VISUAL-OCULAR MOTOR ACTIVITY IN THE MACAQUE PREGENICULATE COMPLEX

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ABSTRACT  The anatomical connections of the pregeniculate complex (PrGC) with components of the visual-ocular motor system, suggested its contribution to ocular motor behavior. Subsequent studies reported saccade-related activity in the primate PrGC. To determine its contribution, we characterized pregeniculate units (n = 128) in alert macaques during ocular motor tasks and visual stimulation. 1. We found that 36/109 saccade-related units exhibited post-saccadic bursts or pauses in tonic discharge for saccades of any amplitude or direction. In contrast to previous results, 46/109 responses preceded or coincided with the saccade, while 47/109 responses were directionally tuned. 2. Pregeniculate units were modulated not only in association with saccades (109/128), but also with smooth eye movements and visual motion (20/128), or eye position (23/128). 3. Multiple ocular motor signals were recorded from 19% of the units, indicating signal convergence on individual neurons. 4. Visual responses were demonstrated in 51% of PrGC units: Visual field illumination modulated the resting discharge of 33 units; the responses of 37 saccade-related units and all 23 position-dependent units were modulated by visual stimulation. Early saccadic activity in the PrGC suggests that it contributes more to gaze than post-saccadic modulation of visual or ocular motor activity. The patterns of saccadic responses and the modulation of PrGC activity in association with a variety of visual-ocular motor behaviors suggest its potential role as a relay between the parietal cortex and elements of the brainstem ocular motor pathways, such as the superior colliculus and pretectal nucleus of the optic tract.

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INTRODUCTION

The primate pregeniculate complex (PrGC) is a retinorecipient component of the ventral thalamus that lies dorsal and medial to the lateral geniculate nucleus (LGNd) (Livingston and Mustari 2000; Niimi et al. 1963; Polyak 1957). The prominent anatomical connections of the PrGC with cortical and brainstem areas that are critical components of the ocular motor system suggest that it contributes significantly to visual-ocular motor behavior. Notably these anatomical connections include projections from the occipital and parietal visual cortices, and reciprocal connections with the pretectal nucleus of the optic tract (NOT) and the superior colliculus (for review see Harrington 1997; Livingston and Mustari 2000). The contribution of the PrGC to visual-ocular motor behavior is suggested also by studies of the homologous nucleus in non-primates, the ventral lateral geniculate nucleus (LGNv) (Graybiel 1974; Harrington 1997; Jones 1985; Niimi et al. 1963). The LGNv is also retinorecipient and is extensively interconnected with critical visual and ocular motor structures; its proposed role as an integrative component of the visual and ocular motor systems is well supported (Agarwala et al. 1989; Conley and Friederich-Ecsy 1993; Crossland and Uchwat 1979; Graybiel 1974; Hada et al. 1985; Hada et al. 1986; Harrington 1997; Mathers and Mascetti 1975; Swanson et al. 1974).

In primates, pregeniculate involvement in ocular motor behavior is suggested further by the saccade-related (SR) discharge of PrGC neurons (Büttner and Fuchs 1973; Livingston 2000; Magnin and Fuchs 1977). Fuchs and colleagues reported that some PrGC neurons exhibit a post-saccadic burst in discharge, while other tonically active
neurons exhibit a post-saccadic pause in activity (Büttner and Fuchs 1973)*. Similarly, the discharge of many neurons in the LGNv of cats is modulated in association with saccades and the quick phases of vestibular or optokinetic nystagmus (Magnin et al. 1974; Magnin and Putkonen 1978; Putkonen et al. 1973). In cats LGNv neurons are modulated also during oscillatory head motion in complete darkness. These results suggest the possibility that the LGNv plays a role in vestibular responses, and this is supported by studies demonstrating an anatomical association of the LGNv with the vestibular nuclei (Magnin and Kennedy 1979; Matsuo et al. 1994). This contrasts with the results of related experiments in primates, in which the responses of pregeniculate units were recorded during horizontal angular acceleration or during smooth pursuit of a visual target: no vestibular responses or alteration of pregeniculate discharge in association with the smooth eye movements were observed (Magnin and Fuchs 1977). However, these authors restricted their recordings to those pregeniculate units that exhibited the distinctive post-SR activity, as originally reported. It is likely that use of this restrictive criterion for identification and testing of pregeniculate units resulted in an incomplete characterization of the PrGC.

In our studies to determine the contribution of the PrGC to saccadic behavior in primates, we found patterns of saccadic activity that are significantly different than previously reported. We report here early (pre- to peri-) saccadic activity in many units, as well as directionally selective SR responses similar to those reported for the cat LGNv (Magnin et al. 1974). We present evidence that neurons in the primate PrGC are modulated in association with both saccades and smooth eye movements. Eye position-dependent modulation of PrGC activity is also demonstrated. These results are more
consistent with those obtained in other species (Hada et al. 1986; Harrington 1997; Hayashi and Nagata 1981; Hughes and Ater 1977; Hughes and Chi 1983; Magnin and Putkonen 1978; Mathers and Mascetti 1975; Pateromichelakis 1979; Spear et al. 1977; Sumitome et al. 1979). We confirm the presence of visual responses in PrGC units, and show that the discharge of PrGC units may be modulated in response to movement of the visual field. Our results indicate that the PrGC exhibits a variety of visual and ocular motor responses, and that earlier studies in which recordings were restricted to neurons exhibiting classical post-saccadic responses, may have been biased due to selective recording of only a subset of pregeniculate neurons. Our characterization of pregeniculate activity raises several issues. First, the presence of early and late saccadic activity in the PrGC suggests that it contributes to additional aspects of saccadic or gaze behavior than were proposed based on reports of only post-saccadic activity. Second, the multiple visual and ocular motor signals shown to converge in the PrGC are suggestive of activity observed in the parietal cortical areas that are known to project to the PrGC. Our current results in conjunction with previous demonstrations of reciprocal anatomical connections of the PrGC with brainstem structures such as the pretectal nucleus of the optic tract and superior colliculus, suggest that the PrGC acts as a relay between the cortex and brainstem pathways. Visual modulation of pregeniculate activity suggests that one function of the PrGC is the integration of visual input with ocular motor signals that are relayed through this ventral thalamic structure.
METHODS

Experiments were performed in alert, behaviorally trained non-human primates, following procedures approved by the Institutional Animal Care and Use Committee of the University of Texas Medical Branch, Galveston, and conforming to the NIH “Guide for the Care and Use of Laboratory Animals.” All neuronal data was obtained from animals with chronically implanted recording chambers allowing access to the central nervous system, head stabilization lugs, and scleral eye coils for simultaneous recording of eye position. Neurons (n=128) were recorded in 3 rhesus (Macaca mulatta, 86 units) and 1 cynomolgous (M. fascicularis, 42 units) macaque. No differences or trends were found in the discharge properties of units, or in the percentage of unit types recorded in these 2 species; therefore the unit data from all 4 animals is reported together.

