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The role of the superior colliculus in saccade initiation: a study of express saccades and the gap effect

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Abstract

Neural mechanisms underlying the initiation of saccadic eye movements were studied by recording the activity of neurons in the superior colliculus of rhesus monkeys that had extensive experience on the gap task using targets restricted to one visual field. The superposition of visual activation upon the increased excitability occurring on gap trials facilitates the occurrence of a motor burst with extremely short latency; the motor burst is tightly coupled to saccade onset for the full range of saccadic reactions times, both regular and express. We found no evidence that express saccades are a special class of saccades triggered directly by visual responses. The low frequency activity, necessary for the occurrence of express saccades, neither initiates express saccades nor serves as an accurate predictor of the direction or latency of saccades. Based upon these findings, the hypothesis that the motor burst of collicular neurons serves as a signal for triggering saccade onset can now be extended to express saccades.

Keywords: Superior colliculus; Saccade initiation; Gap effect

1. Introduction

The translation of sensory signals into commands for initiating and controlling action is a fundamental problem of integrative neuroscience that requires answers to many questions. For example, how are the direction, amplitude, and speed of a movement controlled by the spatial and temporal pattern of neuronal activity observed in widespread subcortical and cortical areas? In a situation in which many alternative courses of action are appropriate, how is a particular movement selected for execution? And what factors determine when that movement will be initiated? Results described in this report build upon recent advances in understanding the neural mechanisms involved in determining when a movement will be initiated.

If subjects are asked to look as quickly as possible to a visual target that appears immediately after an original fixation stimulus disappears, saccadic reaction times are usually between 180 and 220 ms. The average reaction time is significantly reduced (the 'gap effect') if the fixation stimulus is extinguished and the eccentric target appears after an interval (the 'gap') of 200–600 ms (Saslow, 1967). Given extensive practice on the 'gap' task, subjects may generate a bi- or tri-modal distribution of reaction times (Fischer & Boch, 1983; Fischer, Boch & Ramsperger, 1984) and the modal value of the earliest distribution can be in the range of 80–100 ms. Saccades with these very short reaction times are called express saccades. Moreover, these short latency saccades are movements made in response to visual stimuli, not merely anticipatory movements based upon prediction of target location or time of occurrence (Rohrer & Sparks, 1993). Thus, the neural bases of express saccades are of particular interest because after afferent and efferent delays are subtracted from the reaction time interval, very little time remains to compute the location of the target and to program the direction and amplitude of the movement.

Attentional mechanisms (e.g. Mayfrank, Mobashery, Kimmig & Fischer, 1986; Fischer, 1987; Fischer & Breitmeyer, 1987; Braun & Breitmeyer, 1988), anticipatory movements (Kalesnykas & Hallett, 1987; Kowler, 1990), release from an active fixation process (e.g. Reuter-Lorenz, Hughes & Fendrich, 1991; Kingstone &

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Klein, 1993; Tam & Stelmach, 1993), increased general response readiness (e.g. Ross & Ross, 1980, 1981; Kingstone & Klein, 1993), and early preparation of eye movements (e.g. Becker, 1989; Kowler, 1990; Reuter-Lorenz et al., 1991; Kingstone & Klein, 1993; West & Harris, 1993) have been proposed as factors underlying the gap effect and express saccades. A number of recent experiments have focussed on two hypotheses about the generation of express saccades-hypotheses that emerged from behavioral studies (Sommer, 1994; Pare & Munoz, 1996; Sommer, 1997), lesion experiments implicating the superior colliculus (SC) in the generation of express saccades (Schiller, True & Conway, 1980; Schiller, Sandell & Maunsell, 1987; Schiller & Lee, 1994), experiments demonstrating that the frequency of occurrence of express saccades is altered by pharmacological manipulation of the rostral SC (Munoz & Wurtz, 1992, 1993), and studies of neuronal activity during regular and express saccades (Dias & Bruce, 1994; Dorris & Munoz, 1995; Munoz & Wurtz, 1995; Edelman & Keller, 1996; Dorris, Pare & Munoz, 1997; Edelman & Keller, 1998; Everling, Pare, Dorris & Munoz, 1998b). According to the visuomotor hypothesis of Sommer (1994), the bimodal distribution of saccade latencies observed during the gap task results from the interaction of an active fixation process and the activity of visual-motor cells in the SC. Another hypothesis (Dias & Bruce, 1994; Pare & Munoz, 1996; Dorris et al., 1997; Sommer, 1997) proposes that express saccades occur when visual activity is superimposed upon a preexisting state of increased neuronal excitation.

Previous studies of collicular activity during express saccades compared the activity associated with saccades with regular latencies with the activity accompanying saccades with express latencies. These experiments were performed in animals with extensive exposure to gap trials in which targets were presented in both left and right visual fields. We re-examined the role of the SC in the generation of express saccades by measuring the latency of the target-related and movement-related activity of visual, motor, and visual–motor cells during trials in which the full range of reaction times, both the regular and express, were generated. These recordings were obtained from animals in which training on the gap task was restricted to trials in which the target was presented in only one visual field.

2. Methods

Neuronal activity was recorded from the superior colliculi of two adolescent rhesus monkeys (*Macaca mulatta*). All experimental protocols were reviewed and approved by the Institutional Animal Care and Use Committee of the University of Alabama at Birmingham and conformed to all standards set forth in the National Institutes of Health's Guide for the Care and Use of Animals. Each subject underwent two sterile surgical procedures under sodium pentobarbital anesthesia. A head restraint device and a scleral search coil (Fuchs & Robinson, 1966; Judge, Richmond & Chu, 1980) were implanted in the first procedure. In the second, a stainless steel receptacle for a hydraulic microdrive was mounted over a 10 mm diameter craniotomy centered on the midline at stereotaxic coordinate zero (anterior–posterior). Except during recording sessions, the receptacle was sealed with a sterile teflon plug.

2.1. Recording procedures

Using the scleral search coil technique (Robinson, 1963), eye position signals were digitized at 500 Hz and stored for later analysis. Single unit, extracellular recordings were made from the SC with commercially available, parylene coated, tungsten electrodes using standard chronic recording techniques (Mays & Sparks, 1980). The spike signal was filtered above 3 kHz and below 300 Hz before being passed to a window discriminator to generate a standard pulse. The interspike interval was measured with a 100 μs resolution and stored in digital form.

2.2. Behavioral tasks

In most experiments, an array of light-emitting diodes (LEDs) served as targets. The array consisted of 11 rows of 13 LEDs, equally spaced at 4° intervals, that extended $\pm 24°$ horizontally and $\pm 20°$ vertically from a central fixation position. Each LED subtended a visual angle of approximately 0.2°. In a few experiments, the visual target was a small spot of light presented on a large screen oscilloscope (Hewlett-Packard 1310 or Hewlett-Packard 1321).

Data were obtained while the subjects were performing the three tasks described in Fig. 1. During the step task (Fig. 1B), monkeys were required to maintain fixation of a central target (T1) for a variable period of time (200–1400 ms varied in increments of either 100 or 400 ms). At the end of this interval, the fixation light was extinguished, and, simultaneously, a second peripheral target (T2) was illuminated. Reward was contingent upon looking to the location of the new target within 500 ms. During the delayed saccade task (Fig. 1C), subjects were required to maintain fixation of a central target (T1) while a second eccentric target (T2) was presented. After 100–500 ms, the central fixation target was extinguished and reward was contingent upon looking to the peripheral target within 500 ms. During recordings obtained while the animal was performing this task, visual activity coupled to the onset of a visual stimulus was separated in time from activity

coupled to saccade onset. Thus, cells displaying increases in activity 50–100 ms after target onset were labeled visual cells whereas cells displaying increases in activity 10–50 ms before saccade onset on trials with 300–500 ms delay intervals were labeled motor cells. Some cells met both criteria and were categorized as visual-motor cells. In the gap task (Fig. 1D), the offset of the fixation target (200–1400 ms duration; 100 or 400 ms increments) was followed by an interval (the 'gap') in which the monkey was required to direct the line of sight to the position of the (now absent) central fixation target. At the end of this period, a target (T2) was presented at an eccentric location. If a saccade directed gaze to the new target within 500 ms, a reinforcement occurred.

