

# Starting and stopping movement by the primate brain

Roger Lemon and Alexander Kraskov

Brain and Neuroscience Advances

Volume 3: 1–6

© The Author(s) 2019

Article reuse guidelines:

[sagepub.com/journals-permissions](http://sagepub.com/journals-permissions)

DOI: 10.1177/2398212819837149

[journals.sagepub.com/home/bna](http://journals.sagepub.com/home/bna)



## Abstract

We review the current knowledge about the part that motor cortex plays in the preparation and generation of movement, and we discuss the idea that corticospinal neurons, and particularly those with cortico-motoneuronal connections, act as ‘command’ neurons for skilled reach-to-grasp movements in the primate. We also review the increasing evidence that it is active during processes such as action observation and motor imagery. This leads to a discussion about how movement is inhibited and stopped, and the role in these for disfacilitation of the corticospinal output. We highlight the importance of the non-human primate as a model for the human motor system. Finally, we discuss the insights that recent research into the monkey motor system has provided for translational approaches to neurological diseases such as stroke, spinal injury and motor neuron disease.

## Keywords

Motor system, motor cortex, corticospinal, mirror neuron, monkey

Received: 20 February 2018

To move things is all that mankind can do ... for such, the sole executant is muscle, whether *whispering* a syllable or *felling* a forest

Charles Sherrington’s memorable words emphasise the central importance of the motor system for all types of brain function. Although modern neuroscience is increasingly focused on our special cognitive abilities, the importance of movement actually remains unchanged, not least because we are more aware of the amazing links between our cognitive ability and the myriad variety of motor movements which give that ability expression and meaning.

However, it must also be admitted that there are still many unsolved questions about how we generate a movement or indeed how we prevent or stop an unwanted movement: a crucial (and probably underrated) facility in our highly sophisticated social interactive world (Carpenter and Noorani, 2017). Following a century of detailed anatomical tract-tracing, electrophysiological investigation and careful lesion studies, our knowledge of the executive pathways through which ‘commands’ for movement must pass is unrivalled, yet we are still some way from really understanding how a movement is generated, which structures and pathways are involved and how they interact during the period leading up to movement onset. On the one hand, we know, ever since the discovery of the ‘readiness potential’, that self-generated movements are preceded by a build-up of activity over several seconds in major motor circuits. Even in primary motor cortex, often considered the hub for executive ‘commands’ to be delivered to the spinal machinery for movement, the evidence suggests that activity precedes movement onset by well over a

hundred milliseconds. On the other hand, the actual conduction time from the motor cortex to muscle is, by comparison, vanishingly brief, taking a few tens of milliseconds.

Thus, it is clear that a great deal of brain activity goes on before the ‘brake’ is released and movement is initiated. Indeed, in situations such as motor imagery or mental rehearsal of motor tasks, we now know that even in motor cortex and its spinal targets, activity changes can be clearly detected without any overt movement taking place.

The motor control literature makes liberal use of the expression ‘motor command’. A motor command must, by definition, be both delivered and received. We shall discuss that, for example, neurons in the primary motor cortex can be considered as having the properties of command signal, but far less is known about how these signals are received by the spinal cord, to allow transformation into motoneuron activity and movement. Commands may not only initiate a movement, but also continue to guide and update it until the action is completed and the goal is achieved. For this to happen, the command signal must contain detailed kinematic and dynamic information appropriate for the

Sobell Department of Motor Neuroscience and Movement Disorders,  
Institute of Neurology, University College London (UCL), London, UK

## Corresponding author:

Roger Lemon, Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London (UCL), London WC1N 3BG, UK.

Email: [r.lemon@ucl.ac.uk](mailto:r.lemon@ucl.ac.uk)



context of the movement. Importantly, the command signal can also act to stop, inhibit or withhold movement.

## Evoked versus natural movements

Early investigators were impressed by the ease with which movements could be 'evoked' by electrical stimulation of the brain, and these strong impressions undoubtedly reinforced ideas of 'motor commands' that the generation of a movement was not dissimilar to the effects of electrical stimulation, which somehow hijacked the brain circuits responsible. However, there are major differences in the timing, structure and nature of the activity that precedes natural versus electrically evoked movements (Lemon, 2014). Electrical or magnetic stimulation of the motor cortex induces an intense transsynaptic bombardment of pyramidal output neurons, and leads to high-frequency (~600 Hz) repetitive discharge in these neurons and the characteristic 'D'- and 'I'-waves in the corticospinal tract (Edgley et al., 1997; Patton and Amassian, 1954). Even a single intracortical stimulus can recruit indirect, transsynaptic responses in a high proportion of corticospinal outputs (Maier et al., 2013), and these effects can be evoked both from within motor cortex and from connected premotor areas (Schmidlin et al., 2008). However, during natural movements, pyramidal neurons rarely exhibit these high-frequency discharges (di Lazzaro et al., 2008), and modal discharge frequency is much lower, typically below 100 impulses/s.

