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Role of the Rostral Superior Colliculus in Gaze Anchoring During Reach Movements

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Reyes-Puerta V, Philipp R, Lindner W, Hoffmann KP. Role of the rostral superior colliculus in gaze anchoring during reach movements. *J Neurophysiol* 103: 3153–3166, 2010. First published March 31, 2010; doi:10.1152/jn.00989.2009. When reaching for an object, primates usually look at their target before touching it with the hand. This gaze movement prior to the arm movement allows target fixation, which is usually prolonged until the target is reached. In this manner, a stable image of the object is provided on the fovea during the reach, which is crucial for guiding the final part of the hand trajectory by visual feedback. Here we investigated a neural substrate possibly responsible for this behavior. In particular we tested the influence of reaching movements on neurons recorded at the rostral pole of the superior colliculus (rSC), an area classically related to fixation. Most rSC neurons showed a significant increase in their activity during reaching. Moreover, this increase was particularly high when the reaching movements were preceded by corresponding saccades to the targets to be reached, probably revealing a stronger coupling of the oculo-manual neural system during such a natural task. However, none of the parameters tested—including movement kinematics and target location—was found to be closely related to the observed increase in neural activity. Thus the increase in activity during reaching was found to be rather nonspecific except for its dependence on whether the reach was produced in isolation or in combination with a gaze movement. These results identify the rSC as a neural substrate sufficient for gaze anchoring during natural reaching movements, placing its activity at the core of the neural system dedicated to eye-hand coordination.

INTRODUCTION

Reaching for objects is part of the everyday life of primates as is the exploration of the external visual space by means of saccadic movements. Generally this reaching behavior is visually guided, i.e., primates reach for objects that have been visually located or even fixated. Such visually guided behavior relies strongly on the coordination of the gaze and arm movements that must be implemented by a dedicated neural system (Crawford et al. 2004). Because only hand motion directly affects the external world, gaze movements are the aid in this system, optimizing vision for the guidance of hand motion. This has been proven in many tasks in which the gaze direction predicted and led the trajectory of the hand—suggesting that an interplay between reach-related and gaze-related brain areas occurs in this process (Ariff et al. 2002; Gowen and Miall 2006; Horstmann and Hoffmann 2005; Johansson et al. 2001). In this respect, interactions have been observed in both ways, i.e., gaze direction or gaze movements influencing activity in reach-related cortical areas (Baker et al. 1999; Batista et al. 1999; Mushiake et al. 1997), and hand position or movements influencing gaze-related areas (Mushiake et al. 1996; Thura et al. 2008).

To achieve optimal performance in reaching movements, gaze and arm movements have to be precisely coordinated: gaze has to arrive at the target before the hand (timing) and has to stay there until the hand has reached its goal (stability). These two properties of the oculo-manual neural system, which have been already proven in humans, are important for guiding the final part of the hand trajectory by visual feedback. The gaze movement prior to the arm movement allows early fixation of the target (Lünenburger and Hoffmann 2003; Lünenburger et al. 2000; for studies on the temporal coupling between gaze and reach, see Helsen et al. 1998). Further, the prolongation of the fixation during the entire reaching movement provides a stable image of the object in the retina—proven to be true at least in single-target reaching movements (Neggers and Bekkering 2000, 2001; for behavioral measurements associated to sequential target contact tasks, see Bowman et al. 2009; Hayhoe et al. 2003; Johansson et al. 2001). So far, it is unknown which neural substrates are responsible for these two properties of the oculo-manual neural system. In this study, we searched for neural substrates accounting for the gaze anchoring effect, namely the prolongation of the fixation during the complete reach movement.

The superior colliculus (SC) has been extensively studied for its involvement in the generation of saccadic gaze movements (for review, see Sparks and Hartwich-Young 1989). It has been also shown to contain neurons coding for arm movements in gaze-related coordinates as well as gaze-independent reach activity (Stuphorn et al. 2000). Further, the simultaneous presence of neurons related to gaze and reach movements suggest the possibility that the SC plays a major role in eye-hand coordination (Lünenburger et al. 2001; Neggers and Bekkering 2002).

A group of neurons located at the rostral SC (rSC)—called fixation neurons by several authors—has been interpreted as showing fixation-related activity, firing tonically during fixation and pausing during saccades (Munoz and Wurtz 1993a,b). This functional description has been recently extended, proposing the activity of the entire SC as a signal representing the error between the current gaze direction and the target goal location (Guitton et al. 2004). On the contrary, the rSC neuronal activity has been interpreted as representing potential target locations close to the fovea, contributing to the generation of small saccades, microsaccades and smooth pursuit (Krauzlis 2004; Krauzlis et al. 2000; Missal et al. 2002). Despite a considerable amount of functional and anatomical

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data, the potential contribution of the rSC to visual fixation is still under debate (Büttner-Ennever et al. 1999; Choi and Guitton 2006; Gandhi and Keller 1999; Hafed and Krauzlis 2008; Hafed et al. 2008, 2009). Investigating fixation in different contexts should add helpful information to this debate.

In the present experiments, we investigated whether the activity of neurons located at the rSC is influenced by reaching movements. To do that, monkeys were trained to perform reaches during fixation and reaches accompanied by saccades, both directed toward visual targets. Neurons that were recorded at the rSC during these tasks revealed a critical influence of reaching movements on their activity. Furthermore, we tested which factors—like movement kinematics and target location—could additionally modulate the rSC activity during reaching. The results are discussed in the context of eye-hand coordination, proposing neurons at the rSC as a neural substrate for gaze anchoring during reaching movements.

METHODS

Two male rhesus monkeys (*Macaca mulatta, CL* and *CI* weighing 11 and 9.5 kg, respectively) were trained to perform different combinations of saccades and reaches toward visual stimuli. The monkeys were seated comfortably in a primate chair and engaged in a setup with the body restrained but the head generally free. They faced a 60 cm wide circular translucent tangent screen at a distance of 27.5 cm. Visual targets [red, yellow and blue light-emitting diodes (LEDs); 1 cm diam, 1.5 cd/m^2] were rear-projected on the screen via galvanometer driven mirrors under home-made software control. Further visual input was avoided by performing the experiments in total darkness. The monkeys' behavior was monitored by means of the software that recorded the spike events, behavioral events, gaze direction, and hand position. All procedures were approved by the local ethics committee and followed the European and the German national regulations (European Communities Council Directive, 86/609/ECC; Tierschutzgesetz) as well as the National Institutes of Health Guidelines for Care and Use of Animals for Experimental Procedures.

Surgery

After a preoperative training, the monkeys were premedicated with atropine sulfate (0.05 mg/kg), and anesthetized with ketamine hydrochloride (10 mg/kg im) followed by pentobarbital sodium (25 mg/kg iv). Supplementary doses of pentobarbital sodium were administered intravenously as needed. Deep analgesia was maintained by intravenous bolus applications of fentanyl (3 $\mu g \cdot kg^{-1} \cdot h^{-1}$). A stainless steel head holder was implanted on the animal's skull, and a chamber was placed on the midline over the occipital pole, tilted backward 45° from the vertical—therefore providing perpendicular access to the SC surface. Search coils were implanted under the conjunctiva around each eye (Judge et al. 1980). A connector for the eye coils was fixed in the acrylic cement that was connected to the head holder. Body temperature, blood pressure, heart rate, and SPO_2 were monitored during the surgery. Analgesics (Flunixin) were administered for 2 days, and antibiotics (enrofloxacine) were administered for one week postoperatively.

Recording

Extracellular recordings of single neurons were performed using glass-insulated tungsten microelectrodes (impedance: 2–3 MΩ measured at 100 Hz). The electrodes were lowered within a guide tube through the dura by a microdrive that was mounted on the recording chamber (Narishige, Tokyo, Japan). The activity of single cells was detected in real time by means of a computer controlled multi-channel spike sorter (Plexon, Dallas, TX). Single-unit discharges were separated using an on-line time-amplitude window discriminator and sampled with 1 ms time resolution.

Gaze direction was measured using a magnetic search coil system (Remmel, Katy, TX). Separate horizontal and vertical direction signals were sampled with a frequency of 500 Hz. The gaze direction signal was used to monitor stable fixation in a window of 3° radius around the fixation points during the tasks.

Hand position was recorded by means of the magnetic miniBIRD system (Ascension Technology, Burlington, VT) with a frequency of 91 Hz. Reaching movements were performed using the arm contralateral to the SC being recorded. A sensor was attached to the monkeys at the level of the corresponding wrist. The cable was pasted to the arm at the level of the biceps as well so that the monkeys could move their hand freely. The hand was considered to reach a specific target location when the sensor was inside a three dimensional window of radius 2.5–5 cm. This flexible range was used to account for the variability of reaches and tasks performed.

All data were fed into a PC-ISA multifunction board (Intelligent Instrumentation PCI-20098C) controlled by home-made software, which monitored the behavior of the animals during the tasks and stored the recordings.

Behavioral tasks

Two main tasks were arranged to test the influence of arm movements on the activity of rSC neurons: the fixation-reach (FR) and the coupled saccade-reach (CSR) tasks. Both tasks were performed in blocks so that the monkeys could anticipate which one to perform at the beginning of each trial. Although the tasks were somewhat different for the two monkeys, the basic behavioral patterns were comparable. The first monkey made center-out reach movements to several target locations on the screen, whereas the second monkey performed comparable reach movements from the hip. In the following, the description of methods will focus on the second animal. However, all of the observations and conclusions refer to the data obtained from the two monkeys.

In addition, also standard fixation and saccade tasks containing blinks of 300–600 ms were used to characterize and validate the recorded rSC neurons in the lack of any arm movements (see following text). For a detailed description of these tasks see Reyes-Puerta et al. (2009).

FIXATION-REACH. In the FR task (Fig. 1*A*), monkeys had to reach to a cued target while maintaining fixation at a specific point during the whole trial. In some of the conditions, the fixation and cued reach targets were the same so that a reaching toward a foveated target was performed. In some other conditions, the fixation and reach targets were at different locations; in this case, reaching movements toward peripheral targets were performed.

At the beginning of each trial, monkeys had to touch a metal bar at their waist level and fixate a red light appearing on the screen during a randomized interval of 0.5–1.5 s (fix epoch). Then a blue light appeared, cueing the location of the reaching target for a randomized interval of 0.5–1.5 s (cue epoch). Afterward the fixation spot changed its color from red to yellow, instructing the animal to touch the reach target with the hand (go epoch lasting until the start of the reach movement). The reach epoch lasted from the start to the end of the reaching movement. Once the reach movement was finished, monkeys had to hold the hand at the target for a randomized interval of 0.5–1.5 s (hold epoch). Subsequently a liquid juice reward was given when the trial was performed correctly.

