Comparison of the Discharge Characteristics of Brain Stem Omnipause Neurons and Superior Colliculus Fixation Neurons in Monkey: Implications for Control of Fixation and Saccade Behavior

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Everling, Stefan, Martin Paré, Michael C. Dorris, and Douglas P. Munoz. Comparison of the discharge characteristics of brain stem omnipause neurons and superior colliculus fixation neurons in monkey: implications for control of fixation and saccade behavior. *J. Neurophysiol.* 79: 511–528, 1998. Fixation neurons (SCFNs) in the rostral pole of the superior colliculus (SC) and omnipause neurons (OPNs) in the nucleus raphe interpositus (rip) in the pons share similar discharge properties. Both types of neurons discharge tonically during periods of visual fixation and pause for saccadic eye movements, and their activation by electrical stimulation suppresses saccade generation. On the basis of these similarities and the projection from the rostral SC to the rip, it was hypothesized that SCFNs provide a major excitatory input to OPNs. We investigated the role and relationship of SCFNs and OPNs with respect to both fixation behavior and saccade generation by comparing their activity recorded in the same monkeys performing a gap saccade task. In this task, the central fixation point was extinguished 200 ms before the presentation of an eccentric saccadic target, and the discharges of OPNs and SCFNs were contrasted during visual fixation, nonvisual (gap) fixation, and saccade generation. During visual fixation, the mean discharge rate of OPNs was higher and more regular than that of SCFNs. During the gap period, SCFNs decreased their discharge rate before target appearance, whereas no change in discharge rate was observed in OPNs. For both SCFNs and OPNs, the activity level before target appearance was not correlated to saccadic reaction time. In contrast to SCFNs, several OPNs responded with a transient phasic increase in discharge immediately after the target presentation. Before their saccade-related pause, there was a gradual reduction in the activity of SCFNs, whereas OPNs had an abrupt cessation of discharge. SCFNs paused earlier than OPNs, but the OPN pause onset was better synchronized to saccade onset than the SCFN pause onset. OPNs resumed firing after their pause in activity earlier than SCFNs, and the OPN pause end was better synchronized to saccade end than the SCFN pause end. These physiological data reveal differences in the discharge properties of SCFNs and OPNs that are irreconcilable with the hypothesis that the discharge pattern of OPNs reflects simply the excitatory input from SCFNs. It is most likely that additional inputs to OPNs compensate for the reduction in discharge of SCFNs during these periods.

INTRODUCTION

Saccades are fast conjugate eye movements that shift the visual axis from one point in the visual field to another. The saccade-related input to extraocular muscle motoneurons arises from a saccade-generating circuit composed of burst neurons located in the paramedian pontine reticular formation and the rostral interstitial nucleus of the medial longitudinal fasciculus (for review, see Fuchs et al. 1985; Moschovakis and Highstein 1994). These burst neurons discharge a high-frequency burst of action potentials for saccades and are silent during intersaccadic periods. Omnipause neurons (OPNs), which are located near the midline in the caudal pontine reticular formation within the nucleus raphe interpositus (rip) (Büttner-Ennever et al. 1988; Langer and Kaneko 1990), exhibit the reciprocal discharge pattern: they discharge tonically during intersaccadic periods and pause completely for saccades made in all directions (in monkey: Cohen and Henn 1972; Keller 1974; Luschei and Fuchs 1972; in cat: Evinger et al. 1982). OPNs project extensively onto burst neurons (in monkey: Büttner-Ennever and Büttner 1978; Strassman et al. 1987; in cat: Langer and Kaneko 1983; Ohgaki et al. 1987, 1989), and act as a tonic inhibitory gate for the saccade burst generator (in monkey: Horn et al. 1994; in cat: Curthoys et al. 1984; Furuya and Markham 1982; Nakao et al. 1980, 1988). This is perhaps best demonstrated by the immediate suppression of saccades that occurs when rip is stimulated electrically (in monkey: Becker et al. 1981; Keller 1974, 1977; King and Fuchs 1977; in cat: Evinger et al. 1982). A pause in the discharge of OPNs thus is required to release the burst generator from inhibition and initiate a saccade.

A subset of neurons that share many discharge properties with OPNs recently has been identified in the rostral pole of the superior colliculus (SC) (in monkey: Munoz and Wurtz 1992, 1993a; in cat; Munoz and Guitton 1989, 1991; Peck 1989). In the monkey, these neurons—the SC fixation neurons (SCFNs)—were found to exhibit a tonic discharge when the animal maintains fixation of a visual target (even when the target is blinked momentarily) and a pause in activity for saccades. Electrical stimulation of the rostral SC delays saccade initiation and, when delivered during the saccade, interrupts them in midflight (Munoz and Wurtz 1993b). The similar properties of OPNs and SCFNs suggest that both these neurons subserve a similar function: that of preventing saccade generation. Moreover, it was hypothesized that SCFNs provide a major excitatory input to the rip (Munoz and Guitton 1989, 1991; Munoz and Wurtz 1993a, 1995b). This hypothesis is supported by the following observations: the rostral SC sends a selective anatomic projection to OPNs in the monkey (Büttner-Ennever and Horn 1995); electrical stimulation of the OPN region activates SCFNs antidromically in both monkey (Gandhi and Keller 1996;

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Istvan et al. 1994) and cat (Munoz and Guitton 1989, 1991); and stimulation of the SC in both monkey (Raybourn and Keller 1977) and cat (Paré and Guitton 1994) excites OPNs monosynaptically with a greater efficacy from stimulation of the rostral pole (Paré and Guitton 1994).

Despite the functional similarities between SCFNs and OPNs and the evidence for projections between the rostral SC and rip, it is not clear whether inputs from the SCFNs can account for the discharge properties of OPNs. The activity of monkey OPNs has not been hitherto compared with that of SCFNs. In fact, the discharges of these neurons have not been studied in similar experimental paradigms; OPN activity has been recorded mostly during spontaneous saccades (Cohen and Henn 1972; Keller 1974; Luschei and Fuchs 1972). Such a comparative study is important to clarify the role and relationship of these neurons with respect to both fixation behavior and saccade generation. In addition, the activity of SC neurons, including the SCFNs, recently has been studied in relation to saccadic reaction time (SRT) (Dorris and Munoz 1995; Dorris et al. 1997). It therefore is of interest to investigate the activity of brain stem neurons, targets of the SC, to reach a comprehensive understanding of the neural basis of saccade initiation. The objective of the present study is to perform a quantitative comparison of the discharge characteristics of SCFNs and OPNs in the same monkeys performing saccades in the gap saccade task (Saslow 1967). This behavioral paradigm permits the characterization of both the saccade-related responses and the tonic fixation-related activity during periods of visual and nonvisual fixation. In addition, the variability in reaction time inherent to the saccades produced in this task allows for the determination of relationships between SRT and specific neuronal activity (Dorris et al. 1997).

Some of the discharge characteristics of SCFNs in this behavioral paradigm already have been reported (Dorris and Munoz 1995; Dorris et al. 1997). Preliminary reports of the data presented in this report have appeared in abstract form (Everling et al. 1997a,b).

METHODS

Experimental procedures

All procedures were approved by the Queen's University Animal Care Committee and were in accordance with the Canadian Council on Animal Care policy on use of laboratory animals.

We recorded single-neuron activity from neurons in the rostral SC and rip of two male rhesus monkeys (*Macaca mulatta*) weighing between 5 and 7 kg. The procedures used for preparing the animals have been described recently (Dorris et al. 1997; Paré and Munoz 1996). Eye movements were monitored by the magnetic search coil technique (Fuchs and Robinson 1966), which had a spatial resolution of 0.1°. Two stainless-steel cylinders were implanted for single-neuron recordings. One cylinder was centered on the interaural axis and tilted 25° lateral of vertical and allowed recordings from neurons in the left SC and OPNs in rip. The other cylinder was centered on the midline and tilted 38° posterior of vertical and allowed recordings from neurons in both SC.

Behavioral paradigms, visual displays, and storage of data were under the control of a 40846 IBM-compatible computer running a real-time data acquisition system (REX) (Hays et al. 1982). Single neurons were recorded by the use of tungsten microelectrodes (Frederick Haer) with impedances of 0.5–5 MΩ. Electrodes were driven through stainless-steel guide tubes that were held in position by a delrin grid fixed inside the recording cylinders (Crist et al. 1988). During the experiments, which lasted 2–3 h, the monkeys were seated in a primate chair with the head restrained. They faced a tangent screen 86 cm in front of them for which they had an unobstructed view of 70 × 70°, i.e., ±35° of center. Red light emitting diodes (2.0 cd/m^2) were back projected onto the screen to produce visual targets. During the intertrial intervals, the screen was illuminated diffusely (1.0 cd/m^2) to prevent the animals from becoming dark adapted. The extinction of the background lights signified the start of a trial.

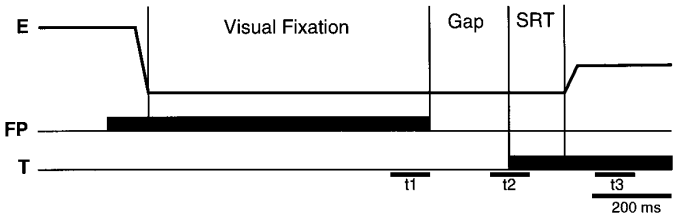

FIG. 1. Schematic representation of the gap saccade task. Monkey had to fixate a central fixation point (FP) that was turned off for 200 ms before the eccentric target (T) appeared. Saccadic reaction time (SRT) was defined as the time from target appearance to the onset of the saccadic eye (E) movement. See METHODS for additional details.

Behavioral paradigm

The monkeys were trained to perform the gap saccade task (Fig. 1). Once the fixation point (FP) appeared in the center of the screen, the animals were required to look at it and maintain steady visual fixation for 500–1000 ms. The FP then was extinguished, and there was a period of no visual stimuli (gap) before an eccentric target was presented. Within a block of trials, the gap period was set at a constant duration of 200 ms. The target was presented at two possible positions randomly interleaved and with equal probability, either 10° to the left or 10° to the right of the FP. A liquid reward was given to the monkey if it maintained steady fixation during the visual fixation and the gap periods and made a saccade to the target within 500 ms after its appearance. A monkey typically would complete between 1,000 and 2,000 trials in each experimental session. They received water until satiation, after which they were returned to their home cage. Records were kept of the weight and health status of the monkeys, and additional water and fruit was provided as needed.

Data collection and analysis

Single-neuron discharges were sampled at 1 kHz after passing through a window discriminator that produced a pulse for each spike that met both amplitude and time constraints. Horizontal and vertical eye position signals were digitized at 500 Hz and stored on a hard disk. The off-line analysis was performed on a SUN Sparc 2 Workstation with the use of a computer program that identified and marked the onset and termination of each saccade using velocity and acceleration threshold criteria (Waitzman et al. 1991). Each trial was inspected visually, and identification failures were corrected if necessary.

To evaluate the relation between neuronal discharge and specific events (such as FP disappearance, target appearance, or saccade onset), we produced rasters and a spike-density function (MacPherson and Aldridge 1979; Richmond and Optican 1987) aligned on these events. To generate the spike density function, a Gaussian function with a width of 10 ms was substituted to each spike, and then all of the Gaussians were summed together to generate a continuous function in time. Large values of the spike-density func-

tion represent a greater probability of the occurrence of a spike. A mean spike-density function was calculated by averaging the spike densities over a series of trials.

To quantify neuronal activity during visual fixation, we measured the interspike intervals during the visual fixation portion of each available trial, i.e., the interval (500–1,000 ms) starting from when the monkey started to fixate the FP and ending when the latter disappeared at the start of the gap period. This period excluded perisaccadic discharges.

