Quantitative Assessment of the Timing and Tuning of Visual-Related, Saccade-Related, and Delay Period Activity in Primate Central Thalamus

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Submitted 23 January 2003; accepted in final form 24 April 2003

Wyder, Melanie T., Dino P. Massoglia, and Terrence R. Stanford. Quantitative assessment of the timing and tuning of visual-related, saccade-related, and delay period activity in primate central thalamus. J Neurophysiol 90: 2029–2052, 2003. First published April 30, 2003; 10.1152/jn.00064.2003. This study investigates the visuomotor properties of several nuclei within primate central thalamus. These nuclei, which might be considered components of an oculomotor thalamus (OcTh), are found within and at the borders of the internal medullary lamina. These nuclei have extensive anatomical links to numerous cortical and subcortical visuomotor areas including the frontal eye fields, supplementary eye fields, prefrontal cortex, posterior parietal cortex, caudate, and substantia nigra pars reticulata. Previous single-unit recordings have shown that neurons in OcTh respond during self-paced spontaneous saccades and to visual stimuli in the absence of any specific behavioral requirement, but a thorough account of the activity of these areas in association with voluntary, goal-directed movement is lacking. We recorded activity from single neurons in primate central thalamus during performance of a visually guided delayed saccade task. The sample consisted primarily of neurons from the centrolateral and paracentral intralaminar nuclei and paralaminar regions of the ventral anterior and ventral lateral nuclei. Neurons responsive to sensory, delay, and motor phases of the task were observed in each region, with many neurons modulated during multiple task periods. Across the population, variation in the quality and timing of saccade-contingent activity suggested participation in functions ranging from generating a saccade (presaccadic) to registering its consequences (e.g., efference copy). Finally, many neurons were found to carry spatial information during the delay period, suggesting a role for central thalamus in higher-order aspects of visuomotor control.

INTRODUCTION

Nearly two decades have passed since Schlag and Schlag-Rey published a two-part account of the properties of neurons in primate central thalamus (Schlag and Schlag-Rey 1984; Schlag-Rey and Schlag 1984). Despite some intriguing findings and provocative interpretation, these two reports remain the only full accounts of the visual- and oculomotor-related properties of neurons in a group of central thalamic regions that collectively might be considered to constitute an oculomotor thalamus (OcTh). Oculomotor regions of thalamus include several nuclei within and at the borders of the internal medullary lamina (IML), a band of fibers that roughly bisects the thalamus into medial and lateral halves. Included within Schlag-Rey and Schlag’s original description of areas having gaze-related activity are the paracentral (Pc), centrolateral (CL), and central superior lateral (CSL) nuclei. These 3 nuclei are found within the IML and are considered members of the rostral intralaminar group (Groenewegen and Berendse 1994; Van der Werf et al. 2002). Also included as part of OcTh are regions that border the IML, including paralaminar regions of the mediodorsal (MD), ventral anterior (VA), and ventral lateral (VL) nuclei as well as the lateral dorsal nucleus (LD), which is found at the superior extreme of the IML.

In separate reports, Schlag-Rey and Schlag (1984) and Schlag and Schlag-Rey (1984) provided thorough qualitative accounts of neurons that were active in association with self-paced spontaneous saccades and neurons that were responsive to visual stimulation in the absence of any specific motor requirement. Although rudimentary by today’s standards, the spontaneous saccade and fixation tasks used in these studies revealed neural activity related to visual stimuli, saccades, active fixation, and eye position.

At the time of Schlag and Schlag-Rey’s reports, most published accounts of neurons with visual and/or oculomotor activity were from recordings of the midbrain’s superior colliculus (SC; for review see Sparks 1986), with a handful of studies targeting regions downstream (e.g., pontine gaze centers. Hepp and Henn 1983; King and Fuchs 1979; motor nuclei, Fuchs and Luschei 1970, 1971; Robinson 1970; Schiller 1970) or upstream (e.g., frontal eye fields, Bizzi 1968; Goldberg and Bushnell 1981; Schiller 1980) to the SC. Although clearly visual-related or saccade-related, the properties of neurons recorded in central thalamus were in many ways distinct from those recorded in the SC and downstream structures more directly associated with motor outflow. Comparatively, thalamic response types were more diverse, less stereotyped in their relation to the physical parameters of saccades (e.g., amplitude, direction), and exhibited little or no systematic topography. This, along with the fact that the intralaminar nuclei (ILN) were known to have widespread cortical and subcortical connections, led Schlag and Schlag-Rey to propose a “higher-order” role for signals in oculomotor thalamus. Rather than carry precise information about “what” would occur, Schlag and Schlag-Rey proposed that central thalamic...
signals contributed to determining “when” and “how” a saccade occurred by coordinating the function of cortical visuomotor regions as a saccade was being planned and executed.

Conceptually, at least, Slagl and Schlag-Rey’s postulate of central thalamus as a “controller” seems timely, given recent advances regarding the neural basis of cognitive functions such as attention, working memory, and perceptual-motor decision making (for reviews see Colby and Goldberg 1999; Glimcher 2001; Miller and Cohen 2001; Schall and Thompson 1999).

Electrophysiological studies have greatly expanded knowledge of how frontal eye fields (FEF), supplementary eye fields (SEF), posterior parietal (PPC), prefrontal (PFC), and cingulate cortices function in these capacities. Paralleling studies in cortex, however, has been a growing appreciation for the importance of cortical–subcortical interactions in sensorimotor control. As such, concepts of basal ganglia (Mink 1996; Redgrave et al. 1999) and cerebellar function have been dramatically revised in recent years to accommodate their potential roles in mediating most, if not all, of the aforementioned cognitive functions (Albin et al. 1989, 1995; Graybiel et al. 1994; Hikosaka et al. 2000; Houk et al. 1996; Kim et al. 1994; Middleton and Strick 1994; Mink 1996; Thach 1996).

Although electrophysiological studies of central thalamus remain few, accumulating anatomical evidence continues to strengthen the link between these regions and visuomotor function by placing the ILN and paralaminar regions of MD, VA, and VL at the center of several putative computational loops. Thalamocortical loops consisting of reciprocal connections with FEF, SEF, PPC, and PFC have been established (see Groenewegen and Berendse 1994; Jones 1985; Macchi and Bentivoglio 1986 for reviews). Paralaminar VA is an obligatory synapse in the basal ganglia “oculomotor loop” (Alexander et al. 1986), which originates within the FEF and SEF (Lynch et al. 1996; Shook et al. 1991), flows through the caudate nucleus, the substantia nigra pars reticulata (SNr), and thalamus [ventral anterior nucleus (VAmc)] before returning to its point of cortical origin. Along with cortical terminations, the anterior intralaminar nuclei and paralaminar regions of VA and VL (McFarland and Haber 2000) project to regions in the caudate nucleus that are also targeted by FEF and SEF, a projection that may serve to modulate activity within the so-called oculomotor loop (see Groenewegen and Berendse 1994 for review). A projection from paralaminar MD to FEF is known to carry information from the SC (Sommer and Wurtz 1998, 2002) and may thus be the final link in a cortico–subcortical loop that originates and returns to FEF (FEF–SC–MD–FEF). OcTh also mediates the influence of deep cerebellar nuclei on cortical activity. The gaze-related cerebello-thalamic projection arises from the dentate nucleus and terminates in paralaminar VL (Area X of Olszewski) that in turn projects to both the FEF and the SEF (Lynch et al. 1994, 1996; Shook et al. 1991).

Despite compelling anatomical evidence of a central thalamic role in visuomotor control, little is known about the visuomotor properties of neurons in these regions. Only very recently have a few studies examined the activity of these neurons using controlled behavioral tasks. Although not in the context of a saccadic task, recordings from the centre median–parafascicular complex (Cm–Pf) of the caudal intralaminar group indicate that neurons in this region represent behaviorally relevant sensory stimuli (Matsumoto et al. 2001) and may participate in attentional orienting (Minamimoto and Kimura 2002). Most recently, Tanibuchi and Goldman-Rakic (2003) reported that neurons in MD show spatially selective activity in the context of visually guided and memory-guided saccade tasks, a finding that is consistent with known connections between MD and PFC.

In this study we systematically evaluated the capacity for central thalamic neurons to represent information relevant to the performance of goal-directed saccadic eye movements. Recordings were concentrated in areas previously investigated by Slagl and Schlag-Rey (1984a,b), including paralaminar regions of the VA and VL nuclei along with nuclei of the IML. In contrast to the original studies of these regions, we used a visually guided delayed saccade task. This task couples a specific sensory stimulus, by an instructed delay, to a specific saccadic response. This task readily distinguishes between the sensory-contingent and saccade-related activities of individual neurons and permits classification based on their conjunction. Determining whether a neuron is visual-related, motor-related, or visuomotor is relevant for understanding the processing stage or stages to which it contributes. Having identified sensory- and motor-related response components, we further characterized neurons by quantifying both the timing and spatial selectivity of these components.