COUPLED SACCADE-REACH. In the CSR task (Fig. 1*B*), monkeys were instructed to perform a reflexive saccade-reach movement toward a common target. When humans or primates try to perform a simultaneous movement, a saccade is usually performed first, tightly followed by the reaching movement (Helsen et al. 2000); thus in this

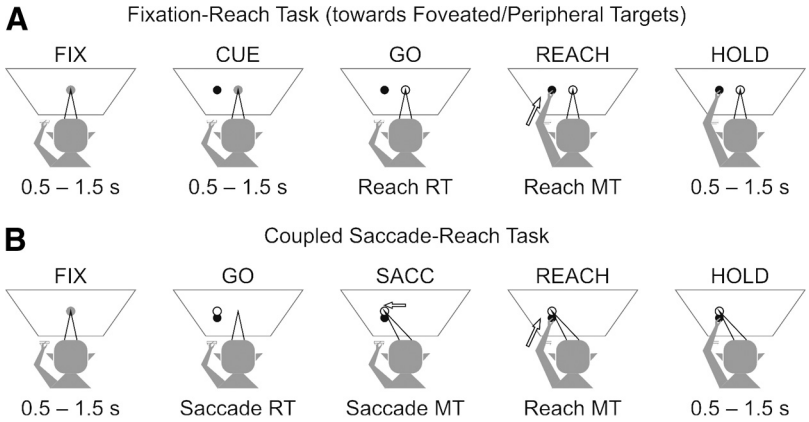

FIG. 1. Behavioral tasks. *A*: fixation-reach task. The complete sequence of behavioral events was the same for all target locations but illustrated here for only 1 of them. The name of each epoch is written above, and the temporal duration of each epoch is illustrated below the corresponding monkey-screen scheme. RT, reaction time; MT, movement time. Details can be read in METHODS. *B*: coupled saccade-reach task: same conventions as in *A*.

task, the reach movements were always performed toward previously foveated targets. Further, the location of the saccade-reach targets were in this case not cued beforehand; therefore a more reflexive and natural behavior was expected here than in the previous task.

Each trial started by monkeys touching a metal bar at their waist level and fixating a red light appearing on the screen during a randomized interval of 0.5–1.5 s (fix epoch). Afterward the fixation spot jumped to a new location changing its color to yellow, and at the same time, the reach target appeared just below the yellow (saccade) target. These two simultaneous events instructed the monkeys to perform a coupled saccade-reach movement to the target location (go epoch). Generally the saccade was completed (SACC epoch) before the corresponding reach movement (reach epoch). After completing the reaching movement, monkeys had to hold the position of the hand for a randomized interval of 0.5–1.5 s (hold epoch). A liquid juice reward was given after completion of each correct trial.

Data analysis

All off-line analyses were performed in Matlab (The Mathworks). Neurons fulfilling the following criteria—adapted from Munoz and Wurtz (1993a) and Krauzlis et al. (2000)—were validated and further analyzed. *1*) *Visual Receptive Field.* Only neurons recorded during penetrations containing foveal or parafoveal visual receptive fields were included, i.e., when the distance between the center of the receptive field and the center of the fovea was $<2.5°$. Receptive fields were registered at superficial layers at the beginning of each penetration. *2*) *Depth.* Neurons had to be recorded between 0.8 and 3.5 mm below the dorsal surface of the SC. *3*) *Firing Rate Stability.* Neurons had to show stability in the firing rate during recordings. Recording stability was ensured by computing the coefficient of variation in mean firing rate of trials for every block. The coefficient of variation had to be <1.0 in each block to accept stability and validate the neural recording. If one of the blocks from a cell failed this validation, then the cell was rejected. The used time interval was the whole length of each trial. *4*) *Activity during fixation.* Neurons had to have a minimum firing rate of 5 spike/s (average) during prolonged fixation. *5*) *Pause in activity during saccades.* Neurons had to show a pause in activity during saccades. Pause is considered as having a firing rate during the saccade period $<50\%$ of the firing rate during prolonged fixation. The saccade period is defined as the time period between 30 ms before saccade onset until saccade offset. *6*) *Fixation activity during blink.* Standard fixation and saccade tasks containing a blink were used to discard neurons showing purely visual activity. Thus neuronal firing rate had to be higher than 5 spike/s during the blink period of blink tasks, which is also the minimum accepted firing rate during prolonged fixation.

Spike density functions (SDFs) were computed using a Gaussian kernel of 10 or 20 ms SD and a time resolution of 1 ms. SDFs were used for the presentation and analysis of individual neurons' activity.

Gaze direction signals were filtered using a second-order low-pass Butterworth filter (28 Hz cutoff frequency). Velocity and amplitude criteria were used to detect the onset and offset of gaze movements. For medium and large saccades ($>3°$ amplitude) the onset and offset velocity thresholds were calculated as 2.5 times the SD of the filtered gaze velocity signal. Due to the presence of fixational gaze movements and small saccades during the fixation period, it was not possible to automatically designate intervals of the signal as being "at rest;" thus the SD of the filtered gaze velocity signal was computed using the whole trial period for the CSR task, i.e., including both fixation and saccade periods. This approach actually improved the stability and robustness of the automated detection algorithms without affecting significantly their performance because the small proportion of data related to the large saccade elevated slightly the thresholds for saccade detection—thus avoiding the identification of microsaccades and small saccades as target related ones. However, in the FR task, the SD of the signal was computed using only periods of fixation as no large saccades were produced here. For microsaccades and small saccades (between $6'$ and $3°$ amplitude) the onset and offset velocity thresholds were set to $20°/s$. We performed additionally repetitive visual inspections of the data to insure the performance of the detection algorithms. Only those trials recorded in the FR task containing no detected medium or large saccades were taken into consideration for analysis; in the CSR task, trials had to contain just one detected medium or large saccade.

Hand position signals were filtered using a second-order low-pass Butterworth filter (7 Hz cutoff frequency). Absolute velocity (speed) and amplitude criteria (computed using the *x, y,* and *z* components of the signal) were applied to detect the onset and offset of hand movements. The onset and offset speed thresholds were calculated as 0.5 times the SD of the filtered hand speed signal. The SD of the filtered speed signal was again computed using the whole signal, i.e., including periods at rest and periods where the arm was moving. Only hand movements of >20 mm amplitude were detected. Trials recorded in the FR task or the CSR task containing a different quantity than one detected hand movements were discarded.

As previously stated, all reaching movements were done using the arm contralateral to the SC being recorded. All our data refer to the right SC—and therefore to the left arm. Data obtained when the monkey was using the right arm (left SC) were converted to a mirror left arm image (right SC).

Statistical tests were used to test the hypothesis that two independent samples containing firing rates or activity ratios represent similar distributions. Generally the following approach was used. First each distribution of data were tested for normality (D'Agostino-Pearson test) within each group. A minimum sample size of 20 was set to ensure proper performance of the D'Agostino-Pearson test (Zar 1999). If both samples were normally distributed and the sample size in both was ≥ 20, parametric tests (independent sample *t*-test) were applied at the 5% significance level for between-group comparisons. If at least one sample deviated significantly from normality or had a small size

(<20), nonparametric tests (Mann-Whitney *U* test) were performed—again at the 5% significance level.

RESULTS

A total of 55 neurons were recorded in the intermediate layers of the rSC of two monkeys during 45 penetrations. In all of these penetrations, neurons at the superficial layers had visual receptive fields near and in the fovea (<2.5° eccentricity). Of the 55 rSC neurons recorded, 27 fulfilled all the criteria to be considered as fixation-related neurons (criteria listed in METHODS following Munoz and Wurtz 1993a). In short, the validated neurons lie in the intermediate layers of the rostral SC. They show tonic activity during fixation and pause shortly before and during saccades. When the fixation spot is extinguished, they maintain a tonic activity, disclosing that they are not just purely visual neurons. A careful validation process was applied to warrant a homogeneous group of cells similar to those previously described. The remaining 28 neurons violated one or several of the applied criteria and were discarded from the main analysis (Supplemental Table S1).[1]

All of the 27 validated neurons were recorded in the FR task and 16 of them additionally in the CSR task. Generally each neuron was recorded in a subset of conditions; therefore several of our population analyses were performed using a subset of the total number of neurons.

Individual neuron responses

A typical response of a rSC neuron in a 25° contraversive saccade-only task, in the FR task and in the CSR task can be observed in Fig. 2. Here we compare directly the responses of *neuron CI-029702* in the three tasks.

Throughout the contraversive saccade task (Fig. 2*A*), this neuron shows tonic activity before (mean: 48.8 spike/s) and after (mean: 57.6 spike/s) the saccade. However, a clear pause is observed shortly before and during the saccade itself (mean: 1.3 spike/s in the range between 30 ms before saccade onset and saccade offset).

The activity of this neuron in the FR task is outlined in Fig. 2*B*. The activity is constant during the fixation period (57.6 spike/s), increasing slightly after the cue (68.3 spike/s) and strongly after the go signal (99.4 spike/s, already 297 ms before the reach movement starts). Afterward, the activity of this neuron increases further to show the highest activity during the reaching movement (directed toward a foveated target, 142.3 spike/s) and then maintains a relatively high activity during the holding period (91.3 spike/s, 319 ms after reach onset).

One critical concern was the possible influence of head movements on the activity of rSC neurons as the animals were generally free to move their heads during the tasks. Regarding the production of conjugated head-eye movements, two major strategies were found. In the first strategy only an eye saccade was produced to foveate the peripheral target (*top traces* in the panel showing horizontal head position). Thus in many of the trials, the head was still facing the center of the screen when the reach movement actually began. During the reach epoch, only small and slow head movements were produced by the start and end of the reach movements. The peak speed was slightly higher for the head movement produced at reach offset (median: 23.2°/s). Only afterward larger head movements were

[1] The online version of this article contains supplemental data.

