Progression in Neuronal Processing for Saccadic Eye Movements From Parietal Cortex Area LIP to Superior Colliculus

MARTIN PARÉ AND ROBERT H. WURTZ
Laboratory of Sensorimotor Research, National Eye Institute, National Institutes of Health, Bethesda, Maryland 20892

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Paré, Martin and Robert H. Wurtz. Progression in neuronal processing for saccadic eye movements from parietal cortex area LIP to superior colliculus. *J Neurophysiol* 85: 2545–2562, 2001. Neurons in both the lateral intraparietal area (LIP) of the monkey parietal cortex and the intermediate layers of the superior colliculus (SC) are activated well in advance of the initiation of saccadic eye movements. To determine whether there is a progression in the covert processing for saccades from area LIP to SC, we systematically compared the discharge properties of LIP output neurons identified by antidromic activation with those of SC neurons collected from the same monkeys. First, we compared activity patterns during a delayed saccade task and found that LIP and SC neurons showed an extensive overlap in their responses to visual stimuli and in their sustained activity during the delay period. The saccade activity of LIP neurons was, however, remarkably weaker than that of SC neurons and never occurred without any preceding delay activity. Second, we assessed the dependence of LIP and SC activity on the presence of a visual stimulus by contrasting their activity in delayed saccade trials in which the presentation of the visual stimulus was either sustained (visual trials) or brief (memory trials). Both the delay and the presaccadic activity levels of the LIP neuronal sample significantly depended on the sustained presence of the visual stimulus, whereas those of the SC neuronal sample did not. Third, we examined how the LIP and SC delay activity relates to the future production of a saccade using a delayed GO/NOGO saccade task, in which a change in color of the fixation stimulus instructed the monkey either to make a saccade to a peripheral visual stimulus or to withhold its response and maintain fixation. The average delay activity of both LIP and SC neuronal samples significantly increased by the advance instruction to make a saccade, but LIP neurons were significantly less dependent on the response instruction than SC neurons, and only a minority of LIP neurons was significantly modulated. Thus despite some overlap in their discharge properties, the neurons in the SC intermediate layers showed a greater independence from sustained visual stimulation and a tighter relationship to the production of an impending saccade than the LIP neurons supplying inputs to the SC. Rather than representing the transmission of one processing stage in parietal cortex area LIP to a subsequent processing stage in SC, the differences in neuronal activity that we observed suggest instead a progressive evolution in the neuronal processing for saccades.

INTRODUCTION

The production of sensory guided movements entails a sequence of neural events distributed throughout the neural axis, and it is imperative that the processing hierarchy linking different brain regions be determined if we wish to understand fully their respective contributions within a functional circuit. To this end, a common approach has been to contrast results obtained in independent studies each performed in the distinct brain regions composing a distributed system. Such studies, however, generally permit only coarse comparisons, and experimental discrepancies render impractical the description of subtle but possibly significant differences between brain regions. A more rigorous alternative consists of performing a systematic comparison of the neuronal signals that are closely ordered within the neural sequence and collected under identical experimental conditions. The present study uses this approach to help elucidate the progression in processing linking two structures within perhaps the best-understood sensorymotor circuit in the primate brain, the visuo-saccadic system.

Neural pathways underlying the production of visually guided saccadic eye movements extend through the visual cortex and converge in the brain stem. One of these pathways involves the posterior parietal cortex and the superior colliculus (SC), and a body of literature has described their neuronal activation as transitional between sensory and motor processing stages. Neurons within the SC intermediate layers display, along with their typical visual and saccade-related activation, a low-frequency "prelude" of activity that can precede movement production considerably (Glimcher and Sparks 1992; Mohler and Wurtz 1976; Munoz and Wurtz 1995; Sparks 1978). Within the parietal cortex, the lateral intraparietal (LIP) area contains a distinct population of neurons with visual and saccade-related activation (Andersen et al. 1987) and projects to the SC intermediate layers (Andersen et al. 1990; Asanuma et al. 1985; Lynch et al. 1985). A sustained low-frequency activity between visual stimulation and saccade execution, resembling that of SC neurons, is a prevailing characteristic of these parietal neurons (Barash et al. 1991a,b; Colby et al. 1996; Gnadt and Andersen 1988). Thus independent studies indicate a clear overlap within the activity patterns of the SC and LIP neuronal populations, and we previously showed that this was also the case for the LIP neurons projecting to the SC (Paré and Wurtz 1997a). These observations suggest that area LIP could account for certain aspects of SC activation, particularly the low-frequency activity. The key question is whether there are differences between the activation of LIP and SC neurons, and if so, do they suggest a shift in neuronal processing away from visual processing and toward saccade production?

Present address and address for reprint requests: M. Paré, Dept. of Physiology, Queen's University, Botterell Hall, Rm. 438, Kingston, Ontario K7L 3N6, Canada (E-mail: pare@biomed.queensu.ca).

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To address this question, we directly compared signals in both brain regions in two monkeys performing identical tasks and, most importantly, we limited the comparison to neurons closely ordered within the neural sequence by identifying antidromically the LIP neurons projecting to SC. Using the well-known motor characteristics of SC neurons as a reference to elucidate any progression in processing occurring between the LIP output and the SC, we concentrated our investigation on the neuronal activity that develops after target presentation but in advance of saccades. Understanding this activity is a central issue because it may reveal the nature of covert processes linking sensory representations and motor commands. One existing hypothesis surmises that such delay activity represents a "motor intention" or "preparatory process" (Dorris and Munoz 1998; Dorris et al. 1997; Mazzoni et al. 1996; Platt and Glimcher 1997; Snyder et al. 1997). According to this *motor preparation* hypothesis, the activity's relationship with movement production must be highly predictive when advance information is provided (Evarts et al. 1984; Requin et al. 1991), and its intensity must be largely independent from sustained sensory stimulation. Conversely, neuronal activity being unrelated to the impending movement production and depending strongly on sensory stimulation may rather simply construct a *sensory representation*. Thus if there were a neuronal progression in the processing leading to visually guided saccades, the dependence of this neuronal activity on visual stimulation would gradually lessen while the relation to the impending movement would gradually strengthen.

To examine whether there is such a progression in saccade processing between LIP and SC, we recorded neuronal samples during two behavioral tasks. We dissociated the timing of saccades from visual stimulation with a delayed saccade task to reveal the extent of any delay activity, and we manipulated advance response instruction with a delayed GO/NOGO saccade task to assess the extent to which this delay activity relates to the future production of a saccade. To determine whether the activity was independent of visual stimulation, variations of both tasks allowed us to compare the activity in advance of saccades guided either by a continuously present visual stimulus or by its remembered location. From area LIP to SC, we found a significant increase in the dependence of the delay activity on response instruction and a significant decrease in its dependence on sustained visual stimulation. These findings thus offer evidence of a progressive shift in saccade processing from area LIP to SC.

Brief reports have been presented elsewhere (Paré and Wurtz 1997b; Sommer et al. 1997).

METHODS

Animal preparation

Two male rhesus monkeys (*Macaca mulatta,* 6–11 kg) were prepared for chronic recording of single neurons and eye position in a single surgical procedure carried out under general anesthesia and aseptic conditions. All animal care and experimental procedures were approved by the Institute Animal Care and Use committee and complied with Public Health Service Policy on the humane care and use of laboratory animals.

Just prior to the start of surgery, the animals were given an analgesic (2.0 mg/kg im Flunixin meglumine), and a 10-day treatment of antibiotics (25 mg/kg im Cefazolin) was initiated. They were also premedicated with glycopyrrolate (15 μg/kg im). After induction of anesthesia with ketamine HCl (10 mg/kg im) and diazepam (1 mg/kg im), an endotracheal tube was positioned to permit subsequent gas anesthesia, and an intravenous catheter was inserted in the saphenous vein for fluids to maintain hydration. Anesthesia was continued with isofluorane, and the monkey's head was fixed in a stereotaxic frame throughout the surgery. Scleral search coils were inserted subconjunctivally (Judge et al. 1980), and the connector leads were embedded in a dental acrylic implant that was firmly anchored to the skull by titanium screws inserted into drilled and tapped holes. The implant also included a plastic (ULTEM resin) head-holding device and two plastic recording cylinders (18 mm diam), each positioned over a trephined hole of identical dimension. The first cylinder was directed toward the SC (15 mm above and 1 mm posterior of stereotaxic zero) and was centered on the midline with its top tilted 42° posterior of vertical. The second cylinder was centered on the stereotaxic coordinates P 5.0 and L 12.0 mm and tilted 30° lateral of vertical to allow recordings from area LIP neurons.

Brain imaging procedure

Before the experiments began, an image of each monkey's brain was obtained using magnetic resonance imaging (MRI) technology. In preparation for being positioned within the MRI magnet (1.5 T GE SIGNA scanner), the animals were given an analgesic (0.1 mg/kg im Butorphanol) and premedicated with glycopyrrolate. Anesthesia was induced and maintained with ketamine HCl and diazepam. The animal's head was immobilized with a stereotaxic device (aluminum, brass, and plastic) positioned in the MR scanner to align the imaged sections with the stereotaxic planes. The MRI procedure was a fast SPGR T1-weigthed inversion recovery pulse sequence, and series of coronal and sagittal sections were obtained at 1-mm intervals. We positioned tungsten microelectrodes within the cylinders prior to the MRI scans and directed them near the SC and the lateral bank of the lateral intraparietal sulcus to delimit these brain regions and subsequently provide an anatomical reference to locate the relative position of the penetrations made during experimental sessions.

Experimental procedures

Animals were trained to execute visuooculomotor tasks for a liquid reward. Behavioral paradigms, visual displays, and data acquisition were controlled by a personal computer running a UNIX-based real-time data acquisition system (REX) (Hays et al. 1982). Eye positions were monitored by the magnetic search coil technique (Robinson 1963). Single neurons were recorded with tungsten microelectrodes (Frederick Haer, 1.0–2.0 MΩ at 1 kHz) that were inserted into the brain via a sterile guide tube (13 gauge) positioned in the cylinder with the use of a grid system (Crist et al. 1988). The SC guide tube ended ~5 mm above the surface of the SC, whereas the length of the LIP guide tube was carefully measured and adjusted to allow the microelectrodes to pass through the dura mater while avoiding damage to the cortical tissue as much as possible. Neuronal signals were conventionally amplified, filtered (band-pass 300 Hz to 5 kHz), and displayed on an analog oscilloscope while being played on an audio monitor. They also were transmitted to an additional computer acting as a digital oscilloscope (50 kHz), where action potentials of single neurons were isolated with the use of window discriminator software that excluded action potentials that did not meet amplitude and time constraints. Isolated action potentials, along with horizontal and vertical eye position signals, were digitized at 1 kHz.

During the experiments, monkeys were seated in a primate chair with their head restrained. They faced a vertical tangent screen (Crist and Robinson 1989) positioned exactly 57 cm in front of their eyes, and for which they had an unobstructed view of 80° × 80° (±40° in any direction from straight-ahead). Visual stimuli (<0.5° diam) were generated by a video projector (Sharp 850, 60 Hz) and back-projected

onto the tangent screen. The colors of the visual stimuli were blue ($CIE_{x,y}$ 0.15, 0.07; luminance 0.3 cd/m^2), red ($CIE_{x,y}$ 0.61, 0.38; luminance 1.5 cd/m^2), and green ($CIE_{x,y}$ 0.20, 0.75; luminance 2.0 cd/m^2).

Fluid intake was controlled during training and recording sessions, during which the animals performed until satiated. Fruits and additional fluids were provided regularly. Animal weight, health status, and fluid intake were monitored closely under the supervision of the institute veterinarian.

Behavioral paradigms

All behavioral trials were initiated by the appearance of a visual stimulus, referred to as the fixation point, in the center of the screen. The monkey was required to look at the fixation point within 1,000 ms of its appearance. Once the eyes entered a computer-defined window (±1°) centered on the fixation point, the latter remained on for 500–800 ms (fixation period). If fixation was successful, one of the tasks described below proceeded; otherwise the trial was aborted. Because of the background illumination (0.1 cd/m^2) of the video projector, the behavioral trials were performed only in partial darkness. During the inter-trial interval (randomized between 1,000 and 1,500 ms), the screen was illuminated with diffuse white light (0.6 cd/m^2), and the monkey was not required to fixate.

DELAYED SACCADE TASK. Neurons initially were characterized with the delayed saccade task, which was designed to dissociate temporally the neuronal activity related to visual stimulation from that related to saccade initiation (Fig. 1*A*). After the initial fixation of a red fixation point, a green peripheral stimulus was presented, but the fixation point stayed illuminated for an additional 500- to 1,000-ms period of maintained fixation (delay period). The fixation point disappearance acted as the visual cue signaling the monkey to make a saccade to the stimulus within 500 ms and then maintain eccentric fixation on it to correctly perform the task and be rewarded. Two versions of the delayed saccade task were used to control for the possible contribution of the visual stimulus presence to the neuronal activation. In the visual version of the task, the peripheral stimulus remained present throughout the trial. In the memory (nonvisual) version, the stimulus was only briefly presented (100-ms flash), and the monkey had to make a saccade to the remembered location of the target.

GO/NOGO SACCADE TASK. An additional instructed-delay saccade task with a GO/NOGO paradigm was designed to dissociate temporally the neuronal activity related to visual stimulation, response instruction, and behavioral response (Fig. 1*B*). First, the monkey was required to look at a blue fixation point. If fixation was maintained, a green peripheral stimulus then appeared (stimulus period). After 800–1,200 ms, the fixation point changed color to instruct the monkey that the peripheral stimulus will (green = GO instruction) or will not (red = NOGO instruction) become a saccadic target. After another 800–1,200 ms (instruction period), the fixation point turned back to its original blue color (choice period), the cue signaling the monkey to make a saccade to the stimulus location within 500 ms (GO) or maintain fixation for an additional 1,000 ms (NOGO) before being rewarded. Thus correct behavior in both GO and NOGO trials were rewarded, i.e., the reward procedure was symmetrical.

