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Neural correlates of target selection for reaching movements in superior colliculus

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Song JH, McPeek RM. Neural correlates of target selection for reaching movements in superior colliculus. *J Neurophysiol* 113: 1414–1422, 2015. First published December 10, 2014; doi:10.1152/jn.00417.2014.—We recently demonstrated that inactivation of the primate superior colliculus (SC) causes a deficit in target selection for arm-reaching movements when the reach target is located in the inactivated field (Song JH, Rafal RD, McPeek RM. *Proc Natl Acad Sci USA* 108: E1433–E1440, 2011). This is consistent with the notion that the SC is part of a general-purpose target selection network beyond eye movements. To understand better the role of SC activity in reach target selection, we examined how individual SC neurons in the intermediate layers discriminate a reach target from distractors. Monkeys reached to touch a color oddball target among distractors while maintaining fixation. We found that many SC neurons robustly discriminate the goal of the reaching movement before the onset of the reach even though no saccade is made. To identify these cells in the context of conventional SC cell classification schemes, we also recorded visual, delay-period, and saccade-related responses in a delayed saccade task. On average, SC cells that discriminated the reach target from distractors showed significantly higher visual and delay-period activity than nondiscriminating cells, but there was no significant difference in saccade-related activity. Whereas a majority of SC neurons that discriminated the reach target showed significant delay-period activity, all nondiscriminating cells lacked such activity. We also found that some cells without delay-period activity did discriminate the reach target from distractors. We conclude that the majority of intermediate-layer SC cells discriminate a reach target from distractors, consistent with the idea that the SC contains a priority map used for effector-independent target selection.

reaching; superior colliculus; target selection

THE NEURAL MECHANISMS OF TARGET selection for visually guided actions such as saccades and arm-reaching movements are typically studied separately and are usually grounded in the distinct neural substrates subserving the response effector. For example, activity related to eye-movement target selection has been identified in oculomotor structures that control the planning and execution of eye movements, including the superior colliculus (SC), frontal eye field, lateral intraparietal area, and supplementary eye field (e.g., Basso and Wurtz 1998; Burman and Segraves 1994; Glimcher and Sparks 1992; Goldberg et al. 2006; Krauzlis and Dill 2002; McPeek and Keller 2002; Schall and Hanes 1993; Shen et al. 2011; So and Stuphorn 2010; Thomas and Pare 2007; White and Munoz 2011). Likewise, for reaching movements, target selection activity has been identified in skeletomotor structures involved in the planning and execution of reaches such as the dorsal premotor area (PMd), the parietal reach region (PRR), and motor cortex (Cisek and Kalaska 2005; Pesaran et al. 2008; Scherberger and Andersen 2007; Song and McPeek 2010; Thura and Cisek 2014). However, we recently found that the SC, which lies near the output of the saccadic eye movement system, plays a causal role in target selection during a reaching task. Specifically, we demonstrated that temporary focal inactivation of the SC causes monkeys to be biased against selecting a reach target located in the inactivated part of the visual field and that this effect cannot be explained as a simple visual or motor impairment (Song et al. 2011). This result promotes the idea that the SC is part of a general-purpose, rather than effector-specific, target selection system (Nummela and Krauzlis 2010; Song et al. 2011).

The involvement of the deeper layers of the SC and the underlying reticular formation in producing reaching movements has been well-documented: the activity of some deep-layer SC neurons is well-correlated with the activity of muscles involved in reaching (Stuphorn et al. 1999; Werner et al. 1997), electrical microstimulation in this region can elicit forelimb movements in monkeys (Philipp and Hoffmann 2014) and perturb ongoing forelimb movements in cats (Courjon et al. 2004), and fMRI studies have identified reach-related activity in the human SC (Himmelbach et al. 2013; Linzenbold and Himmelbach 2012). However, aside from the inactivation study of Song et al. (2011) showing that SC inactivation can bias the selection of reach goals, we still know little about the activity of SC neurons during reach target selection.

To understand better the mechanisms of reach target selection in SC, we conducted single-unit recordings in nonhuman primates in a task in which a color oddball target was presented with distractors, and monkeys were rewarded for reaching to touch the target while maintaining fixation at a central fixation point. Since our inactivation experiments had targeted the intermediate layers of the SC (Song et al. 2011), we focused on recording the activity of intermediate-layer SC neurons in this task. To characterize further the cells according to conventional criteria, we also recorded each cell in a delayed saccade task, which allowed us to test for the presence of visual, delay-period, and saccade-related activity.

MATERIALS AND METHODS

All experimental protocols were approved by the Institutional Animal Care and Use Committee at the Smith-Kettlewell Eye Re-

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search Institute and complied with the guidelines of the Public Health Service *Policy on Humane Care and Use of Laboratory Animals*. A head-holder system and stainless steel recording chamber to access the SC bilaterally were implanted under isoflurane anesthesia and aseptic surgical conditions in two rhesus monkeys (*Macaca mulatta*). Antibiotics (cefazolin sodium) and analgesics (buprenorphine hydrochloride) were administered as needed during the recovery period under the direction of a veterinarian.

In each recording session, a tungsten microelectrode (FHC) with impedance ranging from 1 to 2 MΩ at 1 kHz was lowered into SC using a motorized microdrive (NAN Instruments). A Plexon Multichannel Acquisition Processor (MAP) system amplified and bandpass filtered the microelectrode signal and was used to identify action potentials. Spike-sorting was verified offline using the Plexon Offline Sorter analysis software. Only well-isolated single units were included in the analyses.

Behavioral Procedures

Testing was performed in a dimly illuminated room. Experimental control, data acquisition, and presentation of visual displays were carried out by a custom real-time MATLAB program on a Macintosh G4 computer using the Psychophysics Toolbox (Brainard 1997; Pelli 1997). Visual stimuli were presented on a 17-in. color CRT touch-sensitive monitor (Elo Touch Solutions) positioned 25.5 cm in front of the monkeys. The monitor had a spatial resolution of 800×600 pixels and a refresh rate of 75 Hz. Stimulus contrast was calibrated with a Minolta CS-100 spectrophotometer. Eye position was sampled at 1 kHz using an EyeLink 1000 infrared video tracker (SR Research).

