Contextual Modulation of Central Thalamic Delay-Period Activity: Representation of Visual and Saccadic Goals

Melanie T. Wyder, Dino P. Massoglia, and Terrence R. Stanford. Contextual modulation of central thalamic delay-period activity: representation of visual and saccadic goals. *J Neurophysiol* 91: 2628–2648, 2004. First published February 4, 2004; 10.1152/jn.01221.2003. This study examines the influence of behavioral context on the activity of visuomotor neurons in primate central thalamus. Neurons that combine information about sensory stimuli and their behavioral relevance are thought to contribute to the decision mechanisms that link specific stimuli to specific responses. We reported in a previous study that neurons in central thalamus carry spatial information throughout the instructed delay period of a visually guided delayed saccade task. The goal of the current study was to determine whether the delay-period activity of thalamic neurons is modulated by behavioral context. Single neurons were evaluated during performance of visually guided and memory-guided variants of a saccadic choice task in which a cue designated the response field stimulus as the target of a rewarded saccade or as an irrelevant distracter. The relative influence of the physical stimulus and context on delay-period activity suggested a minimum of 3 neural groups. Some neurons signaled the locations of visible stimuli regardless of behavioral relevance. Other neurons preferentially signaled the locations of current saccadic goals and did so even in the absence of the physical stimulus. A third group signaled only the locations of currently visible saccadic goals. For the latter 2 groups, activity was the product of both stimulus and context, suggesting that central thalamic neurons play a role in the context-dependent linkage of sensory signals and saccadic commands. More generally, these data suggest that the anatomical substrate of sensorimotor decision making may include the cortico-subcortical loops for which central thalamus serves as the penultimate synapse.

INTRODUCTION

Voluntary, goal-directed saccadic eye movements engage a broadly distributed neural network consisting of several cortical and subcortical structures. A critical function of processing within this network is to ensure that gaze shifts are both timely and appropriate given current behavioral objectives. Saccadic eye movements are not random and choices of where to look are informed both by extrinsic factors, such as the inherent salience of stimuli that compose the visual scene, and intrinsic factors, including expectation, motivation, and anticipated outcome. Simply put, the sensory stimuli that represent possible goals must be combined with cognitively derived signals that reflect the behavioral context in which they occur. As a result of this process, only those stimuli that are consistent with the current behavioral goals gain access to the downstream oculomotor machinery.

Previously, we reported on the visual- and saccade-related properties of neurons in several central thalamic nuclei as revealed through the use of a visually guided, delayed saccade task (Wyder et al. 2003a). This task, which coupled a specific sensory stimulus to a specific saccadic response by an instructed delay, revealed that many thalamic neurons represented the times of occurrence and locations of visual stimuli and the saccades made to acquire them. In addition, we found that many thalamic neurons maintained veridical spatial information throughout the instructed delay period during which the monkey was required to withhold responding to the stimulus. Spatially selective delay-period activity may be the hallmark of a neuron that participates in “higher-order” aspects of sensorimotor function. In many regions, including the lateral intraparietal area (LIP), supplementary eye field (SEF), frontal eye field (FEF), and dorsolateral prefrontal cortex (PFCdL), the temporal evolution of delay period activity has been shown to correlate with cognitively driven events 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). Common to all of these studies is the demonstration that the magnitude of delay-period activity is a function of both the physical stimulus and the context in which the stimulus occurs.

The observation that central thalamic neurons maintain spatial tuning throughout an imposed delay period, though suggestive, is not strong evidence for involvement in a context-dependent process of linking sensory stimuli to saccadic commands. Such activity might simply indicate the presence of a visual stimulus within the neuron’s receptive field, independent of task context. The objective of the present study was to determine whether, in fact, these neurons carry information about both the stimulus and its relevance within the context of the behavioral task. To do so we evaluated the activity of single central thalamic neurons in association with both a single-target delayed saccade task and a 2-stimulus saccadic choice task. Whereas in the single-target task, the lone visual stimulus [whether within or beyond the neuron’s response field (RF)] was known from the outset to be the target of an eventual saccade, the choice task contained a period of ambiguity during which the 2 simultaneously present stimuli (one within and one outside of the neuron’s RF) had equal potential to become...
either the saccadic goal or an irrelevant distracter. This period was followed by a cue identifying the target and distracter.

The single-target and choice tasks permitted comparison of activity evoked by the same physical stimulus in the neuron’s RF in 4 different behavioral contexts: 1) a single stimulus known to be the saccade target; 2) 2 stimuli, one in and one out of the RF, each with the potential to become a saccade target (or distracter); 3) 2 stimuli, a known target in the RF and a known distracter out of the RF; and 4) 2 stimuli, a known distracter in the RF and a known target out of the RF.

The logic of the single-target/choice task comparison is straightforward, with “stimulus-bound” activity predicted to be relatively unaffected by the changing context and more “goal-related” activity differentiating between potential targets (and distracters), known targets, and known distracters. We included “memory” variants of the single-target and choice tasks to further distinguish stimulus-related and goal-related activity. Whereas the prediction for purely stimulus-related activity is relatively trivial—a cessation of activity when the RF stimulus is extinguished—that for apparently “goal-related” activity is more interesting. In principle, the representation of a saccadic goal could be stimulus-independent, persisting after the stimulus has disappeared, or stimulus-dependent, specifying the locations of currently visible goals only.

There are to date very few published accounts of the visuomotor properties of neurons in central thalamus (Schlag and Schlag-Rey 1984; Schlag-Rey and Schlag 1984; Wyder et al. 2003a; see Sommer 2003 for review) and, to our knowledge, only preliminary findings have shown the capacity for delay-period activity to carry information related to behavioral context (Schall and Thompson 1994). In brief, we observed some central thalamic neurons that were consistent with each of the stimulus/goal-related outcomes described above. One group signaled the presence of a visual stimulus independent of task goals, a second group signaled the location of a current saccadic goal independent of the continued presence of the stimulus, and a third group signaled the presence of currently visible saccadic goals. The latter 2 groups indicate that delay-period activity in central thalamus can convey combined information about sensory stimuli (both past and present) and the behavioral context in which they occur. Considered along with the anatomical position of central thalamus, these data suggest that activity within cortico-subcortical loops plays a role in the context-dependent linkage of sensory signals and saccadic commands.

Some of these data previously appeared in preliminary form (Wyder et al. 2003b).

**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). Details of the surgical and recording procedures were previously described (Wyder et al. 2003a). Briefly, 3 rhesus monkeys (*Macaca mulatta*) were prepared for chronic single-unit recording. Before behavioral training, under general anesthesia, an MRI-compatible titanium post was attached to the skull and an eye coil was implanted in one eye (Judge et al. 1980). During subsequent training/recording sessions, the post served to restrain the monkey’s head while 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 tasks (see following text). Once trained to criterion levels of performance, a second surgery was performed to place a recording cylinder (Crist Instrument) over the central thalamus. Daily recording sessions began on full recovery (2–3 wk).

**Recording procedures**

Eye position was sampled and stored at 500 Hz. Neural activity was recorded using parylene-coated, tungsten microelectrodes (Micro Probe) having impedances of between 1.0 and 1.5 MΩ at 1 kHz. Electrodes were inserted through a dura-piercing cannula and advanced to the thalamus by a hydraulic microdrive. Activity was monitored using an oscilloscope and an audiomonitor, and the action potentials of single neurons were isolated using a time/amplitude window discriminator. Spike times were stored at a resolution of 10 μs.

**Behavioral tasks**

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). At a viewing distance of 57 in., adjacent LEDs were separated by either 1 or 2° of visual angle (Cartesian coordinates) and 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).

This report presents neural data associated with performance of 2 variations of a saccadic choice task (Fig. 1). The primary objective of this experiment was to evaluate the degree to which the “delay period” activity of central thalamic neurons reflects behavioral context. The logic of the tasks (which are detailed below) is straightforward. In each version of the choice task the RF stimulus remains physically invariant, but changes in behavioral relevance are dictated by a cue that designates it as either the target of a rewarded saccade or as an irrelevant distracter.

