Role of Primate Magnocellular Red Nucleus Neurons in Controlling Hand Preshaping During Reaching to Grasp

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Van Kan, Peter L. E. and Martha L. McCurdy. Role of primate magnocellular red nucleus neurons in controlling hand preshaping during reaching to grasp. J Neurophysiol 85: 1461–1478, 2001. Reaching to grasp is of fundamental importance to primate motor behavior and requires coordinating hand preshaping with limb transport and grasping. We aimed to clarify the role of cerebellar output via the magnocellular red nucleus (RNm) to the control of reaching to grasp. Rubrospinal fibers originating from RNm constitute one pathway by which cerebellar output influences spinal circuitry directly. We recorded discharge from individual forelimb RNm neurons while monkeys performed a reach-to-grasp task and two tasks that were similar to the reach-to-grasp task in trajectory, amplitude, and direction but did not include a grasp. One of these, the device task, elicited reaches while holding a handle, and the other, the free-reach task, elicited reaches that did not require any specific hand use for task performance. The results demonstrate that coordinated whole-limb reaching movements are associated with large discharge modulations of RNm neurons predominantly when hand use is included. Therefore RNm neurons can at best only make a minor contribution to the control of reaching movements that lack hand use. We evaluated relations between the discharge of individual RNm neurons and electromyographic (EMG) activity of forearm muscles during the reach-to-grasp task by comparing times of peak RNm discharge to times of peak EMG activity. The results are consistent with the view that RNm discharge may contribute to EMG activity of both distal and proximal muscles during reaching to grasp especially digit extensor and limb elevation muscles. Relations between the discharge of individual RNm neurons and movements of the metacarpi-phalangeal (MCP), wrist, elbow, and shoulder joints during individual trials of task performance were quantified by parametric correlation analyses on a subset of neurons studied during the reach-to-grasp and free-reach tasks. The results indicate that MCP extensions were consistently preceded by bursts of RNm discharge, and strong correlations were observed between parameters of discharge and the duration, velocity, and amplitude of corresponding MCP extensions. In contrast, relations between discharge and movements of proximal joints were poorly represented, and RNm discharge was not related to the speed of limb transport. Based on our data and those of others, we hypothesize that cerebellar output via RNm is specialized for controlling hand use and conclude that RNm may contribute to the control of hand preshaping during reaching to grasp by activating muscle synergies that produce the appropriate MCP extension at the appropriate phase of limb transport.

INTRODUCTION

The magnocellular red nucleus (RNm) is a source of origin of the rubrospinal tract, which is part of the lateral system of descending motor pathways (Kuypers 1963, 1982). A large body of evidence from behavioral, anatomic, and electrophysiological studies supports a role for RNm in controlling limb movements (for reviews: Keifer and Houk 1994; Massion 1967). The RNm is somatotopically organized and includes spatially distinct regions related to movements of the forelimb, hind limb, and face (Pompeiano and Brodal 1957), and because of prominent divergence in rubrospinal connectivity (Shinoda et al. 1982), individual forelimb neurons influence muscles at distal and proximal joints (Belhaj-Saif et al. 1998; Horn et al. 1993; Sinkjaer et al. 1995). The main input to RNm derives from the output of intermediate cerebellum via nucleus interpositus (NI) (Houk et al. 1988; Humphrey and Rietz 1976; Kennedy et al. 1986). Therefore understanding the role of the RNm in motor control would constitute a major step toward understanding how the cerebellum influences descending motor pathways.

The view that RNm commands movements is well supported. Discharge patterns are largely phasic and, for the appropriate movement, burst onset and offset precede movement onset and offset, respectively (Gibson et al. 1985b). Discharge of individual RNm neurons correlates with kinematic variables of limb movements, such as movement velocity (Cheney et al. 1988; Gibson et al. 1985b; Kohlerman et al. 1982) and torque rate (dT/dt) (Cheney et al. 1988; Ghez and Kubota 1977; Ghez and Vicario 1978; Mewes and Cheney 1994), and facilitates or correlates with electromyographic (EMG) activity of forearm muscles, particularly digit and wrist extensor, and shoulder flexor muscles (Belhaj-Saif et al. 1998; Horn et al. 1993; Miller and Houk 1995; Miller and Sinkjaer 1998; Miller et al. 1993; Padel and Steinberg 1978; Sinkjaer et al. 1995; Soechting et al. 1978). The extensor bias reported for the primate RNm is also evident from electrical stimulation in the cat RNm (Ghez 1975; Maffei and Pompeiano 1962; Rho et al. 1999). The combined evidence supports the hypothesis that discharge of RNm neurons represents motor commands. The exact representation of these commands, however, whether they are specified in terms of kinematic and dynamic variables of limb movement (Cheney et al. 1988; Ghez and Kubota 1977; Ghez and Vicario 1978; Gibson et al. 1985b; Kohlerman et al. 1982; Mewes and Cheney 1994) or as muscle activation patterns (Miller and Houk 1995; Miller and Sinkjaer 1998) remains an unresolved issue in motor control.

To understand the contribution of cerebellar outflow to mo-
tor command signals transmitted via the rubrospinal system, it is important to define the movements that may be controlled or influenced by this system. One approach toward this objective is to fractionate complex multi-joint movements into individual joint components. Testing movement specificity of individual RNm neurons revealed, however, that only a subset of RNm neurons was well related to movements restricted to individual distal or individual proximal joints (Gibson et al. 1985a). Many RNm neurons did not modulate discharge during any of the single-joint movements tested despite large discharge modulations of the same neurons during reaching to grasp, particularly during phases of the reach that involved use of the distal extremities. These results suggested that RNm is heavily biased for controlling coordinated movements of the most distal joints, a view supported by observations that the strongest device-related discharge modulations were associated with twisting a shaft, which required coordination of wrist and digit and, possibly, elbow and shoulder joints (Gibson et al. 1985a,b).

Additional support for a role of RNm in controlling coordinated movements of the most distal joints derives from studies of interpositus (NI) neurons. Like RNm neurons, many NI neurons also failed to modulate discharge during movements of single or closely related forelimb joints or lacked joint specificity, indicating that intermediate cerebellar output is most likely not organized based on individual joints (Van Kan et al. 1993). As was true for RNm neurons, nearly all NI neurons modulated discharge strongly during reaching to grasp (Van Kan et al. 1993). The same neurons that were strongly activated during reaching to grasp were either not or only weakly activated during reaching movements that were similar in trajectory and amplitude but did not include a grasp, indicating that NI contributes little to controlling coordinated movements of the proximal limb in isolation (Gibson et al. 1996; Van Kan et al. 1994). Moreover, reach-to-grasp-related discharge of NI neurons did not depend on variations in trajectory, amplitude, and direction of limb transport but, instead, was contingent on grasp (Gibson et al. 1996; Van Kan et al. 1994). These results suggest specialization of cerebellar output. Intermediate cerebellar output may be specifically related to aspects of hand use and may contribute to controlling coordinated, whole-limb movements only when these movements include movements of the hand and fingers (Gibson et al. 1994).

The present experiments have aimed to clarify the contribution of forelimb RNm neurons to reaching to grasp. No quantitative studies exist that have attempted to relate RNm discharge to specific aspects of reach-to-grasp behavior. Our experimental approach was to analyze quantitatively discharge of individual RNm neurons, EMG activity of forelimb muscles, and kinematics recorded while monkeys performed three stereotyped reaching tasks that were similar in upper arm involvement but differed in the extent of hand use required. Our main objectives were to determine whether the large reach-to-grasp-related discharge modulations of RNm neurons are also contingent on hand use and to identify specific aspects of hand use that may be controlled or influenced by the discharge of RNm neurons during reaching. The results demonstrate that RNm neurons are not activated strongly during coordinated, whole-limb reaching movements that do not include hand use and that RNm discharge is more strongly related to metacarpi-phalan-gal (MCP) extension than to movements of the wrist and more proximal forelimb joints. A brief report of some of the results has been published (Van Kan and McCurdy 1998).

METHODS

We studied neurons in the RNm of two male rhesus monkeys (*Macaca mulatta*, 7–10 kg) during various reaching tasks. All animal care and experimental procedures complied with the United States Public Health Service Policy on Humane Care and Use of Laboratory Animals, conforming to the National Institutes of Health “Guide for the Care and Use of Laboratory Animals,” and were approved by the Institutional Animal Care and Use Committee.