The above description of the task corresponds to the trials in which the instruction period followed the stimulus period; hereafter referred to as poststimulus instruction trials (Fig. 1*B*, *top*). We also used prestimulus instruction trials (Fig. 1*B*, *bottom*), wherein the instruction period preceded the stimulus period. In addition, visual and memory versions of the GO/NOGO saccade task were used to control for the possible contribution of the visual stimulus presence to the neuronal activation. The eccentric stimulus was visible either for 200 ms (memory version; Fig. 1*B*, black T) or until the end of the trial (visual version; Fig. 1*B*, gray T). Ten to 30 repetitions of each individual trial (visual and memory versions of pre- and poststimulus instruction trials) were randomly interleaved. Single-neuron recording experiments began after the performance of the two monkeys had reached 98% correct trials; we only considered either false alarms

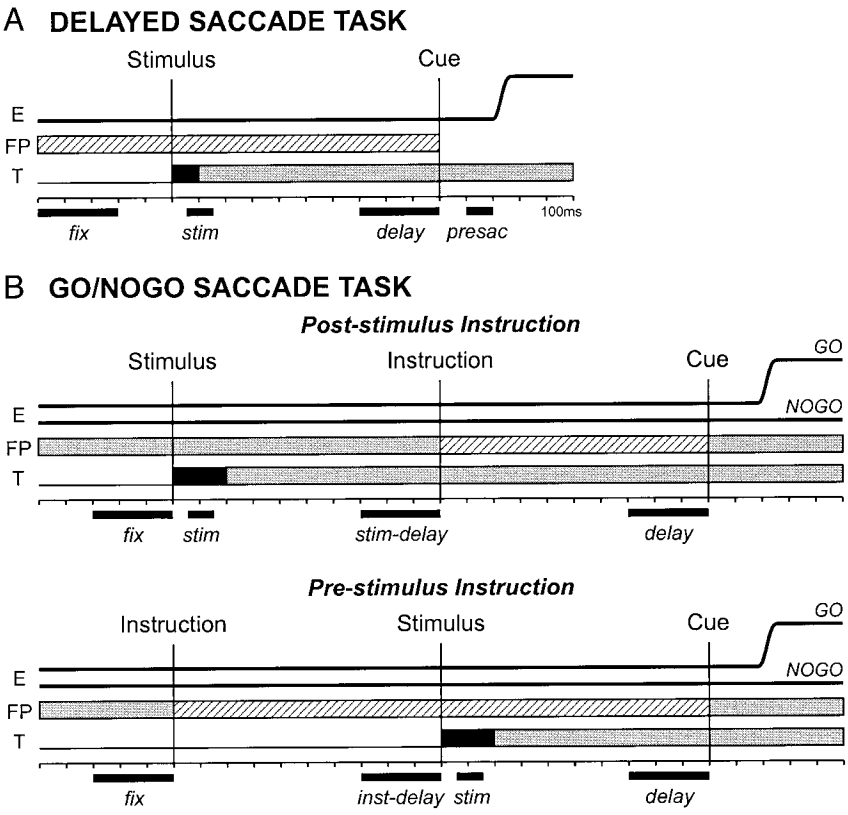

FIG. 1. Schematic representations of the delayed saccade task (*A*) and GO/NOGO saccade task (*B*) employed in this study. In each task, the eye position (E) and the presentation of the visual stimuli (central fixation point, FP; eccentric saccade target, T) are shown as a function of time. Neurons initially were characterized with the delayed saccade task, which is designed to dissociate temporally the *stimulus* presentation from the *cue* (FP disappearance) to produce the saccade. The GO/NOGO saccade task dissociated temporally the stimulus presentation, the response *instruction*, and the *cue* to produce the response. In this task, the stimulus presentation preceded the instruction in the *poststimulus instruction trials*, whereas the reverse sequence occurred in the *prestimulus instruction trials*. The thick horizontal bars below the time axis depict the analysis epochs used to quantify the neuronal activity (see METHODS, an additional analysis epoch estimating the activity at saccade onset is not shown). The striped section of the FP horizontal bar portrays the (GO/NOGO) instruction provided by the change in color. As shown by the black and gray sections of the T horizontal bar, the visual stimulus was presented either for a brief interval (memory trials) or until the end of the trial (visual trials), respectively.

(targeting saccades in NOGO trials) or misses (absence of saccades in GO trials) as behavioral errors. This high performance level was maintained throughout the period that the neuronal data were collected. Early in the data collection, the first ten SC neurons were tested only with visual trials.

RESPONSE FIELD MAPPING. We evaluated the general discharge properties of a neuron using the visual delayed saccade task and determined its response field (the neuron's movement field, or its visual receptive field if it had no saccade-related discharges) by varying systematically (step of 1°) the position of the visual stimulus. This was accomplished by graphically displaying on-line rasters and histograms of the spike occurrences aligned on the onset of the saccades made to each stimulus position. After the center of the response field (the target position for which neurons discharged optimally) was well defined, we collected data, first, in a block of randomized visual and memory delayed saccade trials and, second, in a block of GO/NOGO trials. In these blocks, the visual stimulus was presented with equal probability either in the center of the neuron's response field or at a position equidistant relative to the fixation point but in the diametrically opposite direction. The responses of all SC and LIP neurons were spatially selective, and no significant activity was therefore observed when the visual stimulus was presented outside the response field, except for some postsaccadic discharges. Consequently, we only analyzed quantitatively trials with the stimulus within the response field.

Neuronal identification techniques

Before the recordings in area LIP began, we first determined the location of the SC and the organization of its topographical representation of saccades. The exact depth of the intermediate layers that contain saccade-related neurons (~1–3 mm below the SC surface) was delimited using tungsten microelectrodes to determine both the presence of neuronal activity time locked to saccade onset and by the ability to evoke saccades with stimulation trains of low-intensity pulses (10 μA or less). We then identified area LIP physiologically by the concentration of neurons with significant visual and saccade-related activities within the lateral bank of the intraparietal sulcus and studied only the neurons that were antidromically activated from tungsten monopolar stimulating microelectrodes at predetermined locations within the SC intermediate layer map of saccades. These stimulating microelectrodes (Frederick Haer, impedance 50–100 kΩ at 1 kHz) were moved with a microdrive during each session or held fixed semi-chronically (1–5 wk) to the cylinder's grid with epoxy. The electrical stimulus used for antidromic activation was a single biphasic pulse (see Fig. 2*A*), whose duration was kept short (~0.15 ms for each phase) to optimize axon activation and minimize shock artifact. For each neuron, we determined the threshold intensity to evoke LIP spike responses by SC stimulation, the latency of the evoked responses, and whether the responses could be collided with self-generated orthodromic action potentials. The threshold intensity was defined as the intensity that evoked a response on ~50% of the stimulus presentations. The response latency was the interval from the onset of the stimulus (at 1.2 times threshold intensity) to the onset of the evoked action potential. The collision test verified the antidromic nature of the responses by triggering the stimulus after variable delays relative to the occurrence of an orthodromic action potential. The antidromic responses were abolished (collision, dashed trace in Fig. 2*B*) if the delay between the orthodromic action potential and the stimulus was within the collision interval (Lemon 1984). Throughout the recording session, the occurrence of the collision was monitored routinely (during the inter-trial interval) to confirm the isolation.

Data analysis

To visualize the collected data, rasters of neuronal discharges and continuously varying spike density functions (MacPherson and Aldridge 1979; Richmond et al. 1987) were aligned on specific events in the paradigms. To generate the spike density function, a Gaussian pulse (σ = 10 ms) was substituted for each spike, and then all Gaussians were summed together to produce a continuous function in time. Computer software determined the beginning and end of each saccade using velocity and acceleration threshold and template matching criteria (Waitzman et al. 1991).

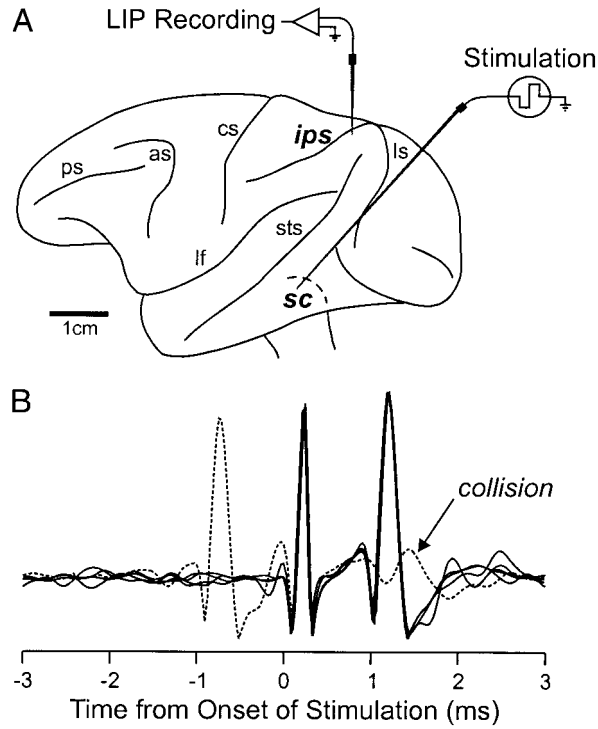

FIG. 2. Neurons recorded in the lateral intraparietal area (LIP) within the intraparietal sulcus were antidromically activated by stimulation of the ipsilateral superior colliculus (SC). *A*: lateral view of a rhesus monkey brain illustrating the stimulation and recording setup. *B*: records of the antidromic responses of an isolated LIP output neuron (*solid trace*), including one trial (*dashed trace*) demonstrating the absence of an antidromic response because of a collision with a self-generated (orthodromic) action potential that triggered the electrical stimulus. as, arcuate sulcus; cs, central sulcus; ips, intraparietal sulcus; lf, lateral fissure; ls, lunate sulcus; ps, principal sulcus; sc, superior colliculus; sts, superior temporal sulcus.

Several sampling epochs were considered for the analysis of the neuronal activity, which was measured from the raw spike counts, with only one exception. In the delayed saccade task, the activity of neurons during fixation was measured by taking the mean discharge rate during a 300-ms epoch within the fixation period, from 500 to 200 ms before the target presentation (Fig. 1*A*, *fix*). The stimulus activation was the mean discharge rate during the 50- to 150-ms interval after the visual stimulus presentation (Fig. 1*A*, *stim*). The delay activity was the mean discharge rate displayed during the last 300-ms interval of the delay period, ending at the fixation point disappearance (Fig. 1*A*, *delay*). The presaccadic activity was the mean discharge rate during the last 100 ms before saccade onset (Fig. 1*A*, *presac*). This interval was employed to establish whether the neurons had specific discharges that could contribute to the generation of the saccade (Colby et al. 1996). The magnitude of the *saccade* activity was determined as the peak rate of the saccade-related burst of activity found within ±20 ms from saccade initiation (not shown). We chose this temporal window because SC neurons are known to discharge maximally at the beginning of saccades (e.g., Dorris et al. 1997), and we measured the peak discharge using the spike density functions constructed from rasters of action potentials aligned on saccade onset.

In the GO/NOGO saccade task, the activity during fixation was the mean discharge rate during the final 300 ms during the fixation period

(Fig. 1*B*, *fix*). The stimulus-related activity was the mean discharge rate during the 50- to 150-ms interval after the visual stimulus presentation (Fig. 1*B*, *stim*). The delay activity, after both the stimulus and the instruction had been presented, was estimated as the discharge rate displayed during the 300-ms interval before the response cue (Fig. 1*B*, *delay*). Two additional analysis epochs were computed for the sustained activity present: *1*) when only the stimulus had been presented in the poststimulus instruction trials (Fig. 1*B*, *stim-delay*) and *2*) when only the instruction had been provided in the prestimulus instruction trials (Fig. 1*B*, *inst-delay*). These epochs consisted of the last 300 ms of the instruction and the stimulus periods, respectively.

In both the delayed saccade task and the GO/NOGO saccade task, neurons significantly active in advance of saccade initiation were defined as those that had activity in the *delay* epoch significantly greater than their activity in the *fixation* epoch in either visual or memory trials (Wilcoxon signed rank test, $P < 0.01$). These were referred to as delay responsive neurons.

The majority of the data set composed nonnormal distributions as determined by the Kolmogorov-Smirnov test ($P < 0.01$), and we therefore conducted statistical comparisons within and between samples with the nonparametric Mann-Whitney *U*-test and Wilcoxon signed rank test, respectively. For comparisons of several samples, we used the nonparametric Kruskal-Wallis ANOVA, followed by an all-pairwise multiple comparison procedure (Student-Newman-Keuls of Dunn's method). Results of the statistical analyses were considered significant only if they exceeded a level of $P < 0.01$, except for the pairwise multiple comparison procedures ($P < 0.05$). All statistical tests were performed with the SigmaStat software (Jandel Scientific).

RESULTS

Single-neuron recording in the two monkeys yielded sufficient data from 102 neurons in the SC intermediate layers that displayed characteristic saccade (or delay) activity and 41 neurons in area LIP that had peripheral excitatory response fields. All LIP neurons were identified as output neurons projecting to the ipsilateral SC, wherein stimulation produced antidromic activation (see Fig. 2) with an average latency of 1.9 ms (range 0.8–6). The antidromic current threshold was minimal for stimulation delivered within the intermediate layers (Paré and Wurtz 1997a) and averaged 182 μA, with 90% of the neurons activated with a current <400 μA.

