Posterior Cingulate Cortex: Sensory and Oculomotor Properties of Single Neurons in Behaving Cat

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The posterior cingulate cortex of the cat is strongly linked to cortical areas with sensory and oculomotor functions. We have now recorded from feline posterior cingulate neurons in order to determine whether they are active in conjunction with sensory events and eye movements. The results described here are based on monitoring the electrical activity of 195 single neurons in the posterior cingulate cortex of three cats equipped with surgically implanted scleral search coils and trained to fixate visual targets. Posterior cingulate neurons carry tonic orbital position signals and are phasically active in conjunction with saccadic eye movements. Activity related to eye movements and gaze is attenuated but not abolished by the elimination of visual feedback. Posterior cingulate neurons also are responsive to visual, auditory, and somatosensory stimulation. Systematic testing with visual stimuli revealed that responses are sharply reduced due to refractoriness at rates of stimulation greater than a few per second. These results conform to the theory that posterior cingulate cortex is involved in processes underlying visuospatial cognition.

The feline posterior cingulate cortex (CGp), a well-defined cortical district with a distinctive pattern of cytoarchitecture and thalamic input, occupies the ventral bank of the splenial sulcus and the adjacent parasplenial gyrus (Rose and Woolsey, 1948; Robertson and Kaitz, 1981; Musil and Olson, 1988, 1992). CGp is indicated by shading in Figure 1*C*, a flat map of cortex forming the medial face of the cerebral hemisphere. As may be seen in this figure, CGp adjoins visual (17, 20b) and somatosensory (5, 3a) areas and commonly is divided into several component areas, based on cytoarchitectural and other criteria, which include splenial visual area (SVA), ventral splenial area (VSA), cingular area, and granular (RSg) and agranular (RSa) sectors of retrosplenial cortex (Olson and Musil, 1992).

The cingulate cortex, including CGp, has long been held to serve as a cortical substrate for emotion (Papez, 1937). However, on the basis of recently reported connectional results, it would appear that CGp more probably is involved in sensory, motor, and memory-related processes (Olson and Musil, 1992; Musil and Olson, 1993). By far the strongest inputs to CGp derive from neocortical association areas with sensorimotor integration functions. Moreover, insofar as limbic afferents are present in CGp, they derive primarily from structures considered to subserve memory rather than emotion, notably the parahippocampal gyrus and anterior thalamic nuclei.

A broad intermediate division of CGp (the "ocular" zone of Fig. 1*D*) is strongly linked to numerous cortical areas with visual and oculomotor functions, including area 7, the frontal eye fields, the granular insula, the posterior ectosylvian gyrus, area 20, and several lateral suprasylvian visual areas (Olson and Musil, 1992; Musil and Olson, 1993). The inference that this zone is involved in processes related to vision and eye movements has received support from functional studies showing that neurons in it are visually responsive in anesthetized cats (Kalia and Whitteridge, 1973) and that neurons in an apparently homologous division of rabbit cingulate cortex exhibit phasic excitation during the rapid eye movements of nystagmus (Sikes et al., 1988). The aim of this study was to investigate more fully the functional properties of neurons in the ocular subregion of CGp, and in particular to assess patterns of activity related to voluntary visually guided eye movements.

Cerebral Cortex Nov/Dec 1992;2 485–502; 1047–3211/92/$4.00

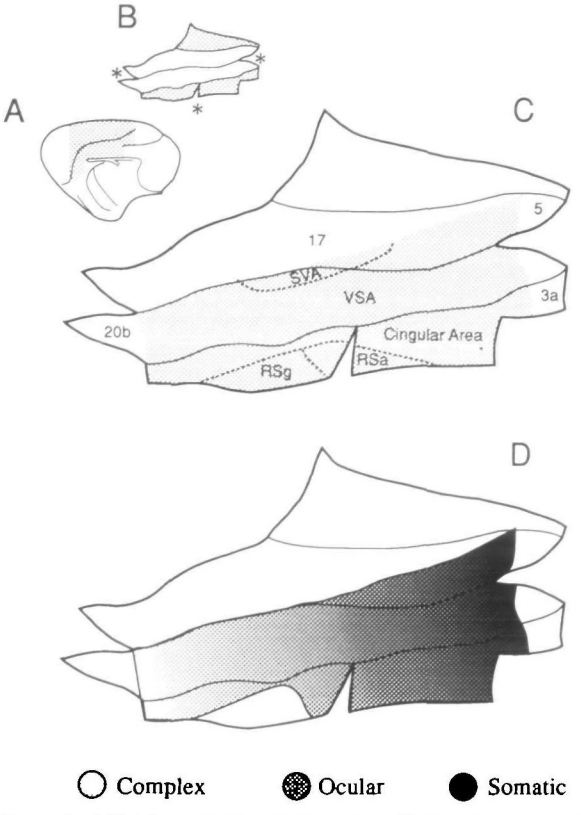


Figure 1. *A*, Medial view of left cerebral hemisphere. *Shading* indicates extent of cortex represented in flat map. *B*, Flat map of CGp and adjacent areas. *Shading* indicates cortex exposed on gyral surfaces prior to flattening. *Unshaded area* encompasses dorsal and ventral banks of splenial sulcus. *Asterisks* indicate incisions placed in the cortical sheet to permit undistorted flattening. *C*, *Shading* indicates CGp. *D*, Internal regional organization of CGp as inferred from topography of afferent connections. At rostral levels, projections from somesthetic and somatomotor areas terminate; at intermediate levels, projections from visual and oculomotor areas terminate, at caudal levels, projections from "complex" areas including prefrontal cortex terminate (Olson and Musil, 1992)

Materials and Methods

Subjects

The experiments were carried out on adult cats, free of eye and ear infection, weighing 2–3 5 kg. All aspects of the experiments were in accord with guidelines published in the *NIH Guide for the Care and Use of Laboratory Animals,* Publication Number 86-23.

Surgery

Pretreatment and Anesthesia

Cats were food deprived for 12 hr prior to surgery and were pretreated on the day of surgery with atropine sulfate (0.2 mg/kg, i.m.) and penicillin (Durapen, 300,000 U, i.m.). Dissociative anesthesia was induced with an intramuscular injection of Ketaset (ketamine hydrochloride, 30 mg/kg). Following cannulation of a forelimb vein, deep anesthesia was induced with Brevital (methohexital sodium, 10 mg/ml, i.v.) and maintained thereafter with additional intravenous doses of Brevital as needed. During surgical procedures involving the eye and surrounding tissue, the local anesthetic lidocaine hydrochloride (2%) was applied topically to the conjunctiva.

Implant

The scalp was incised at the midline and the muscle and periosteum were retracted. Skull screws were placed at the perimeter of the exposed skull. A 5-mm-diameter craniotomy was placed over the cortical area of interest, with care taken to maintain the underlying dura intact, and a recording chamber, its base flush with the dural surface, was fitted snugly into the hole. A pedestal of dental acrylic was then built up over the entire area of the exposed skull. The acrylic block firmly enclosed the heads of the skull screws and the outer wall of the recording chamber. Also embedded in it were the electrical connector leading to the scleral search coil and attachment mounts for the head-restraint device. Particular care was taken to produce a smooth surface at points where the acrylic contacted the skin and connective tissue of the scalp.

Scleral Search Coil

A scleral search coil was implanted on the right eye by a procedure adapted from Judge et al. (1980). First the scleral surface of the globe was fully exposed by cutting and blunt-point dissection of the conjunctiva along the entire perimeter of the limbus. Then a previously prepared coil was slipped onto the globe in frontoparallel orientation and sutured to the sclera at four points with fine sutures. The leads of the coil were passed subcutaneously from the periorbital space to the area above the skull exposed by incision of the scalp skin. The ends of the wires were then soldered to an electrical connector.

Postsurgical Treatment

Penicillin (Durapen, 300,000 U, i.m.) was administered on alternate days for 1 week following surgery. At least twice weekly, throughout the entire period of the subsequent experiment, the skin surrounding the implant and the interior of the chamber were cleansed with hydrogen peroxide (3%) and rinsed with sterile saline.

Behavioral Apparatus

Restraint

The cat was placed in an adjustable nylon-mesh zippered vest fixed to an immobile frame (Alice King Chatam, Inc., Los Angeles, CA). The vest allowed free movement of the extremities and permitted the cat to assume a variety of comfortable postures, sitting or standing. The cat's head was held rigidly in place at a natural angle by a clamp that attached to the steel tubes embedded in the acrylic pedestal.

Eye-Position Monitoring

The cat's head was centered within a 24 inch field coil. Signals generated by the field coil and picked up by the scleral search coil were monitored through a lead attached to the connector on the acrylic pedestal. Circuits designed by Remmel (1984) and manufactured by Indiran Instruments (Cambridge, MA) generated the field-coil signal and transformed the

search-coil signal into voltages representing the horizontal and vertical angles of the eye with a noise level corresponding to approximately 0.1°.

Visual Targets

The cat faced a horizontal perimeter at a distance of 30 cm. The perimeter contained five visual stimulus devices, one straight ahead of the cat and the others at 10° and 20° to the left and right. Each device consisted of a 4 × 4 array of yellow LEDs. The luminance of the LEDs was 11 ft-lamberts, one log-unit above the standard level of background luminance, and each array subtended a visual angle of 2.3°.

Reward

The reward was beef puree (0.1 ml) delivered intermittently under air pressure through a retractable spigot placed beneath the mouth. At the time of delivery of each reward, the spigot was raised for several seconds and then lowered. The inaccessibility of the spigot between food deliveries prevented its becoming a source of distraction during task performance.

Training

(1) The cat was accustomed to restraint by giving it access to food within the apparatus over a period of days. (2) The eye coil system was calibrated by use of a program that permitted the experimenter to activate any stimulus device and record automatically the output voltages at the termination of the resulting spontaneous saccade. (3) Over a period of several days, the cat was trained to make visually guided eye movements by a procedure that involved the direct participation of the experimenter. For several hours each day, the experimenter activated stimulus devices and delivered reward under push-button control. Reward was delivered only if the cat made an eye movement toward the stimulus, as determined by inspection of a display in which the instantaneous angle of gaze was indicated by the position of a spot and the locations of targets were indicated by windows. (4) A period of automatic training on visual-target fixation ensued. Under computer control, stimuli were presented at intervals of approximately 10 sec in pseudorandom sequence. In order to receive reward, the cat was required to fixate the stimulus for a specified period that was increased gradually over the course of a few sessions to 2.5 sec. (5) Finally, the cat was trained under computer control to make saccadic eye movements between visual targets. The regimen was identical to that employed in step 4 except that after 1 sec of fixation on target 1, this target was extinguished and target 2 simultaneously appeared. Over a period of weeks, requirements for speed and accuracy were gradually made more stringent. At the end of training, cats initiated nearly all saccades to the second target at a latency between 100 and 300 msec. The size of the window, centered on the target, within which the cat had to maintain fixation in order for the trial to proceed to successful completion, was subject to continuous adjustment throughout the period of training and data collection. It was maintained at an extent, commonly 1° beyond the fixation point in each direction, such that fewer than 80% of trials were completed successfully.

