Rapid and Long-Lasting Plasticity of Input-Output Mapping

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Yamamoto, Kenji, Donna S. Hoffman, and Peter L. Strick. Rapid and long-lasting plasticity of input-output mapping. J Neurophysiol 96: 2797–2801, 2006. First published August 23, 2006; doi:10.1152/jn.00209.2006. Skilled use of tools requires us to learn an “input-output map” for the device, i.e., how our movements relate to the actions of the device. We used the paradigm of visuo-motor rotation to examine two questions about the plasticity of input-output maps: 1) does extensive practice on one mapping make it difficult to modify and/or to form a new input-output map and 2) once a map has been modified or a new map has been formed, does this map survive a gap in performance? Humans and monkeys made wrist movements to control the position of a cursor on a computer monitor. Humans practiced the task for ∼1.5 h; monkeys practiced for 3–9 yr. After this practice, we gradually altered the direction of cursor movement relative to wrist movement while subjects moved either to a single target or to four targets. Subjects were unaware of the change in cursor–movement relationship. Despite their prior practice on the task, the humans and the monkeys quickly adjusted their motor output to compensate for the visuo-motor rotation. Monkeys retained the modified input-output map during a 2-wk gap in motor performance. Humans retained the altered map during a gap of >1 yr. Our results show that sensorimotor performance remains flexible despite considerable practice on a specific task, and even relatively short-term exposure to a new input-output mapping leads to a long-lasting change in motor performance.

INTRODUCTION

An important feature of primate behavior is the ability to use tools and operate complex devices. Humans learn to operate a computer mouse and drive a car. Similarly, monkeys can be trained to operate complex manipulanda (Kakei et al. 1999) and to use tools like a rake to gather food treats (Iriki et al. 1996). An important element in these tasks is that subjects learn an “input-output map” for the device, i.e., how their movements relate to the actions of the device. For example, skilled operation of a computer mouse requires knowing that forward movement of a mouse on a surface results in upward displacement of a cursor on a computer monitor.

Recently, the paradigm of “visuo-motor rotation” has been developed to explore plasticity of input-output maps (Cunningham 1989; Kagerer et al. 1997; Klassen et al. 2005; Krakauer et al. 2000; Paz et al. 2003). In this paradigm, subjects first learn the relationship between movements of a device (like a computer mouse) and the actions of a cursor on a computer monitor. Then, displacement of the cursor is rotated relative to movement of the device. To make accurate cursor movements, subjects must rotate their movements in an equal and opposite direction to the imposed cursor rotation. Subjects quickly adjust their movements to the altered conditions (Imamizu et al. 2000; Kagerer et al. 1997; Klassen et al. 2005; Krakauer et al. 2000; Paz et al. 2003).

Here we used the paradigm of gradual visuo-motor rotation to examine two questions about the plasticity of input-output maps: 1) does extensive practice on one mapping make it difficult to modify and/or to form a new input-output map and 2) once a map has been modified or a new map has been formed, does this map survive a gap in performance?

METHODS

We trained three right-handed human subjects (2 females and 1 male; age, 41–53 yr) and two male rhesus monkeys (Macaca mulatta, 7.5 kg) to make rapid step-tracking movements of the right wrist (Hoffman and Strick 1999; Kakei et al. 1999, 2001). The human studies were approved by the Institutional Review Board of the University of Pittsburgh, and all subjects provided informed consent according to the Declaration of Helsinki. Experimental procedures in monkeys were conducted according to National Institutes of Health guidelines and were approved by the animal care and use committees of the University of Pittsburgh and the Pittsburgh VA Medical Center. Subjects sat in a chair with the forearm supported. They grasped the handle of a two-axis manipulandum with the forearm fully pronated. Two potentiometers attached to the manipulandum measured wrist angle in the extension–flexion (vertical) and ulnar–radial (horizontal) planes (Hoffman and Strick 1986). Subjects faced a computer screen that displayed a cursor and a target. The cursor moved in the same direction as the wrist (i.e., upward displacements of the cursor were caused by upward movement of the handle, rightward displacement of the cursor was associated with rightward movement of the handle, etc.). At the start of the task, a target (an open circle with a diameter of ~4° of wrist angle) was placed at the center of the screen. Subjects moved the handle of the manipulandum to place the cursor inside the target. After a variable hold period, a second target appeared at one of eight peripheral locations. Subjects were asked to move the cursor from the central to the peripheral target, which required a 20° change in wrist angle. Subjects did not have a view of their hand and wrist during the experiment.