Behavioral paradigm

During behavioral training and recording sessions, the animals were seated upright in an adjustable primate chair with their backs and feet supported and their thighs positioned horizontally. The animals were restrained loosely by a flexible neck collar and a waist plate. Both forelimbs as well as the animal’s head were unrestrained during experimental sessions. To optimize stable conditions for single-unit recording in monkeys without head restraint, we were vigilant in focusing the monkey’s attention either at the task or at receiving food or water rewards at all times. This minimized occurrence of abrupt head movements, which frequently are the cause of losing recording stability. The primate chair did not restrict the workspace of the “reaching” limb.

The monkeys were trained in three reaching tasks (free-reach, device, and reach-to-grasp) that were similar in their involvement of the proximal forelimb but differed in the extent of hand use required. The animals reached with their right forelimb for water or for cereal rewards presented at four target locations in front of them. Two target locations (left and right) were at shoulder height at angles of 31° to the left and 28° to the right of the parasagittal plane through the shoulder. The other two (upper and lower) were within the sagittal plane through the shoulder at angles of 56° above and 5° below the horizontal plane through the shoulder. The reaches started from a common location near the waist where the monkeys held onto a handle. The amplitude of reaches to the left, upper, right, and lower targets were 460, 500, 460, and 410 mm, respectively. Illumination of a different color light-emitting diode (LED) at the target indicated the type of task to be performed at a given trial and, in addition, served as cue to move. During an intertrial interval of variable duration (3–5 s), the animals received water reward for holding the handle steady at waist level while a mechanical arm (Scorbot ER-III, Eshed Robotec) moved the target assembly in a pseudorandom order to one of the four target locations.

FREE-REACH TASK. The animal reached to position its right hand to interrupt simultaneously two perpendicularly oriented infrared beams at the center of the target zone (Fig. 1, A and C). The target zone comprised a volume of space in front of the target LED; it had no visible boundaries. During the free-reach task, hand and finger movements were not, or only minimally, constrained by the intrinsic properties of the target. That is, no specific hand and finger movements were required during task performance. Following the reach, the animals held the limb steady at the center of the target zone for 5–8 s to receive water reward.

DEVICE TASK. This task elicited a reaching movement while holding onto a handle (Fig. 2, A and B). The device was multi-articulated so as not to restrict the trajectory of the movement. Potentiometers on the rotation points of the device were used to define electronically a volume of space in front of the LED that served as a reward zone. The device was counter balanced with springs to minimize the load on the animal’s forelimb. A small amount of friction applied at the device articulations ensured that the handle remained stationary when released. The device did not have sufficient lateral rigidity to support the
monkey’s arm by applying sideways pressure, and its handle rotated freely to minimize grip adjustments during operation.

**REACH-TO-GRASP TASK.** Simultaneously with cue onset, a cereal (Froot Loop, Kellogg, thickness: ~6 mm; diameter: ~19 mm) was dispensed by a computer-controlled air cylinder into a 50-ml glass beaker (clear; diameter: 32 mm) at the target location. The beaker was tilted at a 45° angle toward the animal, and a whole-hand grasp was required to retrieve the cereal. The animal released the handle, reached, and inserted four digits into the beaker to grasp the cereal in one smooth, coordinated motion (Fig. 1, B, D, and E). The longitudinal axis of the beaker was specifically set at each target location to minimize the need for radial or ulnar deviation at the wrist during retrieval of the cereal.

On isolating a unit, we performed various free-form tests to determine its movement specificity. Neurons were tested for relations between discharge and movement of specific body parts by visual observation and video recording. Neurons with discharge that was better related to movements of body parts other than the forelimb were not considered for further study. Relations to forelimb movements were dissociated from relations to head and eye movements by eliciting reaching movements with either forelimb. Hind limb relations were tested by eliciting movements by lightly touching the sole of the foot or the hairs on the toes. Relations to movements of the mouth and face were studied during the limb holding periods when the animal received water reward and during ingesting cereal and raisins.

We were careful to restrict the range of movements tested in our behavioral tasks; the space covered by reaching to the tested targets represented part of the workspace of the reaching forelimb. Restricting the range of movements tested minimized visually observable postural adjustments of head and trunk that accompanied forelimb reaching, and therefore task-related discharge modulations under our conditions were related to forelimb movements rather than to associated movements of other body parts.

**Surgical preparation**

Following completion of behavioral training, the monkeys were prepared for chronic recording. Under surgical anesthesia (1–1.5% isoflurane) and aseptic conditions, a stainless steel recording cylinder (19 mm ID) and headholder were fastened above a craniotomy with 4–40 stainless steel skull screws and dental acrylic cement. Atropine sulfate (0.1 mg/kg sc) was administered preoperatively; postoperatively the animal received antibiotics (amoxicillin, 200,000 U/d for 5 days), and analgesics (buprenorphine, 0.02 mg/kg im every 10 h for 2 days) for preemptive control of anticipated postsurgical pain associated with swelling and tenderness of muscles. The recording
cylinder was centered on stereotaxic coordinates A3.0 and L0 and tilted 35° laterally in the coronal plane. It was positioned above the right (ipsilateral) cerebral cortex. Daily treatment of the wound minimized the risk of infection.

Implantation of fine bipolar EMG electrodes was done under ketamine anesthesia (12 mg/kg im). Each of 21 forelimb muscles (Table 1) was implanted with a pair of Teflon-coated multistranded stainless steel wires (AS-632 Bioflex, Cooner, Chatsworth, CA). Each wire of a pair was back fed into a 22-gauge hypodermic needle and inserted transcutaneously into the muscle belly. The wires were exposed for 2 mm at the tips, and the tips of a pair were separated by 5–10 mm (Loeb and Gans 1986; McKiernan et al. 1998). Electrode locations were confirmed by observing appropriate movements evoked by electrical stimulation through the electrode pair. Electrode wires were anchored in place with elastic adhesive tape (Johnson and Johnson No. 5174). Following implantation, the animals were returned to their home cages wearing a one-sleeved vest, which protected the implants.

The vest was removed during recording sessions to minimize the risk of infection. The monkeys adapted readily to this procedure and following recovery from anesthesia immediately used the implanted arm without signs of pain or discomfort.

Data collection

Discharge of individual RNm neurons was recorded with epoxylite-coated tungsten microelectrodes (exposed tip: 15–25 μm) in daily recording sessions of 2–3 h duration. Microelectrodes were inserted through the dura with a microdrive (Narashige) that was modified to minimize deflection of the electrode by installing a stainless steel guide tube that extended to the surface of the dura. The microdrive assembly was covered by a lightweight cylinder (100 mm diam) that was fastened to a bolt imbedded in the acrylic cement of the animal’s implant. Periodically, accumulation of dural scar tissue was removed surgically under ketamine anesthesia (12 mg/kg im). Reproducibility of stereotaxic placement of microelectrodes was achieved by cross-referencing microelectrode coordinates with an optical zeroing device (Gibson et al. 1985a). The microelectrode signal was amplified, filtered (half-amplitude band-pass: 100 Hz and 10 kHz, ±3 dB), and fed into a window discriminator circuit that produced a standard pulse for each action potential. Discriminated pulses were used as a computer-clock trigger to collect interspike intervals with 100-μs precision.

The 35° angle of the recording chamber relative to the midsagittal plane ensured that the microelectrode traversed the oculomotor nuclei as it crossed the midline before entering the contralateral (left) RNm. The oculomotor nuclei are located on either side of the midline, ~1 mm dorsal to the RNm, and they extend over approximately the same distance as the RNm in the sagittal plane. Motoneurons of extraocular muscles are easily recognized by their distinct eye-position-related

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**TABLE 1. Forelimb muscles studied during task performance**

