Activity Properties and Location of Neurons in the Motor Thalamus
That Project to the Cortical Motor Areas in Monkeys

Kiyoshi Kurata

Department of Physiology, Hirosaki University School of Medicine,
Hirosaki, 036-8562 Japan

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Address correspondence:

Dr. Kiyoshi Kurata
Department of Physiology
Hirosaki University School of Medicine
Hirosaki 036-8562, Japan
Tel: +81-172-39-5011
Fax: +81-172-39-5013
E-mail: kuratak@cc.hirosaki-u.ac.jp

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ABSTRACT

The activity of neurons in the motor nuclei of the thalamus that project to the cortical motor areas (the primary motor cortex, the ventral and dorsal premotor cortex, and the supplementary motor area) was investigated in monkeys that were performing a task in which wrist extension and flexion movements were instructed by visuospatial cues prior to the onset of movement. Movement was triggered by a visual, auditory, or somatosensory stimulus. Thalamocortical neurons were identified by a spike collision, and exhibited two distinct types of task-related activity: (1) a sustained change in activity during the instructed preparation period in response to the instruction cues (set-related activity); and (2) phasic changes in activity during the reaction and movement time periods (movement-related activity). A number of set- and moment-related neurons exhibited direction selectivity. Most movement-related neurons were similarly active, irrespective of the different sensory modality of the cue for movement. These properties of neuronal activity were similar, regardless of their target cortical motor areas. There were no significant differences in the antidromic latencies of neurons that projected to the primary and nonprimary motor areas. These results suggest that the thalamocortical neurons play an important role in the preparation for, and initiation and execution of the movements, but are less important than neurons of the
nonprimary cortical motor areas in modality selective sensorimotor transformation. It is likely that such transformations take place within the nonprimary cortical motor areas, but not through thalamocortical information channels.

**Key words:** motor thalamus, cortical motor areas, antidromic stimulation, sensory cues, wrist movement
INTRODUCTION

Many motor areas exist within the primate cerebral cortex, and each cortical motor area has been suggested to contribute to specific aspects of motor control of a forelimb via distinct neuronal activity (see Evarts et al. 1984; Kurata 1994a; Tanji 1994). It has been proposed that the specific information for each specialized cortical motor area is processed through corticocortical networks (Jones and Powell 1970, 1969; Pandya and Kuypers 1969; Wise et al. 1997), or through networks involving subcortical motor centers, such as basal ganglia and cerebellum, through the motor nuclei of the thalamus (the motor thalamus) (Alexander et al. 1986; Allen and Tsukahara 1974; DeLong and Georgopoulos 1981; Evarts and Thach 1969; Houk and Wise 1995; Kemp and Powell 1971). The latter view is supported by anatomical and physiological data.

Anatomically, each cortical motor area has a specific connection to the cerebellum (Dum and Strick 2003; Holsapple et al. 1991; Kelly and Strick 2003; Orioli and Strick 1989) and basal ganglia (Alexander et al. 1986; Hoover and Strick 1993; Middleton and Strick 2000). The anatomy of these connections suggests that the motor thalamus plays a key role in providing the specific channels from the basal ganglia and cerebellum to the cortical motor areas (Asanuma et al. 1983; Darian-Smith et al. 1990; Percheron et al. 1996; Sakai et al. 1996, 2002; Steriade et al. 1997). The
main inputs to the ventral and dorsal premotor cortex (PMv and PMd, respectively) come from Area X and the rostral portion of the nucleus ventralis lateralis, pars caudalis (VLcr), respectively, whereas the primary motor cortex (MI) receives dense projections from the nucleus ventralis posterior lateralis, pars oralis (VPLo) and the caudal portion of the nucleus ventralis lateralis, pars caudalis (VLcc) (Kurata 1994b; Matelli et al. 1989; Schell and Strick 1984). The nucleus ventralis lateralis, pars oralis (VLo) serves as a main source of input to the supplementary motor area (SMA) (Rouiller et al. 1994; Sakai et al. 2002; Shindo et al. 1995).

Recordings of the activity of neurons within the motor thalamus supports the idea that the thalamocortical system channels information about the initiation and execution of movement (Anderson and Turner 1991; Butler et al. 1992; Nambu et al. 1991; Strick 1976). In the aforementioned studies, it was reported that the neurons were active shortly before the onset of movement (referred to as movement-related activity). Subsequently, van Donkelaar et al. (1999) reported that thalamic neurons discharged differently in visually or internally guided movements; specifically, neurons in VPLo and Area X tend to be active during sensorially (visually) triggered movements, whereas neurons in the VLo and parvocellular portion of the ventral anterior nucleus (VApC) were more active during internally generated limb movements. These findings correspond closely to the findings that neurons in the PMv and PMd are active preferentially during
visually guided movements, whereas the SMA contains neurons that are more active during internally guided movements (Kurata and Wise 1988b; Mushiake et al. 1991; Okano and Tanji 1987; Thaler et al. 1988). Furthermore, movement-related neurons in the SMA (Tanji and Kurata 1982) and in the PMd and PMv (Kurata and Tanji 1986) were reported to be active preferentially in response to different modalities of sensory signal (visual, auditory, and somatosensory); whether the same is true for thalamocortical neurons is not known.

In addition to movement-related activity, the cortical motor areas exhibit distinctive ‘set-related’ activity, which refers to a sustained change in activity throughout a preparation period that precedes movement in response to instruction signals for forthcoming movements. Such activity is considered to reflect motor preparation for forthcoming forelimb movements, mainly because it frequently showed a preference for the direction of movement (Alexander and Crutcher 1990; Crammond and Kalaska 2000; Hoshi and Tanji 2002; Johnson et al. 1999; Johnson et al. 1996; Kurata 1993; Riehle and Requin 1989; Tanji and Evarts 1976; Tanji and Kurata 1985; Tanji et al. 1980; Weinrich and Wise 1982). In the primate thalamus, neurons in the nucleus centralis (Wyder et al. 2004) and the nucleus medialis dorsalis (MD) (Watanabe and Funahashi 2004a, b) exhibited sustained activity during a delay period that preceded saccadic eye movement, and those in the VA and VL were active during a delay period
maintaining a memory (Fuster and Alexander 1973). However, it is not clear whether neurons in the motor thalamus exhibit set-related activity that reflects preparation for impending limb movements. There are only a few reports of neuronal activity in the motor thalamus related to hand/wrist movements of awake behaving monkeys in which inputs from basal ganglia and/or cerebellum and outputs to the cortical motor areas were identified physiologically (Anderson and Turner 1991; Nambu et al. 1988, 1991). It is not known whether thalamic neurons that project to specific cortical motor areas exhibit set- and movement-related activity or whether different types of information are conveyed by differential neuronal activity reflecting sensorimotor transformation for the determination of the direction of an impending wrist movement.

