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Direct and Indirect Corticospinal Control of Arm and Hand Motoneurons in the Squirrel Monkey (*Saimiri sciureus*)

M. A. MAIER,[1] E. OLIVIER,[1] S. N. BAKER,[1] P. A. KIRKWOOD,[1] T. MORRIS,[2] AND R. N. LEMON[1]
[1]*Sobell Department of Neurophysiology, Institute of Neurology, London WC1N 3BG; and* [2]*Department of Laboratory Animal Science, SmithKline Beecham Pharmaceuticals, Harlow, Essex CM19 5AW, United Kingdom*

Maier, M. A., E. Olivier, S. N. Baker, P. A. Kirkwood, T. Morris, and R. N. Lemon. Direct and indirect corticospinal control of arm and hand motoneurons in the squirrel monkey (*Saimiri sciureus*). *J. Neurophysiol.* 78: 721–733, 1997. Anatomic evidence suggests that direct corticomotoneuronal (CM) projections to hand motoneurons in the New World squirrel monkey (*Saimiri sciureus*) are weak or absent, but electrophysiological evidence is lacking. The nature of the corticospinal linkage to these motoneurons was therefore investigated first with the use of transcranial magnetic stimulation (TMS) of the motor cortex under ketamine sedation in five monkeys. TMS produced early responses in hand muscle electromyogram, but thresholds were high (compared with macaque monkey) and the onset latency was variable. Second, stimulation of the pyramidal tract (PT) was carried out with the use of chronically implanted electrodes in ketamine-sedated monkeys; this produced more robust responses that were markedly facilitated by repetitive stimulation, with little decrease in latency on the third compared with the first shock. Finally, postsynaptic potentials were recorded intracellularly from 93 arm and hand motoneurons in five monkeys under general chloralose anesthesia. After a single PT stimulus, the most common response was a small, slowly rising excitatory postsynaptic potential (EPSP), either alone (35 of 93 motoneurons) or followed by an inhibitory postsynaptic potential (39 of 93). The segmental delay of the early EPSPs was within the monosynaptic range (mean 0.85 ms); however, the rise time of these EPSPs was slow (mean 1.3 ms) and their amplitude was small (mean 0.74 mV). These values are significantly slower and smaller than EPSPs in a comparable sample of Old World macaque monkey motoneurons. The results show that CM connections do exist in the squirrel monkey but that they are weak and possibly located on the remote dendrites of the motoneurons. The findings are consistent with earlier anatomic studies. Repetitive PT stimulation produced large, late EPSPs in some motoneurons, suggesting that, in this species, there are relatively strong nonmonosynaptic pathways linking the corticospinal tract to hand motoneurons.

INTRODUCTION

In primates, many different lines of evidence suggest that the capacity to perform relatively independent finger movements (RIFM) is dependent on the direct corticomotoneuronal (CM) projections from motor cortex to the motoneurons supplying hand and finger muscles (Bernhard et al. 1953; see Porter and Lemon 1993 for a review). Comparative studies on different primate species have suggested that the degree of digital dexterity is well correlated with the extent to which these CM projections are present (see Heffner and Masterton 1983). A recent anatomic study by Bortoff and Strick (1993) made a direct comparison of the corticospinal projections in the New World squirrel (*Saimiri sciureus*) and cebus (*Cebus apella*) monkeys. In the more dexterous cebus monkey, there were abundant projections from the primary motor cortex to the dorsolateral part of Rexed lamina IX, where motoneurons innervating intrinsic hand muscles are located. These projections were not present in the squirrel monkey, which does not use precision grip (Costello and Fragaszy 1988). However, the absence of corticospinal terminations in dorsolateral lamina IX does not exclude the possibility that corticospinal neurons establish direct connections with hand motoneurons by synapsing on dendrites located beyond the boundary of lamina IX (Bortoff and Strick 1993; Porter and Lemon 1993).

The aim of the present study was to investigate the corticospinal system in the squirrel monkey with the use of electrophysiological techniques. In the first part of the study we utilized noninvasive transcranial magnetic stimulation (TMS) of the motor cortex to look for electromyographic (EMG) responses in arm and hand muscles. Such responses have been extensively studied in humans and in the macaque monkey, and it has generally been assumed that short-latency responses elicited by TMS are mediated by fast corticospinal neurons with monosynaptic connections (see Baldissera and Cavallari 1993; Edgley et al. 1990, 1997; Rothwell et al. 1991). This study demonstrates that short-latency responses can be evoked in the intrinsic hand muscles of the squirrel monkey, although it was not possible with the use of noninvasive methods to determine unequivocally whether the responses were mediated by CM connections.

The second part of the study looked for more direct evidence of CM connections with the use of intracellular recordings made from arm and hand motoneurons. Postsynaptic responses to stimulation of the corticospinal tract in the medullary pyramid were examined. This approach demonstrated unequivocally the existence of monosynaptic CM connections to hand motoneurons in squirrel monkeys, although the excitatory postsynaptic potentials (EPSPs) were small and had rather slow rise times. This finding is compatible with a relatively remote dendritic origin of EPSPs, in agreement with anatomic findings of Bortoff and Strick (1993).

Preliminary accounts of these data have been published previously (Lemon et al. 1996; Olivier et al. 1996).

METHODS

This study was performed in five male squirrel monkeys (*S. sciureus*) weighing between 1.0 and 1.6 kg. The animals had been obtained as young adults from a feral Peruvian source via the Pan

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American Health Organisation and had been imported into the United Kingdom 3 yr previously. They appeared to be of a similar age and phenotype. Animal care and use was in accordance with the UK Animals (Scientific Procedures) Act 1986.

TMS in sedated monkeys

Recording of EMG responses to TMS of the motor cortex was performed under ketamine sedation. After dose ranging studies in the first animal, an initial dose of 15 mg/kg, followed by further doses of 8 mg/kg of ketamine, was used with the aim of providing a consistent level of sedation. The final dose rate at the end of each experiment was 0.83 ± 0.11 (SD) $mg \cdot kg^{-1} \cdot min^{-1}$ ($n = 5$). Body temperature was maintained at 37–39°C with a thermostatically controlled heating blanket.

Responses to TMS were recorded with intramuscular electrodes from the following muscles: biceps brachii, extensor digitorum communis (EDC), and an intrinsic hand muscle [either abductor pollicis brevis (AbPB) or 1st dorsal interosseous (1DI)]. The correct location of the intramuscular electrodes was confirmed by electrical stimulation through them. Surface electrodes were also used to record thenar muscle activity. M responses and F waves were elicited by supramaximal electrical stimulation of the median nerve or ulnar nerve at the wrist and recorded in AbPB or 1DI, respectively. EMG activity was digitized on-line at 5 kHz with the use of a personal computer with 1401plus interface (CED, Cambridge, UK) and analyzed off-line.

Monkeys were then placed in a hammock that was suspended on a metal frame, which allowed stabilization of the monkey's head. Magnetic stimuli were delivered with the use of a Magstim 200 stimulator (Magstim, Dyfed, UK) and a 7-cm-OD figure-eight coil (maximum magnetic field 2.2 T). The coil was held with the handle pointing in the lateromedial direction, so that current flow in the coil was from the lateral to the medial side of the stimulated hemisphere (see Werhahn et al. 1994); coil position was adjusted to optimize the amplitude of short-latency EMG responses evoked in intrinsic hand muscles. Background EMG activity, which was present in all muscles under ketamine sedation, was augmented in the tested muscles by gentle manipulation of the hand or forearm. Once the optimal coil position was determined, a series of 20 suprathreshold stimuli was given to determine the shortest latency of EMG responses to TMS. Subsequently, a series of stimuli at three to four different intensities was delivered in a random sequence, to determine the threshold of EMG responses to TMS. Threshold was taken as the lowest intensity that yielded a response probability ≥0.2. This value was obtained from linear regression analysis of response probability and the range of intensities used.

The latencies of M responses, F waves, and responses to TMS were measured from single traces and used to calculate the mean and SD. For responses to TMS, the 10th percentile of the response latencies was computed and used to define the shortest latency; this was done to minimize possible error due to outliers. The peripheral motor conduction time (PMCT) from the spinal cord to intrinsic hand muscles was then computed as follows

$$\text{PMCT} = (M + F - 1)/2$$

where M and F are shortest latencies of M responses and F waves, respectively, and 1 ms is the absolute refractory period of the fastest motor fibers (see Kimura 1989). We calculated the ''central delay'' for the responses to TMS, defined as

$$\text{central delay} = \text{EMG}_{\text{lat}} - \text{PMCT}$$

where EMG_{lat} is the shortest latency of responses to TMS in intrinsic hand muscles.

