博士論文

Visuomotor Map as a Common Foundation for Human Motor Control and Learning

(ヒト運動制御・学習の共通基盤としての視覚運動写像)

by

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Organization of Manuscript

The manuscript consists of the following chapters:

In Chapter 1, I introduce the background and general purpose of my research. This includes general perspectives of motor control and learning, relationships between psychophysical, neurophysiological, and theoretical studies, introduction of visually guided reaching, and unsolved problems on motor control and learning that I aimed to investigate.

In Chapter 2, I describe my investigations in the association of motor control (feedforward and feedback controls) and motor learning. Previous studies have investigated motor control and learning separately. Here, I illustrate that a visuomotor map, which transforms visual information of a target into movement execution, is a common foundation of human motor control and learning mechanisms in behavioral experiments.

In Chapter 3, I propose a possible computational principle of the influence of motor learning on the subsequent motor learning. First, I show that the experimental results described in Chapter 2 cannot be reproduced by a current computational model. Then, inspired by previous neurophysiological studies, I explain that rotation of preferred direction of motor primitives plays a key role in motor learning mechanisms.

In Chapter 4, I summarize my research and discuss perspectives. In addition, I offer implications of my research on practical situations such as sports, functional rehabilitation, and education.

The studies in this thesis are based on the following published papers:

1. Hayashi, T., Yokoi, A., Hirashima, M., and Nozaki, D. (2015). Visuomotor map determines how visually guided reaching movements are corrected. Translational and Computational Motor Control.
2. Hayashi, T., Yokoi, A., Hirashima, M., and Nozaki, D. (2016). Visuomotor map determines how visually guided reaching movements are corrected within and across trials. eNeuro, 3:1-13.
3. Hayashi, T. and Nozaki, D. (2016). Improving a bimanual motor skill through unimanual training. Frontiers in Integrative Neuroscience, 10:25.

Chapter 1

General Introduction

Movement is essential for our ability to interact with the world, such as moving from place to place, manipulating tools, or communicating with others. Without movement, we cannot perform even the most basic of human activities; we cannot feed ourselves, reproduce, or express our feelings and thoughts. Hence, movement is regarded as one of the most essential human abilities.

The body and limbs have complex structures. The situations, contexts, and environments are not fully observable because of noises and delays in sensory feedback. This suggests that the brain continuously faces severe challenges to control the body and limbs with complicated kinematics and dynamics amid these uncertainties. However, the brain seems to be able to control for these challenges seemingly easily in daily life. Here, one fundamental question arises: How does the brain control the body and limbs? This is a problem of "motor control."

Motor control is not always innate. Indeed, the brain acquires novel motor skills with practice. In the case of acquisition of tennis stroke, the movement is initially slow, clumsy, and inconsistent, but with practice becomes quicker, more accurate, and automatic. Here, another fundamental question arises: How does the brain acquire novel motor skills? This is a problem of "motor learning."

The goal of my research was to elucidate the mechanisms behind motor control and learning. In Chapter 1, I review traditional and current approaches of motor control and learning from psychophysical, neurophysiological, and theoretical studies.

1.1 Concise History

Early psychophysical research on motor control and learning began in the early twentieth century (Adams, 1987; Fuchs, 1998; Schmidt and Lee, 2011). At that time, studies investigated fundamental features of movement, such as accuracy, reproducibility, and timing of motor control (Bowditch and Southard, 1882; Stevens, 1886; Woodworth, 1899; Leuba, 1909), as well as transfers, plateaus, and savings of motor learning (Book, 1908; Hill et al., 1913), which still remains a topic of debate. Notably, most studies of this era focused on sports (e.g., baseball, football, basketball, and fencing) (Scripture, 1894; Griffith, 1931) and educational and industrial skills (e.g., writing, typing, receiving and sending Morse codes, and production-line assembly movements) (Bryan and Harter, 1896; Bryan and Harter, 1897; Book, 1908; Gilbreth, 1909; Stimpel, 1933). These experimental tasks were very practical but too complex to be described with mathematical equations than, for example, reaching movements.

Conversely, early neurophysiological studies investigated very simple movements, such as spinal cord reflexes (Sherrington, 1910; Liddell and Sherrington, 1924). Thus, there were few hypotheses concerning the neural function behind motor control and learning linking early psychophysical and neurophysiological findings.

Bernstein and von Holst were among the first to place emphasis on the neural control of movement, at around the middle of the twentieth century (Bernstein, 1967; Bernstein, 1996; von Holst, 1950; von Holst, 1954). Bernstein claimed that movement could not be grasped as the chain of simple reflexes, and that movement had to be concisely defined before scientists were able to investigate it. Von Holst suggested that, in order to accomplish a successful movement, the brain needs to receive sensory information from the peripheral organs (e.g., the retina in the visual system and muscle spindle in the proprioceptive system), and that such “afference” should be the key information for accurate motor control (the term “afference” was created by von Holst in contrast to “efference”). These appealing ideas were not so prevalent at the time, perhaps due to the languages of their books (Bernstein published his work in Russian and von Holst in German).

In another important field, theoretical neuroscience, Craik considered the brain as a kind of a computer, in which the brain obtained misalignment between target and actual movements via sensory feedback, processed the information in the cortex of the brain, and executed actions to the environment with limbs to compensate for and reduce the misalignment (Craik, 1948). At the same time, Wiener, who was dedicated to the field of control engineering, proposed that the brain could be regarded as negative feedback controller, in which the controller included in the brain generated negative control signals if the brain obtained an error between a desired and actual state (Wiener, 1948). Based on observations of movements of patients with cerebellar disorders, Wiener proposed that this calculation was processed in the cerebellum, which is generally accepted even now.

One of the most influential scientists in theoretical neuroscience, David Marr, insisted that computational formulation may be the only way to understand brain function (Marr and Poggio, 1976; Marr, 1982). In his landmark book, "Vision," Marr stated that scientists needed to clarify three different levels in order to understand the brain. The first was the level of computational theory, accounting for what a goal of the brain is and why the goal is appropriate for the brain. The second was the level of representation and algorithm for transformation from input (movement goals) to output (movement executions), showing how the brain can solve several problems when achieving the goal. The third was the level of hardware implementation, discovering how representation and algorithm are implemented in the brain. Importantly, these three levels are highly dependent on each other. For example, there are many kinds of representations and algorithms to achieve a particular movement goal, and they are constrained to the neural architecture. Marr's idea, which is called the "Tri-Level Hypothesis", reminded scientists of the importance of computational approaches, and also influenced subsequent motor control and learning studies.

1.2 Current Approach

Current studies of motor control and learning have been more focused on the tripartite relationship between psychophysical, neurophysiological, and theoretical studies. Here, I will review the current literatures with a focus on theoretical studies; this is because only the theoretical explanation can account for the mechanisms behind motor control and learning according to Marr's "Tri-Level Hypothesis" (Marr and Poggio, 1976; Marr, 1982).

1.2.1 Complexities of Reaching Movement

Considering the case when we try to move a cursor on a computer screen toward a certain position, the sensorimotor system must understand accurate transformation between motion of the computer mouse (or hand) and that of the screen cursor. Additionally, the sensorimotor system does not move the hand directly but contracts muscles that induce joint motions. Thus, to accomplish a desired movement of the hand, the sensorimotor system accurately understands the relationship between motion of the hand and that of the joint angles of the limb. Furthermore, even if the desired states are identical, such as a gait, different movements are required for walking on concrete, sand, and ice. When we manipulate some objects, such as a tennis racket, a cup, or chopsticks, the sensorimotor system has to know the kinematics and the dynamics of the objects. From these examples, it is reasonable to propose that the sensorimotor system operates input-output mapping with regard to contexts and environments, which is called the "internal model" (Kawato, 1989; Wolpert et al., 1998).

The experimental paradigm of visually guided reaching movement has been developed since around 1980 (Morasso, 1981; Morasso and Mussa Ivaldi, 1982; Flash and Hogan, 1985). In the planer reaching movement task, participants perform shoulder and elbow joint movements. The hand position (h_x, h_y) is mathematically determined by these joint angles (q_s, q_e) and limb lengths (l_1, l_2) as follows:

$$h_x = l_1 \cos(q_s) + l_2 \cos(q_s + q_e) \tag{1.1}$$

$$h_y = l_1 \sin(q_s) + l_2 \sin(q_s + q_e) \tag{1.2}$$

where 1 and 2 denote the upper and lower arms, and s and e denote the shoulder and elbow joints, respectively (Figure 1.1).

If desired kinematics of the reaching movements are given, namely desired angular positions (q_s, q_e), velocities $(\dot{q}_s, \dot{q}_e)$, and accelerations $(\ddot{q}_s, \ddot{q}_e)$, are given, torques of the shoulder and elbow joints (τ_s, τ_e) are determined as follows:

$$\begin{aligned}
\tau_s &= (I_1 + I_2 + m_1 c_1^2 + m_2(l_1^2 + c_2^2 + 2 l_1 c_2 \cos(q_e))\ddot{q}_s \\
&\quad + (I_2 + m_2 c_2^2 + m_2 l_1 c_2 \cos(q_e))\ddot{q}_e \\
&\quad - (m_2 l_1 c_2 \sin(q_e))\dot{q}_e^2 - (2 m_2 l_1 c_2 \sin(q_e))\dot{q}_s \dot{q}_e && (1.3) \\
\tau_e &= (I_2 + m_2 c_2^2 + m_2 l_1 c_2 \cos(q_e))\ddot{q}_s \\
&\quad + (I_2 + m_2 c_2^2)\ddot{q}_e + (m_2 l_1 c_2 \cos(q_e))\dot{q}_s^2 && (1.4)
\end{aligned}$$

These equations (1.3) and (1.4) indicate that the muscle torques are essentially dependent on the several parameters, which are: inertia (I), limb length (l), mass (m), and center of mass (c). This suggests that the reaching movement is counter-intuitively very complex and that the kinematics and

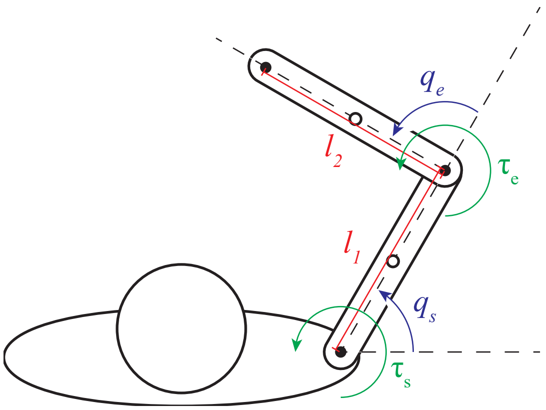

Figure 1.1: **Schematic Model of Human Arm.** A planer reaching movement with shoulder and elbow joints is easy to be described because the hand position is mathematically determined by the joint angles of the shoulder and elbow (q_s, q_e) and upper and lower limb lengths (l_1, l_2). Thus, the reaching movement from the start position to the target position is defined as time-dependent changes of these joint angles (q_s, q_e), in other words, these joint torques (τ_s, τ_e).

the dynamics are related each other. Thus, the parameters and the mapping must be organized so that the sensorimotor system performs accurate reaching movements.