Discharge properties in the delayed saccade task

ACTIVITY PATTERNS. In the delayed saccade task (see Fig. 1*A*), SC and LIP neurons displayed a range of activity patterns that included a burst of activity in response to visual stimulation, a sustained activity during the delay period, and a presaccadic increase in activity. Figure 3 shows examples of these activity patterns in the visual version of the task, i.e., when the visual stimulus presented within a neuron's response field remained on from its onset to the end of the trial. Within the SC sample, we observed many neurons with two bursts of activity time locked to the onset of either the visual stimulus or the saccade, along with a low-frequency sustained activation during the intervening delay period (Fig. 3*A*). A smaller subset of SC neurons showed only a sustained delay activity without a clear burst of activity associated either with stimulus presentation or saccade execution (Fig. 3*B*). Finally, we encountered several SC neurons whose primary discharge was a high-frequency saccade-related burst of activity (Fig. 3*C*), which occasionally could be preceded by a transient stimulus-related response. These three example neurons were comparable to those previously referred to as *1*) "prelude bursters" (Glimcher and Sparks 1992) or "buildup" neurons (Munoz and Wurtz 1995), *2*) "quasi-visual" neurons (Mays and Sparks 1980), and *3*) "sac-

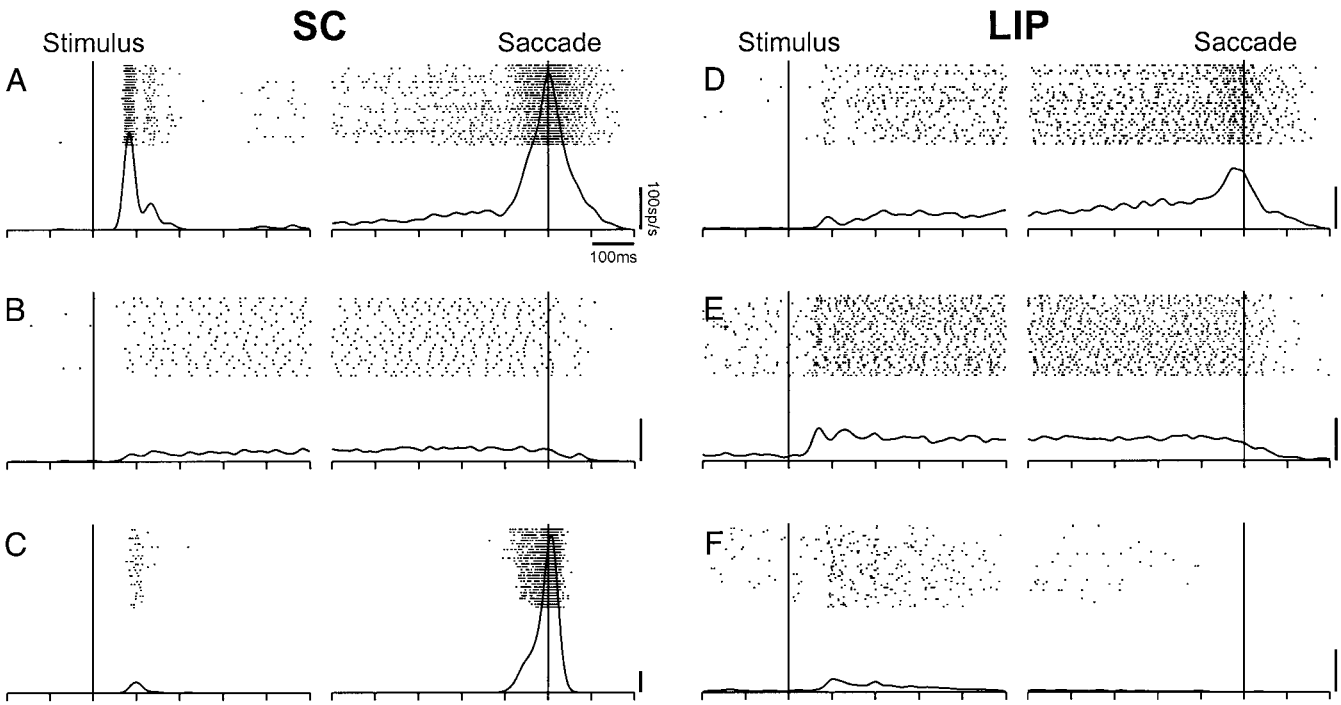

FIG. 3. Examples of 3 SC (*A–C*) and 3 LIP (*D–F*) neurons illustrating the range of activity patterns observed in the delayed saccade task, in which the visual stimulus remained on from its onset to the end of the trial (visual trials). Rasters and spike densities show the activity aligned on either the onset of the visual stimulus or the saccade. These data were collected with the visual stimulus positioned in the center of the neuron's response field.

cade-related burst neurons" (Mays and Sparks 1980) or "burst neurons" (Munoz and Wurtz 1995).

The activity patterns of the LIP output neurons, like that of many SC neurons, generally consisted of a sustained activation lasting from visual stimulation to saccade execution. Nonetheless, even when this activation ended in a saccade-related burst of activity (Fig. 3*D*), its magnitude generally was smaller than that of SC neurons (compare Fig. 3, *A* and *D*). A subset of LIP neurons that were active during the delay period but without such a burst resembled more closely those recorded in the SC (compare Fig. 3, *B* and *E*). In striking contrast to the SC neuronal sample, we encountered no LIP neurons that displayed saccade-related discharges without preceding delay activity. Last, along with nine neurons located in the SC superficial layers (described in the last section of RESULTS), one LIP neuron was found to show only a transient activation triggered by the visual stimulus presentation (Fig. 3*F*).

The graphs in Fig. 4, *A* and *B*, depict the magnitude of both the *stimulus* activity and the *saccade* activity plotted against the magnitude of the *delay* activity for each of the LIP and SC neurons in the visual version of the delayed saccade task. The salient observation is that the stimulus and delay activities of LIP and SC neurons show a remarkable overlap (Fig. 4*A*), whereas a difference appears in the combinations of their saccade and delay activities (Fig. 4*B*). In this latter case, LIP output neurons all cluster along the abscissa indicating that they possess delay activity but modest saccade activity, whereas the SC neurons are scattered and nearly cover the full range of activity patterns. These graphs also emphasize the continuum of activity patterns both within and between the two neuronal samples, with the exception that the absolute magnitude of the saccade activity is greater in SC neurons (Mann-Whitney rank sum test, $P < 0.001$). Nevertheless, both the SC and the LIP neuronal samples significantly increased their discharge before saccade initiation. Table 1 emphasizes this characteristic by giving the levels of delay and presaccadic activity of the LIP and SC delay responsive neurons.

In summary, the sample of LIP neurons projecting to the SC resembled the sample of neurons in the SC intermediate layers. Their stimulus and delay activity was remarkably similar. The two neuronal samples also displayed significant presaccadic discharges, but the saccade activity of LIP neurons was weaker than that of SC neurons, and, unlike the latter, it never occurred without any preceding delay activity.

DEPENDENCE ON VISUAL STIMULUS PRESENCE. The LIP and SC neurons were also recorded in a memory version of the delayed saccade task, i.e., when the visual stimulus was only briefly presented and therefore absent during both the delay period and the saccade execution. The graphs in Fig. 4, *C* and *D*, depict the corresponding levels of activity for each of the LIP and SC neurons and reveal that they qualitatively resemble those observed in the visual version of the task (compare with Fig. 4, *A* and *B*). The statistical analysis of the LIP and SC activity in advance of saccades, however, demonstrates one major quantitative difference: the delay and presaccadic activity of LIP neurons, but not that of SC neurons, was significantly reduced

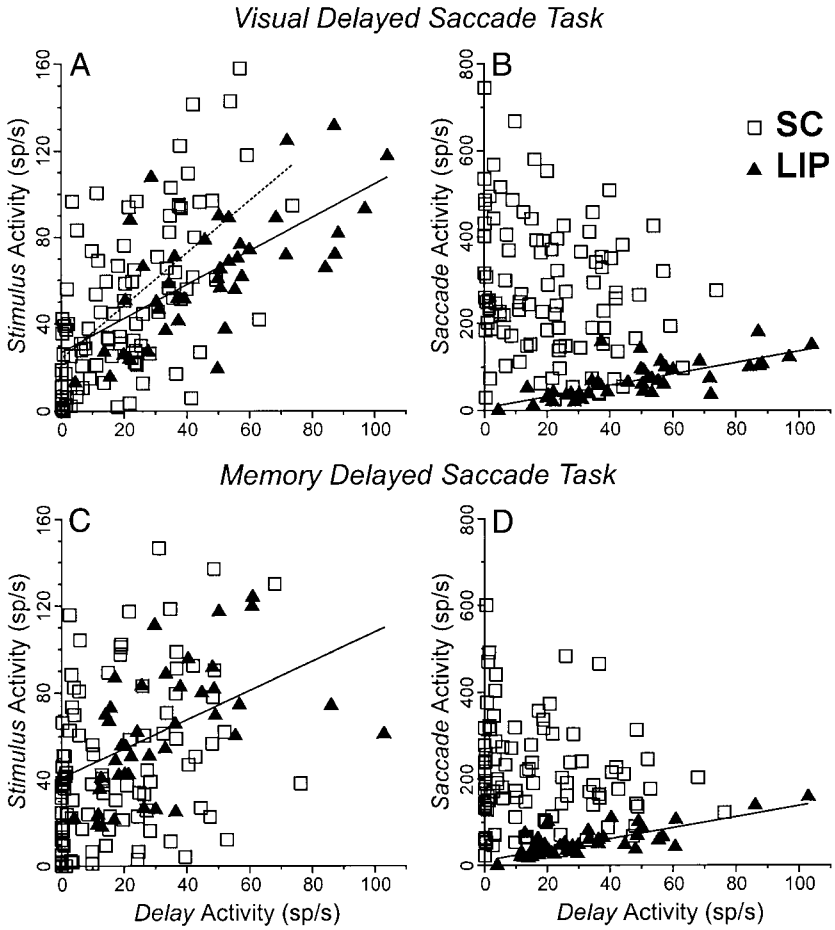

FIG. 4. Discharge properties of LIP (▲, $n = 41$) and SC (□, $n = 102$) neurons in the visual (*A* and *B*) and the memory (*C* and *D*) trials of the delayed saccade task. *A* and *C*: scatter plots of the magnitude of the *stimulus* activity against the magnitude of the *delay* activity. *B* and *D*: scatter plots of the magnitude of the *saccade* activity against the magnitude of the *delay* activity. Each data point indicates the mean value of each parameter for each neuron. The *stimulus* activity was the mean discharge rate during a 100-ms interval starting 50 ms after stimulus onset, while the *delay* activity was the mean rate during the last 300 ms of the delay period. The *saccade* activity was the peak rate that occurred within ±20 ms from saccade initiation (derived from the spike density functions aligned on saccade onset). The SC neurons generally had a lower saccade activity in memory trials than in visual trials, and we presume that this change is related to the well-established change in saccade dynamics between the saccades produced in these 2 types of trials (Gnadt et al. 1991; White et al. 1994). The stimulus and saccade activity of LIP neurons is correlated to the delay activity ( ), and the parameters of the linear regression equations (solid lines, $P < 0.01$) are as follows: *A*: $b = 27$, slope = 0.77, $r = 0.64$; *B*: $b = 11$, slope = 1.23, $r = 0.70$; *C*: $b = 41$, slope = 0.67, $r = 0.49$; *D*: $b = 16$, slope = 1.22, $r = 0.76$. For the SC sample, only the visual activity in visual trials was significantly related to the delay activity: $b = 16$, slope = 1.42, $r = 0.58$ (*A*, dashed line).

TABLE 1. *Discharge properties of LIP and SC neurons in the delayed saccade task*

	Delay	*Presaccadic*
	Lateral intraparietal area	
Visual	50.1*	55.0*†
Memory	27.1	37.1†
	Superior colliculus	
Visual	25.9	107.3†
Memory	24.2	103.4†

Activity level of delay responsive neurons in the lateral intraparietal area (LIP; $n = 40$) and the superior colliculus (SC; $n = 69$) during the *delay* and *presaccadic* epochs (see Fig. 1*A* and METHODS) in the visual and memory versions of the delayed saccade task. Neuronal activity levels are presented as median discharge rates (spikes/s). Within each neuronal sample, there was a statistically significant difference among the groups (Kruskal-Wallis ANOVA on ranks, $P < 0.0001$). An all pairwise multiple comparison (Student-Newman-Keuls methods, $P < 0.05$) additionally revealed whether the delay and presaccadic discharges in each sample were significantly different between the visual and memory trials (*) and whether the pre saccadic activity in either trial type was significantly different than the delay activity (†). Delay responsive neurons were those that had delay activity significantly greater than their fixation activity in either visual or memory trials (Wilcoxon signed rank test, $P < 0.01$).

in the absence of the visual stimulus (Table 1). This difference may indicate that LIP neurons are less involved in the early covert processes directly related to saccade production. To perform a meaningful comparison, however, one needs to compare quantitatively the normalized discharge properties of the LIP and SC neuronal samples. To do so, we chose not to use a ratio or contrast index based on mean discharge rates. This approach unfortunately relies on the assumption of normal population distributions, and this was often untenable in our data set (e.g., Fig. 5*B*). Rather, we opted for a nonparametric measure of the separation between the distributions of neuronal activity observed in visual and memory trials.