Comparison of responses to TMS and to direct stimulation of the pyramidal tract

A few months later the same animals were used in acute, terminal experiments. Three of the monkeys were sedated with ketamine (15 mg/kg im), and TMS procedures identical to those above were repeated. General anesthesia was then induced via a mask and maintained with an endotrachial tube with the use of 1.5–2.5% isoflurane in a 1:1 O_2:N_2O mixture. All anesthetic procedures were supervised by a veterinary anesthetist. In three monkeys, two varnish-insulated tungsten electrodes (tip impedance ~20 kΩ at 1 kHz) were implanted under stereotaxic control 4 mm apart in the medullary pyramidal tract (PT), at stereotaxic levels A3 and P1, 1 mm from the midline. Electrodes were positioned at the lowest threshold point for evoking an antidromic cortical volley recorded through a burr hole over the primary motor cortex; in all cases the threshold of the antidromic volley from at least one of the electrodes was <50 μA (stimulus duration 0.1 ms). Correct placement of electrodes was later confirmed by postmortem histology (see Fig. 9). PT electrodes were secured to the skull with dental cement and all wounds were closed and infiltrated with bupivacaine (Marcaine, Astra, Kings Langley, UK), a long-acting local anesthetic.

In two monkeys, after removal from the stereotaxic holder, isoflurane anesthesia was discontinued. EMG responses to PT stimulation (intensity 100–200 μA, duration 0.1 or 0.2 ms) were recorded under ketamine sedation, with the same muscle electrodes used to record the responses to TMS. A direct comparison of the responses in the same animal was therefore possible. Both single and repetitive PT stimulation (3 shocks at 333 Hz) were used. In one animal, recording of the descending corticospinal volley from the PT was made during delivery of TMS to the ipsilateral motor cortex. Records were made with the use of a specially designed amplifier to which a mute pulse could be given so as to reduce the TMS-induced stimulus artifact (see Baker et al. 1994).

Intracellular recording of postsynaptic responses in arm and hand motoneurons to PT stimulation

Under general anesthesia (1.5–2.5% isoflurane in a 1:1 O_2:N_2O mixture), cuff electrodes were placed on the radial nerve (Ra), median nerve (Ma), and ulnar nerve (Ua) at the axilla, and on the deep radial nerve (DR) just above the elbow. An extensive cervical laminectomy was carried out. When surgery was complete, the monkey was given chloralose (50–80 mg/kg iv) and the isoflurane was discontinued. The animal was mounted in a spinal frame and headholder, with clamps on the vertebral column at T_4 and in the lumbar region. The animal was paralyzed with pancuronium bromide (Pavulon, Oregon-Technika, Cambridge UK) at a dose of 0.3 $mg \cdot kg^{-1} \cdot h^{-1}$ iv and was artificially ventilated. A bilateral pneumothorax was carried out. The dura was opened and the spinal cord was covered in warm mineral oil. The adequacy of the anesthesia was continuously assessed by reference to the blood pressure, heart rate, and pupillary reflexes. Supplementary doses (1–5 mg/kg iv) of pentobarbitone sodium (Sagatal, Rhone Merieux, Harlow, UK) were administered when necessary. Body temperature was maintained between 37 and 39°C. Fluid balance was maintained with the use of a slow infusion of lactated Ringer solution into the femoral vein. Routine analysis of blood gases was carried out, supplementary bicarbonate solution was added to the Ringer solution as required, and each animal remained in good physiological condition throughout the recording.

In three monkeys, descending corticospinal volleys in response to PT stimulation were recorded from the surface of the dorsolateral funiculus (DLF) at two different levels of the spinal cord (C_2–C_3 and C_8–T_1). The latency difference in the arrival of the volley at the two levels was determined, the conduction distance between them was measured, and the values were used together to estimate

the conduction velocity of the fastest CS axons in this part of the corticospinal tract. In one animal, the volleys evoked by TMS over the motor cortex were recorded from the surface of the DLF at C_8–T_1.

In the two monkeys without implanted PT electrodes, the dorsal surface of the medulla oblongata was exposed and a single stimulating electrode was advanced toward the bulbar pyramid just lateral (0.7 mm) and rostral (1 mm) to obex. The depth of this electrode could be varied, and it was positioned at a point that yielded a CS orthodromic volley, recorded from the DLF at C_2–C_3, that had a low threshold (<10 μA) and was near maximal, with an intensity of 200 μA. In all five monkeys there was little increase in the volley amplitude when the intensity was increased from 200 to 500 μA.

In all five monkeys, intracellular recordings were made from motoneurons with glass microelectrodes filled with 3 M potassium acetate and having resistances of 4–10 MΩ. The motoneurons were located in the C_8 and T_1 segments and were identified antidromically from one of the cuff electrodes. Intracellular and surface recording, taken from the DLF immediately rostral to the site of motoneuron recording, were digitized directly at 10 kHz with the use of a 1401plus interface (CED). Membrane potential was monitored throughout the recording, and only data from stable periods of recording were used for analysis (membrane potential >50 mV). Stimuli were delivered to the PT (50–200 μA, duration 0.1 ms, rate 3 Hz). Responses to either single or up to four repetitive stimuli (at 333 Hz) were tested. Extracellular recordings were taken immediately after withdrawal of the electrode. For analysis, measurements of the latency, rise time, and amplitude of postsynaptic potentials were all made from single sweeps. Amplitudes of EPSPs evoked by the third of three PT shocks were measured from the voltage at the start and peak of the EPSP, without any assumptions about underlying baseline trends.

At the end of the experiment the animal was killed with an intravenous overdose of pentobarbitone, and perfused through the heart with fixative. Brain and spinal cord were examined histologically for location of stimulating and recording electrodes.

RESULTS

Activation of corticospinal tract neurons by TMS

The initial part of this investigation determined whether noninvasive TMS of the squirrel monkey motor cortex can give rise to short-latency EMG responses in arm and hand muscles. Activation of corticospinal neurons by TMS was demonstrated by direct recording of the descending corticospinal volleys from the implanted PT electrodes (1 monkey under ketamine sedation) and from the DLF at the C_8–T_1 level (1 monkey under chloralose anesthesia). When recordings were taken from the PT, the initial component had a latency to the first positive peak of 0.5 ms, almost identical to the onset latency of the antidromic response recorded from the motor cortex and activated from the same PT electrodes (0.55 ms). This demonstrated that, in the squirrel monkey, the volley generated by TMS was a result of direct rather than indirect activation of the corticospinal neurons. Similar results have been reported previously in the macaque (Baker et al. 1994; Edgley et al. 1990, 1997).

Results from recordings from the DLF at C_8–T_1 are shown in Fig. 1*A*. TMS evoked a complex series of volleys: a large initial wave (D), followed, after a short delay, by a succession of smaller waves (I_1–I_4). The latency of the first inflection in the D wave (Fig. 1*A*, open arrow) was 1.45 ms. This marks the arrival time of the volley at the segmental

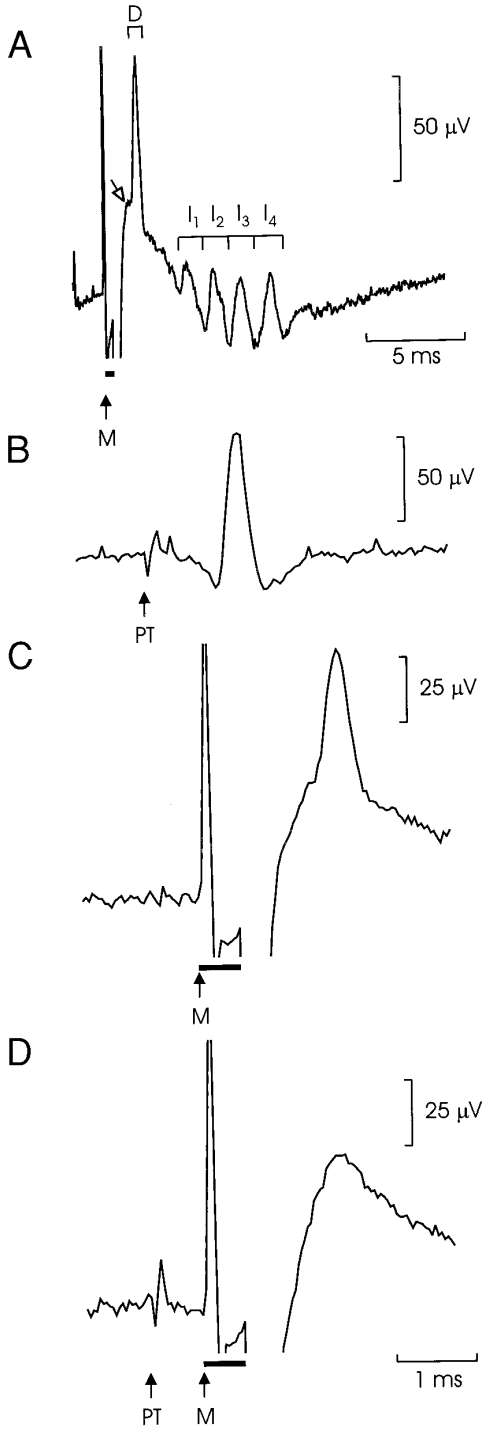

FIG. 1. Single sweep recordings of volleys excited by transcranial magnetic stimulation (TMS) and pyramidal tract (PT) stimulation. Recordings made from surface of dorsolateral funiculus at C_8–T_1 segment. *A*: TMS, delivered at arrow marked M, elicited early direct, D wave and several later I waves (I_1–I_4); open arrow indicates onset of D wave. Intensity: 60% of maximum stimulator output. Horizontal bar above arrow: duration of mute pulse applied to amplifier input to reduce stimulus artifact. *B*: corticospinal volley evoked by PT stimulation (intensity 200 μA, duration 0.2 ms). *C*: expanded portion of *A* to show D wave response to TMS. *D*: identification of this response as corticospinal by collision with volley evoked by preceding shock to PT; PT-TMS interval 0.7 ms.

levels at which the motoneurons innervating the thenar muscles are presumably located (cf. Jenny and Inukai 1983). The D-I_1 interval was 2.4 ms and the interval between successive I waves was 1.4 ms. The latter interval is similar to previously reported values in Old World primates (Amassian et al. 1987; Edgley et al. 1997; Kernell and Wu 1967).