In initial testing, the two monkeys did not demonstrate a consistent hand preference, so both monkeys were trained to use their right hand for the task. However, *monkey J* showed a consistent preference for contacting the touchscreen with his index finger (D2), whereas *monkey H* preferred the middle digit (D3). Consequently, as in Song et al. (2008), a small reflective hemisphere was temporarily taped ~1 cm from the tip of the right index finger (D2) for *monkey J* or the right middle digit (D3) for *monkey H* to measure reach movement trajectories. The reflective hemisphere was illuminated by infrared light and optically tracked in three dimensions at a rate of 60 Hz using a Northern Digital Polaris tracker. The monkeys' left arms were loosely restrained, and their heads were fixed during each testing session.

In all tasks, the sizes of the peripheral target and/or distractor stimuli were scaled according to the cortical magnification factor to keep their salience constant across eccentricities (Rovamo and Virsu 1979). At an eccentricity of 10°, the target and distractor stimuli subtended 2.5°. Trials were immediately aborted when monkeys failed to maintain required eye fixation within a 1–1.5° window during trials.

Reach target selection task. As in our study of reach target selection in the PMd (Song and McPeek 2010), we used a reaction-time target selection task (Fig. 1). This task has been used extensively to study saccade and reach target selection in both humans and monkeys, providing substantial information about the behavioral and neural mechanisms (Basso and Wurtz 1998; Bichot and Schall 1999, 2002; Ipata et al. 2006; Kim and Basso 2008; McPeek 2006; McPeek and Keller 2002, 2004; Schall and Hanes 1993; Thomas and Pare 2007; Thompson et al. 1996). Thus using this task to study reach target selection in the SC has the advantage of facilitating comparisons with this prior literature. Furthermore, a reaction-time target selection task encourages immediate selection with no enforced delay period between stimulus and movement onset. Thus it may provide a more natural situation in which monkeys are free to respond whenever they are ready, potentially reducing the influence of activity related to anticipation of the go signal in delay tasks. Detailed behavioral characteristics of reaching movements in this reach target selection task have been previously reported (Song and McPeek 2009; Song et al. 2008).

At the beginning of each trial, two vertically adjacent fixation points were presented in the central position. Monkeys were trained to fixate the upper fixation point (white square subtending 0.25° with a luminance of 1.5 cd/m²) with their eyes and touch the lower fixation point (2° yellow square with a luminance of 1.5 cd/m²) with the finger that had the attached reflective hemisphere. This hand/eye fixation position was held for 500–1,000 ms. At the end of this initial fixation interval, a color oddball target stimulus was presented with three distractors. One target and three distractor stimuli were presented at equal eccentricity from fixation, separated by angles of 90° (Fig. 1). The locations of the stimuli were adjusted for each recorded neuron so that on every trial either the target or a distractor was presented at the center of the response field (RF) of the neuron. The eccentricity of the stimuli ranged from 2.5 to 20° depending on the RF of the recorded cell. Our precision in mapping RF centers was 5° for directional angle. For cells coding eccentricities >10°, our precision in mapping the optimal eccentricity of each RF was 2°; for cells coding eccentricities from 5 to 10°, our precision was 1°; and for the 3 cells that we recorded coding eccentricities <5°, our precision was 0.5°.

The target was a red or green disc with a luminance of 1.2 cd/m² on a dark homogenous background of 0.2 cd/m², resulting in a Michelson contrast of ~71%. The distractors were of the same luminance as the target but were of the opposite color. The colors of the target and distractors were randomly switched between red and green on a trial-to-trial basis. As soon as the stimulus array was presented, the lower (hand) fixation point disappeared, whereas the upper (eye) fixation point remained illuminated.

Monkeys were rewarded for lifting their hand from the screen and moving it to touch the target while maintaining central eye fixation. Specifically, the first point at which the hand touched the screen was required to be within a hand-position tolerance window around the target stimuli, which was made equal to the stimulus eccentricity divided by 3. Furthermore, monkeys were required to continue to hold their hand at the target location for at least 500 ms after touchdown. The trial was aborted if eye fixation shifted outside of the 1–1.5° fixation window during the trial or if no response was made within 2 s after the search array onset.

Delayed saccade task. At the beginning of each trial, a white square subtending 0.25° with a luminance of 1.5 cd/m² appeared in the central position against a homogenous dim background of 0.2 cd/m². Monkeys were required to keep their eyes within a 1–1.5° window around the fixation point during an initial fixation interval of 450–650 ms. At the end of this interval, a single target stimulus was presented at a peripheral location aligned with the RF of the cell, whereas the fixation point remained illuminated. Monkeys were required to maintain central fixation until the disappearance of the fixation point 500 ms later. Once the fixation point disappeared, the monkeys were rewarded for making a saccade to the peripheral stimulus. Eye-position tolerance windows around the target stimuli were made equal to the stimulus eccentricity divided by 5. As in the target selection task, the target was randomly chosen in each trial to be a red or green disk with luminance of 1.2 cd/m². The delayed saccade task was used
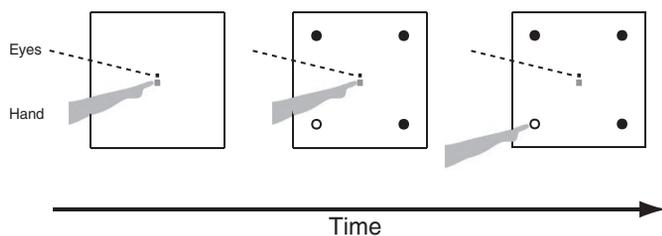
Fig. 1. Reach target selection task. After the eyes and hand were at central fixation for 500–1,000 ms, an odd-colored target was presented with 3 distractors. Monkeys reached to the color oddball while maintaining fixation at the center. Target position was randomized among 4 locations, and 1 position was always aligned with the response field of the cell.

to search for each recorded cell, and we tested any isolated SC cell from which we could evoke visual, delay-period, or saccade-related responses in this task.

