Cortical Control of Motor Learning

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ABSTRACT

The execution of the simplest gestures requires the accurate coordination of several muscles. In robotic systems, engineers coordinate the action of multiple motors by writing computer code that specifies how the motors must be activated for achieving the desired robot motion and for compensating for unexpected disturbance. Humans and animals follow another path. Something akin to programming is achieved in nature by the biological mechanisms of synaptic plasticity; that is, by the variation in efficacy of neural transmission brought about by past history of pre- and postsynaptic signals. However, robots and animals differ in another important way. Robots (at least those of the current generations) have fixed mechanical structure and dimensions. In contrast, the mechanics of muscles, bones, and ligaments change over time: the length of our limbs varies as we grow into adulthood; some part of our body may lose its functionality following a lesion or a degenerative process; muscle mechanics may vary over just a few minutes of intense activity. Because of these changes, the central nervous system must continuously adapt motor commands to the mechanics of the body. Adaptation — the ability to carry previously learned
motor skills into new mechanical contexts — is a form of motor learning. In this chapter, we present a view of motor learning that starts from the analysis of the computational problems associated with the execution of the simplest gestures. We discuss the theoretical idea of internal models and present some evidence and theoretical considerations suggesting that internal models of limb dynamics may be obtained by the combination of simple modules or “motor primitives.” Then, we review some experimental results on the activity of neurons in the cortex during a learning task. These findings suggest that the motor cortical areas include neurons that process well-acquired movements as well as neurons that change their behavior during and after being exposed to a new task.

12.1 DYNAMICS

According to the laws of Newtonian mechanics, in order to impress a motion upon an object one must apply a force directly proportional to the desired acceleration. This is Newton’s equation $f = m \, a$.

A desired motion of an object is a sequence of positions $x(t)$ that one wishes the limb to occupy at subsequent instants of time $t$. Such a sequence is called a trajectory and is mathematically represented as a function, $x = x(t)$. To use Newton’s equation for deriving the needed time-sequence of forces, one must calculate the first temporal derivative of the trajectory, the velocity, and then the second temporal derivative, the acceleration. Finally, one obtains the desired force from this acceleration. This is an example of inverse dynamic computation. The problem of direct dynamics is to compute the trajectory resulting from the application of a force.

One of the central questions in motor control is how the central nervous system solves the inverse dynamics problem and generates the motor commands that guide our limbs. A system of second-order nonlinear differential equations is generally considered to be an adequate representation for the passive dynamics of a limb. A compact expression for such a system is as follows:

$$D(q, \dot{q}, \ddot{q}) = \tau(t)$$

where $q$, $\dot{q}$ and $\ddot{q}$ represent the limb configuration vector — for example the vector of joint angles — and its first and second time derivatives. The term $\tau(t)$ is a vector of joint torques at time $t$ — it plays the role of $f$ in Newton’s equation. In practice, the expression for $D$ — which corresponds to $m \, a$ — may have a few terms for a two-joint planar arm (Figure 12.1) or it may take several pages for more realistic models of the arm’s multiple-joint geometry. The inverse dynamics approach to the control of multiple-joint limbs consists in solving explicitly for a torque trajectory $\tau(t)$ given a desired trajectory of the limb $q_d(t)$. This is done by replacing $q_d(t)$ for the variable $q$ on the left side of Equation 12.1:

$$\tau(t) = D(q_d(t), \dot{q}_d(t), \ddot{q}_d(t))$$

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Early models of motor control\textsuperscript{2,3} suggested that the nervous system may store specific solutions of Equation 12.2 corresponding to the desired motions of the body. However, simple considerations about the geometrical space of meaningful behaviors are sufficient to establish that this approach would be inadequate.\textsuperscript{4} An alternative

