Lack of Monosynaptic Corticomotoneuronal EPSPs in Rats: Disynaptic EPSPs Mediated Via Reticulospinal Neurons and Polysynaptic EPSPs Via Segmental Interneurons

B. Alstermark, J. Ogawa, and T. Isa
1Department of Integrative Medical Biology, Section of Physiology, Umeå University, S-901 87 Umeå, Sweden; 2Department of Orthopaedic Surgery, Kyorin University School of Medicine, Mitaka-shi, 181-8611, Japan; and 3Department of Integrative Physiology, National Institute for Physiological Sciences, Myodaiji, 444-8585 Okazaki, Japan

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INTRODUCTION

The monosynaptic corticomotoneuronal (CM) excitation has for long time been considered to be decisive in the control of independent digit movements of the hand in primates and man, and it has been proposed that such connections are the basis for the ability to make independent digit movements in primates and man, it has been inferred that the monosynaptic CM connection in the rat is likewise important for skilled prehension. Comparison of intra- and extracellular recordings from forelimb motoneurones in anesthetized rats, revealed no monosynaptic CM excitatory postsynaptic potentials (EPSPs). The fastest descending excitation in forelimb motoneurones was disynaptically mediated via a corticoreticulospinal pathway and slowly conducted excitation via corticospinal fibers and segmental interneurons. The findings stress the importance of di- and trisynaptic excitatory corticofugal pathways to forelimb motoneurones in the control of skilful digit movements.

Alstermark, B., J. Ogawa, and T. Isa. Lack of monosynaptic corticoreticulospinal EPSPs in rats: disynaptic EPSPs mediated via reticulospinal neurons and polysynaptic EPSPs via segmental internurons. J Neurophysiol 91: 1832–1839, 2004. First published November 5, 2003; 10.1152/jn.00820.2003. In the rat, some findings have been taken to suggest the existence of monosynaptic corticomotoneuronal (CM) connections. Because this connection is believed to be largely responsible for the ability to make independent digit movements in primates and man, it has been inferred that the monosynaptic CM connection in the cat is likewise important for skilled prehension. Comparison of intra- and extracellular recordings from forelimb motoneurons in anesthetized rats, revealed no monosynaptic CM excitatory postsynaptic potentials (EPSPs). The fastest descending excitation in forelimb motoneurones was disynaptically mediated via a corticoreticulospinal pathway and slowly conducted excitation via corticospinal fibers and segmental interneurons. The findings stress the importance of di- and trisynaptic excitatory corticofugal pathways to forelimb motoneurones in the control of skilful digit movements.

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fast corticoreticulospinal (CRS) pathway. Long-latency di- and trisynaptic excitation (mainly trisynaptic) of motoneurons is mediated by segmental interneurons in C₆–C₈ segments.

METHODS

Preparation

The results have been obtained from 42 rats (42 Wistar rats; 35 females and 7 males) with averaged body weights of 258 g (182–495) and age of 5 mo (4–12). The animals were first anesthetized with a mixture of fentanyl and midazolam (2.8 ml/kg ip) and then by α-chloralose (60 mg/kg iv). Atropin (0.5 mg), dexamethasone (2 mg), and penicillin (0.5 ml) was always given (intramuscular) just after anesthesia. Occasionally strychnine and pentobarbital sodium (Nembutal) was added in doses of 1 mg/kg and ephedrine in doses of 1 mg (intravenous). Pneumothorax and artificial respiration were always performed, the animals being immobilized with gallamine triethiodide (Flaxedil; 12 mg/h). Rectal temperature was maintained at 36–38°C, and the heart rate and expiratory CO₂ were monitored continuously and kept within a physiological range. This investigation was approved by the ethical committee of Umeå University.