The gap-related changes in neuronal activity were quantified by measuring the discharge rate of individual neurons during two different intervals in the 200-ms gap saccade task (Fig. 1): the final 100 ms before the FP was extinguished, while the monkey was fixating the FP (visual fixation epoch, *t1*), and the interval from 50 ms before target appearance to 50 ms after target appearance in 200-ms gap trials (end of gap epoch, *t2*). The relationship between SRT and the discharge rates during the *t1* and *t2* epochs were determined using linear correlation procedures (Pearson product-moment correlation coefficient *r*).

The onset and end of the saccade-related pause in activity were defined to be, respectively, the times of the last action potential preceding the pause and of the first action potential after it. The pause onset time was defined as the interval from the beginning of the saccade to the onset of the pause in activity, whereas the pause end time was defined as the interval from the end of the saccade to the end of the pause.

The postsaccadic changes in neuronal activity were quantified by comparing the discharge rate during the visual fixation (*t1*) epoch with the discharge rate during the interval 50–150 ms after saccade end (*t3*) in individual neurons (Fig. 1). The monkey was fixating a visible red stimulus during both intervals. Further, we calculated a postsaccadic enhancement index for each individual neuron by dividing the mean discharge rate during the *t3* epoch by the mean discharge rate during the *t1* epoch (Munoz and Wurtz 1993a). This index was >1.0 for an increased postsaccadic discharge and <1.0 for a decreased postsaccadic discharge.

All the data were expressed as means ± SE if not stated differently. SCFNs and OPNs were compared with unpaired Student's *t*-tests or, if a test of normal distribution failed (Kolmogorov-Smirnov test), with nonparametric Mann-Whitney *U* tests. Statistical comparisons within SCFNs or OPNs were conducted with a paired Student's *t*-test or, if a test of normal distribution (Kolmogorov-Smirnov test) failed, with the nonparametric Wilcoxon signed-rank test. For group comparisons, a nonparametric Kruskal-Wallis analysis of variance (ANOVA) was used. Posthoc comparisons were conducted with the Student-Newman-Keuls method. Correlation procedures (Pearson product-moment correlation coefficient *r*) were used to evaluate the relationship between the times from target appearance to saccade onset and target appearance to pause onset and the relationship between the times from target appearance to saccade end and target appearance to pause end. Significance was accepted at the $P < 0.05$ level.

Neuron identification

To be classified as SCFNs and included in our analysis, neurons had to be located from 1.5 to 3.0 mm below the dorsal surface of the rostro-lateral pole of the SC and had to possess the following discharge characteristics (Dorris and Munoz 1995; Dorris et al. 1997; Munoz and Wurtz 1993a): tonic activity >10 spikes/s during both the visual fixation (*t1*) and end of gap (*t2*) epochs, i.e., while the monkey fixated the FP even when it was removed momentarily and was required to maintain the same eye position (this excluded visual neurons with a foveal receptive field); and a pause in activity during all ipsiversive 10° saccades and most contraversive saccades.

To be classified as an OPN, a brain stem neuron had to possess the following discharge characteristics (Keller 1974; Luschei and Fuchs 1972; Raybourn and Keller 1977): a high tonic discharge rate during fixation and a pause in activity for saccades in all directions. OPNs were located ventromedial to abducens nucleus along the midline, between burst neurons discharging for leftward and rightward saccades, respectively.

RESULTS

We obtained sufficient data from 21 OPNs in rip and from 43 SCFNs in the rostro-lateral pole of the SC to allow a quantified analysis and comparison of discharge characteristics in the gap saccade task. The activity of one OPN and one SCFN in the gap saccade task is illustrated in Fig. 2 for 200-ms gap trials, and the target presented 10° left or right. Both neurons discharged at a tonic rate during visual fixation and displayed a discrete pause in activity associated with the saccades. During the gap period, the level of activity of the SCFN was reduced momentarily, whereas that of the OPN remained unchanged. In the subsequent sections, we contrast quantitatively the discharge properties of the 21 OPNs and 43 SCFNs in the gap saccade task: activity during visual fixation of the FP, activity during nonvisual fixation during the gap period, target-related responses, saccade-related responses, and postsaccadic responses.

Neuronal activity during visual fixation

Although both OPNs and SCFNs discharged tonically during the period of visual fixation preceding the gap period, OPNs discharged at a higher and more regular rate than SCFNs. This difference in the regularity of discharge during visual fixation is illustrated in Fig. 3, in which we contrast the distribution of interspike intervals for two SCFNs and two OPNs (see METHODS). The range of interspike intervals among the SCFNs (Fig. 3, *A* and *B*) was much greater than the range obtained from OPNs (Fig. 3, *C* and *D*). To compare the variability of discharge between OPNs and SCFNs, we calculated the coefficient of variation (standard deviation/mean), which takes into account the different mean discharge rates of OPNs and SCFNs. Figure 4 shows the distribution of mean interspike intervals and coefficients of variation for individual SCFNs and OPNs. The mean ± SE interspike interval for SCFNs was 27.0 ± 2.1 ms (range 9–61), and for OPNs, it was 9.9 ± 0.8 ms (range 7–18). The mean coefficient of variation was 1.16 ± 0.12 (range 0.40–3.33) for SCFNs and 0.63 ± 0.60 (range 0.29–1.39) for OPNs. These differences in both mean (Mann-Whitney *U* test, $P < 0.0001$) and coefficient of variation (Mann-Whitney *U* test, $P < 0.0001$) were highly significant.

Gap-related neuronal activity

To quantify the discharges of SCFNs and OPNs during the gap period, we compared the mean discharge rates during the visual fixation (*t1*) epoch with the end of gap (*t2*) epoch in 200-ms gap trials (see METHODS). Figure 5 contrasts the mean discharge rate of 43 individual SCFNs (solid circle) and 21 OPNs (open circle) during the *t1* epoch plotted against the mean discharge rate during the *t2* epoch. The discharge rate of SCFNs was significantly different from OPNs during both the *t1* (Mann-Whitney *U* test, $P <$

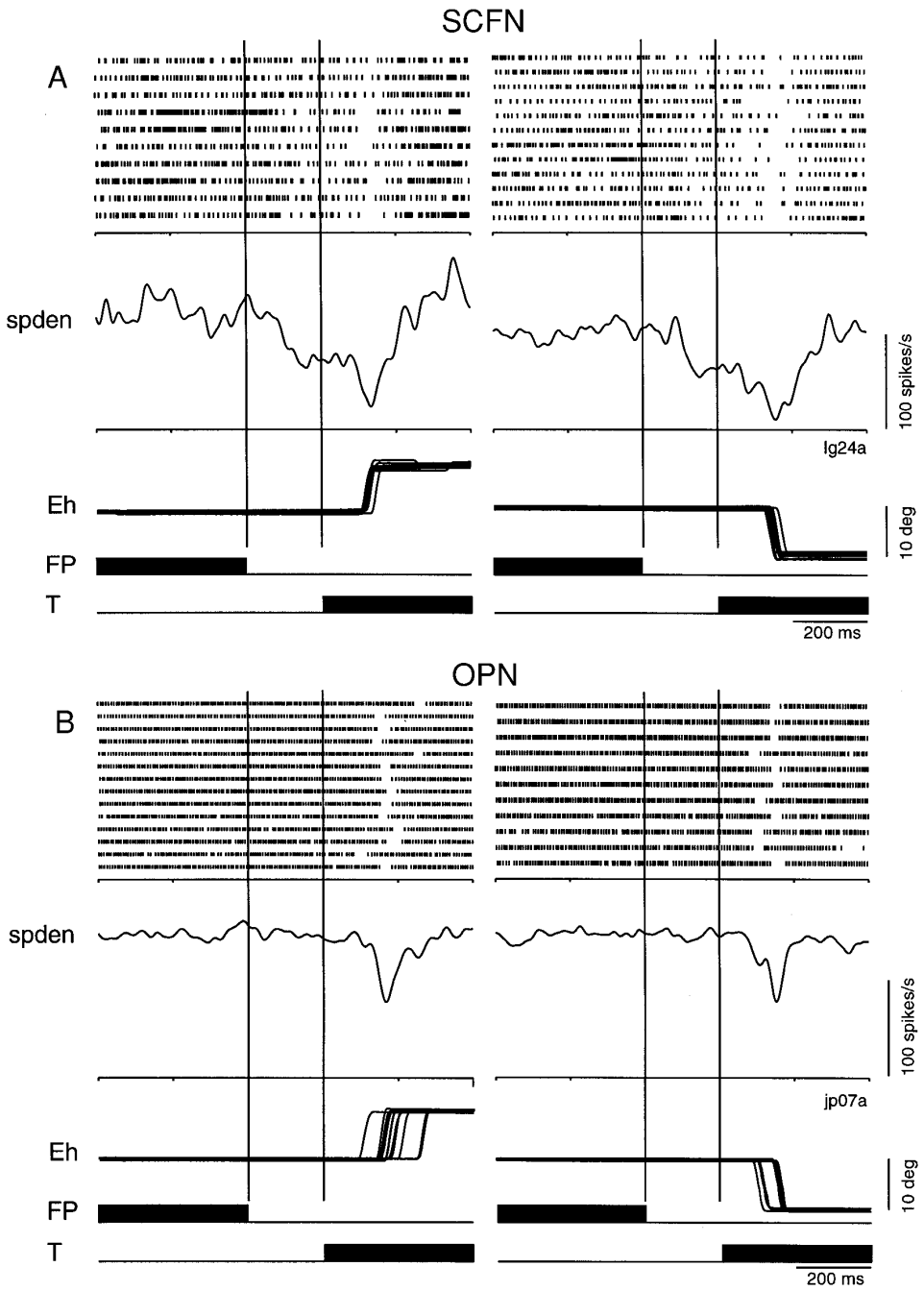

FIG. 2. Activity of a superior colliculus fixation neuron (SCFN, *A*) and an omnipause neuron (OPN, *B*) while the monkey performed the gap saccade task. FP was extinguished 200 ms before the target (T) appeared 10° left or right. Individual rasters of neuron discharge, the spike-density functions (spden), and the horizontal eye position (Eh) are shown for both neurons. Upward deflections denote rightward saccades, downward deflections denote leftward saccades. SCFN decreased its discharge rate during the gap period, whereas the OPN maintained its tonic discharge rate during the gap period.

0.0001) and the *t2* epochs (Mann-Whitney *U* test, $P < 0.0001$). The mean discharge rate of SCFNs was reduced from 50.9 ± 4.4 spikes/s (range 11.8–151.4) during the *t1* epoch to 38.6 ± 18.9 spikes/s (range 14.4–110.0) during the *t2* epoch. This reduction in the mean discharge rate of SCFNs during the gap period was highly significant (Wilcoxon signed-rank test, $P < 0.0001$). The mean discharge rates of OPNs during the *t1* and the *t2* epochs did not differ (Wilcoxon signed-rank test, $P = 0.99$). This is apparent in Fig. 5, where all the open circles fall neatly along the unity (dashed) line. The mean discharge rate of OPNs was 118.7 ± 7.1 spikes/s (range 57.4–161.6) during the *t1* epoch and 118.7 ± 6.8 spikes/s (range 56.8–163.2) during the *t2* epoch. Thus although SCFN activity diminished during the gap period (see also Dorris and Munoz 1995), the activity of OPNs remained unchanged.

