Modulation of Cortical Motor Output Maps During Development of Implicit and Explicit Knowledge

Alvaro Pascual-Leone, Jordan Grafman,* Mark Hallett

The excitability of the human motor cortex during the development of implicit and declarative knowledge of a motor task was examined. During a serial reaction time test, subjects developed implicit knowledge of the test sequence, which was reflected by diminishing response times. Motor cortical mapping with transcranial magnetic stimulation revealed that the cortical output maps to the muscles involved in the task became progressively larger until explicit knowledge was achieved, after which they returned to their baseline topography. These results illustrate the rapid functional plasticity of cortical outputs associated with learning and with the transfer of knowledge from an implicit to explicit state.

Knowledge can be developed or expressed in two distinct ways (*1*). Explicit knowledge is expressed by the deliberate recollection of information that is bound to a specific time and context. Implicit knowledge is expressed by behavior that demonstrates that previous exposure to a task has resulted in improved performance on that task without the subject consciously recalling being exposed to the task before. Different forms of knowledge may be associated with different mechanisms of cellular plasticity (*2*) and with different amounts and patterns of activation of the neural networks that support memory representations, operations, and features (*3*).

Proficiency in a motor task may require modulation of the cortical motor outputs to accommodate the new ability. In previous experiments, we demonstrated the modulation of cortical motor outputs when explicit knowledge was associated with improved motor performance (*4*). We have now studied the effects on cortical motor outputs of the development of implicit knowledge and of the transfer of implicit to explicit knowledge of a task that requires sequential finger movements.

We used a variation of the serial reaction time test (SRTT) described in (*5*). The subject (*6*) sat in front of a computer screen at eye level behind a response pad with four buttons numbered 1 to 4. The subject was instructed to push each button with a different finger of the right hand (index finger for button 1, middle finger for button 2, ring finger for button 3, and little finger for button 4). The "go" signal consisted of a number (1, 2, 3, or 4) displayed in the middle of the screen. The go signal subtended 2.4° of visual angle. On appearance of the go signal, the subject was supposed to push the appropriate button as fast as possible with the appropriate finger. Response time (RT) was measured from the go signal until the button press. When the correct response button was pushed, the go signal disappeared and the next go signal appeared 500 ms later. If an incorrect button was pushed, the go signal remained on until the subject made the correct response (*7*).

Ten normal volunteers were randomly assigned to two groups of five subjects (a test group and a control group) that were matched for age and sex distribution. The control group received randomly presented go signals during the SRTT. The test group received a sequence of 12 cues whose order was repeated 10 times in each block of trials. However, test subjects were not told about this repeating sequence. At the end of each block (120 trials), all subjects were asked whether the order of the cues was random or repeating. If the answer was "repeating," the subject was prompted to generate as much of the sequence as possible. The number of sequence items generated correctly was recorded. The ability to generate the entire 12-item sequence correctly was considered complete explicit knowledge of the sequence.

At the beginning of the experiment, we used focal transcranial magnetic stimulation (TMS) to map the cortical motor outputs to the right first dorsal interosseus (FDI), abductor digiti minimi (ADM), forearm finger flexors (FLEX), and abductor pollicis brevis (APB) muscles in each subject (*8*). Keeping the stimulation intensity and the scalp positions constant, we repeated the TMS mapping after every two blocks of the SRTT. Therefore, we were able to compare performance on the task with the modulation of cortical outputs to muscles involved in the task (FDI, ADM, and FLEX) and to uninvolved, neighboring muscles (APB).

The baseline cortical maps of motor outputs to any of the muscles did not differ between the test and control groups. In both groups, TMS evoked motor potentials (MEPs) of ≥60% of the maximal amplitude from three to five scalp positions for each muscle. Performance during the first block of trials was the same for both groups (mean RT, 329.4 ± 38.8 ms for the test group; 327.5 ± 41.9 ms for the control group).