Four questions were addressed in the present study. First, do thalamic neurons project to more than one cortical motor area? Second, does the location of the thalamocortical neurons correspond to previous anatomical findings? Third, do thalamocortical neurons exhibit set-related activity? Finally, are movement-related thalamocortical neurons preferentially active in response to different modalities of sensory cue? To answer these questions, thalamic neurons that projected to four cortical motor areas (MI, PMv, PMd, and SMA) were identified electrophysiologically by spike collision, and the activity of these neurons was analyzed quantitatively. Using signals to instruct wrist movement directions and trigger cues with
different sensory modalities to initiate the movement, two types of neuronal activity, set- and movement-related, were examined to elucidate the role of the motor thalamus in the preparation and execution of movements.
METHODS

Subjects and apparatus

Two male Japanese monkeys (Macaca fuscata) were used in the present study. They were cared for in the manner prescribed in Guiding Principles for Research Involving Animals and Human Beings of the American Physiological Society. Each monkey was seated comfortably in a primate chair and was trained to perform sensorially cued wrist extension/flexion movements. Both upper extremities were rigidly fixed to L-shaped plastic casts with the elbow flexed at 90°. On the tip of the left plastic cast was a vertical manipulandum (made of 10 x 10 cm plastic plate) to which monkey’s right hand was bandaged with the fingers extended. The proximal end of the manipulandum was attached to a pivot, and the axis of the pivot and the wrist joint were aligned to permit extension and flexion movements around the joint. A potentiometer monitored the angle of the wrist joint.

Visual cues were provided by a horizontal row of 15 light-emitting diodes (LEDs) (Fig. 1A), each of which could emit three colors (green, red, and orange). The LEDs were placed 15 cm in front of the monkey. Each LED was separated by 5 mm and the central LED was aligned with the monkey’s midline. The angle of the wrist joint was indicated by the green illumination of one of the 15 LEDs. Each LED represented 5.0° of wrist
angle except for the central LED with a range of 1.0° for the central holding zone. Above the LEDs, a loudspeaker was placed to provide an auditory cue. A probe connected to a DC motor to provide a somatosensory cue was attached on the radial surface of the right forearm at a point 2 cm proximal to the right wrist joint.

**Behavioral task**

Each trial was initiated by red illumination of the central LED that indicated the central holding zone. The monkeys were required to align their hand positions on the central holding zone. When their hand positions were aligned on the central holding zone, the central LED turned green from red. Then, the monkeys were required to withhold a movement for a randomized period of 2.0-3.5 s (the holding period) until a trigger signal (either visual, auditory, or somatosensory) for movement initiation was presented. During the holding period, a visual directional instruction signal was selected randomly and was presented 0.5 s after trial initiation. The instruction signal (IS) was provided as follows: the third LED from the end of the row turned red to indicate the target location of a flexion (left) or an extension (right) movement (Fig. 1A). The LED that provided the IS was illuminated until the trigger signal (TS) for movement was presented. The sensory modality of the TS (visual, auditory, or somatosensory) was selected randomly for each trial. The visual trigger signal was a change of
the central LED color from green to orange. The auditory signal was a pure 1 kHz tone at an intensity of 18 dB above the background noise level. The somatosensory cue for movement was a 40 Hz vibrotactile stimulus with an amplitude of 150 µm on the right forearm, delivered through the probe. The trigger signal remained present until the monkeys hit the target. If the monkey initiated a required movement within 700 ms of the presentation of the trigger signal (reaction time limitation), reached the target within 500 ms (movement time limitation), and maintained its hand position for at least 500 ms within the target zone, then a drop of juice (0.1 ml) was delivered as a reward. If the wrist position moved out of the holding zone during the holding period (the preinstruction and delay periods, combined), or moved out of the holding zone in a direction that was opposite to that which had been instructed after the trigger signal presentation, the animal was required to restart the trial.

Movement onset was defined as the time at which the wrist position left the holding zone in the instructed direction. The end of the movement was defined as the time at which the wrist position entered the target zone. Accordingly, reaction time (RT) was equal to the period between the onset of the trigger signal and movement onset; movement time (MT) was equal to the period between the onset and end of the movement.
Recording and stimulation methods

After the behavioral training, stimulus electrodes were implanted chronically within the cerebral cortex and a stainless steel recording chamber (16 x 27 mm) and head fixation bolts were attached to the skull under aseptic conditions. Monkeys were anesthetized by pentobarbital sodium (30 mg/kg, i.m.) following the administration of ketamine hydrochloride (8 mg/kg, i.m.) and atropine. During surgery, ketamine hydrochloride was supplemented if necessary. The bone over the four cortical motor regions (MI, PMv, PMd, and SMA) was removed. The location of the implanted electrodes was determined using established cortical landmarks (Gentilucci et al. 1988; Kurata 1993; Kurata and Hoffman 1994; Kurata and Tanji 1986; Luppino et al. 1991; Rizzolatti et al. 1988; Tanji and Kurata 1982, 1985). After the location of the central sulcus, the arcuate sulcus, the arcuate spur, the superior precentral sulcus, and the superior sagittal sinus had been identified by visual inspection of the dura mater, the forelimb region of the MI was identified by surface stimulation of the dura that covered MI. Thereafter, a hand-driven microdrive (Narishige, SM-11) was used to insert 16 stimulation electrodes (8 pairs of bipolar electrodes) into the cortical motor areas (three pairs for the MI, two pairs for the PMd and SMA, and one pair for the PMv) at the depth of 2 mm from the cortical surface (Fig. 1B). The electrodes were glass-insulated Elgiloy electrodes that had an impedance of <0.1 MΩ at 333
Hz. An enamel-coated copper wire (100 µm in diameter) was attached to each electrode. The free end of each wire was soldered to a socket that was fixed near the recording chamber; this end was connected to the isolator of an electrical stimulator (Dia Medical DPS-165B) during recording sessions. After insertion, the stimulus electrodes were fixed to the skull by dental acrylic. Following the completion of stimulus electrode implantation, the recording chamber was placed horizontally over the skull. The center of the chamber was located at A12.0 and L3.0 of the Horsley Clarke coordinates, which is an area that lied above the motor thalamic nuclei (shaded area in Fig. 1B). Antibiotics and analgesics were applied to prevent postsurgical infection and pain.

After allowing for complete recovery from the surgery (at least 7 days), glass-insulated Elgiloy microelectrodes (1.5-2.0 MΩ at 333 Hz) were vertically inserted through the dura mater with a hydraulic microdrive (Narishige, MO-951), and neuronal activity was recorded from the motor thalamus during task performance. Thalamocortical neurons that projected to the cortical motor areas were identified using spike collision (Fuller and Schlag 1976; Tanji and Kurata 1985), which is based on electrical stimulations delivered through the pairs of bipolar electrodes implanted within the cortical motor areas. Both polarities of stimulation in each pair of electrodes were examined to identify thalamocortical neurons. The stimulus responses were recorded and displayed on a digital memory scope
(Panasonic VP-5720A), and the trace data were transferred to a computer for storage via a GPIB interface. When a neuron was isolated, the somatosensory responses to cutaneous and deep stimuli were also examined to differentiate the VPLc from VPLo. Deep stimuli included passive joint rotation, muscle palpation, and tendon taps. The VPLc neurons responded briskly to cutaneous stimuli, whereas the VPLo neurons responded mainly to deep stimuli (Jones and Friedman 1982; Strick 1976; Vitek et al. 1994). Combining the examinations with histological reconstruction (see below), neurons outside the motor thalamus were not included in the database.

