Activity Changes in Monkey Superior Colliculus During Saccade Adaptation

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Takeichi N, Kaneko CR, Fuchs AF. Activity changes in monkey superior colliculus during saccade adaptation. J Neurophysiol 97: 4096–4107, 2007. First published April 18, 2007; doi:10.1152/jn.01278.2006. Saccades are eye movements that are used to foveate targets rapidly and accurately. Their amplitude must be adjusted continually, throughout life, to compensate for movement inaccuracies due to maturation, pathology, or aging. One possible locus for such saccade adaptation is the superior colliculus (SC), the relay for cortical commands to the premotor brain stem generator for saccades. However, previous stimulation and recording studies have disagreed as to whether saccade adaptation occurs upstream or downstream of the SC. Therefore we have reexamined the behavior of SC burst neurons during saccade adaptation under conditions that were optimized to produce the biggest possible change in neuronal activity. We show that behavioral adaptation of saccade amplitude was associated with significant increases or decreases, in the number of spikes in the burst and/or changes in the shape of the movement field in 35 of 43 SC neurons tested. Of the 35, 29 had closed movement fields and 14 were classified indeterminate because the movement field could not be definitively diagnosed. Changes in the number of spikes occurred gradually during adaptation and resulted from correlated changes in burst lead and duration without consistent changes in peak burst rate. These data indicate that the great majority of SC neurons show a change in discharge in association with saccade amplitude adaptation. Based on these and previous results, we speculate that the site for saccade adaptation resides in the SC or that the SC is the final common pathway for adaptive changes that occur elsewhere in the saccadic system.

INTRODUCTION

The function of saccadic eye movements is to point the high-acuity portion of the retina, the fovea, at objects of interest. Because the fovea is small and the accuracy of saccades must be maintained throughout life in the face of growth, disease (e.g., Kommerell et al. 1976), aging (e.g., Warabi et al. 1984), or trauma, neural mechanisms exist to continually adjust (adapt) saccade amplitude so the eyes land accurately on target. The midline cerebellum, the vermis and the caudal fastigial nucleus (cFN), are likely to be involved in this adaptation because lesions of those structures affect a primate’s ability to adjust saccade amplitude (e.g., Optican and Robinson 1980; Ritchie 1976; Villis and Hore 1981; see Hopp and Fuchs 2004 for review). Inactivation of the cFN impairs saccade adaptation, but if the animal recovers from the inactivation in the dark, a latent adaptation is revealed (Robinson et al. 2002). This result suggests that adaptation occurs upstream of the cFN. A major saccadic input to the oculomotor cerebellum originates in the nucleus reticularis tegmenti pontis (nrtp) (e.g., Brodal 1980; see Scudder et al. 2002 for review), which relays signals from the superior colliculus (SC). Recently we showed that saccade amplitude adaptation causes a statistically significant change in the discharge of over half of the saccade-related burst neurons in nrtp (Takeichi et al. 2005a). This observation raises the possibility that the effects of adaptation either are induced within the nrtp itself (e.g., by long-term potentiation) or take place centrally and are conveyed to the nrtp by one or more of its inputs, possibly those that originate in the SC.

Previous investigations have reached opposite conclusions as to whether the site of the neural mechanisms that underlie saccade amplitude adaptation lies downstream or upstream of the SC. On one hand, if saccadic eye movements are elicited by electrical stimulation of the SC (Fitzgibbon et al. 1986; Melis and van Gisbergen 1996), they remain unaffected after saccade amplitude adaptation, suggesting that such adaptation occurs in the SC or upstream of it. In contrast, stimulating the SC at lower current intensities than those used in the two previous studies elicited movements that were affected by saccade amplitude adaptation (Edelman and Goldberg 2002). Moreover, when Frens and van Opstal (1997) recorded saccade-related burst neurons in the SC during amplitude adaptation, the discharge of some of their SC neurons remained unchanged during saccade adaptation, leading them to suggest that the SC actually does not command the adapted saccade size that is changing during the course of adaptation but that it encodes the desired saccade size, i.e., essentially the size of the target step, which is unaffected by adaptation. The latter two studies suggest that saccade adaptation occurs downstream of the SC.

To attempt to resolve these conflicting results, we recorded the activity of SC burst neurons during saccade adaptation under conditions that were deliberately chosen to promote the greatest possible change in neuronal discharge. We expected to confirm that adaptation does not alter SC firing and that the site of adaptation indeed is downstream of the SC (Frens and van Opstal 1997). We reasoned that this expected result combined with previous findings that adaptation occurs upstream of the cFN and affects the response of neurons in the nrtp (Takeichi et al. 2005a) would identify the nrtp as the location of the changes underlying saccade adaptation. Instead, we found that >80% of SC neurons do show changes in their discharge patterns in association with saccade amplitude adaptation, suggesting that the changes in the nrtp might reflect changes in it’s collicular inputs. A preliminary report on some of these findings has appeared in abstract form (Takeichi et al. 2005b).
METHODS

The methods used in this study are identical to those used in our recent study on the effects of saccade adaptation on nrtp activity (Takeichi et al. 2005a), and therefore are summarized only briefly here.

Animal preparation, training, and recording

Three juvenile male rhesus monkeys (Macaca mulatta, 3.6–4.8 kg, K, P, and B) were implanted with acrylic mounds on the skull for head-stabilization, a preformed scleral search coil, and a stainless steel recording chamber under inhalation anesthesia and aseptic conditions. The chamber was centered on the mid sagittal plane, tilted caudally by 38° (monkey K) or 35° (monkeys P and B) from the vertical and aimed at a point 1 mm posterior and 15 mm dorsal to stereotaxic zero to allow access to the SC.