Furthermore, the timing of stimulus evoked versus naturally generated movements is completely different. The intense, synchronised output generated by electrical stimulation of macaque motor cortex evokes responses in hand and digit muscles with onset latencies of only ~10 ms. These latencies are much shorter than the 60–100 ms between the onset of changes in M1 activity and the onset of muscle activity during voluntarily generated movements (Cheney and Fetz, 1980; Porter and Lemon, 1993).

Transcranial magnetic stimulation (TMS), in particular, has revealed a huge amount of knowledge about the connectivity and function of the human motor cortex and the corticospinal system (di Lazzaro et al., 2008). However, the nature of the neuronal activity that it evokes is such that it can teach us much less about how natural movements are generated.

## Motor cortex activity in preparation for movement

It has long been known that motor cortex is active during both the preparation and execution of an action, although classically this activity has been studied using very different approaches. The evolution of motor cortex activity from preparation to execution is under intense investigation (Elsayed et al., 2016; Kaufman et al., 2013). This evolution is seen in the framework of a dynamical systems approach (Erlhagen and Schoner, 2002; Shenoy et al., 2013). This general theoretical framework considers the brain as a physical system whose future state is a function of its current state, its input and some noise. Within this dynamical system, not all motor cortex activity is considered to be driving the spinal cord and muscles. According to this approach, a substantial part of the motor cortex activity might be representing internal processes, possibly reflecting a larger set of different possible movements that are being prepared. Applying this approach to a

large set of simultaneously recorded neurons in motor cortex, Kaufman et al. (2014) suggested that preparation and movement activity occupy different dimensions of a multidimensional neuronal space describing the brain's dynamical system. Thus, the preparation activity does not spread into dimensions linked to the movement execution, that is, preparation activity does not 'spill out' into movement.

The generality of dynamical system framework for understanding movement-related activity of the motor cortex represents its strength, but also its weakness. Abstract dimensions of the multidimensional neuronal space at some point have to be linked back to our accumulated anatomical knowledge about effective connectivity of motor cortex to other cortical and subcortical brain structures and ultimately to the output of motor system, that is, the spinal cord, motoneurons and the muscles they innervate.

The discovery that M1 neurons can become active during observation of the actions of others, but without any overt signs of movement in the observer (Vigneswaran et al., 2013) adds to a long list of evidence that motor cortex can be active in a number of different states, all of which are quite distinct from movement itself (Schieber, 2011). These include preparation for movement (Shenoy et al., 2013), mental rehearsal and imagination (Cisek and Kalaska, 2004; Dushanova and Donoghue, 2010; Macuga and Frey, 2012). Further evidence comes from operant conditioning of M1 outputs (Fetz and Finocchio, 1971) and the use of M1 activity to control a brain-machine interface: a situation in which an ensemble of cortical neurons can become active, but without any associated muscle activity or movement (Schwartz, 2007). Unfortunately, in nearly all of these studies, the neurons have not been identified (Vigneswaran et al., 2011), so we do not know whether all these activities are also seen in M1 output neurons. We do know that pyramidal tract neurons (PTNs) are embedded in the M1 cortical microcircuit (Jackson et al., 2002), and if these circuits play a part in processes such as action observation and mental rehearsal, it is not surprising that M1 PTNs are also involved.

For eye movements, posture and locomotion, there is a well-developed functional schema which suggests that under normal circumstances the networks that initiate these type of movements are held in check by signals from the basal ganglia (BG), specifically output nuclei of BG, the internal segment of the globus pallidus (GPI) and substantia nigra pars reticulata (SNr) (Grillner et al., 2008; Mink, 1996; Nambu et al., 2002). Release of this 'brake', initiated by suppression of BG output via the direct cortico-striatal pathway, allows movement to begin, and the restoration of the pallidal signal via the indirect cortico-striatal-pallidal pathway terminates the movement. These circuits have been observed in the motor system of a wide variety of vertebrates, and are therefore considered to be highly conserved across all species.