1.2.2 Motor Control

A recent motor control framework has developed since around 1980 (Bizzi et al., 1976; Saltzman, 1979; Hollerbach, 1982; Kawato et al., 1987) (Figure 1.2). Previous studies have suggested that motor control requires input-output mappings, which is called the "internal model."

Feedback control As I described above, the motor commands (joint torques: τ_s, τ_e) strongly depend on the current state of the limb ($q_s, q_e, \dot{q}_s, \dot{q}_e, \ddot{q}_s, \ddot{q}_e$). Thus, the sensorimotor system needs to know the current state reliably. One of the important sources for this is sensory feedback. Many studies have suggested that reaching movement varies depending on visual and proprioceptive information (Scott, 2016). However, sensory feedback is not always reliable during reaching movement because of the following two reasons. First, sensory feedback is exposed to noise (Faisal et al., 2008), which means the sensorimotor system is unable to extract authentic information from the sensory feedback. Second, neural processing has inevitable delays (Scott, 2016). For example, proprioceptive feedback takes approximately 60 ms (Pruszynski and Scott, 2012) and visual feedback takes approximately 90 ms or more (Cluff et al., 2015) to convert sensory information into motor commands, meaning that the sensorimotor system does not directly obtain and utilize the current state in real time.

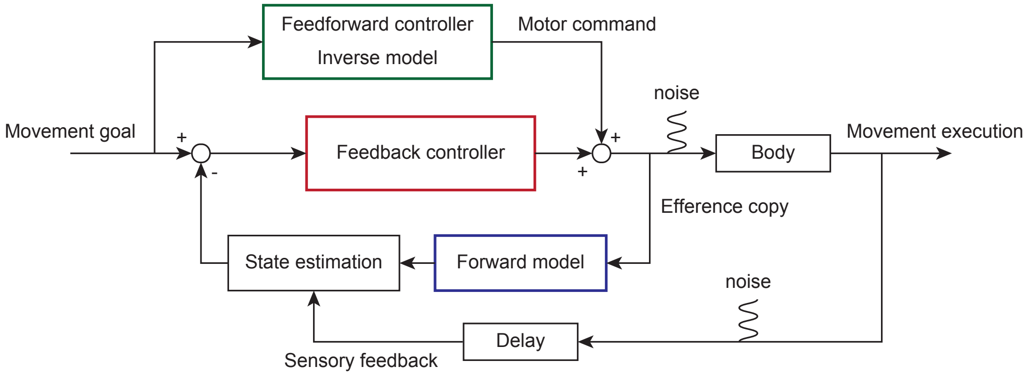

Figure 1.2: **Schematic Model of Motor Control Theory.** Feedback control is incorporated to stable the movement (Red). However, sensory feedback has inevitable noises and delays, which deteriorates a fast and predictive movement. Previous studies have proposed two different mechanisms for the problem. One is predictive control using the inverse model that directly transforms the desired states into motor commands (Green). This type of motor control is called feedforward control. The other is predictive control using a forward model that transforms motor commands into predictive states (Blue). The predictive states by the forward model can be used for the future motor commands. However, it is still unclear as to which controller is implemented in the brain.

Noises and delays in the sensory feedback could devastate a movement, especially during a fast and predictive movement. Then, how does the sensorimotor system overcome this problem?

Predictive Control with Inverse Model In the reaching movement example, hand position moves as smooth and straight as possible towards a target position. Thus, the sensorimotor system accomplishes the reaching movement if the sensorimotor system can transform the desired state (e.g., a desired trajectory and a desired position) inversely at entire points into the motor commands. The mapping is called the "inverse model", which is used for predictive movement control (feedforward control) (Wolpert and Ghahramani, 2000).

Predictive Control with Forward model The other idea is that predictive movement control is generated with the "forward model" that transforms motor commands, the "efference copy," into the predicted sensory feedback. If the sensorimotor system can obtain the future states, the predictive motor commands can be reliably generated.

For example, a computational study by Miall et al. (1993) simulated a tracking task with or without the forward model (Miall et al., 1993; Miall et al., 1986; Miall and Jackson, 2006). They assumed that the motor commands were smoothed by low-passed filter mimicking muscle mechanical properties (Baldissera et al., 1998; Miall et al., 1986) and that the sensory feedback had a delay of a few hundreds ms (Scott, 2016). They found that the correct forward model led to stable and accurate movements, suggesting that the forward model is indispensable for the motor command generation when there are neural delays.

One recent motor control theory, the optimal feedback control theory, implements the forward model (Todorov and Jordan, 2002; Todorov, 2004; Scott, 2012). This theory can reproduce several features of motor control such as movement coordination (Todorov and Jordan, 2002), movement curvature after adaptation to novel environments (Izawa et al., 2008), corrective movement for target jump (Nagengast et al., 2010; Izawa and Shadmehr, 2008), and tool use (Nagengast et al., 2009). The predictive movement control with the forward model is thought to be more plausible than that with the inverse model. However, it remains controversial as to whether the feedforward and feedback controllers can be unified.

Control Policy Another important issue in motor control is how the sensorimotor system alters movement pattern. For example, when we run as fast as possible, the running form must be altered by the running distance; if we run a long distance (e.g., more than 10 km) the running form should be more efficient, while if we run a short distance (e.g., around 100 m) the running form should be more vigorous. This example implies that the sensorimotor system has flexible rather than normative control policy. In other words, the sensorimotor system sets the “control policy” according to tasks, contexts, and environments.

How about reaching movement? Does the sensorimotor system have a normative control policy? Previous studies have illustrated that reaching movement has some typical features: tracing a slightly curved path from the starting position to the target position, and bell-shaped velocity profiles

(Flash and Hogan, 1985). The features are quite universal, suggesting that the reaching movement is based on the normative control policy. Several control policies have been proposed to reproduce these features, such as minimization of jerk (Flash and Hogan, 1985), torque-change (Uno et al., 1989), and variances (Harris and Wolpert, 1998).

1.2.3 Motor Learning

Suppose that we start to practice a fast movement, such as tennis strokes. At first, we have to continuously pay attention to how the body and racket should be moved, but the movement gradually becomes more accurate, quick, and automatic. That is, in the progress of motor learning, the sensorimotor system acquires the correct internal model to predictively generate the accurate motor commands (Kawato, 1989; Albert and Shadmehr, 2016).

This motor learning process can be investigated by applying a novel perturbation during reaching movement. In a typical experimental situation, participants perform reaching movement while holding a planer robotic handle. Participants are required to move the cursor representing the handle from a starting position to a target position displayed on a horizontal screen (Figure 1.3A). The visual rotation paradigm is widely used; the cursor motion is rotated around the start position (Figure 1.3B) (Cunningham, 1989). In this experiment, participants need to shift their movement in the opposite direction to the visual rotation so that the cursor reaches the target appropriately.

The sensorimotor system builds a correct internal model according to the imposed novel environment (Cunningham, 1989; Shadmehr and Mussa-

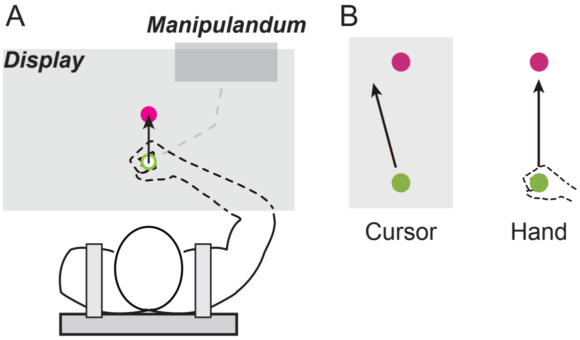

Figure 1.3: **Visual Rotation Task in Reaching Movement A.** Participants hold a planer robotic handle to perform reaching movements. Horizontal screen blocks direct vision of their limb and they move the cursor representing the handle from the start position to the target position in the screen. Unwanted movements (e.g., body trunk and wrist movement) are constrained by using belts and a brace. **B.** To measure how to build the internal model, a visual rotation is typically used (Cunningham, 1989). The cursor is rotated in a clockwise (CW) or counter-clockwise (CCW) direction around the starting position during the reaching movement. In order to compensate for this, the hand movement is altered in the opposite direction to the visual rotation.

Ivaldi, 1994). A current computational framework suggests that building this internal model can be described with the state space model as follows:

$$\begin{aligned} e_t &= x_t + p_t \qquad (1.5) \\ x_{t+1} &= \alpha x_t - \beta e_t \qquad (1.6) \end{aligned}$$

where the movement error (e) is produced by the perturbation (p), then the motor commands (x) are altered with regard to the movement error trial by trial (t). The terms α and β are constants representing retention and learning rates, respectively, which determine the learning dynamics. The state space model is simple but can precisely reproduce the behavior during motor learning, for example, savings (Krakauer et al., 1999; Smith et al., 2006), spontaneous recovery (Kojima et al., 2004; Smith et al., 2006), anterograde interference (Sing and Smith, 2010), and explicit and implicit learning (Taylor et al., 2014; McDougle et al., 2015).

