1996). These procedures are illustrated graphically in the data supplements¹.

RESULTS

Examples of trajectories obtained by stimulating two sites, one in the right SC (*left column*) and one in the right SEF (*right column*), are shown in Fig. 1. The first row shows gaze trajectories evoked with the head-fixed and the second row with the head-free. In both examples, the trajectories appear to be shorter and more convergent toward a fixed position in space with the head-fixed (*A* and *E*) than with the head-free (*B* and *F*), probably due to the contribution of the head to the movements in the latter case. To corroborate this suggestion, we decomposed the head-free gaze trajectories (*B* and *F*) into their two components: movements of the Hs (*C* and *G*) and movements of the Eh (*D* and *H*). For both the Hs and the Eh, the trajectories are plotted until gaze landed on its their final position in space—meaning that only the portion of the head trajectories that contributed to the gaze shifts is taken into account.

For both the SC and the SEF, the Hs and Eh trajectories appear considerably shorter than the overall gaze trajectories, suggesting that both components contributed to gaze. Additionally, Hs trajectories appear less convergent than Eh trajectories, suggesting that the apparent decrease in the convergence of head-free relative to head-fixed gaze was due to the Hs contribution. We found this qualitative pattern of results in the majority of the stimulated sites and in both the SC and the SEF. In general, this qualitative analysis is consistent with the hypothesis that head-fixed trajectories do not reveal the intended movement goal, which is only revealed with the head-free. We will quantitatively test this hypothesis.

To perform such a test, we chose three measurements that have been used in previous studies of visuomotor coding (Klier et al. 2001; Russo and Bruce 1996). Such measurements reflect the average length of the evoked trajectories as well as their position dependency or convergence in space. A comparison between the same measurements in both head-fixed and head-free conditions should reveal either the differences that we hypothesized or similarities that would negate this hypothesis. The first measurement is the length or amplitude of the CV, which represents the vertical and horizontal components of the movement expected to be elicited from the straight-ahead eye and head reference position (calculated from the entire population of gaze trajectories from each site; see METHODS and data supplements).

The second and third measures are the convergence indices (CIa, CId), describing the dependence of individual gaze dis-

¹ The Supplementary Material for this article is available online at <http://jn.physiology.org/cgi/content/full/00330.2003/DC1>.