**VISUALLY GUIDED CHOICE TASK.** Visually guided trials (Fig. 1A) began with the presentation of a yellow central fixation stimulus (Panel 1; fixation) that the monkey had to acquire within 500 ms. After either a variable (some sessions), or fixed, delay (variable = 500 or 750 ms; fixed = 400 ms), 2 eccentric stimuli were illuminated, one red and one green (Panel 2; before-cue). The 2 stimuli were always of equivalent eccentricity and differed in direction by 180°. Stimulus position was randomly assigned such that the stimulus pair could appear at any one of 8 possible orientations (see following text). During the before-cue period, each stimulus was a potential saccade target. After a delay (700 ms, fixed; 500 or 700 ms, variable), the central fixation light changed color, randomly, to either red or green (Panel 3; after-cue), cueing the monkey to the identity of the eventual saccade target (color match) and distracter (nonmatch). The monkey was required to maintain fixation throughout the after-cue period (300 ms, fixed; 300 or 600 ms, variable) until offset of the central fixation stimulus, the go signal, directed a saccade to the target (Panel 4; go/saccade). The monkey was required to look to the target within 500 ms and maintain fixation on the target for an additional interval (200 or 500 ms) to obtain a liquid reward. Note that, together, the before-cue and after-cue periods constitute a delay interval that is analogous to the visual delay period imposed on the single-target visually guided and memory-guided tasks described below.
MEMORY-GUIDED CHOICE TASK. The memory-guided choice task (Fig. 1B) was identical to the visually guided version up to and through the after-cue period (Panel 3). At this point, instead of extinguishing the fixation point to mandate a saccade, both the target and distracter were extinguished (Panel 4), requiring the monkey to remember the location of the target or movement vector throughout an additional interval (memory period; 600 ms, fixed; 500 or 700 ms, variable). The memory period terminated with the go signal (offset of fixation light), signaling the monkey to make a saccade to the remembered location of the target.

Visually guided and memory-guided choice trials were randomly interleaved and equally probable. Variable intervals and/or random interleaving of trial types were a critical element of the experimental design and prevented monkeys from predicting the time of the go signal. At a minimum (20/49 neurons), temporal uncertainty was created by interleaving fixed-interval visually guided and memory-guided choice trials resulting in randomized cue-go intervals of 300 (visually guided) and 900 ms (memory-guided: 300-ms cue interval plus 600-ms memory period). At a maximum (29/49 neurons), 6 Cue-go intervals, ranging from 300 to 1,350 ms, were randomized by interleaving variable-interval visually guided and memory-guided choice trials.

SINGLE-TARGET TASKS. The spatial selectivity of each neuron was also examined in association with single stimulus (target) visually guided and memory-guided saccade tasks. In these tasks (described previously, Wyder et al. 2003a), the fixation light was illuminated red, and a single color-matched eccentric target was subsequently presented. As for the choice tasks, monkeys maintained fixation on the central stimulus for a fixed (1,000 ms) or variable (750 or 1,000 ms) delay period, after which the fixation spot was extinguished (go signal) and a saccade to the target required. On visually guided trials, saccades were directed to a persistent visual stimulus, whereas, on memory trials, the target was extinguished before the go signal and the saccade directed to the location of the now-absent target.

The single-target tasks were used to estimate the direction selectivity of task-related modulations and provided the primary benchmark for evaluating the activity recorded on choice trials (see following text). For approximately one half of the neurons, the 2 single-stimulus and 2 choice tasks were randomly interleaved and equally probable \( (P = 0.25) \), whereas for the remaining neurons, single-stimulus and choice trials were presented in separate blocks. When blocked, single-target trials preceded choice trials.

STIMULUS LOCATION. In all tasks, stimulus locations were selected from a circular array of 8 possible locations (see Wyder et al. 2003a for details). Target direction was randomized across trials and stimuli were presented at a fixed eccentricity of either 6, 10, or \( 20^\circ \) (i.e., the radius of the circle). Eccentricity was chosen based on an on-line estimate of that which produced the strongest task-related modulation.

Data analysis procedures

DIRECTION SELECTIVITY. A neuron’s RF was delineated by estimating a preferred direction for each eccentricity tested. Tuning functions were generated from activity recorded during performance of the single-target tasks and the eccentricity that yielded the greatest direction selectivity was considered for subsequent analyses. Our methods of evaluating direction tuning were previously described in detail (Wyder et al. 2003a). Briefly, average firing rates for each of the 8 target directions were calculated separately for both a visual and a saccade-related epoch. Each epoch was 100 ms in duration and corresponded to intervals of maximal task-related modulation (see Wyder et al. 2003a for details). Plots of average firing rate versus target direction were then fit with Gaussian functions, the means of which provided estimates of preferred direction. The visual epoch was used to estimate preferred direction whenever possible. However, in cases of weak or absent stimulus-related modulation, tuning was based on the motor epoch.

Figures 2 and 3 illustrate, for an example neuron, the procedures for determining preferred direction (Fig. 2) and for evaluating the capacity of single thalamic neurons to discriminate between target and distracter stimuli (Fig. 3). Figure 2 depicts data from single-target visually guided saccade trials for a single neuron. The polar plot of Fig. 2A compares average firing frequency as a function of target direction for a prestimulus baseline period (open circles), with stimulus-related activity clearly illustrating a preference for rightward (contralateral) stimuli. In Fig. 2B, stimulus-related firing as a function of direction is fit with a Gaussian function that yielded an estimate of \( 334^\circ \) as the preferred direction for this neuron.

An estimate of \( 334^\circ \) for the preferred direction corresponds to a location between the 315 and \( 270^\circ \) (360°) stimuli and is consistent with the similarly high rates associated with these 2 stimulus/target locations. Given the generally broad tuning exhibited by these thalamic neurons (see Wyder et al. 2003a), it was common for 2 or 3 points (target/stimulus locations) of similar firing rate to straddle the peak (within-RF) of the Gaussian function. Analogously, the asymptote of the Gaussian function was typically fit to 2 or 3 points of a similarly low firing rate. In all but 2 cases (47/49 neurons), firing rates were each based on averaging the activity across 2 stimulus directions for which rates were comparable. In the remaining 2 cases, sufficiently sharp direction tuning permitted use of a single stimulus direction.
FIG. 2. Analysis of direction selectivity for an example neuron using data from the single-target delayed saccade task. A: polar plot of firing rate as a function of target direction during a 100-ms prestimulus baseline epoch (open symbols, dotted line), and during peak stimulus-associated activation (solid symbols, solid line, 114–214 ms after stimulus onset). B: plot of stimulus-associated firing rate as a function of target direction (same data plotted with solid line in A), and the corresponding least-squares fit Gaussian function. C: rasters (top) and average frequency histograms (bottom) are aligned with target onset (left) and with saccade onset (right). Activity is shown for trials in which the target was inside (black, 315 or 0°) or opposite to (gray, 135 or 180°) the neuron’s response field (RF). Task events are depicted above each set of rasters. Black line within each task box encloses the stimulus positions inside the neuron’s RF (0 and 315°); see text for additional details. Vertical lines mark stimulus onset (left), end of the visual delay period (middle), and saccade onset (right). Short horizontal lines above the histogram in the left panel indicate the baseline- and stimulus-related epochs referred to in A.
Figure 2C plots both rasters (top) and average firing frequency histograms (bottom) for a target within (black; 315 and 0°) and opposite (gray; 135 and 180°) the RF. Task events are depicted above each set of rasters. Activity profiles are shown aligned on stimulus/target onset (left panel) and saccade onset (right panel). Note that, beginning about 100 ms after stimulus presentation (t = 0), activity increases for the within-RF target (black) and decreases (transiently) for the oppositely directed non-RF target (gray). This difference in firing is maintained throughout the delay period and subsequent reaction time (beginning with go signal), leading up to saccade onset (t = 0; right panel), at which time, preferred-direction activity is abruptly suppressed (100-ms baseline and poststimulus epochs used to construct Fig. 2, A and B are indicated by horizontal lines above average firing histogram).