\begin{align*}
D_1 &= (l_1 + l_2 + m_2 l_2 \cos (q_2) + \frac{m_1 l_1^2 + m_2 l_2^2}{4} + m_2 l_2) \ddot{q}_1 + \\
&+ (l_2 + \frac{m_1 l_1 l_2}{2} \cos (q_2) + \frac{m_2 l_2^2}{4}) \ddot{q}_2 - \frac{m_2 l_1 l_2}{2} \sin (q_2) \dot{q}_1 \dot{q}_2 + \beta_1 (q_1, q_2, \dot{q}_1, \dot{q}_2) \\
&- m_2 l_1 l_2 \sin (q_2) \dot{q}_1 \dot{q}_2 \\
D_2 &= (l_2 + \frac{m_2 l_2}{2} \cos (q_2) + \frac{m_2 l_2^2}{4}) \ddot{q}_1 + (l_2 + \frac{m_2 l_2^2}{4}) \ddot{q}_2 + \\
&- \frac{m_2 l_1 l_2}{2} \sin (q_2) \dot{q}_1 \dot{q}_2 + \beta_2 (q_1, q_2, \dot{q}_1, \dot{q}_2)
\end{align*}

\textbf{FIGURE 12.1} Simplified model of planar limb dynamics. The mechanics of the arm are approximated by a two-joint mechanism with angles $q_1$ (with respect to the torso) and $q_2$ (with respect to the forearm, respectively (top)). The dynamics are described by two nonlinear equations (bottom) that relate the joint torques at the shoulder ($D_1$) and at the elbow ($D_2$) to the angular position, velocity, and acceleration of both joints. The parameters that appear in these expressions are the lengths of the two segments ($l_1$ and $l_2$); their masses ($m_1$ and $m_2$); their moments of inertia ($I_1$ and $I_2$). The numerical values used in the simulations are the same as those listed in Table 1 of Shadmehr and Mussa-Ivaldi\textsuperscript{7} and correspond to values estimated from an experimental subject. The terms $\beta_1$ and $\beta_2$ describe the viscoelastic behavior of the resting arm. They are simulated here by linear stiffness and viscosity matrices. (From Reference 4, with permission.)

\subsection{12.2 INTERNAL MODELS}

Early models of motor control\textsuperscript{2,3} suggested that the nervous system may store specific solutions of Equation 12.2 corresponding to the desired motions of the body. However, simple considerations about the geometrical space of meaningful behaviors are sufficient to establish that this approach would be inadequate.\textsuperscript{4} An alternative
approach postulates that the motor system solves the problems of dynamics by constructing internal representations of the way in which limbs respond to applied forces. These representations would allow us to generate new behaviors and to handle situations that we have not yet encountered. A vivid illustration of how explicit representations of dynamics, also called internal models, may facilitate motor learning is offered by the work of Schaal and Atkeson, who studied the task of balancing an inverted pendulum with a robotic arm. They found that robots can be trained to carry out this task successfully when they can build an internal model of the dynamics associated with the balancing act. Such a model may be constructed using data derived from the observation of humans engaging competently in the same task.

The term internal model refers either to (1) the transformation from a motor command to the consequent behavior, or to (2) the transformation from a desired behavior to the corresponding motor command. A model of the first kind is called a forward model. Forward models provide the control system with the means to predict the outcome of a command, and to estimate the current state in the presence of feedback delay. A representation of the mapping from planned actions to motor commands is called an inverse model. Strong experimental evidence for the existence of internal models has been offered by studies of the adaptation of arm movements to perturbing force fields.

12.3 EVIDENCE FOR INVERSE INTERNAL MODELS

One way to test for the existence of inverse internal models is by changing the dynamics that the central nervous system must control in order to execute a desired movement. This approach was adopted by Shadmehr and Mussa-Ivaldi. They asked subjects to make reaching movements in the presence of externally imposed forces. These forces were produced by a robot whose free endpoint was held as a pointer by the subjects (Figure 12.2A). The subjects were asked to execute reaching movements toward a number of visual targets. Since the force field produced by the robot (Figure 12.2B) significantly changed the dynamics of the reaching movements, the subjects’ movements initially were grossly distorted (Figure 12.2D) when compared to the undisturbed movements (Figure 12.2C). However, with practice, the subjects’ hand trajectories in the force field converged to a path similar to that produced in absence of any perturbing force (Figure 12.3).

