

Cortical correlates of learning in monkeys adapting to a new dynamical environment

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In this paper, we describe the neural changes observed in the primary motor cortex of two monkeys while they learned a new motor skill. The monkeys had to adapt their reaching movements to external forces that interfered with the execution of their arm movements. We found a sizable population of cells that changed their tuning properties during exposure to the force field. These cells took on the properties of neurons that are involved in the control of movement. Furthermore, the cells maintained the acquired activity as the monkey readapted to the no-force condition. Recent imaging studies in humans have reported the effects of motor learning in the primary motor cortex. Our results are consistent with the findings of these studies and provide evidence for single-cell plasticity in the primary motor cortex of primates.

In a number of recent studies investigators have shown that when networks of neurons are repeatedly exposed to sensory-motor associations, learning of motor tasks occurs. Primates learn a new task as the result of repeated exposures to sensory signals coming from a variety of visual and proprioceptive sources. The sensory inputs are funneled to the motor areas of the central nervous system each time a movement is produced. The current view is that learning results from a change in the internal structure of the cortical and subcortical networks brought about by sensory and recurrent signals.

Presumably, the iterative sensory-motor process leads to the establishment of an internal model of the controlled dynamics through a gradual change of the synaptic strength (1) of the neurons of the cortical and subcortical motor areas. The internal model is embedded in the newly formed connectivity of a group of neurons, and the activity of these trained neurons generates the neural impulses necessary for the execution of the learned motor task. According to this view, motor learning and the control of dynamics are two facets of the same process. In this paper, we describe the cellular changes in the circuitry of the primary cortical motor area of the monkey during the acquisition of a motor skill.

In the experiments described here, a key feature of the task to which the monkeys were exposed involved a change in the mechanical environment with which their hand interacted. Because of this change, the neural representation of the arm would have to develop a new model to deal with the new dynamics of the environment. In this paper, we present psychophysical evidence for the formation of this new internal model and we describe the neural changes observed in the primary motor cortex as the new model was formed.

Methods

Description of the Motor Task. Two monkeys (*Macaca nemestrina*) were trained to grasp the manipulandum of a 2-df, lightweight, low-friction robot with a force-torque transducer mounted on the handle. Two torque motors were mounted on the base of the robot and produced force fields upon the hand of the monkey as the animal performed reaching movements (see ref. 2 for details).

During an experimental session, each monkey made visually guided reaching movements while holding the manipulandum with the right hand. Starting from a central position, the monkey

made reaching movements toward a series of targets located at a constant radial distance and at 45° intervals. During an experimental session, a monkey would make about 200 reaching movements in the baseline epoch (no-force) and the same number of movements in the force field and in the washout (no-force) epochs, respectively.

The force fields we used in this experiment were viscous (proportional in strength to the instantaneous hand velocity) and directed orthogonally to the instantaneous hand velocity. We used force fields that were rotationally invariant, i.e., they formed the same angle (of $\pm 90^\circ$) with any velocity direction. Such fields were either clockwise or counterclockwise.

Each monkey was presented with the same clockwise force field every day for more than 30 sessions before switching to the counterclockwise force field.

Data Recording and Analysis. Hand trajectories and neural activity were recorded and analyzed off-line. Trajectories were sampled at 100 Hz, and the goodness of the performance was quantified with a correlation coefficient, as defined in ref. 2. Briefly, an ideal trajectory was defined. Trajectories were represented in velocity space and aligned at the velocity peak. The correlation coefficient was the normalized covariance of the actual trajectory with the ideal trajectory. Its values varied between -1 and 1 and were close to 1 for actual trajectories close to the ideal.

Cell activity was recorded with DATAWAVE software and analyzed with MATLAB. During recordings, a threshold-crossing discrimination was used as the criterion for the recording of spikes. Single-spike waveforms were sampled at a frequency of 20 kHz and saved to a disk. Spike assignment to a single cell was done off-line through a manual clustering process, considering the projection of each waveform in the space of its relevant characteristics. After the clustering, the waveforms of each cell were visually inspected for stability. Cells that did not show consistent waveforms throughout the experimental session were discarded.