EVALUATING THE NEURAL DISCRIMINATION OF TARGETS AND DISTRACTERS. The neural discrimination analysis hinged on comparing activity for the same neuron both before and after the stimulus in the RF was revealed to be either a target or distracter. Figure 3 illustrates this for the same neuron depicted in Fig. 2. Rasters and average firing frequency histograms (Fig. 3A) are shown aligned on stimulus onset (left) and saccade onset (right) for activity associated with the visually guided choice task. Trials are separated according to whether the stimulus in the RF was ultimately revealed to be the target (red) or distracter (blue). For comparison, the average firing frequency...
histograms for the single-target trials (black: single target within RF; gray: single target opposite RF) of Fig. 2 are also shown here (trials in which neither a target nor a distracter was within the RF of the neuron were not considered for subsequent analyses).

Corresponding task events for choice trials are shown in the panels above each set of rasters. Stimulus probabilities were set such that, on any given trial, the stimulus in the RF was equally likely to become a target (red rasters) or a distracter (blue rasters) and, critically, targets and distracters were equally likely to be red or green (see bifurcation in the task panels above each set of rasters). In this example, there were 147 trials in which the RF stimulus became the target (76 red, 71 green) and 148 trials in which the RF stimulus became the distracter (68 red, 80 green). The random assignment of color (red/green) and stimulus identity (target/distracter) ensured that, if present, differences in firing rate attributed to stimulus identity (target or distracter) could be distinguished from those attributed to preference for the color of the RF or fixation stimulus (see following text).

As expected, activity during the before-cue period (t = 0–700 ms) did not differentiate between stimuli that, only later in the trial, would become distinguishable on the basis of their relationship to the color of the fixation light (i.e., target or distracter). However, about 200 ms after presentation of the cue, activity evolved to differentiate between a target or distracter within the RF with the difference in level for these conditions approximating or even exceeding that for single-target trials (black: target within RF; gray: target opposite RF). A neuron was considered to have “discriminated” between a target and distracter if, by 300–350 ms after the cue, a statistically significant (t-test; P < 0.05) difference in firing rate had developed. For the example neuron, the mean firing rate for a target in the RF was 95.8 ± 23.2 spikes/s and for a distracter in the RF was 42.6 ± 34.4 spikes/s, a significant difference.

The degree and time course of target-distracter differentiation was further quantified by adapting an analysis previously used for neurons in the FEF and the superior colliculus (SC) (McPeek and Keller 2002; Thompson et al. 1996). The resulting discrimination functions provided a means to visualize and quantify the time course of discrimination, providing bases for comparing individual neurons within the sample and for comparing this sample to comparable data from other reports (e.g., McPeek and Keller 2002; Thompson et al. 1996; see DISCUSSION). We evaluated the degree to which the “target” and “distracter” response profiles differed in 5-ms increments, for each interval calculating the probability that the firing rate on “target” trials would exceed that on “distracter” trials (or vice versa in cases of target-related suppression). The resulting probability value, referred to as the discrimination index (DI), is analogous to the area under a ROC curve and provides an index of how reliably the presence of a target or a distracter in the response field could be predicted based on the response of the neuron.

For each trial, instantaneous firing frequency was calculated by taking the reciprocal of each interspike interval. The resulting plots of instantaneous firing frequency versus time were then binned at 1 ms and subjected to a moving average to yield an estimate of mean firing frequency in 5-ms increments. At each 5-ms time point, the value of mean firing frequency was the product of averaging across 10 (1-ms) bins (5 ms before to 5 ms after). For each 5-ms interval the DI was calculated to give the probability that the firing rate on target trials exceeded that on distracter trials according to the formula

\[ DI = \frac{N_{target} - 0.5N_d}{(N_{target} + 0.5N_d)/2} \]

where \( N_{target} \) is the total number of times the target rate was greater than the distracter rate, \( N_d \) is the number of times the target rate equaled the distracter rate, \( N_t \) is the total number of target trials, and \( N_{distracter} \) is the number of distracter trials (\( N_{target} = \) the total number of comparisons made). Theoretically, values of DI range between 0.5 and 1.0, with 0.5 corresponding to no reliable difference in rate ([target > distracter] and [target < distracter] equally probable) and 1.0 corresponding to nonoverlapping rate distributions (target rate always greater than distracter rate).

Values of DI are plotted in Fig. 3B for the time period beginning 100 ms before the cue interval. Note that values hover near 0.5 during the before-cue interval, begin to rise about 200 ms after the cue, and rise monotonically over the subsequent 150 ms, to reach an asymptotic value of near 0.9. We quantified this time course by fitting functions of DI versus time with the modified cumulative Weibull function given by

\[ P = p_{max} - (p_{max} - p_{min}) \exp\left(-\frac{t}{a}\right) \]

where \( t \) is the time after the cue (fix change), \( a \) is the time at which the curve reaches 64% of its full growth, and \( b \) describes its slope or rate of rise (Thompson et al. 1996). Here max and min are, respectively, the maximum and minimum DI values calculated for a given neuron (Thompson et al. 1996). They were obtained by averaging the DI values during the first and last 50 ms, respectively, of the interval over which the Weibull function was fit. Generally, good fits were obtained using the interval from cue onset until 100 ms after the end of the cue interval (400 ms total), but small adjustments to this interval were made in some cases to accurately capture the discrimination process. The onset and offset of discrimination were estimated as the time at which the best-fit Weibull function reached 25 and 75% of its maximum value, respectively. For the neuron shown in Fig. 3, the discrimination function rose from 0.49 to 0.91, reaching 25% of maximum at a postcue time of 245 ms and 75% of maximum at a postcue time of 315 ms.

For comparison, Fig. 3, C and D illustrate the same analysis, performed on the same data set, but with trials parsed according to the color of the RF stimulus (Fig. 3C) or the color of the fixation stimulus (Fig. 3D). In both analyses, a preference for red is indicated by DI > 0.5 and a preference for green by DI < 0.5. The DI function for RF stimulus color (Fig. 3C) hovers above 0.5, suggesting a weak preference for red over green stimuli. In contrast, the DI function for fixation stimulus color (Fig. 3D) declines to <0.5 after the cue changes, indicating a preference for a green fixation stimulus. Compared with the effect of target/distracter identity, the influences of color are subtle. At 300–350 ms after the cue, the target/distracter DI value differed from 0.5 by 0.34, whereas deviations for RF-color and fixation color were much less pronounced at +0.1 and −0.13, respectively. For all neurons that discriminated between targets and distracters, a 2-way ANOVA was performed to test for main effects of RF stimulus color, fixation stimulus color, and their interaction.

SINGLE-TARGET DISCRIMINATION FUNCTIONS. To provide a benchmark for comparing the degree of discrimination achieved on choice trials, DI analyses were also applied to single-target trials by comparing trials in which the lone stimulus was in the RF to trials in which the stimulus was opposite the RF. Differences between responses to single targets within and opposite the RF were quantified.

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% paraformaldehyde. 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 (cresol violet).

RESULTS

Results are based on the activity of 49 neurons, each recorded in association with visually guided and memory-guided
variants of both single-target delayed saccade and 2-alternative saccadic choice tasks (see Fig. 1). All neurons were recorded in the vicinity of the intralaminar and paralaminar thalamic nuclei and all were deemed to have task-related activity according to the quantitative criteria described in a previous report (Wyder et al. 2003a). The present study is based on a subset of a larger sample that contributed to an earlier report (Wyder et al. 2003a). The majority of neurons were recorded bilaterally from one monkey (n = 42) with minor contributions from 2 additional monkeys (n = 4 and n = 2).

Functional distinctions among central thalamic neurons

As described in the introduction, used in conjunction, the behavioral tasks used here had the potential to reveal important functional distinctions among neurons in central thalamus. In principle, when the activity of the same neuron is considered across single-target and choice trials and visually guided and memory-guided trials, it should be possible to determine whether the task-related activity of that neuron represents the locations of visual stimuli (independent of task requirements), the locations of only those visual stimuli identified as saccadic goals, or the locations of saccadic goals independent of the presence of a visual stimulus.