Data Analysis

All analyses considered only correct trials. Offline data analysis was performed in MATLAB using custom software. Saccades were detected using velocity and acceleration criteria, and eye-movement data from each trial were visually inspected to verify correct marking of saccades. The onset of reaching movements was measured as the time at which the hand was lifted from its initial position in the center of the touchscreen. Reach endpoint was measured as the first location contacted on the touchscreen after movement onset. A trial was classified as an error and excluded from analysis when the reach endpoint was outside of the hand-position tolerance window around the target (described above).

Reach reaction times were defined as the interval between the onset of the target and the onset of the corresponding movement. We excluded trials in which the reach reaction time differed from the mean reaction time by more than 3 SD, a criterion that typically resulted in the exclusion of no more than one or two trials per cell.

To generate continuous spike-density functions, recorded neural events were convolved with a Gaussian kernel ($\sigma = 10$ ms; Richmond and Optican 1987). For statistical reliability, only neurons having at least six correct trials for each condition were included in the analyses. When assessing statistical significance, we adopted a criterion α-level of 0.05.

In the target selection task, we compared the mean activity of each neuron when the target was in the RF of the cell vs. in the diametrically opposite location. When trials were aligned on the onset of the target/distractor array, we measured activity during the early visual epoch, defined as the interval from 50 to 100 ms after stimulus onset, and the late visual epoch, defined as the interval from 150 to 250 ms after stimulus onset. When trials were aligned on the onset of the reaching movement, we measured activity during the pre-reach epoch, defined as the period from 50 to 150 ms before reach onset, and the reach initiation epoch, defined as the period from 50 ms before to 50 ms after reach onset. In the delayed saccade task, we measured the mean visual activity in each cell by subtracting the mean activity during the period 0–100 ms before target onset (baseline period) from the mean activity 50–150 ms after target onset. To quantify the mean delay activity in each cell, we subtracted the baseline activity from the mean activity during the period 300–400 ms after stimulus onset (delay period). Finally, we measured the saccade-related activity by subtracting the baseline activity from the mean activity during the period 50 ms before saccade onset to 50 ms after saccade onset.

RESULTS

We recorded 165 neurons in the reach target selection and delayed saccade tasks. One hundred forty-one of these neurons (39 from *monkey H* and 102 from *monkey J*) met the inclusion criteria described in MATERIALS AND METHODS, and all subsequent data analyses were restricted to this subset of neurons.

Reach Target Selection Task

The reach target selection task (Fig. 1) required the animals to reach and touch a color oddball target while maintaining fixation. Both the endpoints of the reaches (Fig. 2A, *left*) and their trajectories (Fig. 2A, *right*) demonstrate that the reaches to each target location were accurate. Furthermore, eye-position recordings showed that fixation

was successfully maintained during the reaching movements (Fig. 2B). Overall, *monkey H* correctly completed 70% of trials, and *monkey J* correctly completed 68%. Mean reaction times were 401 ms (SD = 67 ms) in *monkey H* and 429 ms (SD = 83 ms) in *monkey J* (Fig. 2C).

In this task, we compared SC responses when the reach target vs. a distractor was in the RF of the cell. An example cell is shown in Fig. 3. When activity is aligned with the onset of the stimulus array (Fig. 3, *left*), the initial phase of the activity of the cell does not discriminate the target from distractors: in both cases, the cell shows a brief transient increase due to the onset of a RF stimulus. However, soon after, activity rises to a higher level when the reach target is in the RF compared with when a distractor is in the RF, and this elevated activity persists throughout the reaching movement. Sustained activity discriminating the reach target can also be seen when the trials are aligned on the onset of the reaching movement (Fig. 3, *right*). This alignment also makes clear that the cell does not show an increase in activity associated with the onset of the reaching movement itself. Thus the activity difference for trials in which the target vs. a distractor was in the RF appears to be sustained visual activity related to target selection rather than movement-related activity.

Similar results are also seen at the population level (Fig. 4) when activity is aligned on stimulus onset (*left*) and reach onset (*right*). The black ribbon represents the mean population activity (± 1 SE) when the target was in the RF of the cell, whereas the gray ribbon represents the mean and SE of activity when the distractor was in the RF of the cell. We confirmed at the population level that early visual activity does not discriminate the target from the distractors [target mean 68.5 ± 5.8 spikes per second (sp/s); distractor mean 68.0 ± 5.9 sp/s; Wilcoxon signed-rank test, $P = 0.5$] but that the later visual activity (measured in the period from 150 to 250 ms after stimulus onset) clearly signals the target location (target mean 49.1 ± 4.1 sp/s; distractor mean 18.1 ± 2.2 sp/s; Wilcoxon signed-rank test, $P < 2.5 \times 10^{-23}$). This difference in activity is sustained throughout the reach initiation epoch, albeit at a slightly lower level (mean 29.9 ± 3.4 sp/s for the target vs. 12.5 ± 1.8 sp/s for the distractor; Wilcoxon signed-rank test, $P < 7 \times 10^{-22}$). However, there was no burst of activity closely related to reach onset: when the target was in the RF, activity during the reach initiation epoch (mean 27.4 ± 2.8 sp/s) was rather slightly reduced compared with the prereach period (mean 34.2 ± 3.7 sp/s; Wilcoxon signed-rank test, $P = 0.02$). As is evident from Fig. 4, elevated activity continues even beyond the reach initiation epoch. We speculate that this activity could be a sustained visual response, occurring because the monkeys are required to maintain their finger actively within the target window for 500 ms after touch-down to receive the reward (i.e., the target continues to be a goal for the hand). However, we were not able to analyze activity occurring after the reach initiation epoch because, as the end of the reaching movement approached, monkeys' hands entered the RF of the cells in trials in which the target was in the RF, potentially confounding analysis.