After the animals had recovered from the surgery, we placed them in a chair that limited movements of the trunk and limbs. By means of the stabilization mounds, we prevented the animal from turning its head and measured eye movements with an electromagnetic technique (Collewijn 1977; Robinson 1963). The monkeys were trained to track a small (~0.3°) target spot, which was rear-projected onto a tangent screen 68 cm away. If monkeys made a saccade within 500 ms of a target step and then maintained eye position within an error window surrounding the stepped target location for 1–1.4 s, they received an applesauce reward. The reward window size was set at ±2° while we searched for a SC burst neuron and then was relaxed to ±3.5° while the monkey made the dysmetric saccades that occurred during saccade adaptation.

We recorded extracellular neuronal activity with homemade tungsten microelectrodes (Takeichi et al. 2005a). The neuronal signal was amplified and filtered (band-pass: 300 Hz to 10 kHz), played over an audio monitor, and displayed on an oscilloscope. Eye and target position signals were digitized at 1 kHz and spike occurrence was monitored on a memory oscilloscope, helped us decide the amplitude and one or two other amplitudes along the estimated preferred direction. If the burst rate increased to a peak and then decreased, the unit had an apparent closed movement field. This preliminary, on-line diagnosis, which was based on both the unit activity placed over an audio monitor and the instantaneous firing rate monitored on a memory oscilloscope, helped us decide the amplitude and direction for saccade adaptation (see next section). It was validated for all neurons post hoc based on all our recorded responses (cf. Soetedjo et al. 2002a). The optimal amplitude was confirmed in our movement field plots. We did NOT quantify changes in the discharge along nonoptimal directions, so when we refer to the neuron’s movement field, we are referring only to changes along the optimal direction for the neuron. Keller et al. (1996) have used the term “amplitude movement field” to refer to the discharge along the optimal direction. Because saccade adaptation affects saccades of similar amplitudes and in nonadapted (here nonoptimal) directions (the adaptation field, see Hopp and Fuchs 2002), which we did not study here, we chose not to use their term.

ADAPTATION OF SACCADE AMPLITUDE. After we had estimated the unit’s preadaptation movement field and collected responses during saccades with a variety of sizes along the preferred direction, we used target step was predictable. Ten to 15 repetitions of each target step comprised the preadaptation data. If, during our initial assessment, the burst rate continued to increase for all saccade amplitudes (≥30°), we designated the unit as having an apparent open movement field (along its preferred direction). If the burst rate increased to a peak and then decreased, the unit had an apparent closed movement field. This preliminary, on-line diagnosis, which was based on both the unit activity placed over an audio monitor and the instantaneous firing rate monitored on a memory oscilloscope, helped us decide the amplitude and direction for saccade adaptation (see next section). It was validated for all neurons post hoc based on all our recorded responses (cf. Soetedjo et al. 2002a). The optimal amplitude was confirmed in our movement field plots. We did NOT quantify changes in the discharge along nonoptimal directions, so when we refer to the neuron’s movement field, we are referring only to changes along the optimal direction for the neuron. Keller et al. (1996) have used the term “amplitude movement field” to refer to the discharge along the optimal direction. Because saccade adaptation affects saccades of similar amplitudes and in nonadapted (here nonoptimal) directions (the adaptation field, see Hopp and Fuchs 2002), which we did not study here, we chose not to use their term.

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the McLaughlin paradigm (McLaughlin 1967) to either increase or decrease the size of saccades along the preferred direction. In that paradigm, the target is made to step either further onward or backward (the adaptation step) as a primary saccade is en route to an initial target step. After a few hundred repetitions, the primary saccade changes in size to land closer to the target location reached after the adaptation step. We used adaptation step sizes that ranged from 2 to 10° or 40 to 53% of the initial step size. We were unable to retain unit isolation long enough to subject the same unit to both amplitude increases and decreases or test it during re-adaptation toward the initial target step.

We selected the saccade amplitude to be adapted and whether the adaptation should be forward or backward so that, based on our on-line estimation of the unit’s movement-field, adaptation would be expected to produce a dramatic change in the burst discharge. If the unit had an apparent closed movement field, we either reduced (n = 10) or increased (n = 19) saccade amplitude. In the former case, we usually chose a small saccade with a modest burst and used backward adaptation to produce a smaller saccade that, based on the movement field, would normally be accompanied by no burst at all (e.g., Fig. 7B, tip of blue arrow). Occasionally, we adapted large-amplitude saccades associated with a minimal burst toward the optimal saccade amplitude associated with the maximal burst (e.g., Fig. 7A, tip of blue arrow). In the latter case, we chose a large-amplitude saccade (i.e., beyond peak discharge) associated with a modest burst and used forward adaptation to reduce the discharge to a minimum (e.g., Fig. 8).

For the 14 apparent open movement field neurons, we always reduced saccade amplitude (backward adaptation) for several reasons. First, discharges associated with larger saccades often are more variable and therefore would increase the noise in a pre- vs. postadaptation comparison. Second, saccade amplitudes large enough (3–50°) to be associated with large changes in discharge become more difficult to elicit at the end of a long adaptation session. Third, some neurons exhibited a saturated discharge as amplitude increased so that forward adaptation would result in little change in discharge. Finally, forward adaptation produces amplitude increases that usually are smaller than decreases and occur more slowly (Straube et al. 1997; see Hopp and Fuchs 2004), so we would have been required to maintain unit isolation for a longer time to discern the changes associated with adaptation.

We monitored the progression of adaptation on an oscilloscope and when saccades had changed by an average of ~20% for backward adaptation and ~18% for forward adaptation, we increased the intra-saccadic adapt step size to encourage further adaptation. Again, the target stepped in a pseudo-random fashion along the neuron’s preferred direction (see Takeichi et al. 2005a).

EVALUATION OF POSTADAPTATION UNIT RESPONSE CHARACTERISTICS. When the on-line plot of saccade gain (saccade size/target step size) began to asymptote (after 400–1,100 trials), we tested the neuron’s discharge in association with saccades to the same size target steps along the preferred direction that we used to determine the preadaptation movement field (see preceding text). We gathered from 10 to 15 saccades at each amplitude target step. We did not blank the target during postadaptation trials, which would retard recovery toward normal gain (e.g., Shafer et al. 2000), because our previous study (Takeichi et al. 2005a) showed that such recovery was so gradual that there was little loss in adaptation over the ~75 saccades required to construct the postadaptation movement field.