For each reaching movement, we recorded the neuronal firing rate during a time window that began 200 msec before the onset of movement and ended at the movement's termination. (Movement onset and termination were defined with a velocity threshold of 4 cm/sec.) A control time window was defined as the 500 msec preceding the presentation of the directional cue. During this time, the monkey was holding the manipulandum in the central position.

In each epoch, we disregarded the first four successful trials in each movement direction and focused our analysis on the neural

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activity that occurred after the initial dip of the correlation coefficient (Fig. 1*B*). Directional tuning curves for each cell were computed in each epoch considering approximately 20 successful trials in each direction.

For the statistical analysis, each cell was analyzed separately. For each epoch, we ran a one-way ANOVA (factor: direction; $P < 0.01$) to assess whether the cell was directionally tuned. Only cells that showed a significant tuning in at least one of the three epochs were considered for further analysis. To assess changes of activity across epochs, we collapsed the data across trials for each epoch and for each direction (we computed the mean), and we subtracted the mean activity recorded during the control time window. The subtraction was done to isolate the effects of the task on the movement-related activity. We thus were left with a 3×8 table (3 epochs \times 8 directions), on which we ran a two-way ANOVA (factors: epoch, direction; $P < 0.05$). We classified as “kinematic” the cells that did not show significant changes across epochs and as “dynamic” the cells that showed significant changes across epochs. These cells were analyzed further by using Tukey’s method: cells that showed a significant difference between the washout activity and the baseline activity were classified as memory cells, and cells that did not have significant differences between the washout and the baseline activities were classified as purely dynamic cells.

Results

Formation of an Internal Model. In the absence of external forces, the monkeys’ hand trajectories displayed approximately straight paths and smooth, bell-shaped velocity profiles (Fig. 1*A*). However, when the manipulandum generated velocity-dependent forces that interfered with the execution of the reaching movements, the hand trajectories were distorted. Through practice, the monkeys’ distorted hand paths converged to the trajectories observed before the application of the field. This convergence was gradual but monotonic and consistent with an adaptive process whose goal was to compensate for the forces imposed by the external field and to return the hand’s trajectory to the path produced before the perturbation (Fig. 1*A*). At the beginning of the washout epoch, we briefly observed that the trajectories displayed distortions (aftereffects) that were opposite in sign to those induced by the force field. The aftereffects indicate that the monkey’s motor system had generated patterns of force that effectively anticipated the perturbing forces that the moving hand was encountering (Fig. 1*A*).

We gathered quantitative evidence of motor learning by recording the path and the velocity of each monkey’s movements and by computing a correlation coefficient between the velocity of an ideal, straight trajectory and the velocity of the actual trajectories. The correlation coefficient allowed us to evaluate motor learning during each session and over the long term. The correlation coefficient varied during a single experimental session. Fig. 1*B* shows the typical trend of the correlation coefficient for each epoch. The correlation coefficient was found to be close to unity during the baseline condition, because our trained monkeys executed the task with almost straight and smooth trajectories when no forces were applied. In contrast, when external forces were present, the correlation coefficient dropped dramatically at first, but recovered somewhat during the second half of this epoch. Finally, during the washout epoch, the correlation coefficient returned close to unity, except for a brief dip at the beginning of this epoch because of the presence of the aftereffects.

We observed a progressive change of the mean correlation coefficient over a period of several months as a consequence of the exposure to a viscous force field during each session. The mean correlation coefficient computed during the force-field epochs progressively increased over days of exposure and