The neurons depicted in Figs. 4 and 5 illustrate the range of “context” dependency exhibited by this sample of central thalamic neurons. At one extreme is a neuron (Fig. 4) that responded unconditionally to the presence of a visual stimulus in its response field. At the other extreme is a neuron (Fig. 5) having a response that was conditional on the knowledge that its response field contained a saccadic goal.

Figure 4 compares response profiles for single-target trials (black: target in RF; gray: target opposite RF) and choice trials (red: target in RF; blue: distracter in RF) for both visually guided (top row) and memory-guided (bottom row) versions of the tasks. Color-coded task panels illustrate the corresponding task events. As described in Methods, targets (or distracters) were equally likely to be red or green (because of space constraints, only the red target/green distracter configurations are shown in this and subsequent figures). The single-target traces (black and gray) show this neuron to be very selective for direction, with a target in the RF evoking a strong early transient (Fig. 4A) followed by a relatively high level of sustained activity. The sustained activation persisted throughout the visual delay period and beyond the go signal (Fig. 4B), declining only after the saccade was initiated (Fig. 4C).

Interpreting sustained delay period activity solely on the basis of single-target visually guided trials is problematic. One plausible interpretation is that delay-period activity signaled the continued presence of a saccadic goal in the response field. Alternatively, this activity, which seemed to increase as the trial progressed, could have been a signal of motor preparation for the impending saccade. Note also that these two possibilities are not mutually exclusive, in that a sensory-contingent goal-related signal could have yielded to a motor preparation signal as the impending saccade drew nearer (e.g., see Sato and Schall 2003; Thompson et al. 1996).

The activity profiles associated with the choice task and memory-guided tasks appear to rule out the “goal-related” interpretations detailed above, instead suggesting that the activity of this neuron signaled the locations of sensory stimuli largely independent of task objectives. For example, when 2 stimuli were present, one within and one opposite the RF (Fig. 4A; red and blue traces), activity was virtually identical to that for a single target in the RF (black trace). Thus the neuron did not distinguish between a stimulus that was known to be a target (black trace) from one that merely had the potential to become a target (red and blue traces). More telling is the after-cue epoch shown in Fig. 4B. Here, it is apparent that activity failed to discriminate between a stimulus that had been identified as a target (red trace) and one that was known to be a distracter (blue trace). This ambivalence to the task relevance of the stimulus even carried into the saccadic period (Fig. 4C), which showed roughly equivalent perisaccadic activity for saccades directed toward or away from the RF.

The activity of the same neuron on memory trials provided further evidence that the presence of a visual stimulus, independent of context, was the primary determinant of this neuron’s response. Figure 4D shows that activity ceased abruptly about 100 ms after the stimuli were extinguished and remained low throughout the saccadic period [although there is some hint of residual saccade-related activation for saccades in the preferred direction (black and red traces)].

The neuron shown in Fig. 5 provides a strong counterexample, in that its activity was conditional on knowledge that the stimulus specified the location of a saccadic goal. Furthermore, once established, this representation did not require the continued presence of the stimulus. On choice trials (red and blue traces), the presence of 2 stimuli (each a potential target) during the before-cue portion of the delay period yielded a response rate intermediate to that for single targets (black and gray traces). However, about 250 ms after the cue identified the target and distracter (Fig. 5B; cue), the activity profiles diverged, with activity increasing if the stimulus in the RF was revealed to be the target (red), and decreasing if revealed to be the distracter (blue).

Figure 5D shows that, whether for single-target or choice trials, direction-selective activity persisted in the absence of the stimulus, maintaining a similarly high level of differentiation during the memory period for both trial types. Likewise, the saccade-related modulation of this neuron was virtually identical, whether for saccades to visual goals or to their remembered locations (Fig. 5, C and E). In either case, sustained activity preceding movement to a preferred-direction goal was sharply suppressed just before saccade onset, a motor-related response pattern not uncommon among neurons in the central thalamus (Schlag and Schlag-Rey 1984; Schlag-Rey and Schlag 1984; Wyder et al. 2003a).

Key differences between the example neurons are apparent in Fig. 6, which quantifies and compares the degree of discrimination for single-target trials (target in RF vs. target opposite to RF) to that achieved for target/distracter discrimination on choice trials. This comparison is made for the neurons of Figs. 4 and 5 (Fig. 6, A and B) and for a third neuron (Fig. 6C) that showed a conditional response that was intermediate to those discussed above. The DI (see Methods; Fig. 3B) is plotted as a function of time for activity synchronized on relevant task events including stimulus onset (left column), cue change (middle column), and stimulus offset (right column; memory trials only). Generally, we found that DI values > 0.65 corresponded to statistically significant differences in firing rate (see Fig. 8).
The discrimination functions shown in Fig. 6A confirm that the "stimulus-contingent" neuron of Fig. 4A is very selective for direction, discriminating at a high level (DI ≥ 0.9) for a target within versus a target opposite the RF for as long as a stimulus is present (thin trace, left and middle columns). In contrast, on choice trials (thick trace) the persistence of DI values near 0.5 throughout the delay period, even after the cue change (top row, middle column), reflects the fact that this neuron fired equivalently for a target or distracter in its RF. On single-stimulus memory trials, the strong preference for a stimulus in the RF was lost because this activity required the physical presence of the stimulus (thin trace, top row, right column).

The evolution of the discrimination index is quite different for the "goal-related" neuron shown Fig. 6B (same neuron as in Fig. 5). On single-target trials (thin trace), the firing advantage for a stimulus/target within the RF developed slowly (middle row; left column), but gradually attained a high level of discrimination (DI ≥ 0.8; middle row; middle column) that was maintained throughout the memory interval (middle row; right column). On choice trials (thick trace) the discrimination function began to rise about 250 ms after the cue was presented (middle row; middle column), with target/distracter discrimi-
nation on choice trials ultimately reaching the same level as the within-RF/oppo-
site-RF discrimination on single-target trials. In both cases, a high level of discrimination was maintained throughout the memory period (middle row; right column).

The neuron shown in Fig. 6C was intermediate; this neuron was direction selective on single-target trials (thin trace) and selective for targets versus distracters after the cue on choice trials (thick trace; bottom row; middle column), but showed discrimination that was strongly dependent on the continued physical presence of the visual goal (bottom row; right column). As such, the activity of this neuron showed a dual dependency, conditional on both the presence of a visual stimulus and the knowledge that the stimulus was the goal of an impending saccade. The activity profiles for this neuron, along with those from a similar neuron, are shown in Fig. 7, A–E and F–J, respectively. The DI functions shown in Fig. 6C (light traces) indicate that neurons of this type were selective for direction on single-target trials for as long as the stimulus was visible. Accordingly, single-target firing rates converged about 150 ms after stimulus offset (Fig. 7, D and I; black and gray traces). The stimulus dependency of the target/distracter discrimination is more obvious on choice trials in which an even larger difference in firing rate, developed during the after-cue period, dissolved within the same time frame (Fig. 7.

FIG. 5. “Goal-related” activity; conventions are as in Fig. 4. For this neuron, task intervals were fixed (cue: 300 ms, memory: 600 ms).
and I; red and blue traces). The after-cue discrimination for these neurons was the product of both increases (for targets, red traces) and decreases (for distracters, blue traces) in firing from a before-cue level that was intermediate to that for single targets within (black traces) and opposite (gray traces) the RF.

**Task-related discrimination across the population**

To characterize discrimination for individual neurons and for the sample as a whole, DI functions were narrowed to 3 values each for single-target and choice trials. These values were computed by averaging DIs over selected 50-ms epochs. For choice trials, these consisted of one interval before cue presentation, one after cue presentation, and one during the memory period. For single-target trials, the temporally corresponding epochs consisted of 2 from the delay-period (one early, one later; see following text) and one from the memory period. The sample intervals are indicated by horizontal line segments in Fig. 6 (middle and right columns). The before-cue period corresponded to the 50 ms leading up to the cue (change in fixation color). The analogous single-target period is referred to as “early delay” and is the interval from 350 to 300 ms before the end of the visual delay period.

