Cortico-motoneuronal system and dexterous finger movements

To the Editor: A recent paper in the *Journal of Neurophysiology* by Sasaki et al. (2004) reports that in macaque monkeys, skilled movements of the digits can survive a large unilateral lesion of the lateral corticospinal tract (LSCT) at the C3 level. This important report forces us to reconsider our views about the pathways mediating control of these movements and to consider the processes involved in plastic recovery mechanisms after spinal injury.

In assessing the evidence presented by Sasaki et al. (2004), the first question is whether the lesion interrupted all of the corticospinal input to the lower cervical cord. The authors carefully addressed this question both by histological reconstruction and by electrophysiological recordings at the end of the experiment. In these recordings, they found evidence for field potentials in C6–C8 and excitatory postsynaptic potentials (EPSPs) in forelimb motoneurons that were evoked by single stimuli to the pyramidal tract. These potentials and EPSPs had longer latencies than the fast cortico-motoneuronal input interrupted by the lesion and are interpreted as arising via disynaptic action of C3–C4 propriospinal neurons (PNs). However, it seems unlikely that these late effects solely reflect this pathway; first, some of them are too early to be disynaptic; second, such effects are not normally evoked by single shocks, and finally, they show little temporal facilitation with repetitive pyramidal tract (PT) stimuli. Indeed, similar effects were reported some years ago by Maier et al. (1998; Fig. 7) in recordings from macaque motoneurons below an acute lesion of the LCST at C3; these authors attributed them to the action of slowly conducting CST fibers that had survived the lesion. Such fibers represent the vast majority of axons in the LCST, are less susceptible to injury than fast conducting axons, and make monosynaptic connections with motoneurons (Porter and Lemon 1993). Thus it may not be safe to conclude “that the CST lesions in the three monkeys were complete.”

The authors suggest that because recovery of precision grip after LCST lesions at C3 is rapid compared with earlier reports of permanent loss of fine movements after lesions at a higher, i.e., PT level, then the key structures must be those innervated at an intermediary level, such as the C3–C4 PNs. However, in earlier reports (Hepp-Reymond et al. 1974; Lawrence and Kuypers 1968), it was only near-complete (>80% of PT fibers destroyed) that produced such impairments. Incomplete lesions, which included unilateral PT lesions, produced slowing rather than abolition of the precision grip (Schwartzman 1978; Belhaj-Saïf and Cheney 2000). The lesion in monkey Y (performance is illustrated in Fig. 3) may not have interrupted the most ventral LCST fibers.

The prediction from the current work is that a C2 LCST lesion, which would interrupt corticospinal input to the C3–C4 system, should produce a much more severe impairment than the C3 lesion. This prediction now needs to be tested by the authors.

A final issue relates to interspecies comparisons. Maier et al. (1998) cautioned against drawing parallels too closely between the cat, in which the functional properties of the C3–C4 system have been so elegantly demonstrated, and other species, including humans. Subsequent studies in rat and monkey have reinforced the need for caution (Alstermark et al. 2004; Nakajima et al. 2000). If future C2 lesions do implicate the C3–C4 system as mediating some precision grip control, then this is in striking contrast to the cat, in which this system is said to be mainly concerned with reaching and is largely uninvolved in the “food-taking” movement.

The authors claim that indirect pathways “have been considered to be of little or no importance in prehension.” This is an overstatement. Indeed, >10 yr ago I wrote: “nevertheless, it may be too sweeping a generalization to suggest that cortico-motoneuronal connections are the sine qua non of independent digit movements” (Lemon 1993).

REFERENCES


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REPLY

To the Editor: Our paper, “Dexterous Finger Movements in Primate Without Monosynaptic Corticomotoneuronal Excitation” by Sasaki, Isa, Pettersson, Alstermark, Naito, Yoshimura, Seki, Ohki (2004) has prompted Dr. Lemon to write a letter consisting of six paragraphs, which we would like to comment upon.

In the first paragraph Lemon writes that our “report forces us to reconsider our views about the pathways mediating control of these movements”, but in the 2nd paragraph, he suggests that our conclusion, that the corticospinal tract (CST) lesions in the three monkeys were complete, may not be safe. His concern is based on the fact that a single stimulus to the pyramidal tract evoked field potentials in the motor nuclei and EPSPs in forelimb motoneurones after the chronic lesion in

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C4/C5 as shown in Figure 1C and 2D, respectively. His first comment is that some of the EPSPs are too early to be disynaptic and he suggests that they could be monosynaptically mediated by remaining slow CST fibres. The shortest segmental latencies were 1.0–1.2 ms as shown in Fig. 2H. In fact, such short latencies have already been reported several times in the cat, which lacks monosynaptic corticospinal connections (cf. Fig. 1; Alstermark, Lundberg, Sasaki, 1984; Fig. 4; Alstermark and Sasaki, 1985) and also in the Macaque monkey after administration of strychnine (Alstermark et al., 1999; cf. below). The segmental latency is to a large extent influenced by the excitability of the intercalated neurones as shown by Alstermark and Sasaki (Fig. 8B; 1986).