Electromyographic (EMG) activity was monitored bilaterally with surface and wire electrodes from the biceps and triceps brachii, deltoid, extensor carpi radialis, flexor carpi ulnaris, trapezius, supraspinatus, infraspinatus, pectralis major, rhomboid, thoracic and lumbar paravertebral muscles, gluteus maximus, quadriceps, and tibialis anterior. EMG activity from each muscle was recorded from each monkey prior to chamber implantation and near the end of data collection period. EMG data and hand positions were sampled at 100 Hz, respectively, through an 8-channel, 12-bit analog-to-digital converter. Data were quantified and stored in the same computer that was used to control behavior and collect data of neuronal activity.
Data analysis

For each of six types of trial (wrist flexion and extension triggered by the three different modalities of sensory signal), raster displays of recorded neuronal activity were aligned either with the instruction signal or the onset of movement, and peri-event histograms (20-ms bin width) were created to display neuronal activity for each type of trial. When the activity was stable for more than 10 trials in each raster display and the neuron showed a consistent activity pattern throughout the recorded trials, the data was added to a database.

Two types of neuronal activity were quantitatively analyzed. The first type was set-related activity, which was a consistent and sustained increase during the instructed delay period in either an extension or flexion trial. The second type was movement-related activity, which was a phasic increase after the TS and before movement onset.

To identify set-related activity quantitatively, two sampling periods were selected: the pre-IS period (a 500-ms period from trial initiation until IS onset) and the instructed delay period (200 ms after the IS presentation until TS onset). Set-related activity was defined as a significant difference in mean discharge rates between these two sampling periods (Mann-Whitney U test, p<0.05, two tailed), for either flexion movements, extension movements, or both. Then, the mean discharge rates during the instructed delay period in individual trials were compared to examine the direction
selectivity for forthcoming wrist extension or flexion movements, using ANOVA with repeated measures (SYSTAT for Windows ver. 8.0.2, Evanston, IL, USA). Set-related activity was considered directionally selective if the difference in discharge rate between the two directions was statistically significant (ANOVA, p<0.05).

When neurons increased their activity phasically before the movement onset after a trigger signal was presented, the activity was regarded as movement-related. Neurons with activity suppression before movement onset were not included. When neurons showed set-related activity, their further increase of activity immediately before movement onset was regarded as movement-related. Movement-related activity was quantitatively defined as follows. First, the mean discharge rate and standard deviation (SD) was calculated in 20ms bin from 1500 to 500 ms before movement onset (termed “premovement” period). If the discharge rate exceeded 3 SDs between the TS and movement onsets in at least two consecutive bins (40 ms), then the neuron was defined as movement-related. The earliest bin that exceeded 3 SDs was defined as neuronal onset of the movement-related activity. The interval between the neuronal and movement onsets was termed “RT” for convenience, and was used to describe and analyze movement-related neuronal activity during the period.

For movement-related activity, the mean discharge rates during “RT” and MT in each trial were calculated, and were used for subsequent
quantitative and statistical analyses. For RT and MT, sensory modalities and directions were used as ANOVA factors to examine sensory and direction preferences of neuronal activity. If the difference in movement-related activity between sensory modalities was statistically significant (ANOVA, p<0.05), then it was defined that the movement-related activity was modality selective. When the difference was statistically significant (ANOVA, p<0.05), post-hoc analyses for preferences to sensory modalities were carried out to determine which pairs of mean discharge rates following sensory cues (visual vs. auditory, auditory vs. somatosensory, or somatosensory vs. visual) differ significantly, using a Bonferroni multiple-comparison test (p<0.05 each). These statistical measures were also applied to behavioral data (RT and MT in Table 1) and quantified EMG data during RT and MT. Similarly, if the difference in movement-related activity between directions was statistically significant (ANOVA, p<0.05), then it was defined that the movement-related activity was direction selective.

The mean discharge rates during a sampling period (the preparation period, RT, or MT) were used to calculate a direction index (DI) using the following equation.

\[ DI = \frac{|Fl - Ex|}{|Fl + Ex|} \]  

(1)
In equation (1), $F_l$ and $E_x$ are the mean discharge rates during flexion and extension trials, respectively, during the sampling period. If the DI was 1.0, then it indicates that, during a sampling period, a neuron increased its discharge rate in one direction and completely ceased its discharge in the other direction. When a neuron showed a 2:1 ratio of discharge rates in the two directions during a sampling period, the DI was 0.33. When a neuron was equally active in the two directions, the DI was 0. Quantified EMG activity during the sampling periods was similarly analyzed as neuronal activity.

Other types of neuronal activity modulation recorded in the motor thalamus included 1) activity change during pre-IS period, 2) inconsistent increase or decrease of activity during the instructed delay period, 3) activity after movement onset, and 4) activity time-locked to reward delivery. These types of activity were not analyzed further.

**Histology**

After the collection of single-unit data, electrolytic lesions were created to mark the location of the recording electrodes by passing 20 µA of direct cathodal current through the microelectrodes for 15 s. Between 9 and 10 days later, the monkeys were anesthetized deeply with pentobarbital (50 mg/kg i.m.) and were perfused transcardially first with saline, then with
fixative (3.7% formaldehyde in 0.1 M phosphate buffer at pH 7.4), and finally with 10% and 20% sucrose solutions in 0.1 M phosphate buffer at pH 7.4. After marking the location of the recording chamber with five pins at the electrode coordinates, the brain was removed from the skull and was photographed. Later, it was sectioned serially at 50 µm in the frontal plane on a freezing microtome. The tissue sections were stained with thionin and were photographed with a digital camera (Nikon DXM1200) attached to a microscope (Nikon E600). The images were processed with Adobe Photoshop (ver. 7.0.1).

In the present study, the atlas and terminology of Olszewski (1952) was employed to describe the topographical distribution of recorded neurons within the motor thalamus. In addition, the modification of Olszewski’s terminology suggested by Holsapple et al. (1991) was used to describe the rostral and caudal portions of the VLc nucleus (namely the VLcr and VLcc, respectively; see also Kurata 1994b).
RESULTS

Behavior

Monkey 1 and 2 performed the behavioral task correctly in 98% and 99% of the trials, respectively. Mistakes were mostly premature movements during the preparation period or the initiation of movements after reaction time limitation (700 ms). The animals seldom made direction errors.

Table 1 shows means and SDs of RT and MT performed by the two monkeys in response to visual, auditory, and somatosensory signals. In the two monkeys, the differences among the RTs in response to the three types of sensory stimulus were statistically significant (ANOVA, p<0.05), and the RT in response to the visual signal was significantly longer than the RTs in response to the other signals (Bonferroni, p<0.05). On the other hand, the differences among the MTs in response to the three types of sensory stimulus were not statistically significant (ANOVA, p>0.05).