In order to transform from the model of the behavior into that of the brain, a neural network model has often been used (Thoroughman and Shadmehr, 2000; Takiyama et al., 2015). The neural network model assumes that each motor primitive encoding a complex movement repertoire corresponds to one neural unit (e.g., single neuron or neural population) and that a weight vector corresponds to the synaptic strengths. Mathematically, the motor commands are determined by the weighted sums (W) of the activities of motor primitives (g) as follows:

$$x_t = W_t g \qquad (1.7)$$

In this framework, motor learning is defined as plastic changes of the weight to minimize cost function (J). The cost function is typically set as sum of the squared weight and the squared error as follows:

$$J = \frac{\alpha}{2} W^T W + \frac{\beta}{2} e^T e \tag{1.8}$$

and, expand the equation with the steepest decent method as follows:

$$W_{t+1} = \alpha W_t - \beta e_t g^T \tag{1.9}$$

An important factor in this equation (1.9) is that degrees of motor learning ($-\beta e_t g^T$) is determined as the activities of the motor primitives. Thus, tuning function of the motor primitives plays a key role for reproducibility. In most cases, and based on the neurophysiological studies, the activity is determined by a target direction (Thoroughman and Shadmehr, 2000) and by a prospective error (Takiyama et al., 2015). The former can reproduce spatial generalization (Donchin et al., 2003; Krakauer et al., 2000; Gonzalez Castro et al., 2011), target-direction dependent decay (Ingram et al., 2013; Takiyama, 2015), and the latter can reproduce structural learning (Braun et al., 2009; Kobak and Mehring, 2012), effects of uncertainty (Körding and Wolpert, 2004; Wei and Körding, 2010), and relevance of errors (Wei and Körding, 2009).

1.2.4 Neural Substrate

When the sensorimotor system generates the motor commands to accomplish the desired movement, the sensorimotor system knows what and where the movement goal is and calculates how the desired movement can be accomplished. The neural functions are characterized in a wide variety of cortical and subcortical brain circuits (Figure 1.4) (Shadmehr and Krakauer, 2008;

Scott, 2004; Scott, 2012). Firstly, the sensorimotor system obtains visual and proprioceptive information processed by visual related area (e.g., primary visual cortex: V1) (Goodale et al., 1986) and the somatosensory related area (e.g., primary somatosensory cortex: S1) (Cohen et al., 1994; Pruszynski et al., 2016). Then the sensory feedbacks are integrated at posterior parietal cortex (PPC) (Batista et al., 1999; Buneo et al., 2002). Next, the sensorimotor system makes the strategy of how the sensorimotor system accomplishes the movement goal in the processes of the prefrontal cortex (Hoshi et al., 1998; Kim and Shadlen, 1999; Hoshi et al., 2000) and basal ganglia (Graybiel et al., 1994; Turner and Desmurget, 2010; Kawai et al., 2015). Finally, based on the strategy, motor related areas (primary motor cortex: M1, supplementary motor cortex: SMA, premotor cortex: PM) (Georgopoulos et al., 1982; Georgopoulos et al., 1986; Georgopoulos et al., 1989; Caminiti et al., 1991; Fu et al., 1995; Kakei et al., 1999; Scott et al., 2001; Rizzolatti et al., 2001a; Rizzolatti et al., 2001b; Kakei et al., 2001; Cisek and Kalaska, 2005) generate the motor commands to the muscles. Simultaneously, the motor commands (the efference copy) are transmitted to the cerebellum for motor learning (Ito, 1984; Fortier et al., 1993; Blakemore et al., 1998; Coltz et al., 1999; Imamizu et al., 2000; Imamizu et al., 2003; Miall et al., 2007).

M1 is the final area descending the signal into the spinal cord, and plays a important role in movement execution (Dum and Strick, 1991; Dum and Strick, 1996; Hoffman and Strick, 1999; Maier et al., 2002; Graziano et al., 2002; Churchland et al., 2012; Shenoy et al., 2013; Griffin et al., 2015). What M1 neurons represent has remained controversial for some time. Importantly, Georgopoulos et al. (1982) found that M1 neurons encode reaching movement

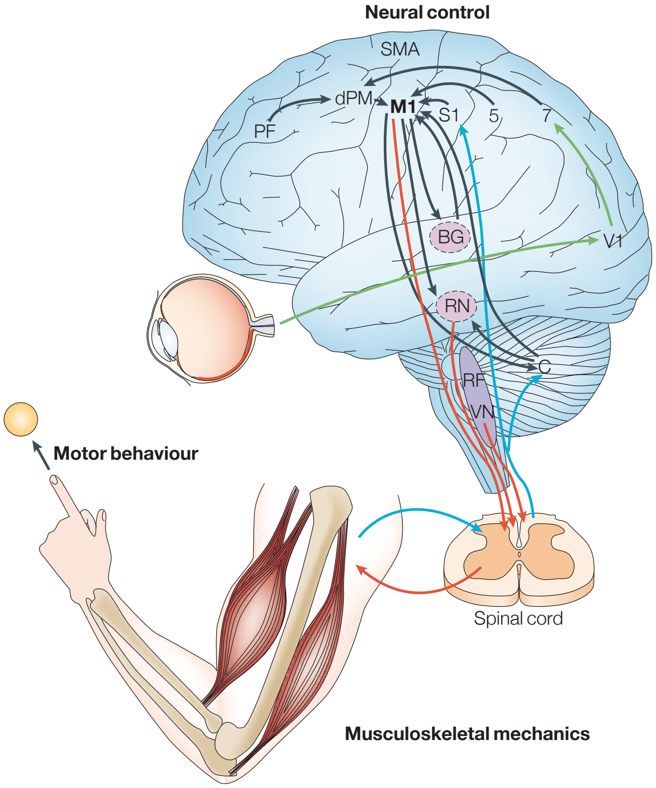

Figure 1.4: **Candidates of Central Nervous System for Motor Control and Learning.** Many cortical and subcortical areas are involved in reaching movements; processing sensory information (Primary visual cortex: V1, and Primary somatosensory cortex: S1), state estimation (Cerebellum: C, Posterior parietal cortex: 7, and Parietal cortex: 5), strategic and cognitive control (Prefrontal cortex: PF, and Basal ganglia: BG), and movement execution (Primary motor cortex: M1, Supplementary motor area: SMA, dorsal premotor cortex: dPM). The brain stem (reticular formation: RF, and Vestibular nuclei: VN) is thought to be more essential for whole-body postural control and locomotion. Adapted from Scott, 2004.

direction, which is called preferred direction (Figure 1.5) (Georgopoulos et al., 1982; Georgopoulos et al., 1986; Kalaska et al., 1989; Caminiti et al., 1991; Scott et al., 2001; Eisenberg et al., 2010).

During motor learning, the neural activities in M1 are changed (Alexander and Crutcher, 1990; Shen and Alexander, 1997b; Shen and Alexander, 1997a; Gandolfo et al., 2000; Li et al., 2001; Paz et al., 2003; Paz and Vaadia, 2004; Crutcher et al., 2004; Arce et al., 2010a; Arce et al., 2010b; Eisenberg et al., 2011; Haar et al., 2015). Li et al. (2001) investigated the alteration of neural activities in M1 when adapting to a novel environment. They found that most of the M1 neurons changed firing frequencies and tuning widths. More interestingly, the preferred directions were systematically rotated in the error (or perturbation) direction (Figure 1.6). Together, these findings suggest that M1 is the key neural substrate not only for motor control but also for motor learning.

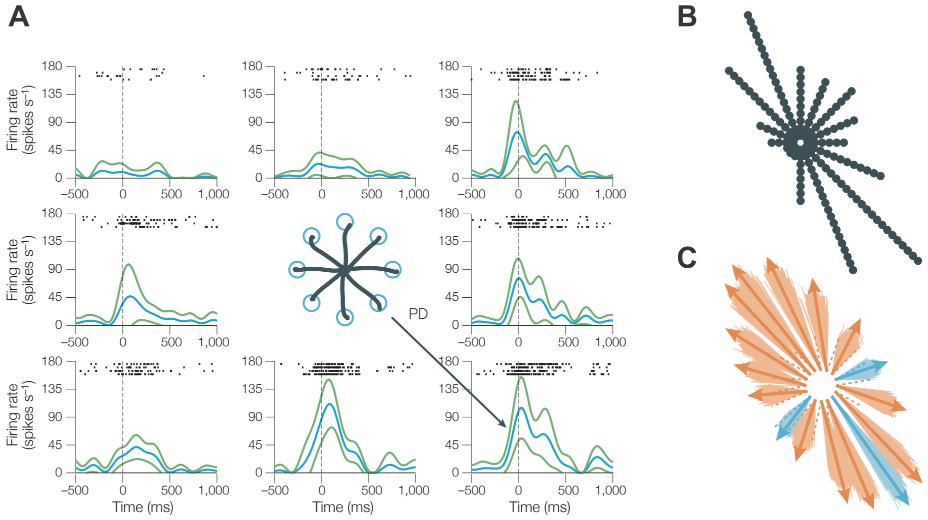

Figure 1.5: **Preferred Direction in M1 Neurons. A.** Firing frequency in an M1 neuron during reaching movement. Monkeys performed the reaching movement in eight directions while recording single neural activities in M1. The neural activity increased when reaching to a particular movement direction (black arrow: right backward direction in this cell), which is called preferred direction of the neural cell. **B.C.** Distribution of preferred direction in M1 neurons. **B.** Each dot denotes the preferred direction of an individual neuron. **C.** Each arrow denotes population activities just after the movement onsets. The vectors are calculated by sum of multiplication of the individual preferred direction. Dotted lines indicate hand movement direction. Blue and orange arrows indicate significant and nonsignificant differences between the angles of hand movements and those of the vectors, respectively. The single neural activities (**B**) and the population activities (**C**) showed skewed distribution when categorized by the preferred direction. Adapted from Scott, 2004.

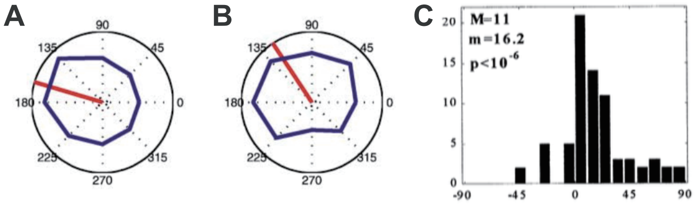

Figure 1.6: **Rotation of Preferred Direction in M1 Neurons. A.B.** Rotation of preferred direction of the representative neuron in M1. After recoding inherent preferred direction in the neuron (**A.** a red line), The preferred direction was rotated in a CW direction after adapting a novel environment (**B.** a red line). **C.** The histogram of M1 neurons categorized by degrees of the rotation of the preferred direction. The rotation was seen in most of the M1 neurons. Interestingly the rotation was directed to the error direction. Adapted from Li et al., 2001.