Subjects’ recovery of performance is due to learning. After the training had been established, the force field was unexpectedly removed for the duration of a single hand movement. The resulting trajectories (Figure 12.4), named after-effects, were approximate mirror images of those that the same subjects produced when they had initially been exposed to the force field. The emergence of after-effects indicates that the central nervous system had composed an internal model of the external field. The internal model was generating patterns of force that effectively anticipated the disturbing forces that the moving hand was encountering. The fact that these learned forces compensated for the disturbances applied by the robotic arm during the subjects’ reaching movements indicates that the central nervous system programs these forces in advance. The after-effects demonstrate that these forces are not the products of some reflex compensation of the disturbing field.
It is of interest to ask what the properties of the internal model are, and in particular whether the model could generalize to regions of the state space where the disturbing forces were not experienced. Recent experiments by Gandolfo and coworkers\textsuperscript{13} were designed to test the generalization of motor adaptation to regions where training had not occurred. In these experiments, subjects were asked to execute point-to-point planar movements between targets placed in one section of the work-space. Their hand grasped the handle of the robot, which was used to record and perturb their trajectories. Again, as in the experiments of Shadmehr and Mussa-Ivaldi,
FIGURE 12.3 Time course of adaptation. Average and standard deviation of hand trajectories executed during the training period in the force field of Figure 12.7B. Performance is plotted during the first (A), second (B), third (C), and final (D) set of 250 movements. (From Reference 7, with permission.)

FIGURE 12.4 After-effects of adaptation. Average and standard deviations of hand trajectories executed at the end of training in the field when the field was unexpectedly removed on random trials. (From Reference 7, with permission.)
adaptation was quantified by the amount of the after-effects observed when the perturbing forces were discontinued.

As a way of establishing the generalization of motor learning, Gandolfo and coworkers\textsuperscript{13} perturbed only the trajectories made to a subset of the targets and searched for after-effects in movements that had not been exposed to perturbations. The amount of the after-effect made it possible to quantify the force field that the subjects expected to encounter during their movements in the trained as well as in the novel directions. The same investigators found that the after-effects were present, as expected, along the trained directions, but the magnitude of the after-effects decayed smoothly with increasing distance from the trained directions. This finding indicates that the subjects were also able to compensate for forces experienced at neighboring workspace locations. Corroborating evidence was recorded by Thoroughman and Shadmehr\textsuperscript{14,15}

The experiments described above have shown that subjects adapt to a new environment by forming a representation of the external force field that they encounter when making reaching movements. Does this representation form an imprint in long-term memory? Brashers-Krug and coworkers\textsuperscript{9} investigated this question by exposing their subjects to perturbing force fields that interfered with the execution of reaching movements (Figure 12.5). After practicing reaching movements, these subjects were able to compensate for the imposed forces (task A) and were able to guide the cursor accurately to the targets despite the disturbing forces. This group of subjects, which was tested 24 hours later with the same disturbing forces, demonstrated not only retention of the acquired motor skill, but also additional learning. Surprisingly, they performed at a significantly higher level on day two than they had on day one. A second group of subjects was trained on day one with a different pattern of forces (task B), immediately after performing task A. In task B the manipulandum produced forces opposite in direction to those applied during task A. When this second group of subjects was tested for retention of task A on day two, the investigators found that the subjects did not retain any of the skills that had been learned earlier. This phenomenon is known as retrograde interference. Next, Brashers-Krug and colleagues\textsuperscript{9} investigated whether the susceptibility to retrograde interference decreased with time. They found that retrograde interference decreased monotonically with time as the interval between tasks A and B increased. When 4 hours passed before task B was learned, the skill learned in task A was completely retained — the initial learning had consolidated. What is remarkable in these results is that motor memory is transformed with the passage of time and in absence of further practice, from an initial fragile state to a more solid state.

In summary, the main findings of these studies are as follows: (1) when exposed to a deterministic field of velocity-dependent forces, arm movements are first distorted and, after repeated practice, the initial kinematics are recovered; (2) if, following adaptation, a field is suddenly removed, after-effects are clearly visible as mirror images of the initial perturbations; (3) adaptation is achieved by the motor system through the formation of a local map that associates the states (positions and velocities) visited during the training period with the corresponding forces; and (4) after adaptation this map — that is, the internal model of the field — undergoes a process of consolidation.
FIGURE 12.5 Motor memory consolidation. The left panels show the learning curves for three groups of subjects. Learning in a perturbing force field was quantified by a correlation coefficient between the trajectories in the field and the average trajectory before any perturbation had been applied. On the right are the mean performances in experiment days 1 and 2. Subjects in the control group (A) practiced reaching movements against a force field (task A) in the first day and then were tested again in the same field during the second day. Subjects in the no-break group (B) during the first day practiced movements in the field of task A. Then they immediately practiced movements in a different field (task B). In the second day they practiced again in the field of task A. Finally, subjects of the 4-hour break group (C) during the first day were exposed to the fields of tasks A and B but with a breaking interval of 4 hours between the two. Their performance was measured on task A on day 2. Learning curves and mean performance were significantly higher on day 2 both for the control group and for the 4-hour break group. In contrast, subjects in the no-break group did not display any difference in performance from day 1 to day 2. (From Reference 9, with permission.)
In order to investigate the neural signals that occur during adaptation, we recently recorded the activity of single neurons from the motor cortical areas of monkeys.