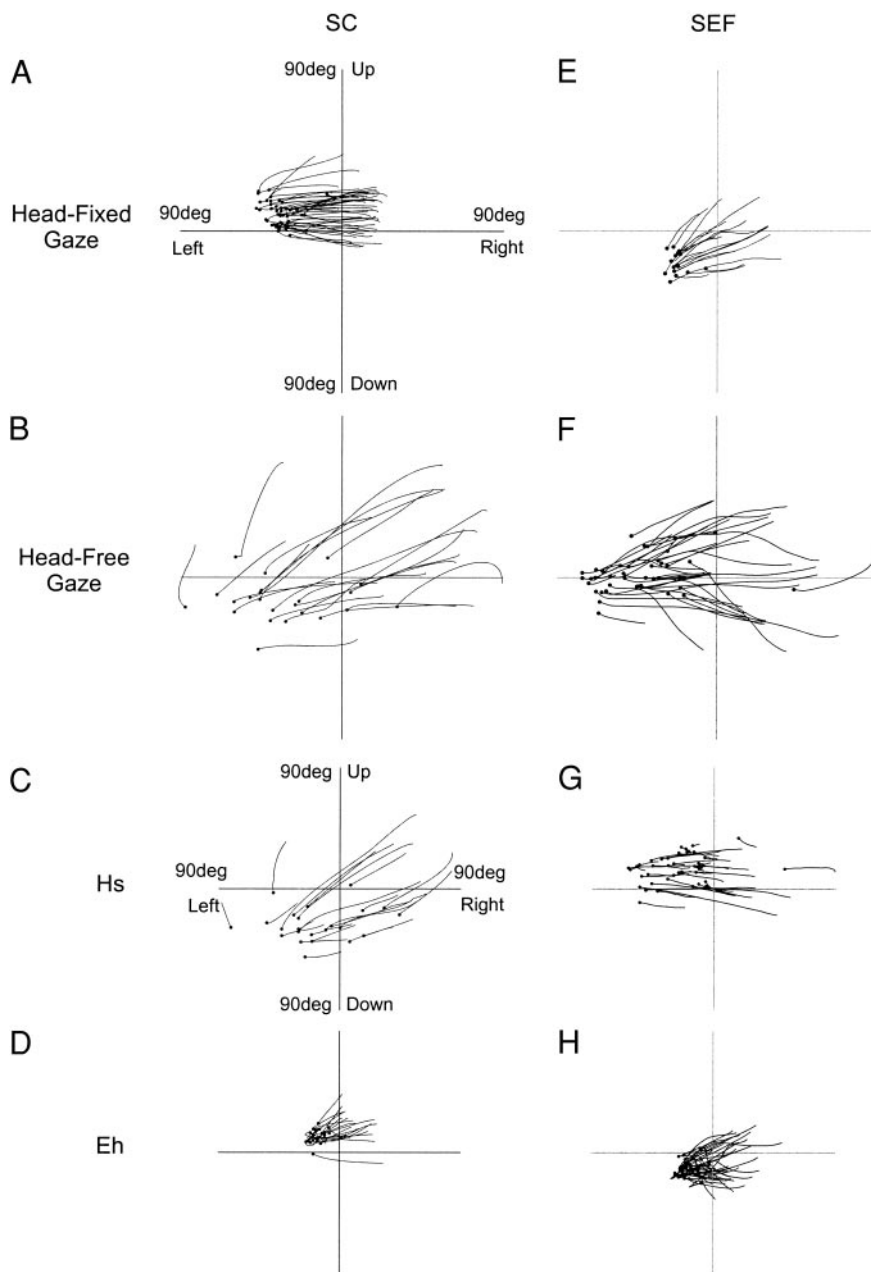


FIG. 1. Trajectories evoked by microstimulating 1 site in the right superior colliculus (SC; *left*) and 1 site in the right supplementary eye fields (SEF; *right*). Solid lines represent gaze trajectories with the head fixed (A and E), gaze trajectories with the head free (B and F), head-in-space (Hs) trajectories with the head free (C and G), and eye-in-head (Eh) trajectories with the head free (D and H). Black circles indicate the final positions of the trajectories. Abscissa and the ordinate represent the vertical and horizontal spatial meridians, respectively.

placements on initial positions. The CIa, along the dimension parallel to the CV, indicates how the amplitude of the movement changes as a function of the initial gaze position. The CI_d, along the dimension orthogonal to the CV, indicates how the direction of the movement changes as a function of the initial gaze position. Values close to -1 indicate a strong convergence or strong initial gaze position dependency of the trajectories, and values close to 0 indicate no-position dependency, i.e., fixed-vector like movements. These measures are particularly relevant because they have been used previously to fit stimulation-evoked gaze shifts to different gaze control models (Klier et al. 2001; Russo and Bruce 1996). A detailed, illustrated description of their calculation is provided in the data supplements.²

Direct quantitative comparisons of CV amplitude, CI_d, and CIa between head-fixed and head-free data are illustrated in Fig. 2. In the *left column*, each scatter-plot displays the same parameter along both axes—with the head-fixed data along the abscissa and the corresponding head-free data along the ordinate. If a parameter would have the same values in both head-fixed and head-free conditions, then the data points should fall along the diagonal (slope of unity). That was not the case. For both data sets (SC; ○) and SEF; ●), the CV amplitude or gaze amplitude (A) was larger ($P < 0.001$, Wilcoxon rank sum test), the CI_d (B) smaller ($P < 0.001$, Wilcoxon rank sum test), and the CIa (C) also smaller ($P < 0.001$, Wilcoxon rank sum test) with the head-free than with the head-fixed.

A simple explanation for these findings is that by fixing the head, one simply removes its contribution to gaze. This leaves the Eh saccade much the same but substantially modifies the

² The Supplementary Material for this article is available online at <http://jn.physiology.org/cgi/content/full/00330.2003/DC1>.