Data analysis

GENERAL DATA PROCESSING. We determined the relation between the burst of a SC neuron and its associated saccade off-line with a homemade interactive program (Takeichi et al. 2005a). The program scrolled the data on a video monitor and identified and stopped at a saccade when either the horizontal or vertical eye-movement velocity exceeded 50°/s. Saccade onset and offset were marked automatically on each component at the points when eye velocity rose above and then fell below 10°/s, respectively. Saccade duration was the time between the first component to start and the last to end. The bursts of SC neurons were marked when the firing rate of the saccade-related discharge exceeded and then fell below 40 spike/s. To find the burst, the computer searched from the time of saccade onset, forward and backward in time, until the discharge rate fell below the firing rate threshold. Each marked saccade and burst were examined on the computer screen and the computer marks were re-adjusted in less than ~1% of the cases, usually when artifacts caused incorrect markings.

The number of spikes was counted during the marked burst duration and the peak frequency was calculated from the average of the five shortest interspike intervals and placed at the center of the duration of the interval that spanned the five associated spikes. The burst lead was the time from the beginning of the burst to the beginning of the saccade and, analogously, the burst lag was the time from the end of the burst to the end of the saccade.

The inspected marked bursts never included a visual response because the program searched backward and forward from the time of saccade onset and the marked burst was over before the burst associated with the target step. Nevertheless, we tested explicitly for the presence of a visual response by aligning the trials on target onset. Only 9 of 43 neurons displayed a visual response. Moreover, of those nine, only three showed a change in the number of spikes with adaptation. All accepted saccades and spikes were stored and analyzed by other homemade or commercial (Igor, WaveMetrics, Lake Oswego, OR; Matlab, Mathworks, Natick, MA) software programs.

TESTS OF EFFECTS OF ADAPTATION. We assessed the effects of adaptation on the burst discharge of SC neurons by two tests. The first examined changes in the burst per se and the second changes in a neuron’s movement field.

In the first test, we examined the changes in the number of spikes in the burst. First, we fit the scatter plots of number of spikes as a function of trial number during adaptation (e.g., Fig. 2, top) with a linear regression and determined whether the slope of the regression was significantly different from zero (P < 0.05 corrected by the Bonferroni correction for multiple comparisons). We will refer to this test as the number-of-spikes test. Second, we compared the average number of spikes associated with the first and last 25 saccades during adaptation using a t-test and a criterion of P < 0.05 (corrected by the Bonferroni correction for multiple comparisons). For every unit reported in the following text, these two measures agreed. Therefore when adaptation is said to be associated with a change the number of spikes, it has affected the slope of the regression during adaptation and caused a significant difference between the number of spikes associated with the first and last 25 saccades during adaptation.

In the second test of the effects of adaptation, we compared the movement fields in a neuron’s preferred direction before and after adaptation. We plotted the fields for both actual saccade size (the saccade amplitude elicited by the initial target step) and desired saccade size (the difference between eye position when the target stepped and the new target position). The fields were plotted against these two different saccade amplitude measures so we could compare our data with those of Frens and van Opstal (1997). We used actual eye position when the target stepped to determine desired saccade size to eliminate trial-to-trial variations in fixation. To compare the pre- and postadaptation movement fields, we considered changes only along the unit’s preadaptation preferred direction.

Examples of our two types of movement fields are shown in Fig. 1. Closed field neurons exhibited their largest bursts for saccades of an optimal vector and smaller bursts for both larger and smaller saccades (Fig. 1A, optimal, ~10°). In contrast, apparent open field neurons (Fig. 1B) discharged their largest bursts for the biggest saccades that we could elicit along the preferred direction (~35–50°). Because open field neurons might have exhibited closed field characteristics (Freed-
man and Sparks 1997) for large head-free gaze shifts, which we were unable to test, we will refer to neurons that did not have closed fields as indeterminate field neurons in the rest of this report. To assess whether movement fields differed before and after saccade amplitude adaptation, we fit plots of the number of spikes versus either actual or desired saccade size (i.e., the difference between eye position when the target stepped and the final target position after the step) by a cubic polynomial function (curve fitting tool, Matlab). In preliminary analyses on indeterminate field neurons, the fits were equally good with the cubic polynomial or a linear regression (cf. Takeichi et al. 2005a). For example, both the linear regression and cubic polynomial fits for the neuron in Fig. 1B accounted for 90% of the variance (i.e., $r = 0.95$). Therefore we based all the comparisons reported here on the cubic polynomial fits, which could be applied uniformly to all neurons. We took the very conservative approach of concluding that the neuron in Fig. 1B had only when the 95% confidence limits of the cubic fits for pre- and postadaptation data did not overlap over $\pm 2^\circ$ of the movement field.

As mentioned in the preceding text, we plotted movement fields not only as a function of actual saccade size, as is done traditionally, but also as a function of desired saccade size. The neurons that changed their movement fields plotted against desired saccade size usually (22/24) also did so when their movement fields were plotted against actual saccade size. Slightly more neurons (77 vs. 56%) showed changes in their movement fields when plotted against actual saccade size.

All experiments were performed in accordance with the recommendations of the National Research Council (Guide for the Care and Use of Laboratory Animals, 1997; Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research, 2003), the Society for Neuroscience, and exceeded the minimal requirements recommended by the Institute of Laboratory Animal Resources and the Association for Assessment and Accreditation of Laboratory Animal Care International. All procedures were evaluated and approved by the local Animal Care and Use Committee of the University of Washington (ACC 2602–01).