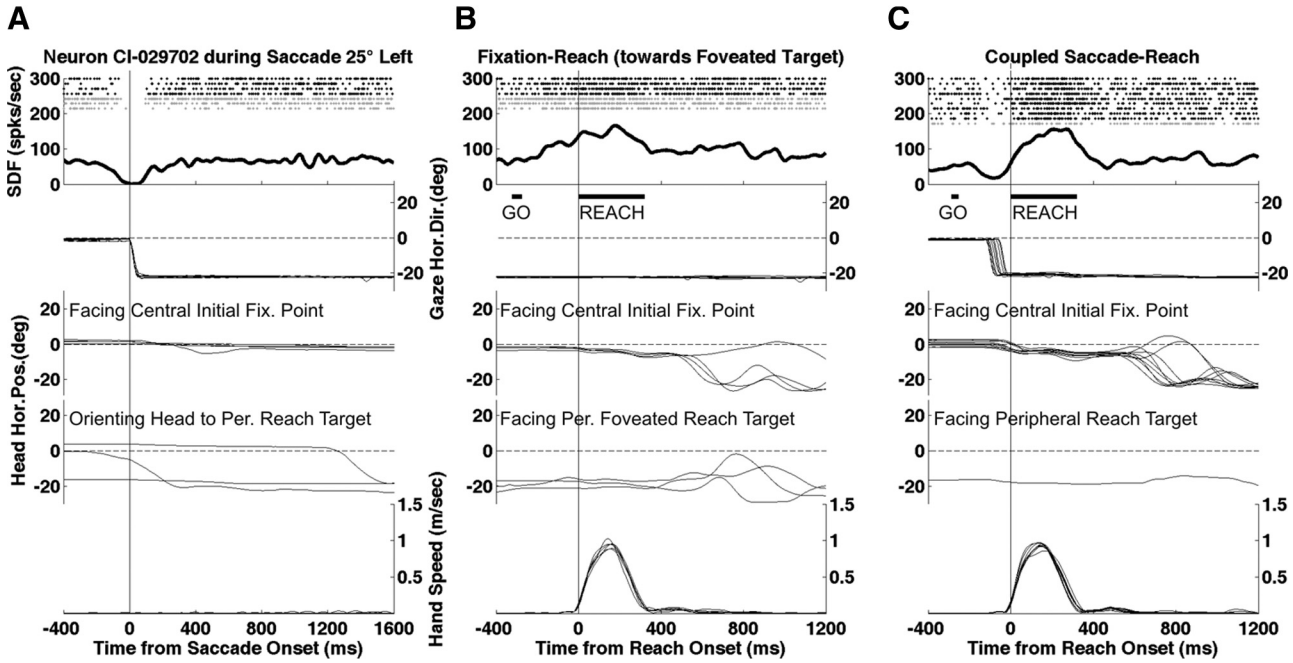

FIG. 2. *Neuron CI-029702* in saccade-only (*A*), fixation-reach (*B*), and coupled saccade-reach tasks (*C*). *A*: activity during 25° saccade to the left. *Top*: a raster plot for each trial aligned on saccade onset. Trials in the raster plot were separated for the 2 head movement strategies described below (black for the 1st strategy and gray for the 2nd); Spike density functions (SDFs) were computed by pooling together both sets of trials. *Second panel*: horizontal gaze direction traces, in which positive values correspond to rightward movements. *Third panel*: horizontal head position. *Top traces*: trials in which the monkey faced the central initial fixation point when the reach movement began. *Bottom traces*: trials in which the monkey oriented his head toward the reach target before the reaching started. *Fourth panel* from *top* represents hand speed in m/s. *B*: activity during a reaching movement toward a foveated target. Trials are aligned on reaching movement onset. Horizontal black bars represent the interquartile range of go-signal and reach movement times. Otherwise same conventions as in *A*. *C*: activity during a coupled saccade-reach movement toward a target 25° to the left. Same conventions are used as in *A* and *B*.

produced to face the peripheral target being held; this larger head movements were produced 321 ms (median) after the reach offset, showing a higher peak velocity as well (median: 55.7°/s). In the second strategy, the head was already facing the peripheral foveated target before the reaching started (*bottom traces* showing horizontal head position); in this case, the head movement facing the reach target was produced before, during or after the eye saccade foveating the peripheral reach target (that is, during the fix or cue epochs). Although no horizontal head movements were registered during the reach epoch in these trials, some faster movements (median: 63°/s) were found 438 ms (median) after the reach offset. These late head movements did not have any clear nor particular purpose for the realization of the task. Finally, no clear differences in neural activity were found between the two described strategies [see separated spike rasters (black and gray) for both strategies in the *top panels*]. In fact head movements were not reflected in the neuronal activity at all.

In the CSR task, the same neuron shows a combination of the saccadic and reaching movement effects (Fig. 2*C*). Again, the activity stays constant during fixation (50.2 spike/s). However, it declines after the go signal, showing a modest activity decrease previous to the saccade (38.5 spike/s, 278 ms before the reaching movement). When aligning the activity on the saccade onset (not shown), a pause can be observed in its activity—which is not as clear as in the saccade-only condition (11.5 spike/s). During the reaching, an increase in the activity can be observed (132.1 spike/s). This increase is comparable to the one observed in the FR task. Afterward the activity stays high during the holding period (66.9 spike/s, 319 ms after reach onset) but not quite as high as in the FR task. In summary, the activity of this neuron in the CSR task could be explained by a combination of the individual effects of both the saccade and the reach.

The head movement behavior observed during the CSR task corroborated the results reported in the preceding text for the saccade and FR task. In the majority of the trials, the head was facing the central fixation point by the start of the reach movement (upper head position traces). Small and slow head movements were produced at reach onset and offset, showing a maximum peak speed by the reach offset (median: 22.7°/s). Larger and faster head movements (median: 58.6°/s) were produced 412 ms (median) after the reach offset. Interestingly, in some few trials, the animals were facing the saccade-reach target even before the go signal was given (represented by 1 trial in this subsample in the lower head position panel). This uncovered a predictive behavior, as the final saccade-reach target position was signaled only after the go signal. As stated in METHODS, the tasks were performed in blocks, so that the monkeys could anticipate which task to perform at the beginning of each trial. Concordantly, we rarely found in these trials significant head movements during the reach or hold epochs.

Several general results can be outlined from the analysis performed on the presented examples, which are representative for the rest of the recorded data. Head position varied across trials, and the precise time of movement onset and offset presented great variability during the fix, cue, and hold epochs. However, neural activity did not show such a trial-to-trial variability correlated with head movements. Second, only small, slow, and stereotyped head movements were registered during the reach epoch that were most likely produced to maintain body posture during the reaching. Third, larger and faster head movements were produced rarely during the fix and cue epochs, very exceptionally during the go epoch, but frequently during the hold epoch. In the last case, the head movements started well after the reach movements were finished, providing an optimal head-eye configuration for the realization of the tasks. All in all, these results make it very unlikely that the increase in firing of rSC cells during the reach was related to head position or head movements.

To demonstrate the wide spectrum of the modulation of rSC neuron activity by reach movements, we give another example of the effects of these tasks in Fig. 3 (*neuron CI-028902*).

This neuron shows tonic activity before (mean: 26.9 spike/s) as well as after (mean: 40.3 spike/s) the 25° contraversive saccade (Fig. 3*A*). Again, a clear pause is present shortly before and during the saccade (mean: 4.6 spike/s).

In the FR task this neuron shows a relatively constant activity pattern (Fig. 3*B*). The activity is tonic during fixation (40.3 spike/s) and after the cue signal (44.2 spike/s), showing a decreased level during the go epoch (19.7 spike/s, 280 ms before the reach movement). Afterward this neuron shows tonic activity during the reaching (31.1 spike/s) and holding periods (31.6 spike/s, 319 ms after reach onset).

In the CSR task, the same neuron shows a very different activity pattern. The activity during fixation stays constant (27.9 spike/s; Fig. 3*C*). It decreases modestly after the go signal (18.6 spike/s, 265 ms before the reach movement). A clear pause can be observed when aligning the activity on saccade onset (1.7 spike/s, not shown). During the reaching, a very high increase of activity can be observed (93.7 spike/s). Here the activity level during reaching is three times higher than the one observed in the FR task. Afterward the activity falls back to a lower firing rate during the holding period (28.0 spike/s, 319 ms after reach onset). In summary, the activity pattern of this neuron in the CSR task cannot entirely be explained by a summation of the individual effects of both the saccade and the reach.

Population responses

To test whether the increase of activity during reaching holds true for the whole population of rSC neurons, we computed the mean activity of individual neurons during the different epochs in both tasks. To perform this computation, we used all the trials recorded in different conditions, grouping them into the FR or the CSR task.

The mean activity of the 27 neurons recorded in the FR task is presented in Fig. 4*A*. Sixteen of those neurons were recorded also in the CSR task, so that their activity could be directly compared (represented by circles); generally the activity of this subgroup of neurons was tonic during fixation (20.3 ± 11.9 spike/s), increasing slightly after the cue (27.1 ± 15.7 spike/s) and go (30.8 ± 17.8 spike/s) signals. The highest activity was observed during the reaching movement (39.1 ± 26.6 spike/s), staying relatively high during the holding period (31.1 ± 20.4 spike/s). For the 11 neurons tested only in the FR task, the activity was not highest during the reach epoch, but instead it was more or less constant from the go through to the hold epochs.

The 16 neurons tested in both tasks showed different results in the CSR task (Fig. 4*B*). Again the activity stayed tonic during the fixation period (26.6 ± 12.6 spike/s), decreasing in

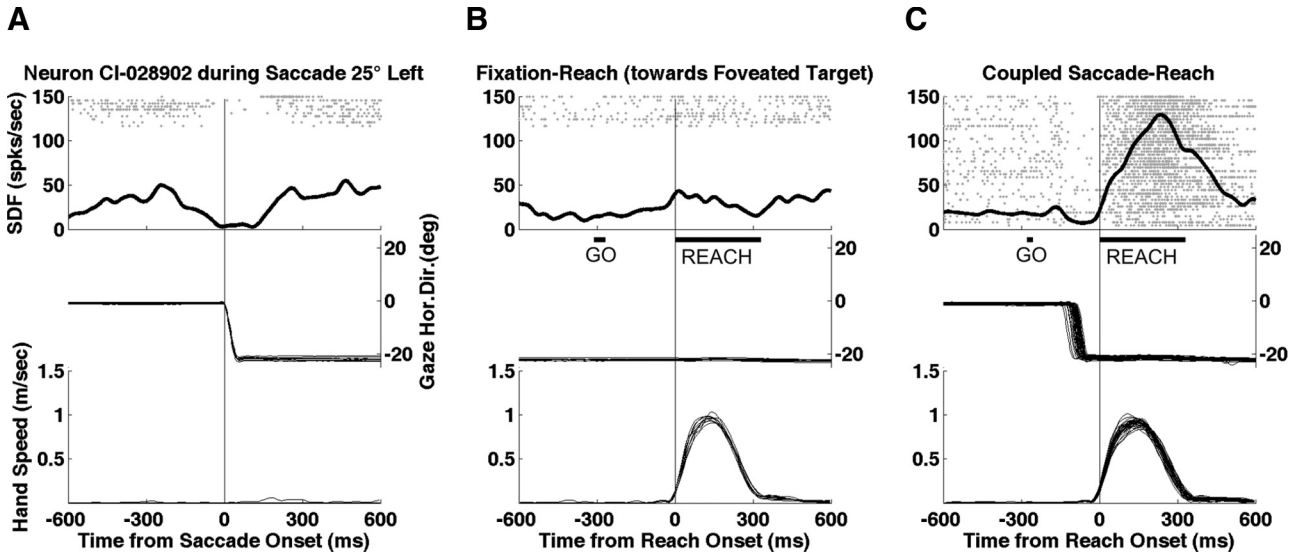

FIG. 3. *Neuron CI-028902* in saccade-only (*A*), fixation-reach (*B*), and coupled saccade-reach tasks (*C*). *A*: activity during 25° saccade to the left. *Top*: a raster plot aligned on saccade onset and SDF; *middle*: horizontal gaze direction traces; and *bottom*: hand speed. *B*: activity during a reaching movement toward a foveated target. Trials are aligned on reaching movement onset. Horizontal black bars represent the interquartile range of go-signal and reach movement times. *C*: activity during a coupled saccade-reach movement toward a target 25° to the left. Trials are aligned on reaching movement onset. Otherwise same conventions are used as in *A*.

this case after the go signal because of the forthcoming saccade (18.8 ± 9.6 spike/s). During the saccade, there was a clear pause on the activity (2.8 ± 3.9 spike/s). Immediately after the saccade the activity increased sharply, presenting its peak during the reaching movement (56.4 ± 32.0 spike/s). During the holding period, the neurons displayed again a relatively high activity (31.4 ± 17.4 spike/s).