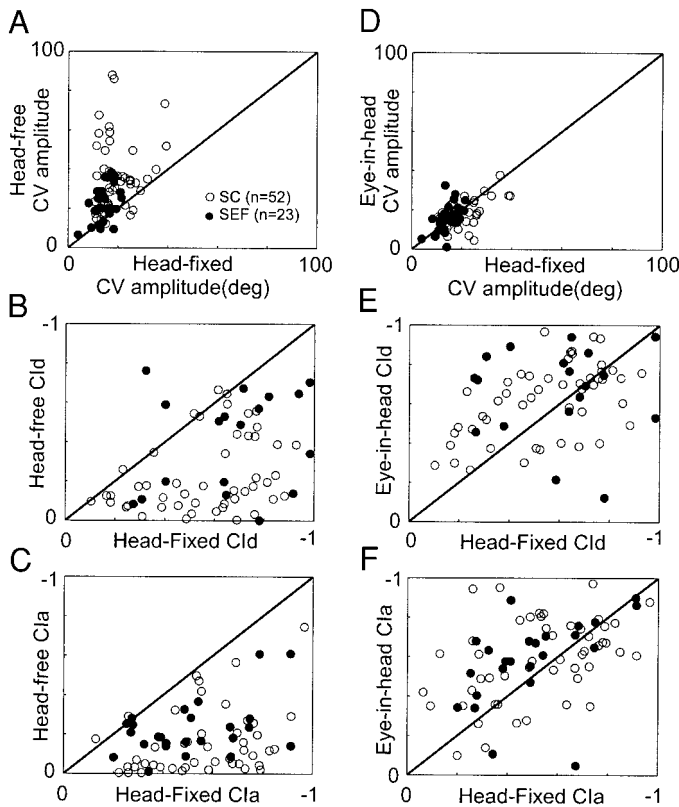


FIG. 2. Parameter comparisons for gaze and eye-in-head data. *Left*: characteristic vector (CV) gaze amplitude (A), convergence index for the movements' direction (Cid) (B), and convergence index for the movements' amplitude (Cla) (C) values for gaze with the head-fixed (abscissa) vs. gaze with the head-free (ordinate). *Right*: CV gaze amplitude (D), Cid (E), and Cla (F) values for gaze with the head-fixed (abscissa) vs. eye-in-head with the head-free (ordinate). Open circles represent data from 52 SC sites, and filled circles represent data from 23 SEF sites. Diagonal lines represent the slope of unity.

gaze trajectory. If this is the case, it is expected that gaze trajectories with the head-fixed and Eh trajectories with the head-free should be similar. The *right column* illustrates these comparisons [the ordinate displays the Eh data (head-free) while the abscissa shows gaze data (head-fixed)].

In these plots, the SEF and SC data are much more evenly distributed along both axes than the data in the head-fixed versus head-free gaze plots (*left column*). In both structures, the three parameters were not significantly different ($P = 0.48$ for gaze amplitude, $P = 0.31$ for Cid, and $P = 0.12$ for Cla in the SEF; $P = 0.41$ for gaze amplitude, $P = 0.13$ for Cid, and $P = 0.14$ for Cla in the SC; Wilcoxon rank sum test). Although these comparisons did not show any significant difference between head-fixed gaze and head-free Eh, the data plotted in Fig. 2, E and F, show a certain bias toward higher CIs for the Eh than for head-fixed gaze.

One possible reason for these small differences in the SC data are that in the head-fixed condition we did not obtain as many different initial gaze positions as we did in the SEF. Another possible explanation is that head-fixed gaze, although more similar to head-free Eh than to head-free gaze, is simply not exactly equivalent to the former. While with the head fixed, the main factor that limits the eye movement would be the oculomotor range, with the head free, other factors such as the VOR could play a critical role modifying the Eh movement (Scudder et al. 2002; Sparks 1999). Moreover, these factors

could depend on the behavioral state of the animal, adding to the noise in these plots. However, note that for both structures, the clear bias seen in the first column (head-fixed vs. head-free gaze) is not present in the second column (head-fixed gaze vs. head-free Eh). These results are consistent with the hypothesis that the systematic change in gaze shifts found with the head-free (Fig. 2, *left column*) is due to the contribution of the head.