EMG

The right extensor carpi radialis (ECR) and flexor carpi ulnaris (FCU) were the prime movers for extension and flexion movements of the wrist, respectively. Figure 2 shows the activity of the right ECR, FCU, and biceps brachii of monkey 2 during the six types of trial. The EMG activity
was similar during extension or flexion movements, regardless of the sensory modality of the trigger signal, and did not change specifically during the preparation period between the presentation of the instruction signal and the trigger signal. Differences in EMG activity during extension and flexion in response to the various cue modalities were not statistically significant (ANOVA, p>0.05). Modest changes in EMG activity were observed in the proximal limb (biceps brachii in Fig. 2C) and trunk muscles, but the activity of these muscles was variable and inconsistent. No specific changes in EMG activity were noted in any of the remaining muscles that were examined.

Neuronal database

Neuronal activity was recorded from 1,632 and 1,710 neurons in the motor thalamus of monkeys 1 and 2, respectively. Of these, 419 and 684 neurons were well isolated long enough to examine collision block and relation to the behavioral task, and 97 and 156 neurons were identified as thalamocortical neurons in monkeys 1 and 2, respectively. Table 2 shows the number of the classified thalamic neurons. All thalamic neurons responded to antidromic stimulation of only one pair of electrodes implanted within the cortical motor areas: none responded to stimulation of more than one pair of electrodes. After collision block had been confirmed, the polarity was reversed. However, no neuron responded to stimulation after
the polarity reversal. In both monkeys, thalamocortical neurons projecting to the MI constituted a majority, whereas SMA-projecting neurons were the least frequent. As shown in Table 2, 85.6% and 94.2% of thalamocortical neurons in monkeys 1 and 2, respectively, were task-related, whereas 57.5% and 52.7% of the neurons in monkeys 1 and 2, respectively, that were not identified as thalamocortical neurons were task-related.

Figure 3 shows histograms of the antidromic latencies of neurons that projected to the MI, PMd, PMv, and SMA. The majority of latencies were 1-3 ms. The antidromic latencies (mean ± SD) for neurons that projected to the MI, PMd, PMv, and SMA was 1.89 ± 1.84, 2.32 ± 1.47, 2.20 ± 1.79, and 1.75 ± 0.90, respectively. The difference in latencies among the different target cortical motor areas was not statistically significant (ANOVA, p>0.05).

Neurons with set- and movement-related activity

Figure 4 shows representative set-related activity of a thalamic neuron that projected to the MI. The antidromic latency was 1.4 ms (Fig. 4, inset). The discharge rate of this neuron started to increase after the presentation of the instruction signal, and this change was sustained throughout the preparation period. The activity of this neuron was defined as set-related, and the neuron exhibited greater set-related activity when extension movements were instructed than when flexion movements were cued. The
differences in discharge rates during different movement directions were statistically significant (ANOVA, p<0.05). This neuron also exhibited movement-related activity during the RT.

Figures 5-8 show representative thalamic neurons that exhibited movement-related activity and that projected to the MI, PMd, PMv, and SMA, respectively. The thalamic neuron shown in Fig. 5 projected to the MI (1.1 ms latency). Movement-related activity in this neuron was direction-selective, but there was no preference for a particular sensory modality. The data in Fig. 6 are for a neuron that projected to the PMd. The neuron exhibited no preference for movement directions (ANOVA, p>0.05), although it exhibited slightly higher activity when the trigger signal was visual than when it was auditory or somatosensory (Bonferroni, p<0.05). The neurons in Figs. 7 and 8 were slightly direction-selective (ANOVA, p<0.05), but there was no preference for a particular sensory modality (ANOVA, p>0.05). Qualitatively, most movement-related neuronal activity was unrelated to the sensory modality of the trigger signal. In the few cases in which the activity in response to different sensory modalities was significantly different, the difference was always modest (Fig. 6). Similar to the movement-related thalamocortical neurons, movement-related thalamic neurons that were not identified as thalamocortical were mostly unrelated to the sensory modality of the trigger signal. In addition, no neuron in the motor thalamus exhibited distinct
phasic response to the visual instruction signal (signal-related activity) (cf. 
(Weinrich et al. 1984).

Table 2 shows the number of thalamic neurons classified as set- and/or movement-related, other task-related (see Methods), and not task-related. As shown in the table, movement-related neurons were observed most frequently, whereas neurons with set-related activity were observed much less frequently, regardless of the target cortical area. In each of the two monkeys, the numbers of the classified task-related thalamocortical neurons in the contingency table were not dependent on their target cortical motor areas (Pearson Chi-square statistic, p>0.05). Thus, each cortical motor area had a similar proportion of each neuronal activity class. Using the data shown in Table 2, the proportion of each class of task-related neuron was also comparable in the thalamocortical neurons projecting to each cortical motor area and unidentified neurons, with no significant difference occurring in monkey 2 (Pearson Chi-square, p>0.05), and only a small, though statistically significant difference, in monkey 1 (Pearson Chi-square statistic, p<0.05).

Quantitative analyses of set-related activity during the instructed delay period

The distribution of DIs for the 47 thalamocortical neurons with set-related activity recorded in the two monkeys is presented in Fig. 9 (left
panels). A majority of the DIs for the set-related activity was less than 0.33 (a 2:1 ratio of discharge rates, see Methods), regardless of their target cortical motor areas. The DI (mean ± SD) of the set-related neurons projecting to the MI, PMd, PMv, and SMA were 0.096 ± 0.092, 0.100 ± 0.078, 0.132 ± 0.193, and 0.078 ± 0.122, respectively. The mean and SD of DI of the set-related neurons that were not identified as thalamocortical was 0.135 ± 0.139. The difference in the DI values for set-related activity among those neurons was not statistically significant (ANOVA, p>0.05).

Fig. 10 shows the relationship between the antidromic latency and the mean discharge rate in the best direction of each set-related thalamocortical activity. As shown by the regression lines in Fig. 10, the discharge rates were usually higher when the thalamocortical neurons had shorter antidromic latencies, regardless of the target cortical motor areas, except for set-related neurons projecting to the PMd in monkey 1. However, only one of the set-related neurons with antidromic latency of 5.6 ms exhibited a very high discharge rate (42.0 imp/s). Without that neuron, the activity properties of neurons projecting to the PMd were similar to the other set-related neurons. Correlations coefficients between the antidromic latency and the mean discharge rate of neurons with set-related activity were relatively small (Table 3), except for neurons that projected to the SMA recorded in monkey 2. However, there were only four neurons with set-related activity that projected to the SMA (Table 2), and none of the
correlations between average discharge rates and antidromic latencies in Table 3 were statistically significant (ANOVA, p>0.05).