A laminectomy was performed that exposed spinal segments C₁–Th₁. The deep radial (DR) and superficial radial (SR) nerves were dissected and mounted on bipolar stimulating electrodes. The DR and SR nerves were used for guidance to check the physiological integrity of the spinal cord after the various lesions. A posterior craniotomy was performed exposing the cerebellum and the caudal brain stem. A series of spinal cord lesions were made to selectively interrupt transmission of different descending tracts as will be explained in more detail in the result section. The dorsal column (DC) was transected at the C₅ level in six rats and at C₂ in nine rats to interrupt the transmission of the corticospinal fibers. A hemisection (without the DC) was made ipsilateral to the recording site at C₂ in nine rats to interrupt transmission of bulbospinal axons and at C₁ in two rats to interrupt transmission of bulbospinal and propriospinal axons. After the C₂ hemisection a C₂ DC transection was made in seven rats to restrict corticospinal input to neurons in the C₁–C₄ segments (see RESULTS). A contralateral hemisection was made at C₂ in one rat. The DC and dorsal part of the lateral funiculus (DLF) were transected together at C₄ in one rat and in C₃ in one rat. All transections were made under microscope using watch makers forceps and Neutral red.

RESULTS

Corticospinal volley and field potential

Figure 1A shows recording from the cord dorsum of the descending corticospinal volley evoked by electrical stimulation in the contralateral pyramid. Recording was made with a silver ball electrode positioned on the dorsal column in the

Stimulation and recording

Corticofugal fibers were stimulated in the contralateral pyramid at 0.5 mm lateral to the midline, 2 mm rostral to the obex level with a rostral angle of 30° using tungsten electrodes (100 kΩ impedance, uninsulated tips of 10 μm diameter). The threshold using 0.1-ms duration pulses was always <10 μA (cathodal) and usually ~5 μA. Optimal placement gave a descending volley that was maximal ~150 μA; 80% in size at 100 μA. A train of two to four stimuli given at 300 Hz and 20–200 μA was usually used. The number of stimuli of the train was always changed to ascertain which pulse was effective for evoking the synaptic effects. Recording of the descending volley was made from the surface of the DC, cord dorsum potential (CDP), in the middle part of the C₅–C₆ segments using a silver ball electrode. Recording was made in each segment for measurements of the conduction time of the corticospinal volley. During intracellular recording, the CDP was recorded in the same segment as the microelectrode. Intracellular records were obtained from 193 forelimb MNs in C₆–C₈ (MN5; 57 DR and 136 unidentified MNs in the same track) using borosilicate glass micro-electrodes, tip diameter ~1 μm and impedance of 3–6 MΩ, filled with 2 M-potassium citrate (pH 7.4) with a minimal membrane potential of ~40 mV. All signals were digitized, stored on hard disk (Digidata 1200, Axon Instruments, Foster City, CA) and analyzed off-line in Clampfit (Axon Instruments).

To calculate the conduction velocity of the descending volley, measurements of the distance was made in situ because we noticed that measurements made from fixed (4% buffered paraformaldehyde) tissue caused large errors due to differences in the amount of fixation. The location of stimulating and recording electrodes was verified and the extent of the lesion reconstructed from sections stained with Neutral red.