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>Digits</td>
<td></td>
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<tr>
<td>Extensor digitorum communis</td>
<td>EDC</td>
</tr>
<tr>
<td>Extensor digitorum two and three</td>
<td>ED23</td>
</tr>
<tr>
<td>Extensor digitorum four and five</td>
<td>ED45</td>
</tr>
<tr>
<td>Flexor digitorum superficialis</td>
<td>FDS</td>
</tr>
<tr>
<td>Flexor digitorum profundus</td>
<td>FDP</td>
</tr>
<tr>
<td>Palmaris longus</td>
<td>PL</td>
</tr>
<tr>
<td>Abductor pollicis longus</td>
<td>APL</td>
</tr>
<tr>
<td>Extensor pollicis longus</td>
<td>EPL</td>
</tr>
<tr>
<td>Wrist</td>
<td></td>
</tr>
<tr>
<td>Extensor carpi radialis</td>
<td>ECR</td>
</tr>
<tr>
<td>Extensor carpi ulnaris</td>
<td>ECU</td>
</tr>
<tr>
<td>Flexor carpi radialis</td>
<td>FCR</td>
</tr>
<tr>
<td>Flexor carpi ulnaris</td>
<td>FCU</td>
</tr>
<tr>
<td>Elbow</td>
<td></td>
</tr>
<tr>
<td>Brachioradialis</td>
<td>BR</td>
</tr>
<tr>
<td>Biceps</td>
<td>BIC</td>
</tr>
<tr>
<td>Triceps (lateral head)</td>
<td>TRI</td>
</tr>
<tr>
<td>Shoulder</td>
<td></td>
</tr>
<tr>
<td>Teres major</td>
<td>TM</td>
</tr>
<tr>
<td>Spino deltoide</td>
<td>spDLT</td>
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<tr>
<td>Latissimus dorsi</td>
<td>LAT</td>
</tr>
<tr>
<td>Acromion deltoide</td>
<td>acDLT</td>
</tr>
<tr>
<td>Cleidodeltoid</td>
<td>ciDLT</td>
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<tr>
<td>Pectoralis</td>
<td>PEC</td>
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FIG. 2. Device task. A: stick-figure reconstruction of the forelimb during a single trial of the device task from the waist to the upper target. Format as in Fig. 1. A and B. The rectangle indicates the spatial location of the target. B: video images of the hand during the same trial shown in A. Format as in Fig. 1. C-E, C–F: kinematics and movement-related discharge during task performance. Reconstructions of wrist trajectories projected on the parasagittal plane through the shoulder are shown for individual trials of the free-reach (●, D), device (●, E), and reach-to-grasp (●, F) tasks. Circle diameter represents single-unit discharge modulation of the same, simultaneously recorded RNm neuron. Discharge modulation was calculated over consecutive 33.3-ms intervals, each corresponding to the duration of a single video frame. D–F: the same trajectories shown in C are offset by 100 mm each for clarity of illustration. □, frame numbers corresponding to reach onset (frame 1) and offset (frames 14, 22, and 11).
tonic discharge patterns, by the regularity of their discharge for a
given eye position, and by their large range of firing rates (0–700
imp/s) (Fuchs and Luschei 1970). The oculomotor nuclei, therefore
serve as useful landmarks for identifying the location of the RNm. On
entering RNm, background activity increased sharply and modulated
during movements of contralateral body parts. The most dorsal neu-
rons encountered were related to movements of the face, mouth,
and/or tongue. Dorsomedially, neurons modulated their discharge
strongly during movements of the forelimb, and ventrolaterally neu-
rons were related to movements of the hind limb. By converting the
chamber coordinates and microdrive readings into three-dimensional
Cartesian coordinates, we mapped the locations of oculomotor neu-
rons and face, forelimb, and hind limb RNm neurons as they would
appear in coronal tissue sections (Fig. 3). Our mapping agrees with
previous descriptions of the somatotopy of RNm based on single-unit
recording (Gibson et al. 1985a), neuroanatomical tracing (Pompeiano
and Brodal 1957; Robinson et al. 1987), microstimulation (Ghez
1975; Larsen and Yumiya 1980), and mapping sensory responsiveness
(Ghez 1975; Larsen and Yumiya 1980; Padel et al. 1988). In addition,
neurons of our sample also showed many electrophysiological char-
acteristics consistent with those reported for RNm neurons in previous
recording studies (Gibson et al. 1985a). RNm neurons had action
potentials of large amplitude (0.4–2 mV) and relatively long duration
(0.5–1.0 ms). Action potentials had negative-positive or positive-
negative waveshapes with prominent IS-SD intervals characteristic of
large cell bodies. Single units were distinguished by the constancy of
their waveform. Most neurons tuned over large distances (typically
~200 μm), and when damaged by advancing the microeleetrode,
neurons often showed separation of their action potential waveshapes
followed by prominent injury discharge.

Times of making and breaking contact with the handle and beaker
were determined by contact sensors as the times of the associated
changes in capacitance. Output signals of the contact sensors were
sampled at 167 Hz by A/D computer inputs (CED 1401plus, Cam-
bridge Electronic Design).

We recorded EMG activity of muscles acting at digit (n = 8), wrist
(n = 4), elbow (n = 3), and shoulder (n = 6) joints (Table 1) during
performance of the same tasks by the same animals, but EMG activity
was not recorded simultaneously with the discharge of RNm neurons.
EMG activity of various combinations of muscles (9 muscles per
session) was collected during nine recording sessions conducted over
a 10-day period in monkey W and during five recording sessions over
a 6-day period in monkey B. EMG signals were rectified, integrated
(time constant: 10 ms), filtered (band-pass 30 Hz-3 kHz), and digi-
tized at 167 Hz by A/D computer inputs (CED 1401plus, Cambridge
Electronic Design).

RNm discharge, behavioral marker signals, and the animals’ move-
ments during task performance were recorded on videotape by an
8-mm video recorder (Sony VTR 1000) and two high-resolution
 cameras (Hitachi KP-M1) with high-speed shutters (1/1,000 s). A
splitter/inserter allowed two images (e.g., side/top view or full/
close-up view) to be recorded simultaneously. A custom video display
system enabled us to record a histogram of discharge rate and behav-
ioral marker signals (e.g., making/breaking contact with the handle
and beaker) in the same video image as the animal’s limb. This
allowed neuronal discharge and other computer records to be cross-
referenced with successive video frames of a given trial, and thus
provided a straightforward means of associating discharge with spe-
cific movements.

Data analysis

For each unit, data collected during task performance were ana-
yzed by grouping together trials to each of the four targets. Each trial
was computer analyzed by marking with a trackball-controlled cursor
the times of making and breaking contact with the handle and beaker
(free-reach and reach-to-grasp tasks) or movement onset and offset as
determined from a record of movement velocity (device task). Reach
onset was defined as the time of breaking contact with the handle
(free-reach and reach-to-grasp tasks) or the time of the first increase
in velocity (device task) and was used to average records or to align
individual trial records in raster displays. Reach offset was defined as
the time of interrupting the infra-red beams (free-reach task) or
contacting the beaker (reach-to-grasp task), or the time velocity re-
turned to zero (device task). Custom software allowed us to synchro-
nize discharge records collected during individual trials on one be-
havioral event (e.g., reach onset) and order them according to another
(e.g., making/breaking contact with the beaker). This technique al-
lowed discharge associations to more than one event to be shown by
the same rasters.

We quantified the amplitude of task-related discharge modulations
during the period of limb transport because nearly all neurons attained
their largest discharge modulations during this period. A record of
discharge rate was derived from the interspike interval record by
calculating discharge rate averaged over consecutive 6-ms periods
taking into account fractional interspike intervals. Task-related mod-
ulations in discharge rate during individual trials were quantified by
calculating the average discharge rate over a 100-ms window that was
moved, 6 ms at a time, between the times of reach onset and reach
offset. Mean peak discharge modulation was defined by selecting the
highest discharge rate and subtracting from it the average rate during
a 0.5-s interval starting 1.0 s prior to movement cue onset during
which the animal sat quietly and held onto the handle at the waist.
Individual trial measurements of mean peak discharge modulation for
each neuron tested during the free-reach, device, and reach-to-grasp
tasks to the four targets were evaluated by ANOVA. There was no
interaction between behavioral task and target location (2-way
ANOVA, P > 0.05), indicating that task-related differences in mean
peak discharge modulations were not due to target location. The mean
peak discharge modulations for each neuron tested during the free-
reach, device, and reach-to-grasp tasks to the target were evaluated sta-
tistically in RESULTS (1-way ANOVA, P < 0.05). Differences between
group means were evaluated with all-pairwise multiple comparison
procedures (Bonferroni i-tests or Dunn’s method).

Task performance was analyzed kinematically from videotaped
images of the moving hand during reaches to the upper target. The
view of one of the cameras was perpendicular to the parasagittal plane
through the shoulder; the other camera was oriented perpendicular
to provide a top view. A video frame grabber board (MIRO 300DCplus)
was used to import successive video frames into commercially avail-
able image software (Adobe Premier, Canvas). Stick figures of the moving limb were reconstructed and joint angles were calculated from the x-y coordinates of the following landmarks: the head of the humerus, the rotation point of the elbow, the proximal end of the carpals, the proximal phalanges, and the proximal interphalanges. The x-y coordinates for these points were identified on successive video frames of the moving limb (resolution: 33.3 ms). Movement trajectories (Fig. 2, C–F) were then reconstructed by overplotting the stick figures obtained from successive video frames.