However, for reaching and grasping movements in the non-human primate (NHP), it appears that the population of cortico-striatal neurons in M1 actually discharges *after* movement onset (Turner and DeLong, 2000), so it cannot be responsible for movement initiation.

## PTNs as 'command neurons'

Evarts (1964, 1968) studied the activity of large corticospinal neurons in primary motor cortex (M1) during simple, natural wrist movements executed by trained macaque monkeys. The

neurons were identified as corticospinal by their antidromic response to stimulation of the medullary pyramidal tract, and referred to as PTNs. Evarts showed that M1 PTNs fired well before movement onset and that their discharge frequency was correlated with the direction and force of the movement. Thus, PTNs seem to be eminent candidates as ‘command’ neurons for movement; a small fraction of them have very fast-conducting axons, some of the fastest in the brain (~80 m/s), and thus conduction delays between cortex and spinal cord are very short.

PTNs exhibit additional features that are consistent with a role as ‘command’ neurons. These include the fact that they make many collaterals to important subcortical motor structures, such as the red nucleus and the pontine nuclei (Ugolini and Kuypers, 1986), thereby providing ‘efference copy’ of ‘commands’ to the cerebellum. Although detailed documentation of the corticospinal ‘connectome’ is still at an early stage (Shepherd, 2013, 2014), it is likely to show species-specific variations: for example, in the macaque, the cortico-striatal projection is quite separate from that comprising the corticospinal and corticobulbar tracts (Pasquereau and Turner, 2011).

If M1 corticospinal neurons, discharging well in advance of movement, act to start reach-to-grasp movements, this puts considerable importance on understanding the inputs to these neurons, including local inhibitory interneuronal circuits, which might act as the ‘brake’ governing PTN discharge. This idea has been tested, but so far the evidence is not clear (Kaufman et al., 2013).

### Cortico-motoneuronal cells with command-like features

A further feature of some primate PTNs is that they make direct cortico-motoneuronal (CM) connections to alpha motoneurons (Porter and Lemon, 1993; Rathelot and Strick, 2006; Zinger et al., 2013), allowing the motor cortex direct access to spinal motoneurons. Of course, the CM system does not act alone, but in parallel with many other local interneuronal mechanisms and other descending pathways (Baker, 2011; Lemon, 2008), segmental (Takei and Seki, 2010) and propriospinal systems (Kinoshita et al., 2012). It is interesting that CM synapses on motoneurons are not subject to presynaptic inhibition (Jackson et al., 2006), suggesting that other systems (e.g. peripheral afferent inputs from the moving limb) do not use this mechanism to modify CM inputs to motoneurons, which would mean that information delivered by CM projections is allowed unfettered influence over target motoneurons.

It is sometimes stated that this influence of direct CM connections is overrated. However, a careful quantitative study by Morecraft et al. (2013) showed that the second greatest number of corticospinal projections from the macaque M1 hand area to the cervical spinal grey matter was found among the motor nuclei of the ventral horn (Rexed lamina IX), and amounted to around a third of the projections to the intermediate lamina VII, in which most of the segmental interneurons are located. Of course, inputs to distal dendrites of motoneurons would also be found in this lamina, so that the numbers of contacts on motoneurons might be even higher than estimated by Morecraft et al. (2013). The CM system can provide a significant proportion of the drive needed to maintain motoneuron discharge in steady state conditions (Cheney et al., 1991) and distal hand and digit muscles may receive a particularly large excitatory drive from CM inputs, loss of which produces a characteristic weakness of the thenar

musculature (the ‘split-hand’ syndrome; Eisen and Kuwabara, 2012; Eisen et al., 2017).

Spike-triggered averaging of electromyography (EMG) demonstrated that the natural activity of PTNs could exert a direct CM action on the target muscle (Fetz and Cheney, 1980; Lemon et al., 1986) and proved that the ‘command’ was received by target motoneurons (Lemon, 2008; Zinger et al., 2013). In macaque hand muscles, post-spike facilitation of EMG activity by CM cells begins around 11 ms, consistent with conduction delays estimated from stimulation studies. Thus, the same pathways that are revealed by electrical stimulation are also employed during natural movements. However, even CM cells show changes in activity long before movement onset, far longer than the estimated conduction delays: thus CM cells exert their influence long before movement starts, but at a level that is subthreshold for motoneuron activation and subsequent movement.