One implication of these results is that freeing the head changes the apparent spatial goals of gaze shifts evoked by SC and SEF stimulation. How might the results of previous head-fixed studies change if one were to free the head in these animals? Figure 3 illustrates this graphically by plotting our data in a format that can be directly compared with the simulated predictions of several gaze-coding models (see Crawford and Guitton 1997; Klier et al. 2001).

The *top two panels* of Fig. 3 plot the Cid as a function of the CV amplitude for the 52 SC sites (*left panel*) and for the 23 SEF sites (*right panel*). The dashed lines represent the predictions of three different models of visuomotor coding—the fixed-vector model, the eye-centered, and the convergent-in-space model. In the fixed-vector model, gaze movements elicited from any initial position will be identical to their CV, so the Cid would always be zero independently of gaze ampli-

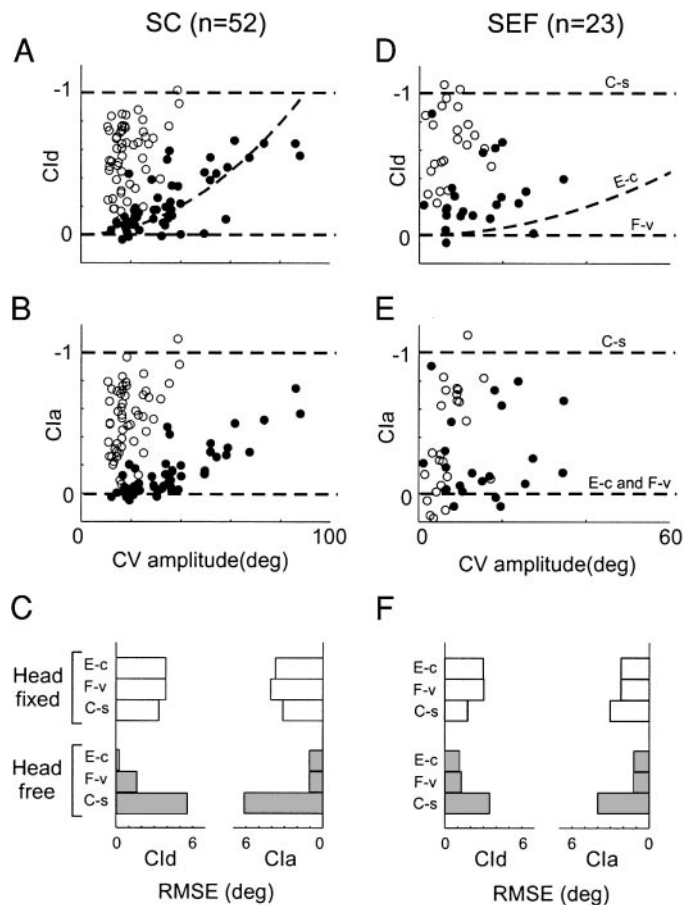


FIG. 3. Cid (*top*) and Cla (*middle*) values as a function of CV gaze amplitude for the SC (*left*) and the SEF (*right*). Open circles represent head-fixed data, and filled circles represent head-free data. Dashed lines represent the predictions of 3 different models of visuomotor coding [eye-centered (E-c), fixed-vector (F-v) and convergent-in-space (C-s)]. *Bottom*: square root of the mean square errors (RMSEs) corresponding to the different models for both the Cid (*left bar graphs*) and Cla (*right bar graphs*) parameters.

tude. In the convergent-in-space model, the evoked trajectories from different initial gaze positions would converge toward a fixed position in space; therefore the CID would assume values of -1 independently of gaze amplitude. Finally, we plot the predictions of a model coding a fixed goal in eye coordinates (like the retina). It has been documented that, due to the nonlinear geometry of eye rotation, this model predicts a nonlinear position-dependent relationship between initial gaze position and the expected gaze trajectory (Klier et al. 2001). As a result, in the eye-centered or retinal model the CID depends on gaze amplitude. As plotted on the graph, the longer the trajectories, the closer to -1 the CID becomes.