The method we adopted is analogous to the ordinal dominance (OD) graphic method (Darlington 1973) and the well-established receiver operating characteristic analysis (Green and Swets 1966), which has been previously employed to characterize neuronal activation (e.g., Britten et al. 1992; Thompson et al. 1996). Figure 5 exemplifies for one SC neuron and one LIP neuron how we calculated the separation between activity distributions. Figure 5, *A* and *B*, contrasts the distribution of the rate of *delay* activity of these neurons. Figure 5*C* shows their OD curves created by plotting the probability that the activity rate in visual trials was greater than a given criterion rate as a function of the probability that the activity rate in memory trials was greater than that same criterion. To create the whole curve, the criterion level was incremented from 0 spike/s to the highest discharge rate in 1-spike/s steps. As the criterion rate increases, the points on the curve thus progress from maximal probability (1.0, 1.0) to null probability (0, 0), through all the intermediate values dictated by the activity distributions. For example, with a criterion rate value of 30 spikes/s, the probability that the visual LIP delay activity in Fig. 5*B exceeds* this rate is 0.87 (26/30 trials) and that of the memory activity is 0.14 (4/29 trials), as indicated on the corresponding OD curve (Fig. 5*C*).

It is the area under each OD curve that captures the amount of separation between the two distributions. This quantitative measure gives the general probability that, given one draw from each distribution of activity rates, the rate from the activity distribution in visual trials would be larger. A chance

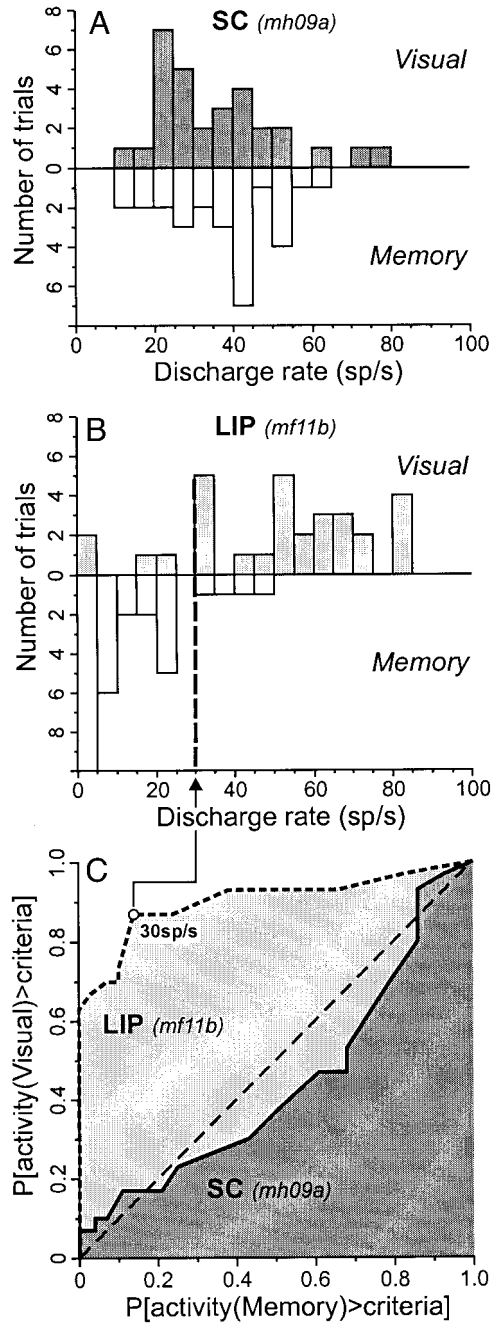

FIG. 5. Distributions of the rate of activity of 1 SC neuron (*A*) and 1 LIP neuron (*B*) during the *delay* epoch in the visual (*top histogram*) and the memory (*bottom histogram*) trials of the delayed saccade task (binwidth is 5 spikes/s). *C*: we used an ordinal dominance (OD) analysis to quantify the separation between the distributions of delay activity in visual and memory trials (see text). The OD curve was generated by plotting the probability that the activity rate in visual trials was greater than a criterion rate as a function of the probability that the activity rate in memory trials was greater than that same criterion. One selected point on the LIP neuron's OD curve highlights the probabilities associated with 1 criterion rate. The shaded area under the OD curve (calculated to be 0.44 for the data shown in *A* and 0.90 in *B*) was used as a quantitative measure of the separation of the 2 distributions, the *visual/memory separation index*.

probability value of 0.5 thus implies completely overlapping distributions. A value >0.5 indicates that the activity distribution in visual trials is greater than that in memory trials, and a value <0.5, the converse. For example, the area under the SC neuron's curve in Fig. 5*C* has a value of 0.44 as the visual and memory distributions roughly overlap, whereas the area under the LIP neuron's curve is 0.90 as the visual distribution is fairly separate from and greater than the memory distribution.

We termed the probability value provided by the area under the OD curve the *visual/memory separation index* and obtained an index value for the delay and the presaccadic activities of each of the SC and LIP delay responsive neurons. Figure 6 shows the distributions of these indexes for both samples of SC and LIP neurons, and the median values of these distributions are given in Table 2. We also indicated in the Fig. 6 histograms the indexes of 0.25 and 0.75 (dashed line) to facilitate the identification of neurons whose activity levels in the two types of trials was significantly different: 0.25, memory > visual; 0.75, visual > memory. The OD analysis actually is closely related to the nonparametric Mann-Whitney rank sum test (Bamber 1975), and the index values of 0.25 and 0.75 approximately coincide with a statistical difference at the significance level of $P = 0.01$. Table 2 additionally gives the percentage of SC and LIP neurons with a visual/memory separation index exceeding these arbitrary thresholds of significance.

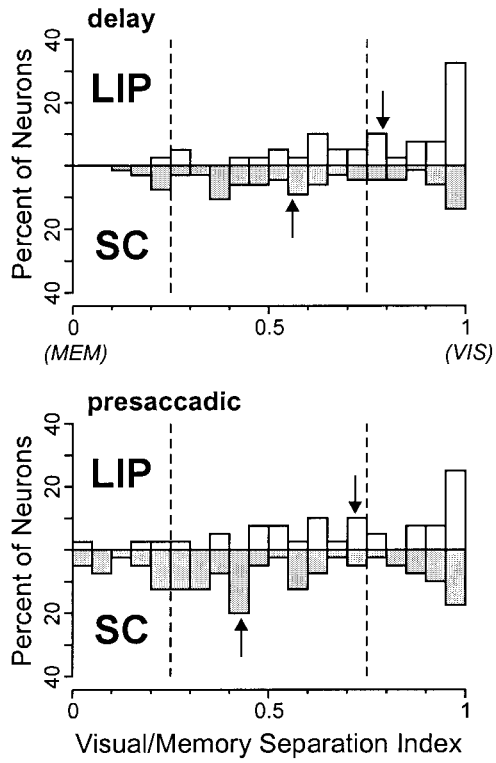

FIG. 6. Distribution of the visual/memory separation index (area under the OD curve) of the activity of SC neurons ($n = 69$) and LIP output neurons ($n = 40$) during the *delay* (*top*) and *presaccadic* (*bottom*) epochs of the delayed saccade task (see Fig. 1*A*). This analysis is based on the distribution of the discharge rates in each analysis epoch (see text). The index can take a value from 0 (*MEM*, memory distribution completely separate from and greater than visual distribution) to 1 (*VIS*, visual distribution completely separate from and greater than memory distribution). A value of 0.5 indicates that visual and memory distributions are indistinguishable. The vertical broken lines at the 0.25 and 0.75 index levels mark the thresholds of statistical significance. Arrow indicates the median index value. Binwidth is 0.05.

TABLE 2. *Visual dependence of LIP and SC neurons in the delayed saccade task*

	Delay	*Presaccadic*
Lateral intraparietal area		
VIS/MEM separation index	0.79	0.72
%Neurons with a significant VIS > MEM distribution separation	58	42
%Neurons with significant MEM > VIS activity difference	2	8
Superior colliculus		
VIS/MEM separation index	0.56	0.43
%Neurons with a significant VIS > MEM distribution separation	31	25
%Neurons with significant MEM > VIS activity difference	12	20

Median value of the visual memory separation indexes for the *delay* and *presaccadic* activity of LIP ($n = 40$) and SC ($n = 69$) delay responsive neurons in the delayed saccade task, along with the respective proportion of neurons with a significant difference between their activity distributions in visual and memory trials of the task: VIS > MEM, index >0.75; MEM > VIS, index >0.25. Delay responsive neurons were those that had delay activity significantly greater than their fixation activity in either visual or memory trials (Wilcoxon signed rank test, $P < 0.01$).

For the SC neurons, neither the delay nor the presaccadic distributions of indexes were significantly different from 0.5 (Mann-Whitney rank sum test, $P > 0.10$). Thus the SC neuronal population activity did not differ in visual and memory trials. In contrast, the LIP index distributions were significantly greater than 0.5 ($P < 0.0001$), thereby revealing that the LIP activity in visual trials generally was greater than in memory trials. When the SC and LIP samples were compared, the distributions of both the *delay* and the *presaccadic* indexes of LIP neurons were statistically different from those of SC neurons (Kruskal-Wallis ANOVA on ranks, $P < 0.0001$; Dunn's test, $P < 0.05$). This difference is expressed by a leftward shift, from LIP to SC, of the index distributions in Fig. 6, which indicates that the delay and presaccadic activity of LIP neurons was more dependent on the visual stimulus presence than that of SC neurons. The majority of LIP neurons with significant indexes had their visual activity greater than their memory activity (Table 2), whereas the proportions of SC neurons with significant indexes were more evenly distributed. Not only were the SC neurons less numerous to be visually dependent, several were even dependent on the absence of the visual stimulus (index <0.25).[1]

In summary, an important difference between LIP and SC neuronal populations was that the intensity of the delay and presaccadic activity of LIP neurons depended strongly on the sustained presence of the visual stimulus, whereas that of the SC neuronal sample did not. We next employed another behavioral task to investigate how the LIP and SC activity relates to the impending production of a saccade.

[1] From the point of view of neurons receiving these inputs, it is impossible to distinguish which SC neurons had either lower or higher discharge rates in visual and memory trials. The influence of SC neuronal signals on downstream elements is reflected in both the proportion and the distribution of the significant visual/memory indexes.

Discharge properties in the GO/NOGO saccade task

We used the GO/NOGO saccade task (see Fig. 1*B*) to provide advance instruction about saccade production and to determine whether this manipulation modulates the subsequent delay activity of LIP and SC neurons. We shall first describe the neuronal responses observed in the version of the GO/NOGO saccade task in which the instruction was presented after the stimulus appearance, the poststimulus instruction trials.

POST-STIMULUS INSTRUCTION TRIALS. Figure 7 illustrates the activity patterns displayed by SC neurons in the visual version of the poststimulus instruction trials of the GO/NOGO saccade task. Following a GO instruction, most neurons (Fig. 7, *A* and *B*) showed a rise of low-frequency sustained activity, which occurred with a considerably longer latency than the earlier stimulus-related activity (e.g., Fig. 7*A*). Such activation did not depend on whether a neuron already displayed some delay activity or a presaccadic increase in activity (compare Fig. 7, *A* and *B*). The sustained activity following a NOGO instruction was greatly reduced relative to that present in GO trials, and, of course, the burst of activity that normally accompanied the GO-trial saccades did not occur during the prolonged NOGO fixation period. A neuron that showed a saccade-related burst of activity but lacked delay activity in the delayed saccade task (see Fig. 3*C*) continued to burst only for the saccades made in GO trials, remaining silent otherwise (Fig. 7*C*). We also found that 19% (13/69) of the SC neurons classified as delay responsive neurons in the delayed saccade task no longer displayed significant delay activity in the GO/NOGO saccade task. This important change in neuronal activation could most probably be attributed to the new behavioral context introduced by the randomly interleaved NOGO trials. Relative to the delayed saccade task, the probability of a saccade being produced was then reduced, and such a manipulation has been shown to affect the excitability of SC neurons (Basso and Wurtz 1998; Dorris and Munoz 1998; Mohler and Wurtz 1976).

Figure 8 illustrates the activity patterns of LIP output neurons also in the visual version of the GO/NOGO poststimulus instruction trials. Following the onset of the instruction, we observed a range of responses from increased sustained delay

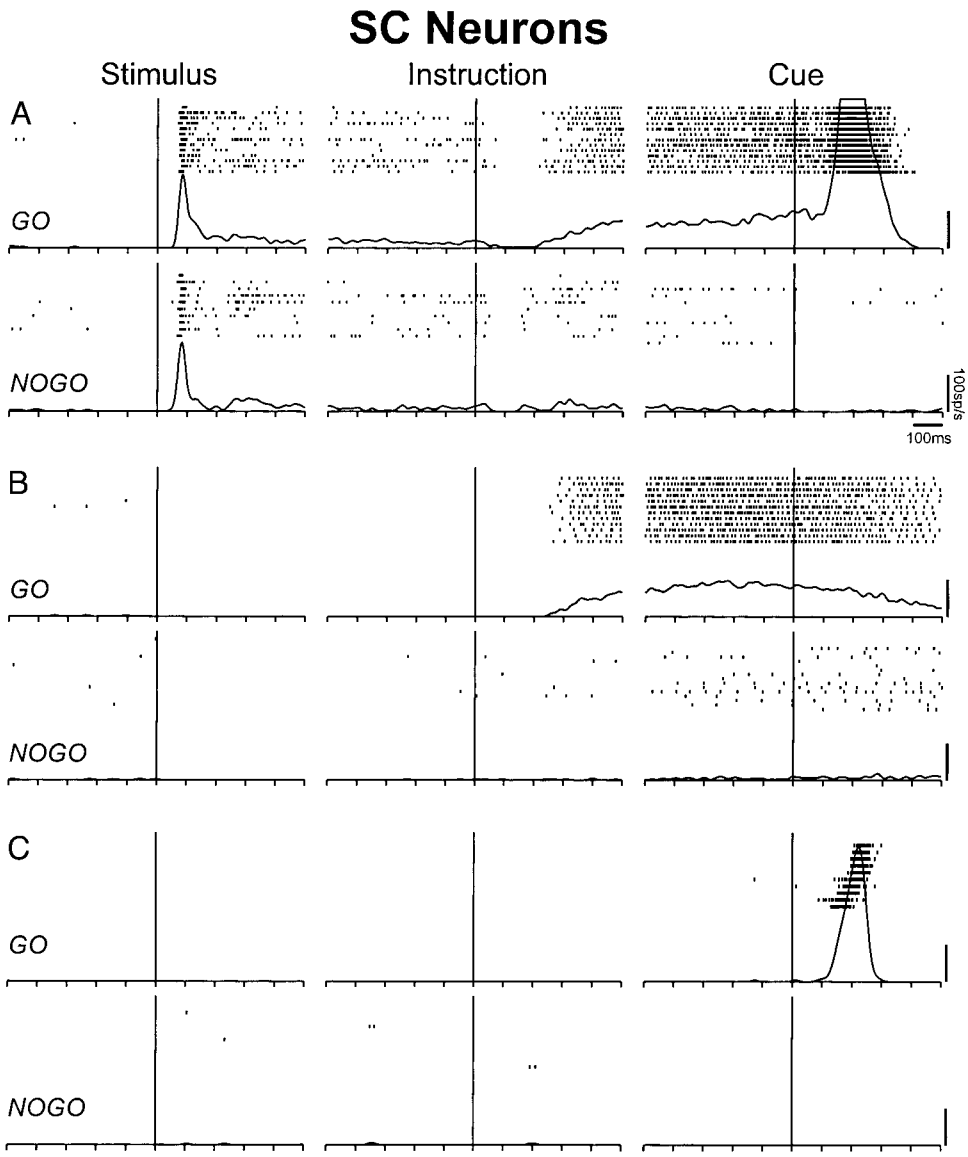

FIG. 7. Activity patterns of 3 SC neurons recorded during poststimulus instruction visual GO/NOGO trials with the stimulus presented in the neurons' response fields. In each panel, the raster of action potentials and the spike density functions of GO (*top*) and NOGO (*bottom*) trials are aligned on the 3 significant behavioral events of this task: stimulus, instruction, and cue signals.