The delayed saccade task also permitted evaluation of each neuron’s capacity to maintain task-relevant information throughout an instructed delay. Spatially selective “delay-period” activity may be the hallmark of a neuron with the potential to participate in “higher-order” aspects of sensorimotor function. In numerous visuomotor regions, such activity has been associated with the neural correlate of factors such as movement selection (Glimcher and Sparks 1992), motor planning (Barash et al. 1991a,b; Bracewell et al. 1996; Mazzoni et al. 1996; see Andersen 1995 for review), spatial attention (see Colby and Goldberg 1999 for review), and perceptual judgment (see Glimcher 2001; Schall and Thompson 1999; Shadlen and Newsome 1996 for reviews). We determined whether—and if so, with what fidelity—thalamic neurons represented spatial information throughout the imposed delay.

In brief we found activity in central thalamus to represent each phase of the visually guided delayed–saccade task with many constituent neurons modulated in association with more than one task period. Across the sample, considerable variability in the timing and spatial selectivity of visual- and saccade-related responses suggested a range of possible functions. We also report that a significant number of neurons were found to carry spatial information throughout the instructed delay period, a finding that supports the idea that central thalamus participates in higher-order aspects of visuomotor control. Preliminary versions of these results have appeared in abstract form (Massoglia et al. 2001; Wyder and Stanford 2000; Wyder et al. 2001).

METHODS

Surgical procedures

All surgical and experimental protocols complied with the National Institutes of Health Guide for the Care and Use of Laboratory Animals, USDA regulations, and the policies set forth by the Wake Forest University School of Medicine Animal Care and Use Committee (ACUC). Three rhesus monkeys (Macaca mulatta) were prepared for

J Neurophysiol • VOL 90 • SEPTEMBER 2003 • www.jn.org
chronic single-unit recording. Each monkey underwent two sterile surgical procedures while under general isoflurane anesthesia. During the first surgery, an MRI-compatible titanium post was attached to the skull using titanium screws and orthopedic bone cement. Also at this time, a preformed loop of Teflon-coated stainless steel wire (eye coil) was implanted beneath the conjunctiva to circumscribe the cornea of one eye (Judge et al. 1980). During subsequent training/recording sessions, the post served to restrain the monkey’s head, whereas the eye coil provided an analog signal of eye position (Fuchs and Robinson 1966; Robinson 1963). Recovery from the initial surgery required 2–4 wk, during which time analgesics and antibiotics were administered as required.

Fully recovered animals were trained on the behavioral task (see following text). Once trained to a criterion level of performance, a second surgery was performed to place an MRI-compatible recording cylinder (Crist Instrument) over the oculomotor thalamus (OcTh). A presurgical MRI was carried out to optimize the stereotaxic coordinates of the cylinder for individual monkeys. The recording cylinder was positioned over a small craniotomy (about 15 mm diameter) and secured with titanium screws and bone cement. Daily recording sessions began on full recovery (2–3 wk).

Recording procedures

Eye position was recorded using the search coil method (Fuchs and Robinson 1966; Robinson 1963). Briefly, the monkey sat in a primate chair with head restrained at the center of a pair of orthogonal (horizontal and vertical) magnetic fields. The magnetic fields induced current to flow within the surgically implanted eye coil. This current, when decomposed into horizontal and vertical components, yielded analog signals proportional to the angular relationships between the eye coil and the horizontal and vertical magnetic fields, respectively (i.e., eye position). Horizontal and vertical eye positions were sampled and stored at 500 Hz.

Neural activity was recorded using parylene-coated, tungsten microelectrodes (Micro Probe) having impedances between 1.0 and 1.5 MΩ at 1 kHz. Activity was amplified, filtered (300 Hz to 4 kHz), and monitored using an oscilloscope and an audio monitor. The action potentials of single neurons were isolated using a time/amplitude window discriminator and spike times stored at a resolution of 10 μs. Electrodes were advanced through a dura-piercing cannula and advanced to OcTh by hydraulic microdrive. Generally, the electrode was advanced rapidly to 15 mm below the surface of the dura and then more slowly to detect landmark changes in background activity. A ‘quiet’ period as the electrode passed through the lateral ventricle was followed by a return of activity on entry into dorsal thalamus. Within the thalamus, oculomotor regions were identified by observing/listening for modulations that coincided with task events (see Experimental design, below). We recorded from any isolated neuron that appeared to be modulated in association with any phase of the task.

Experimental design

During training and subsequent recording sessions, monkeys were seated in a primate chair in a very dimly lit room. The stimulus display consisted of an array of light-emitting diodes (LEDs). The distance between adjacent LEDs was either 1 or 2 in., which, at a viewing distance of 57 in., corresponded to 1 or 2° of visual angle (Cartesian coordinates), respectively. Maximum horizontal and vertical stimulus eccentricities were 24 and 21°, respectively. Standard operant methods were used to train monkeys to look toward visual targets for liquid reward (drop of water or juice). Neural data presented in this report were collected primarily in association with performance of a visually guided delayed-saccade task, diagrammed in Fig. 1. Each trial began with the presentation of a central fixation stimulus (left), which the monkey had to acquire within 500 ms. After a variable interval (300–700 ms), a second stimulus was illuminated at an eccentric location (middle). The monkey was required to withhold eye movement to the eccentric stimulus until the fixation light was extinguished (GO signal, right). This interval, the delay period, ranged from 500 to 1000 ms. Once given the GO signal, the monkey was required to look to the target within 500 ms and maintain fixation on the target for an additional fixed interval (200 or 500 ms) to obtain a liquid reward.

A majority of OcTh neurons were tested for direction selectivity by choosing targets from a circular array of eight target locations. The 8 locations were spaced equally (at 45°) on the circumference of an imaginary circle with 0° (360°) corresponding to straight right. Because LEDs were organized in a Cartesian coordinate frame the polar coordinates of target LEDs were not exact, but chosen to best approximate the desired polar coordinates. Target direction was randomized across trials and presented within blocks of fixed eccentricity at either 6, 10, or 20° (i.e., the radius of the array). The eccentricity that yielded the highest level of activity was estimated on-line and chosen for the first block of trials. Time permitting, direction tuning was tested for a second or third eccentricity. A minority (30/162) of neurons was not tested with the circular target array. For these neurons, targets were presented within the receptive/movement field as estimated on-line by the experimenter.

Data analysis

In the context of the delayed saccade task (see Fig. 1), a prototypical visual-motor neuron generates an early transient burst of activity in response to the sensory stimulus and, after the imposed delay, a motor-related burst associated with the saccade (e.g., see Fig. 4A). In addition, sustained activation that intervenes between the sensory and motor-related bursts is not uncommon (e.g., see Fig. 4A). Analyses were tailored to estimate the direction selectivity and the time of occurrence of sensory and motor-related modulations.

Attempts to describe sensory or motor-related activity with unitary estimates of timing and tuning is complicated by the fact that these response features are not independent. For example, direction selectivity may be different at different times during the course of a trial. Similarly, when (or if) a neuron fires in relation to either a sensory or motor event most often depends on where the target is in space. Ideally, indices of direction selectivity (e.g., tuning width, preferred direction) would be calculated for intervals during which activity is most strongly modulated in relation to task-defined events. Similarly, it is arguable that the most meaningful estimates of the timing (e.g., onset, duration) of event-related modulations are those made for targets/movements that are consistent with the neuron’s tuning preference. Toward this end, a 3-step procedure was used to assess direction selectivity and timing for both visual and motor-related
modulations. First, the interval with the strongest sensory or motor-related activity was identified. Next, direction tuning was estimated based on activity within this interval. Finally, the timing of sensory or motor-related modulations was estimated based on the “preferred” direction derived in Step 2. Figures 2 and 3 illustrate this 3-step method for the saccade-related discharge of a single OcTh neuron.

**Direction tuning**

Figure 2A illustrates average instantaneous firing frequency histograms (bin width = 2 ms) for activity associated with saccades to each of 8 visual targets. The 8 targets were spaced equally at 45° on the circumference of an imaginary circle with 0° (360°) corresponding to straight right. Proceeding counterclockwise, 90, 180, and 270° corresponded to up, left, and down, respectively. Target eccentricity (i.e., radius) was 10° in this example. Each histogram represents the average of multiple trials (N) for movements to a particular target with activity for all trials aligned on saccade onset (t = 0) before averaging. For each target direction, a moving window was used to find the 100-ms epoch for which average firing frequency was highest (Step 1). Searching from 250 ms before to 400 ms after saccade onset (dashed vertical lines), the average firing rate was computed across successive groups of 50 bins (100 ms), each time incrementing the window by 1 bin (2 ms). For each direction, the epoch found to have the highest average firing rate is bracketed by solid vertical lines. Of the 8 epochs defined by this method, that with the highest average firing frequency was selected for the purpose of estimating the parameters of direction tuning (Step 2). In this example, the interval with the highest average firing (gray highlight) corresponded to the time period from 58 ms before saccade onset to 42 ms after saccade onset for movements to the 90° (up) target. The polar plot of Fig. 2B summarizes the relationship between mean firing rate and target direction for this interval that, as expected, shows a strong bias for the 90° target.