Relationship between SRT and neuronal activity

It has been reported previously that the SCFN neuronal activity before target appearance does not predict SRT on a trial-by-trial basis, whereas the activity of a subclass of saccade-related neurons in the caudal SC—buildup neurons (SCBUNs)—is correlated with SRT (Dorris et al. 1997). We performed a similar analysis for our 21 OPNs (see METH-

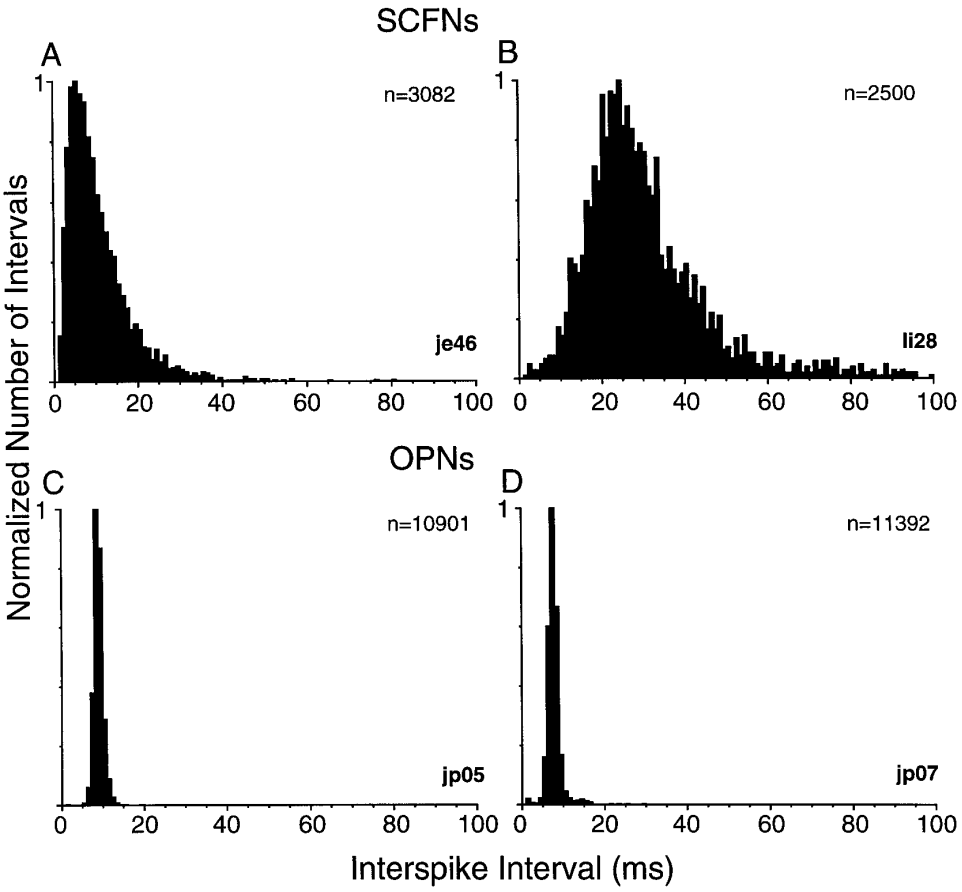

FIG. 3. Distribution of interspike intervals of 2 SCFNs (*A* and *B*) and 2 OPNs (*C* and *D*) during visual fixation. SCFN (*A*) and the OPN (*C*) had a similar mean interspike interval, but the OPN discharged more regularly.

ODS). The mean correlation coefficient between SRT and the discharge rate during the visual fixation (*t1*) epoch was 0.02 ± 0.02 (range -0.17–0.21). None of these correlations was significant. The mean correlation coefficient between SRT and the discharge rate during the end of the gap (*t2*) epoch was 0.04 ± 0.06 (range -0.60–0.65). Significant correlations were found in 14% (3/21) OPNs; two OPNs had a significant positive correlation ($r = 0.65$, $P < 0.05$;

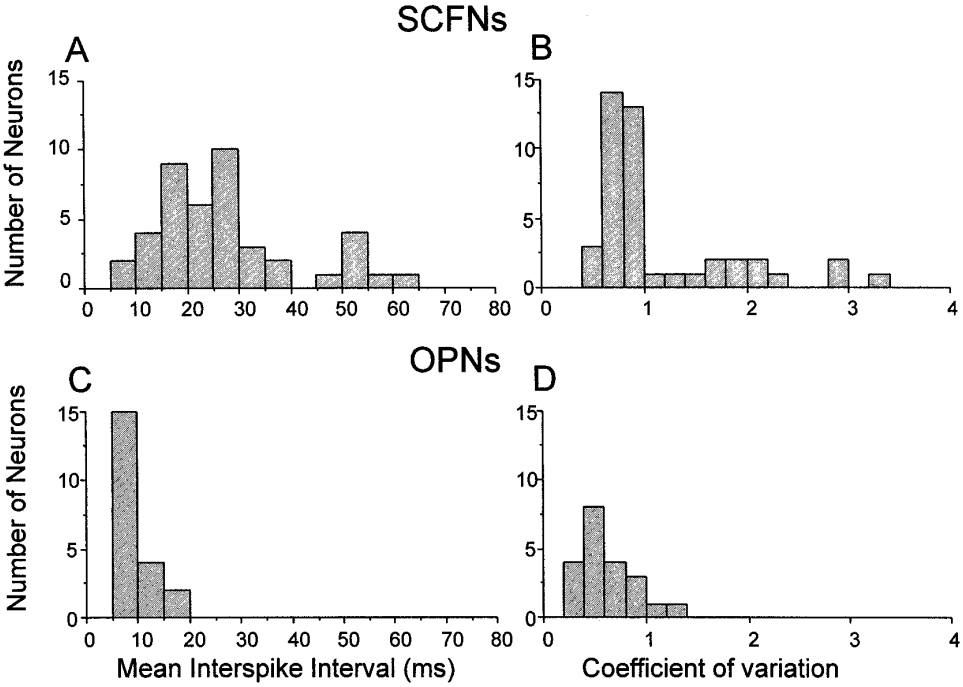

FIG. 4. Plot of the mean interspike intervals of SCFNs (*A*) and OPNs (*C*) and of the coefficient of variation (standard deviation/mean) of SCFNs (*B*) and OPNs (*D*). Binwidth: 5 ms (*A* and *C*) and 0.2 (*B* and *D*). Note the shorter and more regular interspike intervals of OPNs.

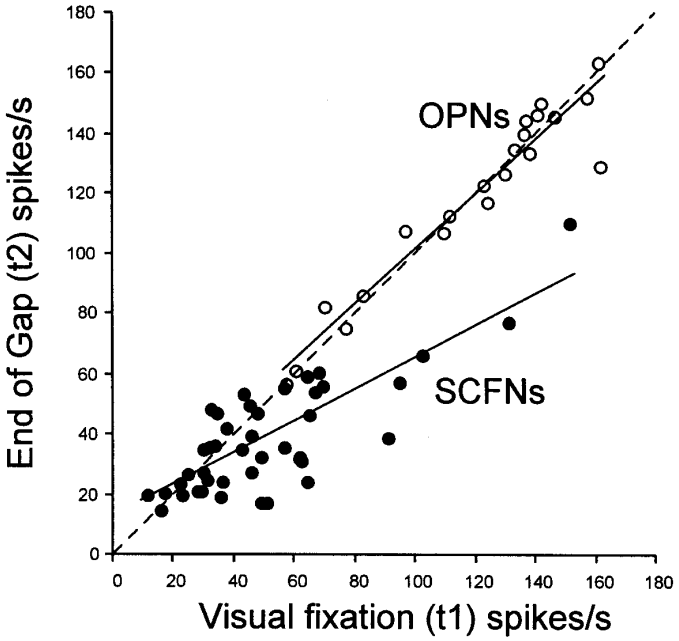

FIG. 5. Mean discharge rates of individual SCFNs (solid circle) and OPNs (open circle) during visual fixation (*t1*) plotted against the mean discharge rates at the end of the gap period (*t2*). Dashed line, unity line (slope = 1). Note that most SCFNs decreased their discharge rates during the gap period (i.e., points lie below dashed line), whereas OPNs maintained their discharge rates (i.e., points lie along dashed line). Straight lines were generated by a linear regression analysis (SCFNs: slope = 0.53, *y*-axis intercept = 11.8, $R^2 = 0.65$; OPNs: slope = 0.91, *y*-axis intercept = 10.8, $R^2 = 0.92$).

$r = 0.38$, $P < 0.05$), and one OPN had a significant negative correlation ($r = -0.60$; $P < 0.01$). Thus the discharge rate of OPNs generally was not correlated with SRT.

The gap saccade task favors the occurrence of saccades with short-latency *express* reaction times (Edelman and Keller 1996; Fischer and Boch 1983; Paré and Munoz 1996; Schiller et al. 1987). These express saccades form a separate peak in the distribution of SRTs at ~100 ms, whereas longer latency *regular* saccades occur ~150 ms. As has been demonstrated previously, SCFNs do not alter their gap-related discharge for express versus regular saccades (Dorris et al. 1997). We performed a similar analysis for OPNs. Express saccades were defined as saccades with reaction times between 70 and 125 ms and regular saccades as saccades with reaction times between 126 and 180 ms.

Target-aligned rasters and spike density functions of the activity of an individual OPN associated with the generation of express and regular saccades are shown in Fig. 6, *left* and *middle*, respectively. This OPN had the same level of tonic activity during the gap period for both types of saccades. The two spike density functions are superimposed in Fig. 6, *right*, and, except for the earlier pause in activity associated with the shorter latency express saccades, there was no difference between them during either the *t1* or the *t2* epochs (Mann-Whitney *U* test, $P > 0.05$). However, this OPN displayed a transient increase in discharge rate for regular saccades, which was absent for express saccades (Fig. 6, arrows). This small burst occurred ~60 ms after target appearance, the time at which the pause in activity started when an express saccade was to be produced.

Sufficient data (≥5 express saccades and 5 regular saccades) was obtained from 12 OPNs for a statistical analysis. None of the OPNs differed significantly in their discharge rates during either the *t1* or the *t2* epochs between express and regular saccades (Mann-Whitney *U* test, $P > 0.5$) (Fig. 7). Before express saccades, the mean discharge rate was 107.9 ± 11.0 spikes/s (range 59–158) during the *t1* epoch and 109.1 ± 10.7 spikes/s (range 59–158) during the *t2* epoch (Wilcoxon signed-rank test, $P = 0.39$). Before regular saccades, the mean discharge rate was 108.8 ± 10.8 spikes/s (range 56–154) and 110.6 ± 10.5 spikes/s (range 59–158) during the *t1* and the *t2* epochs, respectively (Wilcoxon signed-rank test, $P = 0.48$). The mean discharge of OPNs between express and regular saccades did not differ during either the *t1* (Wilcoxon signed-rank test, $P = 0.12$) or the *t2* epochs (Wilcoxon signed-rank test, $P = 0.51$).

Target-related responses

As shown above, many SCFNs reduced their discharge during the gap, thereby indicating a possible visual foveal input to these neurons. In a small percentage of SCFNs and OPNs, we also observed a transient increase in discharge

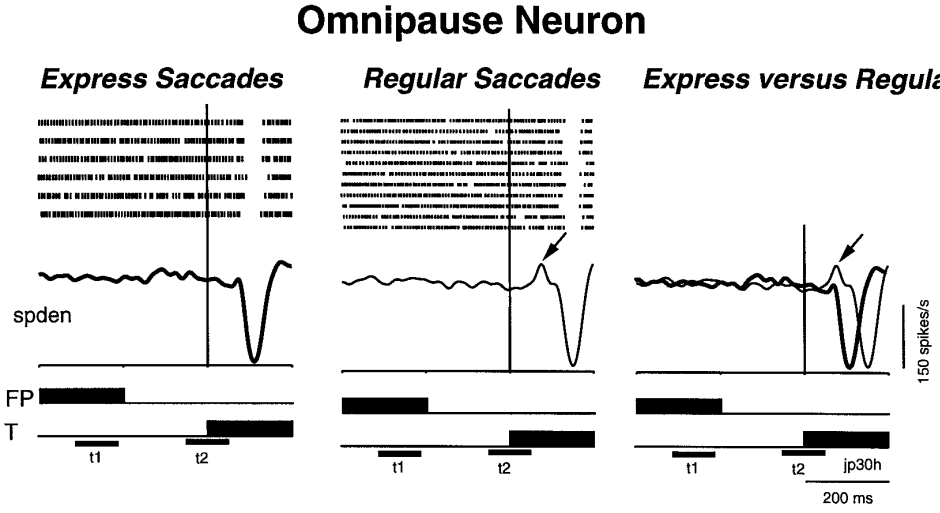

FIG. 6. Activity of an individual OPN preceding express and regular saccades to targets located 10° left. OPN maintained its tonic discharge rate during the gap period before express and regular saccades. This OPN had a weak phasic response (→) ~60 ms after the presentation of the target.