The influence of reaching movements on the neural activity was also computed for individual neurons. We compared for each neuron the activity during the prolonged fixation period to the activity during the reaching movement in the FR task (Fig. 4*C*). Here we can observe in most of the recorded neurons (21 of 27 neurons, 77.8%) a significantly higher activity during the reaching movement as compared with the fixation period ($P < 0.05$). The remaining six neurons did not show significant differences.

Further we did the same comparison for the CSR task by using the 16 neurons recorded in both tasks (Fig. 4*D*). In this

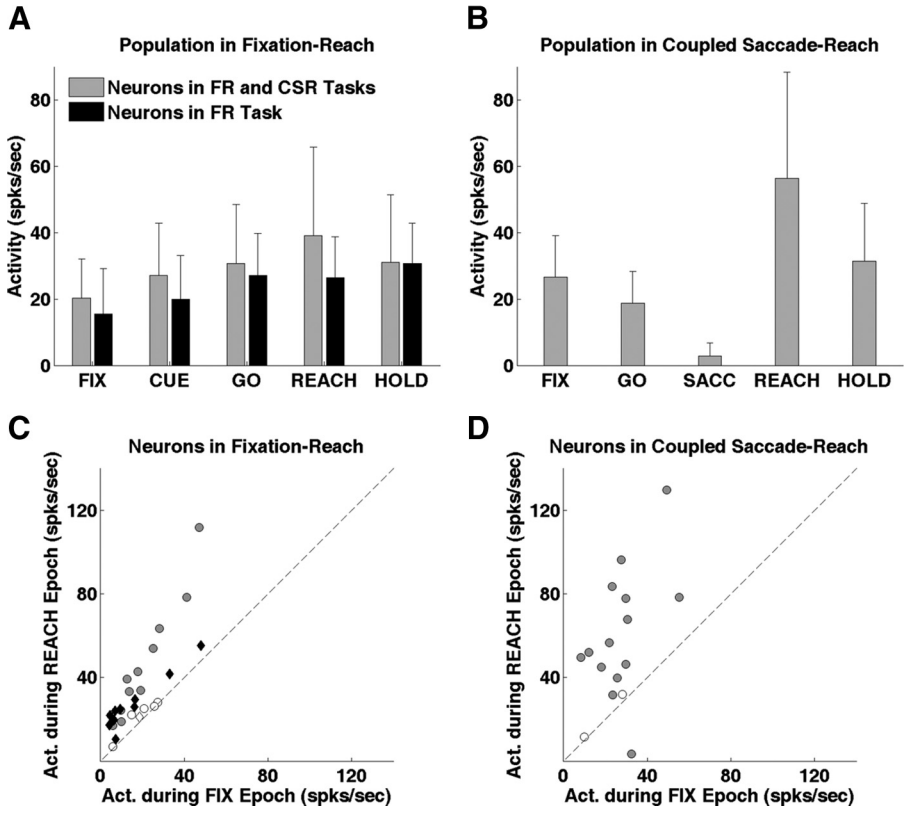

FIG. 4. Population activity in the fixation-reach (FR) and coupled saccade-reach (CSR) tasks. *A*: population activity in the FR task. Each 1 of the bars represents mean ± SD activity for each behavioral epoch, separated for neurons recorded in both tasks and neurons recorded only in the FR task. The mean activity is computed using the mean activity of individual neurons. *B*: population activity in the CSR task. Same conventions are used as in *A*. *C*: comparison of activity during fix and reach epochs in individual neurons in the FR task. Empty symbols, neurons showing no significantly different activity during both epochs; filled symbols, neurons showing significantly different activity ($P < 0.05$). Circles, neurons recorded in both tasks; diamonds, neurons recorded only in the FR task. - - -, unity slope. *D*: comparison of activity during fix and reach epochs for individual neurons in the CSR task. Same conventions are used as in *C*.

case, 13 of the 16 recorded neurons (81.25%) showed a significant increase on their activity, 3 of them (12.5%) no significant difference, and 1 of them a significant decrease.

These results were confirmed by comparing directly for the 16 neurons recorded in both tasks the reaching related activity (i.e., the activity recorded during the reach epoch) in the FR task to the activity in the CSR task. A paired Wilcoxon test showed that the activity of these neurons was found to be significantly higher in the CSR task than in the FR task ($P < 0.01$). To test whether the increased activity in the CSR task was a general effect observable in this population of neurons, we performed the previous comparison for each neuron individually (Fig. 5). As can be observed, there were some neurons for which the activity in these two tasks was comparable, lying close to the unity line (see upwards triangle symbol representing *neuron CI-029702,* previously characterized in Fig. 2). However, some neurons showed a higher activity in the CSR task as compared with the FR task (see downward triangle symbol representing *neuron CI-028902,* previously characterized in Fig. 3). In sum, this comparison confirms that the results obtained for individual neurons in the last section hold true at the level of the population and that the two neurons already analyzed individually are representative for the rest of the population.

All the reported results at the level of the population remained consistent across the two monkeys. Of the 27 neurons recorded in the FR task, 7 were collected in *monkey CL* and 20 in *monkey CI.* All neurons showed higher activity during reaching than during fixation. These differences were significant in two of the seven neurons recorded in *monkey CL* and in 18 of 20 neurons recorded in the *monkey CI* ($P < 0.05$). Of the 16 neurons recorded in the CSR task, 4 were collected in *monkey CL* and 12 in *monkey CI.* In *monkey CL,* all neurons showed higher activity during reaching than during fixation (2 significantly, $P < 0.05$). In *monkey CI,* 11 of 12 neurons did so (all of them significantly, $P < 0.05$). We also compared directly the activity during reaching in the CSR task versus the FR task for the individual monkeys. Of the four neurons compared from *monkey CL,* all of them showed higher activity in the CSR than in the FR task (1 significantly, $P < 0.05$). In *monkey CI,* 11 of 12 did so (9 of them significantly, $P < 0.05$).

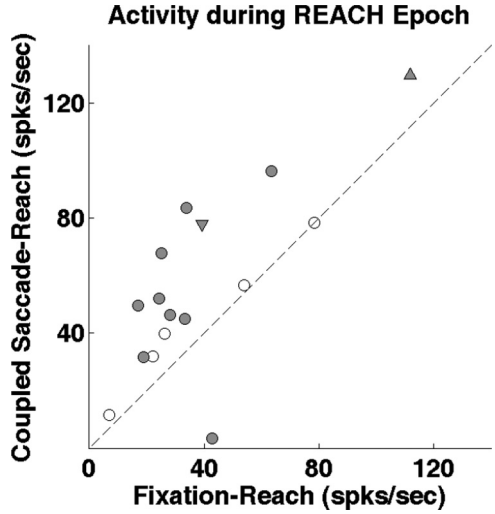

FIG. 5. Direct comparison of activity in FR vs. CSR tasks for the 16 neurons recorded in both tasks. Empty symbols, neurons showing no significantly different activity during both epochs; filled symbols, neurons showing significantly different activity ($P < 0.05$). Upward triangle, *neuron CI-029702* (Fig. 2); downward triangle, *neuron CI-028902* (Fig. 3); dashed line, unity slope.

As stated in METHODS, the animals were generally free to move their heads during the tasks (in particular during the recording of 25 of the 27 validated cells). In many ways, this is more natural and therefore arguably preferable. However, it opens the possibility that cell activity was related to head movement. Therefore we performed a control by analyzing the data from two cells recorded with the head-fixed in one monkey (*CL*). The two neurons showed higher activity during reaching than during fixation in both the FR and the CSR tasks, just as the neurons recorded in the head-free conditions. Further, the activity was significantly higher during reaching in the CSR than in the FR task for one of the neurons ($P < 0.05$). Thus although head movements could not be produced in this case, similar effects were observed on the activity of rSC neurons.

Control for influences of visual stimulation on responses

One specific concern was the possibility that the large increase in activity after the saccade in the coupled saccade-reach task could simply result from visual responses to the additional reach target which has just been brought into the cell's receptive field (RF) by the saccade. This additional RF stimulus by the reach target was not present in the saccade-only condition. In the FR task toward peripheral targets, there was no saccade, so the cell's RF stimulus did not change.

To test this alternative hypothesis, we used the fixation-reach task toward foveated targets. Here the visual stimulus appeared at the beginning of the cue epoch (blue light), cueing the location of the reaching target. Responses to such a stimulus were already described in Munoz and Wurtz (1993a). For our data, they can be seen in Fig. 6. Some rSC neurons showed transient visual responses to the visual stimulus (cue). These responses were actually diverse in their level; the three examples presented here covered the whole range of responses. However, the timing of the responses was very stereotyped. Thus in all cases the transient visual response started after 50 ms and ended before 125 ms from stimulus onset—actually ending a median of 1.15 s before reach movement onset in this task.

If we compare the timing of the transient visual responses to the timing of the reach-related activity profiles, we observe clear differences. As can be observed in Figs. 2C and 3*C,* the activity level of the rSC neurons in the CSR task was increased until the end of the reach movement (>300 ms after the visual stimulation onset). Further, at the population level the neurons usually peaked 225 ms after reach onset (actually 289 ms after the visual stimulation onset, due to the 64 ms median time between saccade offset and reach onset; Fig. 7). Thus it seems highly unlikely that the reported transient responses could cause the differences in activity obtained during the reach.