RESULTS

We recorded the activity of 54 saccade-related burst neurons in the SC of three monkeys (monkey K: 40, B: 6, and P: 8) during saccade adaptation. Thirty-three of the 54 had unambiguous closed movement fields, and the rest had indeterminate fields. To completely characterize the adaptation related changes in neuron discharge, the preadaptation, adaptation, and postadaptation phases required $\approx 1$ h. We lost recording isolation or injured seven neurons during the adaptation phase and were unable to collect postadaptation data on another four due to technical problems. In the analysis in the following text, we consider only the 43 neurons (29 with closed fields) for which we had complete pre- and postadaptation movement fields. For each neuron, we first consider whether there was a difference in the number of spikes test. We will consider then whether there were changes in the movement field, which we will refer to as the movement field test. The two tests did not always agree as to whether adaptation was associated with changes in the burst. Of the 14 of 43 neurons that showed significant changes in the number of spikes test, two did not show significant changes in their movement fields (plotted as a function of desired saccade size). Of the 24 of 43 neurons that showed significant changes in their movement fields, 12 did not show significant changes in the number of spikes test.

Effect of backward adaptation on indeterminate movement field neurons

CHANGE IN NUMBER OF SPIKES. The activity of 14 SC neurons with indeterminate movement fields was recorded during backward (i.e., amplitude reduction) adaptation. In three, the number of spikes after adaptation was significantly different from

FIG. 2.  Change in the number of spikes in a burst during the course of backward adaptation for unit K68. Top: adaptation of saccades made to 18° target steps with adaptation steps of $-6^\circ$ for trials 1 to 358 and $-8^\circ$ from trials 359 to 576. Saccade amplitude (C) and number of spikes (A) are plotted as a function of the number of the adaptation trial. Pre- and postadaptation trials with their mean saccade amplitudes (C) and the mean number of spikes (A) are shown at the left and right, respectively; the $\pm$SDs are about the size of the symbols. Bottom: rasters and histograms of the averaged firing rates (bin width of 10 ms) for trials 1–50, 175–224, 350–399, and 527–576 (between 4099 in top). Averaged histogram for trials 1–50 is superimposed as black outline on the other 3 histograms (gray). \$\Delta$\$\Delta$, increase of presaccadic activity. All rasters and histograms are aligned on saccade onset (A, 1).

SACCADE ADAPTATION AND MONKEY SUPERIOR COLLICULUS 4099
that before. Figure 2 shows a representative indeterminate field neuron (K68) that exhibited a significant increase \((P < 0.001)\) in the number of spikes \((\triangledown)\) from \(9.1 \pm 1.4\) before to \(15.4 \pm 4.4\) (SD) spikes after adaptation (ordinate on the right). This increase occurred gradually as saccade amplitude \((\bigcirc)\) decreased while adaptation progressed and was due mostly to more spikes occurring at the beginning of the burst as can be seen in the rasters and histograms (bin width = 10 ms) in the bottom panels. By trials 350–399, the average histogram (gray) showed increased and earlier discharge than the histogram of the first 50 saccades (black outline). The biggest increase in the number of spikes occurred early in the burst (Fig. 2, \(\searrow\)). Adaptation produced statistically significant increases in the number of spikes in the burst of all three of the indeterminate field units.

In contrast, adaptation produced no change in the number of spikes in the remaining 11 indeterminate field neurons. For the representative neuron in Fig. 3 (P27), the number of spikes in the burst \((\triangle)\) did not change although saccade amplitude \((\bigcirc)\) decreased by 23\%, i.e., from \(7.1 \pm 0.5\) to \(5.5 \pm 0.5\)°. Not surprisingly, the discharge pattern also did not change over the course of adaptation as illustrated by the raster and histogram (bottom; bin width = 10 ms) of the burst during the first (1–50, black outline) and last (519–568, gray bars) 50 adaptation trials.

CHANGE IN MOVEMENT FIELDS. For the 3 of 14 indeterminate field neurons that exhibited a change in the number of spikes, all exhibited a change not only at the adapted desired saccade amplitude (Fig. 2) but also at other saccade amplitudes in the preferred direction. The movement field data for the unit illustrated in Fig. 2 are plotted as a function of desired saccade size in Fig. 4A. After adaptation, the number of spikes \((\bigcirc)\) generally was greater than that before (black dots) at many sizes other than the adapted size of 18° (vertical dashed line). On the other hand, for the unit illustrated in Fig. 3, there was no significant change in the number of spikes (Fig. 4B) and pre- and postadaptation data overlapped at all desired saccade amplitudes (Fig. 4B).

To compare the pre- and postadaptation movement fields quantitatively, we determined whether the 95\% confidence intervals of the cubic polynomial fits for the pre- and postadaptation data (like those in Fig. 4) overlapped. For the unit illustrated in Fig. 4A, Fig. 5A shows that the number of spikes was significantly (no overlap in the 95\% confidence intervals, \(-\)\(-\)) greater after (red) than before (blue) adaptation at desired saccade amplitudes \((A2)\) from \(-25\) to \(32\)° and actual saccade amplitudes \((A1)\) from \(-12\) to \(30\)°. The two other indeterminate field neurons (not shown) showed similar changes in their movement fields. In contrast, for the unit illustrated in Fig. 4B, the 95\% confidence intervals of the pre- and postadaptation movement field fits overlapped for all actual and desired saccade sizes (Fig. 5B).