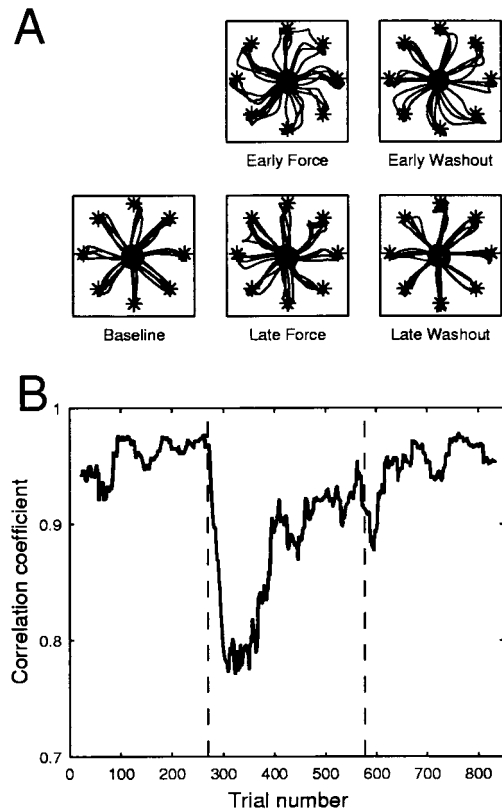


Fig. 1. Psychophysics of motor learning. Data are shown from a representative experimental session. (A) Trajectories in real space. The trajectories are roughly straight when the movements are not perturbed (baseline). When a counterclockwise (CCW) force field is turned on, trajectories are deviated at first (early force). After adaptation has occurred, however, trajectories become straight (late force). After the perturbing force is turned off, the first movements show an aftereffect, inasmuch as they are deviated in the clockwise direction (early washout). Within a few trials, however, the monkey readapts to the unperturbed condition, and trajectories become straight again (late washout). (B) Correlation coefficient. The correlation coefficient (Cc) quantifies the quality of the movements by comparison with an ideal trajectory. The coefficient is close to 1 for straight and smooth movements. In the baseline condition, the Cc is high (≈ 0.95). As the force field is introduced, the Cc drops, returning to high values (≈ 0.9) as the monkey adapts to the external force. When the force field is turned off, the Cc temporarily drops (aftereffect) and returns to its original values as the monkey readapts. The data shown in Fig. 1 were recorded on an early day of training.

reached a steady value after approximately 15–20 sessions in both monkeys.

Plasticity in the Motor Cortex. We recorded the activity of 162 individual neurons from the shoulder region of the contralateral primary motor cortex of two monkeys. The movement-related activity of 143 cells was directionally tuned in at least one of the three epochs. For each of these cells we computed the tuning curve in the three behavioral epochs (baseline, force field, washout). However, in the force-field and washout epochs, we computed the tuning characteristics of the cells only after the recovery of the correlation coefficient from its initial dip.

Not surprisingly, we recorded a variety of cell types, some of which have been described by past investigators recording from the same cortical area. Specifically, we, like others, observed cells that were related to the direction of the arm’s movements (3). Some of these cells preserved the same tuning and general level of activity when the monkeys performed reaching move-