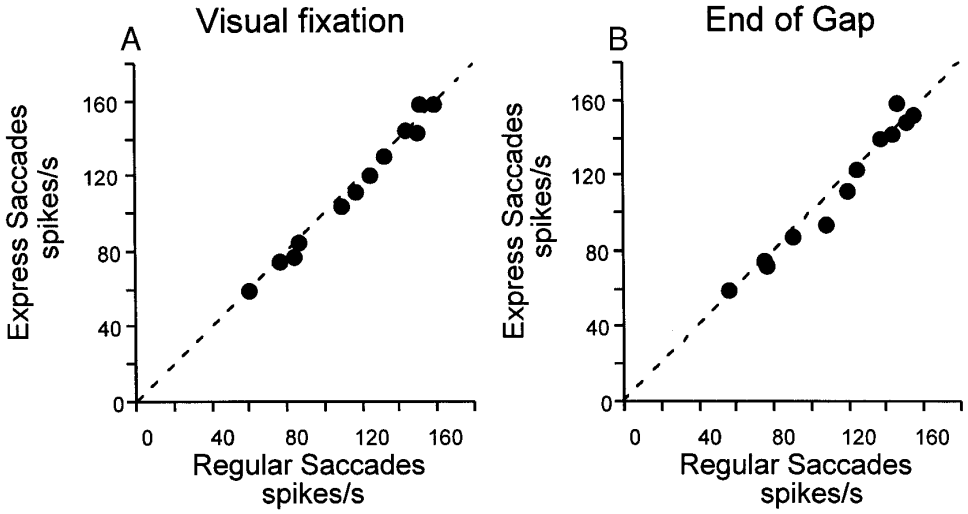

FIG. 7. Discharge rates of individual OPNs before regular saccades (abscissa) plotted against the discharge rates before express saccades (ordinate) during visual fixation (*A*) and at the end of the gap period (*B*). – – –, unity line (slope = 1).

rate after FP disappearance. Figure 8 illustrates, for both a SCFN and an OPN, the modest increase in discharge (Fig. 8, →) after the FP disappearance (¦) in 200-ms gap trials. To test whether these increases in discharge were significant, we compared the mean discharge rate during the control interval 0–40 ms after FP disappearance (*Ctrl* epoch in Fig. 8) with the mean discharge rate during the interval 70–110 ms after FP disappearance (*Vis* epoch) with a one-tailed Student's *t*-test. These intervals were chosen because all neurons with a transient increase exhibited a peak in discharge in the interval 70–110 ms. Significant responses were observed in 24% (5/21) OPNs and 21% (9/43) SCFNs. The OPNs with significant responses increased their discharge rate from 115 ± 8.9 spikes/s (range 91–46) to 138.8 ± 7.9 spikes/s (range 114–159). The SCFNs with significant responses increased their discharge rate from 42.2 ± 2.3 spikes/s (range 27–55) to 54.1 ± 4.01 spikes/s (range 35–73).

We also observed a transient phasic increase in discharge after target appearance 10° right or left in some SCFNs and OPNs in the gap saccade task. For example, the OPN shown in Fig. 6 had a transient increase in discharge ~60 ms after target appearance before regular saccades (Fig. 6, →). We did not attempt to quantify the size of the peripheral visual receptive fields of SCFNs and OPNs here, but we tested whether the presentation of targets at 10° right or left produced a significant elevation of discharge. To do so, we compared the mean discharge rate during the control interval 0–40 ms after target appearance with the mean discharge rate in the interval 50–90 ms after the presentation of the target with a one-tailed Student's *t*-test. Trials with express saccades were excluded from this analysis because OPNs and SCFNs then started to pause during the interval 50–90 ms after target appearance. We found that 52% (11/21) OPNs and 14% (6/43) SCFNs had a significant increase in discharge after target appearance. The OPNs that showed a

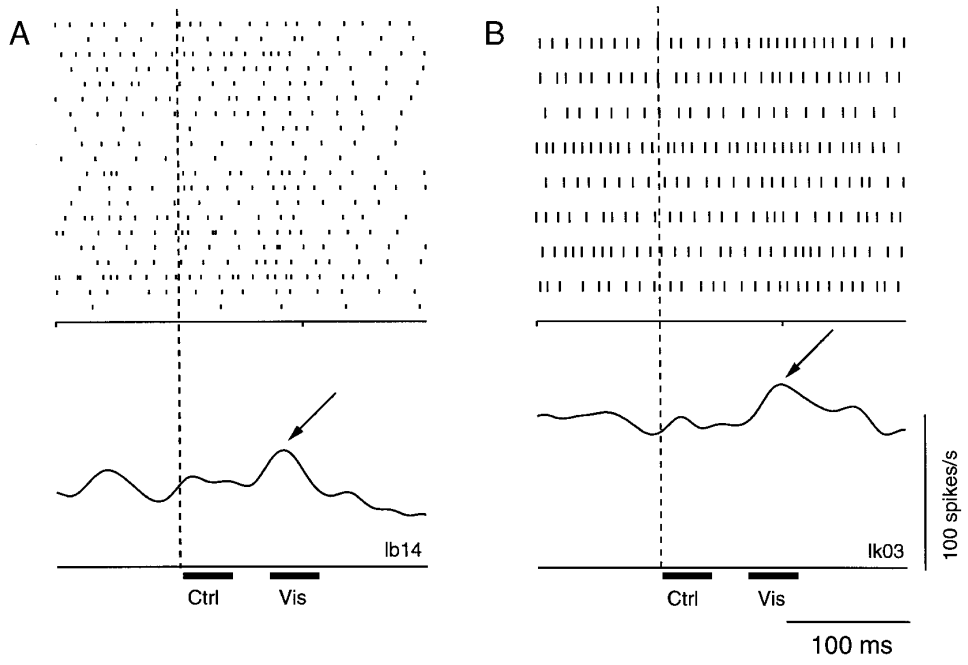

FIG. 8. Responses (→) of a SCFN (*A*) and an OPN (*B*) to the disappearance of the FP (– – –) during 200-ms gap trials. Individual rasters of neuron discharge (*top*) and the spike density functions (*bottom*) are presented. Response magnitude was determined by contrasting the discharge rate during the interval between 70 and 110 ms after FP disappearance (Vis) to a control discharge rate measured during the 40-ms interval after FP disappearance (Ctrl).

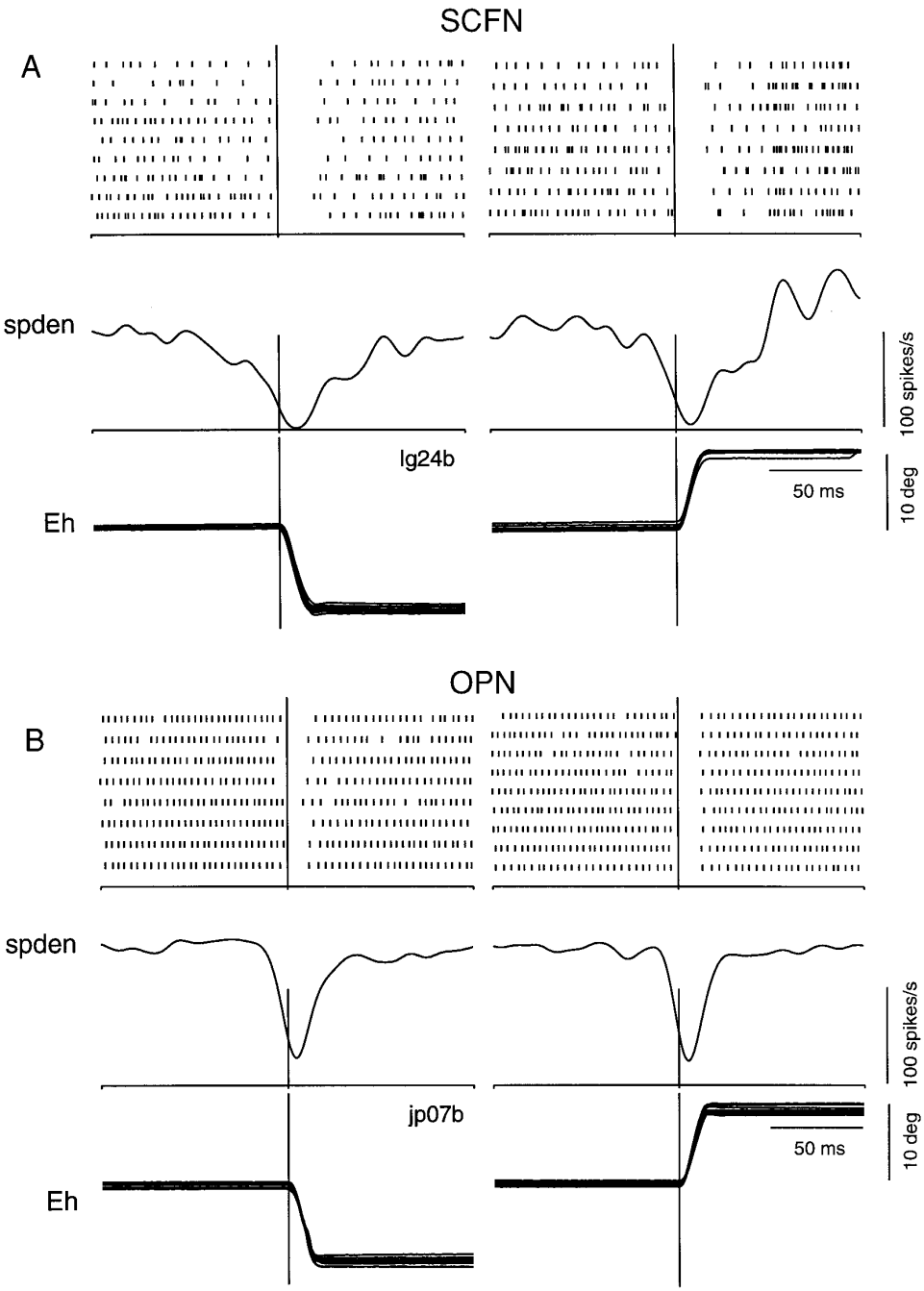

FIG. 9. Activity of a SCFN (*A*) and an OPN (*B*) aligned on the onset of 10° left and right saccades. Individual rasters of neuron discharge, the spike-density functions (spden), and the horizontal eye positions (Eh) are shown for both neurons. Upward deflections denote rightward saccades, downward deflections denote leftward saccades. SCFN decreased its activity gradually before the saccade, whereas the OPN showed a rather abrupt pause in activity.

significant increase elevated their discharge rate from 119 ± 7.9 spikes/s (range 72–152) to 126.1 ± 9.2 spikes/s (range 77–165). Among these, 36% (4/11) had an increase in discharge rate after target appearance 10° left and right. The SCFNs that showed a significant increase elevated their discharge rate from 31.6 ± 7.9 spikes/s (range 9–54) to 45.3 ± 8.7 spikes/s (range 54–75). All of them responded only to targets in the contralateral hemifield.