We evaluated relations between RNm discharge and kinematic variables of movements of the MCP, wrist, elbow, and shoulder joints with correlation and regression analyses similar to those used by Gibson et al. (1985b). The measure of discharge that was correlated with the movements analyzed was the cumulative sum record (Ella-way 1978). The cumulative sum (cusum) record was derived from the interspike interval record of individual trials as follows. The number of action potentials in successive 6-ms bins was adjusted by subtracting the average number of action potentials per bin during a 0.5-s interval starting 1.0 s prior to movement cue onset during which the animal sat quietly and held onto the handle at the waist. The cusum record was then generated by adding up these differences consecutively. The measure of movement was derived from the time plot of joint angle measurements from consecutive video frames by cubic spline interpolation (interval: 6 ms). This algorithm has a smoothing action on the data and does not introduce appreciable distortion. Modulation in discharge rate and movement velocity are represented by the slopes of the cusum and movement record, respectively, and were determined by linear regression of the x, y data points between burst and movement onset and offset times. Scatter plots of discharge versus movement parameters were constructed for each of eight neurons studied during the free-reach and/or reach-to-grasp tasks. Five comparisons were made for each task: burst onset latency versus movement onset latency, burst onset latency versus movement onset offset latency, number of spikes in the burst versus movement amplitude, and frequency within bursts versus movement velocity. Standard regression techniques were used to evaluate each of the five relations.

Rectified, integrated, and filtered EMG signals recorded during individual trials were aligned on reach onset and averaged (binwidth: 6 ms) (Figs. 8 and 9). EMG activity was analyzed quantitatively as described above for discharge of RNm neurons with the exception that the analysis period was extended from 0.25 s before reach onset to 6 ms (Figs. 8 and 9). The measure of discharge that was correlated with the movements analyzed was the cumulative sum record (Ella-way 1978). The cumulative sum (cusum) record was derived from the interspike interval record of individual trials as follows. The number of action potentials in successive 6-ms bins was adjusted by subtracting the average number of action potentials per bin during a 0.5-s interval starting 1.0 s prior to movement cue onset during which the animal sat quietly and held onto the handle at the waist. The cusum record was then generated by adding up these differences consecutively. The measure of movement was derived from the time plot of joint angle measurements from consecutive video frames by cubic spline interpolation (interval: 6 ms). This algorithm has a smoothing action on the data and does not introduce appreciable distortion. Modulation in discharge rate and movement velocity are represented by the slopes of the cusum and movement record, respectively, and were determined by linear regression of the x, y data points between burst and movement onset and offset times. Scatter plots of discharge versus movement parameters were constructed for each of eight neurons studied during the free-reach and/or reach-to-grasp tasks. Five comparisons were made for each task: burst onset latency versus movement onset latency, burst onset latency versus movement onset offset latency, number of spikes in the burst versus movement amplitude, and frequency within bursts versus movement velocity. Standard regression techniques were used to evaluate each of the five relations.

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We evaluated relations between RNm discharge and kinematic variables of movements of the MCP, wrist, elbow, and shoulder joints with correlation and regression analyses similar to those used by Gibson et al. (1985b). The measure of discharge that was correlated with the movements analyzed was the cumulative sum record (Ella-way 1978). The cumulative sum (cusum) record was derived from the interspike interval record of individual trials as follows. The number of action potentials in successive 6-ms bins was adjusted by subtracting the average number of action potentials per bin during a 0.5-s interval starting 1.0 s prior to movement cue onset during which the animal sat quietly and held onto the handle at the waist. The cusum record was then generated by adding up these differences consecutively. The measure of movement was derived from the time plot of joint angle measurements from consecutive video frames by cubic spline interpolation (interval: 6 ms). This algorithm has a smoothing action on the data and does not introduce appreciable distortion. Modulation in discharge rate and movement velocity are represented by the slopes of the cusum and movement record, respectively, and were determined by linear regression of the x, y data points between burst and movement onset and offset times. Scatter plots of discharge versus movement parameters were constructed for each of eight neurons studied during the free-reach and/or reach-to-grasp tasks. Five comparisons were made for each task: burst onset latency versus movement onset latency, burst onset latency versus movement onset offset latency, number of spikes in the burst versus movement amplitude, and frequency within bursts versus movement velocity. Standard regression techniques were used to evaluate each of the five relations.

Rectified, integrated, and filtered EMG signals recorded during individual trials were aligned on reach onset and averaged (binwidth: 6 ms) (Figs. 8 and 9). EMG activity was analyzed quantitatively as described above for discharge of RNm neurons with the exception that the analysis period was extended from 0.25 s before reach onset to 0.25 s following reach offset to determine the times of true peaks in EMG activity of muscles that attained their largest activation before or after the limb transport period (e.g., Figs. 8–10, flexor digitorum superficialis and profundus, palmaris longus, flexor carpi radialis, and biceps).

**RESULTS**

Monkeys performed three reaching tasks that involved similar use of the upper arm but differed in the extent of hand use required. We analyzed task-related discharge from single forelimb RNm neurons, patterns of EMG activity of forelimb muscles, and kinematic data to identify behavioral characteristics that might correspond to differences in magnitude and temporal pattern of task-related RNm discharge.

**RNm discharge during reaching**

One hundred and fifty-seven of 214 RNm neurons in two monkeys were related to movements of the contralateral forelimb. Forelimb neurons were easily recognized by high firing rates and large discharge modulations during reaching to grasp. This report is based on 67/157 forelimb neurons for which complete data sets were obtained during performance of the reach-to-grasp and device tasks. Additional data for the free-reach task is based on a subset (13/67) of these. Results from neurons with partial data sets were consistent with those reported here.

Reaching tasks that involved hand use elicited large discharge modulations of forelimb RNm neurons. Discharge modulations were larger during the reach-to-grasp and device tasks than during the free-reach task (Figs. 2, C–F, and 4). The reach-to-grasp task typically elicited a single burst of discharge (Figs. 2F, 4, C–F, and 5, A–F). The large modulations and high consistency of discharge during multiple trials of the device and particularly the reach-to-grasp task (Fig. 4, B and C) resulted in neuron-specific discharge patterns. The distributions of the mean peak discharge modulations for the three behavioral tasks were significantly different for the neuronal population (1-way ANOVA: $F = 14.380, DF = 2, P < 0.001$; Fig. 14A). Discharge modulations during the reach-to-grasp [$128 \pm 54$ (SD) imp/s], device ($105 \pm 40$ imp/s), and free-reach ($54 \pm 41$ imp/s) tasks represent more than five-, four-, and twofold increases over baseline discharge ($25 \pm 11$ imp/s), respectively. Discharge modulations of most neurons tested were larger during the reach-to-grasp (85%, 11/13 neurons) and device (77%, 10/13 neurons) than free-reach tasks (Fig. 6, A and B, data points above the diagonals). Although the mean peak discharge modulations of the majority of neurons (64%, 43/67) were larger during the reach-to-grasp than device task (Fig. 6C, data points above the diagonals), discharge modulations of some neurons were as large or larger during the device than reach-to-grasp task (Fig. 5, E–G). Thus reaching while holding a handle can be as effective as reaching to grasp in engaging some RNm neurons, suggesting that the device and reach-to-grasp tasks share common behavioral features important to the discharge of RNm neurons.

The timing of discharge modulations of RNm neurons depended on the phase of limb transport. Most neurons attained peak discharge within the period of limb transport (Fig. 7A), and the times of peak discharge relative to the period of limb transport overlapped extensively during the reach-to-grasp and device tasks (Fig. 7B). Most neurons attained their largest discharge modulations within the interval extending from 30 to 80% of the period of limb transport during the reach-to-grasp task (87%, 58/67 neurons; Fig. 7B, □□) and within the interval extending from 20 to 70% of the period of limb transport during the device task (85%, 57/67 neurons; Fig. 7B, □). The interval during which most neurons attained peak discharge was more widespread during the free-reach than device and reach-to-grasp tasks. Seven neurons had discharge modulations $>50$ imp/s during the free-reach task. Three of these seven neurons attained peak discharge near reach onset and one near reach offset. The remaining three neurons attained peak discharge approximately halfway through the period of limb transport. Thus given some delay between neuronal discharge and movement, most RNm neurons exerted their strongest influence during the later two-thirds of the period of limb transport.