Quantitative analyses of movement-related activity during RT

The distribution of DIs for the 195 thalamocortical neurons with movement-related activity during the RT recorded in the two monkeys is presented in Fig. 9 (center panels). A majority of the DIs of the movement-related neurons was less than 0.33, similar to those of the neurons with set-related activity. The DIs (mean ± SD) for the movement-related activity during the RT of neurons that projected to the MI, PMd, PMv, and SMA and of neurons that were not identified as thalamocortical were 0.239 ± 0.215, 0.220 ± 0.166, 0.249 ± 0.235, 0.249 ± 0.223, and 0.228 ± 0.209. The difference in the DI values for movement-related activity during the RT among the thalamic neurons was not statistically significant (ANOVA, p>0.05).

Neuronal activity during the RT was examined to determine whether it was associated with the modality of the triggering signal. Of 67 and 140 thalamocortical movement-related neurons recorded in monkeys 1 and 2, respectively, 66 (98.5%) and 137 (97.9%) neurons were active during the RT, regardless of the modality of the trigger signal. Only four neurons were differently active in response to the three sensory modalities of the trigger signal (ANOVA, p<0.05), although none of these neurons was
exclusively active in response to one particular modality. Of the four neurons that exhibited preference to the modality of the trigger signal, three neurons (one neuron in monkeys 1; two neurons in monkey 2) were significantly more active when the trigger signal was somatosensory than when it was visual or auditory (Bonferroni, p<0.05), whereas only one neuron (monkey 2) was significantly more active when the trigger signal was visual than when it was auditory or somatosensory (Bonferroni, p<0.05).

Fig. 10 (middle panels) shows the relationship between antidromic latency and discharge rate in the best direction of each cell with movement-related activity during the RT. The regression lines in Fig. 10 indicate that, in monkey 2, the discharge rates tended to be higher when the thalamocortical neurons had shorter antidromic latencies, although the relationship was more variable in monkey 2. Table 3 shows that correlations between antidromic latency and mean discharge rate of movement-related activity during the RT were less than 0.5, regardless of their target cortical motor areas, and none of the correlations were statistically significant (p>0.05). Table 4 shows the time preceding movement onset for movement-related thalamic neurons (neuronal onset time). The difference in the neuronal onset time between the thalamocortical neurons projecting to the different cortical motor areas and unidentified neurons were not significant (ANOVA, p>0.05).
Quantitative analyses of movement-related activity during MT

The right panels of Fig. 9 indicate the DI distributions of the thalamocortical neurons with movement-related activity during the MT. Again, a majority of the neurons had a DI of less than 0.33. The DIs (mean ± SD) for movement-related activity during the MT of the 195 neurons that projected to the MI, PMd, PMv, and SMA and of those that were not identified as thalamocortical were 0.327 ± 0.280, 0.359 ± 0.281, 0.357 ± 0.286, 0.358 ± 0.297, and 0.302 ± 0.263, respectively. The difference in the DI values among neurons that projected to the different cortical motor areas was not statistically significant (ANOVA, p>0.05).

Movement-related activity during the MT was examined to determine whether it exhibited preference to the modality of the trigger signal. Of four neurons that exhibited preference to the modality during the RT, three neurons were also differently active during MT in response to the three sensory modalities of the trigger signal (ANOVA, p<0.05). Of the three neurons with such modality preference, two neurons (one neuron each in monkeys 1 and 2, respectively) were significantly more active when movements were initiated in response to the somatosensory signal than when the trigger signal was visual or auditory (Bonferroni, p<0.05), whereas the remaining neuron recorded in monkey 2 was significantly more active.
when movements were triggered by the visual trigger signal (Bonferroni, p<0.05).

Fig. 10 (lower panels) shows the relationship between the antidromic latency and discharge rate in the best direction of each movement-related activity during MT. Similar to the data obtained during the RT, the regression lines between the discharge rates during MT and antidromic latencies in Fig. 10 were variable, particularly in monkey 2. Correlation coefficients between the antidromic latency and the mean discharge rate of movement-related activity during the MT were less than 0.5 (Table 3), regardless of their target cortical motor areas, and none of the correlations were statistically significant (ANOVA, p>0.05).

Location of neurons

An example of an electrolytic lesion that marked the location of a thalamic neuron that projected to the PMv is presented in Fig. 11. The same figure also shows the electrode tracks that were used to reconstruct the locations (see also Fig. 12) of thalamocortical neurons. Neurons that projected to the cortical motor areas were located throughout the motor thalamus including the VLo, VLm, VLcr, VPLo, and Area X. Among these thalamic nuclei, neurons that projected to the MI were densely packed within the VPLo and VLcr. Neurons that projected to the PMv were most numerous within Area X, with a lower density within the VLo and VPLo,
whereas neurons that projected to the PMd were most numerous within the
VLcr, VLo, VPLo, and Area X. The few neurons that projected to the
SMA were located within the VLo, VLcr, and VPLo. Neurons with set-
and/or movement-related activity were intermingled within the thalamic
nuclei, and no differential distribution was observed. However, set- and
movement-related neurons were particularly numerous within the middle
part of the motor thalamus.
DISCUSSION

In the present study, thalamic neurons that projected to the cortical motor areas were identified in monkeys performing a sensory-guided motor task and their activity was examined. This is the first report to describe that thalamocortical neurons exhibited (1) distinct set-related activity with direction selectivity for forthcoming wrist movements and (2) movement-related activity that showed selectivity for movement direction, but not to modalities of trigger cues to initiate the movements. It was also found that various properties of the classified neurons, such as proportion of the cells, antidromic latencies, and direction selectivity, were similar, regardless of their target cortical motor areas. Below, the properties and significance of the thalamocortical neurons during sensorially guided behavior will be discussed with available neurophysiological as well as anatomical findings.

Comparison of location of thalamocortical neurons in anatomical and physiological studies

It was found in the present study that neurons that projected to the cortical motor areas were differentially located within the motor thalamus (Fig. 12). Most neurons that projected to the MI were located within VPLo, VLo, and VLcr. Most neurons that projected to the PMd were located within VLcr, VLo, VPLo, and Area X. Neurons that projected to
the PMv were located largely within Area X, but were also located in VLo and VPLo. Few neurons projected to the SMA, and these neurons were located within VLo, VLcr, and VPLo. These observations are largely consistent with the results of previous anatomical studies showing that neurons were not localized separately to particular thalamic nuclei or regions (Kievit and Kuypers 1977; Kurata 1994b; Matelli and Luppino 1996; Matelli et al. 1989). It is possible that thalamic neurons that projected to the SMA also included those projecting to the presupplementary motor area (pre-SMA), because the location of the stimulating electrodes were determined based on the cortical landmarks in this study (see Methods) and the exact borderline between the SMA and pre-SMA can be determined by thorough investigations using various anatomical and physiological techniques (Luppino et al. 1991; Matsuzaka et al. 1992). It should be also noted that, in the present study, there were errors in the reconstruction of the location of neurons based on microdrive readings. But, such errors seem minimal, because the histological markings and electrode tracks (Fig. 11) were used to reconstruct the location accurately. More importantly, it was frequently observed that neurons that projected to the different cortical motor areas were adjacently located in the same electrode track.