Neuronal activity preceding saccades

Although SCFNs and OPNs both ceased discharging during saccades, there were noticeable differences in their discharge rates preceding the saccade-related pause. Figure 9 shows the rasters and spike density functions of activity of one SCFN and one OPN aligned on the onset of saccades made to the targets presented 10° left or right. Compared with the OPN, which ceased its discharge rather abruptly, the SCFN exhibited a more gradual decrease in its activity leading up to the saccade-related pause. To quantify this difference in discharge between OPNs and SCFNs before the saccade-related pause, we measured the duration of the last three interspike intervals before the pause. Fig. 10*A* shows the mean durations of these interspike intervals of SCFNs and OPNs. There was a significant difference between all three intervals for SCFNs (Kruskal-Wallis ANOVA, $H = 32.11$, df = 2, $P < 0.0001$; Student-Newman-Keuls method, $P < 0.05$). The last three interspike intervals

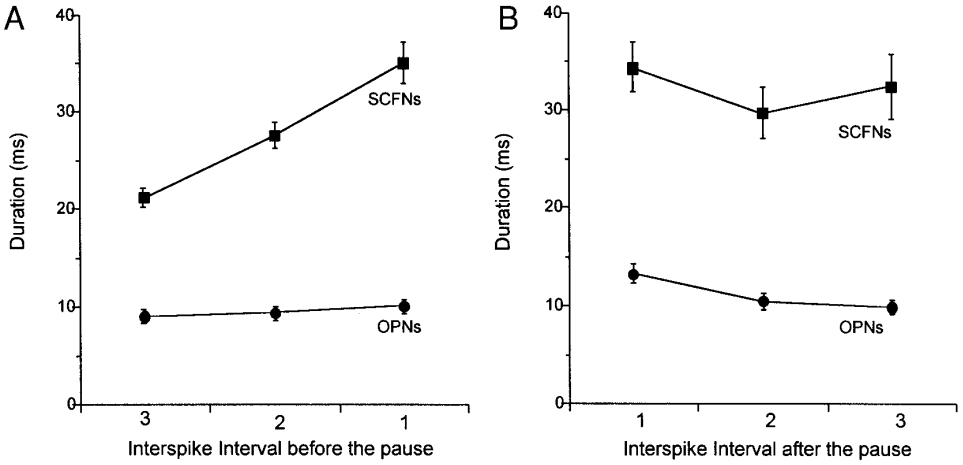

FIG. 10. Plot of the means ± SE of the last 3 interspike intervals before the saccade-related pause in activity (*A*) and of the first 3 interspike intervals after the saccade-related pause (*B*) of SCFNs (■) and OPNs (●).

of OPNs did not differ significantly (Kruskal-Wallis ANOVA, $H = 1.82$, df = 2, $P = 0.40$). Thus SCFNs decreased their discharge gradually preceding the saccade-related pause, whereas OPNs ceased their discharge abruptly.

Temporal relationship between pause and saccade

We studied the temporal relationship between the saccade and the saccade-related pause in activity for OPNs and SCFNs. We separated the analysis for SCFNs into ipsiversive and contraversive saccades. Nine SCFNs, which did not pause for 10° contraversive saccades, were excluded from the paired statistical analyses. Because OPNs from the left and right side are located in very close proximity around the midline of the brain stem (Büttner-Ennever et al. 1988), it was not possible to determine with confidence which side of the brain stem they were located in. Hence, each OPN was analyzed separately for leftward and rightward saccades; three OPNs were tested only for rightward saccades. In sum, this analysis was performed on 43 SCFNs for ipsiversive saccades and 34 SCFNs for contraversive saccades and on 18 OPNs for leftward saccades and 21 OPNs for rightward saccades.

Figure 11 shows the mean time from saccade onset to pause onset for each individual OPN and SCFN. For SCFNs, the mean pause onset time was −30.5 ± 2.5 ms (range −74–1 ms) and −31.7 ± 2.9 ms (range −67 to −10 ms) for ipsiversive and contraversive saccades, respectively (Fig. 11, *A* and *B*). 9% (3/34) SCFNs differed significantly in the pause onset time between ipsiversive and contraversive saccades (*t*-test, $P < 0.05$). For the population of SCFNs, the pause onset time was not significantly different between ipsiversive and contraversive saccades (paired *t*-test, $t = 0.164$, df = 33, $P = 0.87$). OPNs paused on average 10.1 ± 0.9 ms (range 16–3 ms) before leftward saccades and 11.7 ± 0.9 ms (range 10–4 ms) before rightward saccades (Fig. 11, *C* and *D*). For 11% (2/18) OPNs, significant differences in the pause onset time were observed between leftward and rightward saccades (*t*-test, $P < 0.05$). A comparison of the mean pause onset times of all OPNs revealed no significant differences between leftward and rightward saccades (paired *t*-test, $t = 1.05$, df = 17, $P = 0.31$). The difference between the pause onset times of the population of SCFNs (ipsiversive and contraversive saccades) and OPNs (leftward and rightward saccades) was highly significant (Mann-Whitney *U* test, $P < 0.0001$).

We examined the coupling of the saccade-related pauses in activity with the onset of saccades by calculating the correlation coefficients of the relationship between the times from target appearance to saccade onset and target appearance to pause onset for each SCFN and OPN (see METHODS). Figure 12 shows the distribution of these correlation coefficients. For the population of SCFNs, the mean correlation coefficients were 0.82 ± 0.02 (range 0.39–0.98) for contraversive saccades and 0.84 ± 0.02 (range 0.52–0.98) for ipsiversive saccades. For the OPNs, the mean correlation coefficients were 0.97 ± 0.07 (range 0.71–1) and 0.99 ± 0.01 (range 0.89–1) for leftward and rightward saccades, respectively. The differences in correlation coefficients between OPNs and SCFNs were highly significant (Mann-Whitney *U* test, $P < 0.0001$). The higher correlation coefficients of OPNs compared with those of SCFNs indicate that the OPN pause in activity were coupled more tightly to saccade onset than that of the SCFNs.

Figure 13 depicts the temporal relationship between saccade end and pause end. For SCFNs, the mean pause end time was 31.2 ± 5.0 ms (range −15–141 ms) and 30.3 ± 6.7 ms (range −12–173 ms) for ipsiversive and contraversive saccades respectively (Fig. 13, *A* and *B*). The pause end times were significantly shorter for ipsiversive than for contraversive saccades in 24% (8/34) SCFNs (*t*-test, $P < 0.05$). A comparison of the mean pause end times of all SCFNs revealed no significant differences (paired *t*-test, $t = 0.138$, df = 33, $P = 0.89$). For OPNs, the mean time from the end of the saccade to the end of the pause was 2.3 ± 3.8 ms (range −11–53 ms) for leftward saccades and 9.3 ± 3.6 ms (range −13–65 ms) for rightward saccades (Fig. 13, *C* and *D*). This difference between leftward and rightward saccades was significant (paired *t*-test, $t = 4.71$, df = 17, $P < 0.001$). The difference in the pause end time was significantly different for 61% (11/18) OPNs (*t*-test, $P < 0.05$). The difference between the pause end time of the population of SCFNs (ipsiversive and contraversive saccades) and OPNs (leftward and rightward saccades) was significant (Mann-Whitney *U* test, $P < 0.02$).

We evaluated the coupling of the saccade-related pause in activity with the end of the saccade by calculating the

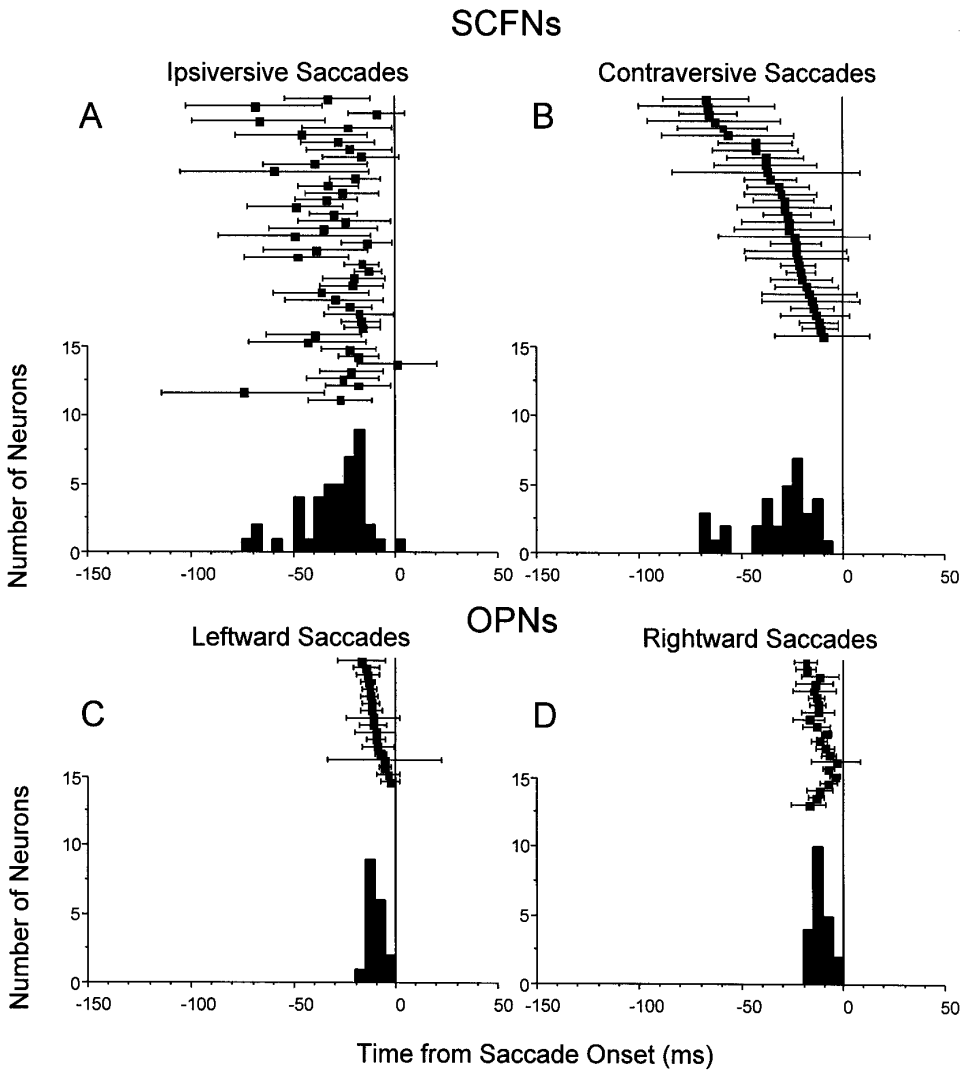

FIG. 11. Distribution of the time from saccade onset to pause onset for ipsiversive (*A*) and contraversive (*B*) saccades in SCFNs and for leftward (*C*) and rightward (*D*) saccades in OPNs. Horizontal lines correspond to data from a single neuron expressed as the mean latency ± SD. Negative values imply that the pause onset preceded saccade onset.

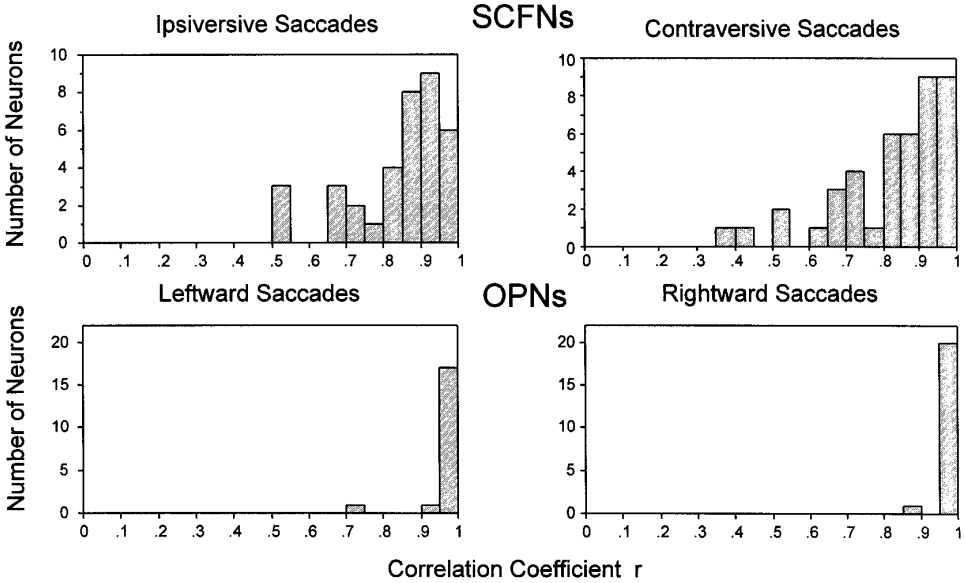

FIG. 12. Distribution of correlation coefficients of the relationship between the times from target appearance to saccade onset and target appearance to pause onset for SCFNs (*A* and *B*) and OPNs (*C* and *D*). Binwidth: 0.05.