To definitely discard this alternative explanation, we performed one further control analysis. We compared again for those neurons recorded in both the FR and CSR task (16 in total) their activity level during reaching; however, in this case, we used a restricted part of the reaching movements time period, specifically the time period starting from 150 ms after reach onset until reach offset. Taking into consideration the 64 ms median time between saccade offset and reach onset, the

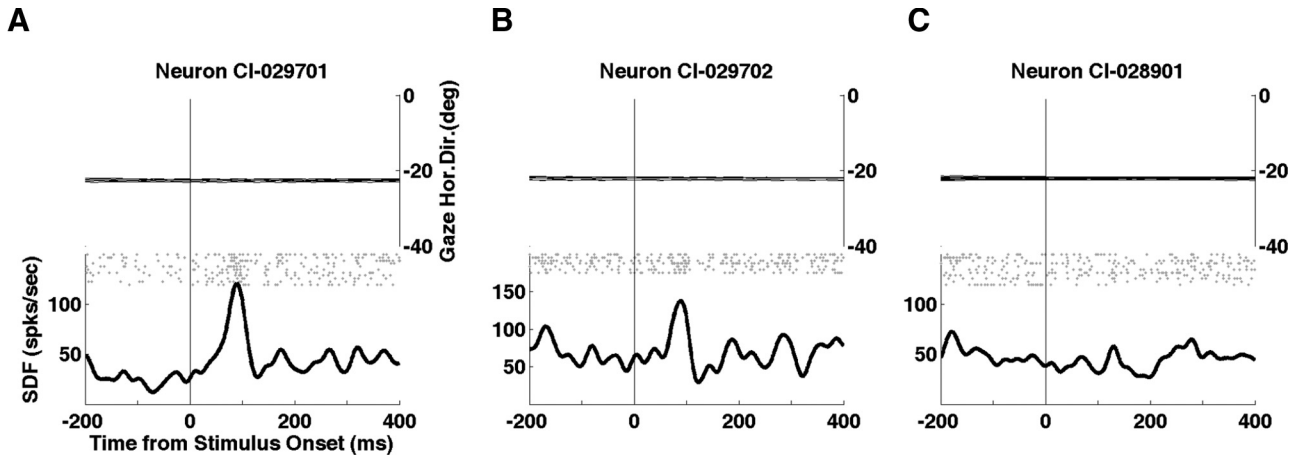

FIG. 6. Transient visual responses associated to the foveated reach target onset. *A*: activity of *neuron CI-029701* aligned on reach target onset (beginning of the cue epoch). *Top*: horizontal gaze direction traces, in which negative values correspond to contralateral (leftward) directions. *Bottom*: a raster plot for each trial and SDF, in this case computed using a Gaussian kernel of 10 ms SD. *B*: activity of *neuron CI-029702* aligned on reach target onset. This neuron is also shown in Fig. 2. *C*: activity of *neuron CI-028901*. Same conventions are used as in *A*.

selected time period would start in median 214 ms after the visual stimulation—thus avoiding completely the time in which the transient visual responses could have had an effect. As a result of this control analysis, the overall activity level increased slightly in both the FR and the CSR tasks, and the statistical difference between both remained unaltered ($P < 0.01$). Further, the differences in firing rate were present in the majority of the recorded neurons as when taking the whole range into consideration (because 12 of 16 neurons showed significantly higher activity in the CSR than in the FR task). Thus the increase in activity in the CSR as compared with the FR task was present in both analyses, i.e., with a possible visual contamination and without (for further details, see Supplementary Fig. S1).

We further tested whether the prolonged visual stimulation caused by the reach target could have an influence on the activity measured during reaching. To test this hypothesis, we computed again the activity level during reaching in the FR task, this time separately for conditions containing reaches toward foveated targets and conditions containing reaches toward peripheral targets. Then we compared directly the activity level of those neurons recorded in the FR task both toward foveated and peripheral targets (14 in total). A paired Wilcoxon test showed that the slight increase of activity observed in conditions involving foveated targets (44.4 ± 32.6 vs. 41.9 ± 25.0 spike/s) was not significant ($P = 0.95$).

With these results, we demonstrate that neither the transient visual responses nor the prolonged presence of the reach stimulus on the fovea had any influence on the differences obtained between the FR and CSR tasks.

Movement kinematics

In this section, we investigate the possibility that some of the reaching movement kinematic parameters modulate the activity of rSC neurons in a stereotypical manner. We approached the relationship between rSC neurons and reach movements in the same way in which the association between neural activity and saccades was studied. Saccadic eye movements do not present a high variability in movement kinematics; however, it has been repeatedly shown that both the saccadic neurons (Sparks 1978) and the rSC neurons (Munoz and Wurtz 1993a) show a clear and stereotyped relation between their activity and the movement patterns. Thus saccadic neurons tend to peak just before the saccade, showing their burst onset 23 ms before the saccade in mean with a SD of only 6 ms (Munoz and Wurtz 1995). Further, rSC neurons showed their pause onset 33 ± 17.2 ms before the saccade onset and their pause end 2.6 ± 7.4 ms before the saccade termination.

The low variability in these saccade-related data showed a clear and stereotyped relation between the activity profiles of SC neurons and the movement patterns. In the case of saccadic neurons, the lower SD found in the time between saccade and burst onset argued for a more consistent relationship between saccade peak acceleration and neural activity. Similarly, the rSC neural activity was found to be better related to saccade peak deceleration than to any other movement parameter (Munoz and Wurtz 1993a).

Here we investigated whether the activity patterns of rSC neurons were as well standardized across the population in relation to the reach movements. More specifically we tested whether the time to peak activity of rSC neurons was related to the time to peak amplitude of several movement kinematic parameters.

As observed in Fig. 2, the patterns of activity of *neuron CI-029702* in the FR and CSR tasks were very similar. Indeed the time to peak firing rate for this neuron in these particular conditions was 181 ms in the FR task and 244 ms in the CSR task (measured from reach onset). The difference in time to peak firing rate between the two tasks could be due to the saccade performed in the CSR task, which introduces a pause in the activity and delays the time point where maximal firing rate is achieved.

However, the patterns of activity of *neuron CI-028902* were somewhat different (Fig. 3). In this case, the time to peak firing rate was very different in both tasks, 15 ms in the FR task and 228 ms in the CSR task. On the contrary, the movement patterns were very similar; this can be observed directly by looking at the hand speed profiles.

To measure the variability of neural activity patterns, we computed the time to peak firing rate (measured from reach onset) for each neuron and each condition. Further, we grouped

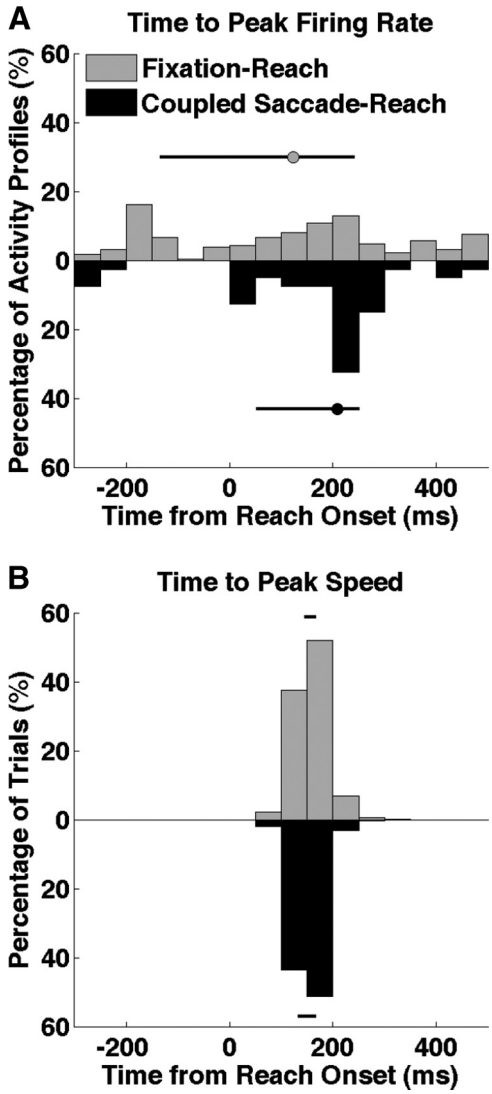

FIG. 7. Movement kinematics and neural activity. *A*: relative frequency histogram of times to peak firing rate for the population of recorded rostral superior colliculus (rSC) neurons. Data were aligned on reach onset, and grouped into FR and CSR tasks. The *y* axis represents percentage of activity profiles, i.e., SDFs of individual neurons in different conditions. The *x* axis represents time from reach onset. The bin size used to compute the histogram was 50 ms. ●, ⊜, median times to peak firing rate; ■ interquartile ranges. *B*: relative frequency histogram of times to peak speed, computed trial by trial. The *y* axis represents percentage of trials. Otherwise same conventions as in *A*.

the data into two distributions of values, one for the FR task and another for the CSR task. Two main conclusions could be drawn from the resulting histograms (Fig. 7*A*). First, both distributions of times to peak firing rate were spread along the time range. There were neurons firing maximally before and some others after the reach onset. Therefore the variability of the data, represented by the interquartile range (IQR), was high in both tasks. Second, the times to peak firing rate were delayed in the CSR task, due to the generation of a pause during the saccade—in fact no neuron discharges maximally during the range of −200 to −100 ms from reach onset, which coincides with the time of saccade execution in this task.

The variability of the movement patterns was also measured by computing the time to peak amplitude of several kinematics parameters (trial by trial). As an example we show the distribution of times to peak speed in Fig. 7*B*. Here we obtain very different histograms to the ones obtained for the times to peak firing rate. First, the variability of the data were in general much lower. For example, in the FR task the IQR of times to peak speed (22 ms) was much lower than the IQR of times to peak firing rate (376 ms). Second, both the FR and CSR tasks had a very similar distribution of times to peak speed. This is due to the fact that the movement patterns were always very regular, independently of the task or condition actually performed (see hand speed traces at Figs. 2 and 3).

The general results related to movement kinematic parameters and activity patterns are summarized at Table 1. As can be observed, the remaining two movement parameters studied (acceleration and deceleration) had as well a very low variability in all tasks, indicating that the movement patterns were generally very stereotyped. Further, the variability was much higher in times to peak firing rate for all tasks. In the FR task, there was no qualitative difference between the conditions in which the monkey reached toward foveated targets, and the conditions in which a reach toward a peripheral target was performed.

Due to the difference in variability measured in times to peak firing rate and times to peak movement parameters, the correlation between these two variables was always found to be low— irrespective of the task or movement parameter tested. The total range of correlation coefficients obtained was −0.23 to 0.12. Therefore and in summary, the activity of rSC neurons was unlikely related to anyone of the tested movement kinematic parameters in a standardized manner.

Target location

As previously shown in Figs. 4 and 5, rSC neurons showed higher increases in activity when the reach movements were preceded by corresponding saccadic movements in a more reflexive and natural task. We initially hypothesized that the difference found between the FR and the CSR tasks could be related to the distance between the fixation point and the target to be reached. Thus in the CSR task, the monkeys always performed reaches toward foveated targets; on the other hand, a mixture of reaches toward foveated targets and reaches toward peripheral targets was performed in the FR task. This initial parsimonious explanation was however rejected (see *Control for influences of visual stimulation responses*). As previously reported, in the FR task the slight increase of activity observed in reaches toward foveated targets (as compared with reaches toward peripheral targets) was not significant (paired Wilcoxon test, $P = 0.95$).

Despite this initial negative result, we further investigated whether the reach target location could have any clear influence on the activity of rSC neurons during the reach epoch. To perform this test, we recorded the activity of 17 neurons in the FR task during conditions containing different fixation points and target locations. At the level of individual neurons, two major subgroups were found. Many neurons were found to show a nonspecific increase of activity during reaching. Some other neurons were found to show mainly a gaze direction effect on their activity. For a clarification of these results, as well as a complete description of the fixation and reach target configurations used, we refer the reader to the *Test of target location* in the supporting material. Due to the characteristics of the neurons described, and taking into account that they are

TABLE 1. *Summary of behavioral and neuronal data in the fixation-reach (FR) and the coupled saccade-reach (CSR) tasks*

	FR Task			
	Foveated	Peripheral	Both	CSR Task
Reach reaction time, ms	283 (54)	277 (42)	278 (43)	274 (35)
Time to peak acceleration, ms	22 (11)	22 (11)	22 (11)	22 (0)
Peak acceleration amplitude, m/s^2	9.17 ± 2.39	10.09 ± 2.84	9.99 ± 2.81	9.58 ± 2.28
Time to peak speed, ms	167 (33)	156 (33)	156 (22)	156 (33)
Peak speed amplitude, m/s	0.98 ± 0.12	0.91 ± 0.19	0.92 ± 0.18	0.87 ± 0.14
Time to peak deceleration, ms	256 (44)	244 (33)	244 (33)	256 (33)
Peak deceleration amplitude, m/s^2	−6.98 ± 1.52	−6.82 ± 1.97	−6.84 ± 1.93	−6.23 ± 1.15
Time to peak firing rate, ms	135 (321)	124 (382)	124 (376)	208 (198)

Times were measured by aligning the data at reach onset and computed in a range from −300 to 500 ms. Therefore all time values are relative to reach onset. For the FR task, values are divided into conditions in which the animal reached toward foveated targets, and conditions in which a reach toward a peripheral target was performed. For simplicity, the mean ± SD were used to present kinematic amplitudes, and the median and interquartile range (IQR) were used to present time related data (reaction times and times to peak).

representative of the population, it is unlikely that the population encoded the reach target location in any of the behavioral epochs. However, it is likely that rSC neurons encoded gaze direction.