Direction tuning was assessed based on the interval identified as having the highest average firing frequency (see Step 2 above). The firing rate within this interval was determined for saccades to each of the 8 targets and plots of firing rate versus saccade direction were fit with a Gaussian function (Fig. 2C). Least-squares fit of the Gaussian function

\[ f(\theta) = C + Re^{-\frac{1}{2}(\theta - b)^2} \]

yielded parameter estimates corresponding to peak (maximum − baseline) average firing rate (R), preferred direction (b), tuning index (a), and baseline firing rate (C). For this example, R, b, a, and C, are 126 spikes/s, 83°, 55°, and 21 spikes/s, respectively. Parameter estimates were accepted for fits in which the correlation coefficient (r) was statistically significant at \( P < 0.01 \).

With the appropriate modifications, the same method was used to evaluate the tuning of decreases in activity. Accordingly, the initial search returned the 100-ms period with the lowest average firing rate (Step 1), and the Gaussian tuning function (Step 2) specified an inverse peak.

**Timing**

For each neuron, the timing of task-related modulations (Step 3) was estimated from average activity profiles that were based on activity for the 3 directions defining the peak of the Gaussian tuning function. Accordingly, for the example in Fig. 2, movements to the 90, 45, and 135° targets were included in the timing analysis (Fig. 2C, gray highlight). The resulting averaged histogram, synchronized on saccade onset (t = 0) is shown in Fig. 3A. With the appropriate average frequency histogram generated, the goal was to identify a statistically significant change in average firing rate. The first step was to choose an appropriate interval for estimating a baseline firing rate. For motor-related activity, we used a 100-ms interval beginning 350
Tuning and timing of visual activity

Figures 2 and 3 illustrate our methods for evaluating motor-related activity. The same 3-step method, with appropriate alterations, was used to quantify sensory-linked increases and decreases in activity. For this, rasters were aligned on target onset rather than saccade onset. The initial search was performed over a 300 ms interval beginning at target onset. Gaussian functions were fit to plots of average firing rate versus target direction, not saccade direction, and the baseline period chosen for the timing analysis corresponded to a period of stable fixation 100 ms before target onset. The bin by bin search for statistically significant modulations in activity proceeded from the time of target onset to the end of the delay period (GO signal).

Modulation index

To compare the strength of sensory- and motor-related modulations for neurons that responded in association with both events (n = 71), a modulation index (MI) was calculated as follows

\[ MI = \frac{(V - M)}{(V + M)} \]

where V and M are the average firing rates during the visual and motor related periods, respectively. The MI could range between -1 and 1, with positive values corresponding to stronger sensory-related modulation in activity and negative values to stronger motor-related modulation in activity. For tuned neurons, target directions and intervals used to calculate mean firing rate for the visual and motor epochs were identical to those defined by the tuning and timing methods described above. For neurons that lacked direction-tuning, epochs were defined by applying the timing analysis to the average response for all directions.

Histology

During a single, final recording session, electrolytic lesions were made by passing 10 μA for 20 s at several locations. Lesion sites were chosen to mark the locations and boundaries of the regions where neurons were recorded. One week postlesion, monkeys were sedated with ketamine, administered an overdose of sodium pentobarbital, exsanguinated, and perfused with heparanized saline and 4% paraf-
maldehyde. The brain was blocked, equilibrated in 30% sucrose, and frozen sections were cut at 50-μm thickness. Every other section was mounted and stained for Nissl substance (cresyl violet).

RESULTS

Results are based on 162 single units recorded from the nuclei composing the OcTh (see Fig. 21 for unit locations). Neurons were recorded bilaterally from two monkeys and from a single hemisphere in a third monkey. Each neuron was studied while the monkey performed the visually guided delayed saccade task depicted in Fig. 1. By decoupling the time of target appearance from the time of saccade onset, the delayed saccade paradigm revealed neurons that were differentially sensitive to the sensory and motor phases of the task. Parsing at the most general level, an OcTh neuron fell into one of 3 categories: “visual-related,” “motor-related,” or “visual-motor,” depending on the combination of visual- and motor-related modulation displayed. “Visual-related” refers to neurons that showed increases or decreases exclusively in association with the stimulus; “motor-related,” to neurons that were only modulated near the time of the saccade; and “visual-motor,” to those that showed both response components. Motor-related neurons constituted the largest group (81/162; 50%), with visual-motor neurons nearly as common (71/162; 44%). Neurons modulated solely during the stimulus period (10/162; 6%) were rarely encountered. This simple classification scheme based on sensory- and motor-related response components serves as a convenient and conventional starting point, although it fails to capture the scope of various task-related activities observed in OcTh. A better account of the breadth of OcTh activity is given in the following sections in which quantitative and qualitative descriptions of the visual-, motor-related, and delay-period activities are provided.

Figure 4 illustrates the task-related activity profile of a representative visual-motor neuron. In most respects, the activity profile of this OcTh neuron is qualitatively similar to that for visual-motor neurons found in areas such as the SC or FEF (see DISCUSSION). In Fig. 4A, rasters (top) and average frequency histograms (bottom) for the same set of trials are shown synchronized both to target onset (left) and saccade onset (right). This neuron displayed two transient bursts of activity, one stimulus-linked and one motor-linked. It is worth noting that, given typical reaction times in the range of 150–300 ms, these bursts could not have been resolved had they been recorded in the context of a simple reaction time task. Along with permitting distinctions between sensory- and motor-related modulations, the delayed saccade task reveals a neuron’s capacity to carry information throughout an instructed delay (see INTRODUCTION). In this example, delay period activation is evident as sustained and increasing activity that effectively bridges the gap between the sensory and motor-related bursts.

A primary objective of this study was to provide a quantitative characterization of neurons in OcTh that would be comparable to those that exist for more commonly and more recently studied visuomotor regions. Toward this end, we focused primarily on the essential measures of timing and spatial tuning for visual- and motor-related modulations (see METHODS). For this example neuron, recorded in the left hemisphere, the sensory burst (Fig. 4A, left) began 68 ms after stimulus onset (t = 0) and endured for 60 ms (i.e., to t = 128 ms; second horizontal black bar). The motor-related burst (Fig. 4A, right) began 64 ms before saccade onset, reached a peak coincident with saccade onset, and declined with saccade execution, returning to baseline near the end of the saccade at a post-saccadic time of 46 ms (second horizontal black bar). Direction tuning was assessed separately for the sensory and motor bursts and the corresponding tuning functions are shown below for the visual-related (Fig. 4B, left; horizontal gray bar in A) and saccade-related periods (Fig. 4B, right; horizontal gray bar in A). Estimates of preferred direction were reasonably consistent at 68° for the visual- and 83° for the motor-related transient, in both cases indicating a preference for stimuli/saccades in the upper quadrant of the contralateral (right) space. Tuning for the visual epoch (35°) was somewhat sharper than that for the motor epoch (55°). Finally, motor-related activity was considerably more vigorous than sensory-related activity as quantified by the estimates of amplitude provided by the fitted Gaussians (visual = 45 spikes/s; motor = 126 spikes/s).

Figure 5 plots the distributions of timing and direction tuning estimates for the entire sample. In general we found the onset times of visual and motor-related modulations to vary considerably ranges, but each distribution to be largely defined by a single mode. As for the example neuron just described, the majority of stimulus-related onset times cluster tightly near a poststimulus time of 100 ms (Fig. 5A). Considering only this primary mode (n = 72; onset <300 ms) and excluding the minor mode consisting of 9 neurons with onset times exceeding 300 ms (see following text, Visual-related activity, for discussion), the mean poststimulus latency was
with the radial target array with 83 (67%) well neurons with motor-related modulations, 124 were tested estimated by least-squares target array. Of these, 46 (65%) showed significant tuning as common as presaccadic (72/152: 47%) modulations in activity. As stated in METHODS, the search for a statistically significant modulation in activity proceeded forward in time from the time of visual stimulus onset to the end of the delay period (a minimum of 500 ms). It can be reasonably argued that the few neurons (n = 9) with very long latencies (>300 ms) are not “visual-related” in any meaningful sense. Inspection of these few examples suggested that these modulations anticipated later saccade-contingent modulations. As noted above, the cluster of onset times near 100 ms is more consistent with that which has been reported for sensory-related activity in other visuomotor areas (see DISCUSSION).

Examples of individual neurons drawn from this population are shown in Fig. 6 to illustrate some of the qualitative features of these neurons. For each neuron, Fig. 6, A–I illustrates rasters and average firing frequency histograms aligned on stimulus onset and composed of responses to preferred direction stimuli (see legend for details). As was true for the example of Fig. 4, many neurons showed a relatively high-frequency transient that was tightly linked to the stimulus onset (Fig. 6, A and B). For others, the transient was less pronounced and, as evident in the rasters, occurred less reliably (Fig. 6, C and D), and for still others, the transient was largely absent (Fig. 6, E and F).

