Effects of Red Nucleus Microstimulation on the Locomotor Pattern and Timing in the Intact Cat: A Comparison With the Motor Cortex

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Rho, Marie-Josée, Sylvain Lavoie, and Trevor Drew. Effects of red nucleus microstimulation on the locomotor pattern and timing in the intact cat: a comparison with the motor cortex. J. Neurophysiol. 81: 2297–2315, 1999. To determine the extent to which the rubrospinal tract is capable of modifying locomotion in the intact cat, we applied microstimulation (cathodal current, 330 Hz; pulse duration 0.2 ms; maximal current, 25 μA) to the red nucleus during locomotion. The stimuli were applied either as short trains (33 ms) of impulses to determine the capacity of the rubrospinal tract to modify the level of electromyographic (EMG) activity in different flexors and extensors at different phases of the step cycle or as long trains (200 ms) of pulses to determine the effect of the red nucleus on cycle timing. Stimuli were also applied with the cat at rest (33-ms train). This latter stimulation evoked short-latency (average = 11.8–19.0 ms) facilitatory responses in all of the physiological flexor muscles of the fore- and hindlimb that were recorded; facilitatory responses were also common in the elbow extensor, lateral head of triceps but were rare in the physiological wrist and digit extensor, palmaris longus. Responses were still evoked in most muscles when the current was decreased to near threshold (3–10 μA). Stimulation during locomotion with the short trains of stimuli evoked shorter-latency (average = 6.0–12.5 ms) facilitatory responses in flexor muscles during the swing phase of locomotion and, except in the case of the extensor digitorum communis, evoked substantially smaller responses in stance. The same stimuli also evoked facilitatory responses in the extensor muscles during swing and produced more complex effects involving both facilitation and suppression in stance. Increasing the duration of the train to 200 ms modified the amplitude and duration of the EMG activity of both flexors and extensors but had little significant effect on the cycle duration. In contrast, whereas stimulation of the motor cortex with short trains of stimuli during locomotion had very similar effects to that of the red nucleus, increasing the train duration to 200 ms frequently produced a marked reset of the step cycle by curtailing stance and initiating a new period of swing. The results suggest that whereas both the motor cortex and the red nucleus have access to the interneuronal circuits responsible for controlling the structure of the EMG activity in the step cycle, only the motor cortex has access to the circuits responsible for controlling cycle timing.

INTRODUCTION

In most mammals, including cats and primates, the red nucleus, via the rubrospinal tract, exerts a substantial influence over the physiological flexor muscles of the fore- and hindlimb (see Keifer and Houk 1994; Kuypers 1964, 1981). Lesion or inactivation of the red nucleus, or of the rubrospinal tract, in both cats (Alstermark et al. 1981, 1987; Ingram and Ranson 1932; Kuypers 1963; Martin et al. 1993; Schmied et al. 1990; Sybir ska and Gorska 1980) and primates (Lawrence and Kuypers 1968b; Ranish and Soechting 1976) leads to deficits in the use of the contralateral distal limb that closely resemble those observed after lesions of the motor cortex or of the corticospinal tract (Armstrong 1986; Drew et al. 1996; Kuypers 1963; Lawrence and Kuypers 1968a; Liddell and Phillips 1944). Further, the results of studies in which both systems have been damaged emphasize not only the importance of these two structures in the control of voluntary movements of the distal musculature but also the ability of one system to compensate for the other in a variety of behaviors (Alstermark et al. 1981; Evans and Ingram 1939; Jiang and Drew 1996; Kuypers 1963; Lawrence and Kuypers 1968b; Martin and Ghez 1988; Pettersson et al. 1997).

The similarities between the two systems are also reflected in the results from unit recording studies. As for neurons in the motor cortex, the discharge frequency of cells in the red nucleus has been found to increase during voluntary movements of the limb and to correlate with different parameters of voluntary movements in both cats (Amlaric et al. 1983; Batson and Amassian 1986; Burton and Onoda 1978; Dormont et al. 1989; Ghez and Kubota 1977; Martin and Ghez 1991; Padel and Steinberg 1978; Schmied et al. 1991) and monkeys (Gibson et al. 1985a,b; Mewes and Cheney 1994; Miller and Houk 1995; Miller et al. 1993).

The role of the red nucleus in the control of locomotion is unclear. Few of the studies involving lesion or inactivation of the red nucleus have specifically studied locomotion, and the lack of any specific comment in the studies listed in the preceding paragraphs suggests that such lesions have only relatively minor outward effects on walking. Nevertheless, the report by Ingram and Ranson (1932) does indicate that deficits in locomotion were observed at least up to 2 wk after a bilateral lesion of the red nucleus and that these problems included “incoordination and stiffness” as well as a lack of “any desire to indulge in the gymnastics that are the habit of normal cats.” That the red nucleus has a role to play in locomotion is also supported by the fact that studies in decerebrate cats have shown that rubrospinal neurons are modulated phasically during locomotion with the majority discharging in a single burst at the end of stance and during the swing phase (Arshavsky et al. 1988; Orlovsky 1972a). Microstimulation of the red nucleus during the swing phase of locomotion in the same preparation (Orlovsky 1972b) enhanced the flexor activity while having no effect on the extensors; stimulation during stance evoked no response. Furthermore the timing of the step cycle was not affected by the stimulation of the red nucleus. These experiments led Orlovsky to suggest that the main function of the red...
nucleus in the control of locomotion is to regulate the level of electromyographic (EMG) activity of flexor muscles during the swing phase.

More recently, however, experiments in our own laboratory in intact cats (Lavoie and Drew 1997) have shown that neurons in the red nucleus increase their discharge frequency during voluntary gait modifications in a similar manner to cells in the motor cortex (Drew 1993). This suggests that, as for discrete voluntary movements of a single limb, the motor cortex and the red nucleus may play a complementary role in controlling voluntary gait modifications, as also suggested on the basis of lesions of the dorsolateral funiculi (Jiang and Drew 1996).

Given the similarity in the discharge characteristics of neurons in the red nucleus and the motor cortex, we wished to determine if microstimulation of the red nucleus in the intact animal would affect the timing of the step cycle in a similar fashion to that observed after motor cortex stimulation (Armstrong and Drew 1985; Drew 1991b; Kalaska and Drew 1993). Further, because in these previous publications we have demonstrated only isolated examples of the effects of motor cortex stimulation on cycle timing, we present a brief quantitative analysis of the effects of motor cortex stimulation to better allow a comparison of the relative effect of those two systems on the step cycle duration. To allow comparison with previous studies of the effects of both red nucleus and motor cortex stimulation in different species, preparations, and behaviors (see DISCUSSION), we also present data on the effects of red nucleus stimulation on the level of EMG activity both at rest and during locomotion.

The results emphasize that although the motor cortex and the red nucleus both affect considerably the level of EMG activity of the flexor and the extensor muscles, only the motor cortex has the ability to produce a reset of the step cycle.

A preliminary report of this study has been published (Rho et al. 1997).

**Methods**

**Red nucleus**

Experiments were carried out on three male cats (weight 4.2–4.5 kg) trained to walk steadily on a treadmill at a speed of 0.40 m/s. After training, the animals were prepared for surgery in aseptic conditions.