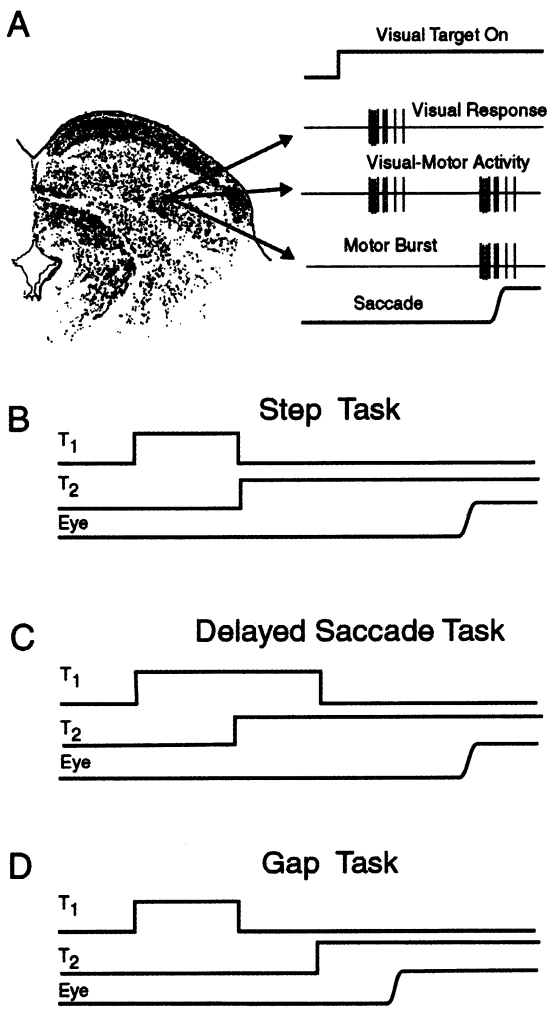

Fig. 1. Schematic diagram of the types of cells recorded and trial types. (A) Three major cell types in the deep layers of the superior colliculus could be involved in mediating express saccades: visual cells with activity linked to the onset of visual stimuli in their receptive fields; motor cells with activity tightly coupled to saccade onset; and visual-motor cells displaying both visual and saccade-related activity. (B) Step task: the eccentric target (T2) appeared immediately after the fixation target (T1) was extinguished. (C) Delayed saccade task. The target (T2) was presented while the fixation stimulus (T1) was present but reinforcement was contingent upon delaying saccade initiation until the fixation stimulus disappeared. (D) Gap task. The offset of the fixation stimulus was followed by an interval of 200–600 ms in which no stimulus appeared. Then the eccentric target was presented.

For all tasks, reward was contingent on the completion of saccades to a spatial window around the target (usually 1.5–2° on either side of the target) within 500 ms, which is much longer than the normal saccade reaction time of monkeys. No additional reward was given for short latency saccades. The inter-trial interval varied randomly between 1 and 3 s.

2.3. Statistical analyses

Velocity criteria (40°/s) were used to automatically define the beginning and end of saccades. Burst onset and offset were defined by instantaneous spike frequency criteria. Burst onset was typically defined as four consecutive spikes in excess of 300 spikes/s; offset as four consecutive intervals with instantaneous frequencies less than 300 spikes/s. Automatic measurements were checked on a trial by trial basis and manual adjustments to the burst onset or offset measurements were made on rare occasions. These measurements were used to generate x–y plots of latency of visual and motor bursts as a function of saccade latency and to calculate the slopes and intercepts of the least-squares lines of best fit.

An analysis of the 'merged' visual and motor bursts was performed using data obtained from nine cells selected because of the reliability of the visual and motor bursts during delayed saccade trials. The amplitude of action potentials often becomes smaller when cells discharge a high frequency burst, but the recordings of the selected cells displayed neither 'drop outs' (instantaneous frequency records that could be accounted for by one missing spike) nor frequencies greater than 1200/s (which can occur when the trigger level is too low and a second cell is recruited into action during a saccade). For each of the nine cells, we selected three or more gap trials in which the visual and motor bursts were clearly separated. For each of the selected trials, all the action potentials occurring during and after the motor burst spike train were shifted, as a block, forward in time by 5 ms. The shifted spikes were combined with the unshifted spikes (the action potentials occurring from target onset until the onset of the motor burst) to create a new instantaneous spike frequency distribution. If the instantaneous firing rate of the derived frequency plot was greater than 1200 spikes/sec, then the spike producing the 'impossible' interspike interval was dropped, and the instantaneous firing rate was calculated using the next spike. This process continued iteratively (using 5 ms increments) until we obtained the 'shifted' instantaneous frequency plots that best matched trials with express latencies in

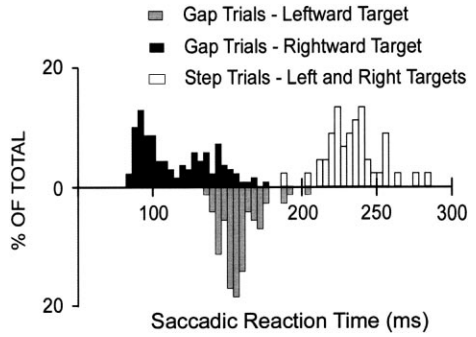

Fig. 2. Distribution of saccadic reaction times obtained during a typical recording session near the end of the experiment. A bimodal distribution of reaction times was obtained on gap trials when visual targets were presented in the right visual field. The distribution of reaction times obtained when targets were presented in the left visual field was significantly reduced compared to the distribution obtained on step trials, but did not contain reaction times in the express range.

which the visual and motor bursts were fused 'naturally'. The 'best' match was determined using the nonparametric Kolmogorov–Smirnov two-sample distribution-free test. Also, this statistic was used to test the null hypothesis that the distribution of interspike intervals of merged bursts artificially created by summing visual and motor bursts was drawn from the same population of interspike intervals associated with 'real' merged bursts.

3. Results

3.1. Saccadic reaction times

Prior to recording sessions, training on gap trials was restricted to a small set of targets presented in the right visual field (activating cells in the left superior colliculus) and a high percentage of express saccades was associated with a restricted range of target locations. Exposure to gap trials was gradually extended to targets in the left visual field as a result of experience obtained during some recording sessions, but as illustrated in Fig. 2, the subjects used in these experiments generated express saccades only to targets presented in the right visual field. Note that all recording data presented in this paper were obtained from neurons in the left superior colliculus.

3.2. Relationships between the latency of visual and motor bursts and saccadic reaction time

We recorded the activity of visual ($N = 9$), motor ($N = 14$), and visual–motor ($N = 18$) cells in the left superior colliculus while monkeys were performing three tasks that produced a large range of reaction times (Fig. 1). Reaction times were usually between 200 and 300 ms on step and delayed saccade trials but between 80 and 220 ms on gap trials. Raster displays of the activity of three cells displaying visual, visual-motor and motor activity are shown in Fig. 3. Activity associated with step (top row), 150 ms gap (middle row) and 300 ms gap (bottom row) trials are shown. Step and gap trials, randomly interleaved during data collection, were sorted according to trial type and arranged in descending order of saccadic reaction time. The visual cell (Fig. 3A) displayed a biphasic response to target onset with a latency of 70–80 ms and also generated a phasic increase in activity as the target image moved across the retina during a saccade. The latency of the activity evoked by target onset was similar on step and gap trials. Variations in saccade latency were not associated with consistent changes in the latency of visual responses (Fig. 3D, Table 1).