The neurons depicted in Fig. 6, A–F show fairly substantial differences along several dimensions (e.g., onset time, transient duration, transient strength, etc.); however, attempts to define classes of neurons based on any single quantifiable metric were not successful. Rather, the variability observed in any given measure was more suggestive of a response continuum than a category boundary. As noted, one clear categorical distinction among sensory-contingent modulations was whether activity

![Image of population histograms of timing and tuning estimates.](image-url)

**Visual-related activity**

Other than response polarity, the summary histograms of Fig. 5, A–C do not provide a strong basis for categorical distinctions among OcTh neurons on the basis of visual-related modulations in activity. As stated in METHODS, the search for a statistically significant modulation in activity proceeded forward in time from the time of visual stimulus onset to the end of the delay period (a minimum of 500 ms). It can be reasonably argued that the few neurons (n = 9) with very long latencies (>300 ms) are not “visual-related” in any meaningful sense. Inspection of these few examples suggested that these modulations anticipated later saccade-contingent modulations. As noted above, the cluster of onset times near 100 ms is more consistent with that which has been reported for sensory-related activity in other visuomotor areas (see DISCUSSION). Examples of individual neurons drawn from this population are shown in Fig. 6 to illustrate some of the qualitative features of these neurons. For each neuron, Fig. 6, A–I illustrates rasters and average firing frequency histograms aligned on stimulus onset and composed of responses to preferred direction stimuli (see legend for details). As was true for the example of Fig. 4, many neurons showed a relatively high-frequency transient that was tightly linked to the stimulus onset (Fig. 6, A and B). For others, the transient was less pronounced and, as evident in the rasters, occurred less reliably (Fig. 6, C and D), and for still others, the transient was largely absent (Fig. 6, E and F).

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increased or decreased. Examples of three neurons with sensory-linked decreases in activity are shown in Fig. 6, G–I. As noted above, just under one-quarter (23%) of the visual-related modulations were decreases in firing rate. Like increases, decreases were varied with some clearly transient (Fig. 6I), others less obviously so (Fig. 6H), and still others clearly sustained (Fig. 6G). Although the timing and tuning distributions for decreases overlapped those of increases (see Fig. 5), decreases were somewhat less likely to be fit by a Gaussian function (decreases: 10/19; 53%; increases: 36/52; 70%) and, when fit, were more broadly tuned for direction (decreases: $38 \pm 29^\circ$; increases: $38 \pm 29^\circ$ t-test, $P < 0.001$).

Although differences in onset latency did not suggest categories of visual response, neurons clearly differed with respect to the quality (i.e., transient/sustained) of the response. Figure 7 summarizes the time course of visual-related modulations for the 72 neurons for which poststimulus modulation occurred within 300 ms. Each neuron is represented as a horizontal line with the start of the line indicating the earliest time (i.e., onset) at which activity differed from baseline (above for increases, below for decreases). Line endings signify times at which activity returned to baseline levels unless occurring at 500 or 750 ms (vertical dashed lines show delay period end), in which case firing was significantly above (increases) or below (decreases) baseline throughout the entire delay period. When present, a dot signifies the time at which a higher-frequency transient gave way to a lower level of firing. The offset times of high-frequency transients were determined with the same procedure used for determining onset times (see METHODS) simply by choosing a posttransient baseline period and searching backward in time for a significant increase above baseline.

Figure 7 parses neurons into 3 groups. Within a given group, neurons are arranged from bottom to top in order of increasing latency. Forty-six of the 56 neurons that were excited by visual stimuli showed an initial transient response component (1–46 on plot). For many ($n = 30$), the relatively high-frequency transient gave way to a lower frequency of sustained activity that often persisted throughout the delay period (e.g., Fig. 6B) and that, in some cases, was preceded by a brief pause in firing (e.g., Fig. 6A). We found no consistent qualitative or quantitative differences between neurons with transient-only and transient-sustained responses. Ten neurons (47–56; shaded) clearly lacked a transient component but demonstrated low-frequency sustained activity throughout the delay period (e.g., Fig. 6F). Neurons 57–72 (unshaded) decreased their activity in association with visual stimuli. Decreases, like increases, could be either transient (e.g., Fig. 6I) or sustained (e.g., Fig. 6G).

**Effect of target eccentricity on tuning for direction**

As described in METHODS, our primary index of spatial selectivity was direction tuning and we attempted to examine direction selectivity at what was estimated on-line to be the most effective of 3 possible eccentricities, 6, 10, and 20°.

### TABLE 1. Number of neurons directionally tuned and with ipsilateral or contralateral preferred directions, shown separately for visual and motor increases and decreases

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean Onset</th>
<th>Number Tested With Radial Targets</th>
<th>Number Fit With Gaussian</th>
<th>Number Ipsilateral</th>
<th>Number Contralateral</th>
<th>Mean Tuning Width</th>
</tr>
</thead>
<tbody>
<tr>
<td>All visual</td>
<td>81</td>
<td>141</td>
<td>71</td>
<td>46 (65)</td>
<td>5 (11)</td>
<td>41 (89)</td>
<td>48</td>
</tr>
<tr>
<td>Visual increase</td>
<td>62 (77)</td>
<td>121</td>
<td>52</td>
<td>36 (69)</td>
<td>3 (8)</td>
<td>33 (92)</td>
<td>38</td>
</tr>
<tr>
<td>Visual decrease</td>
<td>19 (23)</td>
<td>206</td>
<td>19</td>
<td>10 (53)</td>
<td>2 (20)</td>
<td>8 (80)</td>
<td>83</td>
</tr>
<tr>
<td>All motor</td>
<td>152</td>
<td>27</td>
<td>124</td>
<td>83 (67)</td>
<td>37 (45)</td>
<td>46 (55)</td>
<td>55</td>
</tr>
<tr>
<td>Motor increase</td>
<td>109 (72)</td>
<td>11</td>
<td>87</td>
<td>69 (78)</td>
<td>28 (41)</td>
<td>41 (59)</td>
<td>48</td>
</tr>
<tr>
<td>Motor decrease</td>
<td>43 (28)</td>
<td>68</td>
<td>37</td>
<td>14 (38)</td>
<td>9 (64)</td>
<td>5 (36)</td>
<td>87</td>
</tr>
</tbody>
</table>

Percentages are shown in parentheses. Ipsi, ipsiversive; contra, contraversive.
(a few neurons were examined at $4^\circ$). Nineteen visually responsive neurons were examined at multiple target eccentricities for all 8 directions with 8 neurons tested at 2, and 11 neurons tested at 3 eccentricities. Of these 19 cells, 13 were significantly tuned for direction at more than one eccentricity with 2 neurons tuned at 3 eccentricities, 11 at 2 eccentricities, 4 at a single eccentricity, and 2 not tuned. Comparison of Gaussian tuning functions, shown in Fig. 8 for 8 different neurons, illustrates several points. First, direction-selective OcTh neurons are also selective for eccentricity. Considering the peaks of the Gaussian tuning functions, it is apparent that firing rate varied with stimulus eccentricity for most of these example neurons and, furthermore, that different OcTh neurons had different preferred eccentricities. The neuron in Fig. 8A, for example, fired most strongly at an eccentricity of $6^\circ$ (dotted line) with firing rate decreasing monotonically with increasing target eccentricity (solid line: $10^\circ$; dashed line: $20^\circ$). In contrast, the neuron depicted in Fig. 8B responded most strongly at $20^\circ$, the largest eccentricity that we could test with the circular stimulus array (LED board $24 \times 21^\circ$). For these two neurons, the firing rate loosely approximated a multiplicative function of target direction and target eccentricity, the primary effect being on the amplitude of the Gaussian tuning function with other parameters (preferred direction, baseline, tuning index) relatively unchanged. For other neurons, changes in amplitude, tuning index, and baseline were present in varying combinations and to varying degrees, although preferred directions remained fairly congruent across eccentricity.

The examples shown in Fig. 8 suggest that the direction selectivity of OcTh neurons was often the product of both excitation and suppression. The baseline level of activity, obtained during steady fixation before stimulus onset, is indicated as a horizontal dashed line on each of the plots in Fig. 8. Note that, for several of these neurons, activity evoked by stimuli at nonpreferred directions was reduced compared with prestimulus levels (Figs. 8, A, B, D, and E). A somewhat analogous (opposite in sign) phenomenon was observed for neurons that were predominantly suppressed by visual stimulation. Thus for example, the tuning functions shown in Fig. 8G, H are the product of suppression of background activity. In Fig. 8G, tuning at $10^\circ$ eccentricity is the result of suppression at just 3 directions in contralateral space (unshaded), whereas at an eccentricity of $20^\circ$, suppression is much more powerful and extends to all target directions (i.e., $360^\circ$). A similar result is shown in Fig. 8H for a second neuron.
these could be either pre- or postsaccadic. In contrast to visual-related modulations could be either increases or decreases and thus for example, the neurons in Fig. 9, A–C were primarily presaccadic, fired maximally near the time of saccade onset and ceased firing before or near the time of saccade offset. In contrast, those in Fig. 9, D–F began firing later (at, or just after saccade onset), attained peak rate near the time of saccade termination and declined thereafter. Finally, those depicted in Fig. 9, G and H did not begin to fire until approximately 20–40 ms after the saccade had ended.