The Standard Saccade Task

The initial characterization of each neuron involved a procedure to which we will refer as the "standard saccade" task (see Fig. 4). The aim of this task was to indicate whether the firing of the neuron was modulated in conjunction with the execution of saccadic eye movements. This test will be described in detail because it is representative in most regards of all the tests we employed. In the standard task, cats executed rightward and leftward eye movements between targets on the perimeter. Testing was carried out in a dimly illuminated room. The targets were both auditory and visual (both the LEDs and the tone source of the deisgnated device were activated) and they were phasic (flashes and tone bursts of 10 msec duration were delivered in phase at 10 Hz). At the outset of each trial, one target (F, the fixation target) was presented, and the cat was required to attain fixation of it within 500 msec, whereupon it was extinguished for 200 msec and then turned back on. At the instant of re-onset of F, the trial proper began, together with data collection. Target F remained on for 1 sec, and then was extinguished and replaced by a spatially separate target (S, the saccade target), which remained on for an additional 1.5 sec. The cat was required to maintain fixation of target F until its offset and then to transfer gaze to target S and maintain fixation of the latter until its offset, at which point, if the task had been correctly performed, reward was delivered. Cats were allowed 700 msec in which to shift gaze from F to S, although the saccade nearly always occurred at less than 300 msec latency. In one form of the test, righward eye movements were from the device 10° left of center to the device 10° right of center, and leftward eye movements were between the same pair of devices in reverse order. In a second form of the test, utilized during later experiments because it prevented predictive eye movements, all trials began with fixation of the central device and the saccade target was alternately 10° to the left and 10° to the right of center. Data were also collected during spontaneous control periods, 2.5 sec blocks of time when cats were quietly waiting between trials. Trials involving leftward and rightward saccades were interleaved in pseudorandom sequence with each other and with spontaneous control trials according to the rule that in each block of three trials with successful data collection there must be one instance of each condition. Testing was continued, if possible, until data had been collected during 15 trials of each type.

Variants on the Standard Saccade Task

Data were collected during performance of several tasks in addition to the one described above. These were simple variants of the standard saccade task in the sense that the same physical stimuli were employed and in the sense that the same behavioral re-

quirements were present (maintaining fixation on and executing saccades between targets). Cats trained to perform the standard saccade task transferred almost automatically to these tasks. The following variants of the standard saccade task were employed.

Visual Fixation Condition
The aim of this test was to reveal modulations of tonic firing dependent on the direction of gaze during prolonged fixation. Cats maintained steady fixation on a single target that, on pseudorandomly interleaved trials, was at the 10° leftward, central, or 10° rightward position. Each trial was equivalent to a trial in the standard saccade paradigm with the condition that F (the initial fixation target) and S (the saccade target) were identical, with the result that no saccade was required and there was no perceptible transition from F to S.

Orbital Position Condition
The aim of this test was to reveal modulations of tonic firing dependent on the angle of the eye in the orbit under conditions of constant visual feedback. On every trial of this test, the cat maintained steady fixation on the central target. On pseudorandomly interleaved trials, the support frame was rotated, along with the cat's entire body, including the head, so that the head was oriented 10° leftward, straight ahead, or 10° rightward relative to the central target. This required that the angle of conjugate gaze, during fixation of the target, be 10° rightward, central, or 10° leftward with respect to a head-centered coordinate frame.

Darkness Condition
The aim of this test was to assess whether neuronal activity accompanying eye movements was dependent on illumination of the surroundings. On every trial of this test, the cat made a saccadic eye movement between the same two targets. Targets were chosen so as to elicit maximal perisaccadic firing. On pseudorandomly interleaved trials, the light illuminating the room either remained on throughout the trial or was extinguished during a period of 1 sec beginning 200 msec before the onset of the saccade target.

Variable Frequency Condition
The aim of this test was to determine whether phasic responsiveness to a fixated target would emerge if the interflash interval was lengthened beyond the duration of 100 msec employed in the standard saccade task. On every trial of this test, the cat made a saccadic eye movement between the same two targets. On pseudorandomly interleaved trials, the interflash interval was 100 msec, 200 msec, or 500 msec.

Single-Neuron Recording
The recording chamber was a stainless steel tube 8 mm long with an inner diameter of 4 mm. The chamber was sealed between sessions with a tightly fitting plug. During recording, the plug was removed and a microdrive was fitted into the chamber. The solid cylindrical base of the microdrive filled and sealed the chamber. A vertical guide hole penetrated the base of the microdrive at an eccentricity of 1 mm. By rotating the drive with respect to the chamber, it was possible to vary the location of the recording track. Penetrations placed successively through the same chamber with the drive in different positions were parallel and vertical and formed a cylindrical bundle 2 mm in diameter. The advance mechanism was a manually controlled 80 thread/inch screw with 14 mm of travel. Varnish-coated tungsten microelectrodes were used (Frederick Haer Co.).

Data Display and Storage

On-Line Analysis
Amplified neuronal signals were led to an oscilloscope, an audio monitor and a window discriminator, the latter adjusted to produce a single pulse on each occurrence of an action potential. Pulses output by the window discriminator were led to the computer by way of a digital input port. Eye-position signals, in the form of voltages representing horizontal and vertical deviation, were led to the computer by way of analog input ports at sampling intervals of 10 msec. An on-line monitor display, updated under computer control during each trial, included cumulative rasters and histograms of action potentials and traces representing horizontal and vertical eye position as a function of time. By inspection of the on-line display, it was possible to ascertain qualitatively to what degree the activity of each neuron was task dependent and to choose further tests accordingly.

Data Processing
Neuronal and eye position data, together with markers representing the occurrence of key events such as stimulus onset and offset, were stored on disk with 10 msec resolution. The data could be retrieved in trial-by-trial format or in the form of cumulative histogram, raster, and eye-position displays. In cumulative displays, data from successive trials could be aligned at choice on a variety of events including the time of onset or offset of a specified stimulus and the beginning or end of a saccade of specified size and direction.

Statistical Analysis of Data
We utilized three procedures for measuring the statistical significance of task-dependent phasic and tonic changes in neuronal firing. The procedures were fully objective in the sense that they were applied without parametric adjustment, regardless of subjective judgements concerning task-related firing, to data from all neurons. The first step of analysis was to form cumulative histograms representing neuronal activity as a function of time for each trial condition (e.g., trials involving rightward saccades, trials involving leftward saccades, and spontaneous control periods). Bins were 10 msec wide and data from successive trials were aligned on the event of interest. The nature of further analysis depended on the type of response to be analysed: phasic, tonic, or repetitive.

Phasic Responses

This test was used to test for a brief increase or decrease of activity following a sensory event or eye movement. The response was measured as a difference: the number of action potentials fired during 100 msec immediately following the event minus the number of action potentials fired during 100 msec immediately preceding it. The null hypothesis (that a response as strong as that measured would have occurred even in the absence of the event) was tested by sampling activity collected during the 2.5 sec intertrial control periods. At each possible point in the histogram of intertrial activity, a difference score was computed by subtracting the sum of action potentials in the preceding 100 msec period from the sum of action potentials in the following 100 msec period (this procedure yielded 230 measures with 12.5 degrees of freedom). On the basis of the estimated mean and standard deviation of the control-period difference scores, the response was then expressed as a two-tailed Z score. A Z score with an absolute value greater than 1.96 indicated a significant level of responsiveness ($p < 0.05$).

Tonic Responses

This test was used to determine whether the rate of firing was significantly elevated or decreased during a 700 msec block of time centered within the presaccadic fixation period (200–900 msec following trial onset) or the postsaccadic fixation period (1400–2100 msec following trial onset). The response measure was simply the sum of action potentials fired during the stipulated period of time. The null hypothesis was tested by a sampling procedure carried out on the histogram of activity collected during 2.5 sec intertrial control periods. Action potentials were summed within each possible 700 msec block of the histogram of intertrial activity (giving 180 measures with 3.57 degrees of freedom). On the basis of the estimated mean and standard deviation of the control-period scores, the response was then expressed as a two-tailed Z score. A Z score wtih an absolute value greater than 1.96 indicated a significant level of responsiveness ($p < 0.05$).

Repetitive Responses

This test was used to assess activity phase-locked to a regularly repeated stimulus. It was sensitive to depth of modulation without regard to phase or waveform. The first step of analysis was to represent neuronal activity as a function of phase within the stimulus cycle. This was done by summing data from all presentations of the stimulus, both within and across trials, into a single 10-bin histogram representing activity during one stimulus cycle. Thus, in the case of a stimulus presented 10 times at 200 msec intervals on each of 15 trials, each bin of the composite histogram would contain the sum, over 150 presentations, of spikes fired during a particular 20 msec epoch following the stimulus. The null hypothesis (that the level of activity did not vary across bins) was tested by a χ^2 analysis with 9 degrees of freedom. A χ^2 greater than 16.92 indicated a significant level of modulation phase-locked to the stimulus ($p < 0.05$).

Measuring Response Latency and Strength

For quantitative characterization of phasic excitatory and inhibitory responses, we convolved the peristimulus histogram of neural activity with a biphasic square-wave kernel to yield a smoothed and differentiated function in which a local maximum (or minimum) marked any sudden increase (or decrease) in the rate of firing. We generally used a kernel with a full duration of 40 msec (20 msec per phase) because this gave results consistent with subjective estimates. In the case of responses with very slow rise times and poor definition, a kernel of greater duration (up to 120 msec) was used. Latency was taken as the delay between the event evoking the response and the maximum or minimum in the smoothed and differentiated function corresponding to onset of the response. Strength was taken as the height of the maximum or minimum in the smoothed and differentiated function that corresponded to the onset of the response. This yielded a value, in spikes/sec^2, given by the following formula: strength = Diff/(0.5 × Tm × Tr), where Diff = number of spikes in post-onset epoch minus number of spikes in pre-onset epoch, Tm = full duration of square-wave kernel, and Tr = number of trials summed to give histogram.