FIG. 1. Descending corticospinal volley and field potential. A: recordings made with a silver ball electrode on the dorsal column of the corticospinal volley and cord dorsum potential (CDP) in mid C₅–C₆ segments. The corticospinal fibers were stimulated electrically in the contralateral pyramid at a strength of 200 μA. — and □, latency measurement to the onset of the negative component N1 of the corticospinal volley; and ⋆ and ○, the latency to the peak of the negative component N2. B: extracellular recordings of field potentials evoked by pyramidal stimulation at 200 μA. The depths of recording is from the surface of the dorsal column. The angle of the electrode track was 6° lateral from the vertical line. C: latency of N1 and N2 as function of the conduction distance from the pyramidal stimulation to the segmental recording site; • and —, measurements for N1; ○ and ⋆, measurements for N2. Inset: the latencies of N2 vs. N1. The averaged arrival time at C₂/C₃ border is indicated by the red line for N1 and by the blue line for N2. D: transverse section from mid C₅ showing the electrode track used for the extracellular field recordings.
middle of the C2–C6 segments. Due to temporal dispersion, the volley became broader in shape in the caudal segments. To measure the conduction velocity of the fastest corticospinal fibers, the latency was measured from the onset of the stimulating pulse to the onset of the negativity (N1) of the descending volley as is indicated for the recording in C2. The latency for the slower corticospinal fibers was measured to the peak of the negativity (N2) of the descending volley. The peak of the negativity could only be seen down to C4 or C5 in some experiments due to the temporal dispersion at more caudal levels. In Fig. 1C is illustrated the latency for N1 (●) and N2 (○) as function of conduction distance. The inset diagram shows a high correlation of N1 versus N2 ($r = 0.96$). The conduction velocities ranged between 9.7 and 14.7 m/s [12.3 ± 1.8 (SD) m/s, $n = 7$ experiments] for N1 and 6.5 to 8.9 m/s for N2 (8.1 ± 0.9 m/s, $n = 6$ experiments). In Fig. 1C, the arrival on average of the corticospinal volley at the C7/C8 border is shown in red for the fastest corticospinal fibers and in blue for the slower fibers. It can be seen that on average there is a difference of ~1.3 ms.

The slow negative field potential that follows the volley is caused by the EPSPs evoked from the corticospinal fibers. By recording the extracellular field potentials as shown in Fig. 1B from mid C7, we tried to localize the termination of the corticospinal fibers in the forelimb segments. The recording track passed through the dorsal horn, lateral part of the intermediate layers and medially in the motor nuclei (Fig. 1D). A small negative monosynaptic field potential, evoked by a single pyramidal stimulation, appeared at depth 0.2 mm from the surface and became maximal in amplitude at around depth 0.8 mm as shown in Fig. 1B. At depth 1.2 mm, which corresponds to the dorsal part of the motor nuclei, the pyramidial field potential reversed to a positive field potential. This is in good agreement with the anatomy of the corticospinal termination (Casale et al. 1988; Liang et al. 1991). Positive monosynaptic pyramidial field potentials were recorded at depths 1.2–2.0 mm. The threshold for eliciting the monosynaptic pyramidial field potential was sometimes as low as 10–20 µA. These results show that the major termination of the corticospinal fibers is in the intermediate layers and not in the motor nuclei.

Motoneuronal recordings

INTACT SPINAL CORD. Figure 2 (A and B) shows intracellular recordings from a DR motoneuron and the effect of pyramidal stimulation at 200 and 100 µA, respectively. Similar results were observed in the unidentified forelimb motoneurons. A single pyramidal stimulus evoked a small positive potential with the time course of a monosynaptic EPSP. Distinct disynaptic EPSPs appeared after the second and third pyramidal stimuli (red arrows). Threshold for eliciting the EPSPs was near 100 µA in this cell and usually between 50 and 100 µA. Note the clear temporal facilitation with 200 µA in (A) after the third stimuli and that the EPSP consisted of two peaks: one early and one late component. Dorsosventral tracking with the stimulating electrode revealed that the effects were evoked from the pyramid. In another MNs, the early EPSP was very small or absent, whereas the late EPSP was large and had a slow rise time. These late EPSPs were usually evoked already from the second stimulus but with clear facilitation by the third stimulus. In another DR motoneuron, shown in C, a single stimulus at 100 µA evoked a large positive potential (IC; top most traces). In Fig. 1B, it was shown that the negative pyramidial extracellular field reverse to a positive potential in the motor nuclei (i.e., at depths >1.2 mm). We compared the intracellular potential with the extracellular potential recorded just outside the motoneuron as shown in Fig. 2 (A and C; EC). The averaged intracellular and extracellular recordings (C; AV) are virtually identical. Other examples are shown in Figs. 4A and 5A, respectively. We have never observed monosynaptic EPSPs in 104 tested C6–C8 MNs (33 DR motoneurons and 71 unidentified forelimb motoneurons) that could not be explained by the extracellular field and did not show temporal facilitation. Thus, it is necessary to compare the intracellular and extracellular recordings if the extracellular fields evoked by the pyramidial stimulation are large.