The identification of the D wave in these recordings as corticospinal is shown in Fig. 1, *B–D;* it is shown on an expanded time scale in Fig. 1*C.* Stimulation of the PT alone produced an orthodromic volley with a rather similar form and amplitude (Fig. 1*B*), and when this PT stimulus preceded TMS with an interval of 0.7 ms, the D wave was almost completely eliminated (Fig. 1*D*). We investigated the time course of this effect; for technical reasons related to the mute pulse circuitry of the preamplfier, we could only test the D wave response to TMS when the PT stimulus preceded TMS by 0.4–3.0 ms. The D wave was all or partly collided for intervals from from 0.4 to 1.6 ms. The brevity of this effect suggests that it arose by collision (see Edgley et al. 1990).

EMG responses to TMS

In all five monkeys investigated, TMS applied over the motor cortex elicited short-latency EMG responses in arm and hand muscles. Figure 2, *left,* illustrates individual unrectified EMG responses recorded through intramuscular electrodes from AbPB following magnetic stimulation at 60% of the maximal output of the stimulator; the averaged response of rectified EMG is shown at *bottom.* Note the sweep-by-sweep variability in response latency, and the rather complex nature of the responses.

The shortest latency in this monkey, estimated from the 10th percentile (see METHODS), was 8.1 ms. The mean shortest latency in the thenar muscles for the five monkeys investigated was 8.0 ± 0.3 ms. In EDC and biceps, the shortest latency was estimated at 5.9 and 5.6 ms, respectively. The threshold of the EMG responses in Fig. 2 was 40%; the threshold for thenar muscle responses in the different monkeys ranged from 39 to 61% (mean 43%) of maximum stimulator output. The production of EMG responses depended on the center of the figure-eight coil being positioned over the frontal region; no responses were obtained when it was over the occipital region, for example.

Estimation of PMCT and central delay

Figure 3 illustrates M responses and F waves recorded from AbPB after the stimulation of the median nerve at the wrist (same monkey as in Fig. 2). The M response and the shortest F wave had latencies of 1.2 and 8.2 ms, respectively. In this animal, the PMCT was therefore estimated at 4.2 ms [= (1.2 + 8.2 − 1)/2, see METHODS]. In four animals, the PMCT calculated after the median nerve stimulation was 4.3 ± 0.4 (SD) ms. In one animal, the PMCT was assessed after the stimulation of ulnar nerve and was estimated at 4.8 ms. The central delay (shortest latency of EMG responses to TMS minus PMCT, see METHODS) was calculated to be 3.7 ± 0.5 (SD) ms (n = 5).

EMG responses to PT stimulation

SINGLE STIMULI. Figure 2, *right,* shows responses in the AbPB muscle to single PT stimuli via implanted electrodes

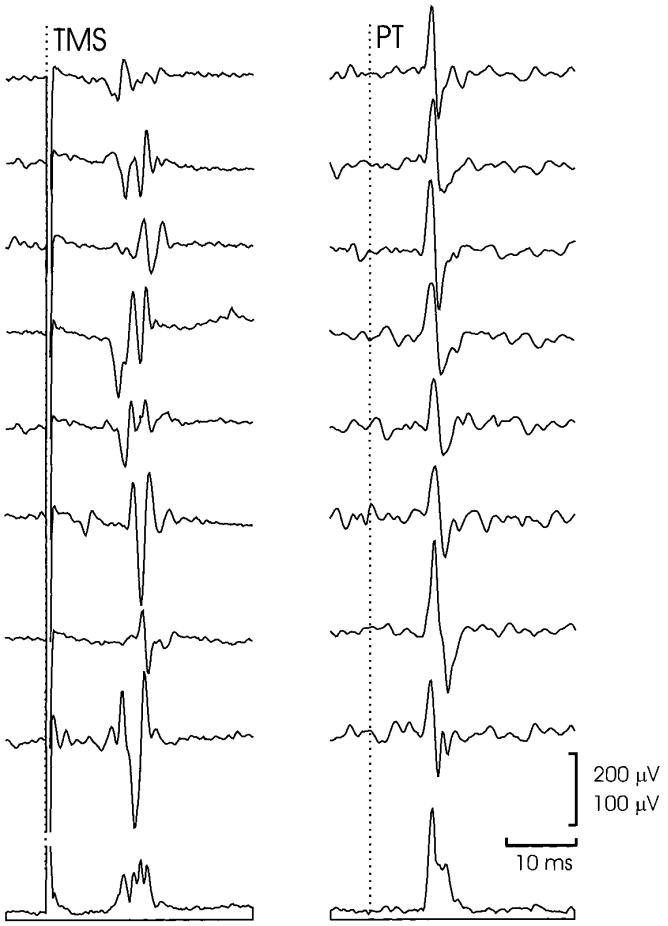

FIG. 2. Single sweeps showing electromyographic (EMG) response to TMS (*left*) and PT (*right*) stimulation recorded from abductor pollicis brevis (AbPB) muscle in squirrel monkey under ketamine sedation. Single PT stimuli (intensity 200 μA, duration 0.2 ms) were delivered at 1 Hz, and TMS at 60% of maximum stimulator output at 0.3 Hz. Vertical dotted line: time of occurrence of stimuli. *Bottom traces* are averages of rectified EMG responses [n = 28 sweeps (*left*) and 31 sweeps (*right*)]. Vertical calibration bar: 200 μV (single sweeps) and 100 μV (averages).

(intensity 200 μA, duration 0.2 ms, rate 1 Hz); these responses were recorded in the same session as those to TMS (Fig. 2, *left*). The response to single PT stimuli had a sharper onset and larger early component, but was still rather complex in appearance. The shortest onset latencies in the thenar muscles for the two monkeys tested for PT stimulation were 6.9 and 7.0 ms. For comparison, the shortest latency of TMS evoked responses recorded in the same muscles was 8.1 ms in both monkeys.

REPETITIVE STIMULI. Figure 4 shows results from the EDC muscle in one monkey in which the response to single (Fig. 4*A*) and repetitive (Fig. 4*B*) stimuli was compared. This was done to see how stable the response latencies were, because responses mediated by oligosynaptic routes should exhibit a greater variability in response latency than those mediated monosynaptically. Figure 4*A* shows the average of 100 responses to a single PT stimulus of 200 μA, delivered while there was clear ongoing background EMG activity in the muscle. The stimulus was just suprathreshold, as shown by the small response; it had an onset latency of 4.8 ms. Figure 4*B* is an average of 63 responses to a train of three

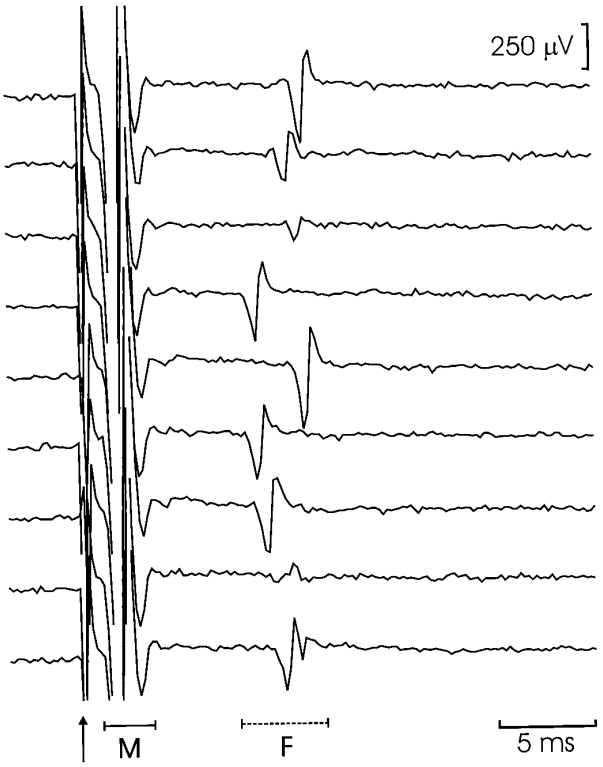

FIG. 3. Nine consecutive traces showing M responses and F waves recorded from AbPB after supramaximal stimulation of median nerve at wrist.