Additionally we investigated whether the influence of gaze direction on neural activity varied dynamically during the progression of the task. During the fix epoch, the majority of these neurons (71%) showed higher activity while gazing at target locations contralateral to the recorded SC as compared with target locations at the ipsilateral side. However, only 35% of them did so during the reach epoch. Figure 8 shows the mean activity of rSC neurons during the different epochs while gazing at contralateral or ipsilateral directions. The difference in mean firing rate was statistically significant during the fix and cue epochs at the population level ($P < 0.01$). However, the statistical significance was lost during the following reach and hold epochs.

Taken together, these results suggest that the differences observed in rSC activity were unlikely due to the reach target location. The only clear factor found on the activity was the gaze direction during the fix, cue, and go epochs, a property already reported by means of standard fixation tasks (Campos et al. 2006; Reyes-Puerta et al. 2009). The influence of this factor was, however, absent during the reach and hold epochs. In conclusion and as previously postulated, the main influential factor found on the rSC activity was whether fixation was produced in isolation or in combination with reaching movements.

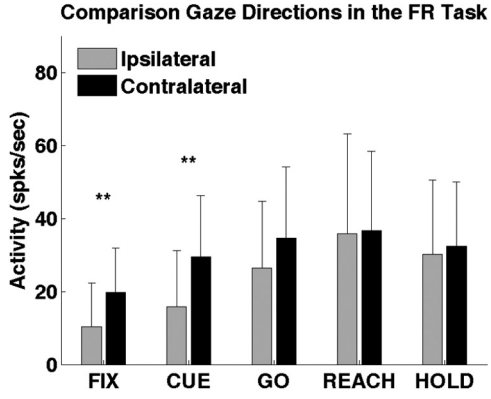

FIG. 8. Comparison of population activity in the FR task while fixating at ipsi- or contralateral fixation points. Each 1 of the bars represents mean ± SD activity for each behavioral epoch while fixating at ipsilateral (□) or contralateral (■) visual locations. The mean activity is computed using the mean activity of individual neurons. $^{**}P < 0.01$.

Small saccades and microsaccades

Microsaccades are the very small involuntary, fast eye movements that occur during fixation (for a review, see Martinez-Conde et al. 2004). Although their role remains unresolved, it seems probable that they are important for the maintenance of vision. Moreover, it is clear that microsaccades lead to neural activity in the visual pathway. Recent studies contributed to unveil the neural mechanisms responsible for their generation, by showing that the activity of rSC neurons is involved in the generation of small saccades and microsaccades (Hafed and Krauzlis 2008; Hafed et al. 2008, 2009).

One important concern is the relation of our data to the generation of small saccades and microsaccades during reaches. To test whether our recorded rSC neurons were involved in this process, we first detected the small saccades and microsaccades present in our data during fixation and reaching. Due to the variety of mean amplitudes and ranges used for their definition in previous studies (Martinez-Conde et al. 2004), and because of the continuum observed in the main sequence of small saccades, we sampled all small saccades in the range of 6′ of arc to 3°. Moreover, only small saccades with a minimum of 20°/s peak amplitude were included. In total, the quality of the gaze direction signals was good enough during the recording of 24 of our 27 recorded neurons, which formed the data basis for this analysis. The gaze direction signals associated to the three remaining neurons showed minor artifacts that impeded the detection and processing of small saccades and microsaccades (in the range of 6′ of arc to 1°).

Data were subsequently aligned on small saccade onset and sorted for contralateral and ipsilataral movements. A considerable proportion of neurons (8 of 24, 33.3%) showed significantly increased activity related to small saccades, measured by comparing the firing rate in the range of −25 to 25 ms to the range of −200 to −150 ms relative to small saccade onset ($P < 0.05$). A clear example of excitatory activity related to small saccades (*neuron CI-026802*) can be seen at Fig. 9*A*. The activity increased preferentially before contralateral small saccades, showing a burst of activity which peaks at small saccade onset. Moreover, the firing rate was high prior to contralateral small saccades but low before ipsilateral ones and also low 100 ms after the small saccades. As reported in Hafed et al. (2009),

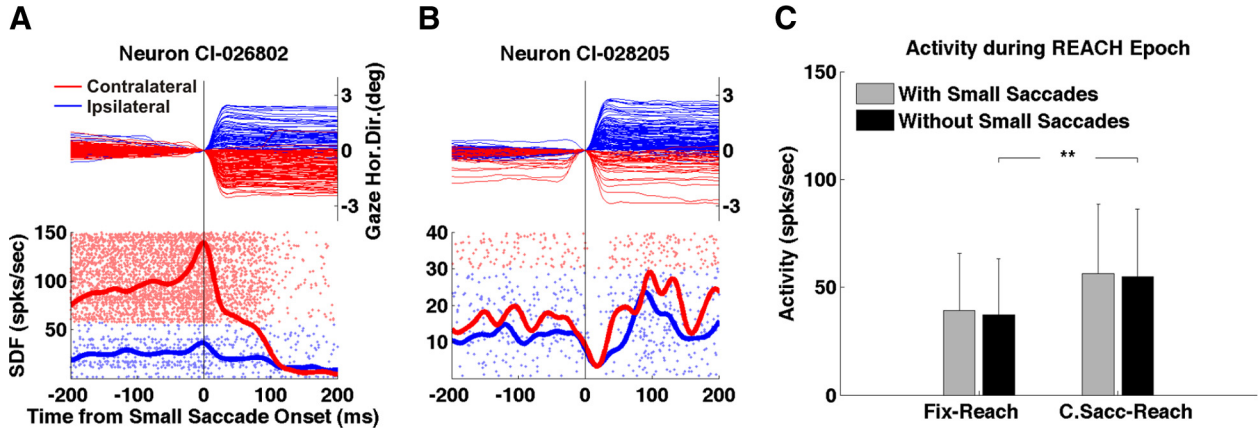

FIG. 9. Activity related to small saccades and microsaccades. *A*: activity of *neuron CI-026802* aligned on small saccade onset. *Top*: horizontal gaze direction traces, in which positive values correspond to ipsilateral (rightward) movements. Small saccades are subdivided into ipsi- (blue) and contralateral (red) small saccades. *Bottom*: a raster plot for each trial and SDFs for each subgroup. *B*: activity of *neuron CI-028205* aligned on small saccade onset. Same conventions as in *A*. *C*: direct comparison of reaching related activity for the 16 neurons recorded in both tasks. Here we compare the data including all trials (□) to the data including only trials without any small saccade or microsaccade (■). Solid bars represent mean reaching related activity. Error bars represent SD. $^{**}P < 0.01$.

this neuron's activity was remarkably similar to the stereotypical saccade-related activity observed in caudal buildup neurons (Munoz and Wurtz 1995) during large saccades except that it happened for the smallest detectable eye movements. Nevertheless this neuron presented clear pauses related to larger saccades (not shown).

Besides this subpopulation of neurons showing increase of activity related to small saccades, we also found a proportion of neurons (4 of 24, 16.7%) showing the opposite effect, i.e., a pause of activity during small saccades. An example can be observed at Fig. 9*B*. Typically these neurons showed low tonic activity during fixation, pausing during small as well as medium and large saccades. The rest of the neurons (12 of 24, 50%) did not show statistically significant effects related to small saccades.

We performed a control analysis to test whether the activity of rSC neurons was mainly influenced by the generation of arm movements or by the generation of small saccades. For this purpose, we used again the 16 neurons recorded in both the FR and CSR tasks because their activity in both tasks could be directly compared. We recomputed for each neuron the reaching related activity; however, in this case, we removed all the trials containing any detected small saccade or microsaccade in the fix or reach epochs, ruling out their possible influence on the neuronal activity. The results are shown in Fig. 9*C*. For comparison, we plot the data including all the trials together with the "desaccaded" data, i.e., data including only trials without any small saccades or microsaccades. As can be observed, only a modest effect of small saccades on the activity (not statistically significant, $P > 0.05$) was observed in both tasks. Further, the increase of activity was again significantly higher ($P < 0.01$) in the CSR task, confirming the results obtained in the previous sections.

DISCUSSION

In the present study, we searched for a neural substrate accounting for a specific property of the oculo-manual system in primates. When primates reach for an object in their vicinity, gaze usually arrives at the target before the hand and stays there until the hand has reached its goal. This behavior—termed gaze anchoring—is important for guiding the final path of the hand by visual feedback (Neggers and Bekkering 2000). We focused our investigation on the rSC, an area that has been classically related to fixation. We hypothesized that the activity in this area could contribute to the prolongation of fixation until the end of the reaching movement.

We present three main findings in our study. First, rSC neural activity was found to be higher during reaching movements than during prolonged fixation. This increase was found to be even higher in a more reflexive and natural task in which the reaching movement was preceded by a saccade foveating the target to be reached. Second, the increase in rSC neural activity during reaching was found to be mainly nonspecific; thus it was not found to be closely related to any of the factors tested, including movement kinematic parameters of the reach and target location. Third, the increase of activity in rSC neurons was found to be independent of small saccade and microsaccade generation, leaving the emergence of reaching movements as the main modulating factor.

Increase of activity during reaching

The increase in rSC neural activity during reaching was manifest both in individual neurons and at the level of the population. As can be observed in Fig. 4*A*, the neural activity was generally higher during the reach epoch as compared with the fix epoch in the FR task. Importantly, this increase was present in most of the neurons (Fig. 4*C*). In the CSR task, the increase in neural activity was even higher than in the FR task (Figs. 4, *B* and *D*, and 5). This could be due to a more task specific coupling of gaze and hand movements in these conditions—and therefore a more important role of rSC neurons in the CSR task.