1.3 Interactions between Feedforward Control, Feedback Control, and Motor Learning

The feedforward controller predictively generates appropriate motor commands based on prior experiences. However, the feedforward controller is not versatile as the movement is challenged by noise and uncertainty in the environment and the central nervous system itself. Thus, when the motor system encounters an unpredicted error resulting from these challenges, the feedback controller needs to generate a motor command to reduce a movement error within the trial. Alternatively, the presence of a movement error implies that the feedforward controller has not generated an appropriate motor command and, in this case, the feedforward controller needs to be updated according to the movement error. This update can be observed as a movement correction in the next trial (motor learning or adaptation).

Thus, the control of human movement is accomplished by cooperation among the feedforward controller, feedback controller, and motor learning mechanisms. However, previous studies have focused on each component separately (e.g., what control policy is optimal for feedforward control (Flash and Hogan, 1985; Uno et al., 1989; Harris and Wolpert, 1998), how early the sensory feedback is utilized for feedback control (Pruszynski et al., 2011; Franklin and Wolpert, 2008), how efficiently can the error information be used for motor learning (Wei and Körding, 2009; Kasuga et al., 2013)), and their cooperative function and relationship have not been fully investigated. Here, I will review some of the literature that has addressed this relationship.

Following this, I will describe the unsolved problems that I investigated in this dissertation.

1.3.1 Feedback Response Could Reflect the Feedforward Control

There are different views on how the feedforward and feedback controllers interact with each other. One view states that the feedforward and feedback controllers exist separately, as shown in Figure 1.2. This assumption tacitly implies that alteration of feedforward control by motor learning does not influence feedback control, and thus feedback control is not altered by motor learning. However, recent studies have revealed that adaptive changes in feedforward control are also accompanied by alteration of feedback responses (Wagner and Smith, 2008; Cluff and Scott, 2013).

Wagner and Smith (2008) first investigated the relationship between the feedforward and feedback controllers by using a very sophisticated experimental paradigm (Figure 1.7). In their experiment, participants were required to acquire feedforward controller adjusting reaching movements to a rotational velocity-dependent force-field environment (Figure 1.7A, middle panel). Thus, after adaptation, the participants successfully performed a reaching movement while generating the force required to counteract the force-field.

Before and after adaptation by the feedforward controller, the feedback responses were induced by assistive or resistive mechanical perturbations immediately after movement onset (Figure 1.7A, right panel). Thus, the participants needed to decrease or increase the movement velocity according to the perturbation. An ingenious point of this study was the use of the error-clamp method to constrain the handle's trajectory to a straight path by a virtual force channel created by the robotic manipulandum. This method allowed measurement of the feedback response i.e., the force exerted against the force channel.

If the motor adaptation to the force field affected the feedback response, the participants should generate feedback motor commands that push the force channel laterally, according to the acquired feedforward controller. On the other hand, if there was no association between the feedforward and feedback controllers nothing should be changed in the feedback response following motor adaptation. Interestingly, the authors found that the feedback force was exerted rightward or leftward after the feedforward controller was adapted (Figure 1.7B), suggesting that the feedback controller reflects the characteristics of the newly acquired feedforward controller.

One of the limitations of the study by Wagner and Smith (2008) was that the feedback responses could be altered by the effects of acquired feedforward control on muscle activity. The motor command for the reaching movement was already modified by motor adaptation and as a result, the muscle activity level was also changed. Such alterations of muscle activity levels could influence the feedback response. Thus, in order to verify the relationship between the feedforward and feedback controllers, it is necessary to test feedback responses while feedforward motor commands remain unchanged by adaptation of the feedforward controller. This seems impossible but, as explained below, this was established in the experimental procedures in this study.

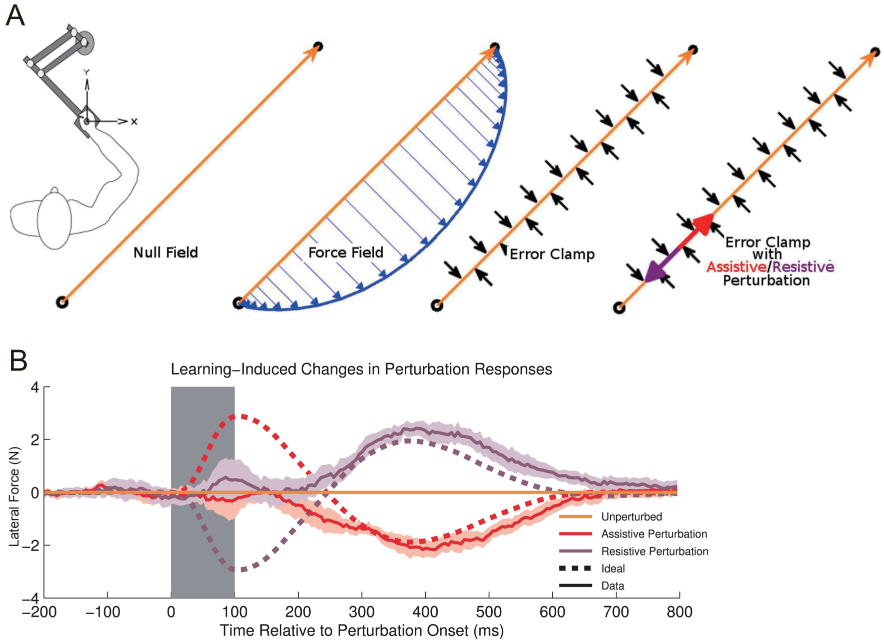

Figure 1.7: **Interaction between Feedforward Control and Feedback Control. A.** Participants in the experiments by Wagner and Smith (2008) adapted their feedforward control to the velocity-dependent force-field. Assistive or resistive mechanical perturbations were then applied in a channel (error-clamp), inducing feedback responses. The authors measured the force generated in response to the channel as an index of the adaptation effects of the feedback controller. **B.** The feedback controller generated lateral force induced by the resistive (purple) and assistive (red) perturbation. Importantly, the output forces (solid lines) matched the ideal forces (broken lines), suggesting that the feedback controller utilized the adaptations acquired by the feedforward controller. Adapted from Wagner and Smith, 2008.

1.3.2 How is Feedforward Controller Corrected Appropriately?

The sensorimotor system has a great ability to alter predictive motor commands according to environmental changes, which contributes not only to correct the movement in the next trial but also to perform consistent movements across trials (van Beers, 2009). A fundamental, yet unsolved, problem regarding the relationship between feedforward control and motor learning is how movements (or feedforward control) are corrected in an appropriate direction. For instance, in experimental procedures using visual rotation (Figure 1.3), even when naive participants are first exposed to the perturbation, they can correct the movement in the next trial in the appropriate direction (i.e., the actual hand movement is always changed in the CW direction if the CCW visual rotation is applied to the cursor (Figure 1.3). Why does the motor system already know which direction to correct the movement to?

This is the effect of "meta-learning" (Harlow, 1949; Braun et al., 2010). Many studies in the field of cognitive neuroscience have shown that the brain, when confronted with a novel task, initially learns slowly by trial and error. Once the brain understands the structure of the novel task it can learn it faster and generalize the knowledge to other tasks (Harlow, 1949). This suggests that the brain learns the general rules of the task while changing behavior.

Braun et al. (2009) illustrated the effect of meta-learning in motor learning (Figure 1.8) (Braun et al., 2009; Braun et al., 2010). In their study, participants were exposed to randomly varied visual rotations while performing reaching movements. Due to the random nature of the changes to visual rotation participant's movements did not change (i.e., no adaptation occurred). However, when they are subsequently subjected to a constant amount of visual rotation they could adapt to it more rapidly than control participants who had not been exposed to the random visual rotation beforehand, suggesting that the sensorimotor system had constructed general rules of how the movement should be altered when a visual rotation is imposed.

1.3.3 Motivation

In Chapter 1, several studies investigating feedforward control, feedback control, and motor learning were reviewed. While cooperation of these processes plays a critical role for movement control, it has not been fully elucidated how these processes are interrelated. In this study, I investigated the relationship by using a visuomotor task (the visual rotation task; Figure 1.3). The visuomotor task should be a more appropriate method of exploring movement control because the kinematics of hand movement can be more easily measured (e.g., position, velocity, and acceleration) than dynamical perturbation (i.e., force-field). In addition, in the visual rotation task, adaptive changes of feedforward control, feedback control, and motor learning can be identified as the alteration of the hand movement direction according to visual information. Furthermore, as explained later, dissociation of feedforward control, feedback control, and motor learning can be achieved by using a novel method inspired by Hirashima and Nozaki (2012) (See Chapter 2), which allows evaluation of the three processes separately.

In the case of the visuomotor task, the feedforward motor command is

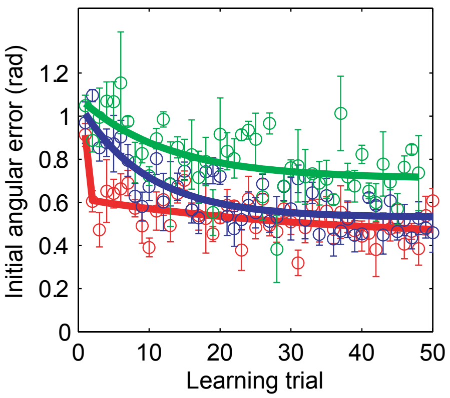

Figure 1.8: **Acquisition of Perturbation Structure.** Each color indicates the learning curve when adapting to a constant visual rotation in the test period; the red group experienced random rotations (i.e., the group had created the structure of the perturbation), the blue group only experienced movements with the null visual rotation, and the green group experienced random linear transforms in which they were separately exposed to x and y components of the visual rotation. The results showed that the random rotation group strongly facilitated later adaptation in the test period (red). Adapted from Braun et al., 2009.

created based on the “visual” target information. The feedback motor command is created according to the “visual” error. That is, the sensorimotor system transforms the visual information into motor commands in both the feedforward and feedback controllers. Hence, I hypothesized that a “visuomotor map” for feedforward control that transforms the visual information into motor commands must be shared between the feedforward and feedback controllers.

Another unsolved issue is how the motor system corrects the direction of movement across. This feat should be impossible without explicit knowledge of the structure representing the relationship between movement error and motor commands. Considering that motor learning in visual rotation is induced by “visual” errors, I hypothesized that the visuomotor map for feedforward control also influences motor learning by providing the structure of how the movement should be corrected based on visual error information.