During the SRTT, the control group remained stable in their performance and their maps of cortical outputs did not change for any of the muscles. The test group, however, showed a significant tendency toward progressively shorter RTs and progressively larger maps of cortical outputs to the muscles involved in the task (FDI, ADM, and FLEX). The map of the control muscle (APB) remained constant. After four blocks of trials, mean RT had shortened to 120.6 ± 21.1 ms ($P < 0.001$), and the maps of cortical outputs to the muscles involved in the task showed significant increases (as compared with baseline values) in peak amplitude ($P < 0.001$) and in number of scalp positions from which TMS evoked MEPs of ≥60% of the peak amplitude ($P < 0.01$) (Figs. 1 and 2). At this point, all subjects knew that the go signals were not presented randomly, although none had complete explicit knowledge of the sequence. Explicit knowledge of the entire sequence was achieved after six to nine blocks, depending on the subject. The progressive enlargement of the maps of cortical outputs to the muscles involved in the task continued in each subject up to this time (Figs. 1 and 2). Thereafter, the maps rapidly went back to their baseline topography despite continued shortening of RTs. After development of explicit knowledge of the sequence, the subjects no longer simply reacted to the go signal but instead anticipated it, as reflected by the extraordinarily fast mean RT of 55.1 ± 6.3 ms at the end of 12 blocks of trials. The maps of cortical outputs returned to baseline configurations within three blocks after development of explicit knowledge (Fig. 2).

Thus, a progressive improvement in RT during implicit learning is correlated with an enlargement in the maps of cortical motor outputs to the muscles involved in the task and with an increase in the intensity of signals within those maps. These results are in accordance with work in other laboratories (*9*). For example, Grafton and co-workers (*10*) have shown that relative regional cerebral blood flow (rCBF) increases in the primary motor area, supplementary motor area, and thalamus as subjects learn a pursuit rotor task, a test of implicit learning.

A. Pascual-Leone, Human Motor Control Section, Medical Neurology Branch, National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health, Bethesda, MD 20892, USA, and the Unidad de Neurobiología, Departamento de Fisiología, Universidad de Valencia, Valencia, Spain.
J. Grafman, Cognitive Neuroscience Section, Medical Neurology Branch, NINDS, Building 10, Room 5S209, Bethesda, MD 20892, USA.
M. Hallett, Human Motor Control Section, Medical Neurology Branch, NINDS, Bethesda, MD 20892, USA.

*To whom correspondence should be addressed.

The development of explicit knowledge resulted in a continued improvement in RT because of a change in the subject's strategy (anticipation instead of reaction), whereas there was a rapid return of the cortical motor outputs to their baseline topography. This return of the maps suggests that as a motor sequence is explicitly learned, the contribution of the motor cortex is attenuated and other brain structures assume more active roles in the execution of the task (*11*). Implicit learning is rarely pure and some contamination with explicit knowledge is expected. However, the fact that the maps contracted only after complete explicit knowledge was attained suggests that learning of the complete sequence was crucial to the change in map size. Supporting evidence comes from the finding that learning of a complicated sequence of voluntary finger movements is associated with increases in cortical and cerebellar rCBF, whereas having learned the motor skill results in rCBF increases in the striatum (*12*).

Alternatively, the transfer from implicit to explicit knowledge may lead to a change in the pattern of cortical motor activation because of the generation of a motor plan that encompasses the entire finger movement sequence rather than individual finger movements in response to each go signal. The cortical sensorimotor representation of a specific body part, as demonstrated, for example, by TMS mapping studies, depends on the momentary level of excitability of the intracortical network that targets it. Neuronal networks targeting different body parts overlap widely and in part share common neuronal elements (*13*). These neuronal elements in multiple networks may maintain a flexible balance that is based on demand and competition by their targets (*14*) and on influences from higher order neuronal networks representing more global motor plans. The generation of explicit knowledge may shift the influence of such higher order networks and alter the motor excitability and the sensorimotor representation of the body parts involved.