FIG. 3. Change in the number of spikes in a burst during the course of backward adaptation for unit P27. Top: adaptation of saccades made to 7° initial target steps with a \(-3°\) adaptation step. Saccadic amplitude \((\bigcirc)\) and number of spikes \((\triangle)\) are plotted as a function of the number of the adaptation trial. Pre- (to the left) and post- (to the right) adaptation trials with their mean saccade amplitudes \((\bigcirc)\) and the mean number of spikes \((\triangle)\) ± SD (\(\sigma\)). Bottom: rasters and histograms of the averaged firing rates (bin width of 10 ms) for trials 1–50 (from 0 to 1st \(\searrow\)) and 519–568 (between last 2 \(\searrow\), 2nd \(\searrow\)). All rasters and histograms are aligned on saccade onset \((\triangle)\)
For the 11 indeterminate movement field neurons in which the number of pre- and postadaptation spikes at the desired saccade size did not differ, 7 also showed no significant change elsewhere in their movement fields. However, like the neuron in Fig. 5C, the remaining four did. For this neuron, the number of spikes was significantly greater after than before adaptation at desired saccade amplitudes between $24^\circ$ and $29^\circ$ (C2) and actual saccade amplitudes from $17^\circ$ to $28^\circ$ (C1). Note that the neurons illustrated in Fig. 5 behave like those reported by Frens and van Opstal (1997) because the number of spikes relative to desired saccade size (vertical - - -) were unchanged after adaptation. However, by constructing the entire postadaptation movement field, we have revealed that adaptation has affected the discharge associated with saccades of other sizes for the neurons in Fig. 5, A and C. In fact, when the number of spikes were plotted as a function of actual saccade size, 11 of 14 indeterminate neurons showed significant changes in their movement fields.

**Effect of backward adaptation on closed movement field neurons**

The activity of 10 closed movement field SC neurons was monitored during backward adaptation. Of the 10, 2 showed a significant increase in the number of spikes test. Both also exhibited changes in their movement fields as illustrated for the unit in Fig. 6A. Based on its preadaptation movement field (●), we attempted to reduce the amplitude of $12^\circ$ saccades (vertical - - -) to $6^\circ$ to produce a large increase in the number of spikes. We produced an actual average change of $2.4^\circ$ (from 12 to $9.6^\circ$) that was associated with a significant increase in the number of spikes ($P < 0.001$). Saccade adaptation also clearly altered the movement field (□). Figure 7, A1 and A2, shows that adaptation was associated with a significantly increased number of spikes for actual saccade amplitudes between 3 and $6^\circ$ and desired saccade amplitudes between 3 and $7^\circ$.

The remaining 8 of 10 closed field neurons exhibited no change of activity according to the number of spikes test but three, one of which is illustrated in Fig. 6B, did show a change in its movement field. For that unit, based on its preadaptation movement field (Fig. 6B, ●), we tried to reduce $8^\circ$ saccades (vertical - - -) to $4^\circ$ to reduce the number of spikes to zero. We actually produced a $1.2^\circ$ (from 8 to $6.8^\circ$) reduction. From the raw data (Fig. 6B), it is unclear whether adaptation was associated with a change in the movement field. Comparison of the pre- and postadaptation movement field fits showed no difference when the fields were plotted against desired saccade size (Fig. 7B2). However, there was a modest increase in the number of spikes for actual saccade amplitudes between $5^\circ$ and $8^\circ$ (Fig. 7B1). This neuron (K118) shows that the change brought about by adaptation could occur for movement fields plotted against one saccade measure, here actual saccade size but not the other.
In summary, for half (5/10) of the closed field neurons, backward adaptation was associated with a significant change in the number of spikes or in the movement field (plotted against desired saccade amplitude) alone. In addition, 9/10 neurons showed significant changes in their movement fields plotted as a function of actual saccade size.

Effect of forward adaptation on closed movement field neurons

Nineteen closed-field neurons were evaluated during forward (i.e., amplitude increase) adaptation. For all these neurons, saccades were adapted from smaller amplitudes associated with a robust discharge toward larger amplitudes associated with a weaker discharge. For 9 of the 19, adaptation caused either an increase (n = 5) or decrease (n = 4) in the number of spikes associated with saccades to the adapted target size. Seven of these nine also showed changes in their movement fields plotted as a function of desired saccade size. The movement field of one, for which adaptation was associated with an increase in the number of spikes, is illustrated in Fig. 8A. When 12° saccades were subjected to forward adaptation, the number of spikes increased significantly not only for saccades to 12° target steps (Fig. 8A, vertical - - -) but also for smaller saccades throughout the movement field. Four of the five neurons that showed an increased number of spikes also showed ranges of desired saccade amplitude within which there was no overlap of the 95% confidence intervals of their pre- and postmovement field fits. For the four where adaptation

![Graph showing number of spikes vs desired saccade size](image)

**FIG. 6.** Comparison of pre- and postadaptation movement fields along the preferred direction for 2 representative closed field neurons (K134 and K118) before (○) and after (□) backward adaptation. The number of spikes is plotted as a function of desired saccade size. Pre- and postadaptation data are fit by a cubic polynomial, — and —, respectively. A: saccades to an initial target step size of 12° (- - -) were backward adapted toward 6° to increase the number of spikes. B: saccades to an initial target step size of 8° ( - - -) were backward adapted toward 4°, to decrease the number of spikes. The actual amount of saccade amplitude adaptation was 2.4° in A and 1.2° in B.

![Graph showing number of spikes vs actual saccade size](image)

**FIG. 7.** Comparison of pre- and post-adaptation movement fields along the preferred direction for 2 representative closed field neurons (K134 and K118) before and after backward adaptation. The number of spikes is plotted both as a function of actual saccade size and desired saccade size for each neuron. Pre- and post-adaptation data are fit by cubic polynomial functions. Note that 95% confidence limits overlap for the number of spikes at the adapted saccade size of 12° because the polynomial was fit to all points (cf. Fig. 6A) and because the criteria of nonoverlap are more stringent than the Bonferroni corrected P < 0.05 for our t-test. Format as in Fig. 5.

![Graph showing number of spikes vs desired saccade size](image)

**FIG. 8.** Comparison of pre- and post-adaptation movement fields along the preferred direction for 3 representative closed field neurons (K101, K60, and K146) before and after forward adaptation. The number of spikes is plotted both as a function of actual saccade size and desired saccade size for each neuron. Pre- and post-adaptation data are fit by a cubic polynomial function. Format as in Fig. 5.
produced significant decreases in the number of spikes, three also showed a significant change in their postadaptation movement fields. For the unit illustrated in Fig. 8B (K60), there was no overlap in the confidence intervals for desired saccade sizes (B2) from ~9 and 18° and for actual saccade sizes (B1) between ~7 and 11 and 18 and 20°.