To illustrate the variability in target discrimination across our sample of cells, Fig. 5 compares the level of activity of each cell for the early (Fig. 5A) and late visual epochs (Fig. 5B) and the reach initiation epoch (Fig. 5C) when the target

A

Reach endpoints   Reach trajectories
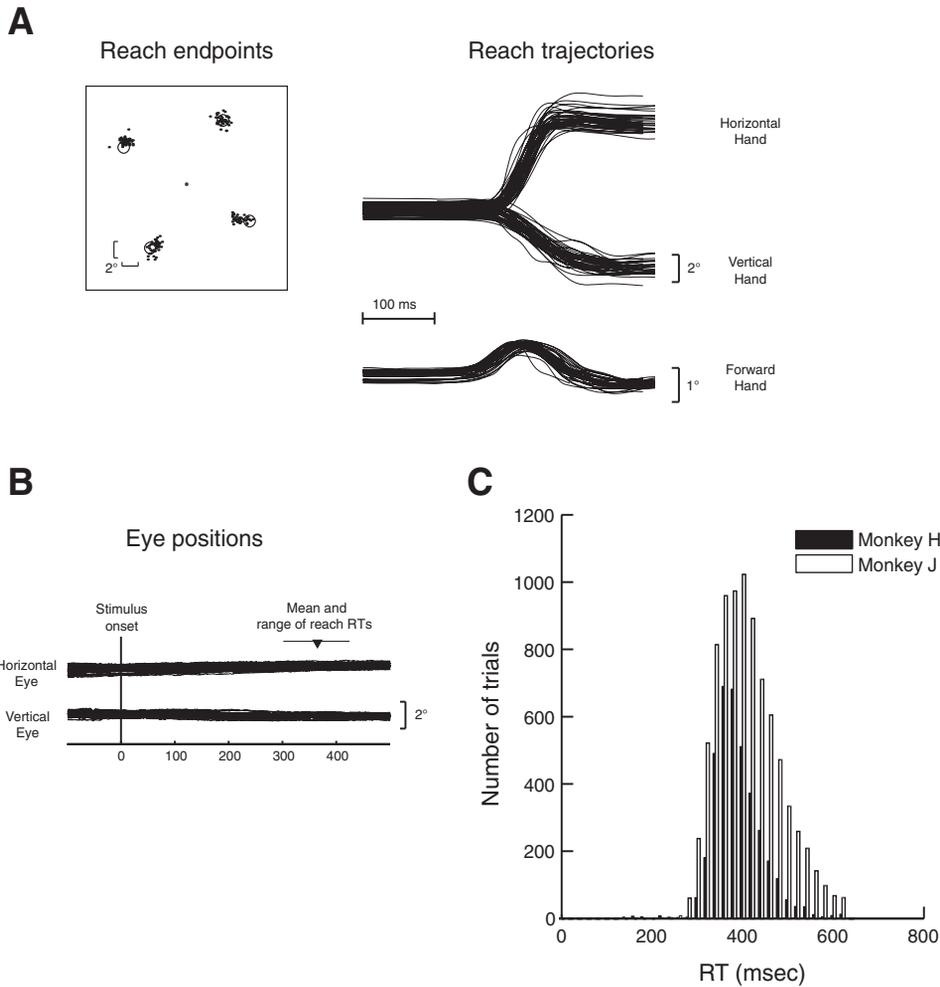
Fig. 2. *A*: reach endpoints and trajectories in a representative block of trials in the reach target selection task. On the *left*, each dot represents a reach endpoint and circles represent targets. Reaches were accurate to each target location. On the *right*, each trace represents hand position in the horizontal, vertical, or forward direction (relative to the screen) over time, aligned on reach onset. The upper and middle traces, respectively, show horizontal and vertical hand position in the plane of the touchscreen, whereas the lower trace shows the forward position of the hand relative to the surface of the touchscreen. *B*: eye positions in a representative block of the reach target selection task. Each trace represents eye position over time, starting 100 ms before stimulus onset. The upper and lower traces, respectively, show horizontal and vertical eye position. The inverted triangle above the eye traces shows the mean reach reaction time (RT), and the accompanying horizontal bar shows the range of RTs in this block. *C*: histograms of RTs for each monkey in the reach target selection task. Data are pooled across all recording sessions. RTs for *monkey H* are shown by black bars, and RTs for *monkey K* are shown by white bars.

vs. a distractor was in the RF of the cell. In Fig. 5, *A–C*, the abscissa represents activity when the target was in the RF of the cell, and the ordinate represents activity when the distractor was in the RF of the cell. When target vs. distractor activity was compared for each cell using Mann-Whitney U tests and an α-level of 0.05, we found a significant difference for only 6 out of 141 SC cells (~4%) in the early visual epoch, with 3 cells having significantly more activity for the target vs. a distractor and 3 having significantly less activity. In contrast, in the late visual epoch, we found that 110 out of 141 (78%) of SC neurons reliably signaled the target location, with 107 cells having significantly more activity for the target vs. a distractor and 3