Surgical Procedures: All surgical procedures were performed under general anesthesia (5:1 Ketamine, 4mg/kg: Xylazine, 0.8mg/kg) using appropriate sterile techniques. Post-surgical analgesics (aspirin, Stadol or Buprenex) were provided. Cylindrical stainless steel recording chambers, ~19 or ~24.5 mm in diameter, were implanted on the bone over a hole drilled in the skull. The chambers were centered above the PrGC using stereotaxic coordinates, 4.7-5.1 mm anterior, and 5.0-10.0 mm lateral to ear bar zero. The bottom surfaces of the chambers were beveled, allowing for electrode tracking at an angle of 0, 20 or 25 degrees from the sagittal plane. The chambers were attached to the skull with dental acrylic, small stainless steel screws, and titanium struts/screws (TiMesh, Medtronic, Memphis, TN). The interiors of the recording chambers were sealed with medical grade silastic (Dow Corning, Midland, MI,
USA) and closed with removable stainless steel caps bolted in place between recording sessions. The stainless steel lug for placement of the head stabilization post (Crist Instrument Co., Inc., Hagerstown, MD) was attached to the skull with dental acrylic. Eye coils (insulated stainless steel, Cooner Wire, Chatsworth, CA) for accurate measurement of eye position were implanted underneath the conjunctiva and stitched to the sclera using techniques similar to those described previously (Fuchs and Robinson 1966; Judge et al. 1980).

**Eye Position Monitoring and Behavioral Training:** During recording, animals were seated comfortably in a standard primate chair, with their heads immobilized. The chair was located within a sound-attenuated, lightproof booth. Eye position was measured using a scleral search coil (Fuchs and Robinson 1966) and a 3’ coil frame and detector system (CNC-Engineering, Seattle, WA). The eye position signal using this system is linear within 20 degrees around the primary direction of gaze and accurate to 15 minutes of arc. Visual stimuli consisting of a discrete (diameter, ~0.25°) red laser spot or a large (~70 x 60 deg) patterned (random dot) image were rear-projected onto a ground glass tangent screen located ~57 cm in front of the animal. Stimuli were projected onto this tangent screen from an optic bench equipped with 2 light paths for presentation and control of the laser spot and large field, patterned stimulus. Both light paths were under either manual or computer control. The visual stimuli were moved independently via x, y mirror galvanometers (General Scanning, Watertown, MA) located along each light path. Each path was equipped with a fast rise time (5 ms) shutter for discrete presentation of the stimuli.
Animals were trained to target fixation or pursuit by electronically comparing laser target and eye positions; when the animals fixated the target, they received an ~0.2 ml applesauce reward. During training, the time required for continuous fixation of the target was gradually increased and the allowable fixation error for reward receipt was reduced. Eye movement signals were calibrated accurately by rewarding the monkey during fixation of the target stepped to known locations in the animal’s visual field. In addition to visual tracking of discrete target steps via saccadic movements, the animals were trained to track smoothly moving targets (typically, sinusoidal oscillation along 4 visual axes: horizontal, vertical and 2 intermediate).

**Single Unit Recording:** Single units were recorded using glass-insulated, tungsten electrodes. The electrodes were advanced through stainless steel cannulae using an hydraulic microdrive (Trent-Wells, Coulterville, CA). The PrGC was identified by characteristic saccadic or smooth eye movement related activity, recorded 150-1350 µm above the dorsal surface of the LGNd. The activity of single PrGC units was isolated with a time-amplitude window discriminator (BAK Electronics, Inc., Germantown, MD) and recorded concurrently with the eye position, laser target and large field stimulus positions. Isolated single unit spikes were converted to TTL pulses and sampled at 1 kHz. Analog signals were digitized to computer (Macintosh Quadra 650 with MIO-16X board [National Instruments, Austin, TX, USA]) through BNC 2080 and custom-built interfaces at 1 kHz. Software for experimental control, data acquisition and analysis were provided by Dr. Albert Fuchs at the University of Washington Regional Primate Research Center, Seattle. Data was digitized concurrently using a 1401-plus CED interface and dedicated software (Cambridge Electronic Design, CED, Cambridge,
England) onto a PC (Optiplex GX1p, Pentium II, Dell Computer Corp, Austin, TX) at a sampling rate of 1 KHz for all signals, except the unit recording which was digitized at 60 KHz. Software protocols for experimental control, data acquisition and analysis using the CED hardware were written by Dr. Andrew Burrows.

**Ocular Motor Testing:** Pregeniculate units were recorded during saccades, smooth eye movements and fixation of the visual target during motion of the large field stimulus. Saccadic testing was performed under 3 conditions: 1) While the animals were seated in the lightproof recording booth in the dark, single units were recorded during saccades evoked by steps (randomly variable amplitude and direction) of the laser target across the tangent screen. 2) To determine the interaction of visual stimulation and SR responses, this test was repeated for saccades across the illuminated large field stimulus. 3) To verify that SR unit activity was not due to visual input, spontaneous saccades performed in complete darkness were also recorded. The activity of PrGC units during smooth eye movements was recorded similarly: To determine if PrGC units responded during smooth pursuit and to test for directional sensitivity, unit activity was recorded during pursuit of a target moving sinusoidally (+/- 10 deg., 0.1-2.0 Hz, along each of 4 visual axes) in the dark or across the illuminated patterned visual field. The responses of some units were recorded during synchronized sinusoidal oscillation of the laser target and the illuminated large field stimulus. To test for sensitivity to visual motion, animals fixated the stationary target during constant velocity oscillation of the large field visual stimulus along each of the 4 visual axes.

To determine the response of PrGC units to visual stimulation, the large field stimulus was sometimes flashed off and on to determine its effect on unit discharge. In
some instances, the large field stimulus was illuminated during saccadic tracking of the laser target to determine how visual input affected the SR discharge of PrGC units.

**Analysis:** Data analysis was performed off-line. Saccade-related neurons were identified by averaging the unit discharge associated with 25-200 saccadic events. The discharge of units during saccades were averaged by aligning each response to saccade onset, defined typically by a 75 deg/sec increase in eye velocity. Cumulative average firing rate histograms were generated to determine if unit discharge was modulated in association with saccades. Responses (pauses or bursts) were classified as pre-SR (onset preceded saccade initiation), peri-SR (coincided with saccade), or post-SR (onset after saccade completion). The average duration and latency of responses were calculated for those units with discharge rates that were regular enough to allow reliable measurements of latency and duration. For units exhibiting a post-SR burst, the peak and average burst frequency were measured. To determine if SR responses were directionally tuned, saccadic data for each unit was sorted into 8 groups: saccades made to the right, left, up, down, up/right, up/left, down/left and down/right. Average firing rate histograms for saccades in each group were generated and compared. To determine if the SR responses of PrGC units were modulated by visual input, the firing rate histograms and average response durations for saccades made under each of the 3 viewing conditions were compared.

Pregeniculate unit discharge during sinusoidal tracking was averaged over 8-30 cycles. Average eye position and associated firing rate histograms were generated after removing intermittent saccades. For neurons that also exhibited SR changes in discharge, saccadic unit responses were removed prior to averaging the unit data. Average firing
rate histograms for pursuit behavior in the dark or across the patterned background were compared. For units that responded more vigorously to pursuit across the patterned background, their response to visual motion was tested explicitly by requiring the animals to fixate the target while the large patterned stimulus was oscillated at a constant velocity. Firing rate histograms were averaged over 10-30 cycles of the patterned visual stimulus. The average firing rates for pursuit (or visual field motion) in each of 8 directions were determined and fit by a Gaussian function to characterize the directional tuning and the depth of direction-dependent modulation for each unit (Mustari and Fuchs 1990; Wallman and Velez 1985). Subsequently the preferred directions (most vigorous discharge) of those units in which directional tuning was fully characterized, were normalized for direction towards (ipsiversive) or away (contraversive) from the side of recording, and plotted together.