Moreover, the increase of activity was found to last generally until the reaching movement was finished. This characteristic of the activity can be observed in Figs. 2 and 3 by comparing the SDFs (*top panels*) to the hand speed (*bottom panels*). As can be seen, the activity is high as long as the hand is moving. At the population level, however, there was no common specific time point related to the reaching movement in which the activity peaks (see histogram of times to peak

firing rate at Fig. 7A). On the contrary, the hand movement patterns were very stable, presenting a much lower variability (see histogram of times to peak speed at Fig. 7*B*). This result showed that the relation between rSC neurons' activity and reach movements was not as stereotypical as the one observed between SC neurons' activity and saccadic movements (Munoz and Wurtz 1993a, 1995; Sparks 1978). However and due to the lack of variability in the hand movement patterns, our data did not present definitive evidence that the activity is not related to movement kinematics at all. Even with big differences in activity levels among different cells, it could be the case that the activity of some or all of the cells would be reduced if the movement velocity were reduced (for example). Related studies have proven that the activity of neurons in motor and premotor cortex is related not only to direction of movement, but also to its time-varying speed (Moran and Schwartz 1999).

Further, we did not find any clear effect of target location on the activity of rSC neurons. However, neural activity was clearly related to the gaze direction (shown previously in Campos et al. 2006; Reyes-Puerta et al. 2009). This gaze direction effect found during prolonged fixation was significantly reduced during the reach related epochs. Thus the increase of activity in rSC neurons during reaching was found to be rather nonspecific.

Several data suggested that the effect observed in rSC activity was unlikely due to head position or movements. First, we found a considerable trial-to-trial variability in the head position that was not reflected in the neural activity. Second, only small head movements were found during the reach, which were almost always slower than 25°/s; however, such slow head movements are not often seen during natural head-free gaze shifts. During small head-free gaze shifts ($<20°$), head movements are very often nonexistent, and during larger gaze shifts, head movements show normally peak velocities $>100°$/s (Phillips et al. 1995). Thus the observed small head movements were most likely produced by adjusting body posture during the reaching, and therefore the increase in rSC activity was not related to head movements produced during natural head-free gaze shifts. Third, larger and faster head movements were seen during the HOLD phase; however, rSC activity was generally higher during reaching than during holding. Fourth, the neurons recorded in a head-fixed setup showed similar effects to those observed in head-free conditions. Nevertheless there could be a partial effect of head position or movements on the rSC activity during the hold phase. This effect, which should be a matter of future research, would be concordant with the observed neck EMG responses following stimulation at the rSC of the monkey (Corneil et al. 2002), and the reported relation between SC neural activity and head-only movements (Walton et al. 2007).

In sum, the results show that neurons show heightened activity during all reaches, even when gaze is not at the goal of the reach. However, a circuit dedicated to anchoring the eyes at the goal of a reaching movement would not, one would think, be activated when the eyes are not in fact at the goal of the movement. Thus the reported effect could be part of a more general neural mechanism supporting eye-hand coordination tasks in primates, a hypothesis which should be tested in future experiments.

Influence of visual stimulation on responses

One general concern was the possibility that some of the observed activity changes could be due to visual influences. For example, when a reach is made toward a foveated target, the hand enters the cell's receptive field at some point, which could possibly account for some of the changes in cell activity during reach.

We found a number of reasons that make unlikely the existence of such visual influences on our data. First, the experiments were made in complete darkness, and the used visual stimuli (red, yellow and blue LEDs projected on a translucent screen, 1 cm diam, 1.5 cd/m^2) were too dim to illuminate the monkey's hand. Second, we rejected those neurons showing purely visual responses by the use of a blink paradigm (see neural validation process in METHODS); therefore the neurons used in our analysis showed activity during fixation also when the fixation spot was extinguished. Third, it has been shown in previous studies that the activity of rSC neurons is task-dependent, even when the visual stimuli used in the different tasks are identical—and therefore not presenting trivial visual effects (Everling et al. 1999; Reyes-Puerta et al. 2009). Fourth, previous publications have shown clearly that the gaze anchoring effect is driven by a proprioceptive, nonvisual signal (Lünenburger and Hoffmann 2003; Neggers and Bekkering 2001).

These arguments suggest that the activity changes observed in our data were not due to visual influences. Further, this conclusion was also supported by the results obtained in two more control analyses. In brief, we showed that the transient visual responses produced by the onset of the reach stimulus did not overlap in time with the higher activity recorded in the CSR task (see Fig. 6 and related text); and the prolonged presence of the reach stimulus in the FR task performed toward foveated targets did not cause a higher activity than when performed toward peripheral targets (see *Control for influences of visual stimulation responses*). Thus despite the fact that we found some residual visual effects on the activity of the rSC neurons, they did not account for the difference in activity observed in the various tasks.

In line with these results, we propose that the increase of activity on rSC neurons during reaching represents the proprioceptive, nonvisual signal producing the gaze-anchoring effect (Neggers and Bekkering 2001). The increase of activity at the rSC could be driven by corollary discharges sent from reach-related premotor or parietal cortical areas or from the reach related neurons in the SC itself (Werner 1993). In this respect, the projections from the arm representations of the premotor cortex to the intermediate and deep layers of the SC might be of great importance (Fries 1984, 1985).

Nevertheless there could be some effect of the visual input on the neural activity in tasks where the hand is visible (also called closed loop conditions) as compared with tasks where it is not visible (open loop conditions, similar to our tasks). Related results can be found in Lünenburger and Hoffmann (2003) showing that vision of the hand reduces saccadic and hand reaction times in tasks involving coordinated gaze-reach movements. In principle, this effect found in behavioral data could be accounted for by differences in SC neural activity, a hypothesis that should be tested in future experiments.

Relation to current models of the rSC

Two prominent models of the rSC activity are the gaze position error (GPE) (Choi and Guitton 2006; Guitton et al. 2004) and the target location hypothesis (Hafed and Krauzlis 2008; Krauzlis et al. 2000). The first hypothesis argues that rSC neurons convey a signal representing the GPE, so that their activity is inversely proportional to the distance to the target—therefore coding for fixation and inhibiting saccades. The second one argues that the whole SC forms a continuous map of target locations, so that rSC neurons represent foveal and parafoveal targets. In general, these two models try to resolve the question of how the same neurons in the rSC participate in the control of two seemingly opposite functions: fixation and microsaccade generation. While the GPE hypothesis argues in favor of a main involvement of the rSC in visual fixation, the target location hypothesis emphasizes its critical role in microsaccade generation.

However, our data suggested that these two hypotheses are actually not mutually exclusive—although at the single neuron level they are contradictory. In concordance with this view, we observed different responses in relation to small saccades and microsaccades even in those neurons that were validated and further analyzed (i.e., those neurons that showed homogenous responses in relation to larger saccades). This suggests that there could be at least two or more different functional types of neurons intermingled in the rSC.

Thus a considerable proportion of the validated neurons (66.7%) showed a pause or no change in their activity during both ipsi- and contralateral small saccades. Further, when we removed the trials containing small saccades and microsaccades, we observed an equal increase of activity during reaching as compared with fixation. Therefore at least a proportion of neurons in the rSC seem to be part of an independent fixation system, which is not related to microsaccade generation. Taking into account the GPE hypothesis, we could argue that the increase of activity in these neurons would increase the activity of OPNs, inhibiting the saccade burst generator (Gandhi and Keller 1999). In addition, the gaze would be stabilized by inhibiting the caudal part of the SC—and thus inhibiting the generation of saccades (Munoz and Istvan 1998).

Further, a substantial proportion of the validated neurons (33.3%) showed an increase of activity related to small saccades and microsaccades (especially toward the contralateral side), albeit showing a pause during larger saccades. These neurons could be part of a subpopulation of rSC neurons responsible for microsaccade generation. However, they showed an increase of activity during reaching just as well (see general effects in Figs. 4, *C* and *D*). Although this property seems to be contradictory, it would also ensure the gaze anchoring effect. If we consider the SC as a continuous representation of goal locations, we could argue that when the activity is mainly located at the rSC only small saccades and smooth pursuit would be performed (Hafed and Krauzlis 2008). In this case, the focusing and increasing of activity at the rostral pole would ensure that the gaze direction remains stable in a reduced portion of the visual space—close to locations which are surrounding the fovea or are already foveated. Thus the elevated activity during reaches could ensure short latency corrective gaze-movements to maintain objects near and in the fovea while performing a reaching movement toward them—and thus producing the gaze anchoring effect.

Conclusions

Taken together, our results showed for the first time the increase of activity at the rSC during reaching movements, providing a possible neural substrate for the gaze anchoring effect. Due to the variability of neurons in the SC (gaze-, head-, and reach-movement related cells), and taking into account our present results, we propose this structure to be part of the distributed neural system for eye-hand coordination in primates.

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DISCLOSURES

No conflicts of interest are declared by the authors.

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SUPPORTING MATERIAL FOR

The Role of the Rostral Superior Colliculus in Gaze Anchoring during Reach Movements

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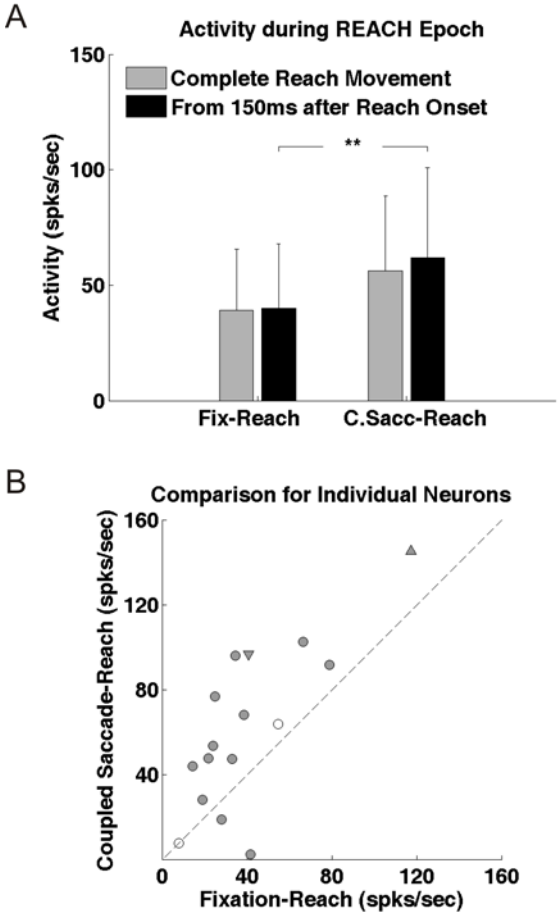
Contents

CLASSIFICATION OF DISCARDED NEURONS

Neuronal Type	Total Number	Percent
Burst during contraversive saccades	8	28.6%
Low general fixation activity (<5 spks/s)	7	25.0%
No pause and no burst during saccades	6	21.4%
Late pause (starting before saccade offset)	5	17.9%
Purely Visual Activity	2	7.1%

Supplemental Table 1: Classification of discarded neurons. Different neuronal types were established in order to present their characteristics. The largest group of discarded neurons (28.6%) showed directional sensitivity in their activity during saccades; generally they showed a pause of activity during ipsiversive saccades and burst activity during (medium and large) contraversive saccades. Seven neurons (25.0%) did not show enough activity during fixation (less than 5 spks/s). Further, six neurons (21.4%) showed neither a pause nor a burst of activity for contraversive saccades; therefore they maintained a tonic activity in those conditions, lacking the pause associated to saccades. Five neurons (17.9%) showed tonic activity during fixation and a late pause during saccades (at least in one or several conditions); in this case the pause started after the saccade onset but before the saccade offset — contrary to the Following Omnipause Neurons (described by Mustari et al., 1997) in which the pause starts after the saccade offset. Finally, two neurons (7.1%) showed low or no activity while the foveated target was briefly extinguished, and high transient visual responses related to target jumps and target foveation; therefore they were considered as purely visual neurons.