Note that in both the SC (Fig. 3A) and SEF (Fig. 3C), the head-fixed data (\circ) scatters widely between the extreme predictions of the fixed-vector model and the convergent-in-space model. Essentially, the head-fixed data does not fit any known model. This is consistent with a number of previous studies (see Klier et al. 2001 for a review of SC studies; Schlag and Schlag-Rey 1987), and from this, it can be observed why it is so hard to use such data to determine which model is being used to code gaze. However, given the result that these data do not show what goals the sites are coding, but only the oculomotor component of gaze, this is not surprising.

In contrast, when the head is freed, the population of SC data (\bullet) shifts toward the eye-centered curve (Fig. 3A), like the result reported by Klier et al. (2001). This shows that head-fixed and head-free results need not contradict each other—they are simply showing different things. A similar shifting of the head-free data toward the eye-centered curve—with the exception of a few clear outliers—was seen for the SEF (Fig. 3B). Clearly, these data suggest that a re-examination of gaze coding in the SEF with the head free is required.

Similar results were obtained for CIA (the amplitude-position dependence; Fig. 3, *middle two panels*). Freeing the head (\bullet) shifted the head-fixed data population (\circ) away from the predictions of the convergent-in-space model and toward those of the fixed-vector or eye-centered models (which are virtually indistinguishable in the CIA plots).

Next, we quantified the goodness of fit of the different models to the head-fixed and head-free data. As a measurement, we used the square root of the mean square errors (RMSE) between the values predicted by the model and the data. The smaller the RMSE, the better the fit. The RMSEs for the different models and for the head-fixed (white bars) and head-free data (dark bars) are shown in the *bottom two panels* of Fig. 3 (*left, SC; right, SEF*). In each panel, the left bars show the RMSEs for the CID and the right bars show the RMSEs for the CIA. With the head fixed, for the SC, the convergent-in-space model had the lowest RMSE, for both the CID and the CIA. The same was true for the CID in the SEF. On the other hand, for the CIA, the convergent-in-space model had the highest RMSE. However, when comparing the values of the mean square errors (MSE) among the different models in both structures and for the CID and CIA, they were not statistically different from each other ($P > 0.05$, ANOVA test) meaning that neither of the three models fits the data better than the other two.

For the head-free data, a completely different picture arises. For the SC, the eye-centered model clearly provides the best fit for the CID data [$P < 0.05$ Wilcoxon rank sum test, when comparing the MSEs of this model against the ones corre-

sponding to the other two models]. For the CIA, the eye-centered and the fixed-vector models provided a better fit than the convergent-in-space model ($P < 0.05$ Wilcoxon rank sum test). However, since the predictions of the former two models are the same, their RMSEs were also the same. Note that neither of these two models do as well at fitting the CIA data as the retinal model fits the CID data, but this could be because these gaze shifts are mainly horizontal and the body is fixed. Since the body contributes horizontally to gaze shifts, particularly to large horizontal gaze shifts with initial eye and head positions deviated toward the goal, freeing the body would be expected to shift the CIA data even further toward the abscissa, for the same reason that freeing the head shifted both the CIA and CID data.

For the SEF, the general pattern of results was similar but not as clear. The main difference with the SC data were that, although the RMSE for the CID was smaller for the eye-centered model, there was no significant difference between the goodness of fit of this model and the one of the fixed-vector model ($P > 0.05$ Wilcoxon rank sum test when comparing the MSEs of the 2 models). When comparing the goodness of fit of the eye-centered model between the SEF and the SC, it was considerably better for the latter. MSEs for the eye-centered model in the SEF were significantly larger than in the SC ($P < 0.05$ unpaired t -test). However, with the head-free for both the SC and the SEF, the convergent-in-space model always performed worse than the eye-centered and the fixed-vector models ($P < 0.05$ Wilcoxon rank sum test).

The set of results for the head-free and head-fixed data can be summarized as follows: 1) with the head fixed, the three models of visuomotor coding fit the data equally in both structures, and 2) with the head free, the eye-centered model clearly provided a better fit to the SC data. For the SEF, although the eye-centered model had the lowest RMSE, the fit was not as good as the SC, and statistically speaking, the fixed-vector model fitted the data equally well. However, note that the convergent-in-space model performed the worst in all head-free cases. Finally, 3) when comparing head-fixed versus head-free, there was a clear shift of the data away from the convergent-in-space model toward the eye-centered model when releasing the head, for both the SC and SEF. The possible meaning of these findings will be considered in the discussion.