For the remaining 10 of 19 neurons, there were no significant differences in the number of spikes according to the number of spikes test. However, for 5 of these 10, adaptation did alter their movement fields as illustrated for unit K146 (Fig. 8C). For this neuron, there was no significant change in the number of spikes at the adapted saccade amplitude of 10° (Fig. 8C2, vertical -- --), but there was a significant difference for desired saccade amplitudes between ~5 and 9° (Fig. 8C2) and actual saccade amplitudes between 5 and 12° (Fig. 8C1). Again, these five neurons behave like those reported by Frens and van Opstal (1997) in that they showed no differences at the adapted desired saccade size. However, they did have alterations to their movement fields away from the adapted target size. Thus forward adaptation produced changes in either the number of spikes or the movement field in 14 of 19 closed movement field burst neurons. Thirteen of the 19 also showed significant changes in their movement fields as a function of actual saccade size.

Summary of the adaptation effects

Figure 9 summarizes the effects of adaptation for the two types of neurons as sorted by their movement fields and adaptation directions. For the 43 neurons that we tested, adaptation was associated with changes in either the number of spikes or the movement field plotted against desired saccade size in 26 (60%), whereas 17 did not (Fig. 9, top left). Of those 26 neurons, 2 (blue) showed a change only in the number of spikes, 12 (red) only in the movement field and 12 in both (purple). Of the 14 neurons that showed a significant change in the number of spikes associated with saccades to the adapted target step, 12 also exhibited changes in their movement fields as plotted against desired saccade size. Of the 24 neurons that exhibited changes in their movement fields, the changes were either toward the adapted direction (n = 6; Fig. 7A), away from the adapted direction (n = 9; Fig. 5C), or occurred rather uniformly throughout the movement field (n = 9; Fig. 5A).

Fig. 9, right, shows the breakdown according to direction of adaptation. Three of the 14 indeterminate field neurons evaluated with backward adaptation showed changes in the number of spikes test and in the movement field test. Four of the remaining 11 showed changes only in their movement fields (Fig. 9, top). Thus saccade amplitude adaptation affected some aspect of the discharge of 7 of the 14 indeterminate field neurons. Of the total of 29 closed field neurons, 2 of 10 evaluated during backward adaptation showed a significant change in the number of spikes. Both of those, as well as three of the other eight, showed changes in their desired-saccade-size movement-fields (middle pie). Thus adaptation affected the discharge of 5 of 10 closed field neurons during backward adaptation. Of the remaining 19 closed field neurons (bottom pie), all of which were evaluated during forward adaptation, 9 showed changes in the number of spikes, and 7 of those 9 in their movement fields. Five of the remaining nine closed field neurons evaluated during forward adaptation showed a significant change only in their movement fields. Thus 14 of the 19 closed field neurons were affected by adaptation. All together, 19 of 29 closed field neurons behaved differently in some way after saccade amplitude adaptation. Whether a neuron was affected by adaptation did not depend on the type of its movement field (closed or indeterminate) or the direction of adaptation (backward or forward).

For our entire population of neurons, the pre- and postadaptation movement fields plotted against desired saccade size were different in 60% (top left), but more (77%; 33/43; Fig. 9, middle left) exhibited changes if movement fields were plotted as a function of actual saccade size. If adaptation changed movement fields plotted as a function of desired saccade size,

![FIG. 9. The effects of adaptation sorted according to the direction (forward or backward) of adaptation and neuron type (indeterminate or closed field). Right: number of neurons that showed significant changes in the number of spikes test, the movement field test as plotted against desired saccade size or both are indicated by the blue, red, and purple sectors, respectively. The white sector identifies the number of units that showed no change in either test. Top left: proportions for the number of spikes test and movement field test as a function of desired saccade size (colors as in the preceding text). Middle: proportions considered as a function of actual saccade size (yellow; both represented by green). Bottom: proportions of all neurons that showed significant changes by ≥1 of the tests: number of spikes only (#sp, blue), movement field as a function of desired saccade size only (ds, red), movement field as a function of actual saccade size only (as, yellow), #sp and ds (purple), ds and as (orange), or as and #sp (green) starting clockwise from leftward.](https://jn.physiology.org/content/vol97/issue6/1403)
it usually (22/24) also changed movement fields plotted against actual saccade size (bottom). In 81% (35/43; bottom) of all our neurons, adaptation caused changes in the number of spikes (14/43), the desired-saccade-size movement field (24/43), and/or the actual saccade-size movement field (33/43).

Adaptation caused specific changes in the burst profile

For the typical neuron illustrated in Fig. 2, the changes in the number of spikes produced by saccade adaptation occurred preferentially during the early part of the burst. To determine whether portions of the burst were affected differentially during adaptation, we examined the effect of adaptation on several discharge parameters. For the 14 units that showed a significant change in the number of spikes test, Fig. 10A shows an increased number of spikes (open circles) or decreased number of spikes (open triangles) above or below, respectively, the line of unity slope. Backward adaptation was associated only with increases in the number of spikes in both indeterminate and closed field neurons (n = 5), whereas forward adaptation of closed field neurons could be associated with either an increase (n = 5) or decrease (n = 4). For most neurons, the increase or decrease in number of spikes was due to a concomitant lengthening (positive numbers) or shortening, respectively, of burst duration (Fig. 10B; r = 0.83, thin black line). If adaptation increased the number of spikes, the increase in duration was due to an increase in burst lead in all neurons (Fig. 10C, open circles lie above the unity slope line) and a smaller and less consistent delay or lag in the end of the burst (Fig. 10D) on average. If adaptation decreased the number of spikes, the modest decrease in duration was often associated with decreases in either burst lead (C, triangles) or burst lag times (D) or both. To illustrate directly the relation between burst lead and increased burst duration, Fig. 10E plots the change in lead against the change in burst duration. The linear fit accounts for 86% of the variance (r = 0.93, thin black line). The difference in the number of spikes and the duration of the burst associated with adaptation cannot be attributed to either the adaptation paradigm per se or to fatigue because some of our SC neurons that were subjected to similar conditions and numbers of trials exhibited no changes in burst parameters (e.g., Fig. 3).