To evaluate eye position-dependent modulation of PrGC unit activity, the average firing rate of units during 50-150 inter-saccadic intervals were measured. Inter-saccadic intervals were defined as being outside of the time course for the SR response of each unit determined by latency and duration measurements. During these inter-saccadic intervals, fixation on a visual target was maintained. For each interval, the firing rate was plotted as a function of the horizontal or vertical component of eye position. Data points were fit using linear regression analysis. If the correlation coefficient was greater than 0.50, the unit was classified as carrying an eye position-dependent signal. For some units this analysis was performed for target fixation in the dark and with the patterned background illuminated.
Visual modulation of PrGC unit activity was evaluated in 2 ways. For neurons in which the overall firing rate was modulated by illumination of the large patterned, visual field stimulus, unit discharge was recorded during alternate periods of illumination and darkness. However, in other PrGC neurons, illumination of the large field visual stimulus did not affect overall firing rate, but did modulate SR responses. In these units the SR response amplitude indicated by average duration or peak burst frequency was determined for saccades performed under each of the 3 viewing conditions.

To determine if one or both eyes mediated visual modulation of PrGC activity, the visual modulation paradigms were repeated for 22 units during binocular, left eye (LEV) and right eye (REV) viewing. The response amplitudes were compared under each of these 3 conditions, and units were classified as binocular, left- or right-eye dominant.

To evaluate the average firing rates of PrGC units, we measured the inter-spike intervals during inter-saccadic periods, while the animals viewed the laser target in the dark. This data was used to calculate the average firing rates for 51 units, and to demonstrate the regularity/irregularity of PrGC unit discharge. Average inter-spike intervals for each unit were calculated to demonstrate the range of firing rates, and a coefficient of variation (CV, standard deviation / mean inter-spike interval) for each unit was calculated (Bialek and Rieke 1992; Goldberg et al. 1984; Goldberg and Fernandez 1971).

**Histological Verification:** To verify that recorded units were located within the PrGC, we noted the location of each relative to the dorsal surface of the LGNd. The dorsal surface of the LGNd was identified by recording neurons with visual responses dominated from the contralateral eye (LGNd layer 6). Visual responses were recorded
during alternating monocular eye patching, as the animals fixated the laser target and the large patterned background stimulus was illuminated. Frequently electrode tracks continued into deeper layers of the LGNd to verify alternation of ocular dominance. Subsequent histological recovery of the electrode tracks provided a clear indication for each animal of the range of distances from the LGNd surface, in which PrGC units were recorded. All units reported were located 150-1350 µm above the dorsal surface of the LGNd. This range was determined based upon tracking angle and the medial-lateral location of electrode tracks (see Fig. 1). Requirement that the location of each unit relative to the surface of the LGNd be verified was stringent, and automatically excluded some unit data. However, verification of each unit’s location within the PrGC was imperative.

**RESULTS**

The PrGC is a thin multi-laminar plate of cells that curves over the dorsal and medial aspect of the dorsal LGNd (Fig. 1A,B). It is separated from the LGNd by the geniculate capsule. The locations of electrode tracks through the PrGC are shown in Fig. 1. The trajectory of tracks at an angle of 25 deg from the sagittal plane is shown in panel C, while vertical tracks from another animal are illustrated in panel D. We recorded the activity of 128 pregeniculate neurons, along tracks comparable to these.

*Saccadic Activity:* Confirming previous results that the PrGC contributes to saccadic behavior, we found that 109 of the 128 (85%) pregeniculate neurons were saccade-related. Thirty-six of the SR units (33%) exhibited post-saccadic modulation similar to that reported previously (Büttner & Fuchs, 1973; Livingston 2000): 22 were
classified as post-saccadic pausers, while 14 were post-saccadic bursters (Fig. 2A, B). Pregeniculate units that exhibit this classical pattern of activity, respond vigorously for saccades of any amplitude or direction. The responses occur late, after completion of the saccadic movement, are prolonged, and variable in duration. Typical responses are illustrated, but it should be noted that for some pausers, the firing rate might require hundreds of milliseconds to return to its pre-saccadic level. For this class of saccadic units the average pause duration relative to saccade initiation was 186 ms (SD 115, range 67-542 ms) for saccades to target in dark, with an average latency of 79 ms (SD 20, range 46-122 ms). Similarly, the post-SR discharge of some bursters was prolonged, with the firing rate diminishing gradually over hundreds of milliseconds (burst durations 83-329 ms). The average duration for classical SR bursts associated with saccades to target in the dark was 181 ms (SD 104), with burst latencies averaging 108 ms (SD 11, range 93-124 ms).

Although 36 SR units in the PrGC exhibited classical post-saccadic responses, we found that in contrast to previous reports, 46/109 (42%) SR units exhibited pre- (n=14) or peri-saccadic (n=32) responses. These early SR responses were seen in both pausers and bursters (Fig. 3). For the unit shown in Fig. 3A, the irregularity of the firing rate made it difficult to define the latency of the pause. However, it is clear that the pause typically begins prior to saccade initiation. The SR-burst illustrated in Fig. 3B is initiated before or during the saccade, reaching its peak frequency during the saccade (average latency - 331.3 ms, average duration 422.2 ms). In addition to early activity, these 2 units illustrate that the SR-response in many pregeniculate units could not be classified as a pure pause or burst. The pause illustrated in Fig 3A is followed by a distinctive increase in the firing
rate that exceeds pre-saccadic levels. The average latency of this burst is 105.9 ms, with a duration of 169.0 ms. Similarly, the peri-saccadic burst shown in Fig. 3B is followed by a distinct pause of variable duration (average latency, 90.9 ms). Various patterns of phasic responses such as these were observed. Many units classified as having post-saccadic bursts due to the prominence of this response also exhibited brief periods of inhibition that preceded the burst and occurred during the saccade. These results demonstrate that significant changes in pregeniculate SR activity are initiated earlier than previously reported, again indicating that the PrGC is associated with more than post-saccadic visual or motor processing.

In addition to early SR activity, we found that 47/109 PrGC units tested, exhibited directionally tuned SR responses. A typical directionally tuned SR response is illustrated (Fig. 4). The SR pause in this unit was most prominent for down/left saccades. There was no response for up/right saccades. The tuning of this response is evident if the pause duration is plotted as a function of saccade direction (Fig. 4C, D). Although many of the PrGC units with directionally tuned saccadic responses, exhibited no response for the opposite direction, some exhibited inverted responses for saccades made in the opposite direction. For example, a unit that burst for saccades towards the right, paused for saccades made towards the left (e.g., Fig. 12A). Of the 47 SR units that were directionally tuned, 25 responded most strongly for saccades made towards the side of recording (ipsiversive), while 22 responded for saccades in the contraversive direction. An additional 9 units had responses tuned for 2 directions, with the responses inverted for saccades made in opposite directions. Unlike the directionally tuned responses seen in collicular neurons, we found no correlation of the SR responses in pregeniculate neurons.
with saccade amplitude. Rather the pattern of directionally tuned saccadic activity seen in the PrGC is more comparable to that reported for some parietal cortical neurons, many of which are only broadly tuned for saccade amplitude and direction (Barash et al. 1991a,b).