PT shocks (frequency 300 Hz, delivered at 1 Hz); these responses were the smallest in the file, and were selected from a total of 103 available sweeps so as to match the earliest component of the response to that of the single-shock condition (Fig. 4*A*). The later components show a great deal of facilitation. Figure 4*C* shows that it was possible to identify reliably the response to each stimulus in the train; a cursor has been placed to mark the onset latency of readily identified components. The distribution of these latencies is shown in Fig. 4*D*. The three responses had mean latencies of 4.8, 4.4, and 4.0 ms, measured from the first, second, and third PT shocks, respectively: a small reduction in onset latency with repetitive stimulation.

Thus, although both TMS and PT stimulation elicited short-latency EMG responses in hand muscles, it was not possible, on the basis of latency analysis alone, to ascribe these responses to monosynaptic activation of the relevant motoneurons by the corticospinal volley (see DISCUSSION). However, activation of motoneurons by a single PT shock does suggest a direct linkage. To clarify the issue, intracellular recordings were made from the motoneurons to determine the nature of their responses.

Conduction time and velocity of the fastest corticospinal fibers

Simultaneous recordings at different spinal levels of the descending corticospinal volley evoked by PT stimulation allowed precise estimates of the conduction velocity of the fastest corticospinal fibers. For three monkeys the values were 50.7, 47.3, and 47.7 m/s, respectively (mean 48.6 m/s). These were estimated from recordings made at the C_2–C_3 and C_8–T_1 levels.

An estimate of the corticospinal conduction time to the C_8–T_1 level was made in three monkeys by adding the onset latency of the cortical antidromic volley from the PT (mean 0.7 ms) to the latency of the orthodromic volley from PT to C_8–T_1 (mean 0.8 ms), giving a total conduction time from the cortex to the cervical enlargement of 1.50 ms (see Table 2 and DISCUSSION).

Intracellular recording of motoneuron responses to PT stimulation

These experiments were carried out to determine how corticospinal inputs are transmitted to motoneurons. A total of 93 motoneurons was sampled; in every case stable recordings were obtained for long enough for the effects of PT stimulation to be fully tested. All were located in the C_8 and T_1 segments. Some of these motoneurons (22) were identified from Ra, and would have innervated muscles acting at the elbow. The remaining 71 motoneurons were identified from the DR (n = 20) or Ma (24) or Ua (27), and would have innervated muscles below the elbow: finger and wrist extensors (from the DR), wrist and finger flexors, and intrinsic hand muscles (from the Ma and Ua).

MONOSYNAPTIC EPSPS. Table 1 lists the responses of motoneurons to PT stimulation. The most common response to a single PT stimulus was an early EPSP, either alone (35 of 93 motoneurons) or immediately followed by an inhibitory postsynaptic potential (IPSP, 39 of 93). The segmental delay of these EPSPs was calculated from the positive peak of the CS volley, signaling its arrival at that segment, to the onset of the EPSP (see Fig. 5*E*). These segmental delays were

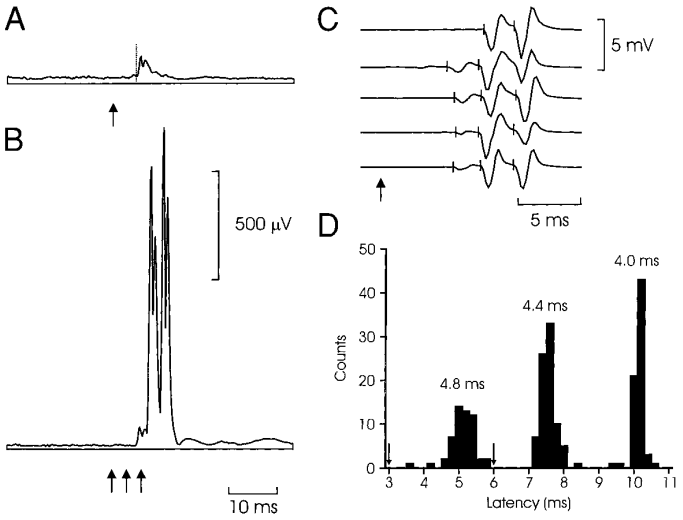

FIG. 4. *A*: average (n = 100) of rectified EMG of extensor digitorum communis (EDC) following single 200-μA PT stimulus (duration 0.2 ms). Dotted line: onset of response at 4.8 ms. *B*: response of EDC to train of 3 200-μA PT stimuli at 300 Hz. Sweeps to compile this average were selected to match size of 1st response peak to that in *A*. *C*: single sweeps of unrectified EMG from same run as in *B*, showing that onset latencies of each response could be clearly measured on some sweeps (tick marks). *D*: histogram of response latency distributions. Numbers above each peak: 10th percentile latency. Arrows: stimulus times (*A*–*D*); 1st stimulus in *D* is at t = 0.

TABLE 1. *Responses of antidromically identified motoneurons to single (PT × 1) and multiple (PT × 3) PT stimuli*

Responses to PT × 1		Responses to PT × 3	
mEPSP	35	mEPSP	13
mEPSP/IPSP	39	mEPSP/IPSP	37
IPSP	15	IPSP	9
		mEPSP/oEPSP	11
		mEPSP/IPSP/oEPSP	22
No response	4	No response	1
Total	93		93

PT, pyramidal tract; mEPSP, monosynaptic excitatory postsynaptic potential; oEPSP, oligosynaptic excitatory postsynaptic potential; IPSP, inhibitory postsynaptic potential.

brief (range 0.6–1.1 ms, 0.85 ± 0.1 ms, mean ± SD, $n = 74$, see Fig. 6*A*), and did not become any shorter with repetitive stimulation (mean 0.82 ± 0.1 ms), indicating that these EPSPs were monosynaptic in origin.

Monosynaptic EPSPs were generally rather small and slowly rising. In the example shown in Fig. 5, the EPSP had an amplitude of 0.5 mV and a rise time of 1.6 ms. The distributions of rise times and amplitudes of monosynaptic EPSPs are shown in Figs. 7*A* and 8*A*, respectively; these EPSPs were recorded in 27 hand and forearm motoneurons (i.e., DR, Ma, and Ua but not Ra) in which no succeeding IPSP was present that might have distorted the rising phase of the EPSP (see below). The mean and SD of results obtained from a similar sample of forearm and hand motoneurons in the macaque monkey (Fritz et al. 1985) are also plotted (Figs. 7*B* and 8*B*). It can be seen that, in the squirrel monkey, the rise time (1.30 ± 0.37 ms, $n = 27$) was significantly ($P < 0.01$, Student's *t*-test) longer than in the macaque (1.05 ± 0.2 ms, $n = 179$), whereas the mean EPSP amplitude was substantially smaller (0.74 ± 0.48 mV, compared with 2.46 ± 1.52 mV, $P < 0.001$). The largest monosynaptic EPSP recorded was 2.0 mV, compared with 7.5 mV in the macaque.

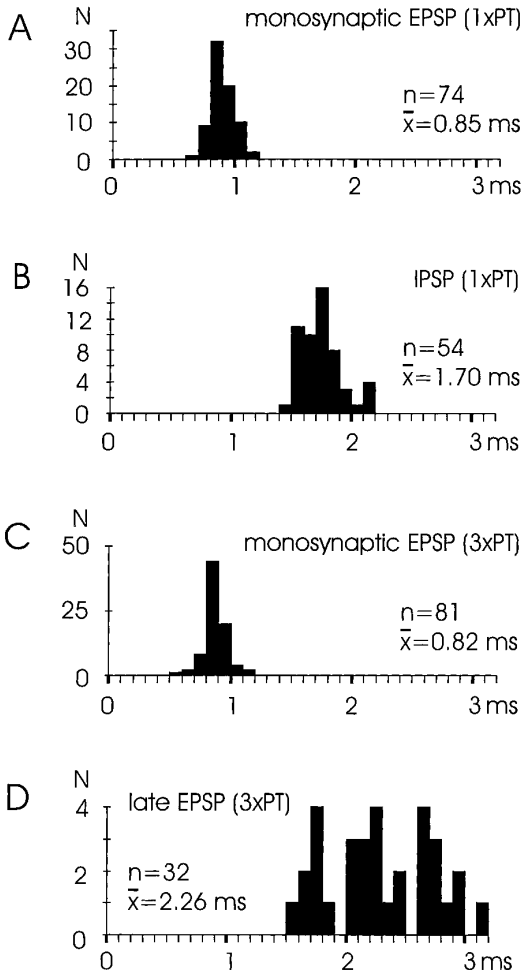

FIG. 6. Distribution of segmental latencies of postsynaptic potentials recorded in sampled motoneurons in response to PT stimulation at 200 μA. *A*: monosynaptic EPSP with single PT shock. *B*: inhibitory postsynaptic potential (IPSP) with single PT shock. *C*: monosynaptic EPSP evoked by 3rd of 3 PT shocks. *D*: late EPSP evoked by 3rd of 3 PT shocks (see text).