In summary, the results demonstrate that coordinated whole-limb reaching movements are associated with large discharge modulations predominantly when hand use is included and therefore aspects of hand use are important to the discharge of RNm neurons.
Activity of forelimb muscles during reaching

Do patterns of muscle activation support a role for RNm in hand use? In the preceding text, we have demonstrated that discharge of RNm neurons is strongly related to reaching tasks only when hand use is included. Therefore we investigated whether the strong coupling between RNm discharge and hand use was also evident in the patterns of activation of forelimb muscles during reaching (Figs. 8 and 9). To assess this relation, we compared the times at which most RNm neurons attained peak discharge during the reach-to-grasp task with the times at which forelimb muscles attained peak EMG activity. Figure 10 compares the average times (mean ± SD) of peak discharge of our sample of forelimb RNm neurons with the average times of peak EMG activity of the forelimb muscles studied. The times of peak EMG activity of digit and wrist extensor muscles closely matched the times of peak RNm discharge for both animals (Figs. 8, A–C, H, and I, and 10, A–E). In contrast, the times of peak EMG activity of digit and wrist flexor muscles (Figs. 8, E–G, J, and K, except FCU in monkey W, and 10, C–F) did not match the times of peak RNm discharge (Fig. 10, A and B). In addition, the times of peak EMG activity of many proximal muscles were also compatible with the times of peak discharge of RNm neurons. For example, the times of peak EMG activity of BIC in monkey W (Figs. 9B and 10, A and H) and BR in monkey B (Figs. 9C and 10, A and F) during individual trials of task performance overlapped the times of peak discharge of RNm neurons completely (Fig. 10, A and B), and partial overlap was observed for spinodeltoid (spDLT, Figs. 9D and 10, A and J) and acromion deltoid (acDLT) in monkey B (Fig. 9F), and for triceps (TRI, Figs. 9A and 10, A and G) and pectoralis (PEC, Fig. 9I) in both animals. In summary, results from analyzing EMG activity of forelimb muscles are consistent with the view that RNm discharge may contribute to the activation of both distal and proximal forelimb muscles during reaching to grasp, especially distal extensor muscles and proximal muscles important for limb elevation. The results are consistent with a role for RNm in controlling muscle synergies required for MCP extension during reaching to grasp.

A second approach we used to relate RNm discharge to
EMG activity of forelimb muscles was to investigate how the times of peak discharge of RNm neurons and EMG activity of forelimb muscles depended on the duration of limb transport. Results of this analysis are shown in Fig. 10, B–J. Linear correlation coefficients for the scatter plots of the time of peak discharge of RNm neurons versus the duration of limb transport were significant at the \( P \leq 0.05 \) level for both animals (Fig. 10B), thus peak RNm discharge occurred later for longer duration of limb transport. The times of peak EMG activity of many proximal (Fig. 10, F–J) and distal (Fig. 10, C–F) muscles were also positively correlated with the duration of limb transport as might be expected because many of the proximal muscles contribute to elevating and extending the limb, and hand preshaping is coupled to the phase of limb transport (for reviews: Jeannerod 1988; Paulignan and Jeannerod 1996). We examined relations between RNm discharge and kinematic data to specify the behavioral relevance of the strong linkages between RNm discharge, EMG activity of forelimb muscles, and hand involvement during the reach-to-grasp task.

Relation between RNm discharge and movement parameters

Comparing discharge of RNm neurons and EMG activity of forelimb muscles to kinematic data during task performance revealed that one aspect of hand use that is strongly correlated with RNm discharge is extension of the MCP joints. Extension of the interphalangeal joints also differed between tasks. RNm discharge, however, probably contributed little to this difference because extension of the interphalangeal joints was much more pronounced in monkey W than monkey B during the reach-to-grasp task (Fig. 1, E, frames 3–9 vs. D, frames 4–7).

FIG. 5. Discharge of 7 RNm neurons (A–G) during performance of the device and reach-to-grasp task to the upper target. The neurons are ordered from top to bottom to illustrate the entire spectrum of discharge relations, from stronger discharge during the reach-to-grasp than device task (A–D), to similar discharge (E), to stronger discharge during the device task (F and G). Format as in Fig. 4. Vertical scale is 350 imp/s for A–D and 200 imp/s for E–G. Number of trials included in the average discharge records for device and reach-to-grasp tasks, respectively, in A: \( n = 6, 7 \); B: \( n = 10, 6 \); C: \( n = 3, 1 \); D: \( n = 7, 6 \); E: \( n = 6, 4 \); F: 6, 7; G: 20, 13.

EMG activity of forelimb muscles was to investigate how the times of peak discharge of RNm neurons and EMG activity of forelimb muscles depended on the duration of limb transport. Results of this analysis are shown in Fig. 10, B–J. Linear correlation coefficients for the scatter plots of the time of peak discharge of RNm neurons versus the duration of limb transport were significant at the \( P < 0.05 \) level for both animals (Fig. 10B), thus peak RNm discharge occurred later for longer duration of limb transport. The times of peak EMG activity of many proximal (Fig. 10, F–J) and distal (Fig. 10, C–F) muscles were also positively correlated with the duration of limb transport as might be expected because many of the proximal muscles contribute to elevating and extending the limb, and hand preshaping is coupled to the phase of limb transport (for reviews: Jeannerod 1988; Paulignan and Jeannerod 1996). We examined relations between RNm discharge and kinematic data to specify the behavioral relevance of the strong linkages between RNm discharge, EMG activity of forelimb muscles, and hand involvement during the reach-to-grasp task.

FIG. 6. Scatter plots comparing mean peak discharge modulation (imp/s) for individual RNm neurons during the free-reach, device, and reach-to-grasp tasks to the upper target for monkey B (○) and monkey W (▲). Each data point represents data from the same neuron. Paired \( t \)-statistics: A, reach to grasp (128 ± 54 imp/s) vs. device (105 ± 40 imp/s), \( T = 5.221, DF = 66, P < 0.05 \); B, reach to grasp (119 ± 49 imp/s) vs. free-reach (54 ± 41 imp/s), \( T = 3.958, DF = 12, P < 0.05 \); C, device (85 ± 33 imp/s) vs. free-reach (54 ± 41 imp/s), \( T = 2.149, DF = 12, P > 0.05 \).
and yet RNm discharge modulations during the reach-to-grasp task did not differ between the animals (Fig. 14A).

The relations between discharge of individual RNm neurons and movements of forelimb joints were quantified by correlation and regression analyses performed on data from a subset of neurons. The subset consisted of neurons that were studied during both the reach-to-grasp and free-reach tasks and had mean peak discharge modulations >50 imp/s for both tasks. We tested for reliable relations between parameters of movements of MCP, wrist, elbow, and shoulder joints and corresponding bursts of discharge during individual trials of task performance. Seven of 13 neurons tested during both tasks fulfilled these criteria, and kinematic data were available for 6 of these. Discharge of five of these six neurons is shown in Fig. 4. We chose to focus the analysis on neurons that were tested during both the reach-to-grasp and free-reach tasks because we reasoned that if RNm discharge is causally related to MCP extension, then correlation and regression analyses should reveal strong relations between parameters of discharge and MCP extension regardless of task. Discharge modulations of RNm neurons differed the most between the reach-to-grasp and free-reach tasks and yet performance of the free-reach and reach-to-grasp tasks was most similar except for clear differences in hand use. Although MCP extension was also associated with performance of the device task, we did not analyze relations between discharge and movements during the device task because the hand gripped a handle during the device task whereas the hand was unconstrained during the free-reach and reach-to-grasp tasks. Holding a handle may be associated with the generation of grip forces (Van Kan et al. 1994) that may have contributed to the differences in muscle activation patterns observed during performance of the device compared with the reach-to-grasp and free-reach tasks (Figs. 8 and 9).

Strong relations between parameters of reach-related RNm discharge and movements were most frequently associated with MCP extension. Movement relations for all 14 cases tested (involving 6 neurons that were tested during both the reach-to-grasp and free-reach tasks, 1 neuron tested only during the reach-to-grasp task, and 1 neuron tested only during the free-reach task) are summarized quantitatively in Table 2. All neurons tested, regardless of task, showed strong relations between parameters of discharge and MCP extension. Figures 11 and 12 show examples of the close correspondence of the detailed time course of MCP extension and the associated modulations in discharge rate for four neurons during individual trials of the free-reach and/or reach-to-grasp tasks. Bursts of discharge preceded associated movements and the frequency of discharge within bursts was larger (steeper slope of the cumulative sum records) and burst duration shorter for faster movements. For all neurons tested, regardless of task, burst onset latency was strongly correlated with the onset latency of MCP extension (Fig. 13, A–C) and burst offset latency was strongly correlated with the offset latency of MCP extension. Slopes of the regression lines were near 1.0 and fell below the line of simultaneity, indicating that burst onset lead movement onset and burst offset lead movement offset. The average onset lead was 71 ± 25 (SD) ms and the average offset lead was 18 ± 31 ms. Burst duration was strongly correlated with the duration of MCP extension (Fig. 13, D–F; Table 2). Linear correlation coefficients were significant for 12/14 cases (5/6 neurons tested during both the free-reach and reach-to-grasp tasks) and averaged 0.86 ± 0.09. The average slope of the regression line was 1.11 ± 0.28. Discharge amplitude (number of spikes in the burst) was strongly correlated with the amplitude of MCP extension (Fig. 13, G–I; Table 2). Linear correlation coefficients were significant for 12/14 cases (5/6 neurons tested during both tasks) and averaged 0.78 ± 0.12. The average slope of the regression line was 0.54 ± 0.24 imp/s. Finally, discharge frequency was strongly correlated with the velocity of MCP extension (Fig. 13, J–L; Table 2). Linear correlation coefficients were significant for 13/14 cases (5/6 neurons tested during both tasks) and averaged 0.80 ± 0.09. The average slope of the regression line was 0.18 ± 0.08 (imp/s)/(°/s). In summary, all RNm neurons tested showed strong relations between parameters of discharge and corresponding MCP extension movements regardless of task.