The timing of saccadic activity in the various types of SR units is summarized in Table I. The timing relationship of activity associated with saccades is illustrated for 49 PrGC neurons, including all types of SR units (Fig. 5). The average response latencies and durations are plotted, paired with their respective average saccade duration. Although most activity is post-saccadic, it is evident that the discharge of many PrGC units is modulated prior to, or during saccade initiation. Also illustrated is the wide range of response durations that were observed in PrGC units. On the basis of previous work and due to the post-saccadic modulation of activity in many PrGC units, we did not expect to find tight correlations between the pregeniculate responses (latencies, durations) and saccade metrics (initiation, duration). We evaluated the pregeniculate response characteristics and found no correlation with saccade metrics (Fig. 6). No correlation was found between the response duration or peak firing frequency (for bursters) and saccade amplitude, duration, or peak velocity. The relationship of response latency and duration is shown as a function of saccade onset and duration in Fig. 6. All data are referenced to saccade initiation. While the saccade duration for each unit tested (n=49) remains relatively constant within a given range, the response latency (or onset) and end time varies widely. The lack of an association between the timing characteristics of the response and saccade suggests that the PrGC is associated with an aspect of visual processing or ocular motor behavior other than saccadic control.
Smooth Eye Movements and Visual Motion: Although sensitivity to head motion, smooth eye movements, or visual motion have never been demonstrated in the primate PrGC, responses to these stimuli are documented for the LGNv in a variety of non-primates. In testing, we found that 20 of 128 (~16%) pregeniculate units were modulated during smooth eye movements or in response to visual motion of the large field visual stimulus. Of the 20 units, 18 PrGC units responded during smooth eye movements; 9 units responded for visual motion during fixation. The neuron shown in Fig 7A responded for smooth pursuit of the target towards the down/left, but exhibited its most vigorous response for pursuit of the laser target towards the down/left across the patterned background stimulus (Fig 7B). This unit responded in a directionally dependent way for visual motion towards the up/right (Fig. 7C). Under this condition, the increase in the unit’s firing rate correlated with the visual slip of the large field stimulus. However, correlation of the unit response during smooth pursuit in the dark does not appear to correlate well with visual slip of the laser target.

Complete directional tuning curves were generated for 11 pregeniculate units that responded during smooth eye movements. Six additional units were tested for direction selective responses. Most (13/17) were tuned for pursuit towards the side of recording (ipsiversive). The directional tuning curve for a unit recorded in the left PrGC that responded most vigorously for pursuit towards the down/left is shown (Fig. 8). The width of the curve about the preferred directional axis (highest predicted firing rate) demonstrates the broad tuning typical of pregeniculate units. The preferred direction of response for 11 PrGC units were normalized for the side of recording and plotted together (Fig. 8B). The predominance of units tuned for the ipsiversive direction (9/11 units) is
evident. Also evident in the plot is the variable amplitude of the directionally tuned responses observed in pregeniculate neurons.

We recorded the pregeniculate responses during smooth eye movements at velocities of 4-80 deg/s. Although we did not rigorously analyze the velocity tuning of pregeniculate units, for those in which multiple velocities were tested, the most vigorous responses were recorded for pursuit at 14-30 deg/s.

Eye Position-dependent Signals: In 23 PrGC units, eye position-dependent modulation of the firing rate was evident. A unit that responded with a clear increase in firing rate for fixation towards the left is illustrated (Fig.9). Steps towards the right result in intermittent drops in the firing rate. Data taken from the target stepping task shown for this position-dependent unit are plotted in Fig. 9B. While a valid correlation cannot be generated from 2 clusters of fixation points, the plots in the right hand panels illustrate valid correlations for 2 other position dependent units (Fig. 9C, D). One unit is biased for rightward and one for leftward gaze. (Both units were recorded in the right PrGC.) The data for each of the 3 units shown was taken for conditions in which the animals fixated in the dark. For 14/23 eye-position dependent PrGC units, firing rate was modulated only in the dark. In contrast, the firing rate of 9/23 pregeniculate units was correlated with eye position only during illumination of the patterned background. The dependence of the eye position signals on the viewing conditions illustrates the integration of visual and ocular motor signals by the PrGC.

Visual Modulation of Firing Rate: Direct retinal input suggests that a population of PrGC units should exhibit visual responses. This in conjunction with previously documented visual responses in primates and non-primates prompted visual testing in our
experiments. In 33 pregeniculate units, the firing rate was modulated by illumination of
the patterned background stimulus. This phenomenon is illustrated by 2 neurons that
were recorded along the same electrode track, 50 µm away from one another (Fig. 10).
The overall firing rate of 1 unit is inhibited dramatically by illumination of the patterned
background (Fig. 10A). This inhibition is tonic, continuing for as long as the visual field
is illuminated. It is independent of eye position or accuracy of fixation. Conversely, the
firing rate of the second unit illustrated is driven by illumination of the visual field (Fig.
10B). This visual effect is independent of eye position, visual task, or target fixation.
These units were recorded just dorsal to the geniculate capsule, and were likely to be
located within the most ventral (retinorecipient) sublayer of the PrGC. However, the
difficulty of identifying the boundary between the dorsal and ventral sublayers precluded
localization of visually responsive PrGC units within an identified subnucleus of the
PrGC. Of 33 PrGC units in which tonic visual modulation was observed, the firing rates
of 16 were decreased, while the firing rates of 17 were increased by illumination of the
visual field. This suggests that at least some retinal input acts via an inhibitory system,
possibly the GABAergic neuronal population within the retinorecipient sublayer.

In addition to the tonic visual modulation described above, in 37 PrGC units
visual modulation of activity was apparent not simply as a change in general firing rate.
Rather, the SR responses of these units were modulated by illumination of the visual
field. In 25/37 units responses were less vigorous for saccades across the illuminated
patterned background, as compared to saccades made in the dark. This is effectively
illustrated by comparing the durations of SR pauses or bursts under different viewing
conditions. The average pause duration was 273 ms (SD 217) for spontaneous saccades
in complete darkness, 169 ms (SD 116) for saccades to target in the dark, and 151 ms (SD 164) for saccades across the illuminated patterned background. The average duration for bursts associated with spontaneous saccades in complete darkness was 269 ms (SD 172), 174 ms (SD 155) for saccades to target in the dark, and 88 ms (SD 91) for saccades across the illuminated background. Such visual modulation of SR responses is similar to that reported by Büttner and Fuchs (1973), who reported a reduction in the amplitude of SR responses subsequent to brief flashes of diffuse light. To verify that the duration of SR responses in complete darkness was not associated with the increased saccade duration characteristic of saccades performed in complete darkness, we compared the response durations for large saccades of equivalent durations made with visual input to those made in complete darkness. We found that the prolonged response duration for saccades in complete darkness was not a function of the increased saccade duration (not illustrated). This finding is consistent with the observation that the timing of SR responses was not correlated with any aspect of saccade metrics.

**Ocular Dominance:** To determine if visual modulation of PrGC unit activity is mediated binocularly, ocular dominance tests were performed for 22 units. In almost all units tested, the visual modulation of discharge is mediated by input from both eyes. This is clearly demonstrated by changes in the duration of SR responses in a unit during viewing with the left eye (LEV), right eye (REV), or binocularly (Fig. 11). This unit exhibited a vigorous post-SR burst for saccades made to target in the dark (response duration, 150 ms). For saccades made across the illuminated patterned background, the average burst duration is reduced to 36 ms. The burst duration associated with saccades across the illuminated visual field while LEV is 81 ms, and while REV is 79 ms.
Reduction of the response duration due to illumination of the visual field is mediated equally by visual input from both eyes. This was typical of the results obtained for most units tested (18/22). Four units exhibited binocular responses that were dominated by the contralateral eye.