The relatively high incidence of post saccadic activity in OcTh is particularly interesting. Such late activity could serve a multitude of functions as putative feedback carrying information about the ongoing or recently completed saccade (see DISCUSSION). Alternatively, the possibility that this activity could be related to something other than the saccade itself had to be considered. Visually guided delayed saccades were made to an LED illuminated against a uniformly black background in a very dimly lit room. Thus one possibility is that activity was the consequence of a saccade that brought the visual stimulus into or through the receptive field. Given an average visual response latency near 100 ms and minimum latencies on the order of 50 ms (see Figs. 5 and 7), this is a valid possibility only for relatively late postsaccadic activity such as that shown in Fig. 9, G and H, which begins after saccade offset. Given these afferent delays, activity that began during a saccade (e.g., Fig. 9, E and F) occurred too early to have been visually evoked. For those with late postsaccadic activation, we compared responses for visually guided saccades and saccades to remembered locations in which the target was extinguished before saccade onset. Examples of two postsaccadic neurons that responded identically for visually guided (gray) and remembered saccades (black) are shown in Fig. 10, A and B (red ticks; saccade offset). Rather than a saccade-induced sensory response, these neurons appeared to carry a late saccade-related signal. The neuron depicted in Fig. 10B reliably fired after small corrective saccades as well and these bursts are evident between 200 to 300 ms after the primary saccade on visually guided trials (correctives rarely occurred on memory trials). In all, there were 23 neurons with a postsaccadic burst that was temporally coupled to the saccade. Of these, 20 were examined for both visual and memory trials with 12/20 appar-

**FIG. 8.** Comparison of visual-period Gaussian tuning functions for different target eccentricities for 8 different neurons. Spike rate is shown on y-axis and target direction is shown on x-axis with 0, 90, 180, and 270° corresponding to straight right, straight up, straight left, and straight down positions, respectively. Shaded portions of graphs indicate ipsilateral space. On each graph, x-axis with 0, 90, 180, and 270° (open square), 10° dashed line. Symbols indicate responses to 6° (open circle), 10° (filled circle), or 20° (open circle) targets; corresponding least-squares fit Gaussian functions (r > 0.83, P < 0.01) are also shown.

**Motor-related activity**

As shown in the summary histograms of Fig. 5, saccade-related modulations could be either increases or decreases and these could be either pre- or postsaccadic. In contrast to visual-related modulations, the timing of the activity with respect to the saccade can clearly be the basis for a functional distinction among neurons with motor-related activity. Examples of 8 neurons, each with a saccade-related transient, are shown in Fig. 9. For each neuron, rasters corresponding to saccades in the preferred direction are shown aligned on saccade onset (black vertical line; t = 0). Tick marks indicating the times of the “GO” signal (i.e., fixation offset, green tick) and saccade offset (red ticks) are shown for each trial. Proceeding from Fig. 9, A–H, the onset of the saccade-related burst becomes progressively later, ranging from 124 ms before saccade onset (Fig. 9A) to 68 ms after saccade onset (Fig. 9H). As suggested by the summary histograms (see Fig. 5), the intervening examples (Fig. 9, B–G) illustrate that pre- and postsaccadic modulation did not represent a simple dichotomy; rather, the temporal relationship between saccade onset and the burst onset varied continuously. The same could be said about other temporal parameters of the transient. Note that, as a group, neither the time of peak firing nor the time of burst offset bore any consistent relationship to the onset or offset of the saccade.
ently motor-related as evidenced by roughly equivalent activity for stimulus-present and stimulus-absent trials.

For 8 neurons, the postaccadic burst was attenuated or completely absent for saccades to remembered target locations. Although it is not possible to rule out the “sensory” explanation for these neurons, we observed that neurons with pronounced differences in firing on target-present and target-absent trials were just as likely to be presaccadic (11/19) as postsaccadic (8/19). For example, the neurons depicted in Fig. 10, it is not uncommon for the motor-related modulations of OcTh neurons. For instance, 5 of the examples shown in Fig. 9 had ipsilateral preferred directions (Fig. 9, C and D) and 3 had contralateral preferred directions (Fig. 9, C–E). Nothing among these examples would suggest any quantitative (e.g., timing) or qualitative differences between ipsilateral- and contralateral-tuned neurons. To verify this, we compared OcTh neurons with contralateral (n = 46) and ipsilateral (n = 37) preferred directions to determine whether they differed with respect to motor-related timing or tuning. Neither mean onset time (contra: 10.7 ± 100.4 ms; ipsi: –7.0 ± 87.5 ms) nor tuning index (contra: 52.6 ± 25.6°; ipsi: 57.6 ± 43°) was significantly different for neurons with contralateral and ipsilateral preferred directions.

Motor decreases

Of all saccade-related modulations, 43 (28%) were decreases. Mean onset time for decreases (68 ± 132 ms) was not significantly different from that for increases (11 ± 103 ms), with both slightly postsaccadic. However, as was true for visual-related activity, the firing rate versus direction functions were less likely to be fit with a Gaussian for decreases (14/37; 38%) than for increases in activity (69/87; 78%) and, when fit, decreases tended to be more broadly tuned (decreases: 87 ± 29°; increases: 48 ± 32°; t-test, P < 0.001). Moreover, compared with increases, a somewhat higher proportion of motor-related decreases (9/14; 64%) had ipsilateral preferred directions (28/69; 41%) (see Fig. 5; Table 1).

Contralateral versus ipsilateral

Presaccadic neurons in principally visuomotor areas like the SC and FEF have almost exclusively contralateral preferred directions (see DISCUSSION). As shown above, ipsilateral tuning was not uncommon for the motor-related modulations of OcTh neurons. For instance, 5 of the examples shown in Fig. 9 had ipsilateral preferred directions (Fig. 9, A, B, and F–H) and 3 had contralateral preferred directions (Fig. 9, C–E). Nothing among these examples would suggest any quantitative (e.g., timing) or qualitative differences between ipsilateral- and contralateral-tuned neurons. To verify this, we compared OcTh neurons with contralateral (n = 46) and ipsilateral (n = 37) preferred directions to determine whether they differed with respect to motor-related timing or tuning. Neither mean onset time (contra: 10.7 ± 100.4 ms; ipsi: –7.0 ± 87.5 ms) nor tuning index (contra: 52.6 ± 25.6°; ipsi: 57.6 ± 43°) was significantly different for neurons with contralateral and ipsilateral preferred directions.
Effect of target eccentricity on tuning for direction

Twenty-six neurons with direction-selective motor-related activity were examined for effects of target eccentricity. Nine neurons were tested at 2, and 17 neurons at 3 target eccentricities. Of these, 20 met the criterion for Gaussian direction tuning at more than one eccentricity with 6 neurons tuned for direction at 3 eccentricities, 14 at 2 eccentricities, and 6 at a single eccentricity. Figure 11 compares the motor-related direction tuning functions obtained at different eccentricities for 6 OcTh neurons. As was true for visual-related activity, saccade-related modulations showed selectivity for eccentricity with a primary effect on firing rate (e.g., Fig. 11A). When significant direction tuning was present at multiple eccentricities, the parameter estimates (e.g., preferred direction) were largely consistent. The example also illustrates that, as expected, tuning for direction breaks down for eccentricities that fail to evoke adequate levels of activity (Fig. 11, B, D, and F; unfitted data points).

Transient and sustained timing

The examples (see Figs. 9 and 10) shown to this point have emphasized saccade-related transient increases, and appropriately so. Most saccade-contingent modulations were increases (109/162; 67%) and the majority (77/109; 71%) of these were transient or had a pronounced transient component. Figure 12A summarizes the timing of neurons with saccade-related transients for both increases (1–77; unshaded) and decreases (78–96; shaded). The conventions are the same as described for Fig. 7, except that dots indicate the time of maximum average firing frequency for each transient. Responses were considered transient if the modulation in activity returned to baseline before the end of the trial. All but a handful of transient activations
FIG. 12. Summary of timing of saccade-related activity. Conventions are as in Fig. 7, except that dots indicate time of maximum average firing frequency for responses with transient component, and responses are aligned on saccade onset at time 0. For reference, dotted lines are plotted at −100, 0, and 100 ms from saccade onset. Increasing (unshaded) and decreasing (shaded) responses are shown for neurons with a transient component (A) or without a transient component (B).
began within ±100 ms of saccade onset with most reaching their peak firing near or just after (within 75 ms) saccade onset. The longest lines in Fig. 12A indicate 2 unusual neurons with a pronounced transient followed by lower frequency sustained activation until the end of the trial. Figure 12B illustrates the same timing for neurons that lacked a transient component to their response. These responses were considered sustained because activity did not return to baseline before the end of the trial (lines ending at 250 ms indicate neurons recorded with a 200-ms target-fixation interval). Once activated, these neurons (32 increases; 24 decreases) often fired for the duration of the trial until reward was issued and the monkey was allowed to break fixation from the target (t = 250 or 500 ms). The distribution of onset times for sustained neurons clearly differed from that for transient neurons, with many sustained modulations beginning more than 100 ms after saccade onset. On average, transients began earlier and closer to saccade onset (5.62 ± 100 ms) than did sustained activations (64.5 ± 128 ms) and this difference was significant (t-test; P < 0.005).