Visual–motor cells generated two transient increases in activity: one associated with target onset, and the other preceding saccade onset (Fig. 3B). The latency of the visual burst (70–80 ms) was relatively constant across trials and trial types. Because the second burst was closely linked to the onset of the saccade, the interval between the sensory and motor bursts decreased as saccadic latency was reduced. At extremely short latencies, the visual and motor burst merged (Edelman & Keller, 1996; Dorris et al., 1997) and the onset or offset of either the visual or the motor burst could not be defined. For this cell, and all other visual-motor cells observed (see Table 1), the latency of the visual burst (Fig. 3E, gray) is a poor predictor of saccade latency whereas the latency of the second motor burst (black) is highly correlated with saccade latency during all trials in which the two bursts are clearly distinguishable. For the trials shown in this panel, reaction times were between 200 and 300 ms on step trials, from 150 to 220 ms on 150 ms gap trials and between 90 and 150 ms on 300 ms gap trials (see histogram insets).

The activity of a cell generating a motor burst but not a visual burst is illustrated in Fig. 3C. During each trial, the cell generated a low frequency prelude of activity and then a vigorous burst. During step trials, reaction times were between 200 and 300 ms (see inset). During 150 ms gap trials the interval between target onset and burst onset was reduced and the reaction time distribution shifted to the left. The interval between target onset and the motor burst ranged from 70 to 150 ms during 300 ms gap trials and this pattern of neural activity was associated with short-latency saccades, many in the express range. The tight coupling between the onset of the motor burst and saccade onset, reported previously for saccades with regular latencies (Sparks, 1978), extends into the short latency express saccade range (Fig. 3F, Table 1).

3.3. The stereotyped pattern of activity observed on gap trials

Raster and average frequency plots of the activity of a cell in the left SC that generated a visual response and a vigorous motor burst before 8° rightward saccades are shown in Fig. 4. A stereotyped pattern of activity was observed during gap trials (panels C–J). The low rate of activity observed during the fixation interval continued for 60–70 ms after fixation target offset (the left dashed vertical line). An approximately 100 ms period of reduced activity linked to the offset of the fixation target followed and then the rate of activity increased. The higher rate of activity was sustained until shortly before a saccade, at which point it either stopped (ipsilateral) or a visual and motor burst occurred (contralateral). An increase in low frequency activity linked to the offset of the fixation stimulus was observed in 12 of the 18 visual-motor cells and four of the 14 motor cells studied.

The increase in low frequency activity, but not the period of reduced discharge rate, was observed previously in studies of neuronal activity in the frontal eye fields (Dias & Bruce, 1994) and SC (Dorris et al., 1997) during gap trials. We observed the reduction in activity in only four cells but comparable periods of reduced excitability, if present, would not have been detected in most cells because of low background firing rates. Thus, we looked for other evidence for a general reduction in excitability following fixation offset. If the reduced activity reflects a period of active inhibition and/or reduced excitability affecting widespread regions of the collicular map, then the visual response of collicular neurons should be reduced on step trials. On step trials, fixation stimulus offset and target onset occur simultaneously and the putative 100 ms period of reduced excitability would include the interval during which visual responses occur. Visual responses on delayed saccade trials should not be affected because visual responses occur before the fixation stimulus is

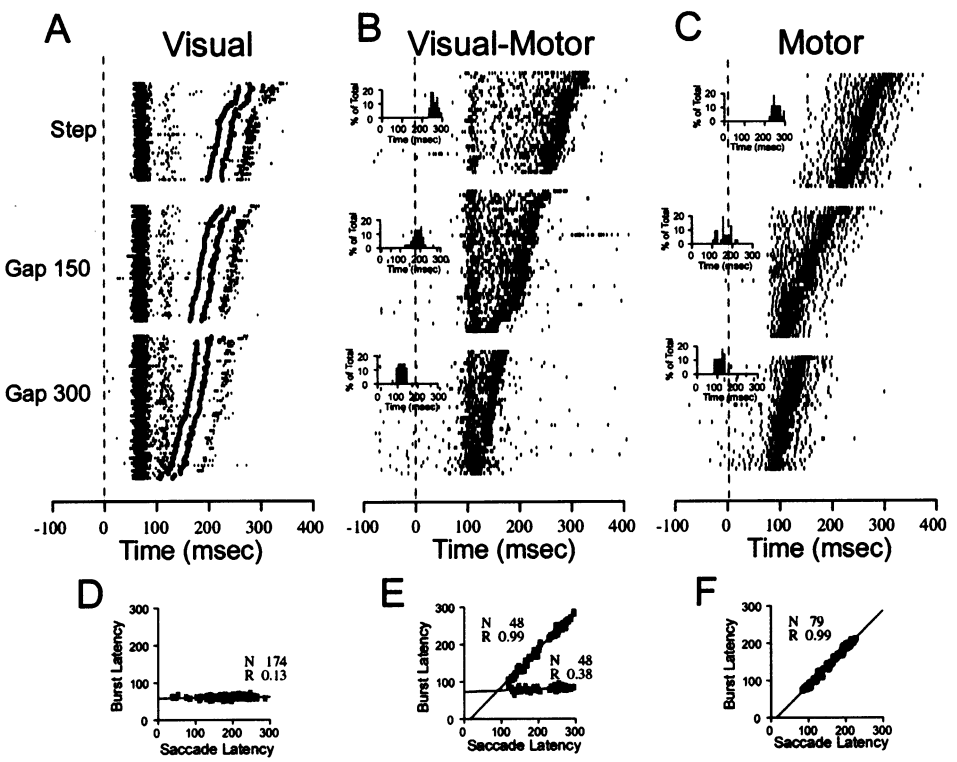

Fig. 3. Raster display of the activity of a visual (A), visual-motor (B), and motor (C) cell during step trials and 150 and 300 ms gap trials. Each tick mark represents the occurrence of an action potential and each row of tick marks represents the activity observed during a single trial. The broad, gray tick marks in panel A represent saccade onset and offset. The visual cell displayed a second period of activation associated with the target image motion on the retina during the saccade. During gap trials, the fixation stimulus was extinguished 150 or 300 ms before the target appeared. The trials are aligned on target onset (the vertical line) and each set of trials is arranged in descending order of saccadic reaction time. Delayed saccade trials, step trials, 150 ms gap trials, and 300 ms gap trials were randomly interleaved during data collection. Histogram insets show the distribution of reaction times observed while recording from the visual-motor and motor cells. (D) Visual burst latency as a function of saccade latency for the visual cell illustrated in panel A. (E) Visual (gray) and motor (black) burst latency as a function of saccade latency for the visual-motor cell illustrated in panel B. Data points for express saccades with the shortest latencies are not illustrated because the onset of the visual and motor bursts could not be defined. (F) Motor burst latency as a function of saccade latency for the cell illustrated in panel C. Saccade onset was defined using a velocity criterion (40°/s). Burst onset was defined as the first of four consecutive instantaneous frequency values greater than 300 spikes/s.