Convergence of Visual and Ocular Motor Signals: Clearly multiple types of visual and ocular motor signals converge within the PrGC. While most of the units illustrated carry a single prominent visual or ocular motor signal, 24/128 (19%) pregeniculate units carry multiple signals. The unit shown in Fig. 12 is an example in which saccadic, visual slip and eye position dependent signals converge. A SR burst for rightward saccades and a longer latency pause for leftward saccades is shown. This unit shows no response for smooth pursuit of a small target across a dark background; however, it does respond to visual slip of the large field stimulus towards the left (Fig. 12B). This visual response is apparent during rightward pursuit across the illuminated patterned background, during which the unit responds vigorously. In addition, the firing rate of this unit is increased for rightward gaze (Fig. 12C). This position dependent signal can be seen superimposed on the response of the unit during pursuit. As shown in the inset (lower right, Fig. 12B), the response associated with the leftward slip of the patterned background extends partly into the rightward slip phase of the cycle; the response continues while gaze is directed towards the right. This unit was recorded from the right PrGC. The combined effect of the signals carried by this unit could collectively contribute to output appropriate for driving the eye during rightward pursuit, interrupted by catch-up saccades.
Irregularity of Firing Rate: A prominent feature of PrGC activity was the wide range of firing rates observed in different neurons. We analyzed the discharge of 51 PrGC units during 5-15 sec of intersaccadic intervals, during which the animals performed stable fixation of the stationary target spot in the dark. (Units that carried eye position-dependent signals were excluded from this analysis.) Under these viewing conditions, the average firing rate was 30.44 Hz (SD 19.0); the range of resting discharge rates for pregeniculate units was 4.09-78.18 Hz. This value contrasts with peak discharge rates ranging from 78.00 to 443.15 Hz observed during SR bursts (average, 128.36 Hz for saccades to target in the dark). We also noted a striking irregularity in the discharge rate of individual pregeniculate neurons. A coefficient of variation (CV) for the interspike intervals was calculated for each unit. The average CV during intersaccadic intervals was 0.97 (range, 0.35-1.99), demonstrating the extremely irregular firing rates of pregeniculate neurons. This irregularity may reflect the convergence of visual and motor signals within the PrGC, and the relay of multiple signals by individual PrGC neurons.

Summary: The distribution of responses that we found among PrGC neurons is summarized in Fig. 13. It must be noted that the results presented here may not represent the entire population of PrGC units. We restricted our analyses to those units whose location relative to the surface of the LGNd could be demonstrated in order to verify their location within the PrGC. A significant number of pregeniculate units are located medial to the LGNd, and so were excluded from this initial study. Further, the difficulty of recording each neuron long enough to test for responses during multiple eye movements and visual stimuli precluded full testing of every unit. Therefore, it is likely that the percentages of neurons with sensitivity to smooth eye movements, visual sensitivity or
convergent signals for example, are under-reported. We also noted that numerous units encountered during tracking in the PrGC did not respond during the ocular motor tasks or visual stimulation described here; these units are not included in this report. Similarly, Büttner and Fuchs also identified a subset of pregeniculate neurons that did not respond during saccadic testing. Therefore the response and discharge characteristics of a subset of PrGC neurons are still unknown.

**DISCUSSION**

The discharge patterns of most PrGC units are different than previously reported. We found that almost 39% of pregeniculate units are associated with non-saccadic visual-ocular motor behaviors, including smooth eye movements (14%), visual slip (7%) and eye position (18%). Although the majority (85%) of PrGC units described here are saccade-related, 67% of these units exhibit timing and discharge characteristics that are significantly different than expected (Fig 13A,B). Notably, 42% of SR responses are not post-saccadic, but occur before or during the saccade. Unlike the original description of saccadic responses in the PrGC, 43% of the responses are directionally tuned. Our findings dictate that previous hypotheses concerning the functional role of the PrGC be modified, and suggest that future experiments evaluate the PrGC in the context of gaze shifts and other aspects of ocular motor behavior. We suggest that one role of the PrGC is the relay of signals from the cortex to the brainstem.

Its potential role as an integrative relay between visual cortical areas and brainstem motor pathways is suggested by the prominence of cortical projections to the PrGC and its reciprocal connections with ocular motor sites in the brainstem (Fig. 14).
Our results demonstrate similarities in the discharge of PrGC units to those in parietal cortex. We also demonstrate convergence of multiple ocular motor signals within the PrGC: 19% of the units carried multiple ocular motor signals. For example, of the SR units that we tested, 9% also exhibited smooth eye movement or visual motion responses, and 13% eye-position dependent signals (Fig. 13C). A small percentage of SR units (3%) exhibited both smooth eye movement and position-dependent signals. The signals recorded in the PrGC are suggestive of activity recorded in those parietal areas that project to the PrGC. Visual modulation of pregeniculate activity indicates that the PrGC integrates these ocular motor signals with visual input. Although limited study of the PrGC to date precludes detailed speculation regarding its functional role, the evidence that is currently available directs that future experiments address its role as an integrative visual-ocular motor relay between the cortex and brainstem. Evidence to support this proposal is discussed further.

*Functional Role of the Pregeniculate Complex:* Our results confirm and extend previous observations regarding neuronal activity in the PrGC. The PrGC is associated primarily with saccadic behavior, and the modulation of many units is post-saccadic. In the absence of any demonstrable correlation between the responses of pregeniculate neurons and saccade metrics (Fig. 6), it is unlikely that the PrGC contributes to saccadic control. Based on these observations, the PrGC might be proposed to play a role in post-saccadic processing of visual or ocular motor signals (Büttner and Fuchs 1973; Livingston 2000). However, the PrGC does not project to the LGNd, a primary site for saccadic modulation of visual input (Ramcharan et al., 2001; Ross et al. 1996; Ross et al. 2001; Wilson et al. 1995). Our results force reconsideration of the pregeniculate role in
visual-ocular motor behavior. Modulation of activity in 42% of SR pregeniculate units before and during saccadic movement suggests that it contributes to more than post-saccadic gating of visual or motor signals.

The range of initiation times and the duration of saccadic unit activity in the PrGC as illustrated in Fig. 5 do not support a role for the PrGC in the control of saccades. Recent studies of other brainstem areas in which the timing of saccadic activity is broadly distributed suggest that late saccadic activity may be associated with aspects of gaze other than saccadic control. Notably, the discharge of many units in the central mesencephalic reticular formation is post-saccadic, and corresponds with the timing of post-saccadic discharge observed in PrGC units. The discharge of these mesencephalic units is associated with head movements (Pathmanathan et al. 2002; Waitzman et al. 2002). Because our recordings were performed in a head-fixed preparation, we cannot address this issue at present. Further behavioral and recording experiments should address the relationship of pregeniculate activity to the later phases of gaze shifts.

Currently there is only weak evidence in primates suggesting that the PrGC may be associated anatomically with the mesencephalic reticular formation (Wilson et al. 1995). However, in a study of the thalamic connections of the LGNv in cats, a reciprocal connection of the LGNv with the MRF was demonstrated (Nakamura and Kawamura 1988). Given the similarities in the timing of activity in the PrGC and the mesencephalic reticular formation, the potential anatomical association between these areas necessitates further study.