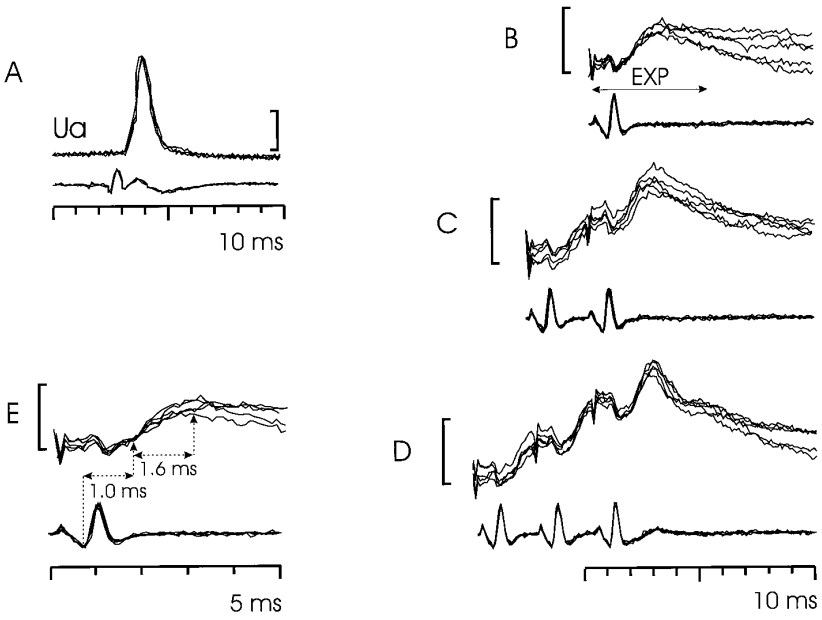

FIG. 5. Monosynaptic excitatory postsynaptic potential (EPSP) in ulnar motoneuron after PT stimulation. *A*: antidromic identification. *Top traces*: antidromic spike from Ua (5 sweeps superimposed). *Bottom traces*: cord dorsum recording. *B–E*: responses to PT stimulation at 200 μA. *Top traces*: monosynaptic EPSP. *Bottom traces*: cord dorsum volley. Responses are to single (*B*), 2 (*C*), and 3 (*D*) PT stimuli, at 300 Hz. Arrow in *B*: region shown at expanded time scale in *E*. This shows segmental latency of monosynaptic EPSP as 1.0 ms after arrival of corticospinal volley in surface recording. EPSP rise time: 1.6 ms. EPSP amplitude: 0.4 mV. Scale bars: 20 mV (*A*), 1 mV (*B–D*).

Monosynaptic EPSPs were only weakly facilitated by three PT shocks (Fig. 5*D*). The segmental delay was unchanged (see Fig. 6*C*). In many motoneurons the EPSP after the third shock was obscured by a large IPSP or a late EPSP; in the 12 motoneurons where this was not the case, the mean amplitude of the EPSP after the third shock was 1.0 ± 0.42 mV, only a modest increase above that obtained with a single shock (0.55 ± 0.36 mV).

CORTICOSPINAL ORIGIN OF THE MONOSYNAPTIC EPSP. This was confirmed in two monkeys by examining the effects of withdrawing the stimulating electrode from the medullary PT (see Fig. 9). With the electrode only 1 mm above the optimal site, there was a sharp reduction in both the size of the corticospinal volley (Fig. 9*C*) and the monosynaptic EPSP recorded from an Ra motoneuron (Fig. 9*A*). At 1.5 mm above both volley and EPSP disappeared; they returned when the electrode was lowered to the optimal site (Fig. 9, control 2).

MONOSYNAPTIC EPSP WITH DISYNAPTIC IPSP. This type of response, obtained in 39 of 93 motoneurons, is illustrated in Fig. 10. In this Ma motoneuron, the early EPSP (segmental latency 0.8 ms) had a slow rise time (Fig. 10*E*), and an IPSP began at 2.1 ms. This IPSP was powerfully facilitated by repetitive PT stimulation (Fig. 10*D*), and this was the case in most motoneurons. In some cases an IPSP was clearly evident on the third shock, but not on the first (see Fig. 5*D*).

PURE IPSPs. Fifteen motoneurons, mainly Ma and DR, responded with an IPSP uncontaminated by any excitatory effects. The mean segmental latency of these IPSPs was 1.70 ± 0.17 ms, and the earliest effects were probably within the disynaptic range (1.1–1.6 ms, see Fig. 6*B* and DISCUSSION). There was a wide range of amplitudes, from 0.2 to 6 mV (mean 1.94 ± 1.78 mV).

LATE EPSP WITH REPETITIVE STIMULATION. A striking feature of many motoneurons (33 of 93, see Table 1) was the appearance of a late EPSP after the second or third PT shock. An example is shown in Fig. 11. This Ra motoneuron showed no response to either a single or double PT shocks,

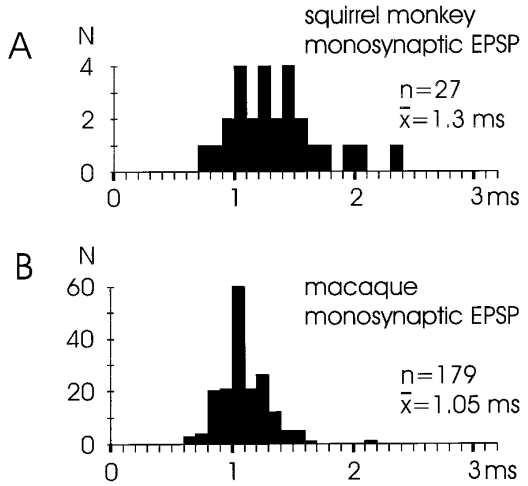

FIG. 7. Distribution of rise times of monosynaptic EPSPs in hand and forearm motoneurons. *A*: monosynaptic EPSP with single PT shock at 200 μA in squirrel monkey. *B*: for comparison, monosynaptic EPSP with single PT shock at 200 μA in macaque monkey (data from Fritz et al. 1985). All motoneurons were identified from Ua, Ma, or DR nerve.

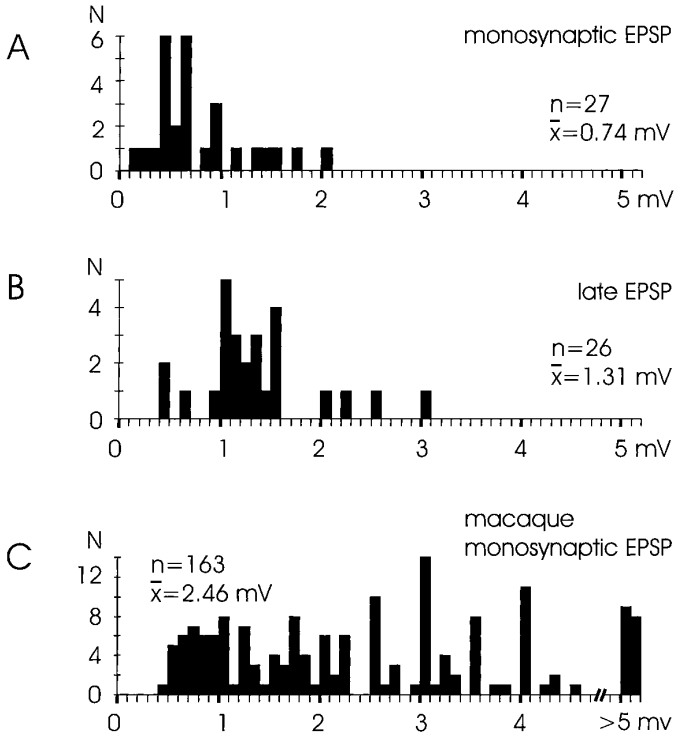

FIG. 8. Distribution of amplitude of monosynaptic EPSPs in forearm and hand motoneurons [i.e., radial (Ra) motoneurons excluded]. *A*: monosynaptic EPSP with single PT shock at 200 μA in squirrel monkey. *B*: late EPSP after 3 shocks at 200 μA in squirrel monkey. *C*: for comparison, monosynaptic EPSP with single shock 200 μA in macaque monkey (data from Fritz et al. 1985).

but responded with a clear, late EPSP on the third shock (Fig. 11*D*). This behavior, and its long segmental latency (1.8 ms, see expanded portion in Fig. 11*E*), both suggest an oligosynaptic linkage. Three further examples are shown in Fig. 12, *A–C;* in every case there was either a very weak or no response to a single PT shock (Fig. 12, *left*) and a pronounced late EPSP with three shocks (Fig. 12, *right*). As shown in Fig. 6*D*, these late EPSPs had a wide range of segmental latencies (1.5–3.6 ms, mean 2.26 ± 0.48 ms, $n = 32$). Their amplitude ranged from 0.4 to 3.0 mV (mean 1.31 mV ± 0.59 mV, $n = 26$, see Fig. 8*B*). In those motoneurons responding to repetitive PT stimulation with both a monosynaptic and a late EPSP, the amplitude of the latter was significantly larger than that of the monosynaptic EPSP, measured after the third shock ($P < 0.01$, $n = 18$, Student's *t*-test).