Our operational definition of “motor-related” included any significant modulation in activity that occurred during the time period from 250 ms before saccade onset to the end of the trial. With rasters aligned on saccade onset, the tendency for impulses to occur at the same time across trials would suggest a temporal linkage to the motor event; however, rather than convey information about the saccade itself (e.g., timing, metrics), activity could reflect (e.g., change in orbital position) or anticipate (e.g., reward) some consequence of the saccade. This possibility seems remote for transients that are tightly linked to the saccade, but seems more likely for sustained activations.

**Eye position-related activity**

For one group of neurons, sustained postsaccadic activation was related to changes in eye position. These neurons fired at a steady rate during periods of stable fixation with firing rate a reflection of eye position in the orbit. Figure 13 shows an example of one such neuron. Figure 13A presents rasters for individual trials aligned on saccade onset (vertical line) for purely horizontal saccades (red tick marks, saccade offset) to contralateral (below) and ipsilateral (above) targets of 10° (gray) and 20° (black) of eccentricity. Before saccade onset, during fixation on central LED, the rate of sustained activity was intermediate to that for fixations to the left or right. The relationship between mean firing rate and eye position (eccentricity) is plotted in Fig. 13B. Each of the 4 sets of data points plots firing rate versus eccentricity for targets along one of the 4 possible axes defined by the 8 target circular target (i.e., horizontal, vertical, 2 diagonals). Note that the function is steepest for fixations along the horizontal axis (circles). Along this axis, the neuron was completely silent for ipsilateral fixation positions but the firing rate increased monotonically as a function of progressively more eccentric contralateral fixation positions. The rate–position functions for fixations along the 2 diagonals are similar but have slopes that are somewhat less steep, whereas there is no systematic trend apparent for fixations along the vertical axis (diamonds). This pattern of results indicates that it was not simply eccentricity, but eccentricity along a preferred axis (horizontal in this case) that determined the firing rate. Consistent with this, Fig. 13C shows good
agreement between the individual curves when the data points are replotted as a function of the horizontal component of eccentricity.

A total of 6 neurons showed a similar pattern of results and are summarized in Fig. 14 (Fig. 14A: same neuron as in Fig. 13). These neurons, all from the same monkey and recorded in close proximity to one another, were most strongly modulated by changes in the horizontal eye position, although “on-directions” could be either contra- (n = 3; Fig. 14, A–C) or ipsilateral (n = 3; Fig. 14, D–F).

Other “motor-contingent” activity

Additional examples of neurons that demonstrated a more remote relationship to the saccade are shown in Fig. 15. In all cases, rasters are aligned on saccade onset (t = 0; vertical line) and reference tick marks to indicate the GO signal (green), saccade offset (red), and reward delivery (blue) are shown. These 6 neurons were all characterized as sustained (see Fig. 12B) and had estimated onset times ranging from 136 ms before saccade onset (Fig. 15C) to 346 ms after saccade onset (Fig. 15F). Unlike the eye position related activity described above, the neurons depicted in Fig. 15 show a gradually increasing rate of activity that lasts until reward delivery. For the example neurons in Fig. 15, A–C activity begins to increase starting well before the saccade. None of these 3 examples showed any preference for direction. The neurons depicted in Fig. 15, D–F were similar in that they demonstrated a gradual increase in rate leading up to reward delivery. However, unlike the first 3 examples, these neurons had a clearly defined onset to the ramp in activity and were tuned for direction. Neurons like those shown in Fig. 15 are representative of many of the sustained neurons shown in Fig. 12B, and such examples indicate that neurons in central thalamus might reflect or anticipate some consequence of the saccade (see Discussion).

Visual-motor relationships

In the preceding sections sensory- and motor-contingent activities were considered independently for the entire sample of neurons. In this section, we examine the relationships between the visual- and motor-related activities for those neurons that were active in association with both the sensory and the motor event. As noted above, 71 neurons were modulated in association with both stimulus presentation and saccade execution. Of these, 53 were tuned for direction during one or both response periods: 14 were tuned during the visual period only, 12 during the motor period only, and 27 were direction-tuned for both epochs. For these 27 neurons, Fig. 16, A–D compares direction selectivity during the sensory and motor periods for relating each of the 4 parameters estimated by the Gaussian fits: tuning index (Fig. 16A), baseline (Fig. 16B), amplitude (Fig. 16C), and preferred direction (Fig. 16D). The scatter plots show tuning index, baseline, and amplitude to be correlated (P < 0.01) for the visual and motor periods, whereas the difference plot shown in Fig. 16D indicates reasonable agreement between estimates of preferred direction. Note that in this context, “baseline” refers to the asymptote of the best-fit Gaussian function, which indicates the levels of activity for nonpreferred directions during the visual or motor periods of the task (not to be confused with prestimulus and premotor epochs that we used to evaluate the timing of visual and motor bursts). Although correlated, there were some differences in tuning for the visual and motor periods. For example, tuning tended to be broader (nonsignificant, P > 0.05, t-test) and baseline rates higher (marginally significant, P = 0.05, t-test)
for the motor period as suggested by the number of points above the line of equality in the plots of Fig. 16, A and B. In contrast, there were no consistent biases in response amplitude (Fig. 16C) or preferred direction (Fig. 16D). When present, differences in the preferred direction (Fig. 16D) were usually associated with weak modulation during one of the epochs.

To evaluate the relative strength of the visual and motor-related modulations regardless of direction tuning, we calculated a modulation index (MI) for all 71 neurons (see METHODS). Values could range from 0 to 1, with negative values indicating stronger motor-related modulation and positive values a stronger visual-related modulation. Figure 16E shows a bias (44/71; 62%) toward negative values, indicating that most of these neurons were more strongly influenced by the motor event. For neurons that decreased during both the visual and motor epochs the sign of the MI was switched to maintain a consistent relationship between the sign of the MI and the epoch (visual or motor) during which modulation was greater.

Neurons tuned for both visual and motor periods (n = 27) were relatively uncommon, but neurons within this group tended to be similar. The majority (20/27; 74%) showed both a visual- and a motor-related increase, and these in turn were most likely (17/20; 85%) to be transient. Interestingly, all 17 of those with transient visual- and motor-related increases had delay-period activity that was either significant (13/17) or approached significance (4/17) for direction tuning. Figure 17, A and B provides examples of two neurons that were among the group with visual-, delay-, and motor-related increases that were tuned for direction. Note that motor-related activity could be either pre- (Fig. 17A) or post-saccadic (Fig. 17B) for this group. Figure 17C shows one of a group of 5 neurons that showed direction-tuned suppression during both the visual and motor-related periods.

Delay-period activity

As stated (see INTRODUCTION), one of our aims was to determine whether OcTh neurons carry task-related information throughout an instructed delay period. As indicated by many of the examples already shown (e.g., Figs. 4, 6, 7, and 17), many neurons were in fact responsive throughout instructed delays. To quantify delay period activity, rasters and average firing frequency histograms were aligned on target onset, and the average firing rate was calculated for the 100 ms preceding the “GO” signal (i.e., fixation offset). Gaussian functions were then fit to plots of average firing rate versus target direction. Forty-one neurons were found to be significantly tuned for direction during the delay period. Of these, 6 were tuned only

Fig. 15. Examples of neurons with motor-contingent activity that have imprecise relationship to the saccade. Rasters (top) and average frequency histograms (bottom) are aligned on saccade onset at time 0, indicated by solid vertical line. Colored tick marks indicate GO signal (green), saccade offset (red), and reward delivery (blue). For neurons shown in A and C, it was apparent during data collection that activity was building to end of trial, so we extended interval to reward delivery to 1,000 ms in some trials; these are the trials shown here. Timing and tuning estimates of motor activity for each example are as follows: A: onset: 168 ms, could not be fit with Gaussian function. B: onset: -74 ms, could not be fit with Gaussian function. C: onset: -136, could not be fit with Gaussian function. D: onset: 120 ms; theta: 358° (contra); tuning index: 77°; amplitude: 10 spikes/s; baseline: 14 spikes/s. E: onset: 148 ms; theta: 57° (contra); tuning index: 27°; amplitude: 16 spikes/s; baseline: 38 spikes/s. F: onset: 346 ms; theta: 325° (contra); tuning index: 40°; amplitude: 21 spikes/s; baseline: 21 spikes/s.

J Neurophysiol • VOL 90 • SEPTEMBER 2003 • www.jn.org
The goal of this study was to examine the ways in which neurons in the central thalamus contribute to visuomotor control. A delayed saccade task was used to permit separate evaluations of a central thalamic neuron’s capacity to carry information during the sensory encoding, instructed delay, and individual neurons that demonstrated spatial selectivity across multiple task periods. Examples are shown in Fig. 19, which compares tuning functions for the visual, delay, and motor-related periods for 3 individual neurons. In each of the examples, delay period activity shows estimated tuning indices and preferred directions that are consistent with those estimated for the visual and motor periods. This pattern was generally true as shown in Fig. 20, which relates direction tuning during the delay period to that for the visual (Fig. 19, A, C, E, and G) and motor periods (Fig. 20, B, D, F, and I) for the sample of neurons tuned during all 3 epochs (open symbols: decreases; filled symbols: increases). The tuning index for delay period activity was correlated, albeit weakly, with that for visual (Fig. 20A) and motor-related (Fig. 20B) activity as was baseline activity (Fig. 20, C and D). Although correlated, shallow slopes indicate that the amplitude of the delay-period tuning function was consistently lower that that for either visual (Fig. 20E) or motor-related (Fig. 20F) activity ($t$-test; $P < 0.01$). Perhaps most important, estimates of preferred direction were consistent (Fig. 20, G and H) across epochs.