Measuring Sensitivity to Orbital Position

This analysis was carried out on data from each neuron studied with the standard saccade test. First, the mean rate of firing was computed for four trial epochs: before and after ipsiversive eye movements and before and after contraversive eye movements. Each presaccadic measurement was based on a period from 200 to 900 msec following the onset of the trial; each postsaccadic measurement was based on a period from 1400 to 2100 msec following the onset of the trial. Then a direction index was computed by use of a formula that should yield a value of +1 for a neuron firing only during contralateral fixation, −1 for a neuron firing only during ipsilateral fixation, and zero for a neuron firing at the same rate under both conditions:

$$\frac{\text{Contra}_{\text{Pre}} + \text{Contra}_{\text{Post}} - \text{Ipsi}_{\text{Pre}} - \text{Ipsi}_{\text{Post}}}{\text{Contra}_{\text{Pre}} + \text{Contra}_{\text{Post}} + \text{Ipsi}_{\text{Pre}} + \text{Ipsi}_{\text{Post}}}.$$

Histology

Tracer Injection

In the single case where recording sites were localized relative to neurons labeled by retrograde transport from area 7, the injection of tracers was carried out 48 hr before perfusion. Under surgical conditions as described above, the cortical area to be injected was exposed by means of a craniotomy and durectomy. Nuclear yellow (NY; Hoechst S 769121; Bentivoglio et al., 1980; 10% suspension) was pressure injected throughout the area of interest by use of a glass micropipette (tip diameter, 50 μm) lowered to a cortical depth of approximately 1 mm. The cortex was

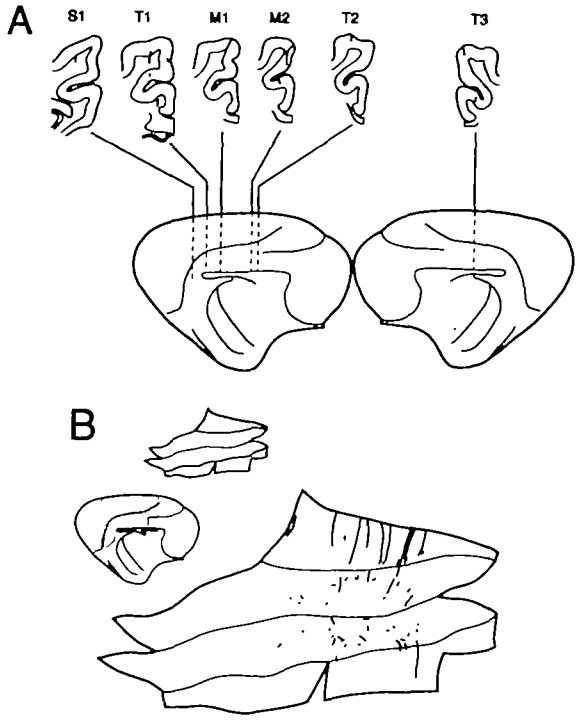


Figure 2. *A*, Each tracing represents a section through the center of one recording chamber. *B*, Reconstructed electrode tracks from all chambers projected onto a standard flattened map of the cingulate gyrus and splenial sulcus.

then thoroughly rinsed with sterile saline and the craniotomy was sealed.

Marking of Recording Sites

Immediately before perfusion, selected recording sites were marked by placing microlesions through recording microelectrodes (10 μA, 10 sec, tip negative) and by inserting through the microdrive microelectrodes that were left in place during perfusion. Reliance was also placed on the visible traces of earlier recording tracks.

Perfusion

Dissociative anesthesia was induced with Ketaset (ketamine hydrochloride, 30 mg/kg, i.m.) and a lethal dose of barbiturate was delivered (Brevital, methohexital sodium, 10 mg/ml, i.v.). The brain was fixed by transcardiac perfusion with 1 liter of normal saline (0.9% NaCl), followed by 1 liter of fixative (10% formalin in 0.1 M phosphate buffer) containing 3% sucrose, followed by 1 liter of fixative containing 10% sucrose. All solutions were administered at body temperature (approximately 38°C). After blocking and removal from the cranium, the brain was stored for approximately 12 hr in a solution consisting of 30% sucrose in 0.1 M phosphate buffer at 5°C.

Tissue Processing

The brain was sectioned in the transverse plane at 50 μm. In cases not involving tracers, all sections through the recording area were mounted on dry, gelatinized slides and dried on a slide warmer at 50°C; they were then stained with cresyl violet and coverslipped. In the case involving fluorescent tracer, all sections through the recording area were mounted on dry, gelatinized slides, and dried on a slide warmer at 50°C. They were then coverslipped, examined for fluorescent labeling, decoverslipped, stained with cresyl violet, recoverslipped, and examined again. In all steps, standard procedures were employed (Olson and Lawler, 1987; Bowman and Olson, 1988; Musil and Olson, 1988).

Microscopy

Tracks and microlesions were recorded by tracing cresyl-stained sections projected at 7× through a vertical projector. Tissue processed for the visualization of tracers was examined with a Zeiss Standard microscope (ultaviolet illumination at an incident wavelength of 360 nm) and labeled neurons were charted onto tracings of the same sections.

Results

Recording Sites

Quantitative analysis was carried out on 195 neurons from CGp in four hemispheres of three cats. Identification of CGp at the time of recording was accomplished by noting the depth at which neurons no longer gave the brisk visual responses characteristic of overlying area 17 and by noting the depth at which the electrode encountered electrical silence characteristic of the splenial sulcus. Tracks that left persistent traces were reconstructed histologically at the end of the experimental period. In Figure 2*A*, each tracing represents a section through the center of one recording chamber, with the A–P level indicated relative to a standard medial view of the hemisphere. Altogether, recording was carried out through five left-hemisphere chambers and one right-hemisphere chamber in three cats (S, T, and M). Reconstructed electrode tracks from all chambers are projected onto a standard flattened map of the cingulate gyrus and splenial sulcus in Figure 2*B*. The entirety of each reconstructed track is shown, including the portion traversing area 17. However, data presented in this article were collected only from portions of tracks confined to CGp (the zone depicted by shading in Fig. 1*C*). A few tracks from each chamber were readily visible on examination of stained sections. These tracks adequately demarcated the zone within which recording had been carried out because all tracks placed through a given chamber formed a narrow bundle a few millimeters in diameter.

Recording sites were concentrated at intermediate levels corresponding to the ocular division of CGp as defined by strong links to visual and oculomotor areas (Fig. 1*D*; Olson and Jeffers, 1987; Olson and Lawler, 1987; Olson and Musil, 1992). This was confirmed, in one case, by injecting a retrograde tracer (NY) into area 7p on the convexity of the right middle suprasylvian gyrus, at the termination of the period of single-neuron recording (Fig. 3*A*). Following a 2 d survival period, neurons labeled by retrograde transport

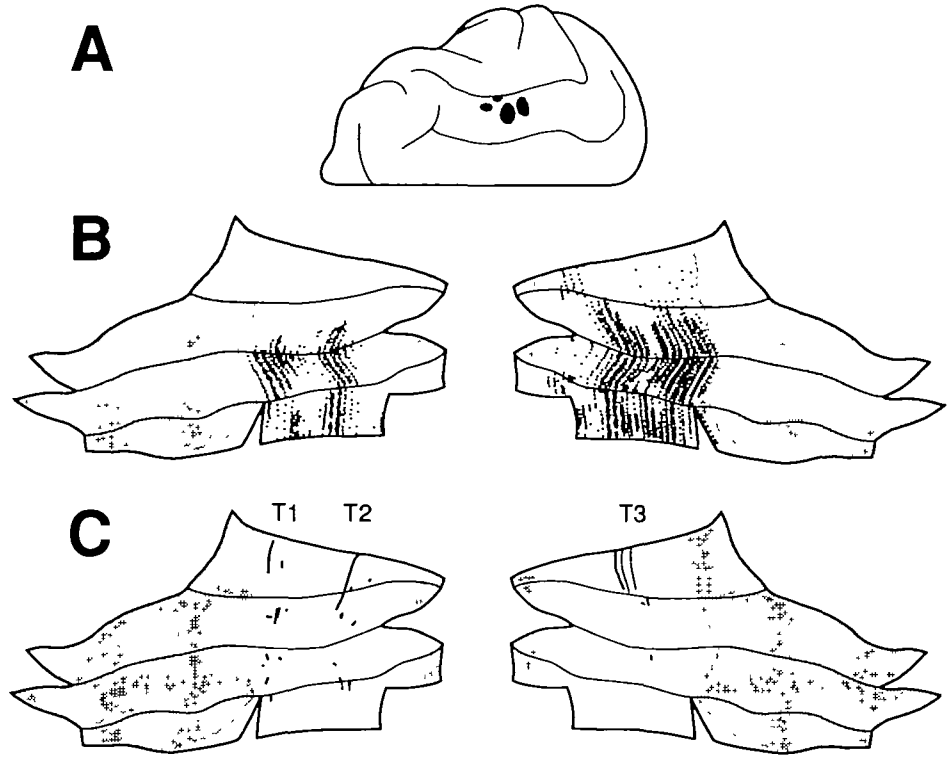


Figure 3. *A*, Deposit sites of NY in cat T. In rostrocaudal extent, these span the central third of area 7p and in mediolateral extent they span the medial half of area 7p (Olson and Lawler, 1987). *B*, Labeled neurons projected onto standard flattened maps of the left and right cingulate districts (map conventions are as in Fig. 1). *C*, Sites of electrode penetrations identifiable on microscopic examination of cresyl-stained sections. Tracks were placed through two chambers in the left hemisphere (*T1* and *T2*) and one chamber in the right hemisphere (*T3*). *Uniform shading* indicates levels at which cortical construction was not carried out because no recording tracks were present.

were charted (Fig. 3*B*) and electrode penetrations were reconstructed (Fig. 3*C*). A high degree of overlap was noted between recording sites and the "ocular" zone of CGp as identified by retrograde transport of tracer from area 7p.

Tonic Changes from Baseline during Periods of Fixation

Standard Saccade Condition

It was common for the rate of tonic firing to deviate from the intertrial baseline rate during periods of fixation preceding and following eye movements in the standard saccade task (Fig. 4). Two examples of fixation-related activity are shown in Figure 5. In each of the illustrated cases, there was a tendency for the rate of firing to rise above the baseline level during contralateral fixation and to fall below the baseline level during ipsilateral fixation. However, other patterns were also observed. To characterize tonic fixation-related firing across the entire population of 195 tested neurons, we asked whether the level of activity differed significantly from the baseline rate ($p < 0.05$, Z score test; for further details, see Materials and Methods) under each of four fixation conditions: contralateral fixation before an ipsiversive saccade, contralateral fixation after a contraversive saccade, ipsilateral fixation before a contraversive saccade, and ipsilateral fixation after an ipsiversive saccade (Fig. 6*A*). The firing rate sof 157 of 195 CGp neurons (81%)

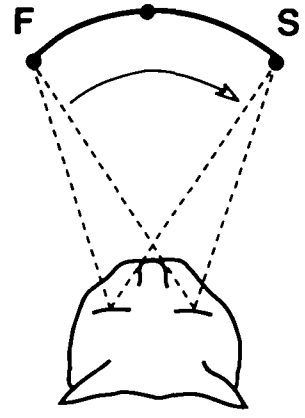


Figure 4. The standard task used for initial characterization of all neurons required the cat to fixate LED targets emitting 10 msec flashes at 10 Hz. Upon cessation of the fixation target (*F*) and onset of the saccade target (*S*), the cat was required to execute a rapid eye movement to S and to maintain fixation for 1.5 sec. Upon completion of the trial, food reward was delivered. The direction of the eye movement was leftward or rightward on pseudorandomly interleaved trials.