Our results extend earlier descriptions of the pregeniculate by demonstrating modulation of PrGC unit activity in association with additional types of eye movements.
The presence of vestibular, smooth eye movement and eye position signals in the homologous LGNv of non-primates, prompted studies to determine if similar activity might be present in the primate PrGC. In contrast to results in chick, rat, rabbit and cats (Hada et al. 1986; Harrington 1997; Hayashi and Nagata 1981; Hughes and Ater 1977; Hughes and Chi 1983; Magnin et al. 1974; Magnin and Putkonen 1978; Mathers and Mascetti 1975; Pateromichelakis 1979; Spear et al. 1977; Sumitome et al. 1979), neither smooth eye movement nor vestibular signals were identified in the primate pregeniculate complex (Magnin and Fuchs 1977). This discrepancy may have been due to the identification of primate pregeniculate units based in part on the presence of classical post-SR bursts. Our results demonstrate that a minority (14/128; 11%) of PrGC units exhibits classical post-SR bursts, and only a small percentage of these might be expected to carry multiple ocular motor signals. It is likely that many pregeniculate neurons were not identified as such in the earlier study, and were not tested for smooth eye movement or vestibular signals. Therefore the possibility of vestibular signals in the PrGC cannot be excluded. Given the similarities between the macaque PrGC and the non-primate LGNv, it is fair to speculate that vestibular signals will be identified in the PrGC.

Relationship of the Pregeniculate Complex to Visual Cortical Areas and the Brainstem: Our results and previous observations indicate that the PrGC may relay information from visual cortical areas to the brainstem motor pathways (Fig. 14): The PrGC receives afferents from several areas of the parietal cortex, including areas 7a, LIP (lateral intraparietal), MT/ MST (middle temporal/medial superior temporal) and the polysensory areas of STS (superior temporal sulcus) (Graham et al. 1979; Leichnetz 1990; Maioli et al. 1984; Maunsell and van Essen 1983b; Norden et al. 1978; Spatz and

Although the saccadic signals recorded in the PrGC could be derived from the superior colliculus, pretectum or cortex, the activity of many saccadic units in the PrGC are comparable to those in the parietal cortical areas that project to it (Andersen et al. 1990; Andersen and Gnadt 1989; Barash et al. 1991a,b; Brotchie et al. 1995; Colby et al. 1993; Kawano et al. 1994). Pregeniculate saccadic activity is not comparable to that of collicular units, as it is post-saccadic and is not correlated with saccade metrics. The SR discharge of only the post-saccadic pausers in the PrGC is similar to that of the pretectal omnipause neurons (Mustari et al. 1994; Mustari et al. 1997). However, there are several similarities in the discharge of parietal and PrGC units. Most notably, responses in many parietal and pregeniculate units are post-saccadic and prolonged. The responses of many SR units in the PrGC are either not tuned for direction or amplitude, or are very broadly tuned; similarly the saccadic responses of many parietal units are only broadly tuned (Barash et al. 1991a,b). Further, just as the saccadic responses in PrGC units do not correlate with saccade metrics, the SR responses of many parietal units are correlated with other aspects of saccadic behavior (Anderson and Buneo 2002; Cohen and Andersen 2002; Colby and Goldberg 1999; Goldberg et al. 2002; Gottlieb et al. 1998; Xing and Andersen 2000). These similarities suggest that saccadic activity in the PrGC is derived from parietal cortical input.
The presence of visual motion, smooth eye movement and eye position signals further suggest that ocular motor signals in the PrGC are derived from cortical input. Cortical projections to the ipsilateral PrGC originate from those parietal areas that play a role in visual motion detection and saccadic behavior, and provide signals for smooth eye movements and saccades (Andersen and Gnadt 1989; Brotchie et al. 1995; Colby et al. 1995; Kawano et al. 1992; Kawano et al. 1994; Komatsu and Wurtz 1988a, b; Newsome et al. 1988; Newsome and Pare 1988; Pierrot-Deseilligny et al. 1995). These parietal areas also process eye and head position signals. Eye position modulates the discharge of cortical units in the lateral intraparietal sulcus and area 7a (Andersen et al. 1990).

In summary, activity in parietal areas MT, MST and STS during visual motion and smooth eye movements is comparable to that of PrGC units. Eye position signals in the LIP and parietal area 7a may also contribute to patterns of unit discharge in the PrGC. Each of these parietal areas is a potential source for the ocular motor signals recorded in the PrGC, supporting our hypothesis that cortical input contributes significantly to pregeniculate unit behavior.

Prominent reciprocal connections of the PrGC with the pretectal nuclei and the superior colliculus provide an anatomical basis by which signals can be relayed from the PrGC to motor pathways in the brainstem (Livingston and Mustari 2000; Mustari et al. 1994; Büttner-Ennever et al. 1996). The distinctive response of the post-saccadic pausers in the PrGC can be compared closely with that of the pretectal omnidirectional pausers (Mustari et al. 1994; Mustari et al. 1997). The discharge characteristics of the pretectal pausers are essentially identical to those of the PrGC units in terms of latency and
duration. Similarly the timing of activity in the distinctive post-SR bursters of the PrGC is comparable to that of the pretectal pausers.

The directional tuning of smooth pursuit and visual slip responses in the PrGC is comparable to that reported for the pretectal nucleus of the optic tract (Hoffmann et al. 1988; Mustari and Fuchs 1990). The majority of PrGC units for which complete directional tuning curves were generated are tuned predominantly for ipsiversive pursuit. Additional units, for which complete tuning curves were not generated, are also tuned predominantly for ipsiversive pursuit. This is comparable to the predominantly ipsiversive tuning of neurons in the pretectal nucleus of the optic tract. Although we did not systematically test the velocity responses in PrGC neurons during pursuit, we did observe vigorous responses at velocities of 4-80 deg/s. This is within the range of velocities at which pretectal units respond vigorously (Hoffman et al. 1992; Mustari and Fuchs 1990). The response properties of NOT units are thought to derive in part from afferents originating in cortical areas MT and MST (Distler et al. 2002; Distler and Hoffmann 2001; Hoffmann et al. 1992). The PrGC was identified previously as an indirect source of cortical input to the pretectal nucleus of the optic tract (Büttner-Ennever et al. 1996). Our observations provide additional evidence to support this hypothesis.

Visual Input to the Pregeniculate Complex: One possible function of the PrGC is the integration of ocular motor signals with visual input (Fig. 14). Ocular motor signals in the PrGC are not dependent on visual input as demonstrated by the presence of robust SR activity in the absence of visual stimulation (Büttner and Fuchs 1973; Livingston 2000). However, these signals may be modulated by visual stimuli. Visual input directly
from the retina, and indirectly from areas 17, 18 and 19 of the occipital cortex (Hendrickson et al. 1970; Livingston and Mustari 2000; Ogren and Hendrickson 1976) suggests that neurons responsive to visual stimulation should be present in the PrGC, notably within the retinorecipient sublayer of the PrGC. Büttner and Fuchs (1973) reported that 10 µs flashes of diffuse light modulated the SR responses of some PrGC units. Similarly, phasic and tonic visual responses were noted for LGNv neurons in cat, rat, hamster, and rabbit (Harrington and Rusak 1991; Hayashi and Nagata 1981; Hughes and Ater 1977; Hughes and Chi 1983; Mathers and Mascetti 1975; Spear et al. 1977; Sumitome et al. 1979). Using prolonged visual stimulation similar to that during natural viewing, we confirmed visual modulation of SR responses in primate PrGC neurons. We also found 2 classes of units, with firing rates that were either tonically increased or decreased by visual stimulation.