**Recording sites**

Figure 21 plots the locations of 145 of the 162 single units included in this report. Eleven of the uncharted 17 units were recorded at anterior–posterior (A-P) levels intermediate to (within 250 um) the representative sections. For the remaining 6 units there is no histology; however, MRI images of electrode placement confirm their location to central thalamus. Recordings from one monkey spanned from A-P 7.0 to A-P 8.5 (Fig. 21, A–D) and those from a second monkey from A-P 10.5 to A-P 11.5 (Fig. 20E). Anterior–posterior levels are estimated based on Olszewski (1952). Similar to Schlag-Rey and Schlag (1984) and Schlag and Schlag-Rey (1984), task-related units were recorded in several central thalamic nuclei, with the majority found in Pce, CL, and paralaminar regions of VA and VL. A few units each were recorded in paralaminar MD, LD, and the lateral edge of CM. One unit (Fig. 21D) appeared to be just beyond the ventral border of thalamus in the vicinity of zona incerta.

We found no clear evidence for topography based on response type. As was also noted by Schlag and Schlag-Rey (1984), it was not uncommon to encounter disparate response types in close proximity within a single penetration. Virtually all recording locations showed a mixture of visual (circles), motor (squares), and visuomotor (triangles) types. Similarly, neurons with delay period activity (red symbols) were recorded at nearly all rostral–caudal levels and showed no clear tendency to cluster within the medial–lateral or dorsal–ventral dimensions. Consideration of quantitative measures of timing and tuning also failed to reveal any clear topographic tendency even when analyses were limited to widely segregated groups of neurons (e.g., Fig. 21, B and E).

**DISCUSSION**

The goal of this study was to examine the ways in which neurons in the central thalamus contribute to visuomotor control. A delayed saccade task was used to permit separate evaluations of a central thalamic neuron’s capacity to carry information during the sensory encoding, instructed delay, and
motor execution phases of generating a simple, visually guided saccadic eye movement. Quantitative assessment of activity during each of these epochs yielded separate estimates of timing and spatial selectivity. As described below, our findings indicate that individual thalamic neurons can carry task-related information throughout all phases of a delayed saccade task, suggesting a possible role in the processes of transforming sensory signals into motor commands. Differences in both the quality and timing of saccade-contingent activity suggested a range of functions, from saccade generation to internal monitoring of motor commands. Along with spatially selective stimulus- and saccade-linked transients, many thalamic neurons were found to have sustained, spatially tuned low-frequency activity that persisted throughout the instructed delay period. Such activity suggests the potential for central thalamic involvement in higher-order aspects of visuomotor control.

Anatomical considerations

As did Schlag and Schlag-Rey (1984), we have recorded visual- and saccade-related activity from a number of nuclei within the central thalamus including nuclei within the internal medullary lamina (primarily Pc and CL) and paralaminar regions of VA and VL. In addition, small numbers of neurons were localized to paralaminar MD and CM. Similar to the findings of Schlag and Schlag-Rey, we found little evidence of significant distinctions among populations recorded in differ-
visuomotor activity in primate central thalamus

Conjunctions of visual- and motor-related activation

Nearly half of our sample (71/162; 44%) of central thalamic neurons discharged in association with both the visual stimulus and the ensuing saccadic eye movement. Thus sensory- and motor-related activity appears to be well-integrated within these regions, with individual thalamic neurons active from the early to late stages of generating a voluntary visually guided saccade. The prevalence of visuomotor activity among thalamic neurons is consistent with that reported for other visuomotor regions. Using similar tasks, other studies have reported mixtures of visual, motor, and visuomotor neurons, and there is some evidence for the existence of differential efferent projections for different neural types (Pare and Wurtz 1997, 2001; Sommer and Wurtz 1998). Presumably, neurons of each type contribute to varying degrees to the processes of sensory encoding, motor execution, and to the intervening processes associated with sensorimotor decision making (e.g., target selection, motor planning). Our data indicate that the vast majority of central thalamic neurons are modulated in conjunction with the saccade. Neurons with both visual-related and saccade-related modulations and those with exclusively saccade-related modulations accounted for 94% (152/162) of our sample.

The prevalence of modulations associated with saccade execution along with the virtual absence of exclusively sensory-contingent modulations emphasizes that a primary function of included substantia nigra pars reticulata (SNr) (41%; Hikosaka and Wurtz 1983) and caudate nucleus (35%; Hikosaka et al. 1989).

To our knowledge, this is one of the first studies to characterize central thalamic neurons in this manner. In their companion reports, Schlag-Rey and Schlag (1984) and Schlag and Schlag-Rey (1984) separately described the visual- and saccade-related activities of largely nonoverlapping samples of neurons. Although it is not possible to infer the degree to which sensory- and motor-related information is segregated or integrated from their data, our results are not construed as inconsistent with these seminal findings. It is plausible, even likely, that a subset of the visually responsive neurons they revealed using a passive visual task (Schlag and Schlag-Rey 1984) would also have shown saccade-related activity if explicitly tested. Similarly, a subset of those with saccade-related discharges (Schlag-Rey and Schlag 1984) might also have been shown to be visually responsive if so tested.

Prevalence of saccade-contingent modulations

Determining whether a neuron is predominantly sensory-related, motor-related, or sensory-motor is a first step in defining its potential contribution to the generation of goal-directed behavior. As noted above, previous studies have shown that both cortical and subcortical visuomotor areas are composed of mixtures of visual, motor, and visuomotor neurons, and there is some evidence for the existence of differential efferent projections for different neural types (Pare and Wurtz 1997, 2001; Sommer and Wurtz 1998). Presumably, neurons of each type contribute to varying degrees to the processes of sensory encoding, motor execution, and to the intervening processes associated with sensorimotor decision making (e.g., target selection, motor planning). Our data indicate that the vast majority of central thalamic neurons are modulated in conjunction with the saccade. Neurons with both visual-related and saccade-related modulations and those with exclusively saccade-related modulations accounted for 94% (152/162) of our sample.

The prevalence of modulations associated with saccade execution along with the virtual absence of exclusively sensory-contingent modulations emphasizes that a primary function of
these central thalamic regions may be to participate in the formulation of the saccadic motor command. Many neurons, like that shown in Fig. 4, culminated in a presaccadic burst that was tuned for saccade direction. In many ways, these neurons are similar to the visuomotor presaccadic neurons commonly found in FEF or SC and that are thought to be causal to voluntary saccade execution. However, we also note that for many central thalamic neurons, saccade-contingent modulations were post-saccadic and thus could not be involved in saccade production. Instead, the activity of these neurons appeared to be the consequence of the saccade. Such neurons, discussed more fully below, could play many roles, including the feedback of information directly related to the saccade (i.e., efference copy), signaling the change in eye position, or carrying information about the expected consequences of the just executed saccade (e.g., reward).

Quantitative estimates of tuning and timing

The broad parceling of neurons based on the presence of visual- and/or motor-related modulation provided a convenient starting point for understanding function; however, quantification of timing and tuning revealed important distinctions between neurons (e.g., presaccadic or postsaccadic) and permitted comparison to other visuomotor areas for which comparable estimates are known. To our knowledge, this is the first study to quantify these parameters for central thalamic neurons.

We found stimulus-linked bursts to be distributed between 90 and 100 ms, which is generally consistent with the first spike latency estimates previously reported for this region (Schlag and Schlag-Rey 1984). This value is consistent with that reported for other visuomotor regions. As discussed by Schmolesky et al. (1998), such long visual onset latencies (i.e., compared with primary visual cortex) are typical for higher-order forms of visual information such as that found in middle-temporal area (MT), FEF, or other cortical regions of the dorsal stream (“where stream”). As discussed above, the similar timing and strong anatomical connections to FEF support the notion that OcTh is a component of this larger visuomotor network.

We found the timing of saccade-related activity in the central thalamus to be broadly distributed, ranging from well before to well after saccade onset. In this regard, OcTh on the whole is clearly distinct from relatively downstream oculomotor-related areas like the SC. Saccade-related signals in the SC play a causal role in saccade generation. Accordingly, saccade-related activity in SC is almost exclusively presaccadic, most often ending with the saccade (Sparks 1978; see Sparks 1986 for review). Although we found many presaccadic OcTh neurons with timing appropriate for a role in saccade generation (e.g., Fig. 5), equally common were neurons that fired too late for such a role. Although some of these late modulations were clearly not saccade-related (e.g., Fig. 15), the majority of postsaccadic modulations consisted of a burst that was tightly linked to saccade occurrence (e.g., Fig. 9). Although sparse or absent in the SC, transient postsaccadic modulations have been reported for several cortical regions, including FEF (Bizzi 1968; Bruce and Goldberg 1985; Schall 1991b), SEF (Schall
1991a), posterior parietal cortex (Barash et al., 1991a), and prefrontal cortex (Funahashi et al. 1991).