In contrast, adaptation had smaller, less consistent effects on the magnitude (F) and no effects on the timing (G) of the peak burst rate. Adaptation caused a modest change in peak burst rate in only some neurons. When adaptation was associated with an increase in the number of spikes, most units showed no change in peak burst rate (for 10 of 14, data lay near unity line, open symbols) although a third, like the unit illustrated in Fig. 2, showed modest increases. Likewise, some but not all units with a decreased number of spikes showed a decrease in peak burst rate.

FIG. 10. Comparison of parameters of the burst accompanying saccades of similar size before and after adaptation for neurons that showed significant changes in the number of spikes test (open symbols) or in the movement field test (solid symbols) during saccade adaptation. Circles represent significant increases and triangles significant decreases. Parameters include mean number of spikes in the burst (A), change in burst duration as a function of the change in number of spikes (B), burst lead (re saccade onset; C), burst lag (re saccade end; D), change in burst lead as a function of the change in burst duration (E), peak discharge rate (F), and timing of peak rate (re saccade onset; G). In B, the linear regression for all points (thick black line) was y = 3.70x + 6.07 (r = 0.75). In E, the linear fit for all points (thick black line) is y = 0.61x + 2.31 (r = 0.87).
All of the preceding noted trends in discharge pattern were also seen in the 12 additional neurons that showed changes only in their movement fields plotted against desired saccade size. To compare pre- and postadaptation discharge, we used desired saccade sizes from the portions of the movement fields for which the 95% confidence limits did not overlap. For the saccades from these 12 neurons, we compared the changes in number of spikes, burst duration, burst lead, burst lag, peak firing rate and timing of the peak discharge (Fig. 10, filled symbols). The changes in the burst were similar to those produced for the 14 neurons that showed differences in the number of spikes test (Fig. 10, cf. open and filled symbols). Specifically, the change in number of spikes and burst lead were also correlated with the change in burst duration (thin dashed lines, \( r = 0.83 \) Fig. 10B and \( r = 0.85 \) Fig. 10E, respectively). For all 18 of 26 the neurons that exhibited an increase in discharge, the spikes were added at burst onset (Fig. 10C). For most of the neurons that showed a decrease in the number of spikes (5/8), the spikes were lost at burst onset.

To test whether saccades remained normometric (i.e., obeyed the main sequence relations between saccade size and peak velocity or duration; Bahill et al. 1975), we also examined whether there were changes in the peak velocity or saccade duration while we were recording from 30 randomly chosen neurons. In contrast to the changes in burst parameters just described, we never observed statistically significant changes in the metrics of the saccade. Similarly, we found no significant change in peak velocity or saccade duration with saccade amplitude adaptation in our nrt study (Takeichi et al. 2005a). Other reports (e.g., Straube et al. 1997) indicate that amplitude adaptation is associated with a trend toward longer saccade duration and lower peak velocity but it was not statistically significant.

**Recording location of SC neurons**

We confirmed our recording sites within the collicular map by histologically reconstructing our tracks in two monkeys (\( K \) and \( P \)), and we identified the location of most neurons on the basis of the chamber map, depth of the recording, the marking lesions, and the gliosis produced by the tracks. Based on these reconstructions, there was no topography of units with closed and indeterminate movement fields or neurons that did or did not exhibit changes in the number of spikes or movement field with adaptation.

**Discussion**

The discharge of the majority (35/43, 81%) of the SC neurons we tested in association with saccade amplitude adaptation showed significant \( (P < 0.05 \) after Bonferroni correction) changes in the number of spikes tests or in their movement field (Fig. 9). For all 14 that showed changes in the number of spikes test, the slope of the number of spikes linear regression with trial number was significant, indicating that the change was gradual. For those 14 and the 12 that showed significant changes in their movement field as a function of desired saccade size, the early part of the saccade-related burst was preferentially affected (Fig. 10). Only 1 of 43 SC burst neurons showed a change only in the number of spikes test, whereas 34 neurons showed changes when the movement field was plotted against either actual or desired saccade size (Fig. 9, bottom left pie). Consequently, the movement field test was a much more sensitive indicator of the effects of adaptation on the discharge of SC neurons than was a measure of properties of the burst at the adapted saccade size. Taken together, our data clearly show that saccade amplitude adaptation produces changes in neuronal discharge by the time that the saccade command is expressed in the SC.

Although adaptation is associated with a variety of alterations in SC neuronal discharge that are not simple multiplicative or additive changes in the burst discharge, several consistent trends emerge. Backward adaptation is associated consistently only with increases in the number of spikes, whereas forward adaptation is associated equally often with increases and decreases. Moreover if the number of spikes test showed an increase/ decrease, the movement field tests also showed an increase/decrease at some location in the postadaptation movement field. However, such changes in the movement field could occur either toward (25%) or away (58%) from the part of the field associated with the adapted saccade or throughout the entire movement field (17%). A dramatic example of a preferential change for some saccade amplitudes occurred for those neurons (42% of altered movement fields plotted against desired saccade size) that developed discharge for amplitudes where there was none before adaptation (Figs. 5C and 8A).

The different types of changes associated with adaptation did not appear to be correlated with the preadaptation behavior of SC burst neurons. In particular, the effects of adaptation were not related to the neuron’s preferred amplitude or direction, the vigor, and time course of the burst or the neuron’s location in the SC. Nor did the number of adaptation trials or the amount of adaptation have any influence. Stated another way, because the SC motor map is defined by its spatial distribution of preferred vectors, our data provide no evidence for topographic changes or remapping of the collicular map in association with adaptation.