DISCUSSION

The present study demonstrates for the first time, that the squirrel monkey does have some rather weak, direct monosynaptic connections to hand and forearm motoneurons. The postsynaptic responses of these motoneurons to corticospinal inputs help to explain the production of EMG responses in hand muscles obtained with activation of the corticospinal system directly by PT stimulation, and noninvasively by TMS over the motor cortex. The results throw new light on the relationship between CM connections and the capacity for RIFM in different primate species. The re-

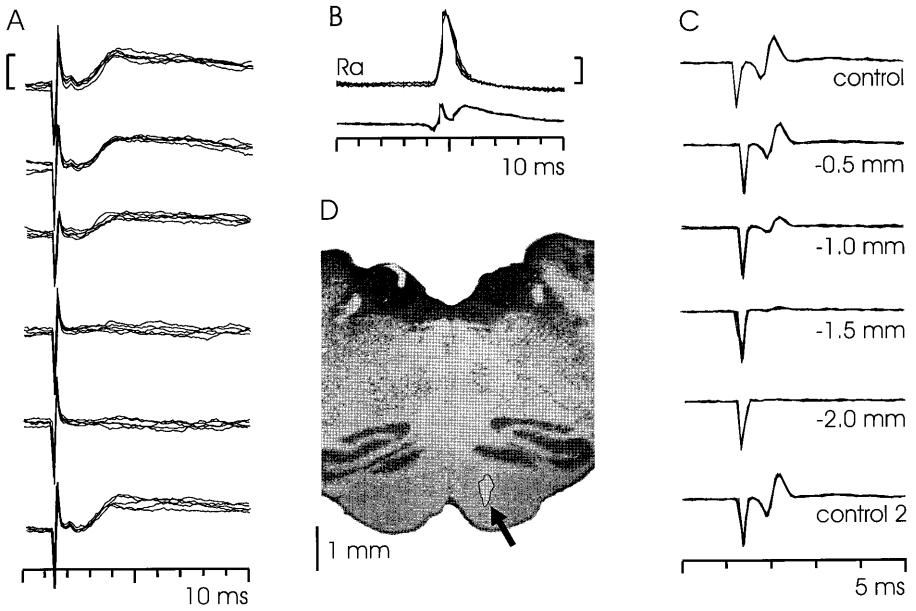

FIG. 9. Location of PT stimulation electrode and effect of withdrawal from tract. Intracellular recordings were made from a radial motoneuron (*A*) and from cord dorsum (*C*) in response to 200-μA PT stimulation. At optimal location of PT electrode (control), this evoked large corticospinal volley (*C, top trace*) and monosynaptic EPSP (amplitude 1.5 mV, *A, top trace*). With dorsal movement of electrode (in steps of 0.5 mm), both volley and EPSP decreased in amplitude, and both disappeared when electrode was 1.5 mm above initial position. *Bottom traces*: return of responses when electrode was again lowered to initial position (control 2). *B*: antidromic identification of motoneuron from Ra. *D*: cross section of medulla. Lesion is clearly visible in center of right pyramid (outline and arrow). Scale bars: 1 mV (*A*), 20 mV (*B*).

sults also help in the interpretation of short-latency EMG responses elicited by TMS.

Corticospinal conduction velocity in the squirrel monkey and other primates

The electrophysiological findings indicate that the fastest corticospinal axons in the adult squirrel monkey conducted at 48.6 m/s (mean from 3 monkeys). This is substantially slower than in the macaque, where, in the adult, the fastest axons conduct at velocities of 80 m/s over the same part of the corticospinal tract (Olivier et al. 1997). These values are in keeping with the observations of Towe (1973) relating the diameter of PT axons to body size: the large macaque has faster axons than the small squirrel monkey. Interestingly, the arrival time of the corticospinal volley at the lower cervical cord is similar in the two species, despite the difference in conduction distance (see volley superimposition in Fig. 13). Verhaart (1966) reported that the largest corticospinal axons found in the pyramid of the squirrel monkey had a diameter of 7 μm; this compares with 12 μm in the macaque (Haggqvist 1937; J. Armand, S. A. Edgley, E. Olivier, and R. N. Lemon, unpublished observations).

Postsynaptic responses of arm and hand motoneurons to PT stimulation

Postsynaptic responses to PT stimulation consisted of an early EPSP, an EPSP followed by an IPSP, or a ''pure'' IPSP. The early EPSPs had segmental latencies that were generally $<$1.0 ms, confirming their monosynaptic origin (see Phillips and Porter 1964). In general, the responses resembled those observed in other primates (Fritz et al. 1985; Landgren et al. 1962; Phillips and Porter 1977; Porter and Lemon 1993; Preston and Whitlock 1961), although by comparison with those in the macaque monkey, the EPSPs were

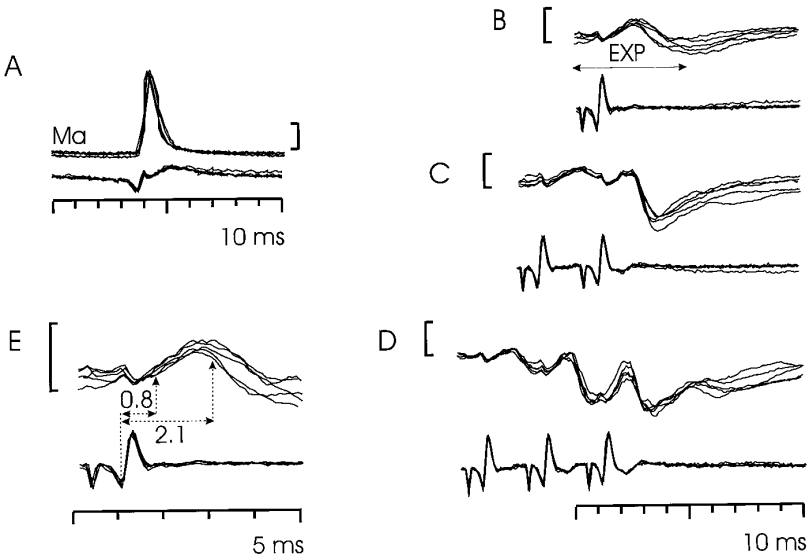

FIG. 10. Monosynaptic EPSP and oligosynaptic IPSP in a median motoneuron in response to PT stimulation. *A*: antidromic identification from Ma. *B*: response to single PT stimulus at 200 μA consisted of monosynaptic EPSP followed by IPSP. *C* and *D*: response to 2 and 3 PT stimuli at 200 μA. Note strong facilitation of IPSP. *E*: region marked in *B* shown at expanded time scale. Segmental latencies of monosynaptic EPSP and IPSP were 0.8 and 2.1 ms, respectively. Scale bars: 20 mV (*A*), 1 mV (*B–E*).

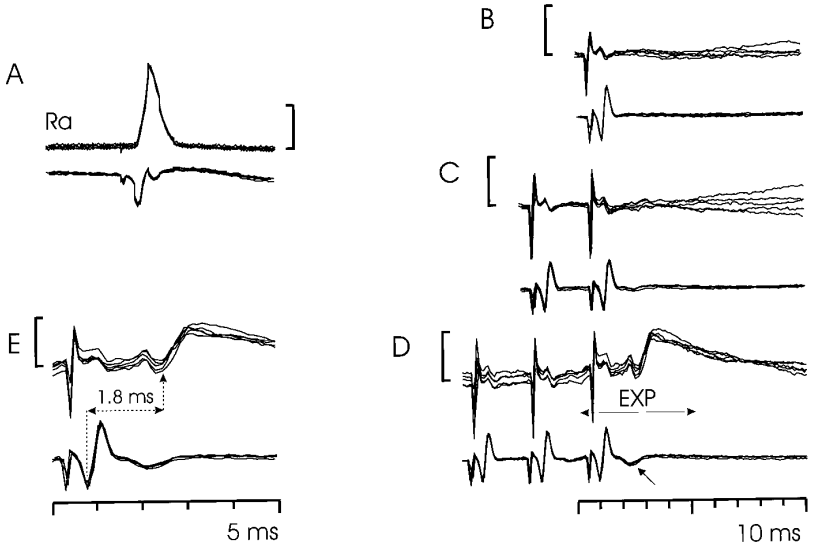

FIG. 11. Late EPSP in a radial motoneuron after repetitive PT stimulation. *A*: antidromic identification from Ra. Stimulation of PT at 200 μA with either 1 (*B*) or 2 (*C*) shocks produced no response, whereas 3 shocks produced large, late EPSP (shown in *D*). *E*: expanded time scale of *D* shows segmental latency of late EPSP as 1.8 ms. Note appearance of late potential in cord dorsum recording (arrow) after 3rd shock. Scale bars: 20 mV (*A*), 1 mV (*B–E*).

small and had a much wider range of rise times. The mean amplitude of monosynaptic EPSPs in this study was only 0.74 mV; this value applies to all Ma, Ua, and DR motoneurons with an EPSP uncontaminated by an IPSP (n = 27). This compares with the mean EPSP amplitude for macaque motoneurons supplying intrinsic hand muscles (3.15 mV), and forearm muscles supplied by the Ma (1.9 mV) and by the DR (1.55 mV). These data are from Fritz et al. (1985) and were recorded in macaques under identical conditions of anesthesia, etc. Interestingly, only 4 of 93 squirrel monkey motoneurons (2 Ma and 2 Ua motoneurons) showed no response at all to single-shock PT stimulation (see Table 1); hand and forearm motoneurons without a monosynaptic EPSP from the PT were also very rare (4 of 209) in the macaque motoneurons recorded by Fritz et al. (1985).