To capture target/distracter discrimination at its fullest development, the after-cue period corresponded to the first 50 ms
after the end of the delay period (i.e., 300–350 ms after presentation of the cue). Although the beginning of this sample period coincided with offset of the fixation stimulus (non-memory trials) or peripheral stimuli (memory trials), visual afferent delays on the order of 100 ms (see Wyder et al. 2003a) preclude the influence of these sensory events on activity during this initial 50 ms. In subsequent text (and figures), this epoch is referred to as “after-cue” (choice) and “late delay” (single-target). Finally, to obtain a steady-state measure of “memory-period” DI, uncontaminated by stimulus (offset)-
related transients, the final sample was drawn from well within the memory period (from 450 to 500 ms).

Figure 8 shows the distributions of DI values associated with single-target (left column) and choice (middle column) trials for each of the 3 sample epochs (Rows 1–3) for the entire sample of neurons. On the single-target tasks, it is apparent (using 0.65 line as reference) that many neurons were tuned for direction and thus discriminated between a single stimulus within and opposite the RF during both the early and late visual delays (Fig. 8, A and B). Overall, 69% (34/49) and 57% (28/49) of the early and late visual delay epochs yielded significant differences (open bars) in mean firing rate ($t$-test; $P < 0.05$), with the means of these distributions nearly identical (early: 0.69; late: 0.70) and indicative of reasonably good spatial selectivity during the period that the stimulus was present. Significant differences in firing rate were less prevalent during the memory interval with 35% (17/49) of neurons discriminating between a stimulus previously present within or opposite the RF. Accordingly, the mean DI was nearer to 0.5 (0.56).

On choice trials, DI values were distributed symmetrically around 0.5 (0.49 ± 0.08) for the before-cue interval, with only 3 (46/49) instances of a significant difference in firing rate ($t$-test; $P < 0.05$). This, of course, is the expected outcome given that the stimulus configurations for the trials that compose these 2 groups were identical with the grouping based on a future change (after cue) in stimulus status (to target and distracter). In contrast, after the cue was presented to signify one stimulus as the target and the other as the distracter, more than one third (17/49; 35%) of the sample developed a significant difference (open bars) in mean firing rate, as evidenced by the rightward shift in mean DI (Fig. 8E, 0.60 ± 0.14). We once again emphasize that the development of discrimination across Fig. 8, D and E reflects a change in RF-stimulus significance, not a change in the physical properties of the stimulus within or opposite to the RF (see Fig. 1 for task description).

On choice trials, the incidence of target/distracter discrimination during the memory interval was identical to that during the after-cue period, with 35% of the cases (14/40) having significantly greater activity for distracters in the preferred direction (Fig. 8F). Overall, the number of observations ($n = 40$) was slightly reduced because of exclusion of neurons for which there were fewer than 7 successful memory trials for each location. For 3 neurons, significant discrimination resulted from greater activity for distracters in the preferred direction (DI < 0.35; open bars, Fig. 8F). This somewhat counterintuitive finding was the result of an apparently active response suppression triggered by offset of the RF target on memory trials.

The scatter plots of Fig. 8, G–I relate DI values for the comparable epochs on single-target and choice trials. As expected, DI values are predominantly below the line of equality in Fig. 8G, indicative of discrimination during the early visual delay period on single-target trials, but not during the before-cue period on choice trials. In Fig. 8, H and I, DI values are more evenly distributed about the line, indicating that, after the cue on choice trials, discrimination between a target and distracter in the RF reached a level similar to that for a single
target within and single-target opposite the RF for many neurons.

**Differential discrimination across sample epochs as a basis for categorization**

The majority of our sample (28/49; 59%), like the 3 example neurons, were selective for direction during the late visual delay period on single-target trials (see Fig. 8B). Our main findings were that many of these neurons did discriminate between targets and distracters and tended to conform to one of the types depicted in Fig. 6. Most “nondiscriminating” neurons were similar to the neuron depicted in Fig. 6A.

For just over half of the neurons with delay-period activity (15/28; 54%), activity after the cue (during the after-cue epoch) on choice trials evolved to discriminate a target from a distracter. For 13 of these target/distracter “discriminating” neurons, there were a sufficient number of memory trials to further define them on the basis of whether discrimination persisted after the stimuli were extinguished. Most (8/13; 62%) were similar to the example shown in Figs. 5 and 6B, with target/ distracter differentiation persisting late into the memory period. The other 5, however, followed the pattern of the example neurons shown in Figs. 6C and 7 such that differentiation was lost soon after the targets were extinguished on choice trials.

The remaining 13 neurons with direction-selective delay period activity failed to discriminate between a target and distracter during the after-cue period on choice trials. Of these, 12 could be further characterized on the basis of memory trials. Most of these neurons (7/12) could be described as “stimulus-bound,” failing to convey spatial information in the absence of the target on either single-target or choice memory trials; these neurons resembled the example depicted in Figs. 4 and 6B. Four of the remaining neurons maintained spatial selectivity during the memory period on single-target trials, whereas 3 of the 5 developed the selectivity during the late memory period on choice trials. For these latter 3 neurons, differentiation occurred very late relative to when the cue was provided and may have reflected preparation for the impending saccade.

Summarizing the breakdown described above, of the 25 neurons that showed direction selectivity during the late delay period, and which could be further defined on the basis of activity on choice and memory trials, 20 conformed to one of the 3 example discrimination profiles shown in Fig. 6A (n = 7), 6B (n = 8), and 6C (n = 5). The number of units in the latter 2 categories could be augmented to n = 9 and n = 7, respectively, by considering 3 additional neurons that approached statistical significance for direction selectivity during the single-target delay period and achieved significance for both the after-cue and memory periods (n = 1; e.g., Fig. 6B) or for the after-cue period alone (n = 2; e.g., Fig. 6C). Unlike these 3, the majority (16/20) of those that did not have direction-selective delay-period activity also failed to discriminate between targets and distracters during the analogous after-cue period on choice trials, as expected.

As noted above, most neurons with spatially selective delay period activity on single-target trials conformed closely to one of the 3 patterns depicted in Fig. 6. Rather than an artificial parsing of a response continuum based on statistical criteria, these groups appeared to be the basis for true qualitative distinctions. Consistency among members within each group is evident by comparing the averaged DI functions shown in Fig. 9, A–C to those for the example neurons shown in Fig. 6, A–C. For the plots in Fig. 9, DI values were averaged across neurons with similar response profiles, as described above. Although averaging substantially reduced the noise, the magnitude and timing of the modulations that characterize the groups remained largely intact.

**Sensitivity to stimulus color**

Tasks were designed so that neural selectivity for the color of either the eccentric stimulus or fixation stimulus would not confound evidence for target/distracter discrimination (see Methods; Fig. 3). Targets and distracters were not associated with a particular eccentric or fixation stimulus color, but were defined by the relationship between the colors presented in the RF and at fixation (match vs. nonmatch). We had no reason to anticipate strong preferences (either neural or behavioral) for a particular stimulus or fixation color as such would not have aided (and could have hindered) task performance. On the whole, we found little evidence of a general preference for color among neurons that were selective for targets versus distracters. When trials were instead parsed according to RF stimulus color or fixation stimulus color, DI values deviated little from 0.5. Based on the same after-cue time interval (300–350 ms) used to compute target/distracter DI values, DI values for RF-stimulus color and fixation stimulus color deviated from 0.5 by ±0.08 and ±0.07, respectively. These deviations are small by comparison to an average deviation of ±0.25 for target/distracter differentiation.