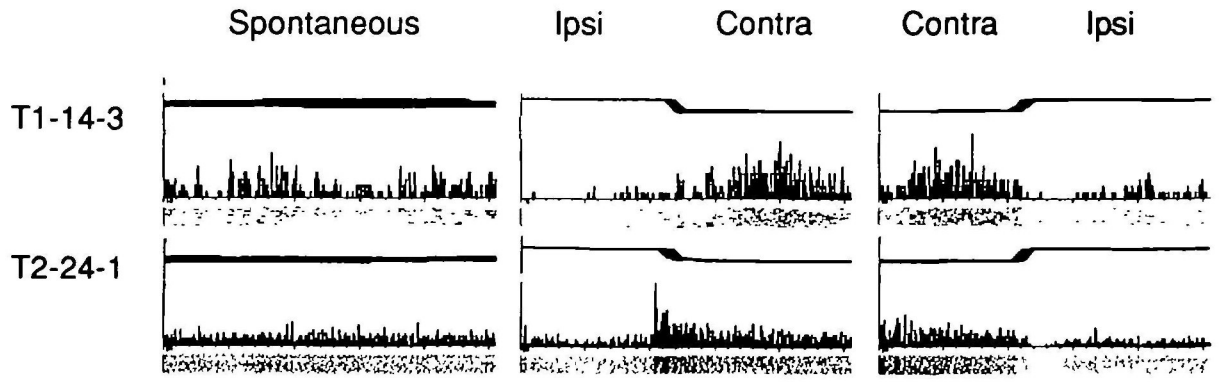


Figure 5. Data from two neurons exhibiting apparent sensitivity to orbital position. Data were collected during performance of the standard task as depicted in Figure 4. Each *histogram* represents mean rate of firing as a function of time (total duration, 2.5 sec) for one condition. In the *raster display* beneath each histogram, each *line* represents one trial and each *dot* represents one action potential. The superimposed traces above each histogram represent horizontal eye position as a function of time for all trials. Rasters and eye traces from successive trials are aligned with respect to the onset of the saccade target. The activity of each neuron was monitored under three conditions presented on pseudorandomly interleaved trials: intertrial periods when no stimulus was presented and the cat's ocular behavior was not under operant control (*left*); trials on which the cat executed contraversive visually guided saccades (*center*); and trials on which the cat executed ipsiversive visually guided saccades (*right*).

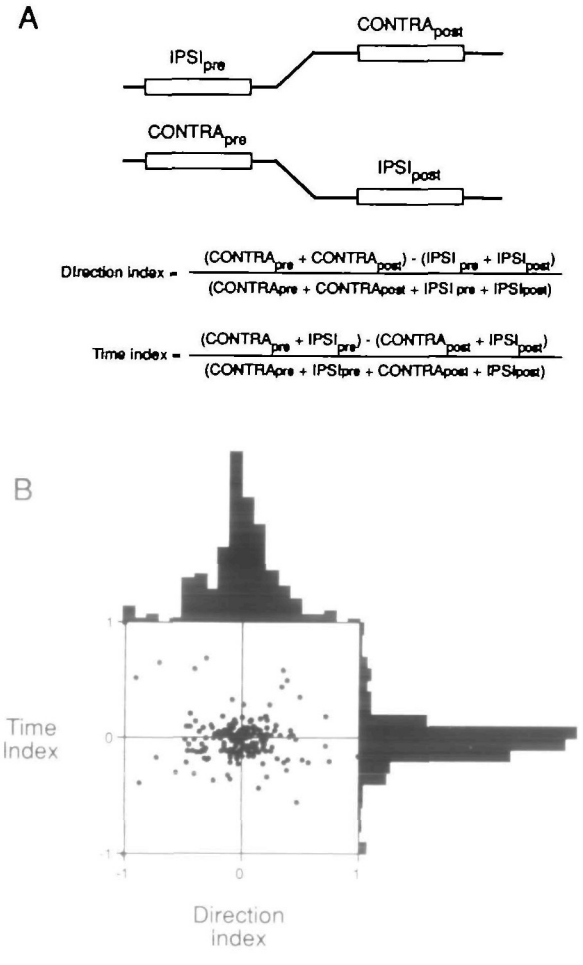


Figure 6. *A*, For all neurons studied while the cat performed the standard task, orbital position sensitivity was characterized by a *direction index* and a *time index*. *B*, The distribution of "direction index" values across the entire neuronal population is shown by the frequency histogram with its base on the *top of the square box*; the distribution of "time index" values is shown by the frequency histogram with its base on the *side of the square box*. In the scatter plot of "time index" versus "direction index" values, each data point represents one neuron.

deviated significantly from baseline in at least one fixation epoch, and significant deviations from baseline were observed altogether in 391 (51%) out of 780 (4 × 195) fixation epochs.

It was our clear impression that in some neurons, including the two on which Figure 5 is based, the rate of firing depended on the direction of gaze. To quantify this tendency, we devised a "direction index" (Fig. 6*A*). The direction index would be +1 for a neuron firing only during contralateral fixation, −1 for a neuron firing only during ipsilateral fixation, and zero for a neuron firing at the same level under both conditions. The mean value of the direction index was very close to zero (mean, − 0.04; SD, 0.315), from which we conclude that neurons in CGp, considered as a group, do not favor either ipsilateral or contralateral fixation. Values of the direction index ranged from nearly −1 to nearly +1. The scatter of values might well reflect neuron-to-neuron variation in the sign and magnitude of the dependence of firing rate on gaze direction, but might equally well reflect stochastic variations in firing rate that, by producing variations in spike counts during the four measured epochs, gave rise to noise-based deviations from the mean. To distinguish between these possibilities, we computed a second index, unrelated to direction of gaze, in which any contribution from stochastic processes should be identical. This "time index" measures the tendency for a neuron to fire during the fixation period preceding the operant saccade as opposed to the fixation period following it (Fig. 6*A*). The time index would be +1 for a neuron firing only during presaccadic fixation, −1 for a neuron firing only during postsaccadic fixation, and zero for a neuron firing equally under both conditions. The mean value of this index was very close to zero (mean, −0.016; SD, 0.217). The values of the time index were not as widely scattered as the values of the direction index, as confirmed both by visual inspection of frequency histograms (Fig. 6*B*) and by the numeric difference between the SDs. The tendency for values of the direction index to be more widely scattered than

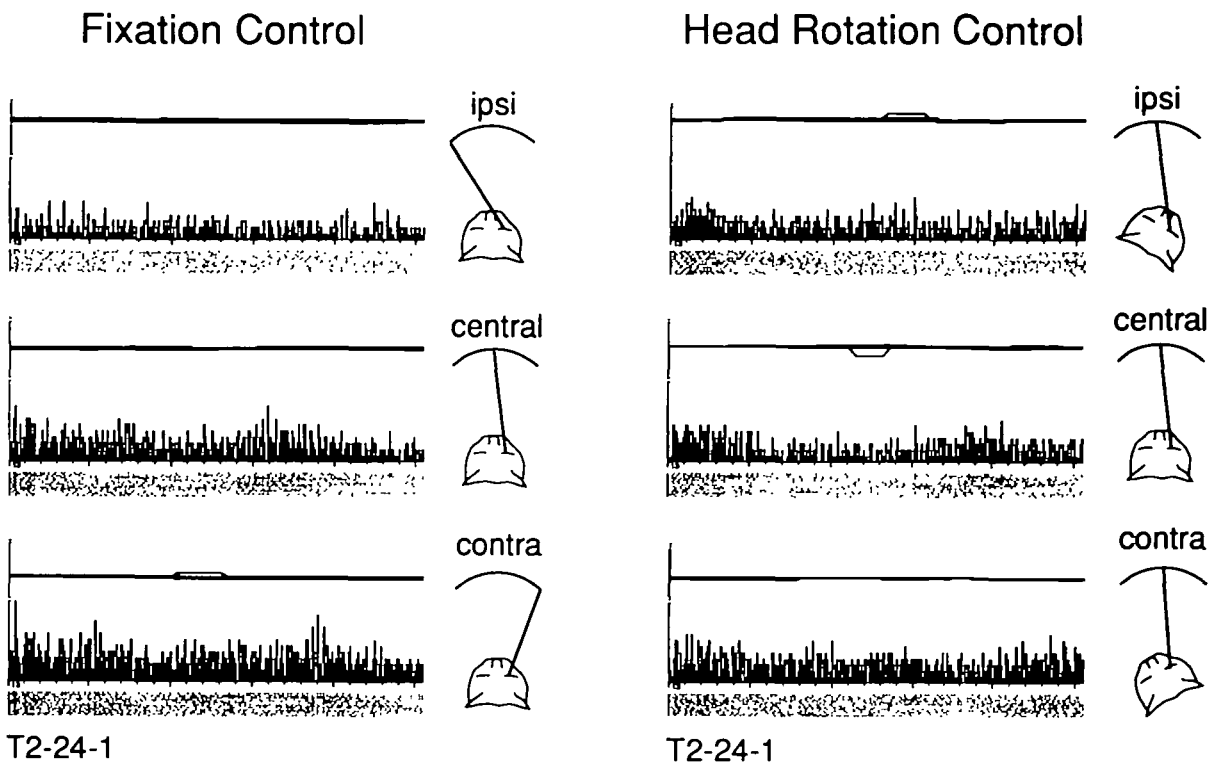


Figure 7. *Data collected from one neuron during periods of steady ipsilateral, central, and contralateral orbital position produced in two ways. Left column,* With the cat's head at constant orientation, target lights were flashed at different locations (10° left, central, and 10° right) *Right column,* With the central target illuminated, the cat was rotated to different orientations (10° right, central, and 10° left). The rotations depicted in the *drawings* are greater than the 10° rotations actually employed.

values of the time index was highly significant ($p < 0.01$, F test for equality of variances). We conclude that neuron-to-neuron variations in the direction index could not be accounted for as noise and instead reflected a genuine dependence of firing on the angle of gaze.