Cats were initially pretreated with a mixture of acepromazine maleate (Atravet, 0.05 mg/kg), glycopyrrolate (Rubinol, 0.01 mg/kg im), and ketamine (11 mg/kg im) and were then anesthetized with isoflurane (1–2% mixed with oxygen). An intravenous line was inserted in a cephalic vein to permit the administration of fluids and of antibiotics (Penicillin G, 40,000 IU/kg) at the beginning and end of the surgery. The head was fixed in a stereotaxic apparatus using atraumatic earbars coated with xylocaine, and petroleum jelly (Vaseline) was put onto the eyes to prevent desiccation. All surgical and experimental procedures followed the recommendations of the Canadian Council for the Protection of Animals and were approved by the local animal ethics committee.

Initially three, 50-μm diam, Tri-ML insulated stainless steel microwires (Cooner Fine Wire, CA) were implanted in the dorsolateral funiculus of the spinal cord at L2 (see Drew et al. 1986) and 21 pairs of Teflon-insulated, braided stainless steel wires were implanted into selected muscles in the forelimbs and hindlimbs to record EMG activity. In the forelimb, electrodes were implanted bilaterally into the brachialis (Br), flexor of the elbow; cleidobrachialis (CIB), protractor of the shoulder and flexor of the elbow; and the triceps brachii, lateral head (TriL), extensor of the elbow. In the contralateral (co) forelimb only, wires were also implanted into the brachioradialis (BrR), flexor of the elbow and supinator of the paw; extensor carpi radialis (ECR), dorsiflexor of the wrist; extensor digitorum communis (EDC), dorsiflexor of the wrist and digits; palmaris longus (PaL), ventroflexor of the wrist and digits; pronator teres (PrT), pronator of the paw; and the teres major (TrM), retractor of the shoulder. During locomotion, all of these muscles, with the exception of TriL and PaL, are physiological flexors and act as a synergistic unit to lift the limb and move it forward during the swing phase of locomotion. The PaL, which is an anatomic flexor, serves primarily as a physiological extensor during locomotion and is active during stance (see Fig. 4) (see also Miller and Van der Meché 1975). In the contralateral hindlimb, electrodes were inserted into the extensor digitorum brevis (EDB), dorsiflexor of the hindpaw digits, semitendinosus (St), flexor of the knee; the tibialis anterior (TA), flexor of the ankle; and the vastus lateralis (VL), extensor of the knee. The anterior head of sartorius (Srt), a flexor of the hip, was implanted bilaterally. All of these hindlimb muscles, except the VL, are active just before or during the swing phase of locomotion (see e.g., Fig. 1 in Widażewicz et al. 1994) and are considered as physiological flexors.

For other studies on unit activity that were carried out in the same animals (Lavoie and Drew 1997), a bundle of three microwires (Drew 1993; Kably and Drew 1998; Palmer 1978) was inserted into the contralateral brachium conjunctivum. A craniotomy was then made in the parietal bone to give access to the red nucleus and a rectangular, stainless steel base plate (10 × 6 mm ID), oriented at 3–5° in the mediolateral plane, was fixed over the craniotomy. The implant was streamlined using dental acrylic, and the animal was placed in an incubator to recover. Analgesics (Buprenorphine; Temgesic Reckitt and Colman Pharmaceuticals, Hull, England, 5–10 μg/kg) were administered for 48 h after the surgery. Antibiotics [Penicillin: amoxicil (50 mg/kg) or apo-cephalex (50 mg/kg)] were administered daily for the duration of the experiment.

**Protocol**

The electrode was advanced through the superior colliculus to the red nucleus, and in most penetrations, unit activity was recorded during locomotion (Lavoie and Drew, unpublished data). In selected penetrations, microstimulation (cathodal current, 11 pulses at 330 Hz; pulse duration, 0.2 ms; maximal current of 25 μA) was applied either at loci at which unit activity that was modulated strongly during locomotion was recorded or throughout the dorsoventral extent of the red nucleus. During the stimulation, the cat was held gently in a prone position on one experimenter’s lap and the nature of the evoked responses was noted. During these exploratory procedures, data were always recorded from seven physiological flexor muscles and two physiological extensor muscles of the contralateral forelimb, from a flexor and extensor of the contralateral hindlimb, and from a flexor and extensor of the ipsilateral forelimb.

After the initial exploratory procedures, evoked EMG responses were digitized on-line on a microcomputer at a frequency of 2 kHz for 25 ms before and 75 ms after the onset of the stimulus train. EMGs were band-pass filtered between 100 Hz and 1 kHz. Stimuli were applied initially at 25 μA and then in 5-μA steps of decreasing current until no further responses were evoked. In some penetrations, the evoked responses were recorded systematically as the electrode was displaced throughout the dorsoventral extent of the red nucleus (see e.g., Fig. 2B), in others, data were quantitatively examined only at a single locus in a penetration. In 21/24 penetrations, this locus corresponded to the site at which the largest responses were evoked in the contralateral forelimb, whereas in 3/24 penetrations, it corresponded to loci at which large responses were evoked in the contralateral hindlimb. In the latter case, three of the forelimb flexor muscles were replaced with additional muscles from the contralateral hindlimb before data collection.
After the microstimulation at rest, the animal was put onto the treadmill to assess the effects of the stimulation during locomotion. Trains of stimuli at 20 or 25 μA (other parameters as at rest) were delivered during every third cycle at different delays with respect to the onset of the activity of the coBr (see Drew 1991a; Drew and Rossignol 1984 for details). Ten repetitions at each delay were made, and each delay was presented in the following pseudorandom order: 100–200–0–400–600–800–1,000–150–300–500–700, and 900 ms after the onset of the activity in the coBr. The responses were recorded on-line as before, and in addition, a continuous record of the EMG activity during locomotion was digitized at either 200 Hz, 500 Hz or 1 kHz. Stimulation during locomotion, with one exception, were applied at a single locus in each penetration, corresponding to that at which the largest responses were obtained.

The duration of the stimulus train was then increased to 200 ms, and trains of stimuli were applied during every fifth step cycle. Three to five trains of stimuli were applied at each delay using the same pseudorandom order as detailed in the previous paragraph. These data were recorded on a Honeywell instrumental tape recorder.

Penetrations were normally made in a grid pattern separated by a minimum of 0.5 mm in both the anteroposterior and mediolateral planes. To aid in histological reconstruction, small lesions (15–35 μA, DC cathodal current) were generally made in one or two penetrations in each row (anteroposterior plane) of penetrations; these lesions were made either just below or just above the limits of the red nucleus as defined by the recordings of unit activity and the microstimulation.

**Data analysis**

The data obtained with the cat at rest were computer rectified and averaged. A custom program allowed us to mark manually the onset and offset of the evoked EMG activity in each muscle using the standard error of the mean of the prestimulus period as a guideline for determining the presence and sign of stimulus-evoked responses. The latency and duration of each response were recorded, and the area under the curve was integrated (sum of each 0.5-ms bin). If more than one response was evoked by the stimulation, only the initial response was quantified. The integrated amplitude of a similar period, before the onset of the stimulus, was subtracted from this value to give the net integrated response.

For the data in which short trains of stimuli were applied during locomotion, an interactive program was used to determine accurately the delay of each stimulus with respect to the onset of the preceding period of activity of the coBr. This delay was then calculated as a phase by dividing it by the average duration of a minimum of 100 interspersed, unstimulated step cycles. Each phase was allotted to 1 of 10 equal periods (groups). The responses evoked by stimuli in each phase were averaged and plotted on a display monitor. The average activity from a similar time period taken from the interspersed, unstimulated cycles then was superimposed on this display (Drew 1991a; Drew and Rossignol 1984). The onset and offset of the response were determined manually using the interval of confidence (P < 0.01) of the standard error of the mean of the control activity as a guideline. The area under the evoked response was integrated and the integrated value of the identical period of the control activity was subtracted from it to give the net response.