12.4 NEURONAL ACTIVITY RECORDED DURING ADAPTATION: LEARNING A NEW DYNAMICS

In a series of recent studies, we investigated how the activity of neurons in the cortical motor areas of the frontal lobe is modified when monkeys learn a new dynamic. To this end, we used the experimental setup of Shadmehr and Mussa-Ivaldi (scaled down). During the experiments, the monkeys sat on a chair and executed reaching movements instructed by targets appearing on a computer monitor, while holding the handle of a robotic arm. Two motors at the base of the robot could exert perturbing forces upon the hand of the monkey. In each session, the monkeys performed center-out reaching movements in three subsequent conditions: Baseline (160 trials, no force); Force (160 trials); and Washout (160 trials, no force). In the Force condition, the monkeys were exposed to either a clockwise (CW) or to a counterclockwise (CCW) viscous force field $F = BV$ with $B = [0 \ -b; b \ 0]$ and $V$ equal to the hand velocity.

The psychophysics of the task, illustrated in Color Figure 12.6*, are essentially the same as those in humans as described by Shadmehr and Mussa-Ivaldi. The hand trajectories are essentially straight in the Baseline and initially become deviated.

* See color insert following page 170.
when the external force is introduced. As the monkey adapts to the perturbation, however, the hand kinematics gradually converge to those observed in the Baseline. In other words, the hand trajectories become straight again and the speed profile returns to its original bell shape. In the Washout, when the force is removed, the monkey displays a few after-effects as the hand trajectories are deviated in a way that mirrors the initial deviation observed in the Force condition. After a short time, however, the hand kinematics return to those observed in the Baseline.

In the analysis of neuronal activity, we essentially disregarded the first adaptation phase in the Early Force condition and in Early Washout, and we focused on movements that had comparable kinematics. Hence, this experimental design allowed for dissociating the neuronal activity related to the movement kinematics (the same in the three conditions) from that related to the movement dynamics (the same in the Baseline and Washout, but different in the Force condition). Most importantly, the experimental design allowed us to dissociate the neuronal correlates of motor performance from plastic changes associated with motor learning. For this dissociation, we compared the activity of neurons recorded in the Washout with that recorded in the Baseline. Indeed, the performance of the monkey (kinematics and dynamics) was essentially identical in the two conditions. The only difference was that in the Washout the monkeys had previously adapted and learned a new dynamic. Hence, changes in the activity in the Washout compared to the Baseline were associated with that learning experience.

Our first study focused on the primary motor cortex (M1). In particular, we recorded and analyzed the activity of 162 individual neurons in a movement-related time window (from 200 msec before the movement onset to the end of movement). As first described by Georgopoulos and colleagues, we found that a large proportion of neurons in M1 were directionally tuned in the Baseline; their activity differed for movements in different directions. Surprisingly, however, we found that some of the neurons that were initially not tuned in the Baseline acquired a new directional tuning in the Force condition following adaptation to the force field. In some cases, these “tune-in” cells maintained their newly acquired directional tuning in the Washout following readaptation to the unperturbed conditions. Conversely, other neurons that were initially tuned lost their directional tuning following adaptation (“tune-out” neurons). The presence of these two groups of cells is an indication of what seems to be an intrinsic property of cells in M1: to be shaped by experience and to undergo plastic changes in a relatively short period of time.

The tune-in and tune-out groups accounted for 37% of the cells recorded in M1. A further analysis, however, revealed another variety of plastic changes associated with motor learning. Specifically, neurons that were directionally tuned throughout the three conditions (Baseline, Force, and Washout) generally changed their preferred direction (PD) as the monkey adapted to the perturbation and readapted to the unperturbed conditions in the washout. Interestingly, in some cases, the final PD in the Washout was different from that originally recorded in the Baseline. These memory cells accounted for a total of 40% of the population of neurons directionally tuned throughout the three conditions.