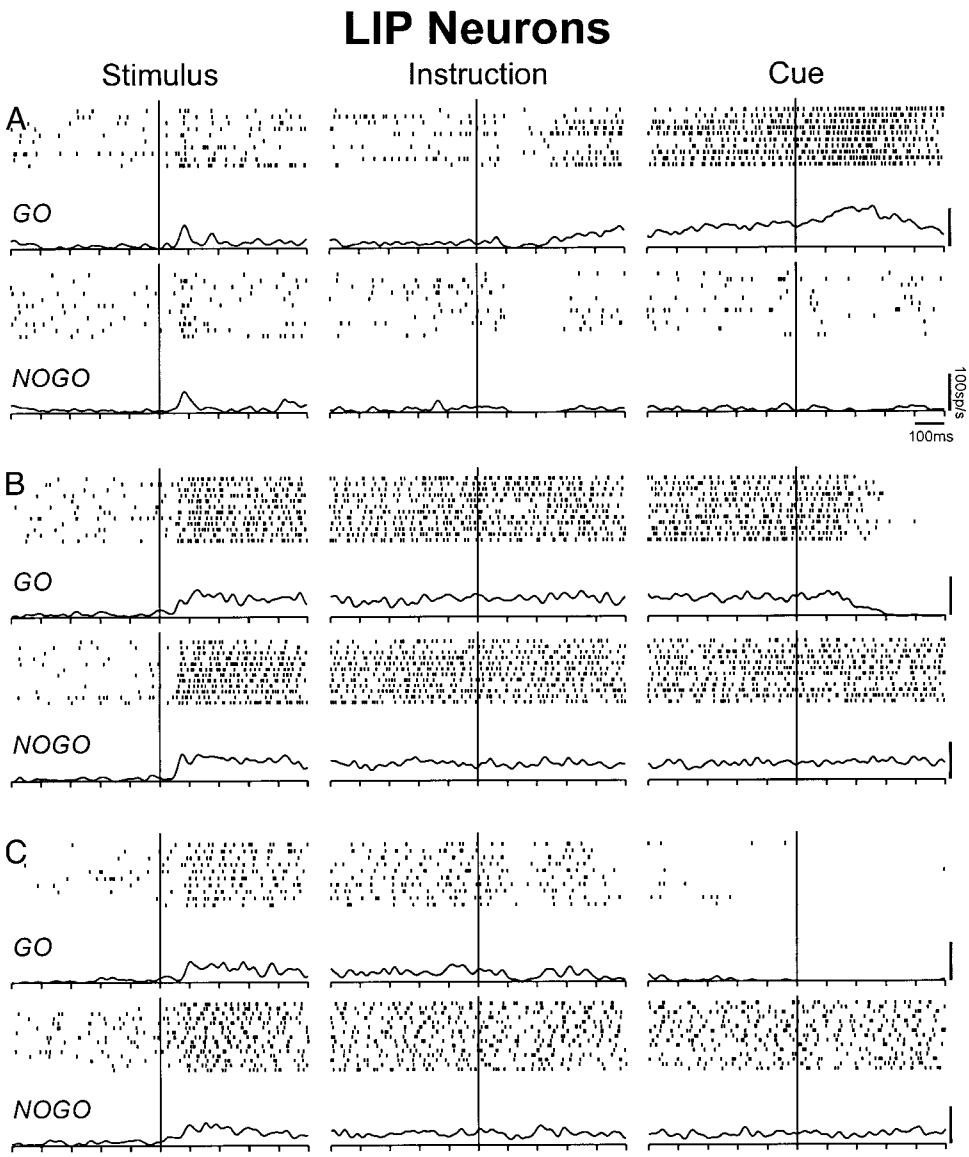

FIG. 8. Activity patterns of 3 LIP output neurons recorded during visual poststimulus instruction trials of the GO/NOGO saccade task. See legend of Fig. 7.

activity only after a GO instruction (Fig. 8*A*), through continuing delay activity unchanged by the instruction (Fig. 8*B*), to persisting activity only after a NOGO instruction (Fig. 8*C*).

To quantify the effect of the response instruction, we considered only the delay responsive neurons. The scatter plots of Fig. 9 show, for each of these SC (*A*) and LIP (*B*) neurons, the mean of their GO and NOGO activity levels during the *delay* epoch of the visual poststimulus instruction trials. The large proportion of data points falling above the equality line indicates that the delay activity generally was stronger in GO trials, and this difference was statistically significant for both SC and LIP samples (Table 3). LIP and SC neurons also were studied in a memory version of the GO/NOGO task (see Fig. 1*B*). In these trials (Fig. 9, *C* and *D*), the difference between GO and NOGO delay activity levels remained significant (Table 3) and was particularly enhanced for SC neurons. Table 4 summarizes the percentage of SC and LIP neurons with significant GO/NOGO activity differences (Mann-Whitney rank sum test, $P < 0.01$). A total of 54 and 70% of the SC neurons showed significant GO/NOGO differences in visual and memory trials, respectively. The proportions of significant differences in the LIP sample (29 and 32% of the neurons) were statistically smaller than in the SC ($\chi^2 = 19.4$, $df = 3$, $P < 0.0005$), and one LIP neuron (see Fig. 8*C*) had a significantly greater NOGO delay activity.

Figure 10 shows the time course of the changes in LIP and SC neuronal activity during the performance of both the visual and the memory versions of the GO/NOGO poststimulus instruction trials, and Table 3 gives the complementary quantification and statistical comparison of the sustained activity observed during the *stim-delay* and *delay* epochs of these trials (see Fig. 1*B*). Both samples displayed a somewhat similar increase in sustained activity ~250 ms following the GO instruction and a subtle decrease in activity following the NOGO instruction. All changes in color of the foveal instruction stimulus also produced a transient reduction in activity possibly reflecting an inhibitory zone in the neuronal response fields (see instruction- and cue-aligned activity traces in Fig. 10). These temporal activation profiles illustrate how the delay activity of SC neurons became particularly more strongly mod-

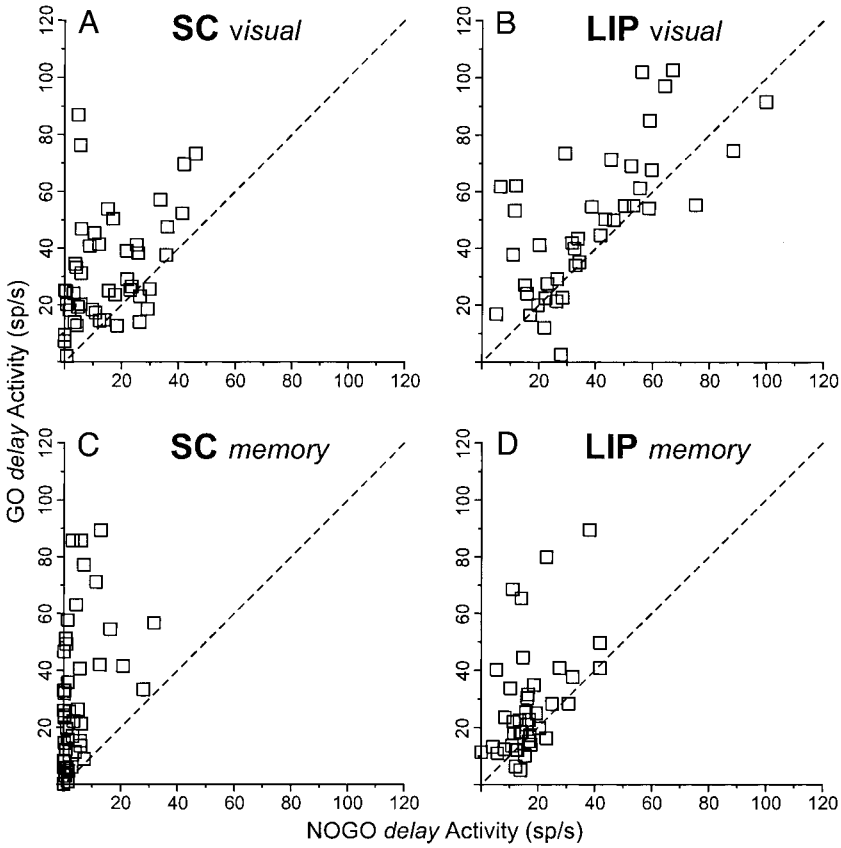

FIG. 9. Comparison between the mean discharge rate of SC (*left*) and LIP (*right*) neurons during the GO and NOGO *delay* epoch of the visual (*top*) and the memory (*bottom*) poststimulus instruction trials of the GO/NOGO saccade task. Included in the graphs are 46 SC neurons and 41 LIP output neurons that were recorded in both the visual and the memory GO/NOGO trials and that had significant delay activity in either type of trials. The dashed line represents the equality line.

ulated by the instruction to make a saccade in memory trials because its magnitude was reduced by the absence of the visual stimulus only in NOGO trials.

To compare quantitatively the effect of the response instruction on the LIP and SC neuronal samples, we used the same OD analysis method described above to estimate the separation between the distributions of delay activity in GO and NOGO trials for each neuron. In this case, the area under the OD curve gives the general probability that the discharge rate in a single trial can be correctly ascribed to a GO or a NOGO trial. A value >0.5 now signifies that the activity distribution in GO trials is greater than that in NOGO trials, and a value <0.5, the converse. We termed this probability value provided by the area under this curve the *GO/NOGO separation index* and obtained an index value for each of the SC and LIP delay responsive neurons. Figure 11 shows the distributions of these indexes for both neuronal samples in the visual and the memory versions of the task, and Table 4 gives the corresponding

TABLE 3. *Discharge properties of LIP and SC neurons in the GO/NOGO saccade task*

	Poststimulus Instruction				Prestimulus Instruction			
	Visual		Memory		Visual		Memory	
	Stim-delay	*Delay*	*Stim-delay*	*Delay*	*Inst-delay*	*Delay*	*Inst-delay*	*Delay*
				Lateral intraparietal area				
GO	45.1	49.7*†	20.4	22.6*†	11.8	44.9*†	10.3	25.0*†
NOGO	41.9	33.0*	18.6	14.9*	10.9	34.4*	10.4	17.2*
				Superior colliculus‡				
GO	7.8	25.4*†	4.7	25.0*†	0.7	29.7*†	0.6	27.1*†
NOGO	8.1	12.2*	5.7	1.6*	0.5	7.6*	0.8	2.0*

Number of LIP neurons is 41; number of SC neurons is 46. Activity level of delay responsive neurons during the delay analysis epochs (see Fig. 1*B* and METHODS) of the GO/NOGO saccade task. Neuronal activity levels are presented as median discharge rates (spikes/s). Within each neuronal sample, there was a statistically significant difference among the groups (Kruskal-Wallis ANOVA on ranks, $P < 0.0001$). An all pairwise multiple comparison (Student-Newman-Keuls method, $P < 0.05$) revealed that in each sample the *delay* activity and the earlier (*stim-delay* or *inst-delay*) activity were significantly different (*), and that the GO and NOGO *delay* activity was significantly different (†). All discharge rates also were significantly greater than the fixation rate (LIP, 10.6 spikes/s; SC, 0.6 spikes/s), except for the activity during the *inst-delay* epochs. Delay responsive neurons were those that had GO delay activity significantly greater than their fixation activity in either visual or memory trials (Wilcoxon signed rank test, $P < 0.01$). ‡ Of 69 SC delay responsive neurons, 13 lost their delay activity in the GO/NOGO saccade task (see RESULTS), and 10 were tested only in the visual version of the task (see METHODS).