Table 1
Relationship between latency of visual and motor bursts and saccade latency for visual, visual-motor, and motor cells[a]

Cell	V_r	V_{slope}	V_n	M_r	M_{slope}	M_n
Visual cells						
da0117	0.32	0.02	107	–	–	–
da0227	0.49	0.09	20	–	–	–
da0303	0.13	0.01	174	–	–	–
da0311	0.04	0.01	55	–	–	–
dc0212	0.15	0.02	75	–	–	–
da1223	0.10	0.01	58	–	–	–
db1223	0.16	0.02	59	–	–	–
dx0107	0.12	0.02	127	–	–	–
dd0401	0.35	0.05	15	–	–	–
Visual-motor cells						
da0109	−0.01	0.00	31	0.98	0.95	31
da0114	0.63	0.12	67	0.99	0.97	35
da0226	0.09	0.02	35	0.99	0.97	36
da0307	−0.01	0.00	15	0.96	0.99	15
da0312	0.30	0.03	50	0.99	1.07	30
da0402	0.29	0.01	18	0.99	1.05	27
da0407	0.25	0.07	35	0.94	0.98	35
da1121	0.25	0.04	76	0.99	1.08	69
dx0130	0.19	0.02	138	0.98	1.01	43
dx0312	0.16	0.02	29	0.99	1.07	29
db0109	0.59	0.05	24	0.99	1.04	23
db0122	0.43	0.10	30	0.97	0.98	30
db0226	0.29	0.04	58	0.98	1.02	29
db0311	0.10	0.02	76	0.99	1.05	56
dx0307	0.58	0.11	46	0.98	0.96	114
dc0402	0.11	0.01	83	0.98	0.92	32
da1122	nd	nd	nd	0.99	1.01	61
db0402	nd	nd	nd	0.99	1.01	73
Motor cells						
da0110	–	–	–	0.98	1.01	109
da0115	–	–	–	0.99	0.97	56
da0128	–	–	–	0.99	1.01	79
da0324	–	–	–	0.99	0.97	87
da0408	–	–	–	0.99	1.05	39
da1104	–	–	–	0.93	0.92	104
da1122	–	–	–	0.99	1.01	66
db0110	–	–	–	0.99	1.02	100
dx0115	–	–	–	0.99	1.00	112
dx1014	–	–	–	0.98	0.94	119
de0212	–	–	–	0.98	1.04	72
da1220	–	–	–	0.99	1.03	104
da1119	–	–	–	0.99	1.03	45
da1125	–	–	–	0.99	1.01	37

[a] Correlation coefficients (V_r, M_r) slope constants, (V_{slope}, M_{slope}), and number of cases (V_n, M_n) for visual, visual-motor, and motor cells.

extinguished. Fig. 5 compares the visual responses of three cells (A, B, C) on step and delayed saccade trials. The number of spikes generated, the peak frequency, and average frequency of visual responses observed on delayed saccade trials were significantly greater than the same measures of visual responses obtained on step trials. As illustrated in Fig. 6, the peak frequency of the transient visual responses on delayed saccade trials was greater than the peak frequency of responses on step trials for 20 of the 23 cells for which sufficient data were available for this analysis.

From inspection of the raster and frequency plots in Fig. 4B–J, the interval between the visual response and the motor burst appears to be related to the level of increased activity present immediately before the visual response. During step trials (panel B) visual responses were superimposed on the low frequency discharge present at the offset of the fixation target and the onset of the eccentric target (dashed vertical line), there was a relatively long interval between the visual and motor bursts, and reaction times were between 200 and 300 ms (see inset). During 150 ms gap trials (panel D), visual responses were superimposed upon a modest increase in activity, the interval between visual and motor bursts was reduced, and the reaction time distribution shifted to the left (see inset). During 300 and 350 ms gap trials (panels H and J), visual responses occurred after a more pronounced increase in discharge rate, the visual and motor burst often fused, and a large number of express saccades were observed (insets).

For the cell illustrated in Fig. 4, the relationships between saccadic reaction time and the level of increased activity observed on 150, 200, and 300 ms gap trials are shown in Fig. 7. An index of the level of increased activity was obtained by counting the number of spikes occurring from 10 to 60 ms after target onset. This interval samples the stereotyped increase in activity for trials with all gap intervals but does not include visual responses of cells in this data set. When the visual targets were in the cell's receptive field (contralateral targets, Fig. 4, panels D–J), visual responses were superimposed upon an increase in activity and reaction time was inversely related to the level of increased activity (Fig. 5, unfilled circles; this relationship is fully documented for a large sample of collicular cells in Dorris et al., 1997). However, when visual targets were not in the cell's receptive field (ipsilateral targets, filled squares), the same levels of increased activity were associated with significantly longer reaction times. Note that the lack of a general relationship between the level of low-frequency activity and saccadic reaction time would probably be obscured in animals trained to generate express saccades to targets presented in both visual fields.

3.4. Merging of the visual and motor bursts of visual-motor cells

During trials with the shortest reaction times, visual-motor cells appear to generate a single burst of activity that may be more vigorous than the visual burst alone (Edelman & Keller, 1996; Dorris et al., 1997). The gradual reduction in the interval between the visual and motor bursts observed when trials are ranked in order of reaction time (e.g. Figs. 3B or 4D–F), suggests that

the merged burst may merely reflect a physiological summation of visual and motor bursts. The data presented in Fig. 8 are consistent with this hypothesis. Panels A–D present instantaneous frequency and horizontal eye position plots for four trials with reaction times of 170, 130, 96, and 94 ms. As reaction time was reduced, the interval between the first (visual) and the second (motor) burst was also reduced until the visual and motor bursts completely overlapped (panel D). The instantaneous frequency plots shown in Panels E, F, and G were formed by: (a) shifting, as a block, all the action potentials occurring during and after the motor burst forward in time by 75 (E), 35 (F), or 10 (G) ms; (b) combining the shifted spikes with the unshifted spikes (action potentials occurring from target onset until the onset of the motor burst); but (c) excluding instantaneous firing rates greater than 1200 spikes/s (see Section 2 for details). For the nine cells that met criteria for this analysis (see methods), the artificial 'merged bursts' (e.g. panels E, F and G) were quite similar to the merged bursts observed during express saccades (e.g. panel H). Moreover, for all nine cells, we were unable to reject the hypothesis that the interspike intervals of the artificially created merged bursts were drawn from the population of interspike intervals associated with 'real' merged bursts.

4. Discussion

During gap trials we observed a stereotyped pattern of collicular activity linked to the offset of the fixation target. A brief (approximately 100 ms) period of reduced activity began about 60–70 ms after the offset of