In conclusion, these data strongly suggest that M1 plays a prime role in motor learning.
Although our M1 results are quite intriguing, they are also somewhat puzzling. They show a surprisingly high degree of plasticity in M1, an area that seems crucial for motor control (for instance, lesions to M1 dramatically disrupt movement generation). Moreover, they show that plastic changes can be induced by a relatively brief exposure to new forces. But how can the same population of neurons effectively support motor performance (after all, movements in the Washout are as good as in the Baseline) and at the same time be flexible enough to support motor learning? A closer inspection of the changes of PD recorded for individual neurons and for the entire population offers a glimpse into this fascinating question.

One of the advantages of our experimental design is that curl force fields (i.e., forces in a direction that is orthogonal to the instantaneous hand velocity) impose strong constraints onto the changes of electromyographic (EMG) muscle activity across conditions. Specifically, when monkeys adapt to a curl force field, the PD of muscles shifts in the direction of the external force (CW or CCW, depending on the force field). The reason for this shift is that the internal forces exerted by muscles sum with the external force field in the Force condition. As a result, the monkey maximally activates any given muscle in the Force condition to execute movements in a direction (the new PD) different from the direction that elicited maximal muscle activation in the Baseline (the old PD). Most importantly, the PD shifts for all the muscles in the same direction, namely the direction of the external force field, independently of the original PD. We verified these predictions empirically by recording in our monkeys the EMG of five muscles of the upper arm (pectoralis, deltoid, triceps, biceps, and brachioradialis). We found that the PD of all muscles shifted in the direction of the external force, on average by 19.2° ($p < 0.005$, $t$ test). In the Washout, the PD of muscles shifted back by –15.4° ($p < 0.05$, $t$ test) so that there was no net shift of PD in the Washout compared to the Baseline (mean shift 4.4°, $p = 0.06$, $t$ test).

These changes of PD observed for the muscle EMG offer a framework for interpreting the activity of neurons. For each neuron in M1 directionally tuned in both conditions, we computed the shift of PD in the Force as compared to the Baseline. Shifts in the direction of the external force were defined as positive. Considering the entire population, we found that the PD of M1 neurons shifted on average by 16.2° in the Force condition compared to the Baseline ($p < 10^{-5}$, $t$ test). In the Washout, the PD of M1 neurons shifted back by 14.2° ($p < 0.001$, $t$ test), so that no net shift was present when comparing the Washout and the Baseline ($p = 0.9$, $t$ test). In other words, the changes across conditions recorded for neurons in M1 as a population matched the changes observed for muscles.

When individual neurons are taken into consideration, an interesting variety of behaviors appears. For one group of neurons, the PD did not change at all across conditions. This group of “kinematic” cells accounted for 34% of the neurons that were directionally tuned throughout the three conditions. For another group of cells, the PD shifted in the Force condition (typically in the direction of the external force field) and shifted in the opposite direction in the Washout, back to the original PD.
In other words, this group of “dynamic” cells (22%) behaved very much like muscles. For the most interesting group of cells, named “memory” cells, the PD in the Washout was significantly different from that in the Baseline. More precisely, we found two groups of memory cells. For “memory I” cells, the PD shifted in the Force condition, typically in the direction of the external force field, and remained in the Washout oriented in the newly acquired direction. In contrast, for “memory II” cells, the PD did not change in the Force compared to the Baseline, and shifted in the Washout, typically in the direction opposite to the previously experienced force field. In total, the two classes of memory I and memory II cells accounted for 19% and 22% of the population, respectively. Thus, a large proportion of individual neurons in M1 maintained a trace of the learning experience outlasting exposure to the perturbation (Color Figure 12.7).