In the present study, thalamocortical neurons with set- and/or movement-related activity were largely intermingled within the thalamic nuclei, and there were no apparent specific distribution. This observation
concerns with the findings of previous studies (Anderson and Turner 1991; Butler et al. 1996; Forlano et al. 1993; van Donkelaar and Lee 1994). Within the motor thalamus, there is a physiologically identified contiguous somatotopic organization through the VPLo and VLo (Vitek et al. 1994; Vitek et al. 1996), but no such organization exists within Area X or the VA (Anderson and Turner 1991; Vitek et al. 1994; Vitek et al. 1996).

Based on anatomical studies of projections from both the basal ganglia and the cerebellum to the cortical motor areas (Holsapple et al. 1991; Hoover and Strick 1993; Kurata 1994b; Matelli and Luppino 1996; Matelli et al. 1989; Middleton and Strick 1994; Rouiller et al. 1994; Sakai et al. 1996, 2002; Shindo et al. 1995), it has been suggested that the SMA primarily receives inputs originating from the basal ganglia (Sakai et al. 2002), whereas the MI primarily receives inputs from the cerebellum (Sakai et al. 2002). On the other hand, the PMv and PMd would appear to receive inputs from both of the cerebellum and basal ganglia (Matelli and Luppino 1996; Matelli et al. 1989). However, these anatomically different channels do not seem to convey very selective information, as far as activity properties of the thalamocortical neurons were examined in this study. As shown in Table 2, the proportions of the classified task-related thalamocortical neurons were similar, regardless of the target motor areas. Furthermore, the proportions of the classified task-related neurons were similar, regardless of whether they were identified or unidentified as
thalamocortical. The results suggest that, even when thalamocortical neurons were not identified due to a limited number of stimulating electrodes, they also conveyed similar information. This contention will be discussed in the following sections.

Information conveyed by set-related activity of thalamocortical neurons

It was found in this study that a proportion of thalamocortical neurons exhibited set-related activity with direction selectivity for forthcoming wrist movements. Some neurons with set-related activity also exhibited movement-related activity. These properties of set-related neurons are comparable to those of neurons in their target cortical motor areas (Hoshi and Tanji 2000; Kurata 1993; Kurata and Wise 1988a, b; Tanji and Evarts 1976; Tanji and Kurata 1985; Weinrich and Wise 1982). Because a majority of the set-related thalamocortical neurons showed directional selectivity, it is likely that the activity conveyed by the thalamocortical system is related closely to preparation for the forthcoming wrist movements. However, it is also possible that set-related activity of the thalamocortical neurons could reflect many other aspects of required behavior dependent on cue modality and its context that has been described for neurons in the SMA (Matsuzaka and Tanji 1996; Tanji and Kurata 1985), the PMd (Boussaoud and Wise 1993; Ohbayashi et al. 2003), MD
thalamus (Watanabe and Funahashi 2004a, b), and central thalamic nuclei (Wyder et al. 2004).

Considering the pathways linking the basal ganglia and cerebellum to the cortical motor areas, set-related activity was recorded in the striatum of monkeys (Alexander and Crutcher 1990), although it is not known whether neurons in the globus pallidus, cerebellar purkinje cells, or deep cerebellar nuclei exhibit sustained activity during delay periods. Accordingly, additional studies are required to examine if set-related activity is generated in these structures and transmitted to the cortical motor area via the motor thalamus. Meanwhile, it is likely that distinct set-related activity recorded in the cortical motor areas is first generated within the cerebral cortex, perhaps through corticocortical information channels, and then is transmitted to the motor thalamus to maintain the sustained activity in the corticothalamic loops (Houk and Wise 1995).

**Information conveyed by movement-related activity of thalamocortical neurons**

It was found in the present study that a number of thalamocortical neurons exhibited movement-related activity with direction selectivity (either wrist extension or flexion). The direction selectivity in a majority of the thalamocortical movement-related neurons during RT or MT was modest (Fig. 9), but it might be possible to obtain more distinct direction
selectivity in movement-related activity, when movements other than wrist extension and flexion were examined. More remarkably, when wrist movements were made in the same direction, most movement-related neurons were similarly active, regardless of the sensory modalities of trigger cues. These observations resembled what occurred within the MI (Evarts 1968; Kurata and Tanji 1986; Lamarre et al. 1983; Tanji and Kurata 1982; Thach 1978) and dentate nucleus (Chapman et al. 1986). Thus, it seems that the motor thalamus, as a part of information channels from the cerebellum to the cortical motor areas, contributes to initiation and execution of wrist movements by providing information about movement parameters, such as direction (Butler et al. 1992, 1996; Strick 1976). However, the results of the present study are very different from those of previous studies of neurons in the PMd, PMv, and SMA. In these areas, movement-related activity was frequently associated with a particular sensory modality of the cue for movement, and it was suggested that the nonprimary motor areas play roles in transformation from specific sensory cues to motor commands (Kurata and Tanji 1986; Tanji and Kurata 1982). Thus, it is likely that the modality specific movement-related activity in the nonprimary motor areas is generated specifically within the cerebral cortex, perhaps via a corticocortical network, but not via the motor thalamus. On the other hand, it is also possible that corticothalamic projections from the MI affect thalamic activity more than do the projections from the
nonprimary motor areas. If outputs from the MI are dominant in the motor thalamus, this would explain why modality specific movement-related activity was not frequently observed in the motor thalamus in the present study. Of course, this finding could also mean that thalamocortical inputs to MI are stronger than those to nonprimary motor areas, and so the MI activity could be better replica of its thalamic inputs for that reason.

It should be noted that, in monkeys performing a task to initiate a limb movement that were either visually triggered or internally generated, movement-related neurons in the motor thalamus that receive cerebellar input tend to be more active during visually-triggered movements than during internally generated movements (van Donkelaar et al. 1999). Therefore, it was postulated that pathways through the cerebellar thalamus (within the motor thalamus) plays a more important role in visually guided motor behavior than in internally guided movements (van Donkelaar et al. 2000). Together with the results obtained in the present study, it is possible that the channel from the cerebellum to the cortical motor areas via the cerebellar thalamus is specialized for behavior guided by various sensory (but not specifically visual) cues.

*Antidromic latencies and location of thalamic neurons that projected to the cortical motor areas*
In the present study, a majority of the thalamocortical neurons had antidromic latencies between 1-2 ms (cf. Nambu et al. 1991). Based on the distance between the motor thalamus and the cortical motor areas (20-30 mm), it is estimated that the conduction velocity of thalamocortical neurons is about 10-30 m/s, which is slower than the fastest conduction velocity of the pyramidal tract neurons (60 m/s) in the MI (Humphrey and Corrie 1978). Thalamocortical neurons with latencies greater than 5 ms were recorded infrequently, but this small proportion might be due to a sampling bias, because their relatively small soma with a thin axon (based on the relatively longer latencies) was more difficult to isolate electrophysiologically (Humphrey and Corrie 1978).