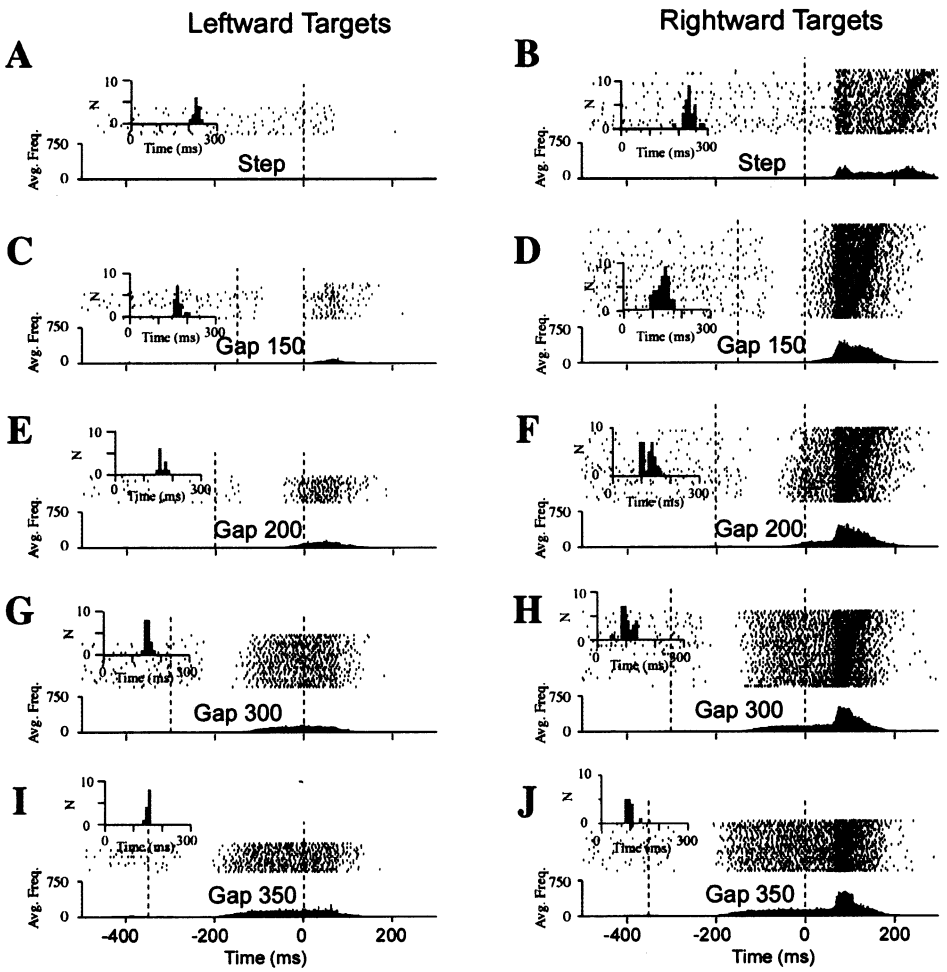

Fig. 4. Raster and average frequency plots of the activity of a cell in the left superior colliculus before and during saccades to leftward (ipsilateral — left column) and rightward (contralateral — right column) targets made during step trials (top row), 150 (second row), 200 (third row), 300 (fourth row), and 350 (bottom row) ms gap trials. During this recording session, two targets were presented: one 8° to the left (left column) and one 8° to the right (right column). The 12 conditions (two targets, four gap intervals, step and delayed saccade trials (not illustrated)) were randomly interleaved. The trials were sorted according to trial type and arranged in descending order of reaction time. Rasters are aligned on target onset. For gap trials, the first dashed vertical line represents fixation target offset and the second represents target onset. Average saccadic reaction time, standard deviation and *N* for the trials in each panel were: (A) 226.3, 11.4, 14; (B) 237.0, 19.9, 30; (C) 168.6, 14.0, 18; (D) 131.9, 21.7, 44; (E) 161.5, 10.9, 13; (F) 120.8, 20.7, 35; (G) 147.8, 20.3, 26; (H) 98.4, 17.9, 36; (I) 147.9, 25.0, 14; and (J) 93.8, 14.1, 25.

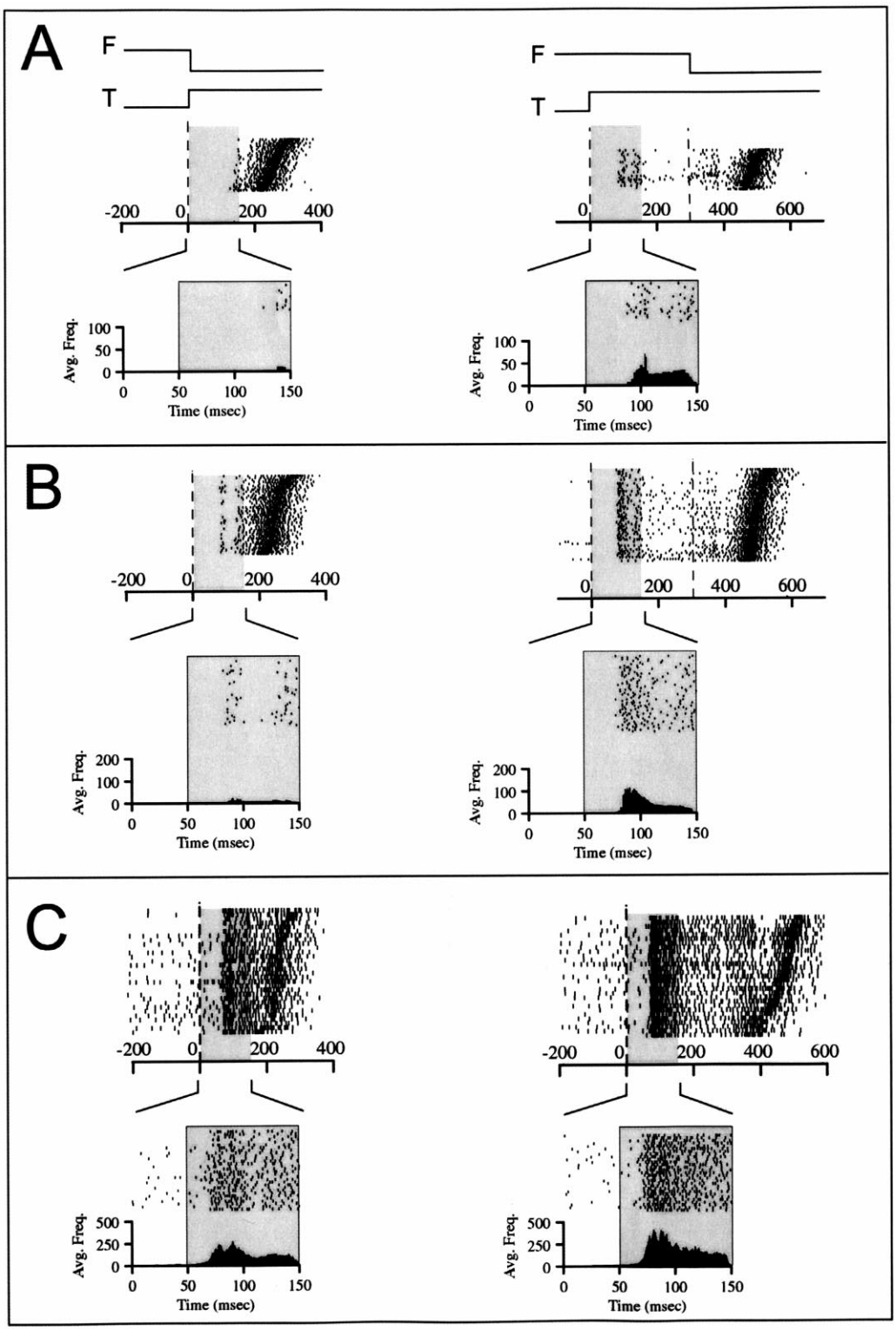

Fig. 5. Comparison of visual responses on step and delayed saccade trials for three cells. F, fixation target; T, eccentric target. In each panel, the top row of rasters displays activity during the entire trial. The 150 ms period following the onset of the eccentric target (shaded area) is expanded in the raster and average frequency plots in the next row. The shaded region in the expanded plot represents the time when the reduced excitability, if present, would be evident. (A) Example of a cell with little or no visual response on step trials, but a clear target-onset related increase in activity on delayed saccade trials. (B) Example of a cell with a weak visual response on step trials but a more pronounced response on delayed saccade trials. (C) Example of an increased response on delayed saccade trials for a cell with a vigorous visual response on step trials.

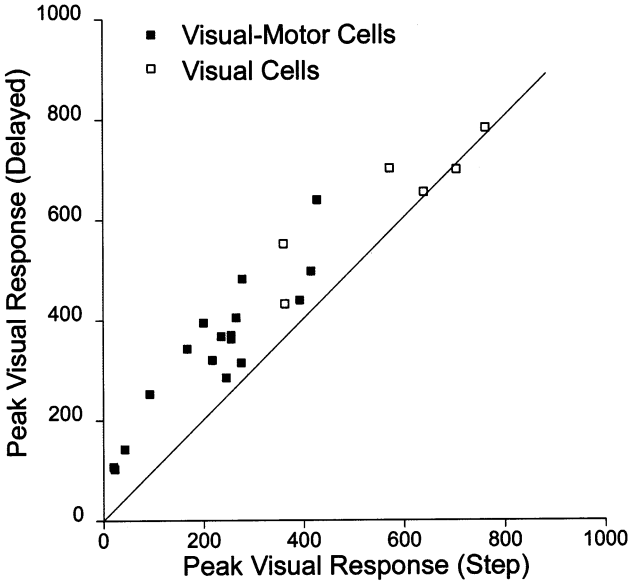

Fig. 6. Comparison of the peak visual response on delayed saccade trials (ordinate) with the peak visual response on step trials (abscissa). Each square represents one cell. Peak visual responses were defined as the maximal value of the average instantaneous frequency response occurring within 100 ms of target onset.