A 2-way ANOVA (RF stimulus color × fixation stimulus color) was performed to further examine the relative potency of the effects of RF stimulus color, fixation stimulus color, and stimulus identity (target vs. distracter selectivity reflected in magnitude of the interaction) on target/distracter-selective neurons. The ANOVA evaluated activity for the same 50 ms after-cue period used to test for significant differences in target versus distracter firing rates (Fig. 8E). The activity of relatively few target-/distracter-selective neurons showed significant main effects for RF-stimulus color (6/16), fixation stimulus color (3/16), or both (3/16). In contrast, in all but one case (which approached significance at P = 0.054), the presence of a significant interaction confirmed selectivity for targets (color matches) versus distracters (color nonmatches). Moreover, in each of the 6 cases in which a main effect of color was observed, the interaction was much larger than the main effect(s). This difference is evident in the corresponding DI values. For neurons that showed a main effect of RF-stimulus color (n = 6), DI values deviated by ±0.12 from 0.5, compared with ±0.28 for target/distracter differentiation for these same neurons. Similarly, for neurons showing a main effect of fixation-stimulus color (n = 3), DI values deviated by ±0.18 from 0.5, compared with ±0.34 for target/distracter differentiation.

**Timing of target–distracter differentiation**

The activity of each of the neurons contributing to the average DI functions in Fig. 9, B and C was differentially modulated in response to the cue identifying the locations of the target and distracter relative to its RF. In principle, this
evolving activity reflects the processes of detecting the cue change, registering the cue color, and identifying the matching stimulus (or by elimination, the nonmatching stimulus). The time course of neural target–distracter discrimination was quantified by estimating the time at which activity began to reflect the changed status of the stimuli and the time at which this gradually increasing difference in activity approached its maximum. As shown in Fig. 3B and described in METHODS, for each neuron, the onset and offset of differentiation were given as the times at which a best-fit cumulative Weibull function reached 25 and 75% of its maximum value. Weibull fits were generally quite good for neurons that discriminated between targets and distracters; correlation coefficients (plots of predicted vs. observed) ranged from 0.81 to 0.98, with a mean of 0.94. The estimates derived from these fits are plotted in Fig. 10. Mean onset time (Fig. 10A) and mean offset time (Fig. 10B) were 171 (±77) and 253 (±60) ms after presentation of the cue, respectively. On average, the DI function rose from minimum (25%) to maximum (75%) over a period of 82 (±42) ms (Fig. 10C). A best-fit line to the scatter plot relating 75 and 25% points on the cumulative Weibull function had less than unity slope at 0.67 and an intercept of 139 ms, suggesting that later starting increases in the DI function required slightly less time to reach their maximum (Fig. 10D). There was no evidence that timing for neurons that differentiated during the memory interval (filled symbols) and those that did not (open symbols) were different by these measures.

Analysis of error trials

Neurons that differentiate between targets and distracters in the RF could contribute to the process of identifying and/or selecting the appropriate stimulus for an upcoming saccade. Presumably then, trials in which the RF stimulus was apparently misclassified would be associated with either less-robust target/distracter differentiation or perhaps even neural discrimination of opposing sign (consistent with incorrect choice). Unfortunately, monkeys made very few choice errors (on average 6 error trials per recorded neuron), providing no opportunity to make statistically meaningful comparisons for an
individual neuron. However, we could evaluate error trials by pooling across all target-/distracter-selective neurons (n = 16). To do so, we compared normalized firing rates for the 4 possible outcomes: 1) correct: target in RF, saccade to target; 2) correct: distracter in RF, saccade to target; 3) error: target in RF, saccade to distracter; and 4) error: distracter in RF, saccade to distracter. For each neuron, the mean firing rate during the after-cue period (300–350 ms after cue) was calculated for each of the 4 conditions and normalized to the rate obtained for correct trials to targets in the RF (set to 1.0). These data indicate that, on average, differentiation on error trials was both less robust (firing rate difference not significant; t-test; P > 0.05) and opposite in polarity to that observed on correct trials. On correct trials, mean firing rate for a distracter in the field (n = 785) was about half (0.52) that for a target in the field (1.0; n = 787). Firing rates were intermediate for error trials with errant saccades to a distracter in the field (n = 56) associated with a higher rate (0.73) than failures to saccade to a target in the field (0.62; n = 42). These data suggest that choice errors resulted when neural activity provided ambiguous or erroneous information about the identity of the stimulus in the RF. We emphasize, however, that a task that deliberately elicits a greater proportion of errors would be needed to provide a rigorous test of this hypothesis.

**Recording sites**

Figure 11 plots the locations of 45 of the 49 neurons included in this report. Two of the remaining 4 units were recorded at a location 0.5 mm rostral to the section shown in Fig. 11A, and for the final 2 units, histology was not available; however, MRI images of electrode placement indicate that these units were located in the central thalamus. Recordings in one monkey ranged from A.P. 6.5 to A.P. 8 (Fig. 11, A–C, section 6.5 not shown), and in the second monkey they were restricted to A.P. 11 (Fig. 11D). Anterior–posterior levels are estimated based on Olszewski (1952). Units were recorded mainly in the central lateral (CL) and paracentral (Pc) nuclei, and in paralaminar regions of the ventral lateral (VL) and ventral anterior (VA) nuclei. In addition, a few units were recorded in the lateral dorsal (LD) nucleus and in paralaminar regions of the medial dorsal (MD) nucleus.

Evidence for regional segregation of discriminating versus nondiscriminating neurons or for the response types highlighted in Figs. 4–7 (see symbol key) was not strong. Although revealing any such topography definitively would require a much larger sample, we note that neurons recorded in the vicinity of rostral CL, caudal Pc, and the paralaminar regions of VL were highly likely to discriminate targets from distracters (filled black symbols) with all cases of choice memory trial differentiation (filled black circles) found in these regions. Much more rostrally, 4 additional discriminating units were localized to the paralaminar VA nucleus (asterisks). Although differentiating between targets and distracters on choice trials, these neurons were not fully evaluated on the memory variant of the task.

**Discussion**

In a previous report (Wyder et al. 2003a), we demonstrated that many neurons in central thalamus maintain spatial information throughout the instructed delay period of a visually...
guided delayed-saccade task. These earlier findings established that the activity of central thalamic neurons can bridge the gap between the sensory encoding and motor execution phases of a delayed-saccade task; however, they did not define a role for these neurons in the context-specific linking of sensory signals to motor commands. As the primary mediators of information transfer from subcortical structures to frontal cortex, we have postulated that central thalamic nuclei could play key roles in the processes that link specific stimuli with specific actions, as required by present circumstances and current behavioral objectives. Consistent with this idea, we report here that the delay-period activity of some central thalamic neurons is a function of both the sensory stimulus and its relevance for guiding a rewarded saccade.

**Functional distinctions among neurons with delay-period activity**

Comparison of delay-period activity across single-target, choice, and memory-trial types revealed that individual thalamic neurons differed in ways suggestive of fundamentally distinct contributions to visuomotor control. As the primary mediators of information transfer from subcortical structures to frontal cortex, we have postulated that central thalamic nuclei could play key roles in the processes that link specific stimuli with specific actions, as required by present circumstances and current behavioral objectives. Consistent with this idea, we report here that the delay-period activity of some central thalamic neurons is a function of both the sensory stimulus and its relevance for guiding a rewarded saccade.

**FIG. 11.** Locations of recorded units from monkeys ML (A–C) and SQ (D). Locations were reconstructed from electrolytic lesions made near recording sites. Units are labeled according to their DI function profiles, as described in the text. Neurons labeled “no discrimination” (open circles) did not discriminate during any of the single-target or choice trial sample epochs used to evaluate discrimination. “Other” (black filled squares) refers to neurons that discriminated during at least one sample epoch, but did not match one of the sample profiles shown in Fig. 9. Approximate anterior–posterior locations of each section relative to the interaural axis are indicated next to panel label. Two units not shown were located 0.5 mm caudal to the section shown in A, and 2 additional units were from a third monkey for which histology was not available. AD, anterior dorsal; CL, central lateral; CM, centromedian; LD, lateral dorsal; MD, medial dorsal; PC, paracentral; VA, ventral anterior; VL, ventral lateral.