having significantly less activity. This target discrimination activity was largely sustained during the reach initiation epoch, as 91 out of 141 (65%) of neurons showed significantly more activity for the target than distractor, and no cells showed significantly less activity in this period. Finally, in Fig. 5*D*, we compared target/distractor discrimination activity (defined as the mean activity when target was in the RF minus the mean activity when a distractor was in the RF) during the prereach and reach initiation epochs and found that across cells, 22 out of 141 neurons (16%) show a small but significant decrease and 8 out of 141 neurons (5%) show a small but significant increase in discrimination during the reach initiation epoch compared with the pre-
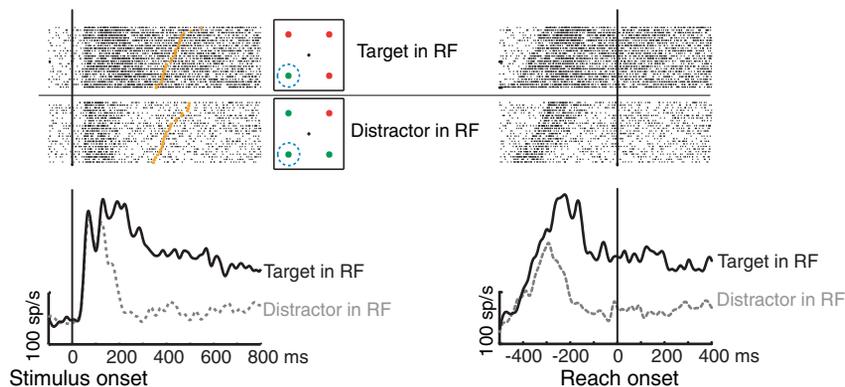
Fig. 3. Activity from 1 example superior colliculus (SC) cell in the reach target selection task. Activity is aligned with stimulus onset (*left*) and reach onset (*right*). Rasters (*top*) are sorted by reach RT. The black trace shows activity when target was in the response field (RF) of the cell, and the dashed gray trace shows activity when a distractor was in the RF. On the *left*, reach onset is indicated in the rasters for each trial by a thick orange tick mark. Activity is elevated when the reach target is in the RF of the cell. When activity is aligned on reach onset, sustained target-related activity is seen before and during the reaching movement, but no burst of activity related to reach onset is seen. sp/s, Spikes per second.
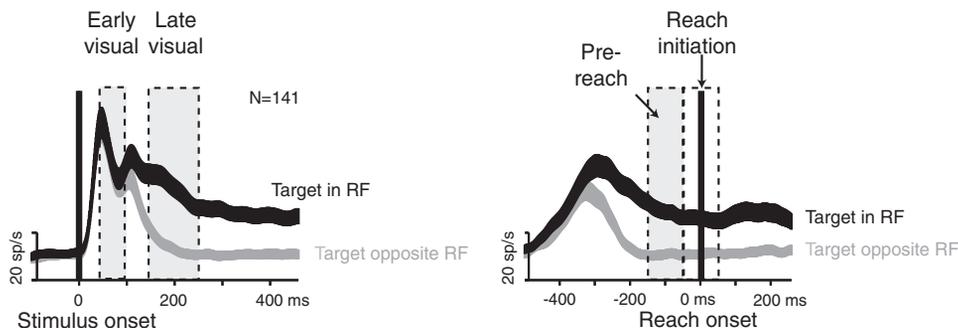
Fig. 4. Population activity of SC neurons in the reach target selection task. Population activity shows mean firing rate ± 1 SE when activity is aligned on stimulus onset (*left*) and reach onset (*right*). The black line represents mean activity when the target was in the RFs of the cells, whereas the gray line represents activity when the distractor was in the RFs of the cells. Marked regions indicate the time intervals for the 4 analysis epochs: the early visual epoch (50–100 ms after stimulus onset) and the late visual epoch (150–250 ms after stimulus onset) are indicated on the *left*, and the prereach epoch (50–150 ms before reach onset) and the reach initiation epoch (50 ms before until 50 ms after reach onset) are indicated on the *right*.

reach epoch. In all plots in Fig. 5, filled circles indicate cells with statistically significant differences in activity (Mann-Whitney *U* test, $P < 0.05$), whereas unfilled circles indicate nonsignificant cells. Together, these results support the notion that these intermediate layer SC neurons are involved in reach target selection but not reach execution.

Characteristics of Cells that Do and Do Not Discriminate the Target in a Reach Target Selection Task

In the previous section, we reported that the majority of recorded SC neurons reliably discriminate the reach target from distractors in a reach target selection task but that some
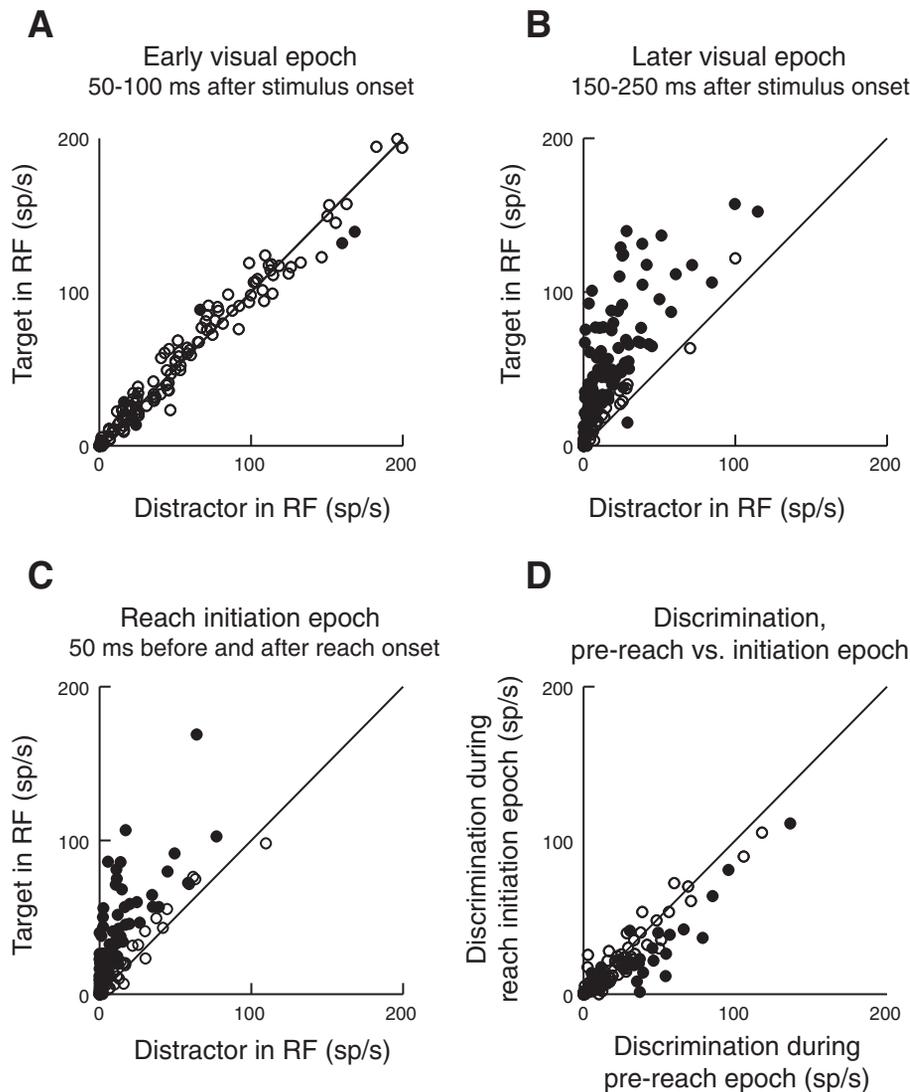
Fig. 5. Comparison of activity in the reach target selection task. In *A–C*, activity is compared in the early visual (*A*), late visual (*B*), and reach initiation (*C*) epochs when the target vs. a distractor was in the RF of each cell in the reach target selection task. Each dot represents a single cell. The abscissae indicate activity when a distractor was in the RF of each cell, and the ordinates represent activity when the target was in the RF of each cell. Overall, early transient visual activity does not discriminate the target from a distractor, but in the late visual epoch, many SC neurons discriminate the target from the distractor. This target discrimination activity is sustained during the reach epoch. In *D*, target discrimination activity in the prereach and reach initiation epochs are compared. There is no increase in discrimination activity coincident with the onset of the movement but rather a small but significant decrease. In all plots, filled circles indicate significant ($P < 0.05$) whereas unfilled circles indicate nonsignificant cells.