The latencies of the pyramidial EPSPs are shown in the histogram, Fig. 2D. They are measured from the effective pyramidal stimulation (usually 2nd or 3rd). The arrival of the corticospinal volley in mid C6-C7 segments was 2.3 ± 0.15 (SD) ms for the fastest fibers ($n = 7$ experiments; red arrow) and 3.6 ± 0.45 ms ($n = 6$ experiments; blue arrow) for the slower fibers. The earliest pyramidial EPSPs had latencies of $0.45 \text{ms (2nd from top) and } 1.8 \text{ms (3rd from top)}$.
2.0 ms (1.8 ms in Fig. 4F), which is earlier than the arrival of the corticospinal volley in the forelimb segments. These results suggest another route for the fastest pyramidal excitation in forelimb MNs (see following text).

SPINAL CORD LESIONS. From studies in the cat we know that disynaptic pyramidal excitation in forelimb MNs can be mediated by C1–C4 PNs, segmental INs and reticulospinal neurons. To differentiate between these possibilities, we first made transection of the corticospinal tract in the dorsal column either in C3 or C2 or both. These lesions spared the reticulospinal pathway. In other experiments, we lesioned the reticulospinal pathways by a complete transection of the lateral and ventral funicules, which spared the corticospinal tract in the dorsal column. Histology of a C3 DC lesion and a C2 hemisection is shown in Fig. 5, E and F, respectively. Recording was made on the side ipsilateral to the lesion/s except for the hemisection made on the contralateral side in C2 as shown in Figs. 6, B and D.

PYRAMIDAL EXCITATION VIA RETICULOSPINAL NEURONS. Figure 3 summarizes the results after dorsal column transection in C5 (A and B) and/or after additional transection in C2 (C and D). Qualitatively similar results were obtained if the C2 corticospinal transection was made alone or after a preceding transection in C4. The experimental arrangement is shown schematically in Fig. 3E. After the C5 and/or C2 corticospinal transections, the latencies of EPSPs ranged between 1.8 and 3.0 ms as illustrated in the histogram in F. Note the fast rise of the EPSPs and the lack of EPSPs with latencies > 3.0 ms. The lesions in C3 and C2 completely abolished the direct corticospinal volley and negative cord dorsum potentials. However, as shown in Fig. 3D a synaptic volley (black arrow) was observed after the second and third pyramidal stimuli (averaged and amplified trace shown below). This volley arrived in C6–C7 ~ 1.5 ms after the third pyramidal stimulus. Measurement made from this volley showed EPSPs with minimal latencies in a monosynaptic range (0.3–0.9 ms) from 1.8 to 2.4 ms. The later EPSPs from 2.4 to 3.0 ms could thus have been disynaptically mediated relative to the synaptic volley. Because the first intercalated neuron must be located rostral to the C1–C2 level, it is suggested that the fastest pyramidal EPSPs are disynaptically mediated via reticulospinal neurons with axons projecting monosynaptically to forelimb MNs (for exclusion of other brain stem systems, cf. DISCUSSION).

PYRAMIDAL EXCITATION VIA SPINAL CORD INS. The result of transecting the CRS pathway in C2 is shown in Fig. 4 (A–C). A schematic diagram of the experiment is shown in E. A single pyramidal stimulation evoked no EPSP as shown in Fig. 4A by comparing the intra- (top) and extracellular (bottom) records (see preceding text). EPSPs with long latencies, >3.2–5.2 ms (Fig. 4F), and slow rising phase were observed after the second and third stimuli as shown in Fig. 4, B and C, respectively. The large positive potential in the cord dorsum after the third stimulus was generated by an extracellular field in the motor nucleus as can be seen in the extracellular record (bottom). The field was larger than usual because strychnine had been given prior to recording. Taking the arrival time of the corticospinal volley into account (cf. preceding text), these results suggest that EPSPs with latencies starting from 3.2 to 5.0 ms could have been disynaptically mediated via the fastest and slower corticospinal fibers and EPSPs with latencies >5.0 ms could be tri- and polysynaptically mediated. It should be emphasized that EPSPs with latencies >5.0 ms was the most common finding after hemisection sparing the dorsal column (-DC) in C2 and/or C5.