Neurons labeled “no discrimination” (open circles) did not discriminate during any of the single-target or choice trial sample epochs used to evaluate discrimination. “Other” (black filled squares) refers to neurons that discriminated during at least one sample epoch, but did not match one of the sample profiles shown in Fig. 9. Approximate anterior–posterior locations of each section relative to the interaural axis are indicated next to panel label. Two units not shown were located 0.5 mm caudal to the section shown in A, and 2 additional units were from a third monkey for which histology was not available. AD, anterior dorsal; CL, central lateral; CM, centromedian; LD, lateral dorsal; MD, medial dorsal; PC, paracentral; VA, ventral anterior; VL, ventral lateral.
quantitative criteria. On the other hand, “discriminating” neurons could be subcategorized on the basis of whether they continued to represent the location of the identified goal after the stimuli (target and distracter) were extinguished on choice memory trials. Thus the delay period activity of some thalamic neurons was conditional on both the physical presence of a stimulus in the RF and the knowledge that the stimulus was the target of an impending saccade.

Unlike the neurons with strictly stimulus-dependent activity described above, a thalamic neuron that differentiated between saccadic goals and irrelevant stimuli must contribute to later stages in the process of linking specific visual stimuli (targets) to rewarded saccades. Such a neuron (e.g., Figs. 5; 6, B and C) could have been either an active participant in the perceptual decision process that identifies the RF stimulus as a target or distracter on the basis of its color, or it may have been involved in the postperceptual process of planning a saccade to the identified target.

The neural correlates of perceptual decision-making (e.g., target selection) and postperceptual motor planning processes are logically and practically dissociable (see Schall 2003 for recent review). In FEF, for example, neurons have been shown to participate in one, the other, or both (Murthy et al. 2001; Sato et al. 2001; Thompson et al. 1996). Generally speaking, studies that have been successful at distinguishing between these 2 alternatives have used tasks that differentially emphasize the perceptual and motor requirements for correct performance (Murthy et al. 2001; Sato et al. 2001), or tasks that disrupt the usual spatial congruence between stimulus and response (Gold and Shadlen 2003; Murthy et al. 2001; Sato and Schall 2003). We emphasize that the tasks used here were not designed for the purpose of distinguishing between these alternatives. Nevertheless, with some reasonable assumptions, we can infer that the rising discrimination functions reported here are more likely to be correlates of the perceptual process (color matching) of identifying the target (or distracter). Consistent with this interpretation, the modulations in firing rate responsible for positive inflections in the neural discrimination functions were time-locked to presentation of the informative color cue, not to the GO signal or to the saccade itself. For example, in the single-neuron discrimination functions of Fig. 6, B and C (middle panels, thick lines), discrimination functions began to rise even before the earliest GO signal (300 ms after the cue) could have been detected by the monkey (350–400 ms after the cue, assuming a reasonable afferent delay). This is also true for the entire population of discriminating neurons, with discrimination functions approaching a maximum value no later than 350 ms after the cue (see Fig. 10B, mean 75% max = 238 ms). Furthermore, recall that random interleaving of variable intervals, along with visually guided and memory-guided trials, precluded reliable anticipation of when the GO signal would have occurred relative to the cue (see METHODS). At a minimum, temporal uncertainty was created by interleaving fixed-interval visually and memory-guided choice trials resulting in randomly presented Cue-GO intervals of either 300 or 900 ms (cue interval, 300 ms; memory interval, 600 ms). At a maximum, 6 Cue-GO intervals, ranging from 300 to 1,350 ms, were randomly presented by interleaving variable-interval visually and memory-guided choice trials.

Despite the substantial temporal uncertainty associated with these tasks, by definition, there was always congruence between the location of the “target” stimulus and the vector of the saccade required for reward. Thus in the choice tasks, the time of target selection was also, theoretically, the earliest time for knowing the required saccade vector. One could argue therefore that, even with an unpredictable GO signal, there would be little cost for advance motor planning. Given this logic, the possibility that postcue increases in activity represented a postperceptual motor readiness signal for a saccade that was held in abeyance cannot be ruled out for those neurons that continued to fire throughout the memory period and up to the time of saccade execution (e.g., Figs. 5, 6B, 9B; see Gottlieb and Goldberg 1999; Snyder et al. 1997). On the other hand, this interpretation seems unlikely to account for those neurons that discriminated between targets and distracters but then ceased firing (and did not resume firing at any time before the saccade) after the targets were extinguished on memory trials (Figs. 6C, 7, 9C). Again, using the same logic, a target-specific motor-readiness signal, once established, would not require the continued presence of the stimulus and should therefore persist until the saccade is executed. In contrast, an evolving target-selection signal, which according to recent models reflects the process of “accumulating sensory evidence” (Shadlen and Newsome 2001; reviewed in Gold and Shadlen 2002; Schall 2003), would require that stimuli remain visible throughout the target/distracter discrimination process.

Based on the arguments outlined above, we suggest that the initial phase of the neural discrimination among thalamic neurons is more likely a correlate of the perceptual process that culminates in selection of the target. Although this interpretation seems especially plausible for those neurons in which the evolving discrimination required persistently visible stimuli, we concede that the case for neurons that continued to convey spatial information during later stages of the choice memory task (i.e., throughout the memory interval and beyond the GO signal) is less clear-cut. As noted above, advance motor planning cannot be ruled out for these neurons, but we do note that the onsets and times to peak discrimination for this group were very similar to those for neurons that required the physical stimulus(i), suggesting that the rising discrimination functions were correlates of the same process for the 2 neuronal groups. However, even if the early discrimination phase (i.e., before the GO signal) is a perceptual correlate, later activity could have been related to motor planning; transitions from perceptual discrimination to motor planning have been demonstrated for neurons in FEF (Sato and Schall 2003). Alternatively, later activity might have been a correlate of spatial working memory for the previously selected, but no longer present, target. Resolution of these questions will require further study with tasks designed specifically for resolving these issues.

Possible role of cortico-subcortical loops in target/movement selection

Our finding that central thalamic neurons can signal both stimulus location and behavioral significance might be viewed as a “missing link,” providing an essential piece of evidence for the argument that cortical-subcortical loops play a role in the evolution of sensorimotor decision-making signals. To date, most, if not all, studies of decision-related signals have centered on visuomotor cortical regions and their downstream targets. Correlates of perceptual discrimination, target selec-
tion, and/or movement selection have been reported in both frontal and parietal visuomotor regions, including the FEF (reviewed in Kim and Shadlen 1999; Schall and Thompson 1999; Sommer and Wurtz 2001; Thompson et al. 1996), PFCdl (Hasegawa et al. 2000; Kim and Shadlen 1999), and area LIP (Platt and Glimcher 1997; Shadlen and Newsome 1996). Subcortical regions in which analogous signals have been observed include the SC (Basso and Wurtz 1998; Glimcher and Sparks 1992; Horwitz and Newsome 1999; McPeek and Keller 2002) and structures of the basal ganglia, including striatum and substantia nigra pars reticulata (SNr) (Basso and Wurtz 2002; Lauwereyns et al. 2002; for reviews see Graybiel et al. 1994; Hikosaka et al. 2000; Mink 1996).

Evidence for decision-related correlates in SC and basal ganglia could simply reflect the descending, feedforward results of computations that are local to cortex. Both the SC and striatum (caudate) receive direct input from neurons in frontal visuomotor regions (Lynch et al. 1985; Shook et al. 1990, 1991; Yeterian and Pandya 1993) with basal ganglia output (by SNr) also directed to the cortico-recipient layers of the SC (reviewed in Hikosaka et al. 2000). Thus both direct and indirect (by basal ganglia) corticofugal influences can shape the SC saccadic motor commands that will be conveyed to downstream saccade generator circuits. Although a “feedforward” interpretation of subcortical decision correlates is reasonable, our finding that neurons in paralaminar VA, VL, and intralaminar regions of central thalamus discriminate between targets and distracters suggests that similar information is present in a major subcortical input to frontal cortex (Ilinsky et al. 1985; Lynch et al. 1994) and raises the possibility that cortico-subcortical loops contribute to evolving decision-related signals.

Nuclei within the central thalamus are the next to last synapse in cortico-subcortical loops involving the basal ganglia and cerebellum. Thus for example, cortico-striato-thalamo-cortical loops originating in FEF and SEF return to cortex by the paralaminar VA (Fig. 12A; Ilinsky et al. 1985). Similarly, a cortico-cerebello-thalamo-cortical loop returns to FEF and SEF by the paralaminar VL (Fig. 12B; Lynch et al. 1994).