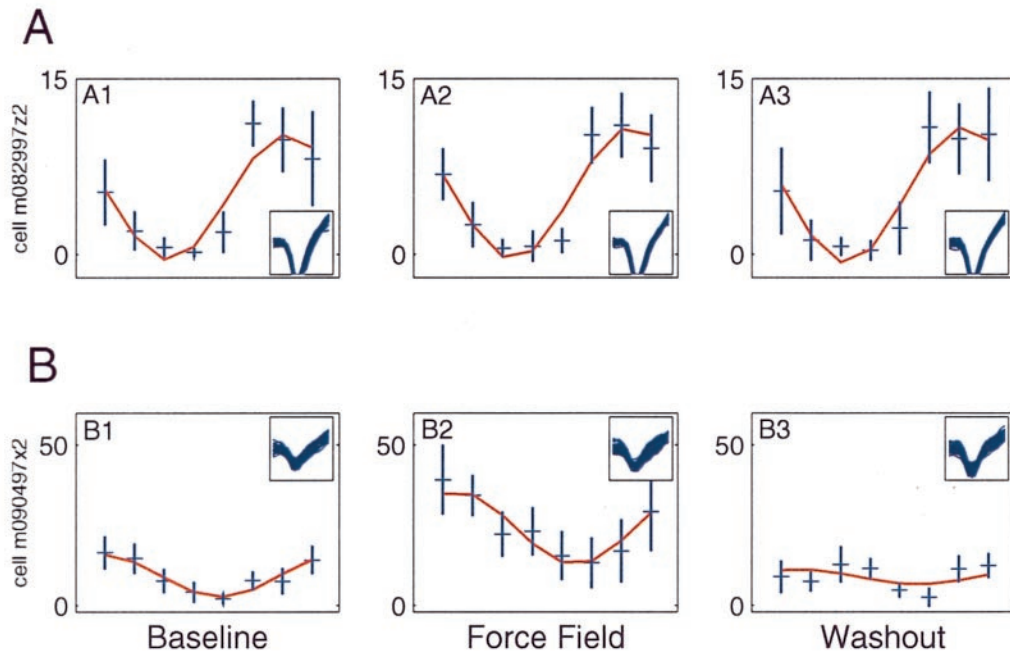


Fig. 2. Examples of cell activity recorded in the primary motor cortex. (A1) The tuning curve of a neuron in the baseline condition. The direction of movement is plotted in the abscissa, and the firing rate (in Hz) is plotted in the ordinate. The firing rate was recorded for approximately 20 trials for each movement direction. The plot shows the average activity and the SD for each direction (in blue) as well as a cosine fit (in red). Waveforms corresponding to single spikes recorded in the baseline are plotted in the bottom right quadrant. (A1–3) A kinematic cell. The tuning curve recorded in the baseline condition (A1) remained unchanged after the adaptation to the force field (A2) and in the following washout (A3). (B1–3) A dynamic cell. The tuning curve recorded in the baseline condition is transformed in the force-field condition (B2), but returns to its original shape during the washout (B3).

ments in all three epochs. These we called “kinematic” cells, because the kinematics of the movements were the same in all three epochs (Fig. 2A). Another sizable group of directionally tuned cells displayed a change in their tuning properties only in the force-field epoch (Fig. 2B). These cells, which correlate with the dynamics of movement, quickly resumed their baseline activity after the force field was turned off.

A novel group of cells—the memory cells—was identified in the course of these experiments. These cells characteristically changed their activity during the force-field epoch and retained the pattern of activity acquired throughout a number of washout epochs.

Fig. 3 illustrates two examples of such memory cells. In Fig. 3A1, a modestly tuned cell recorded during the baseline epoch is displayed. During the force epoch (Fig. 3A2), the firing rate of this cell increased, its tuning became more pronounced, and its preferred tuning shifted in the direction of the applied force. This cell maintained its newly acquired frequency and directional tuning in the washout phase (Fig. 3A3). Another memory cell is displayed in Fig. 3B. In this case, a modestly tuned cell (Fig. 3B1) acquired a pronounced tuning after adaptation to the force field (Fig. 3B2) and maintained its tuning during the washout.

Other cells with memory characteristics were cells with no tuned activity in the baseline epoch that became tuned during the exposure to the force field. This type of cell, like those illustrated in Fig. 3, retained the newly acquired firing rate and tuning through a number of washout epochs (Fig. 4A). Finally, we also observed cells initially tuned in the baseline condition that lost their directional tuning during exposure to the force field, again a change that persisted throughout several washout epochs (Fig. 4B).

Statistical analysis indicated that of the 143 cells considered in this work, 63 cells (44%) did not change activity across epochs (kinematic cells), whereas 80 cells (56%) changed activity across

epochs. Of these, 57 cells (40%) showed a significant difference between washout activity and baseline activity (memory cells). The remaining 23 cells (16%) did not have significant differences between the washout and the baseline conditions (purely dynamic cells). Considering only the directional tuning of cells, we found that 35 cells (24%) became tuned after adaptation to the force, and 19 cells (13%) became untuned after adaptation to the force.