For the data collected when long trains of stimuli were applied, the onset and offset of a selected flexor (coBr) and extensor (coTriL) muscle were measured during the stimulated step cycle as well as during the two steps before and after that cycle. The phase at which the stimulation was applied was calculated as described earlier for the short trains, and the stimuli were grouped into 1 of 10 equal phases as also described in the preceding text. The averaged duration of the stimulated step cycle, as well as the duration of the coBr and coTriL within each group, were calculated for the stimulated cycle as well as for the step cycle before the stimulus was applied (the control cycle). The stimulated cycle was defined as that cycle in which the stimulus fell; the EMGs affected by the stimulation were defined either as those that were active during the stimulus or those bursts after the stimulus if it occurred during the period of inactivity of a given muscle.

For the averaged data in Tables 1 and 2, the swing phase of locomotion was considered to include groups 1–3, and the stance phase, groups 5–9. Groups 4 and 10 were considered to occur during the transition periods and were not included in these averages.

**Histology**

After all experiments were finished, the animal was anesthetized deeply with pentobarbital sodium (Somnotol, 40 mg/kg ip) and perfused transcardially with a solution of phosphate-buffered saline (0.9%) followed by a fixative solution of 4% paraformaldehyde and phosphate-buffered sucrose (4%). The brain stem, cerebellum, and spinal cord were removed and kept in buffered sucrose (20%) overnight. They were then sectioned (30 μm) in the sagittal (brain stem and cerebellum) or transverse (spinal cord) plane and stained with cresyl violet. The locations of the penetrations in each track were localized on tracings of the histological sections using the lesions made during the experiments for orientation.

**Motor cortex**

The data for the motor cortical stimulation were taken from cats previously used for studies on the discharge activity of pyramidal tract neurons during locomotion (Drew 1988, 1991b, 1993). Data were used from three cats (MC7, MC8, and MC11) in which at least eight loci were stimulated in the forelimb representation, around the rostralateral pericruciate cortex, of each cat. (See Fig. 1). Only isolated examples of the results from these microstimulation experiments have been published previously (Fig. 6 in Drew 1991b, taken from cat MC7 and Fig. 11 in Kalaska and Drew 1993, taken from cat MC11). The surgical procedures and other details can be found in Drew (1993).

The protocol and data analysis for these microstimulation experiments were identical to those described above for the red nucleus.

**RESULTS**

The effects of microstimulation were quantified in a total of 24 loci in 23 penetrations in three cats. Most of these loci were located within the caudal two-thirds of the red nucleus (see Fig. 1), corresponding to the magnocellular region of the nucleus, at lateralities varying between 1.2 and 2.4 mm.

**Microstimulation at rest**

The effects of microstimulation of the red nucleus with the cat in a prone position were quantitatively analyzed in 19 penetrations in two cats (RN4 and RN5); for the third cat, the data at rest were only qualitatively examined. In 16/19 of these penetrations, the largest, low-threshold responses were evoked primarily in contralateral forelimb muscles and in the other 3, primarily in hindlimb muscles. The sites at which the largest responses were obtained are referred to as forelimb and hindlimb sites (or loci), respectively. All evoked responses after stimulation at rest were facilitatory. Figure 2A illustrates a representative example of the responses evoked by microstimulation at a forelimb site in a penetration in cat RN4. The stimulation evoked short-latency (range 7–14 ms), facilitatory responses in all contralateral forelimb muscles recorded except in the coPaL. Except for a small facilitatory response in the coSt, there were no responses evoked in either the contralateral hindlimb muscles (coEDB, coSrt, or coVL) or in the ipsilateral forelimb muscles (iBr and iTriL). Displacement of the ele-
trode by 0.5 mm in the dorsoventral plane of the red nucleus with respect to the most effective site (Fig. 2B) was enough to considerably diminish the effectiveness of the responses in the different forelimb muscles recorded, although a larger response was recorded in St when the electrode tip was lowered by 0.5 mm.

Overall, stimulation of all seven forelimb loci examined in cat RN4 evoked facilitatory responses in all of the physiolog-

FIG. 1. A and B: location of the stimulated sites within the red nucleus of cats RN4 and RN5. Loci are shown on tracings of the parasagittal histological sections that best represent the location of each group. ●, forelimb sites; ○, hindlimb sites (see text). Scales beneath each figure indicate the approximate stereotaxic antero-posterior (AP) coordinates for each section.

C–E: location of the sites (●) in the pericruciate motor cortex at which microstimulation was applied in cats MC7, MC8, and MC11. All sites elicited flexion of the contralateral forelimb with the cat at rest. Larger filled circles, those sites at which 200-ms trains of stimuli during locomotion produced decreases in step cycle duration of >25% (see RESULTS). Dotted lines on the surface are placed 1 mm apart. 3N, oculomotor nerve; L, laterality of the section; PG, pontine gray; PT, pyramidal tract; RN, red nucleus; T, track (or penetration); TRN, tegmental reticular nucleus; Ans, Ansate sulcus; Cor, coronal sulcus; Cru, cruciate sulcus; PCD, procruciate dimple; Presylv, presylvian sulcus. D and E modified from Drew (1993).
ical flexors of the contralateral forelimb that we recorded, as well as in the coTrIL (Fig. 2C). Responses were evoked in coPaL at only one locus and were also relatively rare in the hindlimb muscles. Similar results were obtained in the other cat, RN5 (not illustrated). Responses were not observed in the ipsilateral forelimb muscles in either cat. Biomechanically the stimuli in the forelimb sites always evoked flexion of the forelimb, including retraction of the shoulder (10/20 sites), flexion of the elbow (17/20), and either wrist dorsiflexion (10/20) or wrist ventroflexion (3/20) (for 1 site, the biomechanical effects were not noted).

In the three hindlimb loci (not illustrated), large short-latency responses were evoked in coSt and coSrt together with a small response in coTA from one site; none of the sites elicited responses in coVL. In addition, no responses were evoked in the contralateral forelimb muscles in these three loci, except for a small response in coEDC for one site and in coCIB for another.

The averaged latency of the responses evoked in the contralateral forelimb muscles with the cat at rest ranged from 11.8 ms in coBr to 19.0 ms in coPaL (Table 1). When responses were present in the hindlimb muscles, the latencies ranged...
Contralateral triceps brachii, lateral head (−) we recorded.

Muscles from these same forelimb loci was between 3 and 10 (3/21 sites, the threshold for evoking responses in the forelimb of the tested penetrations, except one. In contrast, in all except 3/21 sites, the threshold for evoking responses in the forelimb muscles from these same forelimb loci was between 3 and 10 μA. At >50% of the forelimb sites, in both RN4 and RN5, stimulation at 10 μA elicited responses in all seven of the physiological flexor muscles of the contralateral forelimb that we recorded.