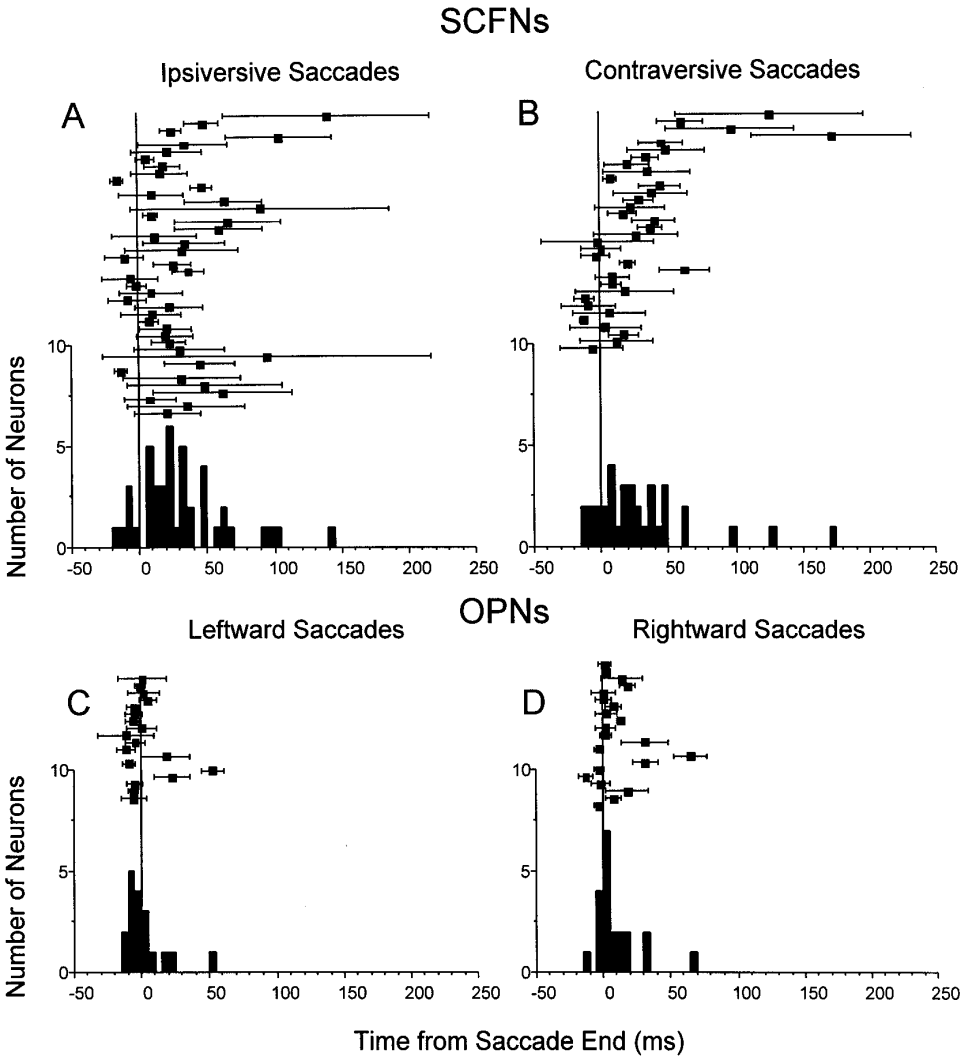

FIG. 13. Distribution of the time from saccade end to pause offset for ipsiversive (*A*) and contraversive (*B*) saccades in SCFNs and for leftward (*C*) and rightward (*D*) saccades in OPNs. Horizontal lines correspond to data from a single neuron expressed as the mean latency ± SD. Negative values imply that the pause offset preceded saccade end.

correlation coefficients of the relationship between the times from target appearance to saccade end and target appearance to pause end for each SCFN and OPN (see METHODS). Figure 14 depicts the distribution of the correlation coefficients of the individual SCFNs and OPNs. The mean correlation coefficients of SCFNs were 0.70 ± 0.03 (range 0.14–1) and 0.63 ± 0.04 (range 0.06–0.99) for ipsiversive and contraversive saccades, respectively. The mean correlation coefficients of OPNs were 0.93 ± 0.02 (range 0.74–1) for leftward saccades and 0.97 ± 0.01 (range 0.88–1) for rightward saccades. The differences between OPNs (leftward and rightward saccades) and SCFNs (ipsiversive and contraversive saccades) were significant (Mann-Whitney *U* test, $P < 0.0001$). Thus the end of the OPN pause was better correlated to the end of saccades than that of the SCFNs.

To determine whether the pauses of SCFNs and OPNs were better correlated with the onset or the end of saccades, we also compared the correlation coefficients of the relationship between the times from target appearance to saccade onset and from target appearance to pause onset with those of the relationship between the times from target appearance to saccade end and from target appearance to pause end. The results revealed that the pause in activity of both SCFNs (Mann-Whitney *U* test, $P < 0.0001$) and OPNs (Mann-Whitney *U* test, $P < 0.01$) was correlated significantly better with saccade onset than with saccade end.

Neuronal activity after saccades

To quantify how OPNs and SCFNs resumed discharging after their saccade-related pause in activity, we measured in each neuron the duration of the first three interspike intervals after the pause. Figure 10*B* shows the mean durations of these three interspike intervals of SCFNs and OPNs, respectively. The first three interspike intervals of SCFNs did not differ significantly (Kruskal-Wallis ANOVA, $H = 2.71$, $df = 2$, $P < 0.26$). Moreover, Fig. 10*B* shows a high variability among SCFN interspike intervals. The first three interspike intervals of OPNs differed significantly (Kruskal-Wallis ANOVA, $H = 7.51$, $df = 2$, $P = 0.02$). A pairwise comparisons showed significant differences between the first interspike interval and the second interspike interval and between the first and third interspike interval (Student-Newman-Keuls method, $P < 0.05$) but not between the second and the third interspike interval ($P > 0.05$). These results indicate that OPNs increased gradually their discharge rate

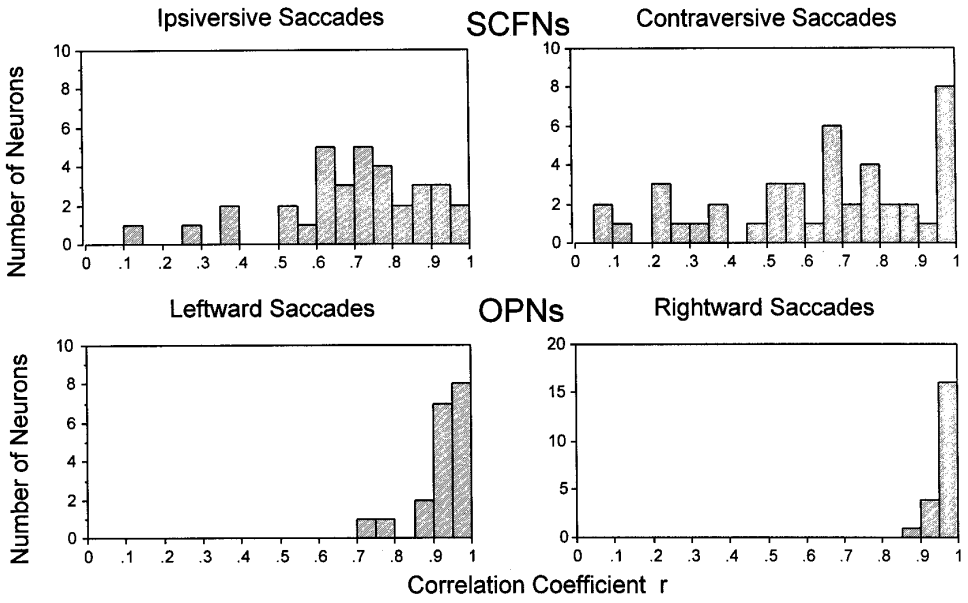

FIG. 14. Distribution of correlation coefficients of the relationship between the times from target appearance to saccade end and target appearance to pause end for SCFNs (*A* and *B*) and OPNs (*C* and *D*). Binwidth: 0.05.

after their saccade-related pause. In contrast, SCFNs had no regular discharge pattern after their pause in activity.

We quantified the postsaccadic discharge rate of SCFNs and OPNs by comparing the mean discharge rates during visual fixation before FP disappearance (*t1*) with the mean discharge rates during visual fixation after the saccade (*t3*). A postsaccadic enhancement index (Munoz and Wurtz 1993a) was calculated by dividing a neuron's mean discharge rate after the end of saccades by that before the FP disappeared (see METHODS). Figure 15 shows the distribution of postsaccadic enhancement indices for SCFNs (*A* and *B*) and OPNs (*C* and *D*). SCFNs changed their discharge rate from 49.8 ± 4.3 spikes/s (range 15–151) before FP disappearance to 55.8 ± 8.4 spikes/s (range 4–257) after ipsiversive saccades (paired *t*-test, $t = 1.06$, df = 42, $P = 0.29$). Their discharge rate changed from 54.4 ± 5.0 spikes/s (range 16–152) to 57.9 ± 7.4 spikes/s (range 13–240) after contraversive saccades (paired *t*-test, $t = 0.75$, df = 35, $P = 0.48$). There was no difference in the postsaccadic enhancement index between ipsiversive and contraversive saccades (paired *t*-test, $t = 0.04$, df = 35, $P = 0.99$). A significant increase in postsaccadic discharge was found in 20.9% (9/43) SCFNs after ipsiversive saccades (paired *t*-test, $P < 0.05$), and in 20.9% (10/36) SCFNs after contraversive saccades (paired *t*-test, $P < 0.05$). Figure 15 also shows that a large number of SCFNs had a postsaccadic

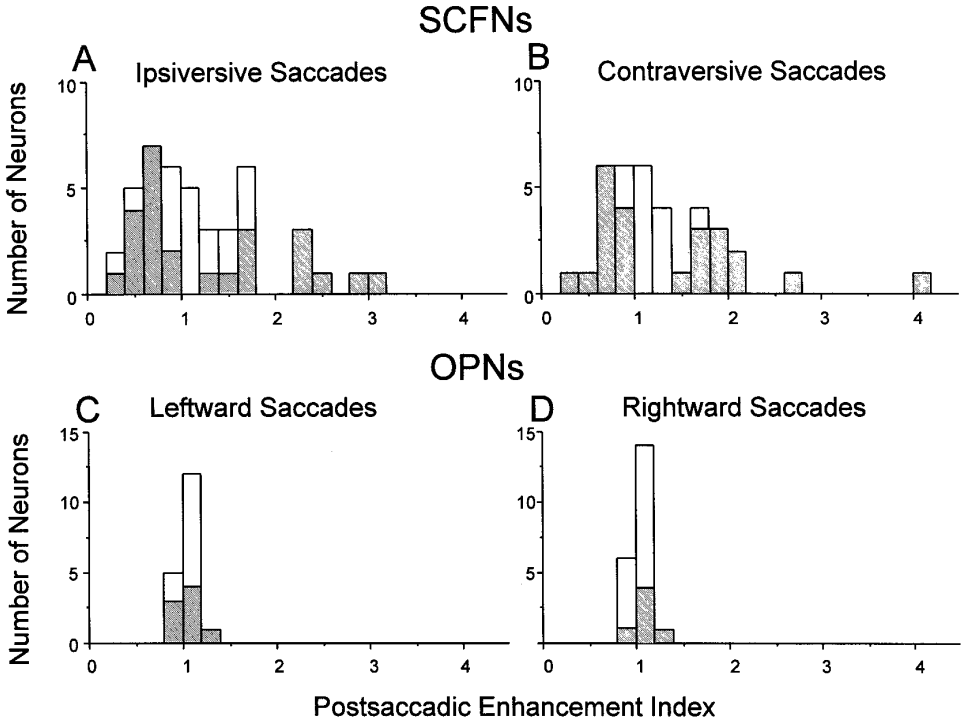

FIG. 15. Plot of postsaccadic enhancement index calculated for SCFNs for ipsiversive (*A*) and contraversive saccades (*B*) and for OPNs for leftward (*C*) and rightward saccades (*D*). Index was calculated by dividing the mean discharge 50–150 ms after the end of a saccade by that in the 100 ms preceding FP disappearance. Neurons with significant postsaccadic discharge differences are shaded.

enhancement index <1.0. A significant decreased discharge rate during the *t3* epoch compared with the *t1* epoch was found in 33% (14/43) SCFNs after ipsiversive saccades and in 33% (12/36) SCFNs after contraversive saccades.