Along with relaying signals from basal ganglia and cerebellum to frontal cortex, thalamic neurons in VA and VL receive a robust input from cortex (see Steriade et al. 1997 for review). It has been suggested that this corticothalamic feedback projection, which arises from layer 6, plays a “modulatory” role, although its function in the current context has not been considered previously (see Sherman and Guillery 2001, 2002 for reviews). Nevertheless, just as the longer basal ganglia and cerebellar loops might contribute to the formation of cortical decision-related signals, more direct thalamocortical interactions could also play an important role. Whether components of long loops, short loops, or both, “discriminating” thalamic neurons would be in a position to provide an early and sustained influence on evolving cortical decision signals.

**Time course of neural discrimination**

The timing of neural discrimination in relation to task events is critical for considering the possible functional relevance (e.g., perceptual discrimination, motor preparation; see above) of the modulated activity. In principle, it could also provide some insight into the relative contributions of the many visuomotor areas in which analogous sensitivities to context have been observed. In practice, however, the utility of such comparisons is compromised by differences in both task design and methods used to estimate timing. For example, neural discrimination in tasks that require search for a feature singleton (i.e., pop-out task) or detecting change in one of several stimulus elements occurs relatively quickly. Using similar pop-out tasks, comparable target detection times have been reported for neurons in FEF (140 ms; Thompson et al. 1996), PFCdl (135 ms; Thompson et al. 1996), and SNr (115 ms; Ilinsky et al. 1985).
ms; Hasegawa et al. 2000), and the SC (139 ms; McPeek and Keller 2002). In each of these tasks, multiple stimuli appeared simultaneously with one stimulus (the target) differing along a single feature dimension (e.g., color, spatial frequency). Using a paradigm in which a change in relative luminance differentiated the target stimulus from surrounding distractors, neural estimates of target detection were on the order of 100 ms for both the SC (Basso and Wurtz 1998) and SNr (Basso and Wurtz 2002).

The similar estimates of neural discrimination from Thompson et al. (1996) and McPeek and Keller (2002) may be compared with some confidence because they are based on virtually identical behavioral paradigms and analytical methods (i.e., signal detection method applied to individual neurons similar to that used here). The values reported by Hasegawa et al. (2000) and Basso and Wurtz (1998, 2002) might be considered “in the ballpark” given differences in behavioral paradigm and estimates of “target selection” times based on the populations rather than individual neurons.

In this study, we used essentially the same analytical method (see Figs. 3 and 4) used by Thompson et al. (1996) and McPeek and Keller (2002), with a slightly different discrimination criterion, but more important, a very different task. Whether we consider the time at which neural discrimination achieved 25% (171 ms) or 75% (253 ms) of its maximum, the times for our sample of thalamic neurons are on average longer than those reported above. This difference is very likely attributable to significant differences in task design. Unlike a simple pop-out task, which requires the monkey to detect the “oddball” stimulus, the choice tasks used here (see Fig. 1) first required detecting the change in fixation light color (instruction cue) followed by evaluation of the eccentric stimuli for match or nonmatch status. Using this same method of cueing (i.e., change in color of fixation stimulus), Sommer and Wurtz (2001) reported on a sample of FEF neurons that, as a population, required 300 to 400 ms to differentiate between a relevant (go trials) and irrelevant (Nogo trials) stimulus in the response field. Although it is not certain that the go/Nogo discriminating neurons (at 300–400 ms) recorded by Sommer and Wurtz (2001) are the same class of FEF neuron as the target-/distracter-discriminating neurons (at 140 ms) described by Thompson et al. (1996), they clearly share the property of representing both stimuli and their behavioral relevance.

Given the above, the use of timing to place thalamus within a functional hierarchy of “decision-related” visuomotor areas, if at all possible, must await future studies in which tasks and analyses are directly comparable.

Related studies of primate central thalamus

To date there have been very few electrophysiological studies of primate central thalamus (see Sommer 2003 for review). In some of the first studies of this region, Fuster and Alexander (1971, 1973) provided evidence that delay-period activity within MD of primates plays a role in working memory. In monkeys trained to perform a delayed manual response, sustained activation conveyed relevant information about an earlier informative cue during the memory (delay) period leading up to the response (Fuster and Alexander 1971, 1973). Until very recently, the seminal studies of Schlag and Schlag-Rey (1984) and Schlag-Rey and Schlag (1984) stood as the only published accounts of visual- and saccade-related activity within nuclei in this region. As stated in the introduction, in the course of surveying the visuo-oculomotor properties of central thalamic neurons (Wyder et al. 2003a), we noted that many had spatially tuned delay-period activity, a finding that motivated the current study.

In parallel with our recent studies, Sommer and Wurtz (2001, 2003b) have explored the role of the SC-recipient region of MD in conveying a corollary discharge signal from the SC to frontal cortex (e.g., FEF). They reported that muscimol inactivation of MD reversibly impaired a monkey’s ability to perform double-step saccades, finding that the vector of the second saccade deviated in a manner consistent with a partially disrupted corollary discharge signal. Accompanying single-unit recordings from identified SC-recipient neurons suggest that MD receives multiple signals from the SC, including saccade-related, visual-delay period, and memory-period activities (Sommer and Wurtz 2003a). Similarly varied response profiles were observed by Tanibuchi and Goldman-Rakic (2003) in their sample of MD neurons, suggesting that MD could, in turn, provide a variety of signals to its principal targets in frontal cortex (e.g., FEF, PFCdl). We observed a similar range of response types in our earlier report (Wyder et al. 2003a), but with the majority of the sample localized to paralaminar VA, VL, and intralaminar nuclei.

Single-unit recording and reversible inactivation studies of skeletonmotor VA and VL suggest that basal ganglia–recipient (VA) and cerebellar-recipient (VL) regions of motor thalamus are functionally distinct (VanDonkelaar et al. 1999, 2000). VanDonkelaar and colleagues propose that internally generated (e.g., to a remembered target location) and visually triggered (to a visible target) limb movements are disproportionately represented within VA and VL, respectively. Whether oculomotor regions of VA and VL display a similar dichotomy is an open question. Although our sample is inadequate to address this issue, we note that several of the target/distracter-selective neurons that showed a strong visual dependency were recorded in the vicinity of VL (e.g., see Fig. 11).

In addition to the ascending projections that form the last leg of cortico-subcortical loops, the central thalamus provides the main subcortical input to striatum. Whereas this projection was once thought to emanate exclusively from intralaminar nuclei, recent studies have documented the existence of sizable projections from VA and VL (McFarland and Haber 2000). The functional significance of thalamostriatal inputs, which are known to contact both medium spiny and cholinergic interneurons, is largely unknown. However, a recent study of the centromedian–parafascicular complex (Cm-Pf) of the caudal intralaminar group suggests that the responsiveness of striatal cholinergic interneurons to salient, behaviorally relevant, sensory events depends on the integrity of the projection from Cm-Pf (Matsumoto et al. 2001).

In summary, despite the recent interest in the central thalamus, studies remain too few and varied to develop a strong conceptual framework for understanding the contributions of its constituent nuclei to visuo-oculomotor control. It is intuitively obvious that some thalamic neurons or regions must play an essential feedback role, providing cortical structures with lower-order information about the progress of ongoing, or the consequences of completed actions (e.g., Sommer and Wurtz 2001, 2003a,b; see also Wyder et al. 2003a for discus-
sion). Our current findings, which show that the activity of some central thalamic neurons evolves to distinguish between behaviorally relevant and irrelevant sensory stimuli, indicate that the central thalamus could play a role in the higher-order processes that link specific stimuli to specific actions. In a broader context, evidence for cognitively derived signals in the central thalamus fits well with developing concepts on the nonmotor functions of basal ganglia and cerebellum and is consistent with the idea that cortico-subcortical loops contribute to the neural computations that guide context-appropriate action.

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