In a previous study (*4*), we found that increased hand use alone was sufficient to induce changes in the cortical output maps, but only after several days of 2-hour practice sessions. In the present study, we did not find significant changes in the control subjects, presumably because of the much shorter duration of the task.

The changes in cortical motor outputs that we identified during stimulation do not necessarily reflect the cortical activation pattern evoked during task performance, because TMS was applied in the inter-block interval. Nevertheless, the consistent coupling between changes in type of knowledge and cortical motor outputs strongly suggests that the latter reflect a sustained cortical modulation associated with motor learning. The rapid time course of this modulation is most compatible with unmasking of previously existing connections, perhaps as a result of decreased inhibition or increased synaptic efficacy in existing neural circuits (long-term potentiation) (*15*). Such flexible short-term modulation seems important in the acquisition of new skills and could lead to structural changes in the intracortical and subcortical networks as the skill becomes more overlearned and automatic (*16*).

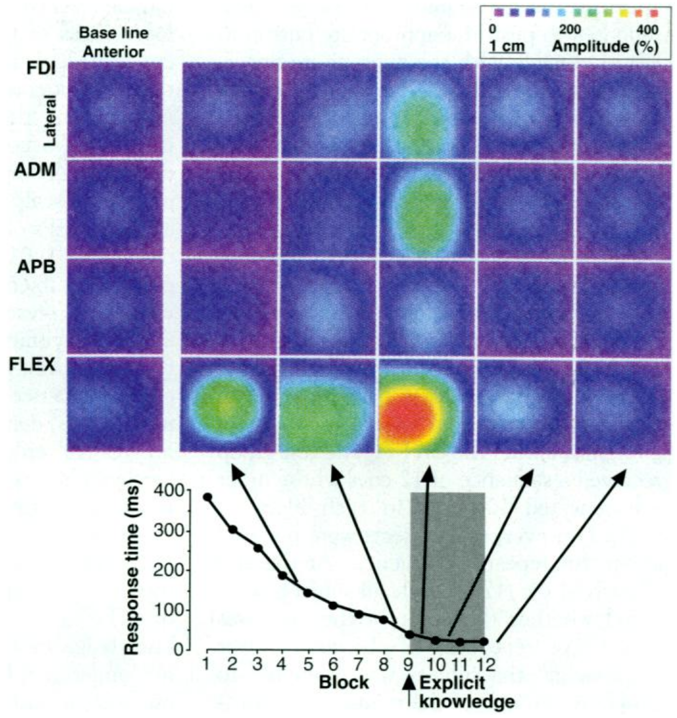

Fig. 1. Response times on the SRTT and cortical motor output maps for all muscles tested in a single representative test subject. Complete explicit knowledge of the sequence is achieved after block 9 (arrow). The baseline motor output maps were obtained before the beginning of the SRTT; the other maps after blocks 4, 8, 9, 10, and 12 of the SRTT (arrows), when subjects were at rest. The maps represent contour plots of the amplitude of the TMS-induced muscle response as a percentage of the maximal MEP generated over the optimal position at the baseline. Each map encompasses an area of 5 by 5 cm centered over the optimal position for activation of each muscle (*8*).

