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The Motor Cortex and Descending Control of Movement

In the latest in our series on Motor Control, Fisher, Soteropoulos and Witham bring us up-to-date on the descending control of somatic movement. In particular, they present recent work that expands our view of the corticospinal tract, which is much more than the connection from the primary motor cortex to the ventral horn of the spinal cord. In this age of functional imaging and gene sequencing, this review is a reminder of the importance of careful anatomical and neurophysiological studies in animals.

Martyn Bracewell, Series editor.

Over the course of evolution the motor areas of cerebral cortex and the corticospinal tract (CST) have become increasingly important for the control of movement. In particular, there has been a relative expansion in the size of the CST and the development of direct synaptic connections between corticospinal neurons and upper limb motoneurons (corticospinal synapses) which is correlated with increased hand and finger dexterity.¹ From new world monkeys such as macaques and then to apes, including humans, there has been a large increase in the number of direct connections to motoneurons. Other mammals such as cats have few if any direct connections (one exception is the racoon, which has both significant direct connections and good manual dexterity).

Primary motor cortex (M1) and the CST are known to be essential for voluntary control of the contralateral skeletal musculature. This is particularly evident in patients with unilateral motor cortical damage (e.g. following stroke). The result, depending on the extent and location of the lesion, is usually paresis of the contralateral limbs. Further functional consequences of CST damage have been described following bilateral surgical lesions to the CST in macaques.^{2,3} It was demonstrated that after an initial period of paralysis, animals actually recovered most gross motor function very quickly and permanent deficits in movement were restricted largely to fractionated finger movements. By contrast, lesioning other descending pathways (rubrospinal & reticulospinal tracts) resulted in permanent loss of grasping and impaired gross movements of the axial and proximal musculature with preserved fine finger movements.

A detailed overview of corticospinal neurons and their role in voluntary movement has been published by Porter and Lemon.⁴ In the past two decades there has been a number of advances in the basic anatomy and physiology of the corticospinal and other descending tracts in primates

including improvements in tracing techniques and recording from deep structures such as the brainstem. These advances may explain some features of recovery seen after stroke and suggest future targets for rehabilitation.

Multiple origins of corticospinal tract

Across species the largest proportion of the CST originates in M1.⁵ However significant populations of corticospinal neurons are found in other frontal and parietal areas such as the supplementary motor area (SMA) and primary somatosensory cortex (S1). Improvements in tracing techniques have led to a better understanding of the origin and termination of different corticospinal populations. For example S1 corticospinal neurons project to the dorsal horn of the spinal cord whereas SMA corticospinal neurons project to the intermediate zone and ventral horn (similar to M1 corticospinal neurons).⁶ Some of the main areas contributing to the CST and their spinal termination are shown in Figures 1A and B.

The CST has multiple functions including control of voluntary movement, gating sensory inputs during movement, control of spinal reflex loops and preparing the spinal cord for movement. The projection patterns of different areas suggest that each serves a different function, however evidence linking discrete areas to different functions is lacking. Groups have recorded from identified corticospinal neurons in different areas in an attempt to understand function. Early studies showed that M1 corticospinal neurons are active approximately 200ms before movement onset and S1 corticospinal neurons are active after M1 neurons (but still in advance of movement).⁷ A recent study has shown that corticospinal neurons in premotor cortex exhibit 'mirror neuron' behaviour, being active both when the monkey performs a precision grip and when the monkey observes the experimenter perform the same action.⁸ Another study has shown that interneurons in the spinal cord are active during movement preparation as well as during movement.⁹