Visual Fixation Condition

In the standard saccade task, relatively brief periods of fixation preceded and followed execution of an operant saccade. To assess fixation-related activity during longer periods of fixation unbroken by operant saccades, we monitored the activity of 20 neurons during performance of a second task in which the cat maintained fixation for 2.5 sec on a single target placed at the midline or 10° to its right or 10° to its left on interleaved trials. Data are presented from a neuron that exhibited a clear contralateral preference in the visual fixation task (Fig. 7, left column) just as it had in the standard saccade task (Fig. 5, bottom row). For all neurons tested by this procedure, a direction index was computed by a formula directly analogous to the one presented above. In Figure 8*A*, direction indices based on data from the visual fixation task are plotted against direction indices based on data from the standard saccade task. Across the population of tested neurons, there was a highly significant ($p < 0.01$) positive ($r = 0.695$) correlation between direction indices obtained under the two conditions although indices based on the visual fixation condition generally were lower (slope of the best-fit line = 0.264). We conclude that the dependence of neuronal activity on the angle of the eye in the orbit persists during prolonged periods of fixation.

Orbital Position Condition

In both the standard saccade task and visual fixation task, the absolute location of the fixation target covaried with the angle of the cat's eye in the orbit. Thus, when a neuron fired at a higher rate during fixation in one direction, it was unclear to what degree the enhancement of firing reflected the angle of the eye in the orbit and to what degree it reflected the angle of the eye relative to the room. To distinguish the influences of these factors, the activity of 18 neurons was monitored during performance of a task in which the orbital angle of the eye was varied while the angle of the eye relative to the room was held constant. On all trials, the cat fixated, for 2.5 sec, a target placed at the same central location on the perimeter. Between trials, the entire restraint frame was rotated about a vertical axis running through the midpoint of the line connecting the nodal points of the eyes; on interleaved trials, the head was oriented 10° to the left, straight ahead, and 10° to the right, relative to a line directed from interocular midpoint to the center of the perimeter (Fig. 7*B*, drawings). Results from a single neuron are depicted in Figure 7*B*. The firing of this neuron was largely unaffected by the angle of the eye in the orbit when angle relative to the room was held constant. For all neurons tested under this condition, direction indices reflecting the dependence

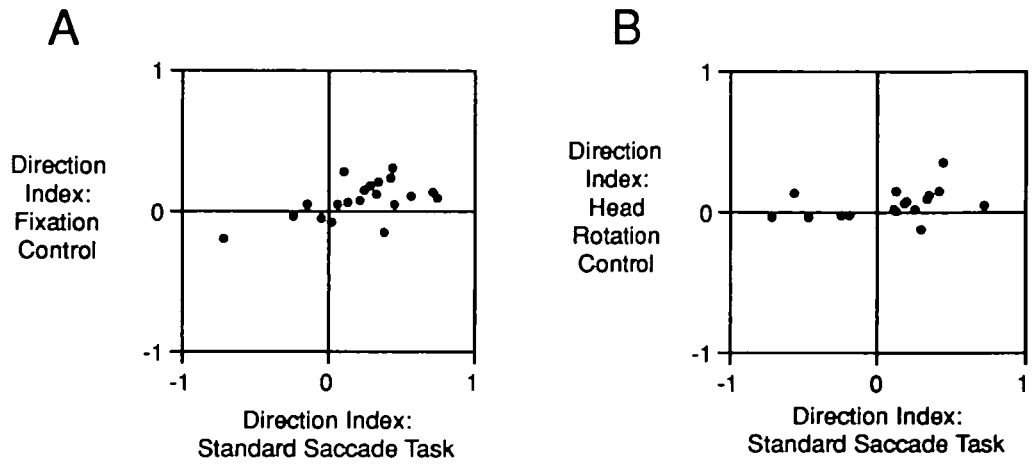


Figure 8. *A*, Direction indices based on the standard saccade task (Fig. 7, left column) are plotted against direction indices based on the standard saccade task (Fig. 4) for all neurons studied under both conditions. *B*, Direction indices based on the head-rotation control task (Fig. 7, right column) are plotted against direction indices based on the standard saccade task (Fig. 4) for all neurons studied under both conditions.

of neuronal firing on the orbital angle of the eye were computed and compared to the analogous indices obtained in the standard saccade task (Fig. 8*B*). Indices derived in the orbital control task are plotted against those obtained in the standard saccade task in Figure 8*B*. The two sets of indices were positively correlated ($r = 0.51$) and the correlation was significant ($p < 0.05$), although indices computed from orbital control data were lower than those computed from standard saccade data (slope of best-fit line =0.139). The findings indicate that neuronal activity is influenced by the angle of the eye in the orbit even under conditions such that visual feedback is held constant. However, the modulation of neuronal activity is not as deep as when shifts in orbital angle are accompanied by shifts of the angle of gaze relative to the room with consequent changes in visual feedback.

Perisaccadic Modulation of Neuronal Responses

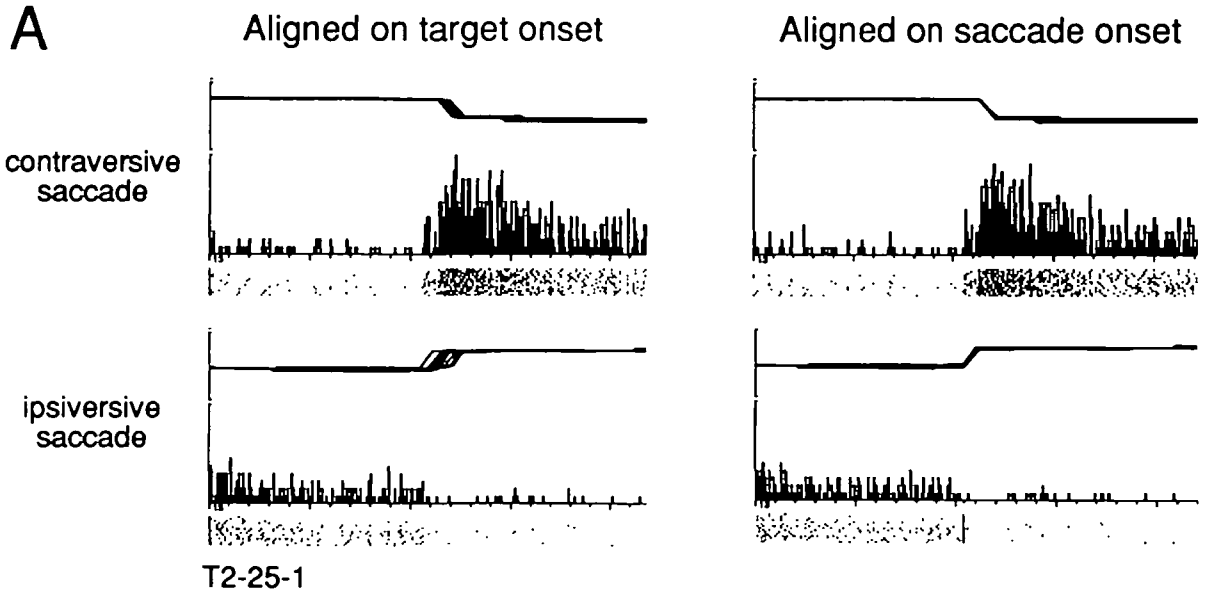
Standard Saccade Condition

Of the 195 CGp neurons studied in the standard saccade task, 97 underwent a phasic increase (98%) or decrease (2%) of activity beginning around the time of initiation of the saccade and persisting for up to several hundred msec (Fig. 9*A*). To characterize the timing of this event relative to the saccade, we analyzed histograms formed by aligning rasters from successive trials on the time of occurrence of the saccade. The time of onset of the response was defined as the point of steepest rise (of an excitatory response) or fall (of an inhibitory response). This was determined automatically by sliding a 40 msec window along the time axis until it was centered on a point at which the difference between mean firing rate during the first 20 msec and the mean firing rate during the second 20 msec was maximal (see Materials and Methods, Measuring Response Latency and Strength). Times of onset ranged from 15 msec before to 70 msec after the initiation of the saccade (Fig. 10).

In an attempt to verify that the time of occurrence of the shift in firing level was correlated with the time of occurrence of the saccade, we compared action-potential histograms obtained by aligning rasters on the onset of the visual target and on the onset of the saccade. Because the cat's behavioral reaction time was variable, a response time-locked to the saccade should appear sharper in the histogram obtained by aligning rasters on the onset of the saccade. Sharpness was defined as the absolute value of the rate of change of firing frequency (spikes/sec^2) over a period of 40 msec centered on the onset of the burst. This corresponds to the absolute value of response strength as described under Materials and Methods. The sharpness of the bursts was not significantly greater when successive trials were aligned on initiation of the saccade than when they were aligned on onset of the visual stimulus. Eye traces and spike histograms obtained by aligning events on target-onset (left) and saccade-onset (right) are shown for a representative neuron (Fig. 9*A*) and for all neurons that were judged by examination of peristimulus time histograms to fire robust excitatory perisaccadic bursts in conjunction with contraversive saccades ($n = 64$) (Fig. 9*B*). It is not clear to what degree this negative result reflects the actual timing of perisaccadic activity as opposed to noise arising from the narrow scatter of behavioral reaction times and the comparatively ragged onset of perisaccadic bursts.

Darkness Condition

Neuronal firing correlated with saccadic eye movements might depend in part or in whole on reafferent visual stimulation that occurs when images of the environment are swept across the moving retina. We assessed the influence of visual feedback by monitoring the activity of 20 neurons, which had evinced perisaccadic firing in the standard saccade task, while the cat made a saccadic eye movement of fixed amplitude and direction under two interleaved conditions: (1) continuous ambient illumination, and (2) ambient illumination extinguished for a period of 1 sec beginning 200 msec before the presentation of