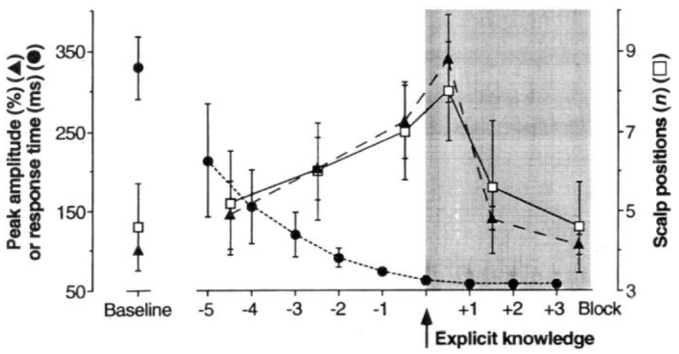

Fig. 2. Response times on the SRTT and peak amplitude and number of scalp positions of the cortical motor output maps for the FLEX muscle from which TMS evoked MEPs of ≥60% of the peak amplitude at the baseline. The values express mean ± SD for the five test subjects after alignment of their results to the block during which they achieved explicit knowledge of the sequence. Baseline values correspond to the cortical output maps obtained before the SRTT and to the SRTT performance in the first block of trials. Negative numbers on "block" axis are numbers of blocks seen before explicit knowledge was achieved.

REFERENCES AND NOTES

1. L. R. Squire and S. Zola-Morgan, *Trends Neurosci.* 11, 170 (1988); *Science* **253**, 1380 (1991); D. L. Schachter, *J. Exp. Psychol. Learn. Mem. Cogn.* 13, 501 (1987); C.-Y. P. Chiu and K. N. Ochsner, *Annu. Rev. Neurosci.* **16**, 159 (1993); S. Zola-Morgan and L. R. Squire, *ibid.*, p. 547.
2. T. J. Carew and C. L. Sahley, *Annu. Rev. Neurosci.* **9**, 435 (1986); R. D. Hawkins, E. R. Kandel, S. A. Siegelbaum, *ibid.* **16**, 625 (1993); R. F. Thompson, *Science* **233**, 941 (1986).
3. Attempts are being made to apply the learning rules derived from the study of single cells and synapses to networks of neurons with computational models [M. A. Gluck and R. Granger, *Annu. Rev. Neurosci.* 16, 667 (1993)]. In addition, lesion studies in humans suggest that different neural structures are critical for implicit and explicit learning (*1*).
4. A. Pascual-Leone *et al.*, *Neurology* **43**, A157 (1993).
5. D. B. Willingham *et al.*, *J. Exp. Psychol. Learn. Mem. Cogn.* **15**, 1047 (1989).
6. All subjects were naïve to the task. All were right-handed according to the Oldfield handedness questionnaire and had normal physical and neurological examinations. All subjects gave written informed consent.
7. We measured RT to the first button pushed in

order to eliminate the self-correction delays. The error rate was extremely low for all control and test subjects across all blocks of trials (>99% accuracy).