Taken together, my hypothesis was that the visuomotor map is a common foundation for the feedforward controller, feedback controller, and motor learning. I tested this hypothesis with a series of behavioral experiments, described in Chapter 2.

Proposing the computational model behind behavior is very important for understanding brain function. In Chapter 3, I propose a novel computational principle based on the findings described in Chapter 2, which is inspired by the neurophysiological studies: rotation of preferred direction of motor primitives. In Chapter 4, I summarize these results and discuss the implications from more general point of view.

Chapter 2

Visuomotor Map for Motor Control and Learning

2.1 Introduction

Our ability to accurately reach toward visual objects is achieved by feedforward control based on a visuomotor map that transforms the spatial information of a target location into an appropriate movement (Johnson et al., 1996; Kalaska et al., 1997; Wise et al., 1997; Pouget and Snyder, 2000). However, feedforward control is not always versatile; the movement could be perturbed by noise and/or uncertainty within our nervous system and environments (Harris and Wolpert, 1998; Hamilton et al., 2004; Faisal et al., 2008; Franklin and Wolpert, 2011). Facing such unexpected perturbations, the sensorimotor system corrects movements in two different ways. Consider a laboratory situation in which a participant is making a reaching movement toward a visual target. When a cursor representing their hand deviates from the target, the sensorimotor system can correct the movement during the movement by feedback control (online correction) (Diedrichsen et al., 2007; Diedrichsen et al., 2010; Scott et al., 2015) and in the next trial by motor adaptation (offline correction) (Shadmehr and Mussa-Ivaldi, 1994; Shadmehr et al., 2010; Wolpert et al., 2011).

Intriguingly, these movement corrections are not necessarily achieved voluntarily (Goodale et al., 1986; Kagerer et al., 1997; Desmurget et al., 1999; Kasuga et al., 2013). Online correction during movements begins very rapidly (less than 150 ms) after visual perturbation (Franklin and Wolpert, 2008; Dimitriou et al., 2013; Reichenbach et al., 2014), much faster than voluntary movement correction (Day and Lyon, 2000; Franklin and Wolpert, 2008; Kobak and Mehring, 2012). As for offline correction, in the trial immediately after the perturbation, the movement inevitably deviates in the opposite direction (i.e., aftereffect), even if participants aim at the target (Wei and Körding, 2009; Kasuga et al., 2013).

Here, I hypothesized that the visuomotor map for voluntary movement control could influence the implicit online and offline movement corrections. To test the causal links between them, I examined how these movement corrections were influenced when the visuomotor map was artificially distorted. Theoretically, if I can distort the visuomotor map as shown in Figure 2.1B, this should result in reaching movements that are less sensitive to differences in the target's direction. Therefore, if both movement corrections refer to the visuomotor map, both types of movement corrections should also decrease following distortion of the visuomotor map. On the other hand, if the movement corrections are independent of the visuomotor map, I should observe the same amount of movement correction, even after the shape of the visuomotor map has been distorted. I tested this prediction by examining the rapid online correction when the target location was moved to another place immediately after the initiation of movement (Figure 2.1C) and the offline correction in the trial immediately after the deviation was imposed on the cursor (Figure 2.1D).

2.2 Methods

Participants Fifty-four right-handed participants (34 males and 20 females; age 15-52 years old) with no reported neurological disorders participated after giving informed consent. The entire protocols were approved by the ethics committee of my university.

General task settings The participants performed reaching movements with their right arm in a horizontal plane while holding the handle of a robotic manipulandum (KINARM End-point Lab, BKIN Technologies, Kingston, ON, Canada). Their trunks were fixed to the chair by two belts at right and left shoulders. Wrist movements were constrained by a brace, and an arm sling was used to support the upper arm horizontally and maintain a constant posture. A white cursor representing the handle position (10 mm diameter), a starting circle (14 mm diameter), and a target circle (14 mm diameter) were presented via a mirror placed over the arm, which occluded direct vision of participants' own arm. They were instructed to move the cursor from the starting circle toward the target circle (movement distance: 15 cm). A warning message “fast” or “slow” was displayed just below the start position

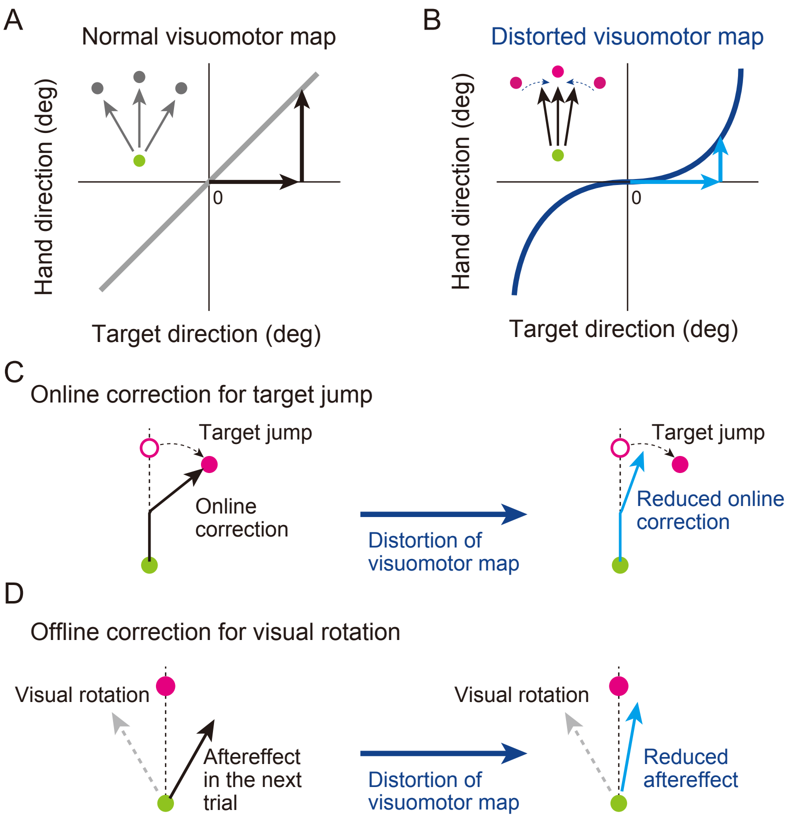

Figure 2.1: **Schematic Representation of My Hypothesis.** The visuomotor map is the relationship between the target direction and hand movement direction. **A.** In ordinary situations, these two directions are almost identical. **B.** If the map can be distorted (represented by a blue solid line), a voluntary reaching movement toward three targets should always result in the same hand movement directed to 0°. Participants cannot voluntarily change the movement direction even if they try. **C.D.** I hypothesized that online movement correction to a target jump (**C**) and offline movement correction observed after imposing visual rotation (**D**) also cannot be changed appropriately.

if the movement velocity was outside 600-750 mm/s (Experiment 1 and 3) and 380-450 mm/s (Experiment 2). In Experiment 2, slow movement was used, so that participants had sufficient time for online movement correction.

Procedure for distortion of the visuomotor map I defined the visuomotor map as the relationship between the target direction and actual hand movement direction. In ordinary situations, these two directions should be almost identical, because we can move our hands accurately to targets located anywhere. I attempted to distort this visuomotor map. In Experiment 1, I confirmed the visuomotor map was altered. Experiment 2 and 3 examined how online (Experiment 2) and offline (Experiment 3) movement corrections were influenced by distortion of the visuomotor map.

To distort the visuomotor map, I used the following method. The target was displayed alternately 30° to either the right or left of the straight-ahead position (0°). When reaching to the right or left target, rightward or leftward visual rotation around the starting position was applied to the cursor representing the handle position (Figure 2.2A). The amount of visual rotation was increased gradually from 0° to 30°, at a rate of 0.5° a trial (61 trials for each target) so participants were not aware of the presence of visual rotation. This procedure implicitly made the movement direction of the handle closer (i.e., inward) even when the participants aimed at the two different targets. I called the participants who experienced this training the inward adaptation group.

I also used another type of intervention, in which visual rotations were applied in the opposite direction (Figure 2.2B). Specifically, when reaching to the right or left targets, leftward or rightward visual rotation around the starting position was applied to the cursor representing the handle position. These rotations made the movement direction of the hand become more distant (i.e., outward). I called participants who experienced this training the outward adaptation group. If participants noticed the presence of visual rotations, the experiment was terminated and the data abolished. In total, the data of 4 participants (2 each for Experiment. 2 and 3) were discarded. In the following sections, the data did not contain these participants.

Experiment 1: Distortion of visuomotor map To confirm the visuomotor map was actually distorted by the intervention described above, I obtained the visuomotor map by having participants ($N = 6$ for each of inward and outward adaptation group) reach to targets located at various positions (0°, ±7.5°, ±15°, ±30°, ±45°, and ±60°; 6 trials for each target) without visual feedback (i.e., the cursor was invisible) before and after the intervention. Before the intervention, participants were asked to reach toward each target (Figure 2.2C), and the cursor became invisible immediately after the color of the target changed. After the intervention, participants reached alternately to 2 targets located at ±30° under 30° visual rotation. Probe trials to each target were randomly interleaved (66 probe trials out of 266 total trials). In the probe trials, the cursor became invisible immediately after the color of the target changed so that unnecessary visuomotor adaptation did not occur. After adapting to the inward (or outward) adaptation, I expected that the movement direction would become less sensitive (or more sensitive) to changes in the target locations.

Experiment 2: alteration of feedback control Sixteen participants were assigned to two groups (N = 8 for each group) according to the type of distortion of visuomotor map (inward or outward adaptation, see Experiment 1). To investigate how the intervention influenced online movement correction, I adopted an experimental paradigm using target jump (Figure 2.2D) (Goodale et al., 1986; Desmurget et al., 1999; Day and Lyon, 2000; Izawa et al., 2008; Gritsenko et al., 2009; Gritsenko and Kalaska, 2010). As shown in Experiment 1, movement to the central target remained unchanged after intervention. Thus, I used movement to the central target as probe trials to investigate online movement correction; More specifically, in probe trials reaching toward the central target, the target location changed to another location (±30°, ±15°, ±7.5°, 0°) after the force to the handle exceeded 1 N when starting reaching movement. The cursor disappeared simultaneously so that unnecessary adaptation did not occur during online movement correction.