Discharge of RNm neurons was poorly related to movements of proximal joints. The speed of limb transport differed between tasks (Kruskal-Wallis 1-way ANOVA on ranks: H = 109.800, DF = 2, P < 0.001), but the differences in speed did not correspond to the differences in task-related discharge modulations (Fig. 14, A vs. B). Limb transport was nearly as fast during the free-reach as the reach-to-grasp task [1.13 ± 0.20 vs. 1.54 ± 0.21 (SD) m/s], but discharge modulations were more than twice as large during the reach-to-grasp than free-reach task (128 ± 54 vs. 54 ± 41 imp/s). In addition, limb transport was more than twice as fast during the reach-to-grasp than device task (1.54 ± 0.21 vs. 0.62 ± 0.07 m/s), and yet discharge modulations were only larger by 22%. Furthermore, scatter plots of discharge modulation as a function of speed of limb transport constructed from data for individual neurons showed no significant correlations for any of the three tasks. Thus these results clearly do not support a role for RNm in controlling the speed of limb transport during reaching. Instead, RNm discharge during the device task may have been...
increased to nearly the level of the much faster reach-to-grasp task because somewhat greater muscle activation may have been required (Figs. 8H and 9, B, F, and I) due to the added inertia of the device or the generation of grip forces while holding a handle.

Correlation analysis of the above defined subset of eight forelimb RNm neurons studied during the reach-to-grasp and/or free-reach tasks also showed that discharge was poorly related to movements of the wrist, elbow, and shoulder joints. Bursts of discharge did not consistently precede corresponding movements across trials. Some bursts were associated with periods of no movement, preceded movements in the flexion direction for some trials but in the extension direction for others, or preceded movements by long intervals, sometimes longer than 0.35 s. Consistent relations between discharge and movements of the wrist, elbow, and shoulder joints were analyzed quantitatively as described in the preceding text for MCP extension, and only these cases are listed in Table 2. Parametric
relations between discharge and movements of wrist, elbow, and shoulder joints were observed much less frequently as compared with relations involving MCP extension, and they were characterized by higher failure rates (Table 2). Failures were scored when movements occurred without discharge (e.g., Fig. 11E). Using an average correlation coefficient >0.5 as a criterion of relatedness, 4 of 14 cases tested (involving 4 neurons) were related to wrist flexion, 2 of 14 cases (involving 2 neurons) were related to elbow extension, and none of 14 cases were related to movements of the shoulder. None of six neurons tested were related to movements of the wrist, elbow, or shoulder during both the free-reach and reach-to-grasp tasks. Figure 12 shows records of discharge and angles of the MCP, wrist, elbow, and shoulder joints for neuron B137-218 recorded during individual trials of the free-reach (A and B) and reach-to-grasp tasks (C and D). Relations between discharge and movements were significant for wrist flexion and elbow extension during the reach-to-grasp task and for MCP extension during both tasks (Fig. 13, left; Table 2). The individual trial records in Fig. 12, A–D, are ordered from left to right according to increasing velocity of MCP extension. Comparing discharge and joint angle records shows that faster MCP extension and faster wrist and shoulder flexion were preceded by larger modulations in discharge rate. The relations between discharge and wrist and shoulder flexion, however, were not consistent across trials during the free-reach task, and the relation between discharge and shoulder flexion was not consistent across trials during the reach-to-grasp task.

In summary, the combined results of our analyses of discharge of individual RNm neurons, EMG activity of forelimb muscles, and kinematic data during the free-reach and reach-to-grasp tasks suggest that RNm’s influence on digit extensor
muscles may produce MCP extension. RNm discharge was poorly related to movements of proximal joints. Discharge was not related to the speed of limb transport, and none of eight neurons tested (14 cases) demonstrated relatedness between parameters of discharge and movements of the shoulder. In addition, movement relations involving the wrist (4 cases) and elbow (2 cases) were observed during the reach-to-grasp but not during the free-reach task, suggesting that for these neurons RNm discharge may not be causally related to movements of the wrist, elbow, or shoulder joints.

DISCUSSION

Testing the same RNm neurons during reaching tasks that differed in hand use emphasized the importance of hand use to the discharge of RNm neurons. We studied neuronal discharge of individual RNm neurons during a reach-to-grasp task and two tasks that were similar to the reach-to-grasp task in trajectory, amplitude, and direction but did not include a grasp. One of these, the device task, elicited reaches while holding a handle and the other, the free-reach task, elicited reaches that did not require any specific hand use for task performance. The results show that, on average, modulations in discharge rate were graded with hand use. The largest modulations in the discharge rate of RNm neurons were associated with the reach-to-grasp task and progressively smaller modulations were associated with the device and free-reach tasks, respectively. Our demonstration with quantitative methods that coordinated whole-limb reaching movements are associated with large discharge modulations predominantly when hand use is included confirms previous qualitative observations of a similar association during free-form testing (Gibson et al. 1985a). Therefore RNm neurons, like interpositus neurons (Gibson et al. 1996; Van Kan et al. 1994), can at best only make a minor contribution to the control of reaching movements that lack hand use.

Several lines of evidence further strengthen a specialized function for RNm in controlling hand use. First, lesions of the rubrospinal tract in monkeys (Lawrence and Kuypers 1968) or the RNm in cats (Sybirska and Gorska 1980) produced temporary deficits that mainly affect hand use. Lesions of the rubrospinal tract combined with lesions of the corticospinal tracts, however, resulted in a profound and permanent impairment of hand use (Lawrence and Kuypers 1968). In contrast to...
the severe deficits in hand use following lesions of the RNm or rubrospinal tract, control of the proximal limb was affected to a much lesser extent. Temporary inactivation of the forelimb RNm in cats trained to reach to grasp a lever produced severe deficits in grasp and only slight impairment of limb transport (Gibson et al. 1994), and whole-limb pointing movements to track moving spots of light, which did not require a grasp, were only minimally affected by kainic acid lesions of RNm (Levesque and Fabre-Thorpe 1990), or combined lesions of RNm and motor thalamus (Lorincz and Fabre-Thorpe 1997) in cats. Second, neuroanatomical studies indicate that most rubrospinal axons terminate among interneurons in the intermediate region along the entire extent of the spinal cord (Holstege and Kuypers 1982; Kuypers et al. 1962; Nyberg-Hansen and Brodal 1964) but the only terminations among motoneurons selectively target pools that innervate digit muscles, especially digit extensors (Holstege 1987; Holstege et al. 1988; McCurdy et al. 1987; Ralston et al. 1988; Robinson et al. 1987). Third, temporary inactivation of the anterior division of NI in monkeys produced deficits in hand preshaping for grasping and inactivating posterior NI produced difficulties in controlling the limb in positions appropriate for grasping (Mason et al. 1998). In conclusion, the combined evidence from studies using a variety of approaches supports the hypothesis that intermediate cerebellar output via RNm is specialized for controlling aspects of hand use.