Discussion

In this study, we have recorded single-cell activity from the primary motor cortex of two monkeys while they acquired a new motor skill. The monkeys’ reaching movements were perturbed by externally applied, velocity-dependent force fields that, for a while, distorted their hand trajectories. Through practice, the monkeys adapted to the perturbing forces, and their distorted hand paths gradually converged to the trajectories observed before the application of the fields. We found that a significant number of cells in the primary motor area changed their tuning properties during the adaptation to the force fields and that these cells retained the acquired tuning during a number of no-force epochs. Basically, these cells took on the properties of the neurons that are involved in the control of movement.

The changes in firing rate and tuning observed in the population of adapted cells did not correlate with skeletal muscle activity. Our analysis of electromyographic activity (EMG) from a variety of arm muscles showed that the EMG changes observed during the force-field epochs quickly vanished in the no-force condition (unpublished results).

That the activity of our adapted cells was not related to skeletal muscle activation has implications for the interpretation of our data. In the primary motor cortex, directionally tuned cells have been shown to contribute to the computation of a population vector (3). We think, however, that it is unlikely that our

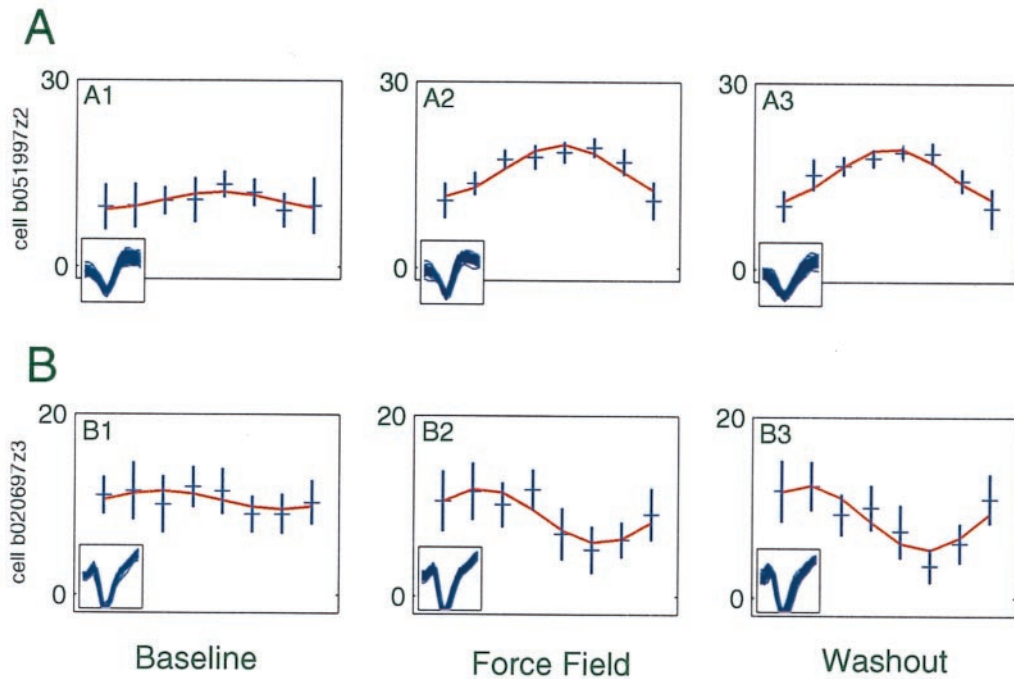


Fig. 3. Two examples of memory cells. (A1–3) A memory cell. This cell is only modestly tuned in the baseline condition (A1), but becomes tuned as the monkey adapts to the force-field condition (A2). In the washout (A3) the field is turned off, but the cell’s tuning curve maintains the shape acquired in the force-field condition. The waveforms plotted in the bottom left quadrants show stable recordings throughout the experimental session. (B1–3) Another memory cell. In this case, the cell increases its average firing rate and becomes tuned in the force-field condition (B2). The tuning curve maintains the same shape in the washout (B3) as in the force-field condition.