DISCUSSION

The fundamental purpose of this study was to quantify the differences in the apparent visuomotor coding between head-fixed and head-free stimulation in the SC and the SEF. Stimulation of both structures with the head fixed does not reveal the goal of the gaze command but only the oculomotor component of a combined eye-head gaze shift. Our results show that the amplitude and position dependence of saccades with the head fixed do not coincide with that of head-free gaze shifts, but rather resemble that of the Eh during these gaze shifts. Compared with head-fixed trajectories, head-free stimulation of the SEF and SC produced longer, less convergent gaze shifts.

To explain the latter point, one needs to consider several aspects of eye-head coordination. First, for a substantial period of a natural or stimulation-evoked gaze shift, both the eye and head move in roughly the same direction (Bizzi 1971; Guitton

1992). Second, as we have shown here, in stimulation-evoked gaze shifts, the head movement does not have large, systematic effects on the kinematics of the saccadic eye movement. Third, as one can see in Fig. 1, head trajectories tend to be much less position-dependent than eye trajectories (Klier et al. 2001). Since head position contributes at least one-half of the initial gaze direction and then adds to the amplitude but less to the position-dependent convergence of the movement, it follows that the stimulus-evoked gaze shifts will be longer and less convergent with the head free.

As we have mentioned before, head-fixed stimulation resembles more the Eh component of a head-free gaze shift than head-free gaze. However, the data in Fig. 2 (2nd column) suggest that this resemblance is not complete, mainly when stimulating the SC. One possible explanation for this result is that while during head-fixed stimulation the VOR is turned off, during a head-free gaze shift, the VOR, although inhibited (Pelisson et al. 1988; Roy and Cullen 2002) is not completely turned off, thereby influencing the Eh movements, especially for large gaze shifts (Scudder et al. 2002; Sparks 1999). These findings could have a number of implications for gaze control; here we focus on the implications for the use of microstimulation for interpreting the spatial coding of gaze.

Head-fixed versus head-free gaze coding in the SC

Previous studies have reported that electrical stimulation of the macaque SC evokes kinematically normal gaze shifts (Freedman et al. 1996; Klier et al. 2001; Stryker and Schiller 1975). Similar results have been reported in the cat (Guillaume and Pelisson 2001; Roucoux et al. 1980). However, the frame of references used to code this gaze signal has been more controversial. Our results provide an explanation for the variability in the reports of previous stimulation studies of visuomotor coding in the SC (see Klier et al. 2001). Given that the oculomotor contribution to gaze increases with the length of the evoked-gaze shifts (Freedman and Sparks 1997) and that the SC possesses a systematic representation of gaze movement amplitudes (more anterior SC sites encode smaller movements while more posterior sites encode larger movements), head-fixed stimulation of the SC would lead into an erroneous estimation of the size and convergence of the movements. Such an error would grow as a function of the anatomical location of the stimulated site, with smaller errors when estimating gaze coding in the anterior SC and larger ones when estimating gaze coding in sites located more posteriorly.

As we have shown here (white bars in Fig. 3C), this leads to results where the data do not follow the predictions of any model. In contrast, when the head is allowed to contribute, the amplitude of the movements increase, and the amount of gaze convergence decreases. The amount of convergence in stimulus-evoked movements still grows—to a lesser degree—with the size of the gaze shift in the head-free preparation, but this is consistent with the predictions of an eye-centered representation of gaze commands (dark bars in Fig. 3C). In such an eye-centered representation, a given SC site would code a fixed goal (location) relative to the fovea on a retinal map (Klier et al. 2001). We hypothesize that the remaining error in fit of the SC data to the eye-centered model in the CIA data (Fig. 3B) arises from fixing the body.