Among the thalamic neurons that projected to the cortical motor areas, most projected to the MI, and relatively few thalamocortical neurons projected to the PMd and the PMv, while neurons that projected to the SMA were the least numerous. There were no significant differences among the latencies of neurons that projected to the different cortical motor areas. This observation suggests that the subcortical information transmitted from the thalamic nuclei is likely transmitted to the different cortical motor areas at a similar speed. In addition, the correlations between the discharge frequency of the set- or movement-related activity and antidromic latency were weak, regardless of the target cortical motor areas (Fig. 10 and Table 3). These results contrast to the properties of the pyramidal tract neurons
in the MI that exhibited larger modulation of movement-related activity when their antidromic latencies were shorter (Evarts 1965). It seems that, in the thalamocortical system, conduction velocity is not very crucial, regardless of the information that the system conveyed.

Finally, it was found in this study (Table 2) that a vast majority of thalamocortical neurons were task-related, whereas those that were not identified as thalamocortical contained a large number of neurons without task-related activity. It has been suggested that thalamic neurons consist of approximately 5-25% of interneurons (Jones 1985), and that they are usually very small (Jones 1985), thus hard to be sampled electrophysiologically (Humphrey and Corrie 1978). So, it is unlikely that a majority of the unidentified neurons were interneurons. If most of those unidentified neurons were thalamocortical, why was the observation obtained? Because, in the present study, the stimulation electrodes were placed around the forelimb region of each cortical motor area (Gentilucci et al. 1988; Kurata 1993; Kurata and Hoffman 1994; Kurata and Tanji 1986; Luppino et al. 1991; Rizzolatti et al. 1988; Tanji and Kurata 1982, 1985), and because the motor thalamus is somatotopically organized (Darian-Smith et al. 1990; Nambu et al. 1991; Vitek et al. 1994, 1996), it is likely that the thalamocortical neurons related to wrist movements were most efficiently activated. It is also possible that, because the number of stimulation electrodes was limited, a large number of thalamocortical neurons escaped
electrophysiological identification, and those without task-related activity were located outside the forelimb region of the motor thalamus. But these possibilities remain to be clarified in future.
REFERENCES


Butler EG, Finkelstein DI, Harvey MC, Churchward PR, Forlano LM, and Horne MK. The relationship between monkey ventrolateral
thalamic nucleus activity and kinematic parameters of wrist movement.

*Brain Res* 736: 146-159, 1996.


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GRANTS

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Figure Legends

Figure 1

Schematic illustrations showing light emitting diode (LED) apparatus (A) and location of the stimulating electrodes implanted in the forelimb regions of the cortical motor areas (B). A: each of the LEDs forming a horizontal array could emit green, red, or orange. One of the LED was illuminated in green to indicate the monkey’s hand position, as detected by a potentiometer. The third LED either from the left or right end was illuminated in red as an instruction signal (IS) for a flexion or an extension movement. The IS also indicated the target location. After the delay period, the central LED turned green to orange, it served as a visual trigger stimulus. See text for detail. B: the areas in which electrodes were implanted were the primary motor cortex (MI), ventral and dorsal premotor cortex (PMv and PMd), and the supplementary motor area (SMA). Each dot shows the location of an electrode. Paired electrodes (e.g., 1 and 2 in the MI) are enclosed within rectangles, and were used for bipolar stimulations. The hatched rectangle covering A6.0–A18.0 and L-1.0–L6.0 (Horsley Clark coordinates) indicates the electrode entry area for recording from the thalamus. Electrodes were inserted into two monkeys in a similar manner. Abbreviations: AS, arcuate sulcus; CS, central sulcus; IPS, intraparietal sulcus; PS, principal sulcus; and SPS, superior precentral sulcus.
Figure 2

Electromyographic (EMG) activity of the right extensor carpi radialis (ECR), flexor carpi ulnaris (FCU), and biceps brahii during the performance of the behavioral task. Summed (upper panels) and trial-based (middle panels) EMG activity was aligned to the onset of movement (Mvt) during extension (Ex) and flexion (Fl) of the wrist in response to a visual (Vis), auditory (Aud), or vibrotactile (Tac) trigger signal. The onsets of the instruction signal (IS) and trigger signal (TS) are indicated by short bars in each EMG trace and the approximate position of each behavioral event is indicated in the traces beneath (lower panel). The right ECR and FCU were prime movers for extension and flexion movements of the wrist, respectively.

Figure 3

Antidromic latencies of thalamic neurons that projected to the cortical motor areas. Data are histograms of the antidromic latencies of thalamocortical neurons within the MI, PMd, PMv, and SMA.

Figure 4

Activity of a representative thalamic neuron that projected to the MI and exhibited set-related activity. Each display was aligned to the onset of the IS. Note that a sustained change in activity was observed throughout the
preparation period between the IS and TS, particularly when wrist extension was instructed. The lower right inset indicates that antidromic response (upward arrow in the lower trace) was blocked when the interval between spontaneous activity and stimulus was shorter than 1.4 ms (upper trace).

Figure 5

Activity of a representative thalamic neuron that projected to the MI and exhibited direction-selective movement-related activity. The histograms (upper panels), rasters (middle panels), and wrist angles (lower panels) were aligned to the onset of movement (Mvt) of wrist extension (Ex) and flexion (Fl) that followed the visual (Vis), auditory (Aud), and tactile (Tac) trigger signals (TS). The lower right inset illustrates that the antidromic response (upward arrow in the lower trace) was blocked when the interval between spontaneous activity and stimulus was shorter than 1.1 ms (upper trace). The neurons did not show differences in activity in response to the various modalities of the trigger signals.

Figure 6

Activity of a thalamic neuron that projected to the PMv and exhibited movement-related activity. The antidromic latency of this neuron was 0.9 ms. Conventions are as in Fig. 5.
Figure 7
Activity of a thalamic neuron that projected to the PMd and exhibited movement-related activity. The antidromic latency was 1.6 ms. Conventions are as in Fig. 5.

Figure 8
Activity of a thalamic neuron that projected to the SMA and exhibited movement-related activity. The antidromic latency was 0.9 ms. Conventions are as in Fig. 5.

Figure 9
Direction index of set-related activity during the preparation period (Set), movement-related activity during reaction time (Mvt-RT), and movement-related activity during movement time (Mvt-MT) of the thalamic neurons that projected to the cortical motor areas (the MI, PMv, PMd, and SMA) and of those that were not identified as thalamocortical. Data are for thalamic neurons recorded in two monkeys. The left and right ordinates indicate the number of neurons and the proportion of bars, respectively.

Figure 10
Each symbol indicates the relationship between the antidromic latency and mean discharge rate of neurons with set-related activity (Set),
movement-related activity during the RT (Mvt-RT), and movement-related activity during the MT (Mvt-MT). Discharge rates were obtained in the best direction during the sampling periods. The oblique lines show fitted regression lines for the relationship between antidromic latency and the mean discharge rate (see also Table 3).

Figure 11

Photomicrograph of a histological section showing an electrolytic microlesion in Area X of the thalamus of monkey 2. The lesion marks the location at which the activity of a neuron that projected to the PMv was recorded.