Postsaccadic modulations are likely to play an important feedback role, providing information about an ongoing or just completed action. One obvious possibility is that this activity represents a corollary discharge of the saccadic motor command (Sherrington 1918; Sperry 1950; see Carpenter 1988 for review). Corollary discharge of ongoing or completed actions is used both by sensory systems and sensorimotor systems. In the former case, information about the distance and direction of eye movement is required to create a stable internal representation of the visual scene. In the latter, this information is critical for planning movement sequences or saccades to remembered sensory goals. To be of value in this role, postsaccadic activity should carry information about saccade metrics. In fact, the majority of the postsaccadic activity we observed was selective for the direction (and when tested, the amplitude) of the saccade (e.g., Fig. 11). Also supportive of this interpretation are recent data from humans (Gaymard et al. 1994) and primates (Sommer and Wurtz 2002) indicating that central thalamic lesions disrupt the ability to perform tasks that specifically require the internal monitoring of motor commands.

Schlag-Rey and Schlag (1984) reported that a substantial number of central thalamic neurons burst after spontaneous saccades. The bursts of these neurons were very tightly linked to saccade offset, usually preceded by a pause, and generally unselective for saccade metrics. As noted by these authors in a short report, such neurons could serve as a more general feedback signal to "ready" the visual system for processing the newly fixated visual information (Schlag and Schlag-Rey 1983). Although we did sample units with this combination of response features, they were less common than other postsaccadic types. However, like Schlag and Schlag-Rey, we found neurons with sustained activity that correlated with the position of the eye in the orbit. Like corollary discharge of motor commands, eye position signals in combination with sensory signals such as those found in the posterior parietal cortex may be critical for establishing the internal reference frames necessary for goal-directed action (see Andersen 1995; Colby et al. 1995 for reviews).

The majority of our sample was tuned during one or more periods of the visually guided delayed saccade task. Although not tested on the same neurons, Schlag and Schlag-Rey reported spatial selectivity for both the visual-related (Schlag and Schlag-Rey 1984) and motor-related (Schlag-Rey and Schlag 1984) populations. Our estimates of direction tuning by Gaussian fit suggests relatively broad spatial selectivity for sensory-, delay-, and motor-related activities. Mean tuning indices ranging from 35 to 60° for visual- and motor-related discharges are remarkably consistent with values between 33 and 58° reported for FEF using the same fitting procedure (Bruce and Goldberg 1985). As was true for timing (see above), spatial tuning in the central thalamus seems to have more in common with FEF than with SC. Using the same index of tuning, Stanford and Sparks (1994) reported values ranging from a minimum of 16° to a
maximum of 35° for a small sample (n = 12) of saccade-related neurons in the SC.

Although quantified in a variety of ways, relatively broad spatial tuning is fairly common in areas that are less closely associated with motor output. In addition to FEF (Bruce and Goldberg 1985; Schall 1991b), similarly broad sensory and/or motor tuning is suggested for SEF (Schall 1991a), parietal cortex (Barash et al. 1991b), prefrontal cortex (Boch and Goldberg 1989; Funahashi et al. 1990), SNr (Handel and Glimcher 1999; Hikosaka and Wurtz 1983), and caudate (Hikosaka et al. 1989), all regions to which OcTh is anatomically linked. As has been reported for most visuomotor regions, including central thalamus (Schlag and Schlag-Rey 1984; Schlag-Rey and Schlag 1984), we found that most units had contralateral best directions. However, the motor-related activity of a small number of neurons preferred ipsilateral saccades. Similar incidences of ipsilateral preference have been reported for parietal (Barash et al. 1991b), prefrontal cortex (Boch and Goldberg 1985; Lynch et al. 1996; Shook et al. 1991), and caudate (McFarland and Haber 2000). Information from SC is conveyed, by paralaminar MD, to FEF (Sommer and Wurtz 1998, 2002) and could be the basis of yet another loop that originates and returns to FEF (FEF–SC–MD–FEF). Although perhaps not the basis for a closed loop, deep cerebellar influences on visuomotor activity in FEF and SEF are also mediated by the central thalamus (Lynch et al. 1994, 1996; Shook et al. 1991).

**Delay-period activity**

Many thalamic neurons were found to carry spatial information during the instructed delay of the delayed saccade task. Nearly one-third (41/132) of the neurons tested with the radial target array were significantly tuned for direction as estimated by Gaussian fit. Unlike the higher-frequency transient bursts that were linked to stimulus onset or saccade initiation (e.g., see Figs. 6 and 9), delay period activation was usually lower in frequency (e.g., see Fig. 17) and bore no strict temporal relationship to either event. As has been observed in numerous studies of other regions, this sustained activity often appeared to bridge the gap between discrete sensory and motor-related bursts. Rarely (6/41) did we observe spatially selective delay period activity that occurred in the absence of a preceding visual-related burst, an ensuing motor-related burst, or both.

Numerous studies suggest that delay period activity represents a context-sensitive link in the process of translating sensory signals into motor commands. Using tasks that call for a more flexible linkage between stimulus and response, these studies have reported neural correlates of cognitive factors such as sensory attention (see Colby et al. 1999 for review), perceptual judgment (see Glimcher 2001; Schall and Thompson 1999; Shadlen and Newsome 1996 for reviews), movement selection (Glimcher and Sparks 1992), and motor planning (Barash et al. 1991a,b; Bracewell et al. 1996; Mazzoni et al. 1996; see Andersen 1995 for review) within the activity that occurs during this interval.

Having used a visually guided delayed saccade task, we can draw no firm conclusions regarding the functional significance of delay-period activity in the central thalamus. However, preliminary findings of our own (Wyder and Stanford 2000) and others (Schall and Thompson 1994; Thompson and Schall 1994) suggest that, in fact, for many neurons, this activity can be modulated by manipulating the meaning of the stimulus in the context of a target/distracter discrimination task. Evaluation of more neurons with this type of task will be required to define thalamic involvement in higher orders aspects of visuomotor control.

**Central thalamus and visuomotor loops**

We can conclude that central thalamic visuomotor neurons are coactive with their counterparts in cortical and subcortical visuomotor structures throughout the entire process of generating a voluntary visually guided saccade. As detailed in the introduction, anatomical connections to these same structures place nuclei of the IML and paralaminar regions of VA and VL at the center of numerous putative visuomotor processing loops. Thalamocortical loops involving all of the major cortical contributors to visuomotor control, including FEF, SEF, PPC, and PFC, have been established (see Groenewegen and Berendse 1994; Jones 1985; Macchi and Bentivoglio 1986 for reviews). Paralaminar VA, along with conveying basal ganglia output to FEF and SEF as part of the so-called oculomotor loop (Alexander et al. 1986; Lynch et al. 1996; Shook et al. 1991), is also part (along with anterior ILN and paralaminar VL) of a major projection to the striatal target of FEF and SEF, the caudate nucleus (McFarland and Haber 2000). Information from SC is conveyed, by paralaminar MD, to FEF (Sommer and Wurtz 1998, 2002) and could be the basis of yet another loop that originates and returns to FEF (FEF–SC–MD–FEF). Although perhaps not the basis for a closed loop, deep cerebellar influences on visuomotor activity in FEF and SEF are also mediated by the central thalamus (Lynch et al. 1994, 1996; Shook et al. 1991).

Although the functional contributions of these circuits are yet unclear, it is important to consider that neurons in all of these regions, including thalamus, are coactive from approximately 60–100 ms after stimulus presentation until the time of saccade generation. This period, which is a minimum of 100 ms (can be much longer for complex tasks), would, in principle, allow for activity to evolve over the course of many iterations through these circuits. It seems plausible that these loops contribute to the sensorimotor decision processes that lead to purposeful action.

**“Reward-related” activity**

We observed a number of neurons with activity that built gradually, leading up to delivery of reward (e.g., Fig. 15). Although these experiments were not specifically designed to test for this capacity, it seems plausible that this activity is, in fact, reward-related. As noted above, these regions of central thalamus project to and receive input (by SNr) from the caudate nucleus, where reward-related activity is frequently observed (Hollerman et al. 1998; Kawagoe et al. 1998; Shimo and Hikosaka 2001; Takikawa et al. 2002). Further, these neurons are remarkably similar to the so-called reward-predicting neurons recently found in SEF (Amador et al. 2000), one of the principal targets of central thalamic projections (Lynch et al. 1996; Shook et al. 1991). Much like those reported here, the activity of an SEF “reward-predicting” neuron begins to build near the time of the saccade and continues to build until reward is delivered.

Future experiments in which reward contingencies are manipulated will be necessary to further explore the possibility that the central thalamus is a component of networks that ascribe reward value to sensory signals and/or pending motor commands. From the results of several recent studies in other visuomotor regions (Kawagoe et al. 1998; Leon and Shadlen...
The functional anatomy of basal decision processes. Consequences of any given action. Anatomically, at least, the central thalamus seems well-positioned to participate in such decision processes.

We thank K. Pearson for providing essential programming support.

DISCLOSURES

This work was supported by National Eye Institute Grant EY-12389.

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