Participants performed 100 reaching movements toward each target located at ±30°, in alternate fashion. A reaching movement to the central target was randomly interleaved (100 trials). Thirty trials were performed with visual feedback (i.e., the cursor was visible), and the remaining 70 trials were probe trials without visual feedback (i.e., target jump trials; 10 trials for each size of target jump). These procedures were performed before and after intervention.

Experiment 3: alteration of aftereffect I investigated how intervention influenced offline movement corrections. Twenty-two participants were randomly assigned to two groups (N = 11 for each group) according to the type of visuomotor map distortion (inward or outward adaptation, see Experiment 1). As in Experiment 2, I used movement to the central target as probe trials. Visual rotations ($-30°$, $0°$, $30°$) were applied to the cursor when participants reached to the central target. In the next trial to reach the same central target, I measured the corrected movement direction in the direction opposite the visual rotation (i.e., aftereffect, Figure 2.2E). I asked the participants to aim at the central target as accurately as possible and not use explicit strategy (Taylor et al., 2014) to change the movement direction. In perturbed trials, I also asked participants not to correct during the movement, so that online movement correction did not influence offline movement correction.

Participants performed 120 reaching movements toward each target located at ±30° positions in alternate fashion. A pair of one visual rotation trial and one probe trial was randomly interleaved (10 pairs for each of 0°, +30°, $-30°$ visual rotations). These procedures were performed before and after intervention.

Data Analysis Data on the kinematics of the handle (position and velocity) and the force on the handle were sampled at 1000 Hz and filtered with a cutoff frequency of 10 Hz using a fourth-ordered Butterworth filter. For the analysis of Experiment 1, I obtained the movement direction by calculating the angle of the line connecting the starting position and handle position at the peak velocity relative to the forward direction. The rightward and leftward movements were defined as positive and negative, respectively.

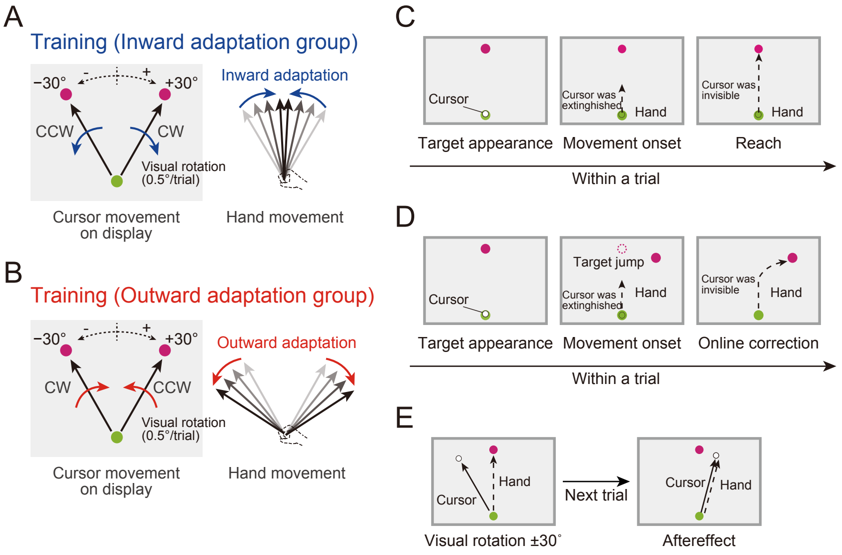

Figure 2.2: **Experimental Setup.** Participants alternately reached toward one of two targets located rightward and leftward. **A.** In inward adaptation group, gradually increasing rightward and leftward visual rotations were imposed on the cursor when reaching to rightward and leftward targets, respectively. This procedure would make the handle movements closer to the target. Participants were not aware of the presence of visual rotation. **B.** In the outward adaptation group, the association of target and visual rotation was reversed, making the handle movements more distant. **C-E**, the participants performed probe trials in order to obtain the visuomotor map (**C**), online (**D**), and offline movement correction (**E**) in Experiments 1, 2, and 3, respectively (see Materials and Methods).

In the probe trials for Experiment 2, the visual cursor was turned off. To ensure if online movement corrections were performed appropriately even when visual feedback was not available, I calculated the angle connecting the starting position with the final handle position (1000 ms after the target jump) as the movement direction. As I will demonstrate in the Results section, there was a linear relationship between the target and movement directions. Therefore, to represent how the participants corrected movement at the end of the trial, I calculated the slope of the regression line for each participant as an index. This slope was compared between period (before and after distortion) and group (inward and outward adaptation) by a 2-way repeated measure analysis of variance (ANOVA) (statistical significance was delineated at $p < 0.05$ throughout the study).

To examine the rapid component of online movement correction, I analyzed the lateral component (i.e., x-component) of force exerted on the handle 170-200 ms after the target jump. The force output depended on the amount of target jump. Accordingly, I calculated the force output for each target jump (small, ±7.5°; medium, ±15°; large, ±30°). The force output for each target jump size was obtained by multiplying the slope of the regression line by the size of target jump. The calculated force output was compared between target jump sizes (small, medium, large), groups (inward and outward adaptation) and periods (before and after distortion) by a 3-way repeated measures ANOVA.

I also considered the influence of other factors, besides the change in the visuomotor map, on the feedback response. Specifically, I examined for changes in the kinematics of the movement to the central target that were caused by the visuomotor map distortion intervention, as even subtle changes in the kinematics could influence the feedback response (Franklin et al., 2012). To this end, I evaluated the peak velocity of the handle, as well as the lateral deviation of the handle at the peak velocity, to examine movement toward the central target when the cursor was visible (30 trials). Second, I evaluated whether the intervention caused changes in the cursor's deviation from the targets. Greater deviations of the cursor from the targets would give the participants more opportunities to correct the movements online, which could strengthen the feedback response (Franklin and Wolpert, 2008). To evaluate this, I measured the lateral deviation of the cursor from a straight line connecting the start and target positions. This was performed for the trials in which the cursor was visible (100 trials each for the left and right targets, and 30 trials for the central target), and then the root mean squared value was calculated for each participant. These values were compared between groups and periods using a 2-way, repeated measures ANOVA.

For the data analysis of Experiment 3, investigating the offline movement correction, I calculated the aftereffect in the trial after the perturbation (i.e., visual rotation) trial. According to the force output data for the online movement correction in Experiment 2 (see Results), the online correction should start approximately 130 ms after movement onset. In order to remove the influence of the online movement correction, the aftereffect was defined as the movement direction 120 ms after movement onset. The calculated aftereffect was compared between periods (before and after distortion) and groups (inward and outward adaptation) using a 2-way repeated measures ANOVA. I also compared movement error experiences for the trial in which the visual rotation was applied in order to confirm participants experienced the same amount of movement error.

I instructed participants not to correct their movement when the visual rotation was imposed; however, it is possible for online corrections to be induced implicitly (Goodale et al., 1986; Desmurget et al., 1999; Day and Lyon, 2000). Since online movement corrections are capable of influencing the offline movement corrections made in the subsequent probe trial (Kawato and Gomi, 1992), I evaluated how the online corrections for the visual rotation trials were different between groups (inward and outward groups) and periods (before and after distortion). To this end, as in Exp. 2, I analyzed the cursor's direction at 500 ms after movement onset from the central target direction and the force output for the movement correction averaged from 170-200 ms after movement onset. A 2-way repeated measures ANOVA was used to compare these measurements across periods and groups.

2.3 Results

Artificial distortion of the visuomotor map In Experiment 1, I characterized in what way the visuomotor map was distorted before and after the respective interventions (inward and outward adaptation groups), before conducting Experiments 2 and 3. Figure 2.3A illustrates the trial-dependent change in the movement direction of the handle for the inward adaptation group ($N = 6$, rotations shown in Figure 2.2A). Before visual rotation was imposed, the direction of movement was toward the respective target (either 30° to the right or left of the straight-ahead position). During the training period, participants in this group experienced an outward visual rotation, and compensated by directing their hand movement in the direction opposite to the rotation (inward). Movement direction became closer to the straight-ahead position as adaptation occurred. Notably, participants were not aware of the visual rotations, as rotations increased gradually by 0.5° per trial. Figure 2.3B shows the trial-dependent change in the movement direction of the handle for the outward adaptation group ($N = 6$), which received visual rotations in the direction opposite that of the inward adaptation group (a leftward rotation occurred in trials involving the right target and a rightward rotation occurred in trials with the left target, as shown in Figure 2.2B). In contrast with the inward adaptation group, participants corrected by directing cursor movement farther away from the straight-ahead position with increasing trials.

Before and after intervention, I measured the visuomotor map by asking participants to reach toward targets located at various positions (0°, ±7.5°, ±15°, ±30°, ±45°, ±60°) without visual feedback from the cursor (Figure 2.2C). As illustrated in Figure 2.3C, prior to intervention, movement directions were almost identical to target directions (broken lines). However, the shape of the visuomotor map was distorted depending on the type of intervention (Figure 2.3C). For the inward adaptation group, the line corresponding to the visuomotor map became flatter around the central target (0°, solid blue line), implying a lowered sensitivity to changes in the target's direction. Conversely, the line corresponding to the visuomotor map of the outward adaptation group became steeper, compared to before the intervention (solid red line), implying that sensitivity increased. Importantly, movement direction toward the central (0°) target remained unchanged by both interventions (Figure 2.3C), indicating that it was unaffected by distortion of the visuomotor map. Therefore, this paradigm was suitable for use of the movement to the central target as a probe trial to compare online (Experiment 2) and offline (Experiment 3) movement corrections, before and after distortion of the visuomotor map.

Gain alteration of online correction Experiment 2 was designed to investigate how online movement corrections were influenced by distortion of the visuomotor map. To this end, I randomly interleaved probe trials in which the central target suddenly jumped to peripheral locations (±7.5°, ±15°, and ±30°, Figure 2.2D) immediately after movement onset. I compared the online movement corrections induced by the target jump between trials before and after distortion of the visuomotor map (Figure 2.4A,B).