Importance of MCP extension to the discharge of RNm neurons

The present study demonstrates that one aspect of hand use that is strongly related to RNm discharge during reaching is extension of the MCP joints. This finding agrees well with accounts of movement relations of individual RNm neurons based on multiple device testing (Gibson et al. 1985a; Miller and Houk 1995). The multiple device approach tests neurons during use of devices designed to elicit movements largely restricted to single or several closely related forelimb joints. Discharge of RNm neurons was preferentially related to use of distal devices rather than the wrist or more proximal devices. The metacarpal and twister devices were the most effective devices in evoking large discharge modulations. Ten of 11 RNm neurons that modulated discharge during use of the metacarpal device, which elicited movements restricted to the MCP joints, were preferentially related to MCP extension (Gibson et al. 1985a). During the free-reach and/or reach-to-grasp tasks, we observed the same strong relations between discharge of individual RNm neurons and MCP extension. Our results also fit well with the observation that the large discharge modulations of neurons during use of the twister device appeared to result from involvement of the fingers in this task (Gibson et al. 1985a). Use of the twister involved rotating a shaft by hand in clockwise and counter clockwise directions, as in operating a motorcycle throttle. None of the neurons active on the twister fired well during isolated wrist movements, whereas 67% of neurons active on the twister fired well during use of finger devices. The remaining 33% of neurons discharged strongly during use of the twister but not during use of finger devices. Perhaps these neurons discharge only when digit and wrist movements occur together. We observed robust discharge for some RNm neurons preceding reach onset when wrist flexion and elevation contributed to MCP extension, suggesting that aspects of coordination of digits and wrist may be important to the discharge of these neurons. The combined data suggest that discharge of some RNm neurons may produce movement restricted to MCP extension but other RNm neurons may produce MCP extension and, in addition, modify aspects of MCP extension related to limb stability or to coordinating MCP extension with limb transport.

### Table 2. Parametric correlations for eight RNm neurons studied during the free-reach and/or reach-to-grasp tasks

<table>
<thead>
<tr>
<th>Neuron</th>
<th>Task</th>
<th>Joint</th>
<th>Dir</th>
<th>( n )</th>
<th>Failures</th>
<th>Duration</th>
<th>Amplitude</th>
<th>Velocity</th>
<th>Average</th>
<th>Mpdm</th>
</tr>
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<tbody>
<tr>
<td>B133-213</td>
<td>FR</td>
<td>MCP</td>
<td>E</td>
<td>10</td>
<td>0</td>
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<td>(0.53)</td>
<td>0.78</td>
<td>0.74</td>
<td>141</td>
</tr>
<tr>
<td>B135-216</td>
<td>RTG</td>
<td>MCP</td>
<td>E</td>
<td>11</td>
<td>0</td>
<td>0.88</td>
<td>0.61</td>
<td>0.82</td>
<td>0.77</td>
<td>159</td>
</tr>
<tr>
<td>B137-218</td>
<td>FR</td>
<td>MCP</td>
<td>E</td>
<td>10</td>
<td>0</td>
<td>0.88</td>
<td>0.82</td>
<td>(0.46)</td>
<td>0.72</td>
<td>94</td>
</tr>
<tr>
<td>W203-202</td>
<td>RTG</td>
<td>MCP</td>
<td>E</td>
<td>7</td>
<td>1</td>
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<td>0.69</td>
<td>0.79</td>
<td>0.81</td>
<td>106</td>
</tr>
<tr>
<td>W209-208</td>
<td>RTG</td>
<td>MCP</td>
<td>E</td>
<td>14</td>
<td>4</td>
<td>0.70</td>
<td>(0.25)</td>
<td>0.19</td>
<td>0.38</td>
<td>53</td>
</tr>
<tr>
<td>B140-222</td>
<td>FR</td>
<td>MCP</td>
<td>E</td>
<td>14</td>
<td>0</td>
<td>0.79</td>
<td>0.87</td>
<td>0.95</td>
<td>0.87</td>
<td>300</td>
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<tr>
<td>B116</td>
<td>RTG</td>
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<tr>
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<td>E</td>
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<td>0</td>
<td>0.82</td>
<td>0.88</td>
<td>(0.03)</td>
<td>0.58</td>
<td>94</td>
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<tr>
<td>Elbow</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>B137-218</td>
<td>MCP</td>
<td>Wrist</td>
<td>E</td>
<td>11</td>
<td>1</td>
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</tr>
<tr>
<td>B140-222</td>
<td>RTG</td>
<td>MCP</td>
<td>E</td>
<td>12</td>
<td>0</td>
<td>0.92</td>
<td>0.81</td>
<td>0.86</td>
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<tr>
<td>W203-202</td>
<td>MCP</td>
<td>Elbow</td>
<td>E</td>
<td>10</td>
<td>0</td>
<td>0.78</td>
<td>0.66</td>
<td>0.71</td>
<td>0.72</td>
<td>86</td>
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<tr>
<td>W209-208</td>
<td>RTG</td>
<td>MCP</td>
<td>E</td>
<td>7</td>
<td>0</td>
<td>0.84</td>
<td>0.92</td>
<td>0.81</td>
<td>0.86</td>
<td>56</td>
</tr>
<tr>
<td>B116</td>
<td>MCP</td>
<td>Wrist</td>
<td>E</td>
<td>11</td>
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<td>0.69</td>
<td>0.90</td>
<td>0.84</td>
<td>0.81</td>
<td>92</td>
</tr>
<tr>
<td>Elbow</td>
<td>10</td>
<td>0</td>
<td>(0.07)</td>
<td>0.69</td>
<td>0.76</td>
<td>0.51</td>
<td>166</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>B133-213</td>
<td>RTG</td>
<td>MCP</td>
<td>E</td>
<td>10</td>
<td>2</td>
<td>(0.60)</td>
<td>0.85</td>
<td>0.84</td>
<td>0.76</td>
<td>167</td>
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<tr>
<td>B220</td>
<td>MCP</td>
<td>Elbow</td>
<td>E</td>
<td>8</td>
<td>0</td>
<td>0.90</td>
<td>0.81</td>
<td>(0.61)</td>
<td>0.77</td>
<td>103</td>
</tr>
<tr>
<td>Wrist</td>
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<td>2</td>
<td>0.74</td>
<td>(0.43)</td>
<td>0.78</td>
<td>0.65</td>
<td>0.49</td>
<td>49</td>
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<td></td>
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\( ^{a} \) Task, free-reach (FR) or reach-to-grasp (RTG) task. \( ^{b} \) Joint, movement analyzed: metacarpi-phalangeal (MCP), wrist, elbow, or shoulder. \( ^{c} \) Dir, direction of joint rotation that was correlated with the neurons’ discharge, extension (E) or flexion (F). \( ^{d} \) \( n \), number of discharge/movement segments analyzed. \( ^{e} \) Failures, number of failures, i.e. movement occurred but was not accompanied by discharge. \( ^{f} r \), correlation coefficients. Parentheses indicate cases in which the correlation was not significant at the \( P < 0.05 \) level. \( ^{g} \) Mpdm, mean peak discharge modulation in imp/s.
The weak representation of relations of discharge of individual RNm neurons and movements of the wrist and more proximal joints during the reach-to-grasp and free-reach tasks observed in the present study is consistent with reports that relatively few RNm neurons are preferentially related to movements restricted to the wrist, elbow or shoulder joints (Gibson et al. 1985a; Miller and Houk 1995). The combined results suggest that RNm discharge does not contribute significantly to the control of parameters such as duration or velocity of movements of proximal joints. Instead, the results support the hypothesis that MCP extension is one aspect of hand use that is coded for by RNm discharge.

**Does RNm contribute to controlling movements or muscles?**

The strong parametric correlations between the modulations in discharge rate of individual RNm neurons and velocity of MCP extension during the reach-to-grasp and free-reach task of the present study are consistent with strong correlations between modulations in discharge rate of individual RNm neurons and velocity of device rotation during use of the metacarpal and twister devices (Gibson et al. 1985b). Although the proposition that the signals transmitted by RNm neurons may serve as velocity commands (Gibson et al. 1985b) may seem to contradict recent results that have emphasized that RNm generates motor commands in a muscle-based coordinate system (Miller and Houk 1995; Miller and Sinkjaer 1998), the strong correlations between RNm discharge and velocity of MCP extension observed in the present study do not exclude the possibility that RNm discharge may have commanded muscle synergies that prominently feature digit extensor muscles. During both the reach-to-grasp and free-reach tasks, the hand and fingers were unconstrained during the periods in which most neurons attained peak discharge, and under these conditions, activation of digit extensor muscles is most likely tightly coupled to MCP extension. The tight coupling precludes a distinction between a preferential role for RNm discharge in controlling movements or muscles, and therefore our results do not resolve the issue whether the observed correlations between discharge and the velocity of MCP extension are secondary to correlations between discharge and EMG activity of digit extensor muscles. It is important to note, however, that the conclusion that RNm discharge is preferentially related to muscle activation rather than kinematic variables (Miller and Houk 1995; Miller and Sinkjaer 1998) is based on correlating RNm discharge with velocity of device rotation rather than with velocity of the animal’s hand and finger movements. Muscle activation and RNm discharge were dissociated from velocity of device rotation in selected trials by accepting variable performance during use of the twister and supination-pronation devices (Miller and Houk 1995). The velocity of
device rotation in the selected trials, however, may not accurately reflect the velocity of hand and finger movements. Therefore in these trials, RNm discharge may have been related to both the velocity of hand and finger movements as well as muscle activation. Kinematic analyses of the animal’s hand and fingers during device operation is essential for resolving the issue. In conclusion, our results are consistent with the hypothesis that signals transmitted by RNm neurons activate muscle synergies that produce the appropriate MCP extension at the appropriate phase of limb transport to ensure that hand preshaping is complete prior to grasp. The results do not disagree with the view that RNm may command muscle activation; in fact they lend behavioral significance to a role for RNm in controlling specific muscle synergies.