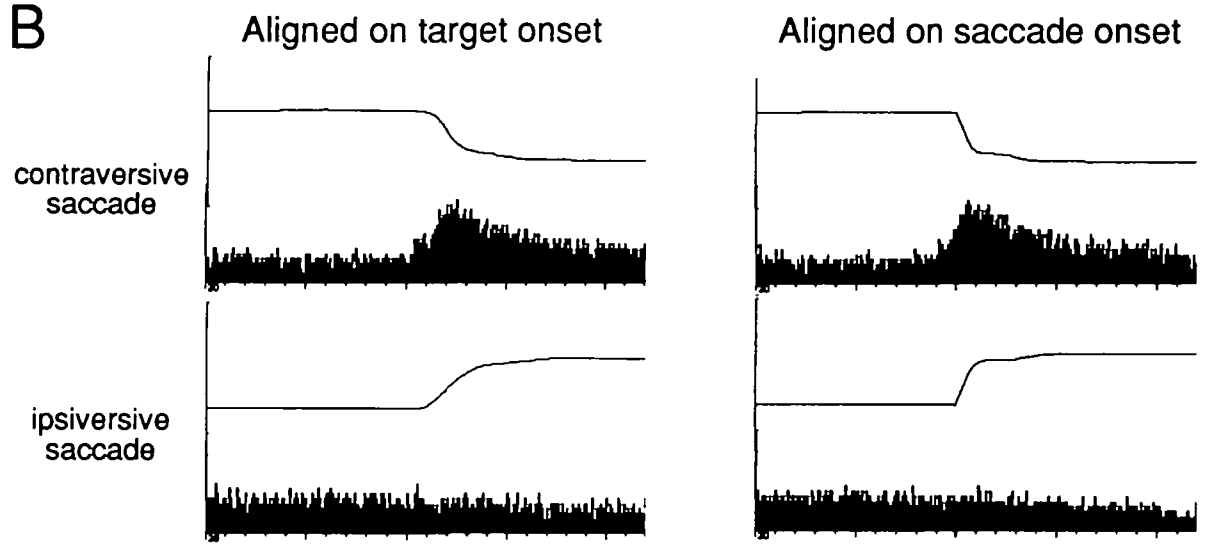


Figure 9. *A*, Example of phasic perisaccadic activation in a neuron studied during performance of the standard task. *B*, Mean firing level and mean eye position for all neurons that exhibited robust perisaccadic excitation at the onset of contraversive eye movements ($n = 64$)

the visual target. The target LED was presented in 10 msec flashes at 200 msec intervals to ensure that in the majority of trials not even the target light would be on at the time of execution of the saccade. All 20 neurons evinced perisaccadic firing under the room-illumination condition. The effect of darkness on perisaccadic firing varied markedly among neurons, ranging, without any obvious clustering, from total attenuation (Fig. 11, neuron T1-5-3) to virtually no effect (Fig. 11, neuron T2-24-1). On average, over all 20 neurons, the strength of the perisaccadic burst (see Materials and Methods, Measuring Response Strength and Latency) was reduced in darkness by a factor of precisely 0.50. A reduction of approximately the same magnitude is seen in a composite histogram based on the firing of the eight most robustly active neurons (Fig. 11, bottom). We conclude from the fact that

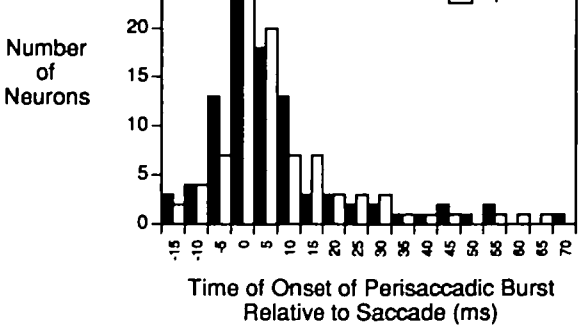


Figure 10. Frequency distribution of the latencies of ipsiversive and contraversive perisaccadic responses with respect to onset of the eye movement. Most perisaccadic responses began after the onset of the eye movement (*positive values*).

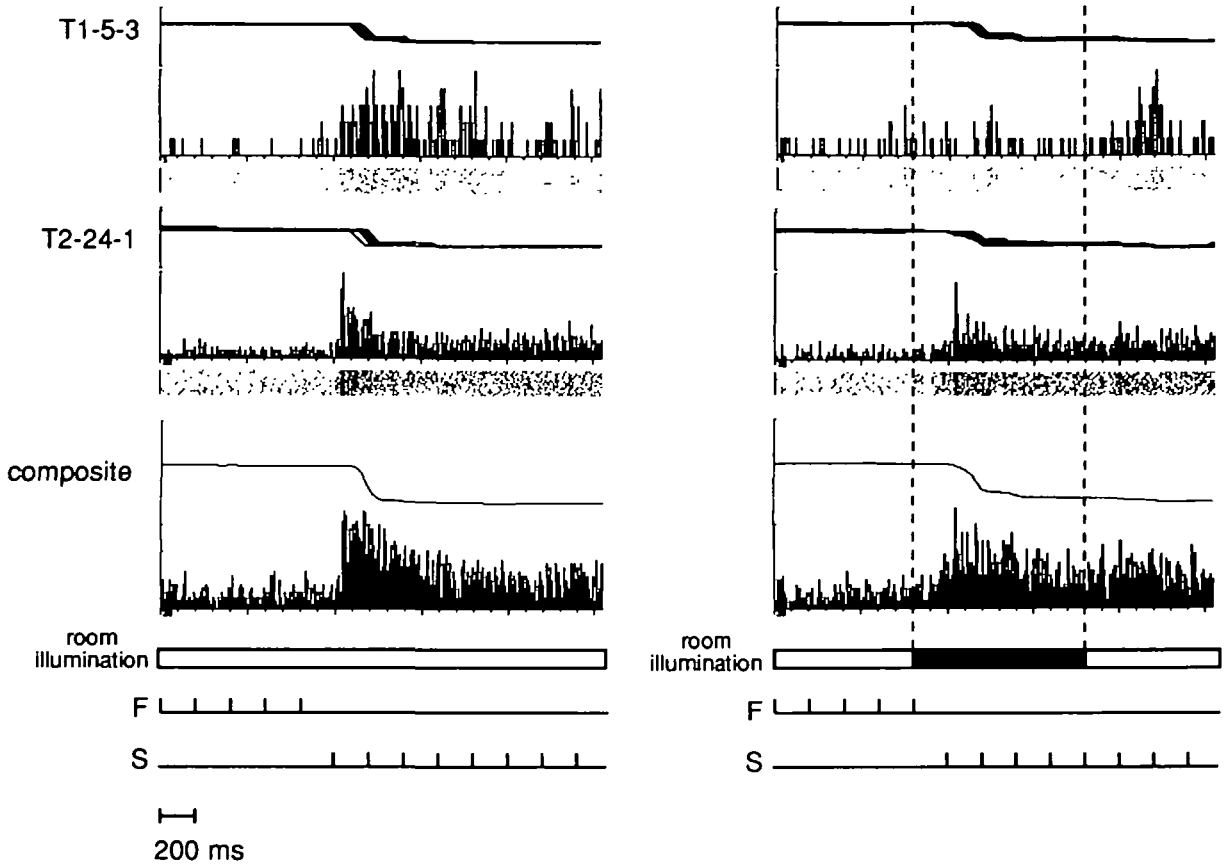


Figure 11. Data from a control task, in which, on randomly interleaved trials, the cat made saccades between identical targets in ambient illumination (*left column*) or in darkness (*right column*). Results are shown for two representative neurons (*top rows*) and for all neurons exhibiting robust perisaccadic activation under at least one of the conditions (n = 8) (*bottom row*)

perisaccadic activity survives in darkness that it does not depend solely on reafferent visual stimulation. However, reafferent visual stimulation, when it occurs, does enhance the strength of perisaccadic bursts.

Phasic Responses to Fixation Targets

Standard Saccade Task

The form of visual responsiveness observed most commonly in this task was a phasic excitatory response to the first flash of the saccade target. An especially strong phasic excitatory response is represented by the tall peak in the middle histogram of the bottom row of Figure 5; time-locking of this neuron's action potentials to the visual stimulus was confirmed by demonstrating that the peak in the histogram was taller and narrower when rasters were aligned on the occurrence of the visual stimulus than when they were aligned on the occurrence of the saccadic eye movement. In the composite activity of all neurons exhibiting excitation during contraversive saccades (Fig. 9*B*, top row, left histogram) a visual response to the onset of the contralateral stimulus takes the form of a small peak preceding the larger and more prolonged burst of perisaccadic activity. This result, rather than the preceding one, is accurately indicative of the properties of cingulate neurons in general. Responses to the onset of the saccade target were neither common nor strong in the population as a whole. Even by an extremely sensitive statistical test for phasic responsiveness (see Materials and Methods) only 14 of 195 (7%) and 8 of 195 (4%) neurons were found to give significant responses to the contralateral and ipsilateral stimuli respectively. Among these neurons, the mean latency of the response was 50 msec.

Responses to stimulation of the area centralis might have been observed in the standard saccade task because both the initial fixation target and the second target on which postsaccadic fixation was maintained were presented in 10 msec flashes at an interflash interval of 100 msec (Fig. 4). However, neurons never exhibited firing obviously phase-locked to the flashes of the fixated target. The absence of responsiveness to stimuli presented on the area centralis during fixation might reflect either absolute insensitivity to central stimulation or adaptation to a stimulus presented repeatedly at the same location. It was not possible to choose between these interpretations on the basis of data from the standard saccade task, because in this task, the period of data collection began after the first target had already begun flashing and the cat had attained fixation (see Materials and Methods), with the result that central adaptation might have occurred before the onset of data collection.

Variable Frequency Condition

To determine whether the absence of firing phase-locked to flashes of the fixated target in the standard saccade task was due to adaptation produced by the rapid repetition of the stimulus, we carried out an additional test in which we varied the frequency at which the fixation target was presented. On interleaved trials, the stimulus was presented at the standard rate (10 Hz) and at lower rates (5 Hz and 2 Hz). Even at the lowest rate, which involved 0.5 sec intervals between flashes of the target, cats exhibited no difficulty in maintaining fixation on the location of the target. The activity of 49 neurons was monitored under these conditions and a statistical test was then applied to determine whether the activity of each neuron exhibited cyclic modulation locked to repeated presentations of the stimulus (see Materials and Methods). The fraction of neurons with activity phase-locked to the stimulus shot up dramatically from 2 of 49 at 10 Hz and 4 of 49 at 5 Hz to 24 of 49 at 2 Hz (Fig. 12*C*). In the low-frequency condition, individual flashes of the target tended to elicit a complicated and prolonged response in which early brief phasic excitation gave way to late prolonged inhibition. This was apparent in data from some individual neurons (Fig. 12*A*) and in the massed activity of all neurons exhibiting statistically significant phase-locking for at least one of the test frequencies ($n = 23$) (Fig. 12*B*). These results support the central adaptation hypothesis and indicate that the process of adaptation initiated by a single flash has a duration of several hundred msec.

Multimodal Sensory Responses

We noted in early recording sessions that some neurons responded to visual, auditory, and somatosensory stimulation outside the context of task performance. To gain an idea of the frequency of responsiveness in different modalities, we subsequently carried out systematic testing in 51 neurons. The activity of each neuron was monitored during repeated manual delivery of the following stimuli: somatosensory (lightly tapping the cat's back), auditory (rapping a stick against a wood block), and visual (onset of room lights) (Fig. 13*A*). To record the time of occurrence of each stimulus, the experimenter closed a switch simultaneously with delivery of the stimulus. Among neurons tested by this procedure, 20 of 51 (39%) responded to stimulation in at least one modality (Fig. 13*C*). The three modalities were approximately equal with respect to their effectiveness at driving cingulate neurons (Fig. 13*B*). Among the responsive neurons, approximately a third (7 of 20) could be driven with stimulation in more than one modality. Data from a neuron responsive to stimulation in multiple modalities are shown in Figure 13*A*.