The degree of correction seemed to decrease or increase depending on the type of distortion each group received. In order to quantify the amount of online movement correction and ensure if the participants tried to correct the movement properly even when the visual information of the cursor was absent, I first determined the angle of the handle position relative to the starting position 1000 ms after the target jump (i.e., final position). Figure 2.4C indicates the relationship between target jump angles and resultant final movement angles. There was a linear relationship between the angles, from which I calculated the slope of the regression line as an index to quantify the degree of online movement correction. A 2-way repeated measures ANOVA revealed that there were significant interactions between period (before and

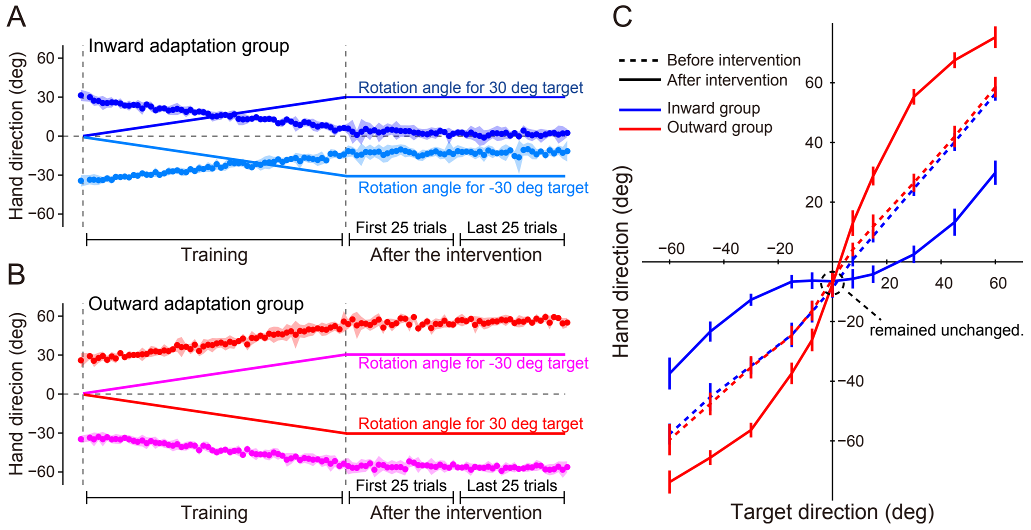

Figure 2.3: **Distortion of Visuomotor Map. A.B.** The imposed visual rotation (solid lines) and the movement direction of the hand in the trial for inward (**A**) and outward adaptation groups (**B**). The hand movements became closer (**A**) and more distant (**B**) to compensate for gradually increasing visual rotation. Data are represented by mean ± SD. **C.** Visuomotor map before (broken lines) and after distortion (solid lines). The shape of the visuomotor map in the vicinity of the central target (0°) was distorted according to the training that each group received. Notably, movement toward the central target remained unchanged. Error bars represent SD.

after distortion of visuomotor map) and group (inward and outward adaptation) ($F(1, 14) = 94.06, p = 1.36 \times 10^{-7}$, Figure 2.4D). The simple main effect of period (before and after visuomotor map distortion) was also significant for both the inward ($F(1, 14) = 38.76, p = 2.21 \times 10^{-5}$) and outward ($F(1, 14) = 56.10, p = 2.92 \times 10^{-6}$) adaptation groups. Specifically, distortion of the visuomotor map resulted in diminished online corrections in the inward adaptation group and exaggerated online corrections in the outward adaptation groups (Figure 2.4D).

Next, to see how early movement correction started, I examined the lateral force exerted on the handle during the online movement correction. Figure 5A and B indicates how the lateral force output changed with time. The force output for the movement correction appeared to emerge approximately 130 ms after the target jump. I averaged the force output between 170-200 ms after the target jump to examine how distortion of the visuomotor map influenced the force output for rapid online movement correction and grouped the responses for each of three target jump sizes (small, ±7.5°: medium, ±15°: large, ±30°). Analysis with a 3-way repeated measures ANOVA (group × target jump size × period) revealed no second-order interaction ($F(2, 28) = 0.15, p = 0.859$); however, there was a first-order interaction between period and group ($F(1, 14) = 9.86, p = 7.24 \times 10^{-3}$), which indicates that the two types of visuomotor map distortions differentially altered the force output for a movement correction. Indeed, there was a simple main effect of period in both the inward ($F(1, 14) = 4.90, p = 0.044$) and outward adaptation groups ($F(1, 14) = 4.95, p = 0.043$; Figure 2.5C). The statistical results were not substantially different when the data for time windows after

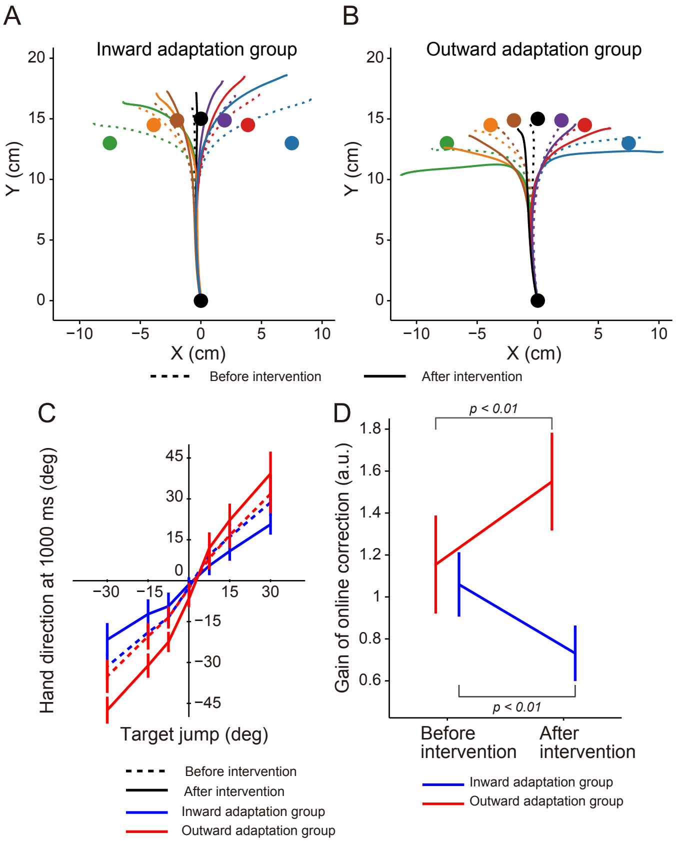

Figure 2.4: **Online Movement Correction. A.B.** Trajectories of the hand before (broken lines) and after (solid lines) distortion of the visuomotor map for the inward adaptation group (**A**) and outward adaptation group (**B**). Each color represents the trajectory for a discrete target jump. **C.** Online movement correction was evaluated 1000 ms after the onset of target jump before and after distortion of the visuomotor map. **D.** The slope of the linear relationship between size of the target jump and corrected movement direction (**C**) significantly decreased after distortion in the inward adaptation group, whereas it significantly increased in the outward adaptation group. Error bars indicate SD.

170 ms (e.g., 175-205 ms, 180-210 ms) were analyzed. Thus, the rapid component of lateral force for online movement correction was decreased (inward adaptation group) and increased (outward adaptation group) depending on the visuomotor map distortion that each group received. Interestingly, as shown in Figure 2.5C, the corrected force outputs during this time window appeared to increase as the size of the target jump became smaller. This is in contrast with a recent study by Franklin et al. (2016), showing that the corrected force was correlated with the size of the target jump. However, the size of the target jump in their study was 7° at maximal, which was much smaller than the target jump in the present study. Thus, it is possible that the online correction was nonlinearly modulated by the size of the target jump. Indeed, Haith et al. (2015) reported that reaction time to a target jump was shorter for a 45° target jump than for target jumps at 90° and 135° (Haith et al., 2015). A similar nonlinear modulation has also been reported in the aftereffect, observed in the trial after the cursor is displaced (Wei and Körding, 2009; Kasuga et al., 2013).

I examined whether changes in the online movement correction could be explained by factors other than distortion of the visuomotor map itself. A 2-way repeated measure ANOVA applied to the peak velocity of the handle toward the central target indicated that there was no significant main effect for group ($F(1, 14) = 0.58, p = 0.46$) or period ($F(1, 14) = 0.15, p = 0.70$), and no significant interaction between them ($F(1, 14) = 0.26, p = 0.62$). The movement trajectories toward the central target when the visual cursor was available are shown in Figure 2.6A,B. While the trajectories before and after visuomotor map distortion largely overlapped (Figure 2.6A,B), a

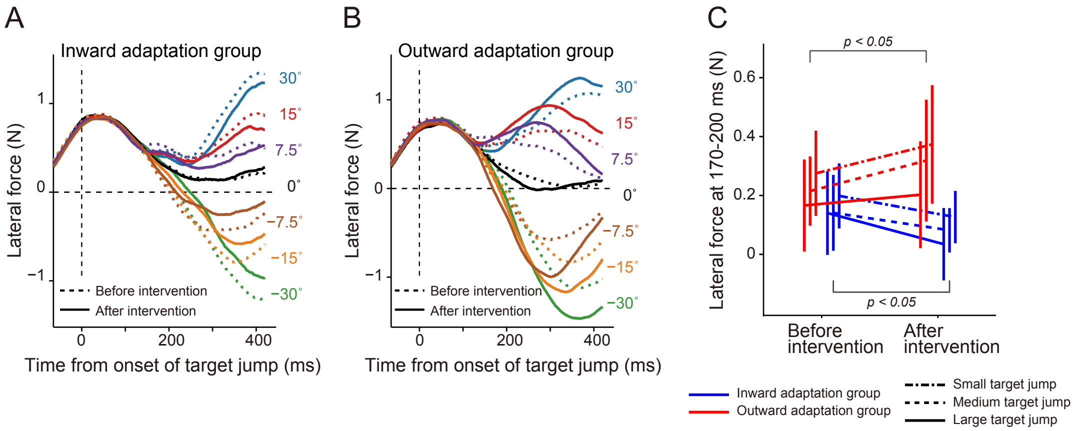

Figure 2.5: **Rapid Component of Online Movement Correction. A.B.** The x-component of force output exerted on the handle before (broken lines) and after (solid lines) distortion of the visuomotor map for the inward (**A**) and outward (**B**) adaptation group. The values shown on the right side indicate the size of target jump. **C.** Force output was averaged between 170 and 200 ms after target jump for each size jump (small, dashed-dotted lines; medium, broke lines; large, solid lines). Error bars indicate SD.