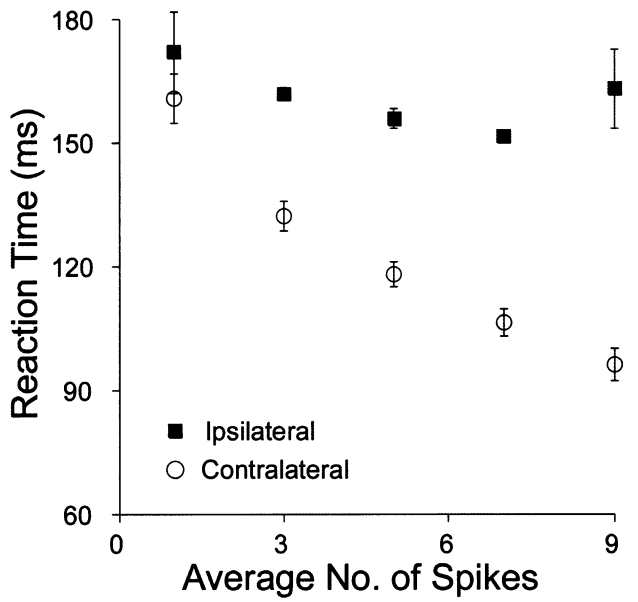

Fig. 7. Mean and standard error of saccadic reaction time as a function of the average number of action potentials in the period from 10 to 60 ms after the onset of ipsilateral (filled squares) or contralateral (open circles) visual targets.

the fixation target and was followed by an increase in activity that continued until saccade initiation. Express saccades occurred when motor bursts had extremely short latencies, events which were only observed when visual responses were superimposed upon the stereotyped increase in discharge rate. These results are discussed in the context of the visuomotor and early activation hypotheses for the generation of express saccades and the role of collicular saccade-related burst neurons in the initiation of regular and express saccades.

4.1. The visuomotor hypothesis

The visuomotor hypothesis of Sommer (1994) attributes the bimodal distribution of reaction times observed on gap trials to an interaction between an active fixation process and the visual and motor activity of visual–motor cells. According to the hypothesis, during step trials an active fixation process negates the effect of the first, visually-triggered, burst of visual–motor cells and saccades are triggered by the second, motor, burst. On gap trials, because the fixation-related inhibitory signal has decayed, the saccade is initiated by the target-related burst of activity. Thus, the prediction is that the onset of the visual burst will be tightly coupled to the onset of saccades with express latencies.

Findings of several studies of the activity of collicular neurons can be related to the visuomotor hypothesis. The discharge rate of neurons with fixation-related activity (Munoz & Wurtz, 1993) is attenuated during the gap period (Dorris & Munoz, 1995). Dorris and Munoz (1995) suggested that this decrease in fixation-related activity disinhibits saccade-related activity, thereby producing a reduction in saccadic reaction times on gap trials. Pharmacological inactivation of neurons in the rostral SC, which includes cells with fixation-related activity, increases the frequency of saccades with express latency (Munoz & Wurtz, 1993). These findings are consistent with the hypothesized decay in the strength of a fixation process but it should be noted that, in general, the activity level of collicular fixation neurons is not highly correlated with either saccadic reaction time or the probability of occurrence of express saccades (Dorris et al., 1997).

Recordings from collicular neurons with both visual and saccade-related activity during gap trials are more directly related to the visuomotor hypothesis. Such studies of the role of the SC in the generation of express saccades have focussed on a comparison of the neural activity observed on trials with 'regular' latency with the activity observed on trials with express latency. Edelman and Keller (1996) and Dorris et al. (1997) noted that the visual and motor bursts of visual–motor cells merged on many trials with express latencies. The peak of target-aligned bursts occurring on trials with express latencies occurs earlier and the bursts are consistently larger than target-aligned bursts observed on trials with regular latencies (Dorris et al., 1997; Edelman & Keller, 1996). Edelman and Keller (1996) concluded that the visual burst of visual-motor cells was more vigorous preceding express saccades and that this more vigorous visual response could play a role in the initiation of express saccades.

Rather that comparing collicular activity on trials with 'regular' and express latencies, we studied changes in the temporal relationship between visual and motor activity during movements having a wide range of reaction times. As reaction time was reduced, the latency of visual responses was relatively constant but the interval between the visual and motor bursts became progressively shorter until, during trials with express latencies, the two bursts fused. Edelman and Keller's (1996) conclusion that the merged burst was not merely the sum of visual and motor bursts was based upon an analysis that did not impose a physiological limit upon predicted instantaneous firing rates. When a physiological limit of 1200 spikes/s was imposed, we were unable to reject the null hypothesis that the distribution of interspike intervals of merged bursts artificially created by summing visual and motor bursts was drawn from the same population of interspike intervals associated with 'real' merged bursts. Thus, the enhanced target-aligned bursts observed during express saccades (Edelman & Keller, 1996; Dorris et al., 1997) probably represents the physiological summation of visual and motor bursts. The enhanced target-aligned bursts cannot be viewed as pure visual responses since it is not possible to determine the onset or offset of either the visual or the motor bursts. While the merged burst may have more spikes than unfused bursts, there is no need to assume that the merged burst represents an unusual case in which saccades are triggered directly by visual activity. During these trials, the bursts of motor cells lacking visual responses continue to be tightly linked to saccade onset (Fig. 4C, Table 1), a finding previously noted by Dorris et al. (1997).

In summary, we see no reason to assume that express saccades are a special class of saccades triggered directly by visual responses. We did not find, as predicted by this hypothesis, a range of saccadic reaction times in which visual (rather than motor) responses were tightly coupled to saccade onset. Instead, we found that the tight coupling between saccade onset and the onset of the motor burst of visual-motor and motor cells, reported previously for saccades with regular latencies (Sparks, 1978), extends into the short latency express saccade range. This would not be the case if express saccades were a special type of movement triggered by a visual burst (see Lee, Helms, Augustine & Hall, 1997 for a recent variant of the visuomotor hypothesis). Our data are consistent with the hypothesis that saccades with express latencies, as well as saccades with other latencies, are triggered by the motor burst of collicular neurons.