8. We delivered TMS with a Cadwell Magneto-electro stimulator 10 (Cadwell Laboratories, Kennewick, WA) through an eight-shaped coil applied to a 5 by 5 grid of scalp positions 1 cm apart over the left sensorimotor cortex. The coil was always held in the same orientation with the handle pointing occipitally and held parallel to the midsagittal line [W. J. Levy, V. E. Amassian, M. Traad, J. Cadwell, *Brain Res.* **510**, 130 (1990)]. Stimulation intensity was 10% above the subject's motor threshold intensity. Motor threshold was defined by the method of limits as the TMS intensity capable of evoking at least five MEPs of 50-μV peak-to-peak amplitude in 10 single trials over the optimal scalp position for activation of each target muscle. The optimal scalp position is the one from which TMS elicits MEPs of maximal amplitude in the target muscles. This technique allows relatively focal stimulation and the generation of restricted topographic maps of cortical motor outputs [L. G. Cohen *et al.*, *Electroencephalogr. Clin. Neurophysiol.* **75**, 350 (1990); P. J. Maccabee *et al.*, *ibid.* **76**, 131 (1990); E. M. Wassermann, L. M. McShane, M. Hallett, L. G. Cohen, *ibid.* **85**, 1 (1992)] that corresponds to the activation of the primary motor cortex, as has been shown by overlay of such maps onto the subject's brain magnetic resonance image [E. M. Wassermann *et al.*, *Soc. Neurosci. Abstr.* **18**, 939 (1992)]. The brain structures stimulated can be inferred from models of the induced electric fields [P. S. Tofts, *Phys. Med. Biol.* **35**, 1119 (1990); B. J. Roth, J. M. Saypol, M. Hallett, L. G. Cohen, *Electroencephalogr. Clin. Neurophysiol.* **81**, 47 (1991); J. M. Saypol, B. J. Roth, L. G. Cohen, M. Hallett, *Ann. Biomed. Eng.* **19**, 317 (1991)]. Electromyographic (EMG) activity was recorded with a Dantec Counterpoint electromyograph (Dantec Medical A/S, Skovlunde, Denmark) with pairs of surface electrodes taped to the skin. Mapping was done with muscles at rest, as verified by EMG monitoring. Motor potentials were printed out on paper for off-line amplitude measurements. Each scalp position was stimulated five times, and we calculated the average amplitude of the MEPs evoked from each scalp position. The cortical output maps were quantified by measurement of the mean amplitude of the five MEPs evoked from the optimal scalp position (peak amplitude) and the number of scalp positions from which TMS evoked MEPs of ≥60% of the peak amplitude. Cortical output maps obtained from the same subject at different times during the experiment were statistically compared by use of a paired *t* test adjusted with the Bonferroni-Dunn correction for multiple comparisons. Response-time data were analyzed with the nonparametric Mann-Whitney test.
9. The nervous system may undergo changes according to patterns of use [M. M. Merzenich, G. H. Recanzone, W. M. Jenkins, K. A. Grajski, *Cold Spring Harbor Symp. Quant. Biol.* **55**, 873 (1990)]. In monkeys, the sensorimotor representation of the preferred hand is more elaborate than that of the nonpreferred hand [R. J. Nudo, W. M. Jenkins, M. M. Merzenich, T. Prejean, R. Grenda, *J. Neurosci.* **12**, 2918 (1992)], and training can result in distortions of body surface and movement representations that lead to behavioral gains [W. M. Jenkins, M. M. Merzenich, G. Recanzone, *Neuropsychologia* **28**, 573 (1990)]. Motor cortical representation of a body part expands after selectively increased activity [J. N. Sanes, J. Wang, J. P. Donoghue, *Cereb. Cortex* **2**, 141 (1992)], and differential stimulation of a restricted skin surface of a finger pad in adult monkeys leads to an enlargement of its somatosensory cortical representation [W. M. Jenkins, M. M. Merzenich, M. T. Ochs, T. Allard, E. Guic-Robles, *J. Neurophysiol.* **63**, 82 (1990)], especially when stimulation has a functional significance [G. Recanzone, W. M. Jenkins, G. T. Hradek, M. M. Merzenich, *J. Neurophysiol.* **67**, 1015 (1992); G. H. Recanzone, M. M. Merzenich, W. M. Jenkins, K. A. Grajski, H. R. Dinse, *ibid.*, p. 1031; G. H. Recanzone, M. M. Merzenich, W. M. Jenkins, *ibid.*, p. 1057; G. H. Recanzone, M. M. Merzenich, C. E. Schreiner, *ibid.*, p. 1071].
10. S. T. Grafton *et al.*, *J. Neurosci.* **12**, 2542 (1992).
11. M. Fabre-Thorpe and F. Levesque, *Behav. Neurosci.* **105**, 176 (1991); C. Weiller *et al.*, *Ann. Neurol.* **31**, 463 (1992).
12. R. J. Seitz *et al.*, *Neuroreport* **1**, 57 (1990).
13. W. J. Levy, V. E. Amassian, U. D. Schmid, C. Jungreis, *Electroencephalogr. Clin. Neurophysiol. Suppl.* **43**, 51 (1991); M. H. Schieber, *Soc. Neurosci. Abstr.* **18**, 504 (1992).
14. Therefore, removal of a target (for example, by amputation or peripheral deafferentation) would result in the takeover of neuronal elements formerly devoted to the network of the removed target by networks targeting neighboring body parts. This would explain the reorganization of the motor outputs targeting muscles proximal to the stump of an amputated limb [L. G. Cohen, S. Bandinelli, T. W. Findley, M. Hallett, *Brain* **114**, 615 (1991)] or an ischemic block [J. P. Brasil-Neto *et al.*, *Neurology* **42**, 1302 (1992); *Brain* **116**, 511 (1993)]. Conversely, increased use of and enhanced sensory feedback from a body part, especially if coupled with functional gain for the subject, may lead to a shift of the balance of intracortical networks toward that body part [A. Pascual-Leone and F. Torres, *Brain* **116**, 39 (1993); A. Pascual-Leone *et al.*, *Ann. Neurol.* **34**, 33 (1993)].
15. H. Asanuma and A. Keller, *Neuroreport* **2**, 217 (1991).
16. T. P. Pons *et al.*, *Science* **252**, 1857 (1991); V. S. Ramachandran *et al.*, *ibid.* **258**, 1159 (1992).
17. We thank B. J. Hessie for her editorial assistance and L. G. Cohen, J. Rauschecker, T. Pons, C. Toro, and E. W. Wassermann for their comments and critical reading of this manuscript.

