

# Skill learning: Motor cortex rules for learning and memory

Jerome N. Sanes

**Primary motor cortex has a complex, interconnected anatomical and functional architecture with dynamic properties. Recent evidence suggests that, concomitantly with regulating muscle activity and movements, the motor cortex makes key contributions to learning and remembering motor skills.**

Address: Fondazione Santa Lucia IRCCS, via Ardeatina 306, 00179 Rome, Italy.  
E-mail: sanes@hsantalucia.it

**Current Biology** 2000, 10:R495–R497

0960-9822/00/\$ – see front matter  
© 2000 Elsevier Science Ltd. All rights reserved.

A key unresolved issue for systems neurobiology concerns the neural sites and mechanisms of motor skill learning. Sherrington and colleagues [1] noted nearly 100 years ago that neural mechanisms in the primary motor cortex seemingly exhibit a form of plasticity, based on observations of ‘instability’ in responses evoked by cortical stimulation. Seminal work in the following decades also suggested that the motor cortex has a role in plasticity [2,3], though none of these studies could readily address whether the primary motor cortex actually contributes to skill learning. Technical and theoretical advances in studying behavioral aspects of motor learning and motor cortex function have now yielded ample evidence that the primary motor cortex in mammals indeed makes a fundamental contribution to learning. A recent study [4] has highlighted the extent to which neurons in the primary motor cortex may mediate skill acquisition and retention. This work, discussed in detail later in this article, demonstrates that neurons in the motor cortex change their discharge properties when monkeys adapt their arm movements to changes in applied forces. First, however, it is useful to review organizational principles of motor representations and prior work that support a role for the motor cortex in skill acquisition.

## Motor corticed representations and networks

The motor cortex map of the body’s output functions has a somatotopically ordered representation for movements (or muscles) resembling a distorted cartoon of the body shape [5,6], with the constituent body parts laid out upon the precentral gyrus. The principal organizing feature incorporates a medial-to-lateral topography of the leg, arm and head and face. Recent evidence upholds the view that the functional subregions representing the leg, arm and head are segregated within the primary motor cortex, while soundly rejecting the idea that regions within a major body part are represented with a precise topography. Instead, the internal organization of each subregion,

such as that representing the arm, best resembles a distributed network that has a mosaic-like, overlapping organization for motor functions [7]. The distributed representations in the primary motor cortex also have an underlying anatomical substrate consisting of horizontal intrinsic connections that are widespread and lengthy [8].

The available data have thus revealed a pattern of organization in the primary motor cortex involving discrete subdivisions representing the major body parts, each of which has an internal distributed and interconnected network. Such an organization may provide for the immense storage capability and richness of function that is characteristic of distributed networks, and also for flexibility — especially if the organization of the network is modifiable.

Neurons in the region of the primary motor cortex that represents the arm commonly show a broad ‘tuning’, with population responses representing movement direction in three-dimensional space [9]. Complex patterns of discharge by relatively few neurons — sometimes as few as twenty — can capture movement parameters, and indeed it has been shown that they can be used to control robotic devices in real-time [10,11]. The ability to capture features of the activity of small numbers of motor cortex neurons on-line, coupled with the distributed representations for diverse movements, may allow for flexible control of a wide variety of motor actions.

## Motor cortex and plasticity

Mammals, especially primates, exhibit a remarkable amount of behavioral flexibility, especially in motor control. Changes in the brain’s motor representations and internal circuitry, especially within the primary motor cortex, are likely to contribute to this wide range of motor behaviors. Indeed, plasticity of the motor cortex is known to occur following pathological damage, such as peripheral nerve injury, and during seemingly everyday experiences, such as movement repetition [7]. Such reorganization can occur within minutes, and can persist under some circumstances for prolonged periods. Both cortical and subcortical mechanisms likely contribute to observed modifications in primary motor cortex representations, but substantial evidence suggests that plasticity occurs directly at this cortical site.

A likely substrate for plasticity in primary motor cortex is the internal system of horizontal connections that span the region. Evidence from several sources indicates that this system of connections functionally associates motor cortex neurons into dynamically structured assemblies that form

motor maps. Manipulations of local and systemic transmission via the inhibitory neurotransmitter  $\gamma$ -amino butyric acid (GABA) has revealed the existence of normally hidden representations of forelimb movements in primary motor cortex [12,13]. Moreover, functional expansion of the output representations of primary motor cortex following nerve injury has been correlated with existing horizontal connections between functional subregions [14]. Synaptic modification most probably mediates the rapid, and perhaps also enduring, changes in motor cortical neuronal mechanisms. A further clue has come from the observation that intrinsic pathways in the primary motor cortex, including those interconnecting neurons horizontally and vertically, have a capacity for long-lasting synaptic modification, with connection strengths that can be adjusted up or down [15].