Delayed saccade task

Reach target selection task
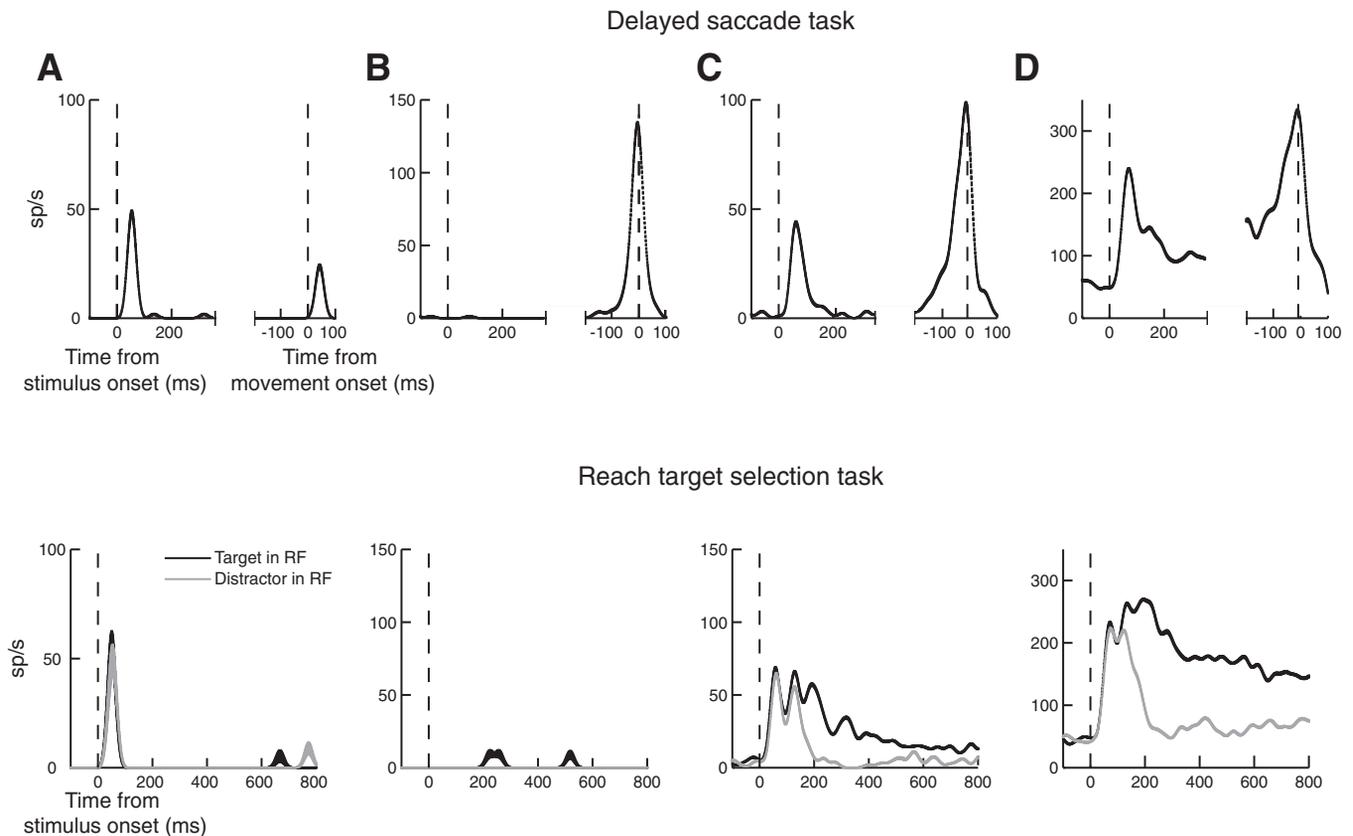
Fig. 6. Examples of SC neuronal responses in the reach target selection and delayed saccade tasks. *A–D* each show mean activity ± 1 SE for a SC neuron in the delayed saccade task (*top*) and in the reach target selection task (*bottom*). In the selection task, the black trace represents activity when the target was in the RF of the cell, whereas the gray trace represents activity when a distractor was in the RF of the cell. On the *top*, the left portion of the plot shows activity aligned on stimulus onset, and the right portion of the plot shows activity aligned on saccade onset. On the *bottom*, activity is aligned on the onset of the target and distractors.

do not. Here, we sought to understand how discriminating and nondiscriminating cells differ and how they fit with conventional SC cell classification schemes. To do this, we used a delayed saccade task that allowed us to isolate the visual, delay-period, and saccade-related responses of each cell.

Given that saccadic buildup (or prelude) neurons have been most strongly implicated in target selection (e.g., Basso and Wurtz 1997; Glimcher and Sparks 1992; Horwitz and Newsome 1999; Krauzlis and Dill 2002; McPeek and Keller 2002; Shen et al. 2011; White and Munoz 2011), we initially hypothesized that target discrimination in the reaching task might be correlated with the presence of significant delay-period activity in the delayed saccade task. Figure 6 illustrates some of the diversity of responses that we observed. Each column in Fig. 6 shows the activity of one SC neuron in the delayed saccade task (*top*) and in the reach target selection task (*bottom*). In the *bottom* panels, the black traces represent activity when the target was in the RF of the cell, whereas the gray traces

represent activity when a distractor was in the RF of the cell. Figure 6*A* shows a transient visual cell, and Fig. 6*B* shows a saccade-related motor cell, neither of which shows significant delay-period activity in the delayed saccade task. These cells (Fig. 6, *A* and *B*, *bottom*) also do not discriminate the reach target from distractors in the target selection task. Another cell, shown in Fig. 6*C*, *top*, also does not show delay-period activity, whereas the cell shown in Fig. 6*D* does, yet both of these SC cells (Fig. 6, *C* and *D*, *bottom*) discriminate the reach target in the target selection task. Thus it appears that SC neurons that do not discriminate a reach target from distractors belong to a subset of cells without saccadic buildup activity. However, some neurons without saccadic buildup activity can still discriminate the reach target from distractors.