Human experiments

Humans performed 400 center-out movements in 1 h as practice before the experimental session. At the start of the experiment (10 min to 7 days later), they performed an additional 200 movements as further practice (Fig. 1, Task). After practice, human subjects performed four movements to a single “experimental target” (left–upward) without cursor feedback (Fig. 1, Pretest). Then, we restored the cursor and subjects made an additional 30 movements to the experimental target. Next, we imposed a “gradual visuo-motor rotation” in

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control experiments

To examine whether our results were specific for making movements to a single target, we carried out an additional experiment in five human subjects (3 females and 2 males; age, 20–33 yr) and the 9-yr monkey. For this experiment, subjects moved to four targets (left-upward, left-downward, right-upward, right-downward) presented in random order. This experiment differed from the human subjects in one important way. After the posttest, we did not train the monkeys on the task for a period of 7 or 14 days. After this gap in performance, the monkeys performed movements to the experimental target without cursor rotation. We took the first trial as the “retest”.

Data collection and analysis

We digitized the signals from the two potentiometers at 1-ms resolution and filtered these signals using a 50-Hz Butterworth low-pass filter. We measured movement onset for each trial as the time when tangential velocity exceeded 55°/s in monkeys or 30°/s in humans. We calculated the direction of each wrist movement as the vector from the starting position of the movement to its location at 200 ms after movement onset. The average SD of movement direction (measured at 200 ms after movement onset) was ±7.0° for the 3-yr monkey and ±5.5° for the 9-yr monkey. Clearly, the two monkeys had learned the mapping between their wrist movements and displacement of the cursor.

Monkey experiments

Monkeys were trained on the task for >9 (9-yr monkey) or >3 yr (3-yr monkey) and completed ~700–1,000 wrist movements each weekday. We estimated that the monkeys made >0.5–2 million wrist movements during their practice on the task. They performed 92–96% of the trials correctly. The average SD of movement direction (measured at 200 ms after movement onset) was ±7.0° for the 3-yr monkey and ±5.5° for the 9-yr monkey. Clearly, the two monkeys had learned the mapping between their wrist movements and displacement of the cursor.

We performed four separate experiments with visuo-motor rotation in each monkey. At least 2 wk of training using unrotated conditions preceded each experiment. The experimental target (left-upward or left-downward) and the direction of rotation (clockwise or counterclockwise) were chosen for each experiment. Visual feedback from the cursor was continuously present because the monkeys did not perform the task reliably without the cursor. In each experiment, the monkey received 10 practice trials to the experimental target; the last five movements were taken as the “pretest.” Then, we rotated the cursor relative to the monkeys’ wrist movements in four increments of 10° each, as in the human experiments. Monkeys performed 30 trials after each increment, and they received 30 extra trials at the final rotation of 40°. Thus they had 150 trials of exposure to cursor rotation and 60 trials at the final rotation. We analyzed the last five movements as the “posttest.” Monkeys completed the 150 trials in ~20−25 min. After the posttest, we did not train the monkeys on the task for a period of 7 or 14 days. After this gap in performance, the monkeys performed movements to the experimental target without cursor rotation. We took the first trial as the “retest”.

Control experiments

To examine whether our results were specific for making movements to a single target, we carried out an additional experiment in five human subjects (3 females and 2 males; age, 20–33 yr) and the 9-yr monkey. For this experiment, subjects moved to four targets (left-upward, left-downward, right-upward, right-downward) presented in random order. Before the experiment, human subjects made practice movements without visuo-motor rotation for 1.5 h, and the monkey performed the wrist task for 6 mo without visuo-motor rotation. We imposed four incremental visuo-motor rotations of 10° each (clockwise for 2 of 5 human subjects, counterclockwise for 3 of 5 human subjects and the monkey). Subjects performed 15 movements to each of the four targets after each 10° increment in cursor rotation. We measured pretest and posttest trials as described in the methods for the preceding experiment. After a performance gap of 1 wk, we measured a retest trial to one of the four targets (randomly selected in each subject). Note that all test trials for the human subjects were made without vision, whereas they were made with vision for the monkey.

In the previous experiment with movements to a single target, subjects performed 120 (human) or 150 (monkey) movements to a single target during the gradual visuo-motor rotation. We thought that it would be asking too much of our subjects to perform the same number of trials to each of the four targets in this control experiment. Therefore subjects performed 60 movements to each of the four targets for a total of 240 movements of gradual visuo-motor rotation. Consequently, compared with the experiment with a single target, subjects received less “local” exposure to the visuo-motor rotation at the expense of more global exposure.
sessions used clockwise and counterclockwise rotations, we simplified the presentation of results by reporting the absolute value of the changes in movement direction. All statistical tests were performed using the Steel-Dwass test (Neuhaus 2001).