2-way repeated measures ANOVA, for deviations in the path of the lateral hand at the peak velocity, revealed a significant interaction between period (before and after the distortion of the visuomotor map) and group (inward and outward adaptation) ($F(1, 14) = 8.251, p = 0.012$). There was a significant simple main effect of period only for the outward group ($F(1, 14) = 15.64, p = 1.43 \times 10^{-3}$; Figure 2.6C). However, the difference was small (approximately 0.2 cm) and this effect was not observed in the inward group ($F(1, 14) = 0.012, p = 0.92$).

I also examined whether cursor movement deviated from the straight path to the target more or less in different groups and periods by calculating the root mean squared values of the lateral deviation for each participant. A repeated measures 2-way ANOVA revealed that there was a significant interaction between group and period ($F(1, 14) = 10.322, p = 6.26 \times 10^{-3}$), and there was a simple main effect of period for the inward adaptation group ($F(1, 14) = 36.07, p = 3.22 \times 10^{-5}$; Figure 2.6D). This indicates that movement accuracy deteriorated in the inward adaptation group; however, there was no simple main effect of period for the outward adaptation group ($F(1, 14) = 2.139, p = 0.17$; Figure 2.6D). Taken together, the procedure to distort the visuomotor map did not change the kinematics and/or the movement accuracy sufficiently to explain the changes observed in the online movement correction.

Gain alteration of offline correction Experiment 3 was designed to examine how distortion of the visuomotor map influenced offline movement correction. To this end, after either intervention, I interleaved visually per-

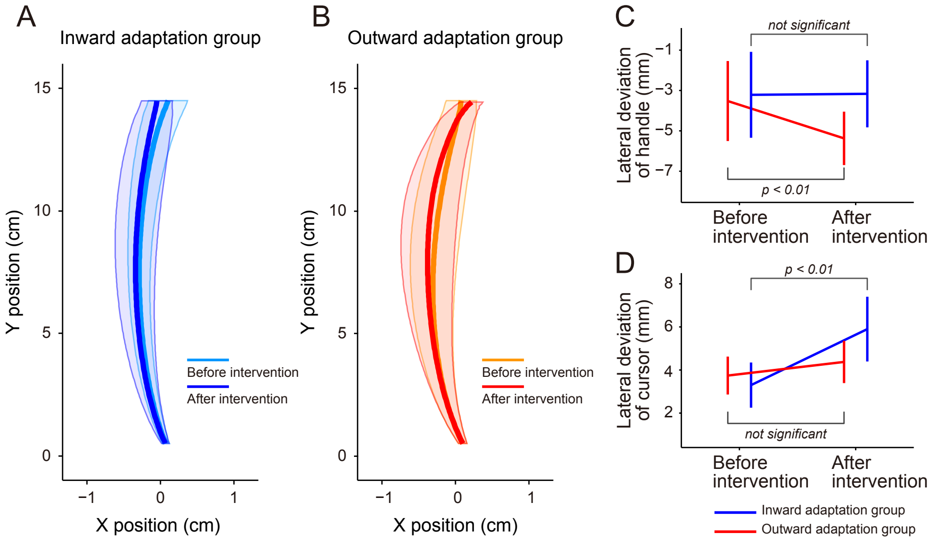

Figure 2.6: **Kinematics of the Movement. A.B.** The trajectories of the handle during movement to the central target (the cursor was visible) before and after intervention for the inward (**A**) and for outward (**B**) adaptation groups are shown. Solid bold lines indicate the averaged trajectory of participants. Shaded areas indicate SD. Note that the scale for the x-direction is exaggerated. **C.**, The handle's x-position during peak velocity was quantified to examine the shape of the trajectories. After intervention, the values became significantly smaller by 1.9 mm only for the outward adaptation group, indicating that the trajectories were slightly curved leftward. **D.** The lateral deviation of the cursor's direction at peak velocity from the target direction (left, central, and right targets) was quantified by taking the root mean squared value for each participant. After intervention, the deviation significantly increased only in the inward adaptation group. In **C** and **D**, error bards indicate SD.

turbed trials (i.e., the cursor was rotated by ±30° around the starting position) and examined the aftereffect observed in the next trial (Figure 2.2E). Figure 2.7 shows the aftereffects for both groups and for both periods. A 2-way repeated measure ANOVA revealed that there was a significant interaction between group and period ($F(1, 20) = 18.54, p = 3.43 \times 10^{-4}$). Furthermore, there was a significant simple main effect of period in the inward ($F(1, 20) = 14.80, p = 1.00 \times 10^{-3}$) and outward adaptation group ($F(1, 20) = 5.03, p = 0.037$), indicating that the aftereffect was decreased (inward adaptation group) and increased (outward adaptation group) depending on the distortion of visuomotor map. A 2-way repeated measures ANOVA was also applied to the error that each group received in the visual rotation trials. There was no significant main effect for group ($F(1, 20) = 0.48, p = 0.50$) or period ($F(1, 20) = 2.07, p = 0.17$), and no significant interaction between the two ($F(1, 20) = 1.02, p = 0.33$), indicating the amount of sensory prediction error itself did not differ between groups and between periods. Again, the effects of group and period on offline movement correction were not explained by differences in the kinematics of the handle; a 2-way repeated measures ANOVA applied to the peak velocity of the handle toward the central target indicated that there was no significant main effect for group ($F(1, 20) = 1.20, p = 0.29$) or period ($F(1, 20) = 2.42, p = 0.14$) and no significant interaction between them ($F(1, 20) = 1.72, p = 0.20$).

I also examined how participants tried to correct their movement during the visual rotation trials. Analysis of the handle trajectories indicated that participants tried to minimize their movement corrections (Figure 2.8A,B) in accordance with the instructions. An evaluation of movement direc-

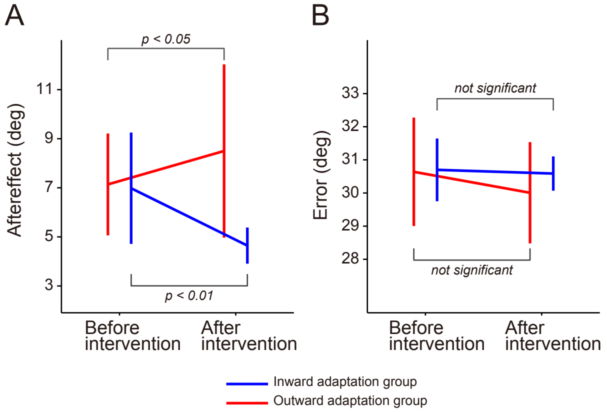

Figure 2.7: **Offline Movement Correction. A.** The aftereffect was quantified in the trial immediately after the perturbation trial (it was evaluated as the movement direction 120 ms after movement onset). The aftereffect significantly decreased after distortion of the visuomotor map in the inward adaptation group, whereas it significantly increased in the outward adaptation group. **B.**, Visual errors in the perturbation trial (the errors should be 30°) were not significantly different before and after intervention. Error bars indicate SD.

tion, at the end of the movement, indicated that a slight correction was made (Figure 2.8C,D). However, a 2-way repeated measures ANOVA showed that the degree of correction was not significantly different before and after the intervention ($F(1, 20) = 0.413, p = 0.53$ for the main effect of period; $F(1, 20) = 3.404, p = 0.08$ for the interaction between group and period). The force output for fast online corrections was also analyzed (Figure 2.9A,B). No significant change in the average of the force output, from 170-200 ms after movement onset, was observed ($F(1, 20) = 1.197, p = 0.287$ for the main effect of period; $F(1, 20) = 1.323, p = 0.264$ for interactions between group and period by a 2-way repeated measures ANOVA). Thus, the procedure to distort the visuomotor map did not change how the participants corrected their movement during the visual rotation trials.

2.4 Discussion

In order to consistently perform accurate reaching movements, the sensorimotor system has two kinds of mechanisms for movement correction within a trial (online correction) and in the next trial by motor adaptation (offline correction). Notably, these corrections could be achieved implicitly, as previously described (Goodale et al., 1986; Kagerer et al., 1997; Desmurget et al., 1999; Kasuga et al., 2013). I hypothesized that the visuomotor map is important for feedforward control during voluntary movement and plays a pivotal role in teaching the sensorimotor system how the movement should be corrected.

I distorted the shape of the visuomotor map by applying the opposite vi-

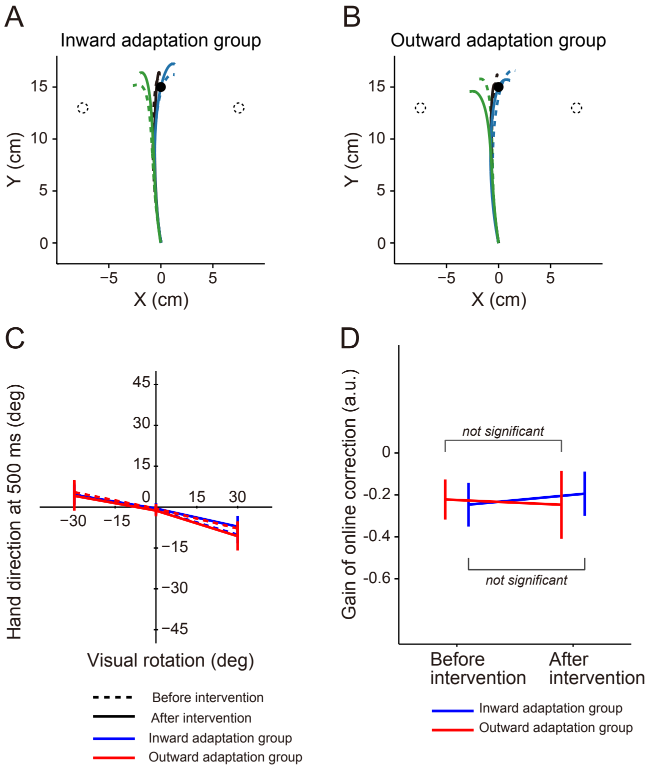

Figure 2.8: **Online Movement Corrections of Hand Position in Experiment 3. A.B.** The trajectory of the handle during movement to the central target in the perturbation trials, before and after the intervention, for the inward (**A**) and outward (**B**) adaptation groups is shown. The dotted circles indicate the corresponding final positions if movements were fully corrected. **C.** Online movement correction was evaluated 500 ms after movement onset, before and after distortion of the visuomotor map. **D.** The slope of the linear relationship between the size of the visual rotation and the corrected movement direction did not change by distorting the visuomotor map, for both experimental groups. Error bars indicate SD.