Figure 12

Anatomical location of thalamic neurons that projected to the MI, PMv, PMd, and SMA in monkey 2. Eight different rostrocaudal levels are presented (A9.0-A13.0).
A. LED Apparatus

LED indicating the hand position

LED indicating the central holding zone and visual trigger signal

10 mm

B. Location of Stimulating Electrodes

Recording electrode entry area for thalamic neurons

5 mm
Fig 2  Kurata

A. ECR  

Ex  

Fl  

B. FCU  

Ex  

Fl  

C. Biceps  

Ex  

Fl  

30°  

1 s
Latency (ms) vs Monkey 1 and Monkey 2 for Total, MI, PMd, PMv, and SMA.

Fig. 3 Kurata
Fig 4 Kurata
Fig 5 Kurata
Fig 6 Kurata
<table>
<thead>
<tr>
<th>Vis</th>
<th>Aud</th>
<th>Tac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ex</td>
<td><img src="image1" alt="Ex Vis" /></td>
<td><img src="image2" alt="Ex Aud" /></td>
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<tr>
<td></td>
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<td></td>
<td><img src="image10" alt="F1 Vis" /></td>
<td><img src="image11" alt="F1 Aud" /></td>
</tr>
</tbody>
</table>

Fig 7 Kurata
Fig 8 Kurata
Kurata Fig. 9

The graphs illustrate the proportion per bar for different conditions.

- **Set**
  - MI
  - PMd
  - PMv
  - SMA
  - Not identified

- **Mvt-RT**
  - MI
  - PMd
  - PMv
  - SMA
  - Not identified

- **Mvt-MT**
  - MI
  - PMd
  - PMv
  - SMA
  - Not identified

Each condition shows a distribution across different direction indices.
Fig. 12 Kurata
Table 1. Means and SDs of reaction time (RT) and movement time (MT) performed by the two monkeys in response to the different modalities of sensory signals.

<table>
<thead>
<tr>
<th></th>
<th>visual</th>
<th>auditory</th>
<th>somatosensory</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monkey 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT</td>
<td>347 ± 55*</td>
<td>249 ± 63</td>
<td>298 ± 39</td>
</tr>
<tr>
<td>MT</td>
<td>243 ± 129</td>
<td>248 ± 133</td>
<td>231 ± 116</td>
</tr>
<tr>
<td><strong>Monkey 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT</td>
<td>377 ± 88*</td>
<td>277 ± 57</td>
<td>262 ± 45</td>
</tr>
<tr>
<td>MT</td>
<td>293 ± 116</td>
<td>290 ± 129</td>
<td>296 ± 130</td>
</tr>
</tbody>
</table>

*In each monkey, the difference among the RTs in response to the three types of sensory stimulus was statistically significant (ANOVA, p<0.05), and the RT in response to the visual trigger cue was significantly longer (Bonferroni, p<0.05). Both extension and flexion movements were included to calculate each value.
Table 2. Number of thalamic neurons projecting to the four cortical motor areas and of those that were not identified as thalamocortical.

<table>
<thead>
<tr>
<th>Monkey 1</th>
<th>MI</th>
<th>PMd</th>
<th>PMv</th>
<th>SMA</th>
<th>Identified subtotal</th>
<th>Not identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Set</td>
<td>7</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>12 (12.3%)</td>
<td>11 (3.4%)</td>
</tr>
<tr>
<td>Movement</td>
<td>31</td>
<td>6</td>
<td>12</td>
<td>5</td>
<td>54 (55.6%)</td>
<td>117 (36.3%)</td>
</tr>
<tr>
<td>Set+Movement</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>8 (8.6%)</td>
<td>16 (4.9%)</td>
</tr>
<tr>
<td>Other task-related</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>9 (9.3%)</td>
<td>41 (12.7%)</td>
</tr>
<tr>
<td>Not task-related</td>
<td>6</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>14 (14.4%)</td>
<td>137 (42.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>20</td>
<td>18</td>
<td>7</td>
<td>97 (100%)</td>
<td>322 (100%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Monkey 2</th>
<th>MI</th>
<th>PMd</th>
<th>PMv</th>
<th>SMA</th>
<th>Identified subtotal</th>
<th>Not identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Set</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>4 (2.6%)</td>
<td>7 (1.3%)</td>
</tr>
<tr>
<td>Movement</td>
<td>57</td>
<td>24</td>
<td>16</td>
<td>13</td>
<td>110 (70.5%)</td>
<td>180 (34.1%)</td>
</tr>
<tr>
<td>Set+Movement</td>
<td>11</td>
<td>7</td>
<td>1</td>
<td>4</td>
<td>23 (14.7%)</td>
<td>55 (10.4%)</td>
</tr>
<tr>
<td>Other task-related</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>10 (6.4%)</td>
<td>36 (6.8%)</td>
</tr>
<tr>
<td>Not task-related</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>9 (5.8%)</td>
<td>250 (47.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>37</td>
<td>20</td>
<td>19</td>
<td>156 (100%)</td>
<td>528 (100%)</td>
</tr>
</tbody>
</table>
Table 3. Correlation coefficients (r) between average discharge rates and antidromic latency of the thalamocortical neurons

<table>
<thead>
<tr>
<th></th>
<th>MI</th>
<th>PMv</th>
<th>PMd</th>
<th>SMA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Set-related</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monkey 1</td>
<td>0.161*</td>
<td>0.512</td>
<td>0.609</td>
<td>-</td>
</tr>
<tr>
<td>Monkey 2</td>
<td>0.235</td>
<td>0.390</td>
<td>0.307</td>
<td>0.909</td>
</tr>
<tr>
<td><strong>Movement-related during RT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monkey 1</td>
<td>0.084</td>
<td>0.080</td>
<td>0.164</td>
<td>0.453</td>
</tr>
<tr>
<td>Monkey 2</td>
<td>0.105</td>
<td>0.170</td>
<td>0.292</td>
<td>0.095</td>
</tr>
<tr>
<td><strong>Movement-related during MT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monkey 1</td>
<td>0.192</td>
<td>0.055</td>
<td>0.537</td>
<td>0.155</td>
</tr>
<tr>
<td>Monkey 2</td>
<td>0.122</td>
<td>0.161</td>
<td>0.241</td>
<td>0.488</td>
</tr>
</tbody>
</table>

*The values were obtained using a linear regression model (Systat ver. 8.0.2).*
Table 4. Means and SDs of neuronal reaction times (ms)* of movement-related thalamic neurons that projected to the four cortical motor areas and of those that were not identified as thalamocortical.

<table>
<thead>
<tr>
<th></th>
<th>MI</th>
<th>PMd</th>
<th>PMv</th>
<th>SMA</th>
<th>Not identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monkey 1</td>
<td>118.4±47.2</td>
<td>135.0±69.9</td>
<td>133.8±60.8</td>
<td>130.0±38.3</td>
<td>128.2±58.3</td>
</tr>
<tr>
<td>Monkey 2</td>
<td>113.8±71.4</td>
<td>114.8±86.0</td>
<td>117.6±70.6</td>
<td>108.7±59.0</td>
<td>111.3±72.4</td>
</tr>
</tbody>
</table>

*See Methods for definition.