Finally, the observed changes were associated with adaptation and not due to other factors. They were not simply the result of fatigue during the long recording sessions because the changes were both increases and decreases in discharge and fatigue would be expected to have the same effect in all experiments. Also the changes in discharge were not due to the inadvertent inclusion of visually evoked spikes because our technique for marking the burst (methods) excluded such discharge. Moreover, only nine of our neurons had an obvious visual response, and only three of those visuomotor neurons showed a change in number of spikes.

**Comparison with other studies**

Our results are consistent with those of Frens and van Opstal (1997), but our conclusion that adaptation affects the discharge of many neurons in the SC differs from theirs because of our movement field analysis. Like their neurons (63%), ~70% of our neurons also showed no change in the number of spikes at the desired saccade size after adaptation. If we consider only our 24 cells tested during backward adaptation (the paradigm that they used), 5 showed changes in the number of spikes during adaptation, whereas 19/24 (79%) showed no change just like the majority (63%) of theirs. However, the data of Frens
and van Opstal (1997) did not exclude the possibility that changes had occurred elsewhere in the movement field, and we show that such changes did occur for 50% (12/24) of this subset of our neurons.

There were other differences between the two studies. All of the neurons reported here were recorded during significant amplitude adaptations, whereas Frens and van Opstal (1997) did not achieve significant saccade amplitude changes while recording 18 of their 30 neurons. We optimized our chances of producing a change in activity during adaptation by concatenating adapt step size, by using many more trials (average = 715 vs. their 250–500), and by allowing the adaptation to proceed as long as it took to produce a significant change. We also tailored the adaptation direction (forward or backward) and the adapted saccade size to produce the biggest change in unit activity based on the shape of the preadaptation movement field. These experimental differences likely explain our much larger percentage (72% cf. 8%) of SC neurons that showed changes of some sort. If we consider significant changes in the number of spikes, desired-saccade-size movement field, or actual-saccade-size movement field, an even larger proportion (81%) of our neurons showed some statistically significant change after adaptation.

Our results refute the early microstimulation results that used supramaximal currents to elicit “saccades” from the SC following adaptation (Fitzgibbon et al. 1985; Melis and van Gisbergen 1996) but are consistent with the later study in which stimulating the SC at lower current intensities showed that elicited movements were affected by adaptation (Edelman and Goldberg 2002). We suggest that our recordings and the lower current stimulation study more accurately reflect the changes in the SC associated with saccade adaptation.

Site of adaptive plasticity

Whereas Frens and Van Opstal (1997) concluded that saccade adaptation occurs downstream of the SC, our data support the proposal that the SC itself might be the site of adaptive plasticity or, at least, that plastic changes produced elsewhere are funneled through the SC. This conclusion is consistent with other behavioral, physiological, and anatomical studies. In non-human primates, adaptation of targeting saccades transfers robustly to express, memory, and delayed saccades (Fuchs et al. 1996), implying that the adaptation occurs at a site common to all these saccade types (see Hopp and Fuchs 2004 for review). The SC, the burst neurons of which discharge for all these saccade types, has been implicated as that site (Hopp and Fuchs 2002). Indeed, several studies (see Scudder et al. 2002 for review) have shown that the SC is the major relay of convergent saccade commands from visual and motor cortical areas that are presumably the origin of the different types of saccades. In turn, all SC premotor neurons are thought to contribute to the drive to the brain stem burst generator (Gandhi and Keller 1997; Istvan et al. 1994; Scudder et al. 1996). We feel that it is unlikely that the adaptive site is downstream of the SC and that the SC receives feedback about those changes. Previously, we showed that the SC receives feedback from the brain stem about on-going saccades (Soetedjo et al. 2002b). However, the changes produced by adaptation cannot reflect feedback about saccade size from downstream sources because brain stem feedback affects the end of the saccade (Soetedjo et al. 2002b), whereas adaptation causes early changes in SC neuron discharge.

The increasingly earlier SC discharge that occurs with adaptation is consistent with changes that have been observed in nrtp and the oculomotor cerebellum. We (Takeichi et al. 2005a) showed that nrtp neurons discharge progressively earlier during adaptation and Scudder and McGee (2003) and Inaba et al. (2003) have observed earlier discharge in caudal fastigial neurons associated with saccade adaptation. Such changes may reflect their input from the earlier discharge we see in SC and nrtp neurons.

Changes in the SC saccade command during adaptation

Our data indicate that adaptation alters the efferent signal emanating from most SC burst neurons. Based on our previous results in nrtp (Takeichi et al. 2005a), we suspect that those neurons that showed increased discharge either in number of spikes or in their movement field with backward adaptation (12/24) impinge on the open field and the few closed field nrtp neurons that also increased their discharge during backward adaptation. That increased discharge, in turn, could cause an increase in vermal discharge that would be sent to the cFN and serve to terminate saccades earlier by one or more of several potential mechanisms (see Inaba et al. 2003; Scudder and McGee 2003). Indeterminate field neurons that showed an increase in discharge during forward adaptation (7/19) might act in a similar fashion. Those few (4/19) SC neurons that displayed a decreased discharge during forward adaptation might project to those few (only 1 of 13) nrtp neurons tested during forward adaptation that decrease their discharge during forward adaptation. Alternatively, they might project only to the saccadic burst generator, thereby supplying a weaker drive that also would produce a smaller saccade.

Conclusion

We have shown that saccade amplitude adaptation is associated with statistically significant changes in the number of spikes in the majority (81%; Fig. 9) of SC neurons. These results along with previous studies of saccade adaptation lead us to hypothesize that adaptive plasticity in the saccade system occurs at the SC or that adaptive changes elsewhere (e.g., the frontal eye fields) are funneled through the SC to the brain stem saccade generator.

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