PT stimulation produced inhibitory effects in many motoneurons either as pure IPSPs or as an EPSP/IPSP sequence; similar observations have been made in the macaque (Fritz et al. 1985; Maier et al. 1996). On the basis of their segmental latencies (Fig. 6*B*), most of the IPSPs would appear to have a disynaptic origin; some may be mediated by Ia reciprocal inhibitory interneurons, as has been shown in the macaque by Jankowska et al. (1976).

A striking feature of the responses in the squirrel monkey was the presence in some motoneurons of longer-latency EPSPs after repetitive PT stimulation (Figs. 8 and 9). These EPSPs had segmental delays of 1.5–3.1 ms, well outside the range for a monosynaptic response. The most likely origin of these disynaptic or oligosynaptic responses is via excitatory interneurons at the segmental level, or relayed through propriospinal neurons in more rostral spinal segments (the C_3–C_4 propriospinal system) (Alstermark and Lundberg 1992). These mechanisms are well established in the cat, which is known to lack any direct CM connections (Baldissera et al. 1981). It is interesting that in many of the cord dorsum recordings a late potential was observed after the third PT

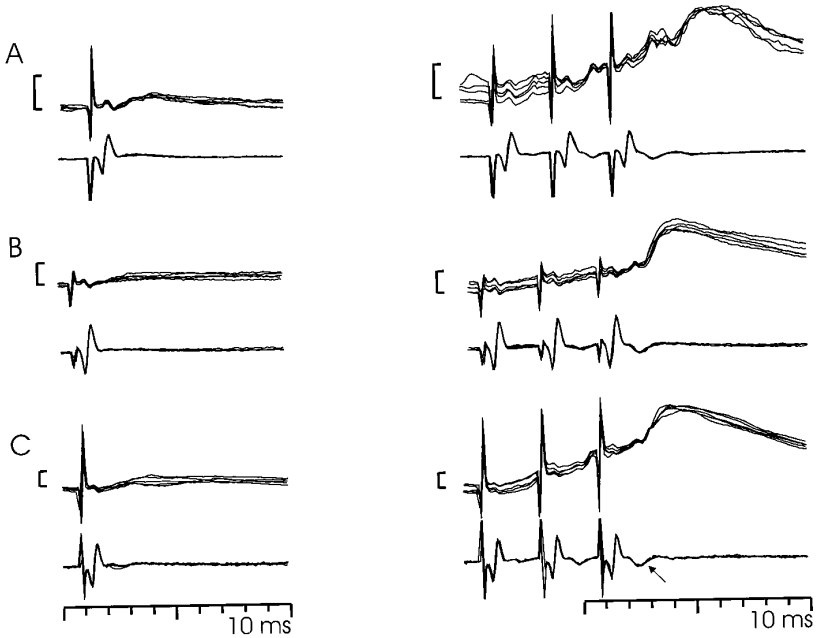

FIG. 12. Three motoneurons (*A–C*), recorded in different squirrel monkeys, with little or no detectable response to single PT shocks at 200 μA (*left*) but with large, late EPSP after 3 shocks (*right*). *A*: ulnar motoneuron, late EPSP amplitude 1.3 mV. *B*: median motoneuron (2.0 mV). *C*: radial motoneuron (2.5 mV). Note progessive increase in late potential (arrow) in cord dorsum recording with number of stimuli in each case. Scale bars: 1 mV.

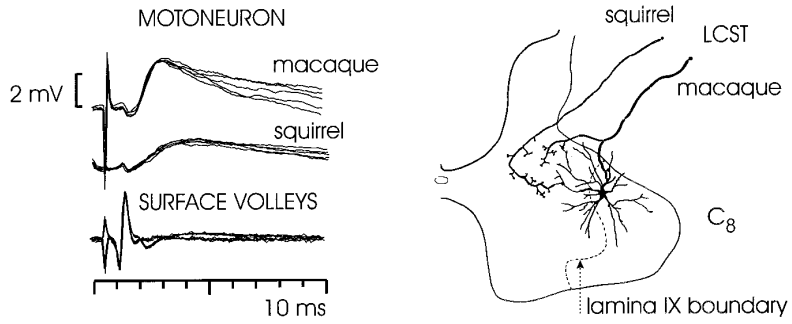

FIG. 13. Hypothetical explanation of more extreme differences in amplitude and rise time of monosynaptic EPSPs in squirrel and macaque monkeys. *Left*: typical intracellular recordings from hand motoneurons in the 2 species. EPSPs are responses to single 200-μA PT stimulus and are shown together with superimposed corticospinal volleys in cord dorsum recordings. EPSP in macaque (Maier, Kirkwood, and Lemon, unpublished observations) is larger and more quickly rising than that in squirrel monkey. Diagram suggests that this is because corticospinal terminals in squirrel monkey are distributed mostly to more distal regions of motoneuron's dendritic tree, located beyond boundary of Rexed's lamina IX (– – –), compared with more numerous and more proximal location of terminals in macaque. Note that the 2 surface-recorded corticospinal volleys superimpose exactly, and this could occur only if longer conduction time due to slower-conducting fibers in squirrel compared with macaque monkey were matched by shorter conduction distance in squirrel monkey.

shock that was not seen after a single shock (see arrows in Figs. 11*D* and 12). This late potential is reminiscent of that observed in the cat, where it is thought to reflect propriospinal activation of motoneurons (Illert et al. 1974). In contrast, PT stimulation in the macaque monkey, in which CM connections are well developed, rarely evokes late EPSPs (Maier et al. 1996; Porter and Lemon 1993, p. 136–137); at present, direct evidence for significant propriospinal transmission of corticospinal excitation is lacking in the macaque.

EMG responses to PT stimulation

EMG responses were obtained in monkeys under light sedation with ketamine, and with some background EMG activity present. Single PT stimuli produced EMG responses in hand muscles with a sharp onset. With repetitive stimulation, there was a powerful facilitation of the EMG response on the second and third shock (Fig. 4*B*), and this suggests that many motoneurons required temporal summation and facilitation of the descending inputs before they could be brought to discharge. It is important to note that, as in the macaque (Fritz et al. 1985; Shapovalov 1975), the monosynaptic EPSP in motoneurons supplying distal muscles was only weakly facilitated by repetitive PT stimulation (see Fig. 5), and therefore the facilitation of EMG may have involved a contribution from the late EPSPs evoked by the second and third PT stimulus. Thus the *earliest component* of the EMG response to each successive shock probably reflects monosynaptic action; the onset of the responses to the second and third responses, relative to the timing of their respective PT stimuli, was only slightly shorter (by 0.4 and 0.8 ms for the 2nd and 3rd response, respectively) than that to the first shock (see Fig. 4*D*). These differences could reflect motoneurons firing earlier in the rising phase of the monosynaptic EPSP, which appears to have a rather long rise time, although the contribution of disynaptic excitation, facilitated by the later shocks, cannot be excluded. Indeed, much of the *later component* of the responses that were facilitated probably resulted from di- and oligosynaptic actions.

TMS and CM connections

The results show that TMS of the squirrel monkey cortex can activate the corticospinal system directly. It was possible to record a large volley from the PT electrodes that had a latency consistent with direct activation within the cortex, similar to observations made in the macaque monkey (Baker et al. 1994). The same volley was recorded from the DLF at spinal levels, and here it could be completely collided from the PT, confirming that it was conveyed by corticospinal axons. It might be expected that stimulating the head of such a small animal with a relatively large TMS coil would result in activation of descending motor pathways originating in the brain stem, as has been claimed to occur in the cat (Haghighi et al. 1995). However, our results show that the generation of EMG responses required the coil to be positioned over the motor cortex, and that the earliest descending volley excited by TMS could be completely collided from the PT, identifying it as corticospinal. None of the EMG or motoneuron responses occurred at latencies shorter than could be explained by the action of the corticospinal D volley, as would have been the case had TMS directly activated brain stem structures.