We calculated the percentage of compensation that remained at the retest relative to that at the posttest as follows:

$$\frac{(Re - Pre)(Post - Pre)}{100}$$

Pre, Post, and Re are the movement directions measured in the pretest, posttest, and retest, respectively.

RESULTS

Humans after modest practice and monkeys after lengthy practice made accurate movements to the single experimental target during the pretest trials. In the three humans, the mean difference between the direction of the experimental target and the direction of wrist movements was $1.9 \pm 4.4, 1.7 \pm 1.7,$ and $3.5 \pm 2.0^\circ$ (SD; $n = 4$ movements; Figs. 1, pretest, Figs. 2 and 3A, top, ●). In the two monkeys, the mean difference between target direction and the direction of wrist movements was $4.9 \pm 4.0$ and $4.2 \pm 3.2^\circ$ ($n = 20$; 4 experiments, 5 trials/experiment; Figs. 2 and 3A, bottom, ○).

Both humans and monkeys quickly altered the direction of their movements during a gradually imposed, visuo-motor rotation of $40^\circ$ (Fig. 2, shaded area). In the posttest trial, humans compensated for the imposed rotation by altering the direction of their movement by $33.8, 36.4,$ and $25.3^\circ$ relative to the target (Fig. 1, posttest, Figs. 2 and 3A, top, ▲). When questioned, the human subjects reported that they were not aware of the change in the relationship between their wrist movements and displacements of the cursor. In four experiments, the monkeys altered the direction of their posttest trials ($n = 5$) by an average of $31.1 \pm 2.9$ (9-yr monkey) and $37.2 \pm 3.2^\circ$ (3-yr monkey; Figs. 2 and 3A, bottom, ▲). These alterations between the pretest and the posttest were significant ($P < 0.05$). Overall, humans compensated for $63–91\%$ of the imposed rotation, whereas monkeys compensated for $73–96\%$ of the rotation. These results indicate that a relatively brief exposure to a gradual visuo-motor rotation was sufficient to overcome 3–9 yrs of training. Thus despite extensive training, the relationship between input and output remains plastic and easily modified.

After the posttest, the monkeys received no further experience with the task for a period of 7–14 days. After this gap in performance, the monkeys made a single movement to the experimental target (retest trial). We found that the direction of movement in the retest trial was rotated by an average of 28.9 (9-yr monkey) and $20.5^\circ$ (3-yr monkey; Figs. 2 and 3A, bottom, ○). These changes were significantly different from the pretest trials ($P < 0.05$). The percentage of compensation that remained relative to the posttest trials averaged 92\% (range, 77–116\%) in the 9-yr monkey and 52\% (range, 34–68\%) in the 3-yr monkey. These results indicate that the new input-output relationship was retained despite a gap in performance. Thus extensive practice on one input-output mapping did not result in poor retention of a new input-output map.

In human subjects, we examined retention of the compensation after a lengthy gap in performance (384–418 days). Although subjects no longer recalled the details of the task from 1 yr earlier, their movements during the retest trials ($n = 5$) remained rotated by an average of $30.6 \pm 2.5, 21.5 \pm 5.5,$ and $16.2 \pm 5.0^\circ$ (Figs. 2 and 3A, top, ○). These changes were significantly different from the pretest trials ($P < 0.05$) but were not significantly different from the posttest trials ($P > 0.05$). The amount of compensation that remained relative to the posttest ranged from 59 to 91\%. These results are especially notable because the human subjects experienced the final rotation of $40^\circ$ for only 30 trials. Thus a small number of trials was sufficient to cause a long-lasting change in motor behavior.
One might argue that our results were specific for movements made to a single target. Therefore in a control experiment, we exposed subjects to gradual visuomotor rotation during movements to four different targets (see Methods). We found that the amount of compensation measured in posttest trials averaged 62% in the one monkey tested (Fig. 3B, bottom) and 63.8% in five human subjects (Fig. 3B, top). One week later, the monkey retained 81.6% of this adaptation (Fig. 3B, bottom) and the human subjects retained an average of 81.2% of their adaptation (Fig. 3B, top). Thus the results after exposure to four targets were comparable with those after exposure to a single target.

**Discussion**

Our results fit many aspects of the term “plasticity.” When some plastics are heated, they can be readily molded into different shapes. Once the hot plastic cools, the new shape is retained until it is reheated and remolded. Similarly, when we exposed humans and animals to an altered input-output relationship, an error correction process resulted in a form of “reheating” that reshaped their behaviors. The behavioral reshaping occurred over a surprisingly small number of trials, even in animals that had an extensive training period in which to establish the original input-output mapping. Our results on long-term retention can be viewed in a similar context. During the gap in performance, the last input-output mapping was stored until the next time subjects performed the task (just as cooled plastic retains its shape). Long-term retention of the last input-output map occurred for both local (1 directional) and global (4 directional) remapping.