Reducing the intensity of the current decreased the amplitude of the evoked responses in all muscles (Fig. 3A). However, even at current intensities just above threshold, evoked responses were observed in almost the same number of muscles as at 25 μA. This can be better appreciated from Fig. 3B where the relative integrated amplitude of the responses is plotted as a function of the current intensity. In this penetration, where the relative integrated amplitude of the responses is approximately linear relationship between the amplitude of the responses in all of the illustrated forelimb groups as at 25 0.45, 0.85)

The phase-dependent nature of the responses in these four muscles, as well as in five other flexor muscles of the contralateral forelimb is shown in Fig. 5 for the example illustrated in Fig. 4, A and B. The data for each muscle are plotted as a percentage of the maximal response evoked in a given muscle at that site. The responses evoked in all of the flexor muscles were largest in swing, although they were not all maximal at the same time. For example, the responses in the coTrM were maximal at the beginning of swing, whereas those in the

### Table 1. Averaged latencies of EMG responses evoked at rest and during locomotion by stimulation of forelimb loci

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Rest n (%)</th>
<th>Onset (ms)</th>
<th>Swing n (%)</th>
<th>Onset (ms)</th>
<th>Stance n (%)</th>
<th>Onset (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contralateral brachialis</td>
<td>16/16</td>
<td>11.8 ± 2.9</td>
<td>70.8</td>
<td>7.8 ± 1.7</td>
<td>11.7</td>
<td>12.8 ± 6.0</td>
</tr>
<tr>
<td>Contralateral triceps brachii, lateral head (−)</td>
<td>15/16</td>
<td>14.9 ± 4.7</td>
<td>55.6</td>
<td>9.6 ± 4.2</td>
<td>16.7</td>
<td>16.8 ± 5.0</td>
</tr>
<tr>
<td>Contralateral triceps brachii, lateral head (−)</td>
<td>0</td>
<td>—</td>
<td>0.0</td>
<td>—</td>
<td>34.2</td>
<td>18.8 ± 8.4</td>
</tr>
<tr>
<td>Contralateral brachioradialis</td>
<td>16/16</td>
<td>15.7 ± 3.7</td>
<td>77.8</td>
<td>10.9 ± 2.7</td>
<td>35.0</td>
<td>18.5 ± 5.6</td>
</tr>
<tr>
<td>Contralateral cleidobrachialis (+)</td>
<td>16/16</td>
<td>14.5 ± 3.4</td>
<td>80.1</td>
<td>6.0 ± 4.0</td>
<td>22.5</td>
<td>12.9 ± 5.8</td>
</tr>
<tr>
<td>Contralateral palmaris longus (+)</td>
<td>1/16</td>
<td>19.0</td>
<td>44.4</td>
<td>12.5 ± 4.2</td>
<td>24.2</td>
<td>11.0 ± 4.2</td>
</tr>
<tr>
<td>Contralateral palmaris longus (−)</td>
<td>0</td>
<td>—</td>
<td>0.0</td>
<td>—</td>
<td>35.0</td>
<td>17.0 ± 7.2</td>
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<tr>
<td>Contralateral pronator teres</td>
<td>12/16</td>
<td>18.1 ± 5.3</td>
<td>75.0</td>
<td>11.0 ± 4.5</td>
<td>49.2</td>
<td>17.7 ± 6.9</td>
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<tr>
<td>Contralateral extensor digitorum communis</td>
<td>14/14</td>
<td>14.4 ± 6.5</td>
<td>75.0</td>
<td>10.4 ± 4.5</td>
<td>60.0</td>
<td>16.3 ± 6.6</td>
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<td>Contralateral extensor carpi radialis</td>
<td>16/16</td>
<td>16.1 ± 6.0</td>
<td>80.6</td>
<td>9.2 ± 2.6</td>
<td>47.5</td>
<td>16.9 ± 7.4</td>
</tr>
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<td>Contralateral teres major</td>
<td>15/16</td>
<td>14.3 ± 4.2</td>
<td>83.3</td>
<td>9.7 ± 3.1</td>
<td>33.3</td>
<td>18.0 ± 6.9</td>
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<td>—</td>
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<td>19.0 ± 5.5</td>
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<td>21.4 ± 7.5</td>
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<td>Contralateral semitendinosus</td>
<td>8/16</td>
<td>21.1 ± 7.2</td>
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<td>18.1 ± 8.6</td>
<td>16.8</td>
<td>18.4 ± 8.3</td>
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<tr>
<td>Contralateral anterior head of the sartorius</td>
<td>3/16</td>
<td>33.0 ± 0.0</td>
<td>22.1</td>
<td>18.2 ± 6.1</td>
<td>9.4</td>
<td>17.0 ± 5.8</td>
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<tr>
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<td>26.2 ± 3.9</td>
<td>16.2</td>
<td>17.4 ± 7.7</td>
<td>14.7</td>
<td>26.0 ± 2.9</td>
</tr>
<tr>
<td>Contralateral vastus lateralis (+)</td>
<td>1/16</td>
<td>33.0</td>
<td>16.2</td>
<td>16.5 ± 4.0</td>
<td>28.2</td>
<td>23.6 ± 6.2</td>
</tr>
<tr>
<td>Contralateral vastus lateralis (−)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>9.4</td>
<td>15.9 ± 8.2</td>
</tr>
<tr>
<td>Ipsilateral brachialis</td>
<td>0/16</td>
<td>—</td>
<td>2.8</td>
<td>27.5 ± 6.4</td>
<td>5.8</td>
<td>27.1 ± 9.1</td>
</tr>
<tr>
<td>Ipsilateral cleidobrachialis</td>
<td>0/16</td>
<td>—</td>
<td>16.7</td>
<td>25.5 ± 11.0</td>
<td>24.2</td>
<td>21.4 ± 7.0</td>
</tr>
<tr>
<td>Ipsilateral triceps brachii, lateral head</td>
<td>0/16</td>
<td>—</td>
<td>12.5</td>
<td>14.3 ± 9.3</td>
<td>25.8</td>
<td>16.6 ± 8.0</td>
</tr>
<tr>
<td>Ipsilateral anterior head of the sartorius</td>
<td>0/16</td>
<td>—</td>
<td>0.0</td>
<td>—</td>
<td>3.3</td>
<td>14.2 ± 6.9</td>
</tr>
</tbody>
</table>

Table gives the mean onset latency (± SD) of the integrated (EMG) responses evoked by stimulation of the forelimb loci with the cat at rest as well as during the swing and stance phases of locomotion. All values are for facilitatory responses unless otherwise specified; when stimulation caused a facilitation in some loci and a suppression in others (e.g., palmaris longus), values are given for both (+ and −, respectively). For the stimulation at rest, n indicates the number of loci in which a response was evoked in cats RN4 and RN5 with respect to the number of loci in which the muscle was recorded. For the stimuli during locomotion, n (%) gives the percentage of groups in which a response was activated for all 3 cats. For example, in swing (groups 1–3), the contralateral brachialis was recorded in 24 loci (=72 groups) and facilitatory responses were evoked in 51/72 of these groups (i.e., 70.8%). Similarly, in stance (groups 5–9), responses in brachialis were evoked in 14/120 groups (i.e., 11.7%). Note that swing and stance always refer to the respective leg.

from 21.1 to 33.0 ms (Table 1). In the three sites that were classified as hindlimb sites, responses were evoked in the hindlimb muscles at latencies ranging from 17.5 ms (coSt) to 29.0 ms (coTA).

Short trains of stimuli during locomotion

Short trains of stimuli at 25 μA (n = 16) or 20 μA (n = 8) were applied during locomotion to 24 loci in 23 penetrations within the red nucleus, including 21 forelimb sites and 3 hindlimb sites. Figure 4 illustrates the effects of stimulating during locomotion for a representative case from cat RN4 (Fig. 4, A and B) and from RN5 (Fig. 4C). Stimulation in the swing phase of the step cycle (Fig. 4, top) evoked large, brief, short-latency responses in the physiological flexor muscles (coBr and coEDC) as well as smaller, short-latency responses in the physiological extensor muscles, coTrIL and coPaL. Stimulation during the stance phase (phase = 0.45, 0.85) evoked small facilitatory responses in coEDC but was, generally, without effect on the coBr. In the extensors, stimulation during stance evoked suppression of both coTrIL and coPaL in the example from cat RN4 (Fig. 4, A and B) and mixed facilitation and suppression in the example from cat RN5 (Fig. 4C, see also Fig. 6).