Head-fixed versus head-free gaze coding in the SEF

The majority of SEF stimulation studies have been conducted in head-fixed conditions (Mitz and Godschalk 1989; Russo and Bruce 1996; Schlag and Schlag-Rey 1987; Tehovnik et al. 1998). More recently it has been reported that stimulation of the SEF evokes gaze shifts composed of combined movements of the eyes and the head (Chen and Sparks 2001; Martinez-Trujillo et al. 2003). Moreover, as with the SC, these evoked gaze movements were indistinguishable from natural gaze shifts (Martinez-Trujillo et al. 2003). However, unlike the SC, previous studies in the SEF have not documented any differences between head-fixed and head-free stimulation evoked gaze shifts; our study is the first to show this difference.

Concerning visuomotor coding in the SEF, there was perhaps even more variability in the results of previous head-fixed stimulation studies than in the SC. Head-fixed results have suggested the existence of multiples codes (Schlag and Schlag-Rey 1987), eye-centered codes (Russo and Bruce 1996), and head-centered codes (Tehovnik et al. 1998). Additionally, single unit studies have reported the existence of object-centered codes (Olson and Gettner 1999). It is difficult to unify these views in a single one, particularly when considering that the SEF is an area in which cell responses seem to be modulated by task-dependent factors such as attention (Bon and Lucchetti 1997), eye movement sequences (Lu et al. 2002), decision making (Coe et al. 2002), and probably other high level cognitive processes.

In our study, we have used a simple fixation task and stimulated the SEF with the head-free and fixed. A conclusion that we can clearly derive from our data is that stimulation with the head-fixed considerably modified apparent visuomotor coding making the trajectories appear to be more convergent in space and more variable and shorter in amplitude relative to head-free stimulation. This clearly biased the results toward a more convergent-in-space-type of code compared with the more eye-centered or fixed-vector type of code revealed with the head-free (Fig. 3F). However, from our data it is hard to estimate whether the eye-centered or the fixed-vector code is the one used by the SEF, particularly when considering that we did not stimulate enough sites encoding average gaze amplitudes larger than 40°. Such sites would allow a better distinction between these two coding strategies (Klier et al. 2001).

At least three different hypotheses can provide an explanation for the relative inability of the three models we have considered here to account for the SEF data compared with the SC data. First, the SEF may encode gaze in eye-centered coordinates or it may use a fixed-vector strategy. However, because our animals had their bodies restrained and because gaze shifts evoked by stimulating the SEF also involve the participation of the body, we may have obtained movements that were hypometric and more convergent than the true movements encoded by each site. Second, the SEF could use multiple motor codes. Finally, the SEF may use some coding system that has not yet been described. To test between these possibilities it may be necessary to stimulate a larger number of sites that encode larger movements and perhaps to consider new models of gaze coding. However, our current results clearly show that, to be useful for testing any visuomotor coding in the SC, SEF, and probably other gaze control struc-

tures, microstimulation should be performed with the head-free.

The authors thank S. Sun and X. Yan for technical support.

DISCLOSURES

E. M. Klier was supported by Canadian National Sciences and Engineering Research Council and Ontario graduate scholarships. J. D. Crawford holds a Canadian Institutes of Health Research operating grant and is a Canada Research Chair.