PYRAMIDAL EXCITATION VIA C1–C4 PNS. To differentiate between effects possibly mediated via C1–C4 PNs and/or INs in the forelimb segments (below C5; denoted as segmental INs), we aimed at making lesions which spared the corticospinal input to either the C1–C4 segments or the segmental segments C6 and caudally. Transection of the cortico-bulbospinal paths in C2 was first made to ensure that pyramidal excitation could be evoked as shown above. We then added a corticospinal transection in C4 as illustrated schematically in Fig. 4E. The only spared descending system to the forelimb segments on the ipsilateral side would be the C1–C4 PNs. In two experiments, we also added strychnine to reduce glycinergic inhibition and...
increase the excitability of synaptic transmission, but without any effect on EPSPs or fields. Intracellular recording from a DR motoneuron, after injection of strychnine, showed that no synaptic response could be evoked from the pyramid after the combined lesions in C2 and C5 (Fig. 4D). Similar results were found in 14 MNs. We also recorded extracellularly, and it can be seen in Fig. 4D that also the negative field potential evoked by pyramidal stimulation was abolished by the combined C2 and C5 lesions. This finding was confirmed in seven experiments. These results suggest that C2–C4 PNs in the rat do not mediate disynaptic pyramidal excitation in forelimb MNs in contrast to previous findings in the cat and monkey (Alstermark and Isa 2002; Alstermark et al. 1999; Illert et al. 1977). However, this finding does not exclude trisynaptic pyramidal excitation to forelimb motoneurons via C3–C4 PNs (see Discussion and Fig. 7).

**Pyramidal excitation via segmental INs.** After transecting the CRS paths and propriospinal axons in C6, the only remaining descending ipsilateral input to the forelimb segments would be from corticospinal fibers to INs in the more caudal forelimb segments as outlined schematically in Fig. 5D. After this transection, pyramidal EPSPs could still be evoked and they had similar shapes and latencies (Fig. 5, A–C) as after a corresponding transection in C2 (Fig. 4, A–C). These findings suggest that disynaptic and trisynaptic pyramidal excitation in forelimb MNs can be mediated via segmental C6–C8 INs. Latencies of EPSPs are shown in Fig. 4F and were similar as after C2 hemisection (-DC).

**Axonal location of CRS pathway.** To further study the axonal location of the fast disynaptic excitatory CRS pathway, we added a transection of the dorsal part of the lateral funiculus after the C2 dorsal column transection because a minor portion of the corticospinal tract is located here. As shown in Fig. 6A, distinct disynaptic EPSPs could still be evoked. This result suggests that the reticulospinal axons, which mediate the fast disynaptic pyramidal EPSPs, are located in the ventral half of the spinal cord. Because some corticospinal and reticulospinal neurons have axons that descend without crossing the midline at the brain stem level but can cross at the spinal level, we also made a hemisection of the contralateral side (to the recording...
side). This hemisection had no effects either on the early or late EPSP components as illustrated in Fig. 6B. The latencies of the EPSPs are shown in Fig. 6C after the different lesions, and it can be seen that they were in a similar range as the EPSPs obtained after corticospinal lesions (cf. Fig. 3F).