What allowed a modified input-output map to be retained during the gap in motor performance? Clearly, monkeys and humans made wrist movements outside the task, and these movements might have caused some decay of the altered mapping. There is evidence that the error correction process is narrowly tuned to the kinematics and/or dynamics of a movement (Kitazawa et al. 1997; Krakauer et al. 2000). Thus one explanation for our observation of limited decay is that the movements made during the gap in performance may have differed in direction and/or velocity from those made during the task. Another potential explanation is that the error correction process during visuomotor rotation may function not at a muscle or joint level of motor processing, but at a higher level of task representation (Krakauer et al. 2000). If this is the case, the limited decay may be caused by the absence of task specific movements during the gap in performance.

Prior results from experiments on prism adaptation suggested that retention of the compensation (=24 h later) depended on the number of practice trials with the prisms in place. Five hundred practice trials led to good retention of the prism adaptation, whereas 250 practice trials did not (Yin and Kitazawa 2001; see also Martin et al. 1996). In contrast, we observed long-term retention of a new input-output mapping with only 30–60 trials of exposure at the final rotation of 45° (and only 120–150 trials of exposure to gradual rotation). The difference between our results and those with prisms may be caused by the nature of the errors produced in the two tasks. In our experiments, subjects were unaware of the visuo-motor rotation because it was imposed gradually and in small increments (Kagerer et al. 1997; Klassen et al. 2005). Thus subjects never experienced a large motor error, and the error correction process occurred implicitly. On the other hand, most experiments with prism displacement introduce a large, observable error that is likely to engage both explicit and implicit movement corrections (Redding and Wallace 1996). If explicit and implicit processes compete or in some other way negatively interact, prism adaptation will require more trials for retention than corrections that are made using entirely implicit processes. This explanation is supported by the finding that a sudden large visuo-motor rotation resulted in less complete adaptation than the same amount of rotation introduced gradually (Kagerer et al. 1997; Klassen et al. 2005). It is also consistent with the observation that a prism adaptation paradigm that included a period in which the displacement was introduced gradually led to a more long-lasting adaptation (Hatada et al. 2006).

One interpretation of our results is that subjects modified a single visuo-motor map (either locally in the 1-target experiment or globally in the 4-target experiment) to correct for the errors introduced by the gradual rotation. Another perspective is that subjects created a new local (single target) or global (4 target) map to compensate for the rotation. We believe that there are several pieces of evidence to support a local or global modification (i.e., a remapping), rather than development of a new, second map. First, subjects received limited practice on the cursor rotation task. This contrasts with evidence in the literature that extensive practice is required to switch between two different visuo-motor maps (Martin et al. 1996). Second, the extent of adaptation showed a small amount of decay over time in some subjects, resulting in a visuo-motor relationship that was intermediate between the pretest and posttest values. The intermediate values argue for a gradual decay of a single, modified map rather than the development of a separate map. Finally, subjects’ lack of conscious awareness of the visuo-motor rotation and our control experiment with four targets make it unlikely that subjects simply developed a contextual or proprioceptive memory of their last move before the gap in performance.

Recent findings suggest that visuo-motor behavior is controlled in part by a highly interconnected cortical network that includes portions of the posterior parietal cortex, ventral premotor cortex, and primary motor cortex (Rizzolatti and Matelli 2003). Anatomical studies have shown that each of these cortical areas is the target of distinct outputs from the cerebellum and thus is a component of multiple cerebro-cerebellar loops (Dum and Strick 2003; Clower et al. 2005). The cerebellum has long been regarded as containing neural mechanisms for error correction, input-output representations (internal models), and motor learning (Gilbert and Thach 1977; Imamizu et al. 2000; Ito and Kano 1982; Kawato 1999; Nagao and Ito 1991; Wolpert et al. 1998). There is evidence that the cerebellum and each of the cortical areas listed above participates in visuo-motor adaptation (Baizer et al. 1999; Clower et al. 1996; Huber et al. 2004; Kurata and Hoshi 1999; Paz et al. 2003; Robertson and Miall 1999). One or more of these areas may be especially important for motor adaptation to gradual perturbations (Robertson and Miall 1999). A challenge for the future is to determine how each node in this distributed neural network contributes not only to short-term adaptive changes but also to the long-term retention observed in our study.
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