Full details of all latency measurements made in this study are given in Table 2. TMS evoked short-latency EMG responses in several upper limb muscles; responses were generally more variable than those to PT stimulation (Fig. 2) and, in the thenar muscles, the shortest-latency responses to TMS (8.0 ms, see Table 2*H*) were ~1 ms longer than those to PT (Table 2*I*). Given that TMS activates the corticospinal neurons at the cortical level (see above), most of this difference can be accounted for by the additional conduction time from cortex to PT, given by the onset of the antidromic cortical volley (0.7 ms, Table 2*B*).

The central delay for the EMG response to TMS was estimated to be 3.7 ms by subtracting the PMCT estimate (4.3 ms, Table 2*J*) from latency of EMG response to TMS (8.0 ms, Table 2*H*). This value can then be compared with a direct estimate of the central delay by adding up the different components that contribute to it: the conduction time from motor cortex to the C_8–T_1 segment (1.45 ms, Table 2*A*)

and the segmental delay (0.85 ms, Table 2*E*). This estimate, based on measurements in a single monkey, comes to 2.3 ms, significantly shorter than the indirect estimate of 3.7. Another direct estimate of the central delay, this time in three monkeys, can be made by adding the segmental delay (0.85 ms) to the sum of the latencies of the antidromic (0.7 ms, Table 2*B*) and orthodromic (0.8 ms, Table 2*C*) volleys evoked from the PT, giving a total of 2.35 ms, similar to the other direct estimate but still significantly shorter than the indirect estimate.

Two factors probably contribute to the differences between direct and indirect estimates of the central delay: first, motoneurons may not discharge at the onset of the monosynaptic EPSPs evoked in them by the TMS-generated corticospinal volley. These EPSPs are likely to have an even longer rise time than that from the PT (mean 1.3 ms, Table 2*F*), because the volley is more dispersed than that from the PT (compare Fig. 1, *B* and *C*). This is probably because activation of corticospinal neurons is less synchronous with TMS than with PT stimulation (Edgley et al. 1997). There is thus the possibility that motoneurons do not discharge until late in the rising phase of the monosynaptic EPSP, or until onset of di- or oligosynaptic EPSPs. A second factor may be that we have underestimated the PMCT, probably because the F wave responses (Fig. 3) are from the fastest-conducting motor units, whereas the *earliest* responses to TMS are from the lowest-threshold, more slowly conducting motor units (Olivier, Baker, and Lemon, unpublished observations).

The particular sensitivity of corticospinal transmission in the squirrel monkey to repetitive activation should make it susceptible to TMS, which is well known to generate multiple descending corticospinal volleys (Burke et al. 1993; Day et al. 1987; Edgley et al. 1990), and direct evidence for such volleys was observed in this study (see Fig. 1*A*). Finally, the thresholds for EMG responses (mean 43%) were generally rather higher than in the macaque investigated under similar conditions (for the macaque, with the butterfly coil, thresholds are typically 15–25%). This might reflect differences in the susceptibility of corticospinal neurons to TMS, or the efficacy of the resulting volley at the spinal level, or both (see Olivier et al. 1997).

TABLE 2. *Summary of mean conduction times in the squirrel monkey*

A. Corticospinal volley: motor cortex to C_8 (evoked by TMS)	1.45 ms
B. Corticospinal volley: antidromic (PT to motor cortex)	0.70 ms
C. Corticospinal volley: orthodromic (PT to C_8–T_1)	0.80 ms
D. Estimated total volley time (motor cortex to C_8/T_1; $B + C$)	1.50 ms
E. Segmental delay of PT-evoked EPSP	0.85 ms
F. Rise time of PT-evoked EPSP	1.30 ms
G. Absolute latency to onset of PT-evoked EPSP	1.55 ms
H. Earliest EMG response to TMS (thenar)	8.00 ms
I. Earliest EMG response to PT (thenar)	6.90 ms
J. PMCT estimate (from F wave)	4.30 ms
K. Central delay estimate ($H - J$)	3.70 ms

TMS, transcranial magnetic stimulation; EPSP, excitatory postsynaptic potential; EMG, electromyogram; PMCT, peripheral motor conduction time; for other abbreviations, see Table 1.

Pattern of CM connections in different primates

Anatomic studies of the squirrel monkey have shown the existence of some sparse corticospinal projections to lamina IX of the lower cervical segments. Bortoff and Strick (1993) found that, at C_8 and T_1, corticospinal projections covered 5 and 1%, respectively, of the cross-sectional area of lamina IX. The sparsity of corticospinal projections in the ventral horn of the cervical segments of the squirrel monkey was also noted by Harting and Noback (1970) and Tigges et al. (1979). Interestingly, Harting and Noback (1970) stressed that these corticospinal terminations were ''limited to the most dorsolateral portion of lamina IX,'' precisely where cell bodies of motoneurons innervating hand muscles are expected to be located (cf. Jenny and Inukai 1983).

Corticospinal projections to lamina IX are much more extensive in both the cebus monkey (86–93% of lamina IX at C_8–T_1) (Bortoff and Strick 1993) and in the macaque, where Armand et al. (1997) found that such projections occupied all of the hand muscle motor nuclei in the C_7, C_8, and T_1 segments. Armand et al. (1997) found that a more sensitive measure of the strength of the corticospinal projection was the area of hand muscle motor nuclei that was occupied by the densest 40% of the projections. In the adult macaque, 20% of the area occupied by these motor nuclei in the caudal C_7 segment was occupied by these strong projections, rising to 81% in caudal T_1. This pronounced caudorostral gradient, which was also reported by Dum and Strick (1996), may reflect the heavier projection to the motoneurons of the intrinsic hand muscles, which are concentrated in the most caudal cervical segments (Jenny and Inukai 1983).

The paucity of corticospinal terminations in lamina IX of the squirrel monkey does not rule out the possibility that some corticospinal neurons could have direct synaptic connections on the dendrites of motoneurons that extend beyond the boundary of lamina IX (Lawrence et al. 1985; Rose and Richmond 1981). Indeed, as indicated in the schematic diagram shown in Fig. 13, we suggest that in the squirrel monkey the small amplitude and slow rise times of some CM EPSPs are just what would be expected from such CM connections. This organization would be consistent with the anatomic data of Bortoff and Strick (1993). We suggest that the larger, faster CM EPSPs, rarely seen in the squirrel monkey but common in the macaque, would be mediated by collaterals synapsing on more proximal dendrites and possibly at multiple sites (Porter and Lemon 1993).

CM connections and RIFM

It is important to examine the significance of the present findings for the hypothesis that CM projections are essential for the capacity to perform RIFM (Bernhard et al. 1953; Kuypers 1962; Lawrence and Hopkins 1976; see Porter and Lemon 1993). The squirrel monkey has a dexterity index of 5, can use only whole hand control (Costello and Fragaszy 1988; Fragazy 1983), and does not manipulate objects within its grasp. This contrasts with another New World monkey, the cebus or capuchin monkey, which can grip small objects between the sides of the digits (Costello and Fragazy 1988). Although it does not possess a truly opposable thumb, the cebus monkey can make a precision grip

between index and thumb and is an expert tool user (Antinucci and Visalberghi 1986). The Old World macaque monkey (dexterity index 6) has a truly opposable thumb, and RIFM are very well developed (Hefner and Masterton 1975, 1983). Thus, both in terms of dexterity and the extent of CM connections, the squirrel monkey would appear to lie in an intermediate position between dexterous primates such as cebus and macaque and nonprimates such as the cat (dexterity index 2), in which direct CM connections are absent (Armand 1982; Baldissera et al. 1981) and independent digit movement is very restricted (Caliebe et al. 1991). Nonmonosynaptic cortical control of forelimb motoneurons, mediated by propriospinal neurons, is well developed in the cat (Alstermark and Lundberg 1992); the later EPSPs seen in some motoneurons with repetitive stimulation in the squirrel monkey may be mediated by a similar mechanism.

Because the squirrel monkey has some CM connections, but clearly lacks RIFM, it can no longer be argued that the presence of these connections alone is sufficient to permit performance of RIFM. We suggest that cortical control of RIFM is mediated by the large, fast-rising EPSPs in hand motoneurons that have been observed in the more dexterous Old World baboon (Landgren et al. 1962; Phillips and Porter 1964) and macaque monkey (Fritz et al. 1985; Porter and Lemon 1993), and that these EPSPs reflect the much denser synaptic termination of corticospinal fibers within lamina IX that are present in the same species (Armand et al. 1997; Olivier et al. 1997). The selective and focused nature of the projection from individual CM neurons has been shown to be important for fractionating the pattern of muscles activity during performance of RIFM (Bennett and Lemon 1994, 1996).

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