CM cells are active for a whole range of different limb movements, including reach-to-grasp, precision grip and during tool-use by macaques (McKiernan et al., 1998; Muir and Lemon, 1983; Quallo et al., 2012). CM connections are particularly well-developed in primates with a high level of dexterity and who use tools. Interestingly, CM cells are characterised by showing not only increases, but also *decreases* in activity before and during precision movements (Maier et al., 1993; Quallo et al., 2012). Indeed, one way that M1 appears to control the pattern of muscle activity during grasp is to ‘disfacilitate’ the excitatory drive to motoneurons.

Rathelot and Strick (2006, 2009) used retrograde transneuronal labelling to show that, in the macaque monkey, most of the CM projections come from corticospinal neurons located in the most caudal part of area 4, which they describe as ‘new M1’, in evolutionary terms (area 4p in humans). Within this region, there is a large representation of each hand muscle which overlaps extensively with that of other hand muscles. There is less extensive, but nevertheless significant overlap with muscles acting at the elbow and shoulder. These spatially overlapping representations may well reflect branching in the terminal distribution of CM terminals among different motor nuclei, but in any event they would allow for close interactions of upper limb musculature during complex reach-and-grasp tasks (McKiernan et al., 1998; Quallo et al., 2012).

In contrast, the more rostral region of ‘old M1’ is characterised by projections to the spinal intermediate zone and to brainstem targets such as the cells of origin of the reticulospinal tracts. A recent study by Witham et al. (2016) showed that microstimulation in the more caudal ‘new M1’ region evoked large excitatory postsynaptic potentials (EPSPs) in some identified upper limb motoneurons which had latencies short enough to be monosynaptic in origin. Short latency EPSPs were not evoked from ‘old’ M1. More commonly, EPSPs had somewhat longer latencies, and some of these could also have been monosynaptic, while others were probably the result of indirect action via interneurons. These longer-latency effects could be obtained from both ‘new’ and ‘old’ M1.

### Corticospinal mirror neurons and motor commands

Some additional insights into the role of the corticospinal system in movement initiation and movement suppression has come about as a result of macaque experiments which showed that

PTNs in both premotor and motor cortex show changes in activity during action observation: watching the actions of others. Given the direct influence of PTNs over muscle activity, it was important to demonstrate that such modulations in discharge occurred without any sign of concomitant EMG activity. This was achieved by monitoring EMG from multiple arm, hand and digit muscles during the action observation condition (Kraskov et al., 2009; Vigneswaran et al., 2013). Thus, PTNs can also be considered as mirror neurons: they discharge during both self-initiated movement and action observation (Gallese et al., 1996). A significant proportion of identified PTNs in both M1 and area F5 of the ventral premotor cortex discharged while monkeys performed a variety of grasps on differently shaped objects, but also discharged as the monkey observed an experimenter perform the same set of grasps.

Interestingly, some PTNs showed contrasting properties for execution versus observation of grasp: they fired vigorously during the monkey's own grasp, but discharge was either partly or completely suppressed during action observation. These were termed 'suppression mirror neurons' by Kraskov et al. (2009) and they may help to inhibit the monkey's own movements as it observes the experimenter's actions. In F5, execution- and observation-related firing rates are similar (Gallese et al., 1996; Kraskov et al. 2009). However, it is interesting that in M1, with direct access to the spinal motor machinery, PTNs were much more active during execution than observation (Kraskov et al., 2014; Vigneswaran et al., 2013). This represents a significant disfacilitation of PTN output to the spinal cord during action observation, which may act to suppress unwanted movement during observation.

## Conclusion: the key contribution of NHP motor neuroscience

This review has touched on several issues that are of fundamental importance to human motor function. Many of the references we have made are to research in the NHP. This is natural because, as that research progresses, it is becoming more and more clear that the human motor system shares important features with that of the NHP, and especially with the Old World macaque monkey. In both species, the corticospinal tract has assumed major importance, and this goes together with the increased influence of the complex cortical and subcortical networks that drive this key output to the spinal cord (Lemon, 2010). The primate corticospinal tract shows many interesting features that distinguish it rather sharply from the rodent pathway. These include the size and distribution of fibres within the tract, with a small but probably very significant population of fast-conducting axons (Firmin et al., 2014). Even the basic electrophysiology of the primate PTN appears different from that of the rodent, including the presence of short-duration action potentials (Vigneswaran et al., 2011), which may allow for brief periods of high-frequency discharge. These 'thin spikes' in macaque pyramidal neurons may, in turn, be related to the membrane expression of Kv3.1b in the fast potassium channel, a feature not found in rat pyramidal neurons (Soares et al., 2017).