The phase-dependent nature of the responses in these four muscles, as well as in five other flexor muscles of the contralateral forelimb is shown in Fig. 5 for the example illustrated in Fig. 4, A and B. The data for each muscle are plotted as a percentage of the maximal response evoked in a given muscle at that site. The responses evoked in all of the flexor muscles were largest in swing, although they were not all maximal at the same time. For example, the responses in the coTrM were maximal at the beginning of swing, whereas those in the
coEDC and coClB were largest at the end of swing. The two extensors, coTriL and coPaL, showed a facilitation during swing but a suppression throughout the stance phase.

As in the examples illustrated in Fig. 5, the amplitude of the maximal response evoked during locomotion was normally larger than that evoked when the cat was at rest. In most cases, this difference was large, as in coTrM and coEDC, whereas in other muscles, such as coBr, the amplitude was almost equal in the two states. However, it should be noted that there was a lot of variability in the relationship between these two values, probably reflecting differences in muscle tonus of the limb when the cat was at rest. For example, in different penetrations, the maximal value of the coBr at rest ranged from 18 to 148% of the maximal value observed during locomotion, and in 7/14 sites the maximum value evoked at rest was 50% of the maximal value evoked during locomotion in 9/14 sites.

In general, the responses evoked by red nucleus stimulation were very reproducible, especially in the flexor muscles, both within and between cats (Fig. 6, A and B). For example, coBr was always activated maximally during the swing phase and showed no or only small evoked responses to stimulation during stance. Similar phase response relationships were observed in coTrM, coClB, coECR, and coPrT (not illustrated). Responses during stance in these muscles were either absent (see e.g., coBr in Fig. 4B) or were substantially smaller than those evoked during swing (see e.g., coBr in Fig. 4C). Large facilitatory responses were also evoked in the coEDC during swing (Fig. 6, A and B) although, in this muscle, substantial responses were also evoked in the stance phase, albeit at a longer latency (see Fig. 4 and Table 1). Responses in the extensor muscles were more variable (also discussed with respect to Fig. 4), although in both coTriL and coPaL, facilitatory responses were evoked during swing in both illustrated cats. In the coTrL, suppression of activity was always evoked in stance in cat RN4, but in only 60% of the penetrations in RN5; in the other 40%, there was either a facilitatory response or no response at all. Although the initial evoked response in coPaL in RN5 was a facilitation, this response was always followed by a suppression during stance. In fact, comparison of the coPaL responses in Fig. 4, B (cat RN4) and C (cat RN5), suggests a difference only with respect to the amplitude of the initial poststimulus response.

The integrated responses evoked in coBr in cats RN4 and RN5 ranged from 337 to 1,931% (689 ± 413%, mean ± SD, n = 15).
of the background locomotor activity in the unstimulated cycles, while the largest responses in the coEDC, irrespective of phase, ranged from 175 to 1951% (613 ± 6472%, n = 17). The third cat examined (RN3) is not illustrated in Fig. 6 but showed the same pattern of responses as for cat RN5.

The averaged latency of the responses evoked by red nucleus stimulation in the contralateral forelimb muscles during swing ranged from 6.0 ms in coClB to 12.5 ms in coPaL (Table 1). During stance, the averaged latency of the responses was slightly longer than in swing, ranging from 11.0 ms in coPaL to 18.8 ms in coTriL, independent of the nature of the primary response (facilitatory or suppression).

For comparison, Fig. 6C summarizes the responses evoked by stimulation of the motor cortex by short trains of stimuli of 25 μA applied within the forelimb representation of the motor cortex of cat MC8. Comparison with Fig. 6, A and B, shows that the pattern of responses evoked in the contralateral forelimb muscles by motor cortical stimulation was very similar to that observed after red nucleus stimulation. As for the red nucleus, the evoked responses were also phase-dependent, with the flexor, coBr, being maximally activated just before and during the swing phase and the coEDC showing responses in both swing and stance. With respect to the extensor muscles, mixed effects were also observed in the TriL during stance although, in this cat, suppression of the locomotor activity was always evoked in the PaL. The amplitude of the integrated responses in the coBr in cat MC8, as a percentage of the amplitude in the unstimulated cycles was similar to that obtained for the red nucleus and ranged from 165 to 977% (486 ± 288%, n = 8) in Br and from 156 to 1,084% (476 ± 275%, n = 11) in coEDC. The latencies of the responses in the motor cortex were comparable with those previously detailed under similar circumstances (Armstrong and Drew 1985).
Stimulation in some of these red nucleus forelimb loci also evoked responses in hindlimb muscles (see Table 1 and Figs. 2 and 3), especially in the coSt, which was activated by stimulation in 18/21 of the forelimb loci. At most of these sites, the integrated amplitude of the responses in the hindlimb muscles was relatively small compared with the size of the responses that were evoked from the three hindlimb loci. Nevertheless, the largest responses evoked in coSt from forelimb loci were sometimes as large as those evoked from hindlimb sites. The averaged latency of the responses evoked in the hindlimb muscles during hindlimb swing by stimulation in these forelimb loci ranged from 16.5 ms in coVL to 19.0 ms in coEDB (Table 1).

Although no responses were ever observed in ipsilateral forelimb muscles when stimulation was applied with the cat at rest, stimulation during locomotion evoked responses in the iTriL in 14/21 loci and in the iClB or iBr in 18/21 sites. However, these responses were small and did not produce any visible mechanical effect. Although we have no means of accurately comparing the amplitude of the responses in the contralateral and ipsilateral forelimbs, the fact that the gains of the amplifiers were adjusted to provide a similar level of EMG activity on the two sides during locomotion makes it possible to provide some comparison. On this basis, the responses in the ipsilateral flexor muscles, during the swing phase of the ipsilateral limb, were generally smaller than those in the contralateral flexor muscles during the swing phase of the contralateral limb and, often, considerably less so. For example, 11/21 sites evoked ipsilateral responses that were <10% of the contralateral responses. Nevertheless, in some other sites larger responses were evoked in the ipsilateral flexors than in those on the contralateral side. In 7/21 of the sites the response in the iTriL was <10% of that in the coTriL, but in 5/21 sites, the responses in the iTriL exceeded those in the coTriL. In general, the latency of the responses evoked in the ipsilateral forelimb muscles was longer that of those evoked in the contralateral forelimb (see Table 1).

As only three hindlimb loci were stimulated, the results for these sites will not be detailed. However, in brief, the responses in the hindlimb muscles were organized in a similar phase-dependent manner to those for the forelimb muscles that have been detailed in the preceding text. Responses in the St were largest late in the hindlimb swing phase and in early stance while VL was generally suppressed during the stance phase and facilitated during swing. Responses evoked in the forelimb muscles from these three loci were all very small compared with those evoked in the same muscles from the forelimb loci. This can be appreciated in Fig. 6, A and B, in which the traces identified by ○ illustrate the relative amplitude of the forelimb responses evoked from hindlimb loci, compared with those evoked from forelimb loci (●).