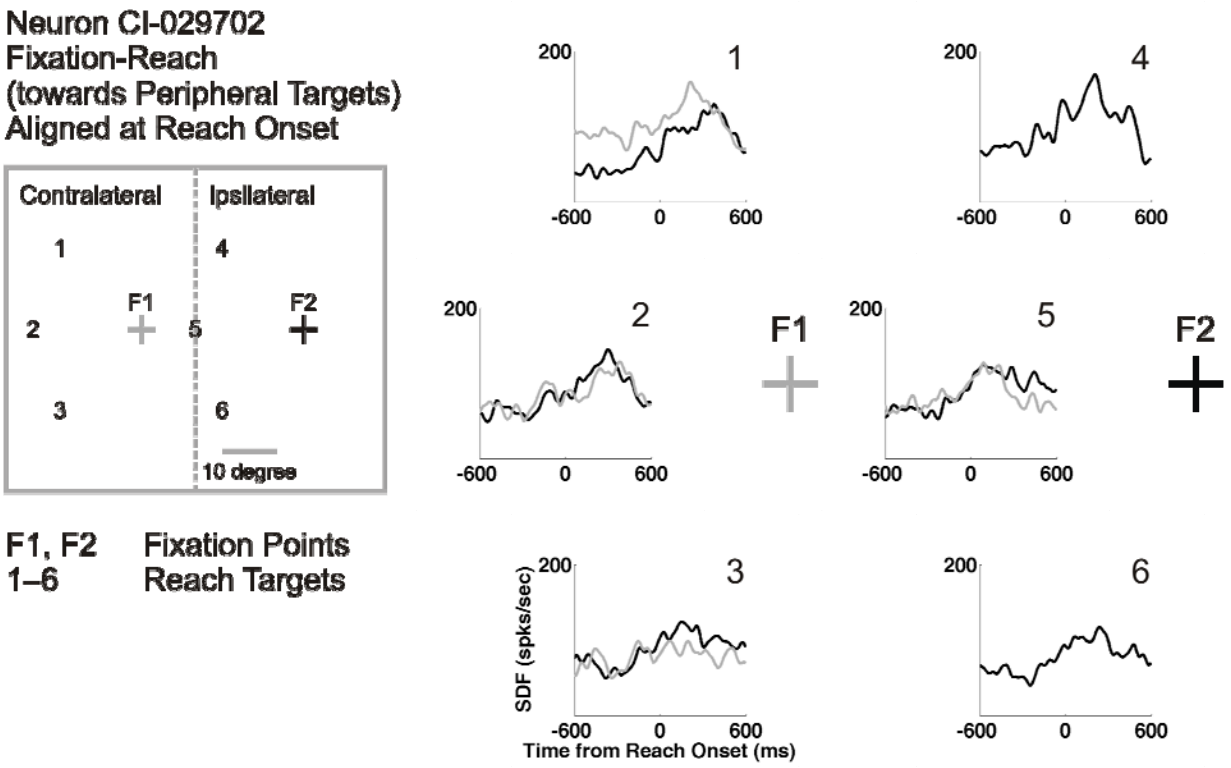
TEST OF VISUAL RESPONSES



Supplemental Figure 1: Direct comparison of activity in Fixation-Reach (FR) vs. Coupled Saccade-Reach (CSR) tasks (control). *A,* Mean reaching related activity for the sixteen neurons recorded in both tasks. Here we compare the data including the complete reaching movements (grey) together with the data including only a restricted part of the reaching movements time period (black). Solid bars represent mean reaching related activity, obtained using the mean activity of individual neurons. Error bars represent SD. **p<0.01. *B,* Comparison of activity during reaching in FR vs. CSR tasks for the sixteen neurons recorded in both tasks (data including only a restricted part of the reaching movements time period). Empty symbols represent neurons showing no significantly different activity during both epochs, while filled symbols represent neurons showing significantly different activity (p<0.05). Upwards triangle symbol represents neuron CI-029702 (Fig. 2). Downwards triangle symbol represents neuron CI-028902 (Fig. 3). Dashed line represents unity slope.

TEST OF TARGET LOCATION

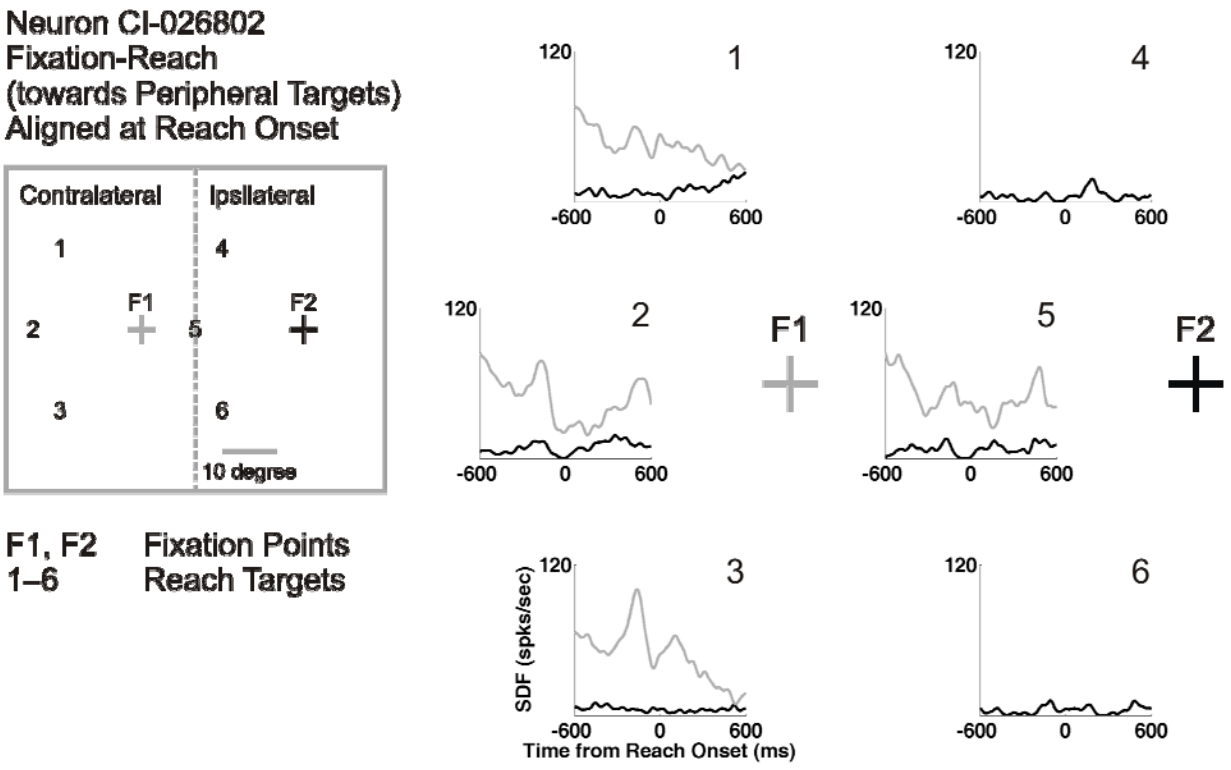
Generally rSC neurons did not show a clearly observable effect of target location on their activity. As an example we show the activity of neuron CI-029702 (previously characterized in the main text, see Fig. 2) during reaches to six different target locations using two different fixation points (Supp. Fig. 2). The scheme at the left side shows the relative locations of the targets with respect to the fixation points.



Supplemental Figure 2: Neuron CI-029702 in Fixation-Reach using different fixation points and target locations. Left side shows the scheme used for fixation points and target locations. Monkeys reached to six target locations (1 to 6) while fixating at two different fixation points (F1 and F2). F1 was located in the contralateral visual hemifield and F2 in the ipsilateral. No reaching movements were performed to targets 4 and 6 when monkeys gazed at F1. Panels 1–6 contain Spike Density Functions (SDFs) of this neuron when monkey reached to the corresponding targets (computed as described in Materials and Methods). The activity is aligned on reaching movement onset. Grey SDFs correspond to the activity of the neuron when monkeys gazed at F1, and black lines when gazing at F2.

The activity (aligned on reach movement onset) was qualitatively similar for the different target locations and the two different fixation points. Nevertheless, a one-way ANOVA performed using the firing rate during reaching as factor revealed a statistically significant difference for the ten different conditions ($p<0.001$). Thus, the condition presenting the highest reach related activity was reaching to target location 4 while gazing at F2 (134.4 spks/s); unfortunately location 4 was not measured while gazing at F1. The condition presenting the lowest activity was reaching to target location 3 while gazing at F1 (88.3 spks/s).

Some other neurons showed an important gaze direction effect in their activity during reaches, as for example neuron CI-026802 (Supp. Fig. 3). This neuron showed also a significant difference for the ten different conditions when applying an ANOVA using as factor the firing rate during reaching ($p<0.001$). The condition presenting the highest activity during reaching in this case was reaching to target location 3 while gazing at F1 (48.0 spks/s). The condition presenting the lowest activity was reaching to the same target location, but while gazing at F2 (3.4 spks/s).



Supplemental Figure 3: Neuron CI-026802 during Fixation-Reach using different fixation points and target locations. Same conventions are used as in Supplemental Figure 2.

This neuron showed always a higher activity in conditions in which the fixation point was in the hemifield contralateral to the recorded SC (mean 40.7 spks/s in conditions fixating F1) compared to the conditions in which the fixation point was ipsilateral to the recorded SC (mean 6.7 spks/s in conditions fixating F2). This result shows that the tuning properties of this neuron were affected more by changes in gaze direction than by changes in target location. This particular characteristic was a general trend in our population. As previously shown (Reyes-Puerta et al., 2009) and in agreement with previous results obtained at the caudal SC (Campos et al., 2006), many of the rSC neurons showed an important gaze direction effect on their activity. Generally the activity of these neurons was higher while gazing at target locations contralateral to the recorded SC as compared to target locations at the ipsilateral side.

Further, another general tendency could be observed in the activity of gaze direction related neurons. As can be observed in Supp. Fig. 3, the difference in activity between the contralaterally and the ipsilaterally fixating conditions reduced after the reach onset, therefore becoming the compared SDFs more similar. For neuron CI-026802, the ratio of mean contralateral to ipsilateral activity was 25.3 (36.8 to 1.5 spks/s) during the FIX epoch, 16.5 (57.3 to 3.5 spks/s) during the CUE epoch, 11.9 (56.3 to 4.7 spks/s) during the GO epoch, 6.1 (40.7 to 6.7 spks/s) during the REACH epoch, and finally 3.5 (30.3 to 8.6 spks/s) during the HOLD epoch. Moreover, this general tendency holds true when analyzing the whole population of recorded rSC neurons (see Fig. 8 in the main article).

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