REFERENCES

- Bizzi E, Kalil RE, and Tagliasco V.** Eye-head coordination in monkeys. Evidence for centrally patterned organization. *Science* 173: 452–454, 1971.
- Bon L and Lucchetti C.** Attention-related neurons in the supplementary eye field of the macaque monkey. *Exp Brain Res* 113: 180–185, 1997.
- Chen LL and Sparks DL.** Supplementary eye field contribution to gaze shifts triggered by electrical microstimulation in head-free monkeys. *Neural Control Movement Abstr* D11, 2001.
- Coe B, Tomihara K, Matsuzawa M, and Hikosaka O.** Visual and anticipatory bias in three cortical eye fields of the monkey during an adaptive decision-making task. *J Neurosci* 22: 5081–5090, 2002.
- Crawford JD, Ceylan MZ, Klier EM, and Guitton D.** Three-dimensional eye-head coordination during gaze saccades in the primate. *J Neurophysiol* 81: 1760–1782, 1999.
- Crawford JD and Guitton D.** Primate head-free saccade generator implements a desired (post-VOR) eye position command by anticipating intended head motion. *J Neurophysiol* 78: 2811–2816, 1997.
- Freedman EG and Sparks DL.** Eye-head coordination during head-unrestrained gaze shifts in rhesus monkeys. *J Neurophysiol* 77: 2328–2348, 1997.
- Freedman EG, Stanford TR, and Sparks DL.** Combined eye-head gaze shifts produced by electrical stimulation of the superior colliculus in rhesus monkeys. *J Neurophysiol* 76: 927–952, 1996.
- Guillaume A and Pelisson D.** Gaze shifts evoked by electrical stimulation of the superior colliculus in the head-unrestrained cat. I. Effect of the locus and of the parameters of stimulation. *Eur J Neurosci* 14: 1331–1344, 2001.
- Guitton D.** Control of eye-head coordination during orienting gaze shifts. *Trends Neurosci* 15: 174–179, 1992.
- Klier EM, Wang H, and Crawford JD.** The superior colliculus encodes gaze commands in retinal coordinates. *Nat Neurosci* 4: 627–632, 2001.
- Lu X, Matsuzawa M, and Hikosaka O.** A neural correlate of oculomotor sequences in supplementary eye field. *Neuron* 34: 317–325, 2002.
- Martinez-Trujillo JC, Wang H, and Crawford JD.** Electrical stimulation of the supplementary eye fields in the head-free macaque evokes kinematically normal gaze shifts. *J Neurophysiol* 89: 2961–2974, 2003.
- Mitz AR and Godschalk M.** Eye-movement representation in the frontal lobe of rhesus monkeys. *Neurosci Lett* 106: 157–162, 1989.
- Olson CR and Gettner SN.** Macaque SEF neurons encode object-centered directions of eye movements regardless of the visual attributes of instructional cues. *J Neurophysiol* 81: 2340–2346, 1999.
- Pare M, Crommelinck M, and Guitton D.** Gaze shifts evoked by stimulation of the superior colliculus in the head-free cat conform to the motor map but also depend on stimulus strength and fixation activity. *Exp Brain Res* 101: 123–139, 1994.
- Pare M and Guitton D.** Brain stem omnipause neurons and the control of combined eye-head gaze saccades in the alert cat. *J Neurophysiol* 79: 3060–3076, 1998.
- Pelisson D, Guitton D, and Munoz DP.** Compensatory eye and head movements generated by the cat following stimulation-induced perturbations in gaze position. *Exp Brain Res* 78: 654–658, 1989.
- Pelisson D, Prablanc C, and Urquizar C.** Vestibuloocular reflex inhibition and gaze saccade control characteristics during eye-head orientation in humans. *J Neurophysiol* 59: 997–1013, 1988.
- Roucoux A, Guitton D, and Crommelinck M.** Stimulation of the superior colliculus in the alert cat. II. Eye and head movements evoked when the head is unrestrained. *Exp Brain Res* 39: 75–85, 1980.
- Roy JE and Cullen KE.** Vestibuloocular reflex signal modulation during voluntary and passive head movements. *J Neurophysiol* 87: 2337–2357, 2002.
- Russo GS and Bruce CJ.** Neurons in the supplementary eye field of rhesus monkeys code visual targets and saccadic eye movements in an oculocentric coordinate system. *J Neurophysiol* 76: 825–848, 1996.
- Schlag J and Schlag-Rey M.** Evidence for a supplementary eye field. *J Neurophysiol* 57: 179–200, 1987.
- Scudder CA, Kaneko CS, and Fuchs AF.** The brainstem burst generator for saccadic eye movements: a modern synthesis. *Exp Brain Res* 142: 439–462, 2002.
- Sparks DL.** Conceptual issues related to the role of the superior colliculus in the control of gaze. *Curr Opin Neurobiol* 9: 698–707, 1999.
- Stryker MP and Schiller PH.** Eye and head movements evoked by electrical stimulation of monkey superior colliculus. *Exp Brain Res* 23: 103–112, 1975.
- Tehovnik EJ, Slocum WM, Tolias AS, and Schiller PH.** Saccades induced electrically from the dorsomedial frontal cortex: evidence for a head-centered representation. *Brain Res* 795: 287–291, 1998.
- Tweed D, Cadera W, and Vilis T.** Computing three-dimensional eye position quaternions and eye velocity from search coil signals. *Vision Res* 30: 97–110, 1990.