Summary histograms showing the distribution of visual, delay-period, and saccade-related responses observed in discriminating and nondiscriminating cells are shown in Fig. 7. The visual response (measured as the mean activity from 50 to
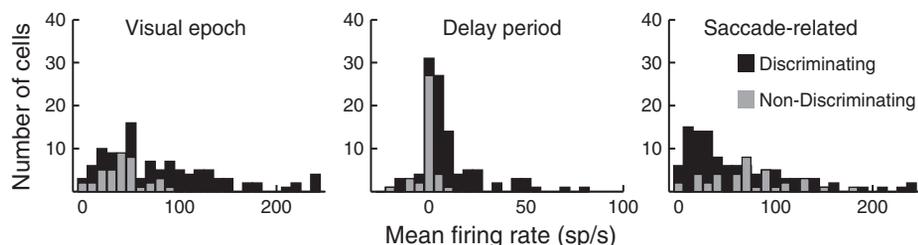
Fig. 7. Histograms showing the distributions of visual, delay-period, and saccade-related activity in the delayed saccade task for cells that discriminated the reach target (black bars) and cells that did not (gray bars).

150 ms after target onset minus the baseline activity measured 0–100 ms before target onset) of cells that discriminated the reach target was significantly higher than that of cells that did not (Fig. 7, *left*; mean $\pm$ 1 SE: 83.5 $\pm$ 7.2 vs. 41.4 $\pm$ 3.6 sp/s; permutation test, $P < 0.001$). Delay-period activity (measured as the mean activity 300–400 ms after target onset minus baseline) was also significantly higher for discriminating cells (Fig. 7, *middle*; 9.4 $\pm$ 1.6 vs. -0.7 ± 0.8 sp/s; permutation test, $P < 0.001$). In contrast, there was no significant difference in saccade-related activity (measured as the mean rate from 50 ms before to 50 ms after saccade initiation minus baseline; Fig. 7, *right*; 81.2 $\pm$ 5.4 vs. 70.4 $\pm$ 6.8 sp/s; $P = 0.36$). In summary, we found that SC neurons with saccadic delay-period activity were highly likely to discriminate the target from distractors in the reach target selection task. In addition, although a lack of saccadic delay-period activity was not always associated with a lack of reach selectivity, virtually all cells without reach selectivity also did not show significant delay-period activity in the delayed saccade task.

Location of Discriminating and Nondiscriminating Cells within the SC

Finally, we investigated whether discriminating vs. nondiscriminating neurons were located in different portions of the intermediate layers of the SC. A post hoc examination of the depths of the recorded cells from the estimated SC surface (defined as the depth at which SC visual responses were 1st audible) did not reveal any notable differences in the depth of neurons that discriminated the reach target and those that did not [Fig. 8A; 2.3 $\pm$ 0.13 (SE) vs. 2.2 $\pm$ 0.18 mm; Mann-Whitney U test, $P = 0.6$]. To estimate the anteroposterior and mediolateral locations of recorded cells within the SC, we transformed the estimated location of the center of the visual receptive field of each cell (measured using the delayed saccade task) from visual field coordinates into SC coordinates using the formulae developed by Van Gisbergen and colleagues (Ottes et al. 1986, 1987) and projected them onto a schematic map of the left SC. Cells from the right SC were merged with cells from the left SC by mirror-reflecting the locations of the right SC cells, thereby preserving their relative

mediolateral position on the combined map. The outcome of this analysis is shown in Fig. 8B. We did not observe any notable tendency toward segregation of discriminating and nondiscriminating cells, although it should be acknowledged that our sample of nondiscriminating cells was limited due to their relative scarcity in the SC intermediate layers.

DISCUSSION

To examine the neural correlates of reach target selection, we recorded the activity of isolated neurons in the intermediate layers of the SC during a reach target selection task. This was motivated by the finding that SC inactivation causes deficits in reach target selection (Song et al. 2011). We found that even when fixation is maintained throughout the trial, activity in a subset of SC neurons discriminates a reach target from distractors. The earliest SC visual activity did not discriminate the reach target from distractors, but approximately 120–150 ms after stimulus onset, activity began to signal reliably whether the target or a distractor was in the RF of the cell. However, cells did not show a burst of activity in association with the onset of the reach.

Some SC neurons exhibit sustained delay-period activity during delayed saccade tasks, and such saccadic buildup (or prelude) activity has been associated in many studies with saccade target selection, distinct from movement execution (Basso and Wurtz 1997; Glimcher and Sparks 1992; Horwitz and Newsome 1999; McPeek and Keller 2002). Here, we demonstrated that neurons having delay-period activity in a delayed saccade task are likely to discriminate a reach target from distractors. Taken together, these earlier results and our current experiments indicate that the majority of SC buildup neurons carry signals related to target selection regardless of the effector that executes the response, consistent with the hypothesis that the SC forms part of a general-purpose priority map that is used to guide a variety of goal-directed actions as well as covert attention.