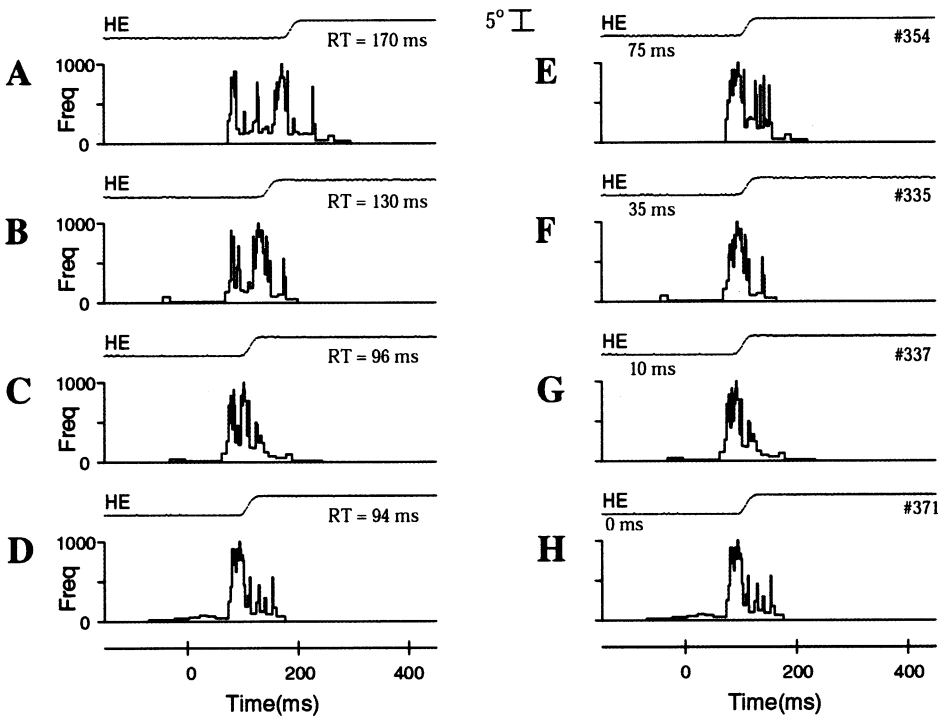

Fig. 8. Eye position (HE, horizontal eye position) and instantaneous frequency plots of the activity of a collicular neuron during trials with reaction times of 170 (A), 130 (B), 96 (C) and 94 (D) ms. Separate visual and motor bursts can be distinguished in A, B and C but not in D. The eccentric target appeared at time zero. The right column illustrates artificial express saccades and associated instantaneous spike frequencies obtained by shifting the motor burst forward in time and combining it with the visual burst (see text for details). (E) Motor burst in panel A shifted by 75 ms. (F) Motor burst in panel B shifted by 35 ms. (G) Motor burst in panel C shifted by 10 ms. (G) Duplicate of the merged visual and motor bursts in panel D shown to facilitate comparison with the activity 'observed' during the artificial express saccades.

4.2. Increase in low frequency activity and the early activation hypotheses

Three sets of experimental findings formed the bases for 'early activation' hypotheses concerning the generation of express saccades. Neurons in the frontal eye fields (FEFs) display increases in low frequency activity beginning about 150 ms after fixation target offset during a gap task (Dias & Bruce, 1994). Dias and Bruce suggested that this 'fixation–disengagement discharge' could prime downstream oculomotor structures so that the subsequent appearance of a visual target would trigger short-latency saccades. Dorris et al. (1997) described an increase in the activity of neurons in the SC on gap trials. The level of presaccadic activity before express saccades was significantly greater than the level of activity observed during trials with regular saccadic reaction times. They proposed that this increase in activity, viewed as the early preparation of an oculomotor program, would bring neurons at a particular location in the collicular motor map so close to threshold that the target-related responses of visual–motor cells trigger short-latency express saccades directly. Sommer (1997) recorded saccadic reaction times to brief visual targets presented while subjects were scanning an array of continuously illuminated LEDs. Although not required by the task, subjects developed stereotyped patterns of scanning movements. When gaze was directed at a particular LED, the probability of making an express saccade to a brief target was related to the frequency of occurrence of movements of that direction and amplitude from that location during the scanning task. Sommer suggested that the spatial preparation of scanning saccades facilitated the generation of express saccades by sensitizing localized regions of the collicular motor map.

The pattern of activity we observed during gap trials is similar to the pattern of activity previously described by Dias and Bruce (1994) and Dorris and colleagues (Dorris et al., 1997). Our observations are consistent with the proposal that express saccades occur when visual activation is superimposed upon a preexisting state of increased excitability. Two additions to this evolving hypotheses are possible based upon our findings. First, the superposition of visual activation upon the increased excitability occurring on gap trials facilitates the occurrence of a motor burst with extremely short latency. Second, while the increase in low frequency activity may be necessary for the occurrence of express saccades, it neither initiates express saccades nor serves as an accurate predictor of the direction or latency of saccades. Referring to Fig. 4, note that the increase in low frequency activity may persist for long periods without saccade initiation. Also, for this cell in the left SC, activity levels observed before leftward saccades with regular latencies are similar to levels observed before rightward saccades with express latencies. On trials in which rightward targets are presented, a visual response is superimposed upon the increased low frequency activity. This superposition, which facilitates the occurrence of a motor burst, is necessary for the occurrence of express saccades. On trials in which leftward targets are presented, visual activity of neurons in the right SC are not superimposed upon the increased low frequency activity and saccades with regular latencies occur. Note that the high correlations obtained between the duration and level of the increase in activity and saccade latency (Dorris et al., 1997; and open circles in Fig. 7 of this paper) were based upon analyses that excluded trials with movements in the opposite direction. The level of low-frequency collicular activity is only predictive if information about the location of the next visual target is also available (see Fig. 7, filled squares).

If animals are trained on gap trials using targets in both visual fields, neurons in both left and right SC would be expected to display increased excitability during the gap interval and visual responses of collicular neurons would be superimposed upon increased low frequency activity if either a leftward or rightward target were presented. In animals trained in this manner, increases in discharge rate during the gap interval generated by cells in the left SC are correlated with reduced latency of leftward saccades (see Dorris & Munoz, 1998). But, presumably, this correlation is present because increases in excitability during the gap interval occurs at multiple sites in both colliculi. Correlations between levels of low frequency activity of collicular cells and saccadic reaction time are higher for contralateral saccades than for ipsilateral saccades (Dorris & Munoz, 1998).

Thus, as suggested by previous workers (Dias & Bruce, 1994; Dorris et al., 1997), it is the interaction between the increase in low frequency activity and visually-evoked responses that is critical for the occurrence of express saccades. Accordingly, the distribution of saccadic reaction times will be influenced by factors which affect the general excitability of collicular neurons, and also by the strength and timing of the superimposed sensory signals. Results of experiments varying the properties of visual stimuli during gap trials support this conclusion. McPeek and Schiller (1994) obtained bimodal distributions of saccadic reaction times during gap trials using stimuli made visible by luminance contrast, color contrast, and motion cues. They found that the relative number of short latency movements and the range of latencies in the early peak of the reaction time distribution depend upon background composition, luminance contrast, chromatic modulation and other aspects of the stimulus display.

Results of neurophysiological experiments using the gap task and stimuli similar to those used by McPeek

and Schiller (1994) would be informative. The expectation is that a bimodal distribution of saccadic reaction times would only be obtained under conditions (such as the gap task) in which a general increase in collicular excitability was observed. Variations in the latency of visual responses to stimuli having different contrast or chromatic properties would produce comparable variations in the modal value of the 'express' peak of the reaction time distribution. Note that the bimodal distribution of reaction times often observed during gap trials does not occur because there are 'reflexive' and 'nonreflexive' modes of activating saccades (e.g. Guitton, Buchtel & Douglas, 1985; Pierrot-Deseilligny, Rivaud, Gaymard & Agid, 1991; Reuter-Lorenz et al., 1991; Everling, Dorris & Munoz, 1998a). Ironically, to the extent that short latency saccades are dependent upon increased excitability of collicular neurons arising from planned sequences of movements (Sommer, 1997), or information about the prior history of target location and probability of occurrence (Basso & Wurtz, 1998; Dorris & Munoz, 1998), the so-called short-latency 'reflexive' saccades are more 'cognitive' than 'regular' saccades.

Since neurons in the FEF display an increase in activity (Dias & Bruce, 1994) similar to that observed in the SC, why are express saccades spared after lesions of the FEF but not after collicular lesions (Schiller et al., 1987)? Several possibilities need to be examined. First, on gap trials inputs from other cortical or subcortical areas may mediate the changes in excitability of collicular neurons necessary for express saccades. Second, intrinsic circuitry providing the recurrent excitation needed to recruit an active population of sufficient size to initiate a saccade may exist at the level of the SC but not in the FEF. Third, the superposition of visual responses and the increase in low frequency activity necessary to drive cells with saccade-related activity into burst mode after extremely short latencies may occur in the SC but not in the FEF. An interesting possibility is that express saccades depend upon the direct connections between superficial and deep layers of the SC (e.g. Moschovakis, Karabelas & Highstein, 1988; Rhoades, Mooney, Rohrer, Nikoletseas & Fish, 1989; Behan & Appell, 1992; Hall & Lee, 1997; Lee et al., 1997; Isa, Endo & Saito, 1998; Pettit, Helms, Lee, Augustine & Hall, 1999).