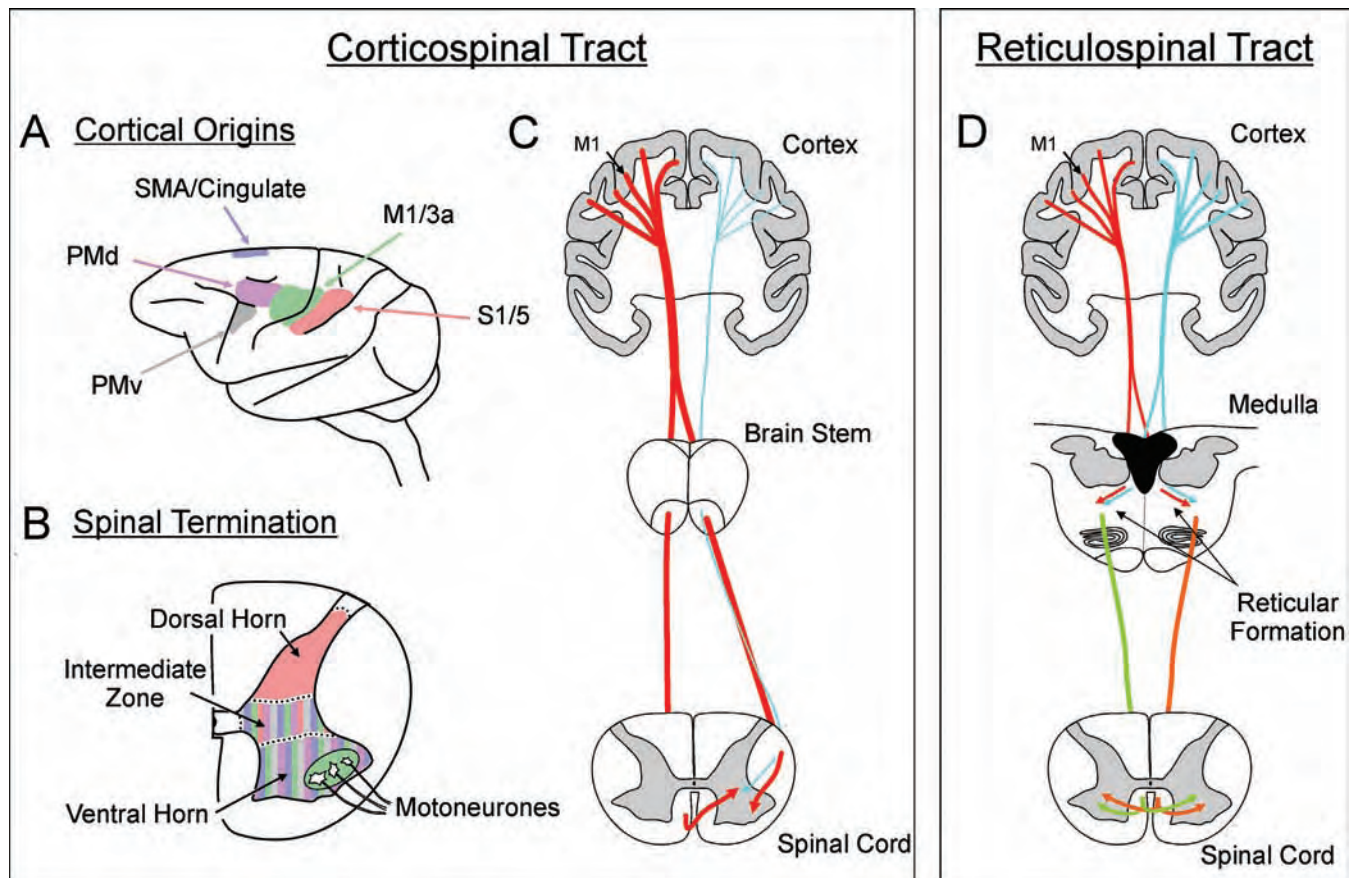


Figure 1. Corticospinal and reticulospinal tracts. A, main cortical origins of the CST. B, simplified spinal terminations of areas in A. C, contralateral (red) and ipsilateral (cyan) projections of the CST. D, bilateral cortical projections to PMRF (red and cyan) and bilateral projection from PMRF to the spinal cord (orange and green).

Anatomical experiments by Rathelot and Strick¹⁰ have shown that corticospinal neurons with direct connections to motoneurons (important in the control of independent finger movement) in monkeys originate in two areas. The main population is in the caudal bank of M1 (85%). A second population originates in somatosensory area 3a; these particular corticospinal neurons are also active before M1⁷ suggesting that the function of the area 3a corticospinal projection is different to the rest of S1.

It is increasingly clear that multiple areas of the cerebral cortex project to different targets in the spinal cord and that these play different roles in motor control.

Ipsilateral corticospinal tract

The extent to which the motor cortex contributes to the control of movements of the ipsilateral limb is poorly understood. It is well supported that neural activity in M1 is modulated with movements of the ipsilateral forelimb – this has been demonstrated with invasive recordings of M1 neurons in monkeys¹¹ as well as with non-invasive (MRI) imaging in humans.¹² Some patients with unilateral motor stroke display deficits in control of the ipsilateral arm, in addition to the more severely affected contralateral arm.¹³ These studies suggest the M1 is more than just a passive bystander during ipsilateral movements.

Anatomically, a small fraction (up to 10%) of the CST projects to the ipsilateral spinal cord; this projection is hypothesised to give M1 access to ipsilateral muscles (Fig. 1B). However recent work¹⁴ has found little evidence that these ipsilateral axons contact ipsilateral spinal circuits. Instead they cross to the contralateral side at the level of the spinal cord. A second study using a more widespread M1 tracer injection has found more extensive crossing of the CST at the level of the spinal cord such that individual corticospinal axons may project contralaterally, ipsilaterally or bilaterally¹⁵. It is unclear at this stage how much of the ipsilateral projection is related to proximal and axial muscles rather than distal forearm and hand muscles.

Beyond the anatomical connectivity, the functional role of these ipsilateral projections is unknown. Activation of M1 in monkeys (via intra-cortical microstimulation) or humans (via transcranial magnetic stimulation – TMS) does not typically evoke ipsilateral muscle responses. Although TMS at maximal intensity can sometimes elicit longer latency ipsilateral muscle responses, these are likely to be mediated by the brainstem descending pathways.¹⁶ A recent study used multiple electrophysiological techniques to identify direct inputs to ipsilateral forearm and distal motoneurons, but failed to find any evidence for such inputs.¹⁷ The lack of ipsilateral corticomotoneuronal connections

suggests that the functional role of the ipsilateral projection differs from that of the contralateral one. Questions still remain regarding how the M1 activity during ipsilateral movements is related to the ipsilateral CST projection, and to other brain regions involved in movement control, and how (if at all) this activity is related to control of ipsilateral movements.