Discussion

Orbital-Position and Perisaccadic Signals

We have found that neurons in the posterior cingulate cortex of the cat fire bursts of action potentials in conjunction with saccadic eye movements and fire tonically during periods of fixation at a level that is determined in part by the angle of the eye in the orbit. Eye-movement-related activity has also recently been noted in the CGp of the rabbit (Sikes et al., 1988) and of the monkey (Olson et al., 1993). It is worthwhile to consider similarities and differences across species as revealed by these studies.

In rabbit, around 14% of CGp neurons fire bursts of action potentials in conjunction with the quick phases of vestibuloocular nystagmus (Sikes et al., 1988). This pattern of activity is comparable to the perisaccadic excitation observed in our experiments in that comparatively brief bursts of activity accompany each rapid eye movement. Eye-movement-related bursts in the rabbit, as in the cat, are not totally dependent on visual feedback, as indicated by their occurrence even in darkness. As in cat, most bursts begin after the onset of the corresponding eye movement. The most salient difference between results obtained in the two studies arises from the failure to observe in rabbit any tonic firing related to the angle of the eye in the orbit. This discrepancy might reflect a species difference or the use of different testing procedures. The rabbits were not trained to maintain active fixation on visual targets.

The study of rhesus monkeys (Olson et al., 1993) was undertaken following the experiments described here, in order to carry out tests for which monkeys, with their greater oculomotor facility, are better suited than cats. We found that neurons in CGp of the monkey undergo modulation during performance of oculomotor tasks. The patterns are directly comparable to those observed in cat and rabbit in the following particulars: neurons fire bursts of action potentials during saccades, the bursts tend to begin at or after the time of onset of the corresponding eye movements, and imposition of darkness has a variable impact ranging from no appreciable effect to total abolition of eye-movement-related firing. In the monkey, as in the cat, CGp neurons fire tonically during periods of fixation. In monkey, the level of tonic firing reflects not only the angle of the eye in the orbit, but also, surprisingly, the amplitude and direction of the saccade by which the current epoch of fixation was initiated. The relative degree to which the parameters of the saccade, as opposed to orbital position, determine the level of firing varies across neurons. Tonic firing related to the parameters of the saccade is, in effect, a memory trace for the movement by which fixation was initiated rather than a signal encoding the current state of the eye. These two potential interpretations of fixation-period firing could not be dissociated in the study of cats because the direction of the eye movement and the orbital angle of the eye during the subsequent period of fixation covaried in our standard saccade paradigm.

We conclude that eye-movement-related activity is present in the CGp of a variety of species and therefore is probably essential to functions dependent on this cortical area. A significant clue to the nature of these functions arises from consideration of the tem-

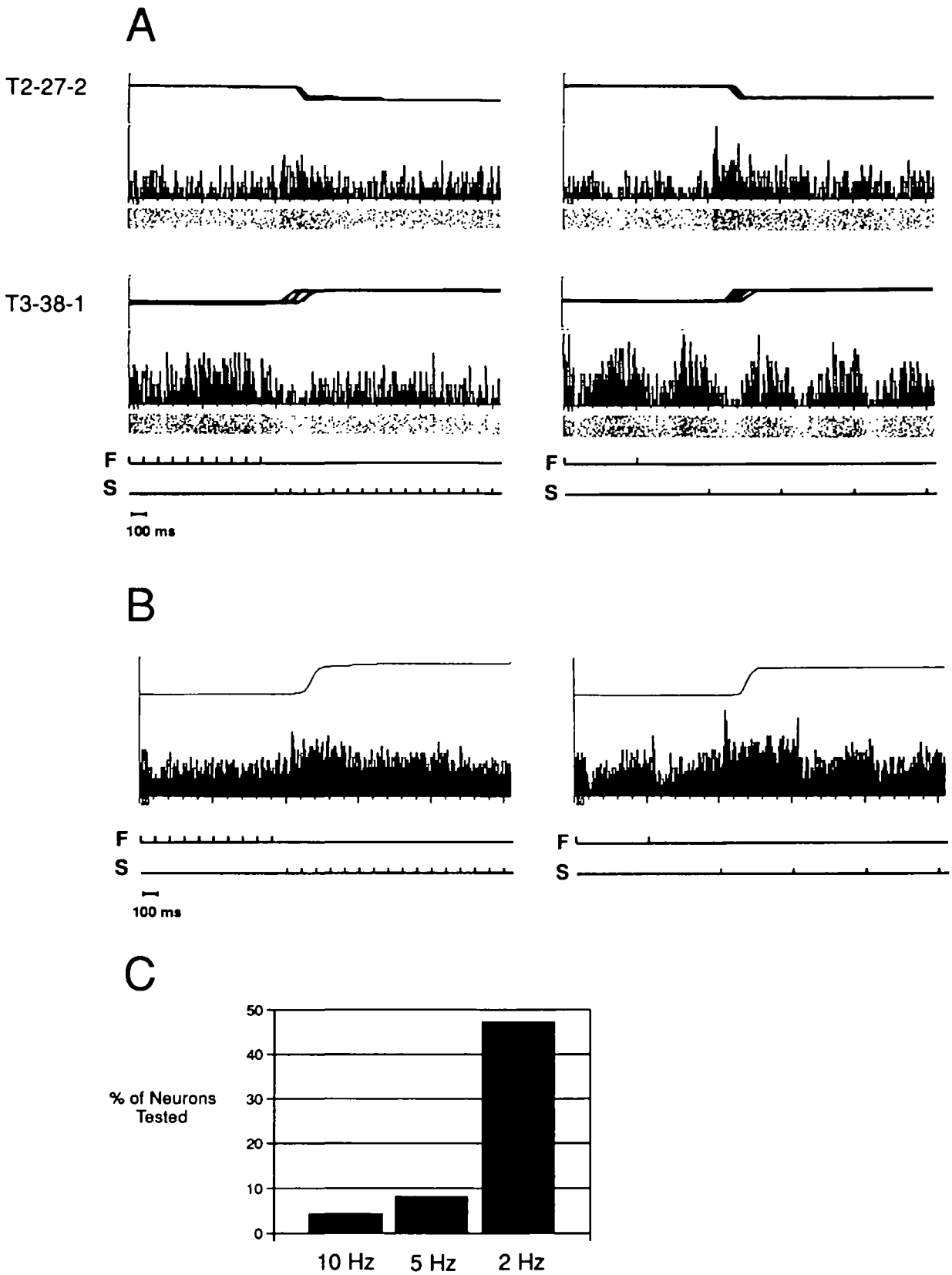


Figure 12. *A*, Data from two neurons phasically responsive to low-frequency flashes of the fixated target (2 Hz; *right column*) but not to high-frequency flashes of the same target (10 Hz; *left column*). *B*, Composite histogram representing the mean rate of firing of all neurons that showed significant phase-locking for at least one of the frequencies tested ($n = 23$). *C*, Percentage of 49 tested neurons exhibiting significant phase-locked firing at 10 Hz, 5 Hz, and 2 Hz.

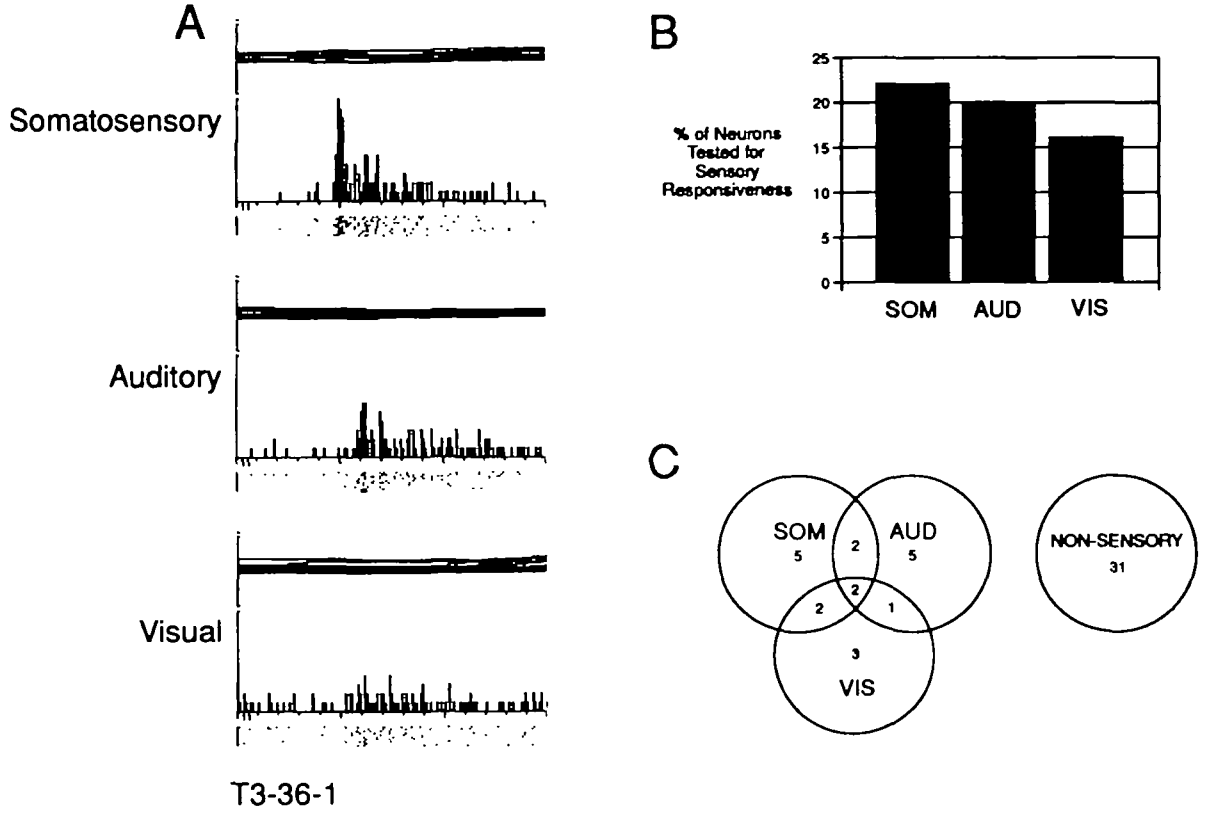


Figure 13. *A*, Histograms representing activity of a neuron responsive to natural stimulation in all three tested sensory modalities. Rasters are aligned on the time of closure of a switch that the experimenter depressed on each delivery of a stimulus. *B*, Percentages of neurons giving statistically significant responses to natural somatosensory, auditory, and visual stimulation ($n = 51$). *C*, Number of neurons exhibiting each pattern of multimodal convergence.

poral relation between eye movements and neuronal activity. In all three species, a majority of CGp neurons begins firing at or after the time of onset of each eye movement. It is reasonable to infer that these neurons are monitoring rather than controlling oculomotor activity.