**DISCUSSION**

**Lack of monosynaptic CM excitation**

Previous electrophysiological investigations in the rat have given different results and suggested the existence of a monosynaptic CM projection (Babalian et al. 1993; Bannister and Porter 1967; Liang et al. 1991). Our results strongly suggest that there is no monosynaptic excitatory CM connection in the rat. Because we could evoke the descending corticospinal volley with a threshold usually 5–10 μA, we also tried to evoke monosynaptic EPSPs at very weak strengths using longer pulse durations to favor activation of slow fibers and also suppressed di- and trisynaptic transmission by giving Nembutal but without any sign of monosynaptic EPSPs. Even the most short-latency EPSPs required temporal facilitation, whereas monosynaptic EPSPs should be possible to elicit by single stimulation. J. B. Nielsen, J.-M. Aimonetti, V. Marchand-Pauvert, and M. Enriquez-Denton have recorded from forelimb MNs and evoked pyramidal excitation and have likewise failed to observe monosynaptic EPSPs (but found di- and polysynaptic pyramidal EPSPs; IUPS meeting 2001, Abstract 2245). A serious problem in small animals like the rat is that extracellular field potentials are very large. If the intracellular recordings are not compared with the extracellular ones, it is possible to mistake the reversed monosynaptic pyramidal field potential for a monosynaptic EPSP. Together with recent anatomical findings based on electron microscopy (Yang and Lemon 2003), it seems safe to conclude that forelimb MNs in the rat lack monosynaptic CM connections. This clarification is important, since it has been proposed that at least part of the skilful digit movements in the rat could have been controlled by such a connection (see Species comparison of forelimb movements).

**Fast disynaptic excitation via CRS neurons**

The shortest latency disynaptic pyramidal EPSPs (1.8 and 2.4 ms) appeared earlier than or almost simultaneously with the direct corticospinal volley. Accordingly, it seems likely that the earliest EPSPs were mediated by another pathway than the corticospinal tract. Because these EPSPs remained unchanged after corticospinal transections (DC and DLF) either in C5 or C 2 and contralateral hemisection in C 2 , we propose that they are mediated via reticulospinal neurons with their axons running in the ventral half of the spinal cord as illustrated schematically in Fig. 7. We can exclude the rubrospinal tract because it was lesioned with DLF transection and also the vestibulo- and tectospinal tracts because they do not receive a direct input from corticobulbar fibers (Brodal 1981). It is interesting that the CRS effects to forelimb MNs in the rat seems to be much more frequent and stronger than in the cat and macaque monkey forelimb motoneurons (Alstermark et al. 1999; Illert et al. 1977). The function of this pathway is unknown, but behavioral investigations in the rat after combined pyramidal tract and red nucleus lesions have shown that bulbospinal systems can compensate and to some extent carry the command for reaching and grasping (Whishaw et al. 1998).

**Corticospinal excitation via segmental INs**

Comparison of the histograms in Figs. 2D (intact), 3F (corticospinal lesion), and 4F (reticulospinal lesion) shows that the
The corticospinal volley makes it difficult to indicate an exact border between di- and trisynaptic transmission. In Fig. 4F, only 6 cells had latencies in the disynaptic time range, whereas 22 had latencies suggesting a trisynaptic linkage. As outlined schematically in Fig. 7, we propose a weak disynaptic excitatory linkage together with a stronger tri- and or polysynaptic pathway. It seems likely that in so far as the intricate control of the paw in the rat depends on the corticospinal tract (Schirmer and Reiser 1993), the trisynaptic pathway probably plays a dominating role.

**Lack of disynaptic CM excitation via C3–C4 PNs**

Corticospinal disynaptic EPSPs (as well as the extracellular fields) were completely abolished by adding a C3 DC lesion (corticospinal fibers transected) after a prior C2 hemisection (without DC; reticulospinal fibers transected). The excitability before adding the corticospinal lesion in C3 was high as can be seen also from the CDP in Fig. 4C. The disappearance of excitation in the motoneurons was not due to strong inhibition of the intercalated neurons because even in the presence of strychnine no EPSPs or fields could be evoked. These results suggest that C3–C4 PNs do not mediate disynaptic corticospinal excitation to forelimb MNs in contrast to findings in the cat and macaque monkey (Alstermark et al. 1999; Illert et al. 1977). However, as outlined in Fig. 7, one possibility is that the longer-latency EPSPs (2.4–3.0 ms; Fig. 3F) after C3 and C2 DC transections could be trisynaptically mediated via a cortico-reticulo-propriospinal pathway to forelimb motoneurons.