OPNs changed their discharge rate from 114.2 ± 7.8 spikes/s (range 56–156) to 116.5 ± 7.6 spikes/s (range 57–164) after leftward saccades (paired *t*-test, $t = 0.93$, df = 17, $P = 0.37$). Their discharge rate changed from 119.9 ± 7.4 spikes/s (range 57–160) to 120.6 ± 7.4 spikes/s (range 61–180) after rightward saccades (paired *t*-test, $t = 0.25$, df = 20, $P = 0.80$). A large number of OPNs had a significantly higher postsaccadic discharge (Fig. 15, *C* and *D*). A significant increase was found in 28% (5/18) OPNs after leftward saccades, and in 23.8% (5/21) OPNs after rightward saccades. A significantly reduced discharge rate was found in 17% (3/18) OPNs after leftward saccades and in 5% (1/21) OPNs after rightward saccades.

DISCUSSION

Monkey OPNs and SCFNs display tonic activity related to fixation behavior and a pause in activity associated with saccades. We have shown in this paper that, despite these similarities, the discharge characteristics of OPNs and SCFNs differ in several aspects. First, OPNs discharged at a higher and more regular level than SCFNs during visual fixation (see Figs. 2–5). Second, SCFNs but not OPNs reduced their activity during the gap period in the gap saccade task (see Figs. 2 and 5). Third, approximately half of the OPNs responded to visual targets presented 10° left or right (see Fig. 6), whereas only a small percentage of SCFNs responded to targets presented in the contralateral visual field only. Fourth, SCFNs exhibited a gradual decrease in activity before the saccade-related pause, whereas OPNs had an abrupt halt in discharge at pause onset (see Figs. 9 and 10*A*). Fifth, the pause onset was better correlated to saccade onset in OPNs than in SCFNs (see Figs. 11 and 12). Sixth, after the saccade-related pause, OPNs resumed discharging significantly earlier than SCFNs, and they were better synchronized to saccade end (see Figs. 13 and 14). These results indicate that the hypothesis that SCFNs provide the main excitatory input to OPNs must be revised. First, we discuss our data with respect to previous studies. Then we discuss possible hypotheses that can account for our results. These differences in the discharge of OPNs and SCFNs and the finding that neither the discharge of SCFNs (Dorris et al. 1998) nor OPNs (present study) is correlated with SRT are discussed in terms of the function of a fixation system within the brain.

General discharge properties of SCFNs and OPNs

Our results confirm and extend many of the properties of SCFNs (Munoz and Wurtz 1993a) and OPNs (Keller 1974; Luschei and Fuchs 1972; Raybourn and Keller 1977) in monkey that have been described previously. Munoz and Wurtz (1993a) reported that the average discharge rate of SCFNs during visual fixation was 50.9 spikes/s. This discharge rate is similar to the mean discharge of our sample of SCFNs (average 47.5 spikes/s). Luschei and Fuchs (1972) reported that the discharge rate of OPNs varied between 75 and 150 spikes/s and that some of the neurons paused for saccades in one direction only. Keller and colleagues (Keller 1974; Raybourn and Keller 1977) described two types of OPNs. One type discharged at a high rate (100–250 spikes/s) and paused for saccades in all directions, the other type discharged at a lower rate (60–140 spikes/s) and paused for ipsiversive saccades only. All OPNs in our study paused for both ipsiversive and contraversive saccades, and their discharge rates during active visual fixation varied from 57 to 162 spikes/s (average 119 spikes/s).

In addition to their higher discharge rates, OPNs discharged at a more regular rate than SCFNs. Our approach of contrasting the coefficients of variation of interspike intervals during visual fixation (see Fig. 4), and the three intervals preceding (see Fig. 10*A*) and after the saccade-related pause in discharge (see Fig. 10*B*) provided quantitative measurements for comparing the variability in discharge rate between SCFNs and OPNs. Earlier reports described that the tonic discharge rate of OPNs was relatively constant for any neuron (Luschei and Fuchs 1972). It was reported previously that SCFNs decrease their discharge rate after the FP disappearance in the gap saccade task (Dorris and Munoz 1995; Dorris et al. 1997). This discharge behavior of SCFNs differed from that of OPNs, which did not show any modulation of their tonic activity during the gap period (see Figs. 2 and 5).

It has been shown that nearly all OPNs in cats have visual responses (Evinger et al. 1982; King et al. 1980). The receptive fields of OPNs in cats are large and always include a representation of the area centralis (Evinger et al. 1982). In contrast, only a small percentage of monkey OPNs have been found to respond to visual stimulation (Fuchs et al. 1985, 1991). This is in contrast to our finding that 52% (11/21) of the OPNs responded phasically to the presentation of the eccentric target and 24% (5/21) to the disappearance of the FP. Although we did not measure the extent of the visual receptive fields of OPNs, the observation that some OPNs responded to stimuli presented both 10° left and right of the FP suggests that at least some monkey OPNs also have very large visual receptive fields, which include both the ipsilateral and contralateral side.

It was reported previously that SCFNs have a foveal visual input (Munoz and Wurtz 1993a). We confirmed this observation in the present study; 21% (9/43) SCFNs had a significant transient increase in their discharge rate 70–110 after the disappearance of the central FP. However, only 14% (6/43) SCFNs showed a significant visual response after the presentation of the eccentric target to the contralateral side at 10°. Therefore, the visual receptive fields of OPNs appear to be much larger in size than the visual receptive fields of SCFNs, which are confined to foveal and parafoveal regions of the contralateral visual field (Munoz and Wurtz 1993a).

SCFNs and OPNs paused before saccadic eye movements. The average pause onset time of OPNs in our study was 11 ms before the saccade's start, which was slightly later than that described previously (16 ms) (Raybourn and Keller 1977). The average pause onset time of SCFNs in our study was 31 ms, which was also slightly later than that described previously (35 ms) (Munoz and Wurtz 1993a). Thus on average, the onset of the saccade-related pause of SCFNs occurred

well before the pause of OPNs. In addition, SCFNs gradually decreased their discharge rate before pause onset, whereas the onset of the OPN pause was abrupt (see Fig. 10).

Munoz and Wurtz (1993a) described some SCFNs that have an increased postsaccadic discharge, and they hypothesized that this response reduces the probability of the occurrence of another saccade by increasing the inhibition of saccade-related SC neurons. We confirmed the observation that a number of SCFNs have increased postsaccadic activity. However, our data indicate that the population of SCFNs generally does not increase its activity after a saccade. In fact, a large number of SCFNs showed a decreased postsaccadic activity. We also found increased and decreased postsaccadic discharge among OPNs.

Projections of SCFNs to OPNs

Munoz and colleagues hypothesized that SCFNs provide an important excitatory input to OPNs (Munoz and Guitton 1989, 1991; Munoz and Wurtz 1993a, 1995b). However, the results presented in the present study do not support the hypothesis that the activity of OPNs simply reflects excitatory input from SCFNs alone. There were two separate epochs in the gap saccade task in which SCFN discharge was reduced and OPN discharge remained constant: during the gap period and before the onset of the saccade-related pause. At least four possibilities could account for the differences in discharge behavior of OPNs and SCFNs. First, OPNs do not receive excitatory inputs from SCFNs. Second, OPNs contain specific membrane properties that allow them to maintain a tonic discharge as long as a critical level of excitation is provided. Third, the major excitatory input responsible for the resting discharge of OPNs does not originate from SCFNs. Fourth, OPNs receive additional inputs that can compensate for the variations in discharge rate of SCFNs during the gap saccade task. In this section, we discuss these alternative hypotheses and argue that the first possibility is unlikely, whereas the other options are consistent with the data.

CONNECTIVITY BETWEEN THE SC AND RIP. Anatomic studies have shown that the intermediate layers of the SC project to the contralateral raphe complex in the paramedian pontine reticular formation in cats where OPNs have been reported (Büttner-Ennever et al. 1988; Langer and Kaneko 1984, 1990; Leichnetz et al. 1987; Olivier et al. 1993). This anatomic projection appears to originate mainly from the rostral SC (Büttner-Ennever and Horn 1995; Büttner-Ennever et al. 1997).

Antidromic stimulation experiments have shown that SCFNs project an axon to or through the OPN region in the rip (in monkey: Gandhi and Keller 1996; Istvan et al. 1994; in cat: Munoz and Guitton 1989, 1991). Moreover, a large proportion of OPNs is driven monosynaptically by electrical stimulation of the SC (in monkey: Raybourn and Keller 1977; in cat: Kaneko and Fuchs 1982; King et al. 1980; Paré and Guitton 1994). It has been demonstrated that OPNs respond preferentially to stimulation of the rostral SC (Paré and Guitton 1994). Taken together, these anatomic and physiological observations support strongly the existence of an excitatory connection from the SC to the OPNs. Furthermore, they suggest that the efficacy of this connection is greatest from the rostral SC where the SCFNs are located.

OPNS HAVE SPECIAL MEMBRANE CHARACTERISTICS. The hypothesis that OPNs contain special membrane properties that explain their constant discharge rate and abrupt pause initially is appealing. If it is assumed that OPNs can maintain a high, stable, tonic discharge rate as long as a critical level of excitatory input is provided, then they would be unaffected by fluctuations in activity of SCFNs during the gap period or by the gradual decrease in discharge before the onset of the pause. We found that some OPNs had transient phasic increases in discharge rate in response to the appearance of the eccentric target or in response to the FP disappearance. Moreover, OPNs resumed firing rather gradually after the saccade-related pause and several OPNs showed either increased or decreased postsaccadic discharge rates. These findings rule out the possibility that OPNs can only discharge at two levels: either active at a constant level or completely silent. Rather, these findings suggest that OPN discharge can change in response to specific changes in environmental stimuli. However, it is still possible that special membrane properties may contribute to the relatively constant discharge of OPNs.

OPN RESTING DISCHARGE DOES NOT ORIGINATE FROM SCFNS. King and coworkers (1980) demonstrated that lesions of the SC had no effect on the resting discharge of OPNs in anesthetized cats. Unfortunately, these lesions spared a small rostro-lateral portion of the SC, where SCFNs are located (Munoz and Wurtz 1993a). Given that lesions of neither the SC nor the cerebellum and visual cortex had any impact on the resting discharge of OPNs, these authors hypothesized that the excitatory drive to OPNs arises predominantly from oculomotor neurons in the reticular formation (burst-tonic, tonic neurons) in the immediate vicinity of OPNs, which also have a high resting discharge.