TABLE 4. *Instructional dependence of LIP and SC neurons in the GO/NOGO saccade task*

	Poststimulus Instruction		Prestimulus Instruction	
	Visual	Memory	Visual	Memory
Lateral intraparietal area				
GO/NOGO separation index	0.63	0.69	0.65	0.66
%Neurons with a significant GO > NOGO distribution separation	41	36	29	32
%Neurons with significant GO > NOGO activity difference	29	32	32	24
Superior colliculus				
GO/NOGO separation index	0.84	0.94	0.91	0.95
%Neurons with a significant GO > NOGO distribution separation	61	72	70	83
%Neurons with significant GO > NOGO activity difference	54	70	56	78

Median value of the GO/NOGO separation indexes for the *delay* activity of LIP ($n = 41$) and SC ($n = 46$) delay responsive neurons, along with the respective proportion of neurons with a significant difference between either their GO/NOGO activity distributions (index >0.75) or their GO/NOGO activity levels (GO > NOGO, Mann-Whitney rank sum test, $P < 0.01$). Delay responsive neurons were those that had GO delay activity significantly greater than their fixation activity in either the visual or the memory version of the GO/NOGO saccade task (Wilcoxon signed rank test, $P < 0.01$).

median values. All index distributions were statistically >0.5 (Mann-Whitney rank sum test, $P < 0.0001$), thereby confirming that the delay activity of both SC and LIP samples increased when the GO instruction was provided. Between task conditions, the *memory* indexes of SC neurons were significantly greater than the *visual* indexes (Wilcoxon signed rank test, $P < 0.0001$), whereas the LIP index distributions were indistinguishable ($P = 0.38$). When the SC and LIP samples are compared, the index distributions of SC neurons in Fig. 11 are shifted rightward from those of LIP neurons, a difference that, however, is statistically significant only in the memory trials (Kruskal-Wallis ANOVA on ranks, $P < 0.0001$; Dunn's test, $P < 0.05$). This difference indicates that, when compared with SC neurons, the delay activity of LIP neurons was less dependent on the instruction to make a saccade when the visual stimulus was absent.

Table 4 summarizes the percentage of SC and LIP neurons with a GO/NOGO separation index exceeding the 0.75 threshold of statistical significance; only a negligible proportion of neurons had an index <0.25 (see Fig. 11). In visual and memory trials, a total of 61 and 72% of the SC neurons had an index >0.75, whereas this was the case for only 41 and 36% of the LIP neurons. These proportions were statistically different ($\chi^2 = 14.3$, $df = 3$, $P < 0.005$).

In summary, the delay activity of both SC and LIP samples significantly increased following advance instruction to make a saccade. Nevertheless, the modulation of LIP neurons was weaker than that of SC neurons, and it involved a smaller proportion of neurons. Altogether, the delay activity of LIP output neurons was less dependent on the instruction than that of SC neurons.

PRE-STIMULUS INSTRUCTION TRIALS. We showed that response instruction modulated the delay activity of both the LIP and SC neurons. In the experiments described so far, however, the instruction appeared after the presentation of the visual stimulus, thereby preventing us from determining whether it also modulated the *stimulus* activity. To address this issue, we had designed the GO/NOGO saccade task to include prestimulus instruction trials, in which the instruction was presented before the visual stimulus presentation (see Fig. 1*B*). Figure 12 shows the average LIP and SC neuronal activation during the performance of both the visual and the memory versions of these types of GO/NOGO trials. In both samples, the foveal instruction signal itself did not trigger any activation, but some activity occurred in anticipation of the visual stimulus in GO trials. Following the stimulus presentation, the initial burst of

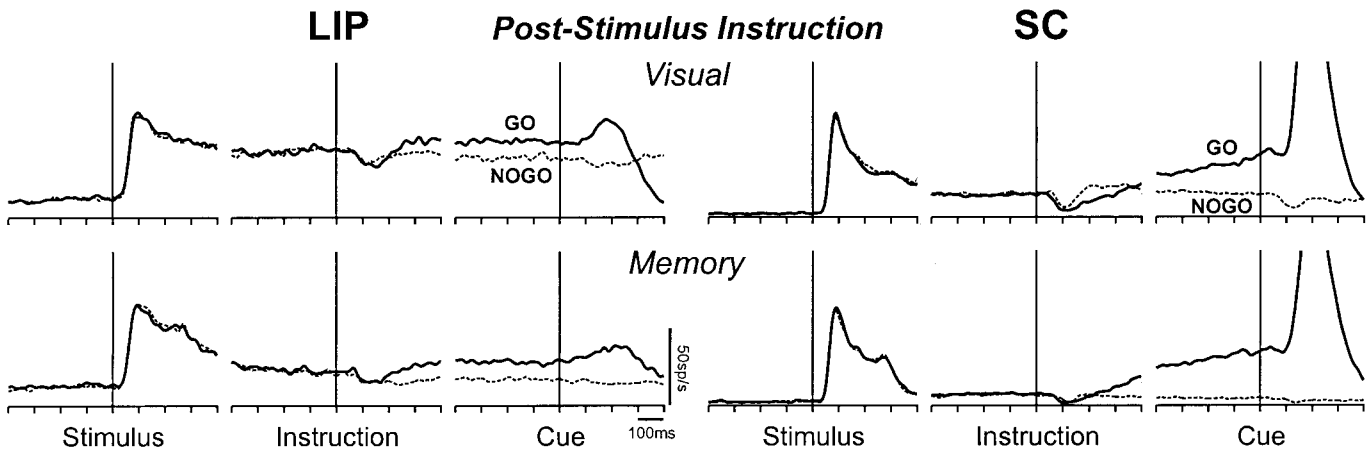

FIG. 10. Comparison between the average activation profile of LIP output neurons and of SC delay responsive neurons in the poststimulus instruction trials of the GO/NOGO saccade task. Average spike density functions of LIP (*left*, $n = 41$) and SC neurons (*right*, $n = 46$) recorded during the visual (*top*) and memory (*bottom*) trials with the stimulus presented in the neurons' response fields. This figure simply illustrates the temporal profile of the LIP and SC activation. Because the weight of each neuron is unknown, it cannot capture the quantitative influence of the neuronal populations. Moreover, comparisons between absolute activity levels across conditions (visual vs. memory) are not warranted because the overall state of the system circuit cannot be safely assumed to be constant. For instance, the fact that the LIP level of NOGO delay activity in visual condition is greater than the GO activity in memory condition cannot be taken as evidence that the LIP activation carries ambiguous instructional information.

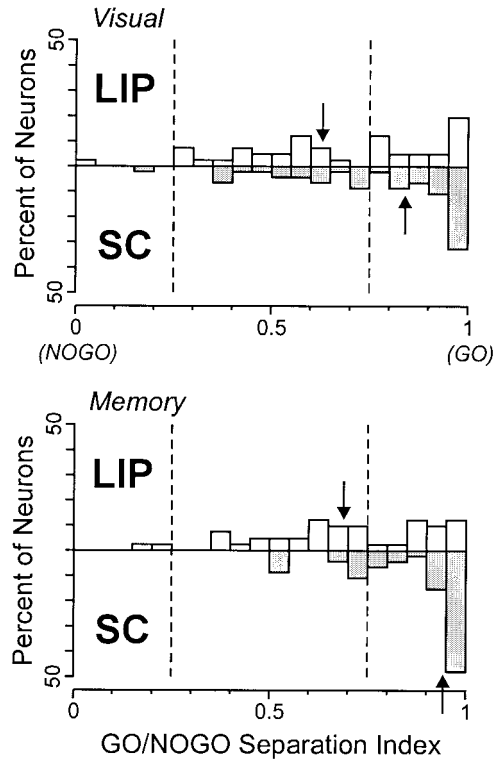

FIG. 11. Distribution of the GO/NOGO separation index (area under the OD curve) of the activity of SC neurons ($n = 46$) and LIP output neurons ($n = 41$) during the *delay* epoch of the visual (*top*) and memory (*bottom*) poststimulus instruction trials of the GO/NOGO saccade task. This analysis is based on the distribution of the discharge rates in the *visual* and *memory* conditions of the task (see text). The index can range from a value of 0 (NOGO distribution completely separate from and greater than GO distribution) to 1 (GO distribution completely separate from and greater than NOGO distribution). A value of 0.5 indicates that GO and NOGO distributions are indistinguishable. The vertical broken lines at the 0.25 and 0.75 index levels mark the thresholds of statistical significance. Arrow indicates the median index value of each distribution curve. Binwidth is 0.05.

activity appeared slightly enhanced when preceded by a GO instruction.

To examine whether the stimulus activity was selectively modulated by the instruction to make a saccade, we compared the activity of delay responsive LIP ($n = 38$) and SC ($n = 49$) neurons during the GO and NOGO *stim* epoch (see Fig. 1*B*) of the prestimulus instruction trials. We considered only the LIP ($n = 38$) and the SC ($n = 49$) neurons with stimulus activity significantly greater than their fixation activity (Wilcoxon signed rank test, $P < 0.01$), and the activity in visual and memory trials was pooled. A control comparison with the poststimulus instruction trials indicated, as expected, no significant difference between GO and NOGO stimulus activity (Wilcoxon signed rank test, $P > 0.14$). In the prestimulus instruction trials, the stimulus activity of SC neurons was not significantly strongest following the GO instruction ($P = 0.09$). Individually, the GO activity of 35% of the SC neurons was statistically greater than their NOGO activity, but it was significantly smaller in 10% of them. The GO/NOGO stimulus activity difference of LIP neurons also failed to exceed the significance level ($P = 0.01$). Individually, the GO activity of only 18% of the LIP neurons was statistically greater than their NOGO activity, and significantly smaller in 3% of them. Furthermore, the GO/NOGO stimulus activity in both pre- and poststimulus instruction trials did not differ statistically for both the LIP and the SC samples (Krukall-Wallis ANOVA on ranks, $P > 0.83$).

To determine whether the weak effect of the response instruction on the stimulus activity was due to a modulation already present before the stimulus presentation, we performed a linear regression analysis between the GO/NOGO activity difference during the *stim* epoch and during the immediately preceding *inst-delay* epoch (see Fig. 1*B*). We found that 47% (LIP) and 60% (SC) of the variance in the stimulus-related modulation could be accounted for by the variance in the earlier modulation ($r = 0.68$ and 0.78, F-test, $P < 0.0001$). In summary, advance instruction about saccade production seemed to affect the magnitude of the neuronal discharges time locked to the stimulus presentation in only a small fraction of neurons in both the SC and LIP samples. Moreover, most of this modulation could be explained by the prior changes in activity anticipating the visual stimulation.

Subsequent to the stimulus activity, the delay activity in the prestimulus instruction trials became significantly greater in GO trials than in NOGO trials (Fig. 12 and Table 3). Across post- and prestimulus instruction trials, all the distributions of

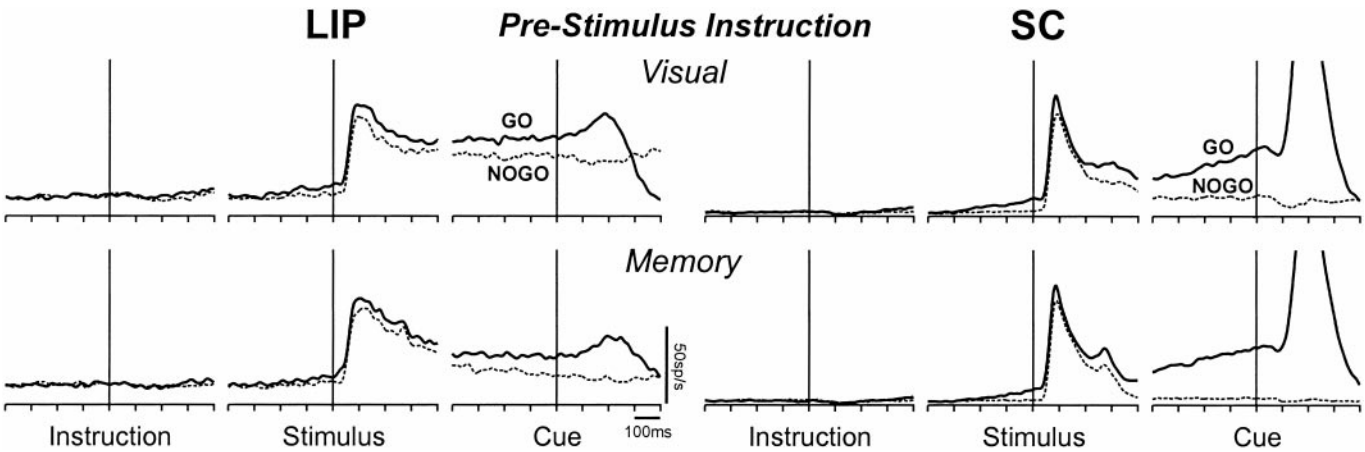

FIG. 12. Comparison between the average activation profile of LIP and SC delay responsive neurons in the prestimulus instruction trials of the GO/NOGO saccade task. Average spike density functions of LIP (*left*, $n = 41$) and SC neurons (*right*, $n = 46$) recorded during the visual (*top*) and memory (*bottom*) trials with the stimulus presented in the neurons' response fields. See legend of Fig. 10.

GO/NOGO separation indexes of the delay activity, except in the visual poststimulus instruction trials, were statistically greater in SC than LIP neurons (Kruskal-Wallis ANOVA on ranks, $P < 0.0001$; Dunn's test, $P < 0.05$). Furthermore, the proportions of neurons with significant GO > NOGO separation indexes and significant GO > NOGO activity differences (Table 4) were statistically larger in the SC sample ($\chi^2 = 50.4$ and 51.2, $df = 7$, $P < 0.0001$). These results further established that the strong delay activity (particularly of SC neurons) was associated with the combined information about the stimulus location and the response instruction.