### **Motor cortex and learning**

As exemplified by the recent work of Gandolfo *et al.* [4], the primary motor cortex appears to have an important role in forming new or adapting existing motor skills. Many examples have been reported of learned modifications to representational maps of the primary motor cortex, in both experimental animals and humans [7]. Such modifications have been shown to occur, for example, in the course of experiments that have involved: alterations to motor task parameters [16]; learning to grip objects precisely [17]; attaining targets more efficiently [18]; practising already learned movements [19,20]; learning a new movement sequence [21]; and adapting limb forces — as in the work of Gandolfo *et al.* [4] — to perform efficient straight line movements [22].

If the primary motor cortex contributes to learning or to storing motor skills, evidence must exist that functional reorganization occurs within motor cortical circuitry, either temporarily or permanently, in association with learning. Evidence has indeed been obtained recently that skill learning leaves a (memory) trace in the primary motor cortex after a new skill has been acquired — horizontal connections in the primary motor cortex of the rat were shown to undergo enduring changes in synaptic efficiency after the animals learnt a novel reaching task [23].

Gandolfo *et al.* [4] have also provided evidence that skill acquisition is tracked and retained by firing properties of neurons in primary motor cortex. These workers investigated whether neural activity in the primary motor cortex of the monkey was modified when the animals had to adapt their arm movement to artificially imposed forces. The task designed by Gandolfo *et al.* [4] was somewhat analogous to experiments testing adaptation of the visual system by using wedge prisms to distort the incoming visual information. After such prisms are put on and a subject is asked to make an arm movement to some target, their reach initially veers in the direction of the distorted

visual scene; their reaching gradually becomes accurate again, however, apparently as approximating corrections are made to compensate for the effect of the prisms.

In the force version of this experiment used by Gandolfo *et al.* [4], the subject had to perform straight-line arm movements after encountering new forces that perturb those movements. Gandolfo *et al.* [4] found that their monkeys, like human subjects [24], readily adapted their reaching to the new situation, ultimately performing straight-line movements with the new perturbing forces. Similarly, when the force to which monkeys became adapted was removed, their movements initially exhibited after-effects and then slowly became straighter after a re-adaptation period.

Gandolfo *et al.* [4] used the directional tuning properties of neurons in primary motor cortex to classify learning and memory related processing of the cells during the adaptation and re-adaptation periods. They found that neurons in primary motor cortex fall into several different categories, two of which have particular relevance to the motor cortex's role in skill learning and memory. A first set of neurons, comprising about 15% of the responsive cells, exhibited 'dynamic' changes in their tuning properties during the adaptation phase, but returned to the baseline state when the monkeys re-experienced the original force field. These neurons may have a role in adaptation, but probably do not participate in skill retention. A second class of neurons, a 'memory' category comprising about 40% of the responsive cells, exhibited changes in tuning during adaptation that endured beyond the learning phase. These memory neurons might provide the necessary substrate for skill retention, and their existence in motor cortex suggests that this brain area may make an important contribution to skill development.

The intriguing results reported by Gandolfo *et al.* [4] furnish important new information about motor cortex functions, but they also invite justifiable comment. The existence of neurons having 'dynamic' and 'memory' properties in motor cortex is indisputable. But the new results provide only initial clues that such cells have roles in motor skill acquisition and retention. A relevant limitation concerns the repeated experience of the monkeys to the same force-field. With continued experience of the imposed force-field, it no longer has novelty — though monkeys still seem to require many trials to adapt to its application — and it remains somewhat uncertain why motor cortex neurons suddenly exhibit novel dynamic and memory properties, when the movement forces have been performed on numerous prior occasions.

One might argue that behavioral adaptation, even for known situations, requires learning and memory related processing. Future work might attempt to track firing of selected neurons for longer periods, even across days, while

monkeys alternate between no force field and a force field, or movements performed against many different imposed loads. In this way, one could address whether novelty alone rules the dynamic or memory like activity. Other issues not addressed concern the laminar location of the neurons and their connectivity. With further elucidation of these issues, the role of primary motor cortex in skill learning and memory should become clearer, and we may know for sure whether motor cortex truly can set rules of behavior.

### Acknowledgements

The Italian Health Ministry grant ICS120.3/RC99 and National Institutes of Health grants AG10634 and NS35376 supported this work. I alone have responsibility for this dispatch, though much of the intellectual content herein developed from long-term collaborative work with Dr. John P. Donoghue of the Department of Neuroscience, Brown University.