The importance of the monkey as a research model of the motor system is of course highlighted by the huge success of Deep Brain Stimulation of the subthalamic nucleus (STN) for

Parkinson's Disease, which is firmly based on NHP research (Blesa et al., 2018; Roelfsema and Treue, 2014), the explosion of interest in the mirror system (Kilner and Lemon, 2013) and the discovery, in the macaque, of the importance of the reticulospinal system for recovery of hand function after stroke (Baker, 2011; Zaaïmi et al., 2012). A further development is the finding that, in some forms of motor neuron disease (amyotrophic lateral sclerosis (ALS)), the CM system may be involved in the spread of the pathology (Braak et al., 2013; Eisen et al., 1992, 2017). The NHP model clearly has plenty to teach us both about motor function in the healthy human and about the many diseases that target the most highly evolved features of that motor function.

## Acknowledgements

We would like to acknowledge the contribution of our many collaborators and colleagues whose work is cited in this review. We also wish to acknowledge the long-term support of The Wellcome Trust.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

## Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

## References

- Baker SN (2011) The primate reticulospinal tract, hand function and functional recovery. *Journal of Physiology* 589(Pt 23): 5603–5612.
- Blesa J, Trigo-Damas I, Del Rey NL, et al. (2018) The use of nonhuman primate models to understand processes in Parkinson's disease. *Journal of Neural Transmission* 125(3): 325–335.
- Braak H, Bretschneider J, Ludolph AC, et al. (2013) Amyotrophic lateral sclerosis – A model of corticofugal axonal spread. *Nature Reviews Neurology* 9(12): 708–714.
- Carpenter R and Noorani I (2017) Movement suppression: Brain mechanisms for stopping and stillness. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences* 372(1718): 20160542.
- Cheney PD and Fetz EE (1980) Functional classes of primate corticomotoneuronal cells and their relation to active force. *Journal of Neurophysiology* 44(4): 773–791.
- Cheney PD, Fetz EE and Mewes K (1991) Neural mechanisms underlying corticospinal and rubrospinal control of limb movements. *Progress in Brain Research* 87: 213–252.
- Cisek P and Kalaska JF (2004) Neural correlates of mental rehearsal in dorsal premotor cortex. *Nature* 431(7011): 993–996.
- Di Lazzaro V, Ziemann U and Lemon RN (2008) State of the art: Physiology of transcranial motor cortex stimulation. *Brain Stimulation* 1(4): 345–362.
- Dushanova J and Donoghue J (2010) Neurons in primary motor cortex engaged during action observation. *European Journal of Neuroscience* 31(2): 386–398.
- Edgley SA, Eyre JA, Lemon RN, et al. (1997) Comparison of activation of corticospinal neurones and spinal motoneurons by magnetic and electrical stimulation in the monkey. *Brain* 120(Pt 5): 839–853.
- Eisen A and Kuwabara S (2012) The split hand syndrome in amyotrophic lateral sclerosis. *Journal of Neurology, Neurosurgery, and Psychiatry* 83(4): 399–403.
- Eisen A, Braak H, del Tredici K, et al. (2017) Cortical influences drive amyotrophic lateral sclerosis. *Journal of Neurology, Neurosurgery, and Psychiatry* 88(11): 917–924.