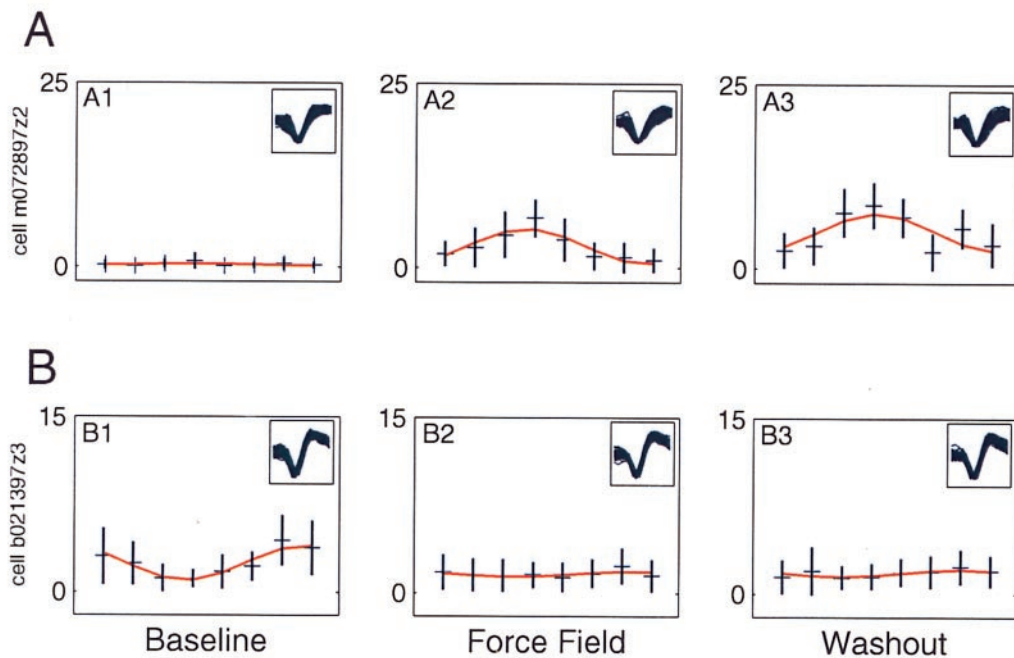


Fig. 4. Two other types of memory cells. (A1–3) This cell is almost silent in the baseline condition (A1), as if it were not related to the task. As the monkey adapts to the force field, however, the cell increases its firing rate and acquires a directional tuning (A2). The cell maintains its tuning curve during washout (A3), when the force is turned off. The waveforms plotted in the top right quadrants show that the recordings were stable throughout the experimental session. Note, in particular, that the activity of the cell at baseline is low, but not equal to zero. (B1–3) In this case, a cell initially tuned in the baseline condition (B1) loses its tuning as the monkey adapts to the force-field condition (B2). During washout (B3), the cell maintains this pattern.

adapted cells represent simple command signals. Rather, the population of newly tuned adapted cells may reflect the formation of an internal model to handle the new dynamics generated by the force fields.

Recent work on the formation of internal models has indicated that models of dynamics are learned from proprioceptive errors in an intrinsic coordinate frame. It is then conceivable that models of dynamics might be encoded in the primary motor cortex because proprioceptive information from the arm reaches this region at short latency (4, 5).

Imaging studies have provided additional evidence that the primary motor area as well as other frontal, parietal, and subcortical areas are involved in motor learning. In a series of studies with positron-emission tomography (6–9) and functional MRI (10–12), the area M1 consistently was found to be involved in the acquisition of motor skills. After motor-skill learning, the topography of representations in the motor cortex has been found to be altered (13–15).

At the cellular level, learning-dependent neuronal activity has been found in the premotor cortex (16), the supplementary motor cortex (17, 18), the supplementary eye field (19), the prefrontal cortex (20, 21), and the somatosensory areas (22). With respect to the primary motor cortex, the study of Wise *et al.* (23) also has shown learning at the level of the cells of this area.

In conclusion, imaging studies as well as single-cell investigations like this one show that motor learning is a process both widespread and selective. On the one hand, a number of brain regions are involved; on the other, the process is selective because distinct population of neurons are transformed by the exposure to learning.

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