In our interpretation, the coexistence of memory I and memory II cells conforms well with the notion that the population of M1 supports both functions of motor performance and motor learning, and offers a glimpse into how it may do so. On the one hand, the PD of memory I cells shifted in the direction of the external force in the Force condition and remained shifted in the Washout. On the other hand, the PD of memory II cells did not shift in the Force condition but shifted in the opposite direction in the Washout. On average, the shifts of PD of memory I and memory II cells cancelled each other in the Washout. (Notably, the percentages of the two classes were similar.)
In order to subserve motor performance, M1 must provide a similar output in the Baseline and in the Washout. And indeed, in a statistical macroscopic sense the activity of M1 is the same in the Washout as in the Baseline, because the changes recorded for the entire population average to zero in the Washout. But in order to subserve motor learning, M1 must maintain after readaptation a trace of the previous learning experience. And indeed, at the microscopic level of individual neurons M1 was very different in the Washout and in the Baseline, because for 40% of neurons the Washout PD was significantly different in the two conditions. Thus, M1 as a population may subserve both functions of motor performance and motor learning by letting individual neurons change their activity when monkeys learn a new dynamic (motor learning), while reorganizing itself at any time to meet behavioral needs (motor performance).16

12.6 NEURONAL PLASTICITY IN OTHER MOTOR AREAS

Recent anatomical studies have identified some 10 or 12 motor areas in the primate frontal lobe.17–19 According to the traditional view, several “premotor” areas host “high” sensorimotor processes and project to M1, which in turn controls movements through its cortico-spinal projections. More recent anatomical work, however, has found that direct projections to the spinal cord originate from a number of motor areas, including the dorsal premotor area (PMd), the ventral premotor area (PMv), the supplementary motor area (SMA), three or four cingulate motor areas, and M1. In a series of studies, we extended to SMA, PMd, and PMv the experiments first conducted on M1.20–22 During the experiments, we imposed a randomly variable delay period between the instruction (cue) and the go signal. In total, we recorded and analyzed the activity of 798 neurons from the 4 areas during a delay time (DT) window (500 msec before the cue) and during the movement-related time (MT) window (from 200 msec before the movement onset to the movement end). Our results can be summarized as follows.

Considering neurons as populations, dynamics-related activity (i.e., significant shifts of PD) are observed during movement planning (DT time window) in PMd and SMA, but not in M1 and PMv. (In fact, very limited directional tuning is observed in M1 and PMv during the delay.) In contrast, during movement execution (MT time window), dynamics-related activity is significantly present in all four areas. Likewise, evidence of neuronal plasticity associated with the learning of a new dynamic is found in all four areas.

12.7 REVIEW OF STUDIES ON CORTICAL PLASTICITY

Vast evidence accumulated in the past two decades shows that sensory and motor areas of the cerebral cortex are plastic. Numerous studies have found extensive cortical reorganization associated with perceptual and motor learning. For instance, in the visual domain, Sakai and Miyashita23 described neurons in the anterior temporal cortex that increased their activation in the delay following presentation of a (nonpreferred) visual stimulus arbitrarily associated with their preferred stimulus.
More recently Erickson and colleagues\textsuperscript{24} were able to induce similar response preference in neurons of the perirhinal cortex after one day of exposure to complex visual stimuli, suggesting that clusters of neurons with similar stimulus preferences are shaped through experience. In the acoustic domain, the cortical representation of the frequency range that monkeys were trained to discriminate was found to be increased in the primary auditory cortex.\textsuperscript{25} In the somatosensory domain, extensive reorganization of the somatosensory cortex was observed after removal of sensory afferent,\textsuperscript{26} and after training.\textsuperscript{27,28} Evidence of short-term neuronal plasticity was also found in the dorsolateral prefrontal cortex of monkeys learning a new conditional association. Asaad and coworkers\textsuperscript{29} found that the latency of neuronal response (directional selectivity) of neurons progressively decreased over the course of learning.

Several studies also found evidence of neuronal plasticity in various areas when monkeys learned a new conditional motor association. In the task of Wise and coworkers, a novel visual stimulus instructed one of four movements, arbitrarily selected, and the monkeys learned the correct association by trial and error. The authors found extensive learning-related plasticity in PMd\textsuperscript{30} and in the supplementary eye fields\textsuperscript{31} for conditional associations that instructed limb and eye movements, respectively. Hikosaka and coworkers recently obtained similar results in presupplementary motor area (preSMA). In a first set of experiments in both humans functional magnetic resonance imaging (fMRI) and monkeys (single-cell recordings and reversible lesions; reviewed in Reference 32), the authors contrasted the activity recorded during execution of new versus learned sequences of arm movements instructed by targets appearing on a computer screen. In particular, they found that neurons in preSMA were preferably activated during the execution of new sequences.\textsuperscript{33} Similar results were obtained by Germain and Lamarre\textsuperscript{34} in the rostral PMd. Finally, plastic changes were also found in the motor cortex of rats learning new sensorimotor associations.\textsuperscript{35}