- Eisen A, Kim S and Pant B (1992) Amyotrophic lateral sclerosis (ALS): A phylogenetic disease of the corticomotoneuron? *Muscle & Nerve* 15(2): 219–224.
- Elsayed GF, Lara AH, Kaufman MT, et al. (2016) Reorganization between preparatory and movement population responses in motor cortex. *Nature Communications* 7: 13239.
- Erlhagen W and Schoner G (2002) Dynamic field theory of movement preparation. *Psychological Review* 109(3): 545–572.
- Evarts EV (1964) Temporal patterns of discharge of pyramidal tract neurons during sleep and waking in the monkey. *Journal of Neurophysiology* 27(2): 152–171.
- Evarts EV (1968) Relation of pyramidal tract activity to force exerted during voluntary movement. *Journal of Neurophysiology* 31(1): 14–27.
- Fetz EE and Cheney PD (1980) Postsynaptic facilitation of forelimb muscle activity by primate corticomotoneuronal cells. *Journal of Neurophysiology* 44(4): 751–772.
- Fetz EE and Finocchio DV (1971) Operant conditioning of specific patterns of neural and muscular activity. *Science* 174(4007): 431–435.
- Firmin L, Field P, Maier MA, et al. (2014) Axon diameters and conduction velocities in the macaque pyramidal tract. *Journal of Neurophysiology* 112(6): 1229–1240.
- Gallese V, Fadiga L, Fogassi L, et al. (1996) Action recognition in the premotor cortex. *Brain* 119(Pt 2): 593–609.
- Grillner S, Wallen P, Saitoh K, et al. (2008) Neural bases of goal-directed locomotion in vertebrates – An overview. *Brain Research Reviews* 57(1): 2–12.
- Jackson A, Baker SN and Fetz EE (2006) Tests for presynaptic modulation of corticospinal terminals from peripheral afferents and pyramidal tract in the macaque. *Journal of Physiology* 573(Pt 1): 107–120.
- Jackson A, Spinks RL, Freeman TCB, et al. (2002) Rhythm generation in monkey motor cortex explored using pyramidal tract stimulation. *Journal of Physiology* 541(Pt 3): 685–699.
- Kaufman MT, Churchland MM and Shenoy KV (2013) The roles of monkey M1 neuron classes in movement preparation and execution. *Journal of Neurophysiology* 110(4): 817–825.
- Kaufman MT, Churchland MM, Ryu SI, et al. (2014) Cortical activity in the null space: Permitting preparation without movement. *Nature Neuroscience* 17(3): 440–448.
- Kilner JM and Lemon RN (2013) What we know currently about mirror neurons. *Current Biology* 23(23): R1057–R1062.
- Kinoshita M, Matsui R, Kato S, et al. (2012) Genetic dissection of the circuit for hand dexterity in primates. *Nature* 487(7406): 235–238.
- Kraskov A, Dancause N, Quallo MM, et al. (2009) Corticospinal neurons in macaque ventral premotor cortex with mirror properties: A potential mechanism for action suppression? *Neuron* 64(6): 922–930.
- Kraskov A, Philipp R, Waldert S, et al. (2014) Corticospinal mirror neurons. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences* 369(1644): 20130174.
- Lemon RN (2008) Descending pathways in motor control. *Annual Review of Neuroscience* 31: 195–218.
- Lemon RN (2010) What drives corticospinal output? *F1000 Biology Reports* 2: 51.
- Lemon RN (2014) Action vocabularies and motor commands. In: Gazzaniga MS and Mangun GR (eds) *The Cognitive Neurosciences*. Cambridge, MA: The MIT Press, pp. 491–499.
- Lemon RN, Mantel GWH and Muir RB (1986) Corticospinal facilitation of hand muscles during voluntary movement in the conscious monkey. *Journal of Physiology* 381: 497–527.
- McKiernan BJ, Marcario K, Karrer JH, et al. (1998) Corticomotoneuronal postsynaptic effects in shoulder, elbow, wrist, digit, and intrinsic hand muscles during a reach and prehension task. *Journal of Neurophysiology* 80(4): 1961–1980.
- Macuga KL and Frey SH (2012) Neural representations involved in observed, imagined, and imitated actions are dissociable and hierarchically organized. *Neuroimage* 59(3): 2798–2807.
- Maier M, Bennett KM, Hepp-Reymond MC, et al. (1993) Contribution of the monkey cortico-motoneuronal system to the control of force in precision grip. *Journal of Neurophysiology* 69(3): 772–785.
- Maier MA, Kirkwood PA, Brochier TG, et al. (2013) Responses of single corticospinal neurons to intracortical stimulation of primary motor and premotor cortex in the anesthetized macaque monkey. *Journal of Neurophysiology* 109(12): 2982–2998.
- Mink JW (1996) The basal ganglia: Focused selection and inhibition of competing motor programs. *Progress in Neurobiology* 50(4): 381–425.
- Morecraft RJ, Ge J, Stilwell-Morecraft KS, et al. (2013) Terminal distribution of the corticospinal projection from the hand/arm region of the primary motor cortex to the cervical enlargement in rhesus monkey. *Journal of Comparative Neurology* 521(18): 4205–4235.
- Muir RB and Lemon RN (1983) Corticospinal neurons with a special role in precision grip. *Brain Research* 261(2): 312–316.
- Nambu A, Kaneda K, Tokuno H, et al. (2002) Organization of corticostriatal motor inputs in monkey putamen. *Journal of Neurophysiology* 88(4): 1830–1842.
- Pasquereau B and Turner RS (2011) Primary motor cortex of the Parkinsonian monkey: Differential effects on the spontaneous activity of pyramidal tract-type neurons. *Cerebral Cortex* 21(6): 1362–1378.
- Patton HD and Amassian VE (1954) Single and multiple-unit analysis of cortical stage of pyramidal tract activation. *Journal of Neurophysiology* 17(4): 345–363.
- Porter R and Lemon RN (1993) *Corticospinal Function and Voluntary Movement*. Oxford: Oxford University Press.
- Quallo MM, Kraskov A and Lemon RN (2012) The activity of primary motor cortex corticospinal neurons during tool use by macaque monkeys. *Journal of Neuroscience* 32(48): 17351–17364.
- Rathelot JA and Strick PL (2006) Muscle representation in the macaque motor cortex: An anatomical perspective. *Proceedings of the National Academy of Sciences of the United States of America* 103(21): 8257–8262.
- Rathelot JA and Strick PL (2009) Subdivisions of primary motor cortex based on cortico-motoneuronal cells. *Proceedings of the National Academy of Sciences of the United States of America* 106(3): 918–923.
- Roelfsema PR and Treue S (2014) Basic neuroscience research with non-human primates: A small but indispensable component of biomedical research. *Neuron* 82(6): 1200–1204.
- Schieber MH (2011) Dissociating motor cortex from the motor. *Journal of Physiology* 589(Pt 23): 5613–5624.
- Schmidlin E, Brochier T, Maier MA, et al. (2008) Pronounced reduction of digit motor responses evoked from macaque ventral premotor cortex after reversible inactivation of the primary motor cortex hand area. *Journal of Neuroscience* 28(22): 5772–5783.
- Schwartz AB (2007) Useful signals from motor cortex. *Journal of Physiology* 579(Pt 3): 581–601.
- Shenoy KV, Sahani M and Churchland MM (2013) Cortical control of arm movements: A dynamical systems perspective. *Annual Review of Neuroscience* 36: 337–359.
- Shepherd GM (2013) Corticostriatal connectivity and its role in disease. *Nature Reviews Neuroscience* 14(4): 278–291.
- Shepherd GM (2014) Diversity and complexity in the pyramidal tract projectome. *Nature Reviews Neuroscience* 15(1): 63.
- Soares D, Goldrick I, Lemon RN, et al. (2017) Expression of Kv3.1b potassium channel is widespread in macaque motor cortex pyramidal cells: A histological comparison between rat and macaque. *Journal of Comparative Neurology* 525(9): 2164–2174.
- Takei T and Seki K (2010) Spinal interneurons facilitate coactivation of hand muscles during a precision grip task in monkeys. *Journal of Neuroscience* 30(50): 17041–17050.
- Turner RS and DeLong MR (2000) Corticostriatal activity in primary motor cortex of the macaque. *Journal of Neuroscience* 20(18): 7096–7108.