The retinorecipient sublayer of the PrGC is largely GABAergic (Livingston and Mustari 2000). These GABAergic neurons may be excited by visual input as illustrated in Fig. 10B, and subsequently inhibit other PrGC neurons. For example, the tonic inhibition of PrGC neurons such as the one shown in Fig. 10A may be mediated by GABAergic neurons intrinsic to the PrGC. GABAergic neurons of the retinorecipient sublayer in conjunction with visual input could also play a role in the modulation of the ocular motor signals relayed through the PrGC (Fig. 14).

*Firing Rates:* The firing rates of pregeniculate neurons are extremely variable, with some units exhibiting high tonic firing rates, while others are relatively inactive, exhibiting extremely low firing rates. Further, the firing rates of individual neurons are extremely irregular, as demonstrated by their high coefficients of variation (CV).
Although the significance of this discharge irregularity is not clear, spike trains with high information content are predicted to exhibit highly irregular discharge, and to include high frequency responses (Bialek and Rieke 1992; Rieke et al 1999). This is the case for pregeniculate neurons, in which we found CV’s of 0.35 – 1.99, and peak discharge rates of 78 to 442 spikes/s. The extremely irregular discharge rates of many PrGC units may reflect modulation of their activity by multiple convergent signals. In addition, there may be sources of input to the PrGC not yet identified, contributing further to firing rate irregularity. Subsequent studies of the PrGC will require more rigorous analysis of how isolated signals modulate PrGC unit behavior, and how the integration of multiple signals impacts pregeniculate discharge.

**Conclusions:** We have demonstrated that the timing of saccade-related activity in the PrGC is broadly distributed in terms of its initiation and duration. We interpret these results in conjunction with other observations, to suggest that the PrGC may play a role in gaze behavior other than saccadic control. The similarity of ocular motor signals in the PrGC to those recorded in parietal areas that project to it, suggests that the PrGC may represent a relay between cortex and brainstem pathways. In support of this hypothesis, projections from visual cortical areas to the PrGC, and in turn from the PrGC to brainstem structures such as the pretectal nuclei and the superior colliculus have been documented. We have also shown that multiple ocular motor signals converge within the PrGC and on single PrGC units. These signals may be modulated by visual input directly from the retina or indirectly from the primary visual cortex. Integration of these visual and ocular motor signals is evidenced by the modulation of PrGC discharge rates and SR responses by visual stimulation.
Text Footnotes

Büttner & Fuchs (1973) originally used the term PGN in reference to the pregeniculate nucleus. To avoid confusion due to the more common use of PGN in reference to the perigeniculate nucleus, we use PrGC in reference to the pregeniculate complex, acknowledging its multiple subnuclei.
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Figure Legends

Figure 1  Photomicrographs illustrating the anatomical location of the PrGC. Medial is towards the left in all panels.  A. Coronal section through the rostral PrGC, showing its location dorsal and dorsomedial to the LGNd. In this section the PrGC has been stained for substance P to demonstrate the multilaminar organization of the rostral PrGC. The retinorecipient sublayer is the most ventral, darkly stained component of the PrGC at this level. The unstained area between the PrGC and LGNd is the geniculate capsule.  B. Coronal section stained for GABA, through the caudal PrGC, showing its location medial to the LGNd, and extending as a thin layer over its dorsal surface.  C, D. Nissl stained coronal sections in which electrode tracks were recovered from 2 of the animals used in this study. The PrGC is stained lightly; fine grey lines mark its boundaries.  C. Two electrode tracks 25° from the sagittal plane are shown. The most prominent track is marked with arrows, and extends through the dorsal to dorsal medial PrGC and into the LGNd. The second track extends through the medial PrGC and does not enter the LGNd.  D. Electrode tracks in the parasaggital plane through the PrGC. The most prominent track through the PrGC, extending into the LGNd is marked with arrows. More medial tracks can be identified faintly. The most medial track shown is located beyond the medial extent of the PrGC. Scale bar, B = 1 mm.

Figure 2  Typical post-saccadic responses recorded in pregeniculate units.  A. A spontaneously active PrGC neuron, recorded during saccades to a visual (laser) target across a darkened visual field. This unit responds with a distinctive post-saccadic pause
in discharge for saccades of any amplitude or direction. The upper traces illustrate the horizontal (He) and vertical (Ve) components of eye position in degrees. Rightward, or upward movement is recorded as an upward deflection in the horizontal or vertical eye position traces, respectively. The dashed line represents gaze directed straight forward. The lower traces are the isolated unit recording and the acceptance pulse for the discriminated unit. B. The averaged SR response of the same unit. The upper traces are the superimposed horizontal and vertical components of multiple saccades, aligned at saccade initiation. The raster display of discharge for each saccade and the cumulative average firing rate histogram are shown beneath the eye position traces. The averaged SR pause in discharge is evident in the cumulative histogram. Histogram bin width, 10 ms. C, D. Another PrGC unit, similarly illustrated, exhibits a distinct post SR burst for saccades of any amplitude or direction. Similar recording conventions are used in all subsequent illustrations.

**Figure 3** A. Pregeniculate unit in which the SR response consists of a pre- to perisaccadic pause. The eye position traces for saccades to target in darkness are aligned for saccade initiation (dashed lines). The firing rate histogram illustrates the average SR discharge for 77 saccades. In many trials the pause begins prior to saccade initiation. The pause is followed by a prolonged post-saccadic burst. B. Pregeniculate unit that responds with a pre-saccadic increase in its discharge rate, leading to a discharge burst during the saccade. The histogram illustrates the average for 128 saccades made to target in the dark; the raster display for 76 trials is shown.
Figure 4  A pregeniculate unit that pauses selectively for saccades towards the down, left.  
A. The top panel illustrates the average response for 47 saccades, made spontaneously in complete darkness; under these viewing conditions, the average pause duration was 194 ms.  
B. The average response for saccades made towards the up, right; there is no response for saccades in this direction.  
C, D. Directional tuning of the SR pause.  
C. The duration of the pause is plotted as a function of direction for 141 saccades: 90°, 180°, 270° & 360° represent upward, leftward, downward and rightward saccades, respectively.  
D. The cumulative rate histograms for saccades (n = 15-26) made in 8 directions are illustrated.  The maximum duration of the pause is for saccades towards 135°-225°.

Figure 5  Illustration of the timing of saccadic responses in 49 PrGC neurons.  For each unit the average saccade duration (grey bars) is paired with the average response duration (black bars).  All data is aligned for saccade initiation (0 ms).  Various types of PrGC unit responses are represented, including both pauses and bursts.  The variability in latencies and duration of responses relative to the saccade is evident in this representation of the data.  These data are for saccades evoked by the laser target in the dark.

Figure 6  Latency and duration of saccadic responses plotted in association with the saccade duration for each of the 49 PrGC units illustrated in Fig. 5.  For these plots, the average response latency (panel A) or the average duration (response end, panel B) for each unit is paired with the average saccade duration.  The circles represent the response and the squares represent the saccade duration.  The pairs of data points have been
ordered with the response latency or duration increasing towards the right along the abscissa. The zero point along the ordinate represents saccade initiation. A. Although the average saccade duration remains fairly level, ranging from >25 ms to <100 ms, the response latencies vary over a wide range; there is no apparent correlation of response latency with saccade initiation or end. Those points below zero represent pre-saccadic responses, points that fall between zero and the saccade duration represent peri-saccadic responses, and those that fall above the saccade duration point represent post-saccadic responses. Nearly half of the responses are pre- to peri-saccadic. B. Similarly, we found no correlation between the termination of the response and the saccade duration or end time. In this plot the pairs of data points are ordered with response duration increasing towards that right. Again, the saccade duration remains relatively constant, while the response duration varies widely.