With respect to motor learning, several studies found evidence of long-lasting changes (long-term plasticity) in M1 following skill acquisition. In humans, it was found that the digit representation of the left hand in the M1 of string players was significantly enlarged.\textsuperscript{36} Similar effects were also found comparing the activation recorded during execution of a motor sequence practiced over a few weeks versus an unpracticed sequence.\textsuperscript{37} Similar findings were obtained with transcranial magnetic stimulation (TMS).\textsuperscript{38} In monkeys, Nudo and colleagues\textsuperscript{39} mapped with microstimulation the cortical representation of digits and wrist/forearm in M1 before and after training in one of two tasks. They found that the digit representation was enlarged following training in a small-object retrieval task, when the digits were actively used. Conversely, the wrist/forearm representation was enlarged following training in a key-turning task. Work by Donoghue and coworkers has found evidence of long-term potentiation (LTP) and strengthening of horizontal connection in the motor cortex of rats after learning a new motor skill.\textsuperscript{40–42}

In other studies investigators have described the changes in neuronal activity that intervene shortly after acquisition of a new motor skill (short-term plasticity). For instance, it was found that the training of one finger movements for 10 minutes changed the direction of movements evoked by focal TMS.\textsuperscript{43} Wise and colleagues\textsuperscript{44} recorded from M1, PMd, and SMA of one monkey adapting to new visuomotor
mappings. In this task — sometimes referred to as acquisition of a new internal model for the kinematics\textsuperscript{45,46} — the experimenters manipulated the association between the visual stimulus and the instructed movement. Wise and colleagues found evidence of learning-related plastic changes in the activity of all three areas.

12.8 CONCLUSIONS AND FUTURE DIRECTIONS ON MOTOR LEARNING

A priori motor learning could be achieved in at least two ways. One possible scenario could be that one or more areas (e.g., M1), “in charge of the usual business,” process movements in already-learned conditions, and supports well-acquired motor skills. According to this hypothesis, other areas hierarchically higher or parallel (e.g., “premotor” areas) would activate when the normal system fails and would play a more direct role in motor learning. An alternative scenario is that learning-related activity is embedded in the motor system, and that the same areas and the same neurons that process well-acquired movements also accommodate the new conditions when necessary.

At least in part, the results of our studies seem more consistent with this second view, for two reasons. First, dynamics-related activity was present in multiple areas, and plastic changes associated with motor learning were similarly found in all of them. Second, plastic changes were often observed among cells that were already active and committed to the task prior to learning. Furthermore, we did not observe a sharp distinction between the classes of cells (kinematic, dynamic, and memory) in any dimension except for the changes of PD across epochs.

Clearly, the emerging view of “embedded memory” is in syntony with the neural networks model of associative memory, where the same variables that represent any given process modify themselves to execute new computations. Two important remarks should however be made in regard to this issue. First, in all areas we also found neurons that only became committed to the task when the monkeys learned the new dynamics (tune-in cells). Second, in our experiments monkeys were learning a new dynamic. The embedded-memory view may well fail for other instances of motor learning, for example when human subjects or monkeys learn more elaborate motor skills.

We conclude this chapter by indicating one important issue that remains open for future research. From a psychophysical standpoint, our task involves both short-term learning (the monkeys adapt to the force field within one session) and long-term learning (adaptation becomes better and faster across sessions). Furthermore, studies in humans have shown that in the hours immediately following training, the newly learned dynamic undergoes consolidation. Both imaging and TMS studies have suggested that M1 plays a somewhat specific role in the early phase of learning and consolidation. Our experiments essentially fail to address the important issue of whether and how the learning-related plasticity observed here plays a functional role in long-term learning. The techniques currently available allow recording from any one neuron reliably only for a limited time (a couple of hours). Thus, we cannot ascertain at this point whether the plastic changes recorded here are long-lasting and persist through consolidation. Advances in the recording techniques will hopefully help to address these questions.
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