**Long trains of stimuli**

Long trains of stimuli of 20 μA were applied to 18/21 forelimb loci within the red nucleus during locomotion. As illustrated by the example in Fig. 7A, stimulation during early swing (phase = 0.05) evoked large facilitatory responses in the coBr with little effect on the coTriL. Behaviorally the stimulation produced an increased flexion of the limb. Although not illustrated, this same stimulation during swing also produced an increased level of activity in all of the other flexor muscles that we recorded. Microstimulation during stance produced no or little response in the Br while producing suppression of the activity in the coTriL. Behaviorally stimulation during stance...
FIG. 6. Summary of the responses evoked in representative muscles of the contralateral forelimb after red nucleus (A and B) and motor cortex (C) stimulation. Amplitude is represented as a percentage of the maximal response of the muscle concerned in all tracks in that cat. Only the initial response evoked by the stimulation at any 1 phase is shown. Shaded rectangles above A and B taken from Figs. 4 and 5, respectively. Shaded rectangles above C calculated from 42 unstimulated cycles in 1 experiment in cat MC8. ●, experiments in which stimuli were applied to forelimb sites; ○, sites in which stimuli were applied to hindlimb sites.
in this locus, as well as in four others, caused the limb to buckle.

The major effects of this microstimulation of the red nucleus was a modification of the amplitude of the muscular activity during the swing phase of locomotion. For example, as illustrated in Fig. 7C, long trains of stimuli applied during the swing period produced a substantial increase in the amplitude of the flexor burst (≥302%) with a concomitant increase in the burst duration (≥163%, not shown). There was also a small augmentation of the amplitude of the coTriL when stimuli were applied during swing (Fig. 7, A and D), although the relative magnitude of this increase was less than for the coBr (≥138%). Although the stimulation during stance in this example caused a suppression of activity in the coTriL, and caused the leg, to buckle, there was a compensatory increase in the level of activity in the coTriL after this suppression so that there was no change in the overall amplitude of the burst during stance (Fig. 7, B and D). Equally, there was no significant change in the duration of the burst.

As indicated by the graph in Fig. 7B, the duration of the step cycle was very little changed, although there was a small but significant decrease (to 92% of control value) of the step duration when the stimulation occurred in midswing and a small, but significant, increase (to 116% of control value) when it occurred at the transition from stance to swing.

Figure 8, A and B, and Table 2 summarize the effects of the long trains of stimuli applied to the red nucleus. As was described for the representative case in Fig. 7, stimulation just before and during the swing phase considerably affected the level of activity of the flexor muscle coBr in most sites stimulated within the red nucleus of all cats. In all sites but one, the stimulation evoked a statistically significant increase in amplitude ranging from 134 to 682% of the control value (Table 2). This increase in the magnitude of the response was accompanied by an increase in the duration of the burst that ranged from 111 to 248%. The amplitude of the response in the coTriL during stance was increased in 15/18 loci, although the relative increase was generally less than in the flexor muscles, ranging from 111 to 164%. There was also a concomitant increase in the duration of the extensor burst in 15/18 sites, ranging from 111 to 137%.

Red nucleus stimulation rarely affected the duration of the
step cycle, as shown in Fig. 8A, and when it did, the changes were always small (see Table 2). There was a small decrease in the cycle duration in 5/18 sites stimulated during the swing phase with the largest reduction of the duration being to 83% of the control value and a small significant increase in cycle duration, ranging from 114–123% in another 5/18 sites (1 locus caused both an increase and a decrease during swing). Stimulation during stance produced a small significant increase in the duration of the step cycle in six loci (Table 2).

As for the stimulation of the red nucleus, long trains of stimuli applied to the motor cortex also produced large increases in the duration and amplitude of the flexor burst during swing. In the

**TABLE 2.** Amplitude and frequency of the responses produced by long trains of stimuli

<table>
<thead>
<tr>
<th>Step Cycle</th>
<th>Swing</th>
<th>Stance</th>
<th>Brachialis</th>
<th>Amplitude</th>
<th>Duration</th>
<th>Triceps brachii</th>
<th>Amplitude</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loci</td>
<td>14/32 (44)</td>
<td>23/32 (72)</td>
<td>27/32 (84)</td>
<td>28/32 (88)</td>
<td>21/32 (66)</td>
<td>25/32 (78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of groups</td>
<td>17/83 (21)</td>
<td>70/110 (64)</td>
<td>63/83 (76)</td>
<td>65/83 (78)</td>
<td>52/110 (47)</td>
<td>55/110 (50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean, %</td>
<td>90 ± 2 (4)</td>
<td>65 ± 15</td>
<td>317 ± 167</td>
<td>191 ± 39</td>
<td>65 ± 15 (10)</td>
<td>62 ± 18 (22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>112 ± 4 (10)</td>
<td>120 ± 3 (3)</td>
<td>162 ± 38 (13)</td>
<td>120 ± 3 (3)</td>
<td>162 ± 38 (13)</td>
<td>120 ± 3 (3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Frequency and magnitude (means ± SD) of the changes produced in the step cycle and in a representative flexor and extensor muscle of the forelimb by long trains of stimuli applied to the red nucleus and motor cortex. Loci: number of sites that produced a significant change in the indicated parameter together with the number of sites that were stimulated. No. of groups: number of groups that produced a significant change in the indicated parameter as a function of the number of groups stimulated. Values in parentheses after these are percentages. A group is defined as any one of the 10ths of the step cycle in which more than one stimulus was applied. Swing was divided into 3 groups (1–3) and stance into 5 groups (5–9). Range: smallest and largest significant response. Mean: gives the average of all of those groups that produced a significant response. If all sites caused a response of a similar type, the value in parentheses is equal to the number of effective loci and is, therefore, not repeated; if stimulation produced one response in some sites and another at other sites, then the value in parentheses is given for each (note that in some sites, stimulation caused a decrease in a value in one phase and an increase in another; see, e.g., the amplitude of the responses evoked in the triceps brachii by stimulation of the motor cortex).
example illustrated in Fig. 9, the duration of the flexor burst was increased to 198% of the control value and the amplitude by 307%. Behaviorally, the increase was reflected by a marked hyperflexion of the contralateral forelimb. Stimulation during stance caused a curtailment of the extensor burst (which was sometimes preceded by an increase in EMG amplitude, as in Fig. 9A) and a premature initiation of the next burst of activity in coBr, thus resetting the step cycle. In the example illustrated in Fig. 9, stimulation early in the stance phase (middle) caused a decrease in the average step cycle duration from 1,013 to 502 ms (see Fig. 9B), i.e., the cycle duration was reduced to 50% of the control value. This decrease in step cycle was accompanied by a decrease in the duration of the coTriL muscle to a minimum of 58% of its control value.

As for the representative case in Fig. 9, most loci (27/32) stimulated produced an increase in the amplitude of the flexor burst during swing (Fig. 10B and Table 2), ranging from 145 to 854% of the control value. This increase in the amplitude was observed both when the stimulation fell in the swing phase, and thus directly affected the EMG amplitude, as well as when it
occurred during stance, and thus affected the amplitude of the subsequent Br burst. In the latter situation, the largest increases in amplitude were frequently seen in those loci in which the stance phase was curtailed (see Fig. 9). As for the stimulation of the red nucleus, this increase in the magnitude of the activity was also accompanied by an increase in the duration of the flexor burst; this change was generally larger than that following red nucleus stimulation and ranged from 136 to 309% (Table 2). The effects on the cycle duration were more variable but frequently much larger than those produced by stimulation of the red nucleus. Stimulation during stance in one other site in MC8 produced a decrease in cycle duration of similar magnitude to that observed in Fig. 9, whereas three other sites produced decreases in the step cycle duration of >25% (i.e., to <75% of control values). Similarly, stimulation during stance in 7/8 sites in MC7 (Fig. 10A) and 5/11 sites in MC11 also produced decreases in cycle duration of >25%. In 4/8 sites in MC7 and in 4/11 sites in MC11, the step cycle duration was decreased by >40% when stimuli were applied at the onset of stance. Overall the average step cycle was decreased to 65% of control by stimulation during stance (Table 2). As indicated by inspection of Fig. 1, C–E, the sites that produced the largest decreases in cycle duration generally were intermingled with the other sites in the relatively restricted region of the cortex that was explored.