4.3. Collicular saccade-related burst neurons and saccade initiation

We studied the role of the SC in saccade initiation by recording collicular activity while monkeys performed tasks that generated a large range of saccadic reaction times. Our results confirm and extend results of earlier experiments demonstrating a tight temporal coupling between the high frequency pre-saccadic burst of collicular neurons and saccade onset (Sparks, 1978). The high-frequency burst of these neurons can be used to predict perfectly the behavior of a monkey performing a behavioral task in which the probability of saccade initiation is manipulated by varying target duration (Sparks, 1978). The hypothesis (Sparks, 1978; also, see Keller, 1979) that emerged from these and other findings — that in normal animals, the motor burst of collicular neurons serves as a signal which triggers saccade onset — can now be extended to express saccades. The saccade-related high frequency burst of motor and visual-motor cells is tightly coupled to saccade onset for the full range of saccadic reactions times, both regular and express.

Other lines of evidence supporting the proposal that the high-frequency motor burst of collicular neurons is involved in the initiation of saccades have been reviewed elsewhere (Sparks & Mays, 1990). The axons of saccade-related burst neurons comprise a major efferent pathway from SC to subsequent oculomotor premotor neurons (for a review, see Moschovakis, Scudder & Highstein, 1996). Reversible inactivation of collicular neurons severely impairs the direction, amplitude, and velocity of movements and produces a profound increase in saccadic latency (Hikosaka & Wurtz, 1985, 1986; Lee, Rohrer & Sparks, 1988). Moreover, pharmacological activation of collicular neurons produces a decrease in saccade latency (Hikosaka & Wurtz, 1985; Sparks, Lee & Rohrer, 1990).

The high-frequency motor burst of collicular neurons cannot be the only mechanism for saccade initiation since animals continue to generate saccadic eye movements after recovery from permanent lesions of the superior colliculus (Wurtz & Goldberg, 1972; Mohler & Wurtz, 1977; Kurtz & Butter, 1980; Schiller et al., 1980; Albano & Wurtz, 1982; Keating, Kenney, Gooley, Pratt & McGillis, 1986; see Sparks & Hartwich-Young, 1989 for a more complete review of the lesion literature). Most of these experiments describe an enduring increase in saccadic latency, a finding that is consistent with the hypothesis that collicular neurons are involved in saccade initiation in normal animals. In animals with collicular lesions, the direct pathway from FEF to pons may be critical for saccade initiation (Schiller et al., 1987). The increases in saccadic reaction time observed following reversible inactivation of the frontal eye fields (Sommer & Tehovnik, 1997; Dias & Segraves, 1999) are associated with a concomitant decrease in saccade-related activity of neurons in the SC (Helminski & Segraves, 1997).

4.4. Reduced activity following fixation target offset

Only four cells had sufficiently high levels of activity during the fixation interval to allow observation of the 100 ms period of reduced excitability that followed the

offset of the fixation target offset. However, visual responses to target onset were significantly reduced on step trials compared to delayed saccade trials for 20 of the 23 cells in which we obtained recordings on both trial types. Thus, the brief period of reduced activity noticeable in a few cells with higher background discharge rates seems to represent a general reduction in the excitability of collicular neurons. Compared to step trials, it is likely that more vigorous visual responses occur on gap trials too (compare the visual responses on step and gap trials in Fig. 3B and Fig. 4B vs. D), but it is difficult to quantify a possible difference. On gap trials with short reaction times, visual and motor activity overlap. When visual and motor responses do not overlap (gap trials with longer reaction times), the visual response is contaminated by the increase in low frequency activity linked to the offset of the fixation target.

The source and functional significance of this brief period of reduced excitability is unknown, but 20–25% of the 'fixation' cells in the rostral SC and many pontine omnipause neurons (OPNs) display a transient increase in activity 70–110 ms after the offset of a fixation target (Everling et al., 1998b). Reductions in OPN activity allow other cells to generate a pulsatile saccadic command signal. The suggestion that the threshold for saccade initiation should be higher during transient increases in OPN activity linked to target onset (Everling et al., 1998b) could be extended to include a brief period following the offset of a fixation stimulus. When viewing natural scenes, only rarely does the object being viewed disappear at the same time that a new object appears. Instead, saccades usually direct gaze from one continuously present target to another. The retinal image of a stationary object does 'disappear' when the eyes move and it would be of interest to compare the visual responsiveness of collicular neurons 60–160 ms after saccade onset (a time that corresponds to the period of reduced excitability on step trials) to responsiveness when the eye is stationary — for this is a period when spatial localization of visual stimuli is compromised (Matin, 1976; Honda, 1991; Dassonville, Schlag & Schlag-Rey, 1992; Honda, 1993; Miller, 1996).

4.5. Summary

Converging lines of evidence from a number of laboratories provide a general picture of the neural events determining when a saccade will be initiated. Cognitive processes involved in planning sequences of eye movements (e.g. Zingale & Kowler, 1987; Kowler, 1990; Sommer, 1997) or, based upon past experience, registering information about the probability of targets appearing at particular times or in certain locations (e.g. Basso & Wurtz, 1998; Dorris & Munoz, 1998) can produce changes in the excitability of populations of neurons residing in localized regions of the motor maps found in the FEF and SC. If sensory activation is superimposed upon this state of increased excitability, cells with saccade-related activity generate a burst of activity, other nearby cells may be recruited into burst mode through local recurrent excitation (Moschovakis et al, 1988; Lee et al., 1997; Pettit et al., 1999), and saccades with extremely short latencies occur. The exact time of saccade initiation depends upon the level of the change in excitability and the latency and vigor of the sensory response. In turn, the level of excitability is a function of factors such as the amount of experience in a particular task, and the latency and vigor of the sensory response are affected by the contrast of the target, the texture of the background, and other stimulus features. The high frequency motor burst of collicular neurons serves as a trigger signal which momentarily removes the tonic inhibition of pontine OPNs and allows downstream brainstem circuits to generate saccadic command signals for the extraocular muscles. The anatomical route by which the collicular burst is converted into an inhibition of OPNs has not been established, but long-lead inhibitory burst neurons could serve as intermediaries (Strassman, Highstein & McCrea, 1986; Scudder, Fuchs & Langer, 1988; Scudder, Moschovakis, Karabelas & Highstein, 1996).

If cognitively-mediated early activation of particular regions of the motor maps is low or if sensory-evoked activity is weak, express saccades do not occur. Current evidence suggests that information about the location of a saccade target gradually develops during the reaction time interval (Sparks, Mays & Porter, 1987) and that 'regular' saccades are initiated when the time integral of FEF or collicular activity exceeds a threshold value (Hanes & Schall, 1996). The high frequency burst of collicular saccade-related burst neurons provides a precise indication of when the threshold is exceeded. Decreases in the strength of an active fixation process, and alterations in neuronal excitation related to global, rather than local, activation of motor map are among the factors that influence the time required for neural activity to exceed the threshold for saccade initiation.

A much richer understanding of the neural mechanisms of saccade initiation will emerge from additional experiments delineating the source and specificity of the cognitive factors influencing the excitability of collicular neurons, the contribution of superficial-to-deep connections, and the functional linkages between the motor bursts of collicular neurons and the discharge of pontine omnipause neurons.

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