17 September 1993; accepted 17 December 1993

Neuronal Plasticity That Underlies Improvement in Perceptual Performance

Ehud Zohary,* Simona Celebrini,† Kenneth H. Britten,‡
William T. Newsome

The electrophysiological properties of sensory neurons in the adult cortex are not immutable but can change in response to alterations of sensory input caused by manipulation of afferent pathways in the nervous system or by manipulation of the sensory environment. Such plasticity creates great potential for flexible processing of sensory information, but the actual effects of neuronal plasticity on perceptual performance are poorly understood. The link between neuronal plasticity and performance was explored here by recording the responses of directionally selective neurons in the visual cortex while rhesus monkeys practiced a familiar task involving discrimination of motion direction. Each animal experienced a short-term improvement in perceptual sensitivity during daily experiments; sensitivity increased by an average of 19 percent over a few hundred trials. The increase in perceptual sensitivity was accompanied by a short-term improvement in neuronal sensitivity that mirrored the perceptual effect both in magnitude and in time course, which suggests that improved psychophysical performance can result directly from increased neuronal sensitivity within a sensory pathway.

Neural circuitry in sensory areas of the cerebral cortex is intricately organized, evoking the impression of an elegantly wired machine that performs stereotyped computations on sensory input. Recent experiments, however, have shown that this circuitry is subject to dramatic plastic changes. Topographic organization can be altered by damage to peripheral afferents or by chronic performance of a sensory task (*1*, *2*). The stimulus-response properties of individual neurons can be modified by pharmacological intervention (*3*), by changes in the behavioral context in which a stimulus is presented (*4*), and by direct manipulation of the sensory environment (*5*). Plasticity thus appears to be a common feature of the adult cortex and may be closely linked to the behavioral ability to respond flexibly to the environment.

We compared neuronal to behavioral plasticity in the context of visual discrimination of motion direction. The monkeys were familiar with this task, having developed asymptotically stable performance over months of training. Within daily sessions, however, the animals often exhibited a steady gain in discriminative ability over the first 300 to 500 trials of a particular task configuration. To search for neural correlates of this phenomenon, we examined the activity of single neurons in two extrastriate visual areas that play a prominent role in motion vision: the middle temporal (MT) and medial superior temporal (MST) visual areas. Neurons in these two areas are typically directionally selective; they respond optimally to motion in a particular

---

Department of Neurobiology, Stanford University School of Medicine, Stanford, CA 94305, USA.

---

*To whom correspondence should be addressed.

†Present address: Centre de Recherche Cerveau et Cognition, CNRS-UPS, Faculté de Médecine de Rangueil 133, Route de Narbonne, 31062 Toulouse Cedex, France.

‡Present address: Center for Neuroscience, University of California at Davis, 1544 Newton Court, Davis, CA 95616, USA.