Muscle synergies depend on the phase of limb transport. Similarly, our results show that the times at which most RNm neurons attained peak discharge depend on the phase of limb transport (Fig. 7), suggesting that individual neurons may contribute to specific muscle synergies. A given neuron may influence movements at distal and proximal forelimb joints in a weighted, neuron-specific fashion according to that neuron’s unique combination of spinal terminations. The population of forelimb RNm neurons may cover an entire spectrum that ranges from influences on distal joints in isolation to influences on combinations of distal and proximal joints. For example, kinematic data are consistent with the view that neurons that attained peak discharge during MCP extension in the early phase of limb transport during the device task in monkey W may have activated synergies of digit and wrist extensor and elbow flexor muscles (Figs. 8, A, C, and H, and 9, B and F). Neurons that attained peak discharge during MCP extension early during limb transport of the reach-to-grasp task in monkey B may have activated synergies of digit and wrist extensor, and elbow and shoulder flexor muscles (Figs. 8, A–C, H, and I, and 9, C and F). Furthermore neurons that attained peak discharge during MCP extension in the later phase of limb

**FIG. 13.** Parametric correlations for 3 RNm neurons (left, middle, and right columns) studied during the free-reach and/or reach-to-grasp tasks. Data points for the reach-to-grasp and free-reach tasks are indicated by □ and △, respectively. A–C: burst onset latency plotted as a function of onset latency of MCP extension. Most data points fall below the line of simultaneity (broken diagonal line), indicating that burst onset led movement onset. D–F: burst duration plotted as a function of duration of MCP extension. Note different scales for E, G–I: number of spikes in the burst plotted as a function of amplitude of MCP extension. J–L: average discharge modulation plotted as a function of velocity of MCP extension. In cases in which data for both the reach-to-grasp and free-form reach task is plotted in the same panel, the correlation coefficient for the reach-to-grasp task is listed above that for the free-reach task.
transport of the reach-to-grasp task may have activated synergies of digit and elbow extensor, and wrist and shoulder flexor muscles (Figs. 8, A–C, J, and K, and 9, A, D, and F). Digit extensor muscles may be common to the many different synergies controlled by individual RNm neurons and may represent the most frequent functional linkages between RNm neurons and forelimb muscles.

The view that RNm discharge may command muscle synergies that include digit extensor muscles in combination with other forelimb muscles is consistent with extensive divergence of individual RNm neurons as revealed by electrophysiological studies in awake intact monkeys and cats (Horn et al. 1993; Miller and Houk 1995; Miller and Sinkjaer 1998; Miller et al. 1993; Sinkjaer et al. 1995). Individual RNm neurons facilitate (Belhaj-Saif et al. 1998; Horn et al. 1993; Sinkjaer et al. 1995) or are strongly correlated with (Miller and Houk 1995; Miller and Sinkjaer 1998; Miller et al. 1993) EMG activity of both distal and proximal forelimb muscles, with a strong bias for digit and wrist extensor muscles. The extensor bias reported for the primate RNm is also evident from electrical stimulation in the cat RNm (Ghez 1975; Maffei and Pompeiano 1962; Rho et al. 1999), which produced flexion of the contralateral fore- or hind limb and activated physiological flexor muscles (e.g., extensor digitorum communis, acromion deltoid) more frequently than physiological extensor muscles (e.g., palmaris longis, latissimus dorsi). Further evidence for prominent divergence of individual RNm neurons derives from neuroanatomical studies. Intra-axonal labeling has shown that single rubrospinal axons in cats have collateral branches that terminate throughout the C₄–C₆ extent of the cervical spinal cord and that even individual branches traverse widely spaced spinal cord segments (Shinoda et al. 1982), confirming similar observations based on electrical stimulation (Shinoda et al. 1977). Thus both electrophysiological studies in awake intact animals and neuroanatomical investigations have shown prominent divergence of individual rubrospinal neurons.

Taken together, our data combined with the previously reviewed studies suggest that the ensemble of muscle synergies commanded by populations of RNm neurons may be the neural basis for producing MCP extension. The strong correlations between discharge of individual RNm neurons and parameters of MCP extension may be secondary to strong correlations between discharge and EMG activity of digit extensor muscles. The weak representation of relations between RNm discharge and movements of the wrist and more proximal joints suggest that RNm’s influences on proximal muscles are small relative to the influences of descending motor pathways other than rubrospinal fibers originating from RNm or that RNm’s influences on proximal muscles may control aspects of MCP extension related to limb stability or coordinating MCP extension with limb transport.

**Functional specialization of cerebellar output via rubrospinal pathways**

Motor commands that preshape the hand while moving the limb in the desired direction may be processed by functional modules that are coupled but are controlled in parallel: one is limb transport and another is grasp (for reviews: Jeannerod 1988; Paulignan and Jeannerod 1996). Although the overall organization of descending motor pathways appears compatible with such a scheme (Kuypers 1982), the relative contribution of a given pathway to control of movements about distal versus proximal joints, and the functional overlap between pathways, remains largely unknown. The rubrospinal tract, for example, originates from two distinct populations of red nucleus neurons that differ in their inputs from cerebellar neurons and in their spinal projections. One population of rubrospinal fibers originates from large size neurons in the RNm and receives input from anterior interpositus (NIA), from dorsomedial regions of posterior interpositus (NIP), and from dorsal regions of the dentate nucleus (NL) in both monkey and cat (Kennedy et al. 1986; Robinson et al. 1987). Ventrolateral NIP and ventral NL have little projection to the RNm (Kennedy et al. 1986; Stanton 1980). A separate population of rubrospinal neurons is located laterally in the parvicellular division of the red nucleus (RNp) in monkeys (Kuypers and Lawrence 1967; Pompeiano and Brodal 1957; Pong et al. 1999). These neurons receive input from a strip of neurons located at the border of NI and NL (Pong et al. 1999) and discharge strongly prior to and during limb reaching in cats with discharge patterns that are broader than those of RNm neurons (Horn et al. 1998). Currently available data on RNm neurons combined with the above data on lateral RNp neurons suggest that the two populations of rubrospinal neurons may preferentially contribute to the control of distal and proximal aspects of reaching, respectively. This view is consistent with results from inactivating cerebellar nuclear regions. Inactivation of NIA produced difficulties in hand preshaping, whereas following inactivation of NIP, monkeys had difficulties holding their arms in positions appropriate for retrieving food from a cylinder, suggesting that NIP contributes to elevating and
stabilizing the arm during grasping (Mason et al. 1998). Additional evidence for functional specialization of RNm and lateral RNp neurons is provided by differences in patterns of spinal terminations. RNm neurons project to interneurons at all spinal levels, including the entire caudal cervical spinal cord (C₅–T₃) (Kuypers et al. 1962) but terminate selectively among motoneuronal pools in C₅–T₃ that innervate digit muscles (Holstege 1987; Holstege et al. 1988; McCurdy et al. 1987; Ralston et al. 1988). In contrast, lateral RNp neurons project to the intermediate gray of predominantly rostral cervical spinal cord (C₅–C₃) (Holstege and Tan 1988), which contains circuitry that innervates proximal and axial muscles. In conclusion, cerebellar output signals via RNm and lateral RNp may contribute to controlling reaching to grasp with a distal and proximal bias, respectively.

Conclusion

We hypothesize that cerebellar output via RNm is specialized for the control of MCP extension. The currently available data suggest that the strong correlations we observed between parameters of discharge of individual RNm neurons and MCP extension movements during reaching tasks are most likely secondary to RNm’s function in commanding muscle synergies required for MCP extension. MCP extension is important for hand preshaping during reaching to grasp, and although MCP extension is considered a specific movement of the digits, it may influence functional linkages with musculature of the entire forelimb. Complex behaviors such as reaching to grasp require coordination of hand preshaping and grasping with limb transport, and signals commanding hand preshaping and/or grasping may well influence proximal muscles to achieve the coordination and stability required for precise digit manipulation to occur. Thus we conclude that RNm may contribute to the control of hand preshaping during reaching to grasp by commanding muscle synergies that produce the appropriate MCP extension at the appropriate phase of limb transport.

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