- Ugolini G and Kuypers HG (1986) Collaterals of corticospinal and pyramidal fibres to the pontine grey demonstrated by a new application of the fluorescent fibre labelling technique. *Brain Research* 365(2): 211–227.
- Vigneswaran G, Kraskov A and Lemon RN (2011) Large identified pyramidal cells in macaque motor and premotor cortex exhibit ‘thin spikes’: Implications for cell type classification. *Journal of Neuroscience* 31(40): 14235–14242.
- Vigneswaran G, Philipp R, Lemon RN, et al. (2013) M1 corticospinal mirror neurons and their role in movement suppression during action observation. *Current Biology* 23(3): 236–243.
- Witham CL, Fisher KM, Edgley SA, et al. (2016) Corticospinal inputs to primate motoneurons innervating the forelimb from two divisions of primary motor cortex and area 3a. *Journal of Neuroscience* 36(9): 2605–2616.
- Zaaimi B, Edgley SA, Soteropoulos DS, et al. (2012) Changes in descending motor pathway connectivity after corticospinal tract lesion in macaque monkey. *Brain* 135(Pt 7): 2277–2289.
- Zinger N, Harel R, Gabler S, et al. (2013) Functional organization of information flow in the corticospinal pathway. *Journal of Neuroscience* 33(3): 1190–1197.