**Figure 7** Pregeniculate unit that responds for target pursuit and visual slip. A. This unit exhibits a direction-sensitive response for target pursuit in the dark. The target is oscillating 20°/s along an axis oriented up/right to down/left, at 45° from the horizontal. The eye position and slip velocity traces, and histogram represent the average for 15 cycles of pursuit. The unit responds weakly for target pursuit towards the down/left. This unit was recorded from the left PrGC. B. Response of the unit for target pursuit across an illuminated patterned background is significantly stronger. The traces and histogram are the average for 8 cycles of target pursuit. C. The response of the unit during fixation of the stationary target accompanied by oscillation of the patterned background. The unit responds for visual motion in the up/right direction, opposite in direction to that of the
response during pursuit. The traces and histogram are the average of 12 cycles. Prior to averaging, saccadic events were removed from the eye position recordings.

**Figure 8** Directional tuning of smooth eye movement activity in PrGC neurons. A. The tuning curve for a neuron recorded from the left PrGC that responded with directional selectivity during smooth pursuit of a target oscillating across an illuminated patterned background. The curve was generated using an algorithm fit to data obtained for tracking in each of 8 directions. The average peak response for pursuit in each direction was determined from 12-32 cycles. The vector indicates the preferred direction (down, left) as indicated by the peak of the curve at 32.6 spikes/s. B. The preferred direction of response for 11 units is plotted. In this plot, the vectors are plotted as ipsiversive (towards right side of graph) or contraversive (left). Note that the majority of units are tuned for ipsiversive pursuit.

**Figure 9** Pregeniculate unit that exhibits an eye position-dependent increase in firing rate. A. The discharge of this unit was recorded while the animal fixated a target spot in the dark. The firing rate of the unit is higher for target fixation 15-25º towards the left. B. The firing rate is plotted as a function of horizontal eye position (r = -0.68). C, D. The firing rates of 2 other PrGC units, plotted as a function of horizontal eye position. Although the position dependence of their firing rates is tuned for opposite directions, both units were recorded from the right PrGC. The data shown is for eye position recorded during target fixation in the dark. C. r = 0.87, D. r = -0.65.
Figure 10  Pregeniculate units that respond to illumination of the visual field.  A. The firing rate of this unit was suppressed by visual field illumination. As shown in the bottom panel, illumination of the visual background mediated a tonic decrease in firing rate.  B. Conversely, the firing rate of this unit was increased by illumination of the visual field. These units were recorded along the same electrode track, 50 µm apart, less than 500 µm dorsal to the LGNd. The visual modulation of each unit’s firing rate was mediated binocularly.

Figure 11  Binocular modulation of visual responses.  A. Pregeniculate unit that responded for saccades with a peri-saccadic pause followed by a post-saccadic burst. The response is the average for 77 saccades to a visual target in the dark during binocular viewing. The average burst duration under these viewing conditions is 150 ms.  B. The post-saccadic burst associated with visually guided saccades (binocular viewing) across an illuminated patterned visual field is reduced in amplitude and duration. The average burst duration for 71 saccades across the illuminated background is reduced to 36 ms.  C,D. The response associated with saccades made across the illuminated visual field while viewing monocularly is reduced but not to as great an extent as during binocular viewing. During left eye (panel C) or right eye viewing (panel D) the average burst durations are 81 ms and 79 ms, respectively.  C is the average of 29 saccades; D is the average of 51 saccades.

Figure 12  Pregeniculate unit that exhibits multiple visual and ocular motor signals.  A. Directionally tuned SR response recorded from the right PrGC. The post-SR response is
distinctly stronger for saccades with a rightward component. The traces and firing rate histogram for rightward saccades are the average of 58 saccades to target across the illuminated patterned background. The post-saccadic burst for saccades towards the left (average of 37 saccades) is attenuated. For leftward saccades, the burst is followed by a period during which the firing rate is reduced. B. Although this unit did not respond for target pursuit in the dark, it does respond vigorously for rightward pursuit across the patterned background (right panel). The response of the unit for leftward visual motion during target fixation suggests that this response is due in part to visual slip (left panel). However the unit discharge during pursuit does not correlate perfectly with visual slip. The unit response during target pursuit is due in part to a position dependent increase in firing rate for rightward eye position (panel C), as evidenced by an increased discharge rate that extends partly into the next phase of the cycle (inset). The responses shown are the average of 26 cycles for pursuit across the patterned background and 20 cycles for target fixation. C. Position dependent increase in firing rate. The unit’s firing rate increases for rightward eye position. The vertical lines indicate brief periods of fixation towards the left, during which the discharge of the unit drops. Firing rate is correlated with eye position in the adjacent plot ($r = 0.54$). For this unit, all signals (visual slip, directionally tuned SR response, and eye position dependent firing rate) could support ipsiversive direction of gaze.

**Figure 13** The percentage of response types recorded in the PrGC. A. The percentage of units from the total population of neurons recorded that exhibited either saccadic, smooth pursuit or eye position dependent signals. All units were tested for saccadic
responses; 85% exhibited some type of saccadic response. Among these SR units, 34% of the population was modulated by visual input. Less than 20% of the units responded during smooth eye movements; more than half of these responded to visual motion. All units with saccadic responses were tested for eye position dependent modulation of their firing rates; those that were responsive constituted 18% of the total population. All of these were modulated by visual input. B. The distribution of types of saccadic responses. All saccadic responses were classified as early (pre- or peri-saccadic) or post-saccadic, and all were analyzed to determine if they were directionally tuned. Approximately 67% of the SR units exhibited either early saccadic and/ or directionally tuned responses. C. The convergence of ocular motor signals on SR units in the PrGC. The percentage of SR units that also carried smooth eye movement or visual slip responses, eye position dependent modulation of their firing rates, or both types of responses.

Figure 14 Schematic diagram illustrating the relationship of the PrGC to visual cortical areas and brainstem structures, represented by the pretectal nucleus of the optic tract (NOT) and the superior colliculus. For simplicity, the PrGC is represented as 2 components: the retinorecipient sublayer and the collective non-retinorecipient components. The primary visual and visual association areas of the occipital and parietal cortices project to the PrGC. (The cortical projections to the individual components of the PrGC have not yet been differentiated.) The ocular motor signals recorded in the PrGC may be derived from the parietal projections to the PrGC. In addition, the retinorecipient PrGC receives direct visual input. In this proposed schema, integration of visual input is mediated by projection of the retinorecipient PrGC to relay neurons in the
non-retinorecipient PrGC (grey arrow). Convergence of signals on the relay neurons would provide a basis for the integration of visual and ocular motor signals within the PrGC. These signals can then be relayed to the brainstem via the reciprocal connection of the non-retinorecipient PrGC with the pretectal NOT and superior colliculus. Signals could also be relayed by the projection of the retinorecipient PrGC to the NOT and superior colliculus.
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<td>Directionally Tuned Pause (n=34)</td>
<td>28 ± 67</td>
<td>169 ± 117</td>
<td>17</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Directionally Tuned Burst (n=31)</td>
<td>88 ± 20</td>
<td>174 ± 155</td>
<td>8</td>
<td>14</td>
<td>9</td>
</tr>
</tbody>
</table>
Fig. 1
Fig. 3
Fig. 4
Fig. 5
Fig. 6
Fig. 8
Fig. 10
Fig. 11
Fig. 12
Fig. 13
Fig. 14