SC superficial layer neurons

In the course of this study, we also examined the activation of nine additional SC neurons recorded presumably within the SC superficial layers. In the delayed saccade task, these neurons lacked significant presaccadic discharges and displayed a phasic discharge time locked to the visual stimulus onset. Sustained delay activity could also persist, but exclusively in the visual version of the delayed saccade task. In the GO/NOGO saccade task, neither the stimulus-related burst of activity of these neurons nor their sustained activity was modulated by advance instruction about saccade production. We excluded these "visual" neurons from our comparative study because the SC superficial layers seem to receive negligible inputs from area LIP, as indicated by anatomical (Lynch et al. 1985) and physiological (Paré and Wurtz 1997a, 1998) methods.

DISCUSSION

We compared the activity of LIP neurons projecting to the SC with that of neurons within the SC intermediate layers to assess the differences in saccade processing between these two brain regions. An examination of activity patterns in a delayed saccade task indicated that LIP and SC neurons have an extensive overlap in their responses to visual stimuli and in their sustained activity during the delay period, as suspected from our previous study (Paré and Wurtz 1997a). LIP output neurons, however, discharged less strongly than SC neurons during saccades, a difference perhaps reflecting dissimilar intrinsic properties between the homogeneous cortical pyramidal neurons and the morphologically heterogeneous SC neurons (Moschovakis et al. 1988). An analysis of the separation between activity associated with trials in which the visual stimulus presentation was either brief (memory trials) or sustained (visual trials) indicated that both the delay and the presaccadic activity levels of LIP neurons, but not of SC neurons, significantly depended on sustained visual stimulation. The output of the LIP population thus appears less directly devoted to saccade processing than the SC population.

An instructed saccade task with a GO/NOGO paradigm examined whether advance instruction about saccade production modulated the delay activity of these neuronal populations. In this task, both the LIP and the SC neurons discharged, on average, more strongly to a visual stimulus positioned in their response fields when it was specified to be a saccadic goal by a foveal color instruction than when the instruction indicated that no movement was requested. These results thus suggest that both neuronal populations could predict the production of an ensuing saccade, even though some level of activity persisted in NOGO trials. Nevertheless, when compared with SC neurons, individual LIP output neurons were significantly less dependent on the advance instruction; only a minority of LIP neurons was significantly modulated. Along with its dependence on visual stimulus presence, the delay activity of LIP neurons therefore continues to appear more remote from the processing for saccade production than that of SC neurons.

Altogether, this study indicates that the LIP neurons projecting to the SC comprise a heterogeneous subset of neurons whose general properties can only partially account for the neuronal activation of its downstream target structure. Indeed, the combined discharge properties predicted by our *motor preparation* framework (visual independence and instructional dependence of the neuronal activity in advance of saccades) was observed almost exclusively in the sample of SC neurons; the activity of the LIP neurons that project to the SC was more closely associated with a "visual representation." Accordingly, the differences in LIP and SC discharge properties suggest a progressive evolution in processing information associated with the production of saccades.

Visual dependence of neuronal activity

In its purest form, neuronal activity associated with saccades must be independent from the sensory signals that trigger the movements. Converging evidence indicates that the saccade activity of SC neurons generally is independent of the presence of a visual stimulus within their movement fields (e.g., Groh and Sparks 1996; Jay and Sparks 1987; Mays and Sparks 1980; Munoz and Wurtz 1995; Wurtz and Goldberg 1971). Nevertheless, differences can be observed when this activity is compared across conditions. For example, Mohler and Wurtz (1976) described a small class of SC neurons (the visually triggered movement cells) that discharge before saccades to a visual stimulus, but not before spontaneous saccades made in the light or the dark. More quantitative studies further demonstrated that, although most SC neurons continue to discharge before saccades made in the absence of a visual stimulus, their activity does generally show signs of visual dependence (Edelman and Goldberg 1997; Sparks and Porter 1983). Because this activity is so intimately linked to saccade execution, its reduced level in nonvisual conditions may be related to the concurrent reduction in saccade dynamics (Gnadt et al. 1991; White et al. 1994). Measuring neuronal activity well in advance of saccades, however, should not be confounding. Apart from our study, the visual dependence of the SC delay activity has been investigated only by Kojima et al. (1996), who found that a minority of SC neurons had a significantly greater delay activity either in the presence (12%) or the absence (14%) of a visual stimulus in their movement fields. Our results indicated a similar proportion of "memory"-dependent neurons (12%), but a greater proportion of visual-dependent neurons (31%).

Very few analogous studies have been performed in area LIP. Our previous paper was the first to demonstrate the strong visual dependence of the delay activity of LIP output neurons projecting to the SC (Paré and Wurtz 1997a). This property subsequently was recognized among nonidentified LIP neurons in different experimental conditions (Gottlieb et al. 1999). Our observation that the visual dependence of the delay activity

significantly diminishes from area LIP to SC therefore extends the previous observations made in independent studies, and we interpret this finding as indicating a progressive shift in saccade processing.

Influence of response instruction on neuronal activity

The manipulation of sensory information to instruct saccade production allowed us to explore the transitional stage between the sensory representation of the saccadic goal and the final achievement of the goal. Such an instruction procedure has proved useful to others who studied such covert processes often interpreted as "preparatory set" or "motor preparation" (Evarts et al. 1984; Requin et al. 1991). Our GO/NOGO saccade task is similar to a GO/NOGO reaching task designed by Kalaska and Crammond (1995), who investigated neuronal activity related to response selection in both parietal and premotor cortex. Briefly, neuronal responses in downstream premotor cortex were found to differentiate between GO and NOGO instructions to a much greater degree than those observed in upstream parietal cortex. These observations thus interestingly paralleled the shift forward in movement processing between area LIP and SC.

Somewhat closer to our study, Glimcher and colleagues studied the delay activity of LIP and SC neurons with a saccade selection task, in which a saccade to one of two peripheral visual stimuli is specified by the color of the fixation stimulus (Glimcher and Sparks 1992; Platt and Glimcher 1997). Data independently collected from each neuronal population showed that neurons generally discharged maximally if the cue dictated a saccade to the stimulus within their response fields rather than outside. From the available quantification, however, it can be estimated that SC neurons were more strongly modulated by the advance instruction than LIP neurons. Overall, the present activity modulation is qualitatively comparable to that observed in this saccade selection task, despite the distinction between the general and the selective inhibition of movements associated with, respectively, GO/NOGO and selection tasks (De Jong et al. 1995). Using a two-alternative force-choice visual discrimination task in which monkeys indicate their choice by correctly directed saccades, Newsome and colleagues (Horwitz and Newsome 1999; Shadlen and Newsome 1996) also recorded from two separate samples of LIP and SC neurons. Differential activation was found to predict the upcoming oculomotor decision in both brain regions, but no comparison is currently available. Other independent studies limited their quantitative investigations to activity patterns present in either area LIP (e.g., Barash et al. 1991a,b; Colby et al. 1996) or SC (e.g., Munoz and Wurtz 1995) often without comparable analyses. The ensemble of these studies thus suggest, albeit qualitatively, that the LIP and SC neuronal populations are functionally overlapping.

Further investigations of instructional influences on LIP and SC neurons are available in studies that employed an antisaccade task, in which the fixation stimulus color specifies either a saccade to a peripheral visual stimulus or a saccade directed diametrically away from the stimulus. Neuronal data collected independently in area LIP (Gottlieb and Goldberg 1999) and SC (Everling et al. 1999) again suggest that saccade instruction alters more the SC than the LIP neurons, but the considerable differences between the experimental designs and data analyses of these two studies preclude any strong comparison. Moreover, the report by Gottlieb and Goldberg (1999) that the activation of most LIP neurons encoded the location of the visual stimulus much more reliably than the direction of the saccade did not refute the possibility that only those neurons with distinct saccade-dependent activation reached the saccadic system, including the SC. This possibility now seems unlikely given that identified LIP output neurons show a similar range of properties as do unidentified populations of LIP neurons.

Our observations that advance instruction about saccade production modulates differently the delay activity of LIP output neurons and SC neurons are therefore consistent with observations made on unidentified neurons recorded in other instruction-based tasks. By using antidromic activation, we have added the important finding that there is no evidence for a motor preparation bias in the LIP neurons projecting to the SC and that the influence of response instruction on neuronal activity is enhanced from the LIP output to the SC. Insofar as the SC delay activity represents a motor preparation signal, its strength would not result from a signal already present in the output of parietal cortex. This progressive evolution in neuronal signals appears to be common within the saccadic system (Ferraina et al. 1999; Segraves and Goldberg 1987; Sommer and Wurtz 2000), but it contrasts with the more abrupt stages seen in visual motion processing (Ilg and Hoffmann 1993; Movshon and Newsome 1996).

Interpretational limitations

Apart from the ubiquitous sampling biases, which more severely affect physiological studies of unidentified neurons, the most serious limitation about the validity of our conclusions arises from the fact that our study did not limit the comparison to SC neurons receiving LIP inputs. The discharge properties of some SC neurons did resembled that of LIP output neurons (neurons with visually dependent and instruction-independent delay activity), raising the prospect that the cortical inputs could be restricted to a distinct sub-group of neurons within the SC population. This would imply that any uniform sampling of SC neurons could produce an apparent sequence of processing. This hypothesis, however, is not supported by our preliminary finding that the SC neurons *orthodromically* activated by LIP stimulation can be either with or without delay activity, and those with delay activity can be visually independent and instruction dependent (Paré and Wurtz 1998). Thus the LIP projection is rather unspecific, and it is reasonable to consider our sample of unidentified SC neurons as putative targets. Accordingly, a progression in saccade processing might emerge from a transformation of the LIP signals within the SC neuronal ensemble via an intrinsic circuitry (Munoz and Itsvan 1998), nonlinear membrane properties (Grantyn et al. 1983), and complex dendritic trees (Moschovakis et al. 1988). Nevertheless, the observation of an evolution in the discharge properties of LIP and SC neurons, by itself, is not sufficient to reveal whether LIP inputs actually are transformed within the SC. The differences between LIP and SC neurons could be due to extra-parietal inputs possibly originating, for example, from the frontal eye field (Everling and Munoz 2000; Segraves and Goldberg 1987; Sommer and Wurtz 1998, 2000; see also Schlag-Rey et al. 1992).

Another intriguing sampling bias issue relates to the fact that the response fields of LIP neurons, including the SC projection neurons, have a three-dimensional configuration (Ferraina et al. 1999; Gnadt and Beyer 1998; Gnadt and Mays 1995); whether SC neurons possess such a property is currently unknown. The fixed-depth visual stimuli used in this study thus might not have succeeded in optimally activating our neuronal samples. Nevertheless, unless the activation in visual, memory, GO, and NOGO trials each had a distinct tuning in depth, the differences between LIP and SC neurons could not have been radically different from what we showed. The exact influence of this factor on visual and instructional dependencies, and particularly on the general properties of SC neurons, nonetheless remains to be determined.

Our hypothesis of a progression in saccade processing assumes that signals transmitted from area LIP to SC necessarily have something to do with sensory-motor processing. It should be noted, however, that a minor fraction of LIP output neurons have other or unidentified properties (Paré and Wurtz 1997a), and these units would need to be accommodated within future schemes. This could easily be achieved for the LIP output neurons that show fixation-related activity by assuming the hypothesized dual function of the SC in fixation and saccade behaviors (Munoz and Wurtz 1993a,b). The remaining population of LIP output neurons that we have previously identified as being unresponsive in visuo-oculomotor tasks could, once we have characterized them fully, either be pronounced developmental anomalies (if their low discharge rates do not carry significant information) or significant players with a function perhaps beyond sensory-motor processes.

Function of area LIP in saccade processing

Area LIP could be ideally suited to convert the product of visual processing into oculomotor programs because it is anatomically interposed between visual cortical areas (Andersen et al. 1990; Baizer et al. 1991; Morel and Bullier 1990) and saccadic centers (SC: Gnadt and Beyer 1998; Lynch et al. 1985; Paré and Wurtz 1997a, 1998; frontal eye field: Ferraina et al. 1999; Schall et al. 1995). The exact function of LIP in saccade processing, however, remains controversial. Two main interpretations currently implicate area LIP in either the planning of saccades (Andersen et al. 1997) or in the formation of an attention map of the salient environment (Colby and Goldberg 1999). Because previous investigations might have focused on different neuronal populations within the intraparietal sulcus region presumed to contain area LIP, it has been particularly difficult to reconcile these seemingly mutually exclusive hypotheses. The participation of LIP neurons in saccade processing is presumably reflected in their connectivity. We therefore reasoned that knowing the signals relayed by the LIP output channels should help to clarify the saccadic role that area LIP plays. Our original characterization of the signals conveyed by the LIP output neurons projecting to the SC established that they could influence saccade processing by means of a visual activation frequently evolving into a presaccadic signal (Paré and Wurtz 1997a). The GO/NOGO saccade task offered an opportunity to elucidate further the relation of this parietal output channel to saccade processing, even though it was not specifically designed to dissociate hypotheses based primarily on motor planning or visuo-attentional mechanisms. Both hypotheses would predict that a GO instruction should increase the LIP activity because of the concurrent planning of the saccade and attentional relevance of the visual stimulus. Our finding that the average LIP delay activity increased in GO trials is therefore compatible with both hypotheses, but the lack of a systematic modulation, along with the persistence of activity during NOGO trials, does not lend strong support to either one. The heterogeneity of the LIP neuronal properties implies either that a single sensory-motor process cannot be attributed to this cortical structure or that the signals carried by LIP output neurons do not reflect a completed process. Hence area LIP does not *impose* a planning or attention signal on SC neurons. In light of the potent instructional influence on SC neurons, we submit that the moderate modulation of the LIP output neurons represents an early stage in the progressive formation of a decision specifying saccade production (cf. Platt and Glimcher 1999; Shadlen and Newsome 1996). In this context, our study highlights the value of comparing the processing taking place in interconnected brain regions to understand their functional contributions.

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REFERENCES

ANDERSEN RA, ASANUMA C, ESSICK GK, AND SEIGEL RM. Corticocortical connections of anatomically and physiologically defined subdivisions within the inferior parietal lobule. *J Comp Neurol* 296: 65–113, 1990.