### References

1. Brown TG, Sherrington CS: **On the instability of a cortical point.** *Proc R Soc Lond [Biol]* 1912, **85**:250-277.
2. Lashley KS: **Temporal variation in the function of the gyrus precentralis in primates.** *Am J Physiol* 1923, **65**:585-602.
3. Gellhorn E, Hyde J: **Influence of proprioception on map of cortical responses.** *J Physiol (Lond)* 1953, **122**:371-385.
4. Gandolfo F, Li C, Benda BJ, Schioppa CP, Bizzi E: **Cortical correlates of learning in monkeys adapting to a new dynamical environment.** *Proc Natl Acad Sci USA* 2000, **97**:2259-2263.
5. Penfield W, Rasmussen T: *The Cerebral Cortex of Man.* New York: The MacMillan Company; 1950.
6. Woolsey CN, Settlage PH, Meyer DR, Sencer W, Hamuy TP, Travis AM: **Patterns of localization in precentral and 'supplementary' motor areas and their relation to the concept of a premotor area.** *Res Publ Assoc Res Nerv Men. Dis* 1952, **30**:238-264.
7. Sanes JN, Donoghue JP: **Plasticity and primary motor cortex.** *Annu Rev Neurosci* 2000, **23**:393-415.
8. Huntley GW, Jones EG: **Relationship of intrinsic connections to forelimb movement representations in monkey motor cortex: a correlative anatomical and physiological study.** *J Neurophysiol* 1991, **66**:390-413.
9. Georgopoulos AP: **Spatial coding of visually guided arm movements in primate motor cortex.** *Can J Physiol Pharmacol* 1988, **66**:518-526.
10. Maynard EM, Hatsopoulos NG, Ojakangas CL, Acuna BD, Sanes JN, Normann RA, Donoghue JP: **Neuronal interactions improve cortical population coding of movement direction.** *J Neurosci* 1999, **19**:8083-8093.
11. Chapin JK, Moxon KA, Markowitz RS, Nicolelis MA: **Real-time control of a robot arm using simultaneously recorded neurons in the motor cortex.** *Nat Neurosci* 1999, **2**:664-670.
12. Jacobs KM, Donoghue JP: **Reshaping the cortical motor map by unmasking latent intracortical connections.** *Science* 1991, **251**:944-947.
13. Ziemann U, Hallett M, Cohen LG: **Mechanisms of deafferentation-induced plasticity in human motor cortex.** *J Neurosci* 1998, **18**:7000-7007.
14. Huntley GW: **Correlation between patterns of horizontal connectivity and the extent of short-term representational plasticity in rat motor cortex.** *Cereb Cortex* 1997, **7**:143-156.
15. Donoghue JP, Hess G, Sanes JN: **Motor cortical substrates and mechanisms for learning.** In *Acquisition of Motor Behavior in Vertebrates.* Edited by Bloedel JR, Ebner TJ, Wise SP. Cambridge, MA: MIT Press; 1996:363-386.
16. Sanes JN, Donoghue JP: **Static and dynamic organization of motor cortex.** *Adv Neurol* 1997, **73**:277-2996.
17. Nudo RJ, Milliken GW, Jenkins WM, Merzenich MM: **Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys.** *J Neurosci* 1996, **16**:785-807.
18. Kleim JA, Barbay S, Nudo RJ: **Functional reorganization of the rat motor cortex following motor skill learning.** *J Neurophysiol* 1998, **80**:3321-3325.
19. Classen J, Liepert J, Wise SP, Hallett M, Cohen LG: **Rapid plasticity of human cortical movement representation induced by practice.** *J Neurophysiol* 1998, **79**:1117-1123.
20. Karni A, Meyer G, Jezzard P, Adams MM, Turner R, Ungerleider LG: **Functional MRI evidence for adult motor cortex plasticity during motor skill learning.** *Nature* 1995, **377**:155-158.
21. Hazeltine E, Grafton ST, Ivry R: **Attention and stimulus characteristics determine the locus of motor-sequence encoding. A PET study.** *Brain* 1997, **120**:123-140.
22. Shadmehr R, Holcomb HH: **Neural correlates of motor memory consolidation.** *Science* 1997, **277**:821-825.
23. Rioult-Pedotti MS, Friedman D, Hess G, Donoghue JP: **Strengthening of horizontal cortical connections following skill learning.** *Nat Neurosci* 1998, **1**:230-234.
24. Shadmehr R, Mussa-Ivaldi FA: **Adaptive representation of dynamics during learning of a motor task.** *J Neurosci* 1994, **14**:3208-3224.