Other descending systems

As well as directly influencing the spinal cord via the CST, the cerebral cortex also has connections to descending motor control pathways which originate in other brain regions. Such alternate pathways are conventionally considered to be less important in humans than in lower species but recent studies in primates have demonstrated that they may form the basis of parallel control systems which are likely to contribute significantly to recovery following damage to the CST. One projection of interest is the reticulospinal tract (RST) which originates in the pontomedullary reticular formation (PMRF) of the brainstem (see review: ref 18). This area receives direct bilateral cortico-reticular input from fibres which originate mainly in motor and premotor cortical areas as well as collateral input from CST neurons projecting to the spinal cord.

The reticulospinal tract itself is a bilateral projection system (Figure 1D). It is highly collateralised, much more so than the CST, and axons

terminate within multiple segments of the spinal cord. These features collectively show that outputs from the PMRF have the potential to influence multiple motoneuron pools and subsequently numerous different muscles. The traditional view is that the RST is largely concerned with control of proximal and postural muscles, however recent work has demonstrated that there are also direct monosynaptic RST projections to the distal musculature;¹⁹ these were found to be weaker than equivalent CST projections but nevertheless were present in primates. Evidence also suggests that there is convergence of CST and RST axons onto the same spinal interneurons.²⁰ The presence of these connections doesn't necessarily mean they have a significant functional role in hand control, but the modulation of reticulospinal activity during reaching movements has been demonstrated in both cats²¹ and primates²² and we can evoke responses which are likely to be of reticular origin in humans (acoustic startle, ipsilateral motor evoked potentials). This evidence together suggests that the RST forms a parallel system of descending control alongside the CST which could act as a potential target for rehabilitation interventions.

Another notable descending motor pathway is the rubrospinal tract which has substantial input from M1 and shares many remarkably similar features with the CST. Both have direct monosynaptic projections to the spinal cord, terminate onto similar interneurons and can influence both proximal and distal muscles. Interestingly there seems to be an inverse relationship between the two tracts so that as the CST expands through evolution the rubrospinal tract diminishes in size.

The rubrospinal tract originates in the red nucleus of the midbrain. In primates this struc-

ture is divided into magnocellular (mRN; giant cells) and parvocellular regions (medium and small cells). The mRN gives rise to the rubrospinal tract and has been shown to be far more developed in the foetal brain than in adult humans,²³ losing prominence alongside the maturation of the CST. However, what remains of the rubrospinal tract following development is a projection system which has preferred access to the distal musculature and a strong extensor bias.

The overlap between rubrospinal and corticospinal systems provides potential compensation following damage to CST. This has been shown in one monkey; whereby a lesion of the pyramidal tract led to remarkable reprogramming of rubrospinal outputs.²⁴ Not only did the muscle targets of the mRN change after the lesion, they changed to a pattern that looked more like the corticospinal system than the rubrospinal. This type of plastic reorganisation suggests that the rubrospinal tract could, like the RST, be a useful target for rehabilitation therapy.

A large body of work has also focussed on other descending tracts although we do not describe these here in detail. Other systems under cortical influence include the vestibulospinal and the tectospinal tracts which predominantly control postural movements and neck muscles respectively.

Although each of the descending motor pathways is specialised it is important to note that there is substantial crossover between many of them. This makes human motor control an extremely complex process and consequently there are many properties and features which remain elusive. However, this complicated matrix of interconnected motor control pathways does explain the recovery of function observed following precise lesions in

animals and gives us an opportunity to provide useful interventional therapy which can promote plastic changes and enhance recovery in patients.

Conclusions and questions for the future

We have highlighted some important recent findings regarding the CST and descending motor control. Firstly, the CST is not equivalent to M1, as more than half of CST fibres come from outside this area. Secondly, the functional connectivity of the CST with ipsilateral motoneurons is not as direct as often assumed. Finally, while M1 and CST are vital for voluntary hand function, other descending systems such as the RST are also able to influence distal forelimb muscles.

Whilst our anatomical understanding of descending pathways has improved recently, the functional role of these connections in voluntary movement is poorly understood. For example, the role of CST neurones originating outside M1 is unknown as well as how these compare with projections which arise within M1. Also unknown is the role of ipsilateral corticospinal terminations given that they are unlikely to be able to directly activate motoneurons. Finally, the relative contribution of the brainstem in the control of voluntary hand movements remains to be elucidated as well as how this is influenced by descending signals from the cortex.

Further work is needed to clarify the functional contribution of the CST at a finer level, taking into account its varied anatomical origins and terminations. This is essential not just for understanding the role of the motor system in normal function but more importantly for the potential avenues it could offer for rehabilitation following cortical damage. ♦

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