ANDERSEN RA, ESSICK GK, AND SEIGEL RM. Neurons in area 7 activated by both visual stimuli and oculomotor behavior. *Exp Brain Res* 67: 316–322, 1987.

ANDERSEN RA, SNYDER LH, BRADLEY DC, AND XING J. Multimodal representation of space in the posterior parietal cortex and its use in planning movements. *Annu Rev Neurosci* 20: 303–330, 1997.

ASANUMA C, ANDERSEN RA, AND COWAN WM. The thalamic relations of the caudal inferior parietal lobule and the lateral prefrontal cortex in monkeys: divergent cortical projections from cell clusters in the medial pulvinar nucleus. *J Comp Neurol* 241: 357–381, 1985.

BAIZER JS, UNGERLEIDER LG, AND DESIMONE R. Organization of visual inputs to the inferior temporal and posterior parietal cortex in macaques. *J Neurosci* 11: 168–190, 1991.

BAMBER D. The area above the ordinal dominance graph, the area below the receiver operating characteristic graph. *J Math Psychol* 12: 387–415, 1975.

BARASH S, BRACEWELL RM, FOGASSI L, GNADT JW, AND ANDERSEN RA. Saccade-related activity in the lateral intraparietal area. I. Temporal properties; comparison with area 7a. *J Neurophysiol* 66: 1095–1108, 1991a.

BARASH S, BRACEWELL RM, FOGASSI L, GNADT JW, AND ANDERSEN RA. Saccade-related activity in the lateral intraparietal area. II. Spatial properties. *J Neurophysiol* 66: 1109–1124, 1991b.

BASSO MA AND WURTZ RH. Modulation of neuronal activity in superior colliculus by changes in target probability. *J Neurosci* 18: 7519–7534, 1998.

BRITTEN KH, SHADLEN MN, NEWSOME WT, AND MOVSHON JA. The analysis of visual motion: a comparison of neuronal and psychophysical performance. *J Neurosci* 12: 4745–4765, 1992.

COLBY CL, DUHAMEL JR, AND GOLDBERG ME. Visual, presaccadic, and cognitive activation of single neurons in monkey lateral intraparietal area. *J Neurophysiol* 76: 2841–2852, 1996.

COLBY CL AND GOLDBERG ME. Space and attention in parietal cortex. *Annu Rev Neurosci* 22: 319–349, 1999.

CRIST C AND ROBINSON DL. A large-field screen with even texture for vision research. *Vis Neurosci* 2: 415–417, 1989.

CRIST CF, YAMASAKI DSG, KOMATSU H, AND WURTZ RH. A grid system and a microsyringe for single cell recording. *J Neurosci Methods* 26: 117–122, 1988.

DARLINGTON RB. Comparing two groups by simple graphs. *Psychol Bull* 79: 110–116, 1973.

DE JONG R, COLES MGH, AND LOGAN GD. Strategies and mechanisms in nonselective and selective inhibitory motor control. *J Exp Psychol: HPP* 21: 498–511, 1995.

DORRIS MC AND MUNOZ DP. Saccadic probability influences motor preparation signals and time to saccadic initiation. *J Neurosci* 18: 7015–7026, 1998.

DORRIS MC, PARÉ M, AND MUNOZ DP. Neuronal activity in the monkey superior colliculus related to the initiation of saccadic eye movements. *J Neurosci* 17: 8566–8579, 1997.

EDELMAN JA AND GOLDBERG ME. Perisaccadic activity of neurons in the intermediate layers of the monkey superior colliculus depends on the presence of a target. *Soc Neurosci Abstr* 23: 843, 1997.

EVARTS EV, SHINODA Y, AND WISE SP. *Neurophysiological Approaches to Higher Brain Functions.* New York: Wiley, 1984.

EVERLING S, DORRIS MC, KLEIN RM, AND MUNOZ DP. Role of primate superior colliculus in preparation and execution of anti-saccades and pro-saccades. *J Neurosci* 19: 2740–2754, 1999.

EVERLING S AND MUNOZ DP. Neuronal correlates for preparatory set associated with pro-saccades and anti-saccades in the primate frontal eye field. *J Neurosci* 20: 387–400, 2000.

FERRAINA S, PARÉ M, AND WURTZ RH. Discharge properties of lateral intraparietal area neurons antidromically activated by frontal eye field stimulation. *Soc Neurosci Abstr* 25: 806, 1999.

GLIMCHER PW AND SPARKS DL. Movement selection in advance of action in the superior colliculus. *Nature* 355: 542–545, 1992.

GNADT JW AND ANDERSEN RA. Memory related motor planning activity in posterior parietal cortex of macaque. *Exp Brain Res* 70: 216–220, 1988.

GNADT JW AND BEYER J. Eye movements in depth: what does the monkey's parietal cortex tell the superior colliculus? *Neuroreport* 9: 233–238, 1998.

GNADT JW, BRACEWELL RM, AND ANDERSEN RA. Sensorimotor transformation during eye movements to remembered visual targets. *Vision Res* 31: 693–715, 1991.

GNADT JW AND MAYS LE. Neurons in monkey parietal area LIP are tuned for eye-movement parameters in three-dimensional space. *J Neurophysiol* 73: 280–297, 1995.

GOTTLIEB J AND GOLDBERG ME. Activity of neurons in the lateral intraparietal area of the monkey during an antisaccade task. *Nature Neurosci* 2: 906–912, 1999.

GRANTYN R, GRANTYN A, AND SCHIERWAGEN A. Passive membrane properties, afterpotentials and repetitive firing of superior colliculus neurons studied in the anesthetized cat. *Exp Brain Res* 50: 377–391, 1983.

GREEN DM AND SWETS JA. *Signal Detection Theory and Psychophysics.* New York: Wiley, 1966.

GROH JM AND SPARKS DL. Saccades to somatosensory targets. II. Motor convergence in primate superior colliculus. *J Neurophysiol* 75: 428–438, 1996.

HAYS AV, RICHMOND BJ, AND OPTICAN LM. A UNIX-based multiple process system for real-time data acquisition and control. *WESCON Conf Proc* 2: 1–10, 1982.

HORWITZ GD AND NEWSOME WT. Separate signals for target selection and movement specification in the superior colliculus. *Science* 284: 1158–1161, 1999.

ILG UJ AND HOFFMANN K-P. Functional grouping of the cortico-pretectal projection. *J Neurophysiol* 70: 867–869, 1993.

JAY MF AND SPARKS DL. Sensorimotor integration in the primate superior colliculus. I. Motor convergence. *J Neurophysiol* 57: 22–34, 1987.

JUDGE SJ, RICHMOND BJ, AND CHU FC. Implantation of magnetic search coils for measurement of eye position: an improved method. *Vision Res* 20: 535–538, 1980.

KALASKA JF AND CRAMMOND DJ. Deciding not to go: neuronal correlates of response selection in a go/nogo task in primate premotor and parietal cortex. *Cereb Cortex* 5: 410–428, 1995.

KOJIMA J, MARSUMARA M, TOGAWA M, AND HIKOSAKA O. Tonic activity during visuo-oculomotor behavior in the monkey superior colliculus. *Neurosci Res* 26: 17–28, 1996.

LEMON R. Methods for neuronal recording in conscious animals. In: *IBRO Handbook Series: Methods in the Neurosciences,* edited by Smith AD. London: Wiley, 1984, vol. 4.

LYNCH JC, GRAYBIEL AM, AND LOBECK LJ. The differential projection of two cytoarchitectural subregions of the inferior parietal lobule of macaques upon the deep layers of the superior colliculus. *J Comp Neurol* 235: 241–254, 1985.

MACPHERSON JM AND ALDRIDGE JW. A quantitative method of computer analysis of spike train data collected from behaving animals. *Brain Res* 175: 183–187, 1979.

MAYS LE AND SPARKS DL. Dissociation of visual and saccade-related responses in superior colliculus neurons. *J Neurophysiol* 43: 207–232, 1980.

MAZZONI P, BRACEWELL RM, BARASH S, AND ANDERSEN RA. Motor intention activity in the macaque's lateral intraparietal area. I. Dissociation of motor plan from sensory memory. *J Neurophysiol* 76: 1439–1456, 1996.

MOHLER CW AND WURTZ RH. Organization of monkey superior colliculus: intermediate layer cells discharging before eye movements. *J Neurophysiol* 39: 722–744, 1976.

MOREL A AND BULLIER J. Anatomical segregation of two cortical visual pathways in the macaque monkey. *Vis Neurosci* 4: 555–578, 1990.

MOSCHOVAKIS AK, KARABELAS AB, AND HIGHSTEIN SM. Structure-function relationships in the primate superior colliculus. I. Morphological classification of efferent neurons. *J Neurophysiol* 60: 232–262, 1988.

MOVSHON JA AND NEWSOME WT. Visual response properties of striate cortical neurons projecting to area MT in macaque monkeys. *J Neurosci* 16: 7733–7741, 1996.

MUNOZ DP AND ITSVAN PJ. Lateral inhibitory interactions in the intermediate layers of the monkey superior colliculus. *J Neurophysiol* 79: 1193–1209, 1998.

MUNOZ DP AND WURTZ RH. Fixation cells in monkey superior colliculus. I. Characteristics of cell discharge. *J Neurophysiol* 70: 559–575, 1993a.

MUNOZ DP AND WURTZ RH. Fixation cells in monkey superior colliculus. II. Reversible activation and deactivation. *J Neurophysiol* 70: 576–589, 1993b.

MUNOZ DP AND WURTZ RH. Saccade related activity in monkey superior colliculus. I. Characteristics of burst and buildup cells. *J Neurophysiol* 73: 2313–2333, 1995.

PARÉ M AND WURTZ RH. Monkey posterior parietal cortex neurons antidromically activated from superior colliculus. *J Neurophysiol* 78: 3493–3497, 1997a.

PARÉ M AND WURTZ RH. Discharge properties of lateral intraparietal sulcus neurons antidromically activated by superior colliculus stimulation. *Soc Neurosci Abstr* 23: 843, 1997b.

PARÉ M AND WURTZ RH. Discharge properties of superior colliculus neurons activated orthodromically by lateral intraparietal sulcus stimulation. *Soc Neurosci Abstr* 24: 1498, 1998.

PLATT M AND GLIMCHER PW. Responses of intraparietal neurons to saccadic targets and visual distractors. *J Neurophysiol* 78: 1574–1589, 1997.

PLATT M AND GLIMCHER PW. Neural correlates of decision variables in parietal cortex. *Nature* 400: 233–238, 1999.

REQUIN J, BRENER J, AND RING C. Preparation for action. In: *Handbook of Cognitive Psychophysiology: Central and Autonomic Nervous System Approaches,* edited by Jennings JR and Coles MGH. New York: Wiley, 1991, p. 357–448.

RICHMOND BJ, OPTICAN LM, PODELL M, AND SPITZER H. Temporal encoding of two-dimensional patterns by single units in primate inferior temporal cortex. I. Response characteristics. *J Neurophysiol* 57: 132–146, 1987.

ROBINSON DA. A method of measuring eye movement using a scleral search coil in a magnetic field. *IEEE Trans Biomed Eng* 10: 137–145, 1963.

SCHALL JD, MOREL A, KING DJ, AND BULLIER J. Topography of visual cortex connections with frontal eye field in macaque: convergence and segregation of processing streams. *J Neurosci* 15: 4464–4487, 1995.

SCHLAG-REY M, SCHLAG J, AND DASSONVILLE P. How the frontal eye field can impose a saccade goal on superior colliculus neurons. *J Neurophysiol* 67: 1003–1005, 1992.

SEGRAVES MA AND GOLDBERG ME. Functional properties of corticotectal neurons in the monkey's frontal eye field. *J Neurophysiol* 58: 1387–1419, 1987.

SHADLEN M AND NEWSOME WT. Motion perception: seeing and deciding. *Proc Natl Acad Sci USA* 93: 628–633, 1996.

SNYDER LH, BATISTA AP, AND ANDERSEN RA. Coding of intention in the posterior parietal cortex. *Nature* 386: 167–170, 1997.

SOMMER MA AND WURTZ RH. Instructional dependence of delay activity in the projection from the frontal eye field to superior colliculus. *Soc Neurosci Abstr* 24: 1146, 1998.

SOMMER MA AND WURTZ RH. Composition and topographic organization of signals sent from the frontal eye field to the superior colliculus. *J Neurophysiol* 83: 1979–2001, 2000.

SOMMER MA, PARÉ M, AND WURTZ RH. Instructional dependence of preparatory discharges of superior colliculus neurons. *Soc Neurosci Abstr* 23: 843, 1997.

SPARKS DL. Functional properties of neurons in the monkey superior colliculus: coupling of neuronal activity and saccade onset. *Brain Res* 156: 1–16, 1978.

SPARKS DL AND PORTER JD. Spatial localization of saccade targets. II. Activity of superior colliculus neurons preceding compensatory saccades. *J Neurophysiol* 49: 64–74, 1983.

THOMPSON KG, HANES DP, BICHOT NP, AND SCHALL JD. Perceptual and motor processing stages identified in the activity of macaque frontal eye field neurons during visual search. *J Neurophysiol* 76: 4040–4055, 1996.

WAITZMAN DM, MA TP, OPTICAN LM, AND WURTZ RH. Superior colliculus neurons mediate the dynamic characteristics of saccades. *J Neurophysiol* 66: 1716–1737, 1991.

WHITE JM, SPARKS DL, AND STANFORD TR. Saccades to remembered target locations: an analysis of systematic and variable errors. *Vision Res* 34: 79–92, 1994.

WURTZ RH AND GOLDBERG ME. Superior colliculus cell responses related to eye movements in awake monkeys. *Science* 171: 82–84, 1971.