**DISCUSSION**

In intact, unrestrained cats, short trains of stimuli applied to the red nucleus evoked phase-dependent responses that were most prevalent in the physiological flexor muscles during the swing phase of locomotion. Microstimulation of the red nucleus had no effect on the cycle duration, even when long trains of stimuli were applied and even though the amplitude of the EMG activity was markedly modified. This in contrast to motor cortex stimulation, which could affect the timing as well as the structure of the locomotor cycle.

**General considerations**

Although the major goal of this study was to determine the influence of red nucleus activity on the locomotion of the intact cat, it is first worthwhile emphasizing that the general results obtained in this study agree well with those that have been reported in other preparations, species, and tasks. As in other reports in the cat (see e.g., Ghez 1975; Maffei and Pompeiano 1962), stimulation with the cat at rest produced flexion of the contralateral fore or hindlimb and evoked EMG responses that were more prevalent in physiological flexor muscles than in the physiological extensors (see Fig. 2). Although this may, at first sight, seem contradictory to the recent results reported for the primate by Cheney and his collaborators (Belhaj-Saif et al. 1998; Cheney et al. 1991; Mewes and Cheney 1991) that have emphasized the effects of the red nucleus on extensor muscles, the only real difference is in the way in which different muscles are classified as flexors or extensors. For example, in both our study and that of Belhaj-Saif et al. (1998), responses were more prevalent in the anatomic extensor, EDC, than in the anatomic flexor, PaL. Similarly, in both
strengths of were evoked simultaneously in at least two muscles at Ghez elicited a response in only one of the three muscles that although 20/51 of the sites that were stimulated in the study of level too low to detect by palpation. It should also be noted that a time. Given the low amplitude of the responses that were electrodes, percutaneously, into a maximum of three muscles at for these differences are not clear, it may be explained partly that the widespread responses are not entirely due to activation of large volumes of the red nucleus. Nevertheless given the compact nature of the red nucleus, it is possible that even this limited current spread might activate multiple representations within the red nucleus. Further it should also be acknowledged that such stimulation might activate presynaptic axons that would activate larger areas of the red nucleus than those activated directly, although both Ghez (1975) and Cheney et al. (1991) present several arguments to suggest that this is not a major consideration.

Widespread responses of the type observed in this study are also consistent with the widespread branching of rubrospinal axons reported in the cervical spinal cord in the cat (Shinoda et al. 1977, 1982) and with the fact that averages, triggered on action potentials of rubrospinal cells in the primate, indicate that some individual cells also innervate both proximal and distal muscles (Belhaj-Saïf et al. 1998). However, these results are in apparent contradiction to Ghez’s (1975) studies in which threshold stimuli, applied to the red nucleus of awake, intact cats, frequently activated single muscles. Although the reasons for these differences are not clear, it may be explained partly by the fact that electrodes were implanted chronically into multiple muscles in the present study, whereas Ghez implanted electrodes, percutaneously, into a maximum of three muscles at a time. Given the low amplitude of the responses that were evoked close to threshold (see Fig. 3), it is possible that other muscles may have been activated in the study of Ghez but at a level too low to detect by palpation. It should also be noted that although 20/51 of the sites that were stimulated in the study of Ghez elicited a response in only one of the three muscles that were recorded at each site, at the other 31/51 sites, responses were evoked simultaneously in at least two muscles at strengths of 10 \(\mu\)A. Although there is always the additional possibility that the widespread effects that we observed are due to indirect activation of the motor cortex by cerebello-thalamocortical pathways, the short latency of the responses, especially during locomotion, argues against them being mediated indirectly. Further Ghez (1975) showed that ablation of the motor cortex had no effect on the responses evoked from stimulation of the red nucleus.

**Location:** phase-dependent responses

In agreement with Orlovsky’s (1972b) results obtained for selected hindlimb muscles in the decerebrate cat, microstimulation during locomotion produced a phase-dependent increase in the amplitude of physiological flexor muscles during the swing phase of locomotion. At a general level, therefore, the results suggest that the same basic mechanisms hold for the intact and decerebrate preparation as well as for the hindlimbs and forelimbs. However, in addition, the chronic recording techniques used in this study have allowed us to extend the original observations of Orlovsky (1972b) to provide new and more detailed information concerning the effects of activating the rubrospinal tract on the basic locomotor pattern. For example, inspection of Figs. 4–6 show that the maximal increase in the level of the EMG activity in flexors was not observed at one fixed point in the step cycle but varied according to the individual muscle. This suggests that the magnitude of the evoked response is dependent on the excitability of spinal neurons. Although it is possible that this result may simply reflect the level of motoneuronal depolarization, the results indicate that the stimulation was not equally effective throughout the period of EMG activity (see e.g., Figs. 4 and 5). In this respect, it is of particular interest that the amplitude of the responses in the EDC were frequently as large during the stance phase of locomotion as during swing (see Figs. 4–6) even though EMG activity was only observed at the beginning and end of the swing phase. Taken together with the fact that monosynaptic connections between rubrospinal terminals and motoneurones are rare in the cat and even when present are observed mostly with the motoneurones of muscles controlling the distal extremities (Holstege and Tan 1988; Hongo et al. 1969; McCurdy et al. 1987; although see Fujito et al. 1991), we suggest that the magnitude of the response is determined by the level of excitability of spinal interneurones and reflects more the functional requirements of the task than the level of motoneuronal depolarization. This is similar to the arguments that we, and others, have made previously for the interactions between cutaneous afferents and the locomotor rhythm (see Rossignol 1996; Rossignol et al. 1988 for reviews) and between the motor cortex and the locomotor rhythm (Drew 1991b; Kalaska and Drew 1993). In addition, the results indicate that the connections between rubrospinal tract fibers and interneurones retain a certain amount of specificity as the phase-dependent responses obtained in the close anatomic synergists, EDC and ECR were, in all three cats, quite different (see Fig. 5).

Our results also suggest some evidence for a topographical specificity, over and above that which has been described for the hindlimb and forelimb representations of the red nucleus (Eccles et al. 1975; Ghez 1975; Holstege and Tan 1988; Padel et al. 1972; Pompeiano and Brodal 1957). Inspection of Fig. 6, for example, shows that there was a large variation in the relative magnitude of the responses evoked in different muscles depending on the site stimulated. Thus although our results do not support Ghez’s (1975) suggestion that small areas of the red nucleus may control individual muscles, they are compatible with his conclusions that different areas of the red nucleus may have a preferential input to different muscles.