Sensory Responses

On systematically presenting stimuli in three modalities, we found that approximately 40% of feline CGp neurons emitted visual, auditory, or somesthetic responses, and that a significant subset of neurons was multimodal. It was our impression, although we did not pursue the issue systematically, that neurons responsive to stimulation in a given modality were not particularly selective either for the spatial location or for the pattern of the stimulus.

The only prior indication of sensory responsiveness in CGp of the cat was obtained by Kalia and Whitteridge (1973). Recording from single neurons in the fundus of the splenial sulcus immediately adjacent to primary visual cortex, these authors noted, in anesthetized cats, the existence of a narrow strip of cortex containing neurons with large visual receptive fields and crude orientation tuning. This cortical strip, termed the SVA (splenial visual area), is projected onto a flattened map of splenial cortex in Figure 1*C*. We believe that the SVA as defined by Kalia and Whitteridge is a part of the much larger "ocular" subregion of CGp explored in the present study. We cannot be certain which of our recording sites, if any, was actually located in the very narrow SVA sector of CGp. However, on connectional grounds, we consider it to be improbable that this strip is different in any fundamental functional sense from the remainder of the ocular subregion. If SVA and the remainder of the ocular subregion are distinct areas, then differential labeling of the two sectors should have been observed following the deposit of tracers in at least a few distant cortical areas, but this has never been reported. On the contrary, uniform labeling of SVA and adjacent cortex is observed in such cases. For example, neurons labeled by transport from area 7 of parietal cortex are distributed throughout the ocular subregion without regard to the boundary between SVA and adjacent parts of CGp (Olson and Lawler, 1987; Musil and Olson, 1993).

Although Cuenod et al. (1965), discovered few signs of sensory responsiveness in the CGp of anesthetized squirrel monkeys, a recent study of alert rhesus monkeys has revealed that CGp neurons respond vigorously to large bright stimuli presented virtually anywhere in the visual field (Olson et al., 1993). It is noteworthy that visual stimuli need not carry behavioral relevance of any kind in order to elicit responses from posterior cingulate neurons in the monkey. Small dim spots elicit no response even when the monkey is actively attending to them and making motor responses toward them, and large bright patterns elicit

a strong response even when the monkey is not required to attend or respond to them.

In rabbit, according to Sikes et al. (1988), around 10% of CGp neurons exhibit clear sensory responsiveness to visual, auditory, or somatosensory stimulation. Gabriel and colleagues, in an extensive series of studies based on multiunit recording (Gabriel et al., 1980, 1988), have documented robust responsiveness to pure-tone auditory stimuli in rabbit CGp. They have also demonstrated that the behavioral relevance of the stimuli influences response strength. When pure tones of different frequencies are employed as the positive conditional stimulus (associated with aversive shock) and the negative conditional stimulus (not associated with shock) in a discriminative avoidance paradigm, there is a progressive diminution during learning of the neuronal response elicited by the negative conditional stimulus. In this paradigm, the positive conditional stimulus comes to differ from the negative conditional stimulus along several dimensions, including ability to capture attention, ability to elicit a motor response, and associative emotional significance, so that the result is open to several interpretations, but, regardless of interpretation, the fundamental conclusion is that the strength of the response is determined by more than the physical properties of the stimulus.

We conclude that sensory responsiveness (including responsiveness to visual, auditory, and somesthetic stimulation) is present in the CGp of a variety of species. CGp neurons either participate in processes underlying the discrimination of sensory stimuli, or form the substrate for some nonperceptual process set in motion by sensory inputs. We favor the latter view on the basis that neurons exhibit little selectivity for specific visual stimuli. It is worth noting, however, that other attributes of CGp neurons, notably their extremely large receptive fields and attenuation of their responses at rates of repetition well below the perceptual fusior threshold, are present also in inferotemporal cortex, which clearly does participate in visual pattern recognition (Miller et al., 1991).

Heterogeneity of Posterior Cingulate Cortex

Nearly all neurons characterized in the present study were at sites demonstrated by direct or indirect analysis to be within the "ocular" subdivision of CGp (Figs. 3, 4). It is characteristic of this zone that it is strongly linked to cortical areas with oculomotor and visual functions (Olson and Musil, 1992), a pattern of connectivity compatible with the finding that neurons here are active in conjunction with eye movements and in response to visual stimulation. It is important to observe that there are other subdivisions of CGp, notably an anterior zone in which connections to somesthetic and somatomotor areas are predominant, and a posterior zone linked primarily to prefrontal cortex and other areas lacking obvious sensory and motor functions. The functional properties of neurons in these divisions remain to be ascertained but would be expected to differ from the properties of neurons in the ocular zone. It is worth noting that, across the six A-P levels at which neurons were recorded in the present study (Fig. 2*A*), the lowest percentage of neurons with task-related activity (20%) was observed at the most posterior location, in a zone of transition between the ocular and complex territories.

Reassessment of Role in Emotion

We had the opportunity to monitor neuronal activity casually under circumstances associated with changes in the cat's emotional state, including delivery of food reward on successful trials, witholding of food reward on error trials, and variations of motivational level associated with the cat's degree of satiation. We did not observe neuronal activity strongly dependent on these circumstances. This negative result, while not conclusive in itself, is in harmony with other available information suggesting that the CGp plays little or no direct role in the regulation or expression of emotional states.

Functional evidence seeming to implicate cingulate cortex in emotional, motivational, attentional, and autonomic functions has arisen from both animal and human studies. Numerous impairments have been reported to arise from cingulate damage in humans, including apathy (Barris and Schuman, 1953; Laplane et al., 1981; Damasio and Van Hoesen, 1983), indifference to pain (Barris and Schuman, 1953), incontinence (Barris and Schuman, 1953; Laplane et al., 1981), distractability (Laplane et al., 1981; Paus et al., 1991), akinetic mutism (Barris and Schuman, 1953; Damasio and Van Hoesen, 1983; Mochizuki and Saito, 1990), and a complex confusional state involving disorientation and vivid daydreams (Whitty and Levin, 1960). Evidence for involvement in complex, if not strictly speaking emotional, processes has also accrued from position emission tomographic studies. Metabolic activation has been reported in the cingulate cortex of normal subjects subjected to thermal pain (Jones et al., 1991; Talbot et al., 1991) or required to carry out demanding stimulus–response tasks involving divided attention (Corbetta et al., 1991), deep semantic processing of the stimulus (Petersen et al., 1988), suppression of an automatic response (Pardo et al., 1990), and deliberate as opposed to automatic execution of a response (Raichle et al., 1991). A major qualification must be attached to all of these results, however, namely, that they concern anterior and not posterior cingulate cortex. The same qualification applies to animal studies, which have implicated the anterior cingulate cortex or adjacent prefrontal cortex in emotion and related processes but have provided little or no support for involvement of CGp (Buchanan and Powell, 1993; Neafsey et al., 1993).

Possible Role in Visuospatial Cognition

The finding that CGp neurons carry eye-movement-related signals and respond to sensory stimuli is compatible with several other lines of evidence pointing toward a role for this area in awareness of the environment and in spatial awareness in particular. The

notion that CGp contributes to spatial awareness was suggested initially by the presence of strong connections to area 7 and the parahippocampal gyrus (Pandya and Yeterian, 1984; McNaughton et al., 1991). Each of these areas has been implicated in a particular form of spatial awareness.

Area 7 is involved in spatial awareness of the immediate extrapersonal environment as evidenced by studies demonstrating that lesions encompassing it compromise the appreciation of object–object spatial relations (Mishkin et al., 1982) and disrupt the ability to reach accurately for visible objects (Perenin and Vighetto, 1988). Area 7 neurons carrying signals related to the parameters of saccadic eye movements (Barash et al., 1991) and the angle of the eye in the orbit (Andersen et al., 1987) may contribute to the analysis of immediate extrapersonal space. Information about the parameters of saccadic eye movements might aid in judging object–object relations because the size and direction of a saccade directed from one object to another are directly proportional to the distance and location of the second object with respect to the first. Information about the orbital angle of the eye could be useful in judging object–body relations because the angle of the eye in the orbit is linearly related to cephalocentric azimuth and elevation of the fixated object.

The hippocampus is involved in spatial memory as indicated by the fact that hippocampal lesions disrupt the animal's ability to remember where it has been recently (Olton et al., 1978) and at what locations particular objects have recently been seen (Parkinson et al., 1988). Hippocampal and postsubicular neurons sensitive to the location and orientation of the freely moving animal (McNaughton et al., 1983; Taube et al., 1990) and to the allocentric direction of gaze of the head-fixed animal (Rolls et al., 1989; Rolls, 1990) may contribute to spatial memory functions by supporting the animal's awareness of its own location and orientation relative to the environment as well as the location and orientation of objects in its field of regard.

The CGp is connectionally intermediate between area 7 and the parahippocampal gyrus in that pathways linking it to each domain are stronger than pathways linking the two domains to each other (Olson and Lawler, 1987; Olson and Musil, 1992). It is of interest, therefore, to ask whether its functions are in some sense intermediate between those of the other two areas. McNaughton et al. (1991) have proposed, along these lines, that the posterior cingulate area is a conduit through which signals arising in parietal cortex and encoding the animal's movements are relayed to the hippocampus, where they update the record of current position and orientation and thus make possible a form of localization based on dead reckoning. This model is difficult to reconcile with the presence in primate area 7 of numerous orbital-position neurons, because the activity of these neurons corresponds to static position rather than to a change in position, but it is compatible with data obtained by recording from single neurons in posterior parietal cortex and CGp of the rat (Chen et al., 1991). Adopting a different approach, one might speculate that neurons in all three structures encoded static position and orientation but that the frame of reference with respect to which these are measured shifts from being predominantly egocentric in area 7 to being predominatly allocentric in the hippocampus, manifesting a transitional or mixed pattern in CGp. Two pieces of evidence lend support to the notion that CGp is involved to a greater degree than area 7 in processes with a world-based system of reference. First, we have found, in cat, that CGp neuronal activity related to the angle of regard is attenuated if the angle of gaze relative to the surroundings remains constant and only the angle of the eye in the orbit varies. Second, it has been demonstrated recently that rats with CGp lesions are impaired on memory-guided navigation in a water maze (Sutherland et al., 1988), and that rats (Markowska et al., 1989) and monkeys (Murray et al., 1989) with extensive cingulate lesions perform poorly on a spatial delayed nonmatch-to-sample task. It is particularly striking that impairments are greater after posterior cingulate than after anterior cingulate damage (Sutherland et al., 1988). It would be of interest in future experiments to ask to what degree CGp neurons in the cat are influenced by changes of location and orientation relative to the environment in the absence of systematic changes in eye position.

Notes

This work was supported by NIH Grant 1 RO1 NS27287 (C.R.O.) and by McDonnell-Pew Program in Cognitive Neuroscience Individual Investigator Award 90-37 (C R O.).

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