The second comment of Lemon is that disynaptic EPSPs are not “normally” evoked by a single shock. Using similar anaesthesia, but without chronic lesions, we have found that disynaptic pyramidal EPSPs could only be evoked frequently in forelimb motoneurones by using 3 or 4 stimuli and intravenous administration of strychnine in the Macaque monkey (Alstermark et al. 1999). However, in the present study with chronic CST lesions, disynaptic EPSPs were evoked in about half of the motoneurones (lesioned side) even without strychnine and by a single shock as shown in Fig. 2D. These findings can be attributed to a considerably higher excitability, which is evident by the presence of a disynaptic field potential and a synaptic volley which appeared already after the first pyramidal stimulus and were markedly facilitated after the second and third shocks (Fig. 1B–C). A disynaptic field potential in the motor nuclei and a synaptic volley is not seen after acute CST lesion, unless strychnine is administered.

The third comment by Lemon is that the EPSPs illustrated in Fig. 2D, showed little temporal facilitation. In the records shown in Fig. 2F, the facilitation was about 70% (comparison between peak amplitudes of the first and third EPSPs). It is not surprising, considering the high level of excitability, that the temporal facilitation was not more pronounced, because of a small subliminal fringe in the pool of intercalated neurones (cf. Fig. 8B; Alstermark and Sasaki, 1986). Furthermore, the third EPSP was cut by an IPSP as shown in Fig. 2F. The important point is that facilitation could be observed, since it indicates temporal summation of excitation in the intercalated neurones. Lemon refers to the work of Maier et al. (1998, Fig. 7), in which the CST lesions were not complete (shown by the authors). It is possible that the EPSP shown in their Fig. 7 could be monosynaptic despite the long latency, since no facilitation was observed as pointed out by these authors. The lack of facilitation of monosynaptic CM EPSPs using a train of stimuli is an important observation, since it rules out the possibility of presynaptic facilitation.

In our study, we have used 3 independent electrophysiological measurements (volley, fields, and EPSPs), each with a resolution to detect a few percentages of spared fibers. Thus, if all these measurements indicate a complete lesion, the probability that a significant part of the lateral CST fibers has escaped the lesion, is indeed low. Of course, it is possible to claim that these measurements mainly assess the extent of the fast component of the CST, and therefore we like to stress that it is an underlying assumption that fast and slow CST fibers do have similar location in the spinal cord. It is important to stress the fact that disynaptic excitation could be evoked in all three monkeys and not only in monkey Y with the smallest lesion, which seems to have just covered the region of the lateral CST. From the histology in Fig. 1A it seems clear that the large lesions in monkeys I and G could not have spared the lateral CST. The intracellular records shown in Fig. 2A–G are from monkey G. We do not find that the comments provided by Lemon violate a conclusion that the lesions were complete.

In response to the third paragraph, we would like to emphasize that the C3–C4 propriospinal neurons (PNs) are just one of several possible candidates for mediating the command for digit movements after the C4/C5 CST lesion. In the article, we first discuss the possibility that brain stem systems (like the rubrospinal pathway) could contribute. In order to distinguish between the different possibilities (which are not mutually exclusive), we have already planned to make experiments in which the CST lesion is made at the C2 level (fourth paragraph of Lemon). As to the fifth paragraph, species-differences are discussed in our paper.

In the sixth paragraph, Lemon claims that our statement, “Indirect (oligosynaptic) CM pathways, which are phylogenetically older than the C5–C6 CST, may be too sweeping a generalization to suggest that cortico-motoneuronal connections are the sine qua non of independent digit movements” (Lemon, 1993; Porter and Lemon, 1993), which two of us have also cited in a review (Alstermark and Isa, 2002). However, recently Lemon has proposed a hypothesis that the phylogenetically older non-monosynaptic (with special reference to the C3–C4 propriospinal system) CM pathways gradually have been replaced with the monosynaptic CM pathway (Nakajima et al. 2000). Our findings in the Macaque monkey strengthen the view that also non-monosynaptic CM pathways may be important in the control of fine finger movements, which is in opposition to the replacement hypothesis.

REFERENCES


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