These experiments in the intact preparation also show that the rubrospinal system may influence the activity in physio-
logical extensor muscles during locomotion both during swing and during stance. Such interactions may be expected given that a number of studies have shown that stimulation of the rubrospinal tract may produce both excitatory and inhibitory post synaptic potentials (PSPs) in extensor motoneurones in the cat (Burke et al. 1970; Endo et al. 1975; Hongo et al. 1969; Powers et al. 1993). In our study, stimulation during the period of the normal activity of the two physiological extensor muscles that we studied produced suppression of activity slightly more frequently than it did facilitation [34.2 vs. 16.7% of effective cases (sites * groups) during stance for the TriL and 35.0 vs. 24.2% cases for PaL]. In this respect, the results have both points of similarity and differences to those obtained by Belhaj-Saif et al. (1998) during a task in which primates made a reaching and prehension movement requiring multijoint co-ordination. In their experiments, most stimulated sites also produced mixed responses in TriL although PaL was almost invariably suppressed. Although the difference in the responses in PaL might appear large, we would emphasize that in our studies the facilitatory responses in PaL during stance were weak and were invariably followed by suppression. However, Belhaj-Saif et al. (1998) also observed suppression in physiological flexor muscles in many cases, whereas we never observed suppression of activity, in any physiological flexor, during its period of activity. In this, there appears to be some difference, although whether this is related to the task or whether it is an interspecies difference is not clear. It is also pertinent that while we observed the effects of stimulation at different phases of the step cycle, when muscles were alternately active and inactive, stimuli were applied throughout the movement sequence in the studies of Belhaj-Saif et al. (1998) so that it is not known whether suppression and facilitation might be observed at different phases, as in the current study. The fact that we frequently (50% of cases for TriL and 44% for PaL, Table 1) observed facilitation of the extensor responses in swing when these muscles were inactive, particularly just before the onset of stance, further supports our view that the effects are mediated by premotoneuronal elements and that they are adapted to the functions of the locomotor cycle. For example, co-activation of flexors and extensors at this phase of the step cycle would serve to stabilize the limb before and during foot contact. It is also interesting to note that the responses in the extensors during stance showed differences between cats RN4 and RN5, suggesting that the relative synaptic efficacy of the rubrospinal connections to excitatory and inhibitory interneurones impinging on extensor motoneurones might be modifiable by experience.

The comparison between the phase-dependent responses evoked by red nucleus stimulation and those evoked by the motor cortical stimulation in cat MC8 suggests that both pathways may modify the locomotor pattern in a similar manner. It is of particular interest that the complicated pattern of phase-dependent responses evoked in the EDC by the red nucleus stimulation was also observed after motor cortical stimulation. Similarly, although not illustrated for the motor cortex, the simple pattern of activation of the ECR was also observed from stimulation of both pathways. Such a similarity is perhaps not unexpected given that the rubrospinal and corticospinal pathways converge onto similar types of interneurones (see Jankowska 1992).

Our analysis of the relative magnitude of the responses obtained after motor cortical and red nucleus stimulation suggests that the two systems also have comparable effects on the level of the EMG activity. This is in contrast to the results presented by Cheney et al. (1991) that suggest that the magnitude of the responses evoked by cortical stimulation in the primate are generally greater than those evoked by stimulation of the red nucleus, particularly at the highest strength used in their study (20 μA). This result may be explained by the relative decrease in the size of the rubrospinal tract that occurs in primates as compared with cats (see Massion 1967) and suggests that in the cat both of these systems have a similar capacity to influence the level of the EMG activity during locomotion.

**Microstimulation: long trains of stimuli**

The experiments in which we increased the duration of the trains of stimuli applied to the red nucleus gave us the opportunity to determine how this structure may interact with the basic locomotor rhythm to modify it. The major result from this part of the study was that although red nucleus micro-stimulation evoked large changes in the duration and amplitude of the flexor muscles, it evoked only very small changes in the timing of the locomotor cycle. This result is in agreement with that obtained by Orlovsky (1972b) in the decerebrate animal although somewhat different from the result of Degtyarenko and colleagues (1993), who found that stimulation of the red nucleus in fictive cats could change the duration of the step cycle. Thus although the red nucleus may have some access to the processes involved in determining the timing of the rhythm generator, it seems that in the walking animal, this access is insufficient to alter cycle timing, presumably because of the stabilizing influence imparted by the rhythmical peripheral afferent feedback in the walking cat (see also Perreault et al. 1994 for a similar argument with respect to the cycle changes produced by stimulation of the medullary reticular formation). This result should be contrasted with those that we have reported previously (Armstrong and Drew 1985; Drew 1991b; Kalaska and Drew 1993), but detailed for the first time in this paper, that similar stimulation of the motor cortex frequently produces significant changes in cycle duration, primarily by reducing the stance duration and initiating a new period of swing. Of course, it is possible that rather than reflecting a true functional difference in these two structures the result simply reflects that the stimulation to the motor cortex was stronger, or more effective, than that to the red nucleus. We feel, however, that such an explanation is insufficient to explain our results. Inspection of Figs. 7 and 9 and of Table 2, for example, shows that stimulation of the red nucleus in the swing phase of locomotion produced responses in the flexor muscles that were just as large as those produced by the motor cortical stimulation. Similarly our analysis of the relative amplitude of the responses produced by the short trains of locomotion (see preceding text) also argues for a similar synaptic efficacy from these two structures. In addition, although the stimulation of the red nucleus during stance was sufficiently strong to completely suppress extensor muscle activity during the burst and, even, to cause a physical buckling of the limb, it never produced a premature activation of flexor muscle activity in the same manner as the motor cortical stimulation, i.e., suppression of extensor activity does not automatically lead to initiation of...
flexor activity. We would argue, therefore, that this result suggests that the red nucleus, although capable of modifying the structure of the step cycle, has little access to the circuits controlling the timing, whereas the motor cortex has access to both neuronal populations.

Such an argument implies that cycle structure and cycle timing are controlled by different interneuronal populations in the spinal cord. There is no direct evidence for such a supposition, but the general idea of separate neuronal populations controlling these two aspects has been discussed frequently since the original suggestion by Lennard (Lennard 1985; Lennard and Hermanson 1985; see also Loeb et al. 1990). For example, Koshland and Smith (1989) have suggested that a division of the spinal central pattern generator into a circuit that controls oscillation and another that controls structure might be the best way to explain conceptually the independence of cycle timing and structure that were observed after deafferentation of the hindpaw in spinal cats. A similar argument has also been made by Feldman and his colleagues (1988, 1990), for the control of the respiratory cycle based, as in the cat and turtle, on the differential effects of afferent feedback on the rhythm and the pattern of activity. In a similar manner Currie and Stein 1989 (see also Stein and Smith 1997) have emphasized that the neural circuits responsible for generating the rhythm in the hip may set the rhythm observed at the other joints. Thus despite the extensive convergence of the two pathways onto similar types of interneurones, the data presented in this study suggest that at least some of the corticospinal fibers must terminate on interneurones that receive no or few rubrospinal inputs and which form part of, or which have access to, the neuronal circuits responsible for controlling the locomotor rhythm. It is assumed that these interneurones would synapse onto other groups of interneurones, which would be responsible for determining the pattern, or structure, of the EMG activity during locomotion. Several lines of evidence suggest that these interneurones might be organized in a modular fashion to allow coordinated changes in activity during stepping (see e.g., Drew 1991c; Grillner 1982; Jordan 1991; Stein and Smith 1997). These modules would receive equally strong inputs from both the motor cortex and the red nucleus, effectively allowing either structure to modify the pattern of activity or the intralimb coordination (see e.g., Jiang and Drew 1996).

In conclusion, the results from this study support the general viewpoint, expressed in the introduction, that the motor cortex and the red nucleus have similar, but obviously not identical, roles to play in motor control. These different aspects of the functions of the two systems are illustrated clearly in the present context by the striking overlap of the effect of rubrospinal and corticospinal activity on the level of EMG activity, in both flexors and extensors, but their very striking difference on the timing of the step cycle. Given that the major input to the red nucleus is from the interpositus nucleus (see e.g., Massion 1967; Toyama et al. 1970) and the putative role of this structure in modifying movements in response to changes in external conditions (see e.g., Allen and Tsukuhara 1974), it is possible that the output from the motor cortex might dictate the movement template while the red nucleus would modulate the level of activity of the muscles in response to changing external conditions.

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