Other Neural Substrates Involved in Reach Target Selection

Our current understanding of the neural substrates of reach target selection involve higher-order cortical move-
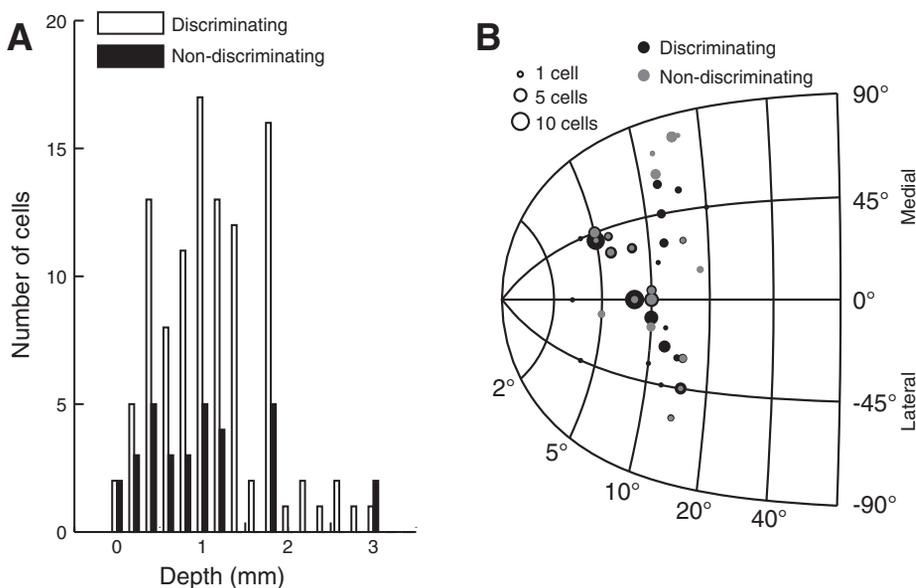
Fig. 8. *A*: estimated depths of recorded SC cells for cells that discriminated the reach target (white bars) and cells that did not (black bars). *B*: estimated location of recorded SC cells within the retinotopic SC map for cells that discriminated the target (black circles) and those that did not (gray circles). Circle diameter represents the number of cells recorded at each marked location. Cells from the right SC have been transposed onto the schematic left SC, which is shown. See main text for details.

ment-planning areas in the frontal and the parietal cortices, including PMd and PRR (Cisek 2006; Cisek and Kalaska 2002, 2005; Hoshi et al. 2000; Scherberger and Andersen 2007; Song and McPeek 2010). For instance, in PRR, Scherberger and Andersen (2007) have shown that neural activity is linked to target choice when monkeys choose one of two sequentially presented targets. Pesaran et al. (2008) demonstrated that information regarding selecting a single reach target from multiple alternatives transfers between PMd and PRR, which may underlie the selection of a common reach goal by the two areas.

Using a task virtually identical to the task used here, we (Song and McPeek 2010) demonstrated that neurons in PMd contain signals related to target selection and movement execution for reaching movements and that different signals are carried by distinct neuronal subpopulations. In light of this as well as the results of our SC inactivation study (Song et al. 2011), we conjecture that information regarding reach target selection may be conveyed from the SC to cortical areas involved in reach target selection and execution. One possibility could be via ascending pathways from SC through thalamus to the PMd or via reciprocal interactions (Matelli et al. 1989; Preuss 2007; Stepniewska et al. 2007).

Potential Roles of Covert Attention and Saccade Planning

One interpretation of the observed SC activity discriminating the reach target might be that it is related to covert saccade planning or to covert visual attention. The SC has been shown to be involved in saccade planning and in covert attention (e.g., Carello and Krauzlis 2004; Cavanaugh and Wurtz 2004; Glimcher and Sparks 1992; Ignashchenkova et al. 2004; Krauzlis et al. 2013; Kustov and Robinson 1996; Lovejoy and Krauzlis 2010; McPeek and Keller 2004; Muller et al. 2005; Munoz and Wurtz 1995), either of which may have accompanied reach planning in this task (e.g., Deubel et al. 1998; Khan et al. 2011). Thus it is difficult to evaluate precisely the extent to which our results are driven by reach target selection signals or by covert saccade planning or attention. However, in our previous SC inactivation study (Song et al. 2011), using a distractor task in which two identical stimuli were sequentially presented with a variable stimulus-onset asynchrony (SOA) as well as in a centrally cued reaching task in which a foveal cue indicated the reach target, we demonstrated a causal role of the SC in reach target selection. These inactivation results indicate that at least some subset of SC neurons is involved in reach target selection. Whether this causal effect is mediated by changes in covert attention or saccade planning remains an open question. Nonetheless, the current study reveals a population of cells that carry signals that would be appropriate for reach target selection. The correlational nature of the experiments do not allow us to establish definitively that the cells described here are necessarily the ones underpinning the effects of SC inactivation on reach target selection. To make a more precise statement regarding the contribution of the cells recorded here, further investigation is needed, including on the relationship between this population of SC reach target selection neurons and pure saccadic neurons.

SC Cells Involved in Reach Target Selection vs. Movement Execution

In contrast to the reach target selection cells that we observed in the intermediate layers of the SC, previous studies have identified a different class of SC neurons that are sparsely scattered in the deeper layers of the SC. These neurons are most numerous near the border of the SC and the underlying mesencephalic reticular formation and exhibit a burst of activity at the onset of, or during, reaching movements even when fixation is maintained (e.g., Stuphorn et al. 2000; Werner et al. 1997). We believe that these neurons form a distinct population of cells, which we did not sample in this study for several reasons. First, we recorded cells in the intermediate layers of the SC, whereas these cells are primarily found in deeper strata. Second, in contrast to what has been observed for the reaching cells, we did not observe an increase in activity related to reach movement onset. Finally, these deeper-layer SC cells do not follow the orderly retinotopic organization shared by other layers, whereas the reach target selection cells we recorded in the intermediate layers showed significant target selectivity when the reach target was located in the part of the visual field corresponding to the traditional retinotopic SC map. Taken together, we conjecture that the SC may play a role in coordinating eye and hand movements toward a common goal via cross talk between intermediate-layer neurons involved in target selection for saccades and reaches and deep-layer neurons involved in reach execution. Future work should clarify the precise functional overlap between these subpopulations and their potential roles in eye-hand coordination (e.g., Reyes-Puerta et al. 2011).

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

J.-H.S. and R.M.M. conception and design of research; J.-H.S. performed experiments; J.-H.S. and R.M.M. analyzed data; J.-H.S. and R.M.M. interpreted results of experiments; J.-H.S. and R.M.M. prepared figures; J.-H.S. and R.M.M. drafted manuscript; J.-H.S. and R.M.M. edited and revised manuscript; J.-H.S. and R.M.M. approved final version of manuscript.

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