The option that the excitatory input to OPNs arises from structures other than the SC also is favored by the contrasting discharge of OPNs and SCFNs during intertrial intervals: OPNs discharge at a high tonic rate between spontaneous saccades in monkeys (Keller 1974; Luschei and Fuchs 1972; Raybourn and Keller 1977), whereas the discharge rate of SCFNs is lower during intertrial intervals compared with the discharge during behavioral trials (Munoz and Wurtz 1993a).

Other afferents to OPNs arise from the vestibular nuclei (Ito et al. 1984; Langer and Kaneko 1990), the nucleus prepositus hypoglossi (Ito et al. 1984; Langer and Kaneko 1984, 1990), the fastigial nucleus of the cerebellum (Langer and Kaneko 1984), the nucleus raphe dorsalis and the locus coeruleus (Ito et al. 1984), nucleus raphe magnus (Langer and Kaneko 1984, 1990), cochlear nuclei, dorsal column nuclei, and the spinal trigeminal nuclei (Langer and Kaneko 1984, 1990). It is difficult to evaluate the contribution of these inputs to the resting discharge of OPNs, but the observation that OPNs (Henn et al. 1984) stop discharging during sleep suggests an important modulatory input from the nucleus raphe magnus, nucleus raphe dorsalis, and the locus coeruleus to OPNs.

OPNS RECEIVE ADDITIONAL COMPENSATORY INPUTS. An alternative explanation of our results is that the constant discharge rate of OPNs observed during the gap period and

before the saccade-related pause may be the result of additional inputs impinging onto OPNs to compensate for the reduced input from SCFNs during these periods. So far, only the discharge of neurons in the caudal SC (Dorris et al. 1997) and in the frontal eye field (Dias and Bruce 1994) has been recorded during the gap saccade task. Both, the caudal SC (Olivier et al. 1993; Paré and Guitton 1994; Raybourn and Keller 1977) and the frontal eye field (Segraves 1992; Stanton et al. 1988) project to OPNs. Neurons in the frontal eye field increase their discharge rate during the gap period (Dias and Bruce 1994). However, the observation that electrical stimulation of the frontal eye field results in a pause in OPN discharge, probably mediated by local interneurons (Segraves 1992), argues against a compensatory excitatory input originating from this cortical area.

A more likely source of the compensatory excitatory input may be the SCBUNs. These neurons increase their discharge rate during the gap period in the gap saccade task in a manner that is reciprocal to that of the SCFNs (Dorris et al. 1997; Munoz and Wurtz 1995a). They also project via the predorsal bundle to or through the OPN region in the rip (Istvan et al. 1994). If both SCFNs and SCBUNs converge onto OPNs, then any reduced excitatory input due to reductions in SCFN discharge would be compensated by a reciprocal increased excitatory input from the SCBUNs during the same periods. Therefore, OPNs could maintain the same tonic level of discharge during the gap period and before the saccade-related pause (see Fig. 16).

This proposed projection of both SCFNs and SCBUNs onto OPNs also could account for another part of our data, namely, the large visual receptive fields of OPNs. SCBUNs have visual receptive fields that include regions of the contralateral visual field (Munoz and Wurtz 1995a). The convergence of SCFN and SCBUN input onto OPNs could provide visual inputs from both the foveal and extrafoveal regions of the visual field. A visual input from neurons in the caudal SC is supported by the observation that bilateral lesions of the SC abolish visual responses of OPNs in cats (King et al. 1980). The finding that some OPNs responded to visual stimuli either to the right or to the left side would indicate that at least some OPNs receive afferents from both the ipsilateral and contralateral SC.

Another unknown in the saccade control circuit is related to the precise source of the signal that causes the OPNs to cease discharging immediately before all saccades. During a saccade, the oculomotor neurons in the brain stem reticular formation (i.e., burst-tonic neurons) may pause for saccades in their off-direction, but they also may burst for saccades in their on-direction. At the time of a saccade most SCFNs stop discharging, but SCBUNs coding for the amplitude and direction of the saccade are active, many of them at high frequencies of discharge (Munoz and Wurtz 1995a). Another class of saccade-related neuron in the SC are the burst neurons (SCBNs), which are silent during fixation and discharge a high-frequency burst of action potentials 20 ms before the initiation of saccades of the optimal amplitude and direction (Munoz and Wurtz 1995a; Sparks 1978). These SCBNs also project an axon via the predorsal bundle into the vicinity of the rip (Istvan et al. 1994; Moschovakis et al. 1988a; Scudder et al. 1996). Microstimulation of the SC not only leads to monosynaptic activation of OPNs, it also leads to polysynaptic inhibition of OPNs (Raybourn and Keller 1977). It is therefore possible that the SCBNs terminate on local pontine inhibitory neurons that could inhibit the OPNs to account for the saccade-related pause in activity. If the efficacy of this inhibitory input to OPNs was of a sufficient strength, it could overcome the proposed excitatory input of SCBUNs onto OPNs.

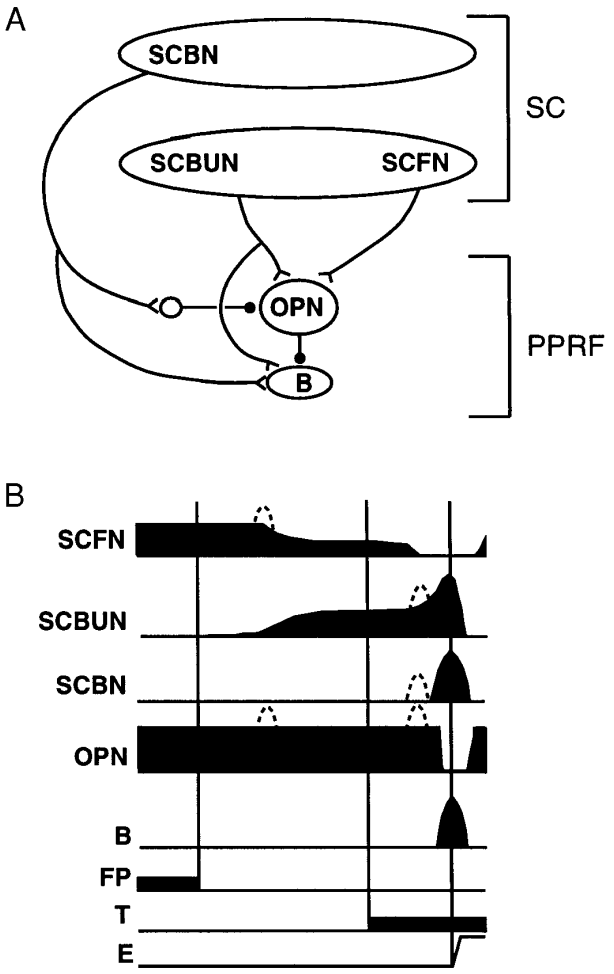

FIG. 16. Schematic representation of the connections from neurons in the SC to the OPNs (*A*) and temporal changes in discharge rate in these neurons in the gap saccade task (*B*). Lines ending in open angles: excitatory synapses. Lines ending in filled circles: inhibitory synapses. B, burst neuron; E, eye position; FP, fixation point; OPN, omnipause neuron; PPRF, paramedian pontine reticular formation; SC, superior colliculus; SCFN, superior colliculus fixation neuron; SCBN, superior colliculus burst neuron; SCBUN, superior colliculus buildup neuron; T, target. Dotted lines in *B*, changes in discharge rate (visual responses) that are only observed in a subset of each class of neurons. See DISCUSSION for details.

To date, no neurons have been identified in the brain stem that burst for saccades in all directions and project directly to the OPNs in the rip. It, however, recently was reported that neurons in the basal interstitial nucleus of the monkey cerebellum discharge a burst of action potentials for saccades in all directions (Kawagoe et al. 1996). A key feature of this activity was that it was best correlated to the temporal aspects of the saccade. These neurons were located in a region of the cerebellum just ventral to the dentate nucleus and this area may project to the rip (Gonzalo-Ruiz et al. 1988). Thus it is possible that they may convey an inhibitory

input to the OPNs to account for the cessation of OPN activity during a saccade.

Fixation system in the brain

Besides SCFNs and OPNs, neurons with fixation-related activity have been found in the frontal eye field (Bruce and Goldberg 1985; Burman and Bruce 1997), supplementary eye field (Bon and Lucchetti 1992; Lee and Tehovnik 1995; Schall 1991; Schlag et al. 1992), prefrontal cortex (Suzuki and Azuma 1977), posterior parietal cortex (Lynch et al. 1977; Sakata et al. 1980), thalamus (Schlag and Schlag-Rey 1984), subthalamic nucleus (Matsumura et al. 1992), zona incerta (Ma 1996), and substantia nigra pars reticulata (Hikosaka and Wurtz 1983). It is currently unclear, however, in what manner these neurons are connected and how the fixation-related activity in one area influences the fixation-related activity of neurons in other areas. If these neurons in these areas form a global fixation system in the brain, then it may be assumed that a change in the activity of neurons in one part of the system has a direct influence on the activity of fixation neurons in other parts. The distinct discharges of OPNs and SCFNs during the gap period and before the initiation of saccades, however, do not support this idea. Alternatively, several independent local fixation systems may exist in the brain that only indirectly influence each other. Fixation neurons at each level may convey their control over saccade generation by local inhibitory connections with saccade neurons on their level.

Recently, it has been questioned whether OPNs and SCFNs play an important role in maintaining fixation and suppressing unwanted saccades, because damage to the OPNs in the rip region with excitotoxic lesions was not found to lead to any apparent fixation instabilities (Kaneko 1996). Such lesions should have reduced the inhibition onto the saccade burst generator. However, it must be considered that a fraction of OPNs surviving the lesions still could have exerted a sufficient functional control on the burst generator. Furthermore, it is entirely possible that monkeys compensated for damage to the OPN region by increasing fixation activity at other levels of the fixation system to reduce excitatory inputs to the burst generator. For example, increased activation of SCFNs within the SC could lead to inhibition of SCBUNs and SCBNs, via hypothesized local inhibitory interactions within the SC (Munoz and Guitton 1989, 1991; Munoz and Wurtz 1993b, 1995b). A similar compensatory mechanism could be activated in the SEF and FEF (Burman and Bruce 1997). This would lead to reduction of the excitatory input to the burst generator and therefore would maintain the stability of fixation.

The idea of a more parallel control of fixation and saccade generation also is favored by our finding that several OPNs have responses to visual peripheral targets. A transient increase in discharge of OPNs during the critical period ~70 ms after stimulus presentation would result in a higher inhibition of the burst generator and also require a stronger inhibitory input onto OPNs to release the burst generator from tonic inhibition. This mechanism—we speculate mediated by a specific projection of the SC saccade-related neurons that display target-related responses—would reduce the number of reflexive express saccades.

Although the high discharge rate of OPNs and SCFNs may help to prevent reflexive express saccades (Munoz and Wurtz 1992), neither the discharge of OPNs (present study) nor that of SCFNs (Dorris et al. 1997) is correlated to SRT. On the other hand, the discharges of SCBUNs (Dorris et al. 1997), saccade neurons in the frontal eye field (Hanes and Schall 1996), and long-lead burst neurons in the brain stem (Everling et al. 1997a) are correlated with SRT. These findings suggest that saccade-related neurons, but not fixation-related neurons, influence SRT.

In summary, we have shown that SCFNs and OPNs share the same general patterns of activity in relation to either fixation or saccade behavior. Beside these similarities, we have demonstrated fundamental differences between the discharges of SCFNs and OPNs indicating that inputs to OPNs, additional to the hypothesized inputs provided by SCFNs, are necessary to control their discharge and gate the occurrence of saccadic eye movements.

We thank A. Lablans, K. Moore, and D. Hamburger for excellent technical assistance.

This work was supported by a group grant from the Medical Research Council of Canada. S. Everling was supported by a postdoctoral fellowship from the Deutsche Forschungsgemeinschaft. M. C. Dorris was supported by a graduate student fellowship from Queen's University. D. P. Munoz is an EJLB Foundation research scholar.

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Received 8 July 1997; accepted in final form 21 October 1997.

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