We are presently recording from identified C3–C4 PNs in the rat and have so far not found evidence in favor of a monosynaptic corticospinal input to them (Ogawa and Alstermark, unpublished findings). Instead, we have observed that C3–C4 PNs can be disynaptically activated from the contralateral pyramidal even after a C2 DC transection of the corticospinal tract.

**Species comparison of forelimb movements**

The lack of disynaptic corticospinal excitation to forelimb MNs via C3–C4 PNs as well as monosynaptic CM excitation in the rat is interesting from a functional point of view. The rat possesses a rich motor repertoire especially with their forepaws, but they do not use their forelimbs as felines in hunting fast moving prey or climbing and jumping in treetops like monkeys. Rats can do reaching movement with their forelimbs, but the movement is rather inflexible if conditions suddenly change (Metz and Whishaw 2000). In this respect, the new finding with a fast disynaptic CRS pathway to forelimb motoneurons is interesting. We know that the reticulospinal neurons in the rat receive convergent excitatory input from motor cortex and tectum (unpublished results), as in the cat (Alstermark et al. 1992). Thus there is a possibility for up-dating of the descending cortical command *en route to the motoneurons* in a similar manner as has been demonstrated in the cat for the C3–C4 MNs (Illert et al. 1977). In view of the present results, we tentatively propose that the disynaptic excitatory CRS tract to forelimb motoneurons in the rat could be viewed as functionally analogous to the C3–C4 propriospinal system in the cat for fast visual control of forelimb movements. It is therefore interesting, that the disynaptic cortico-C3–C4 propriospinal pathway, first shown in the cat, recently has been demonstrated in the macaque monkey (Alstermark et al. 1999) and most likely also exists in man (Marchand-Pauvet et al. 2001). It has been proposed that such spinal premotoneuronal integration is of little or no importance in high primates and man because electrophysiological investigations in the macaque monkey failed to provide clear evidence for the existence of C3–C4 PNs (Maier et al. 1998; Nakajima et al. 2000). According to this view, the monosynaptic corticomotoneuronal connection has replaced the disynaptic one, and this change is correlated with the increased dexterity of digit movements in primates and man (Nakajima et al. 2000). However, the failure to frequently observe disynaptic excitation was shown to be due to a stronger inhibition of the C3–C4 PNs in the macaque monkey compared with the cat (Alstermark et al. 1999; B. Alstermark, Y. Ohki, and T. Isa unpublished observations in the cat). When the inhibition was reduced pharmacologically with strychnine, disynaptic cortico-motoneuronal excitation mediated via C3–C4 PNs could be evoked in virtually all forelimb motoneurons (Alstermark et al. 1999).

The rat as the cat has been underestimated when it comes to digit manipulation for grasping food (Alstermark and Isa 2002; Ivanco et al. 1996). Both species can do fractionated digit movements although not highly independent digit movements like the precision grip in primate. The present results suggest that the dexterity in the rat is not controlled by a monosynaptic CM connection but that skillful digit movements can be effectively controlled by di- and trisynaptic connections. In the cat, it is known that the command for grasping is disynaptically mediated in a manner analogous to the C3–C4 MNs.
mediated via the cortico- and rubrospinal tracts and segmental INs and that it can be taken over by the reticulospinal tract after complete transection of the cortico- and rubrospinal tracts (Alstermark et al. 1981; Pettersson et al. 2000). Recent observations in the macaque monkey after complete corticospinal transection in C₅ show initial impairment of the precision grip, but that it returns already after 6–7 days (S. Sasaki, T. Isa, L.-G. Pettersson, B. Alstermark, unpublished observations). This finding suggests that indirect connections, from the motor cortex to forelimb motoneurons, via interneurons in the spinal cord and brain stem systems may also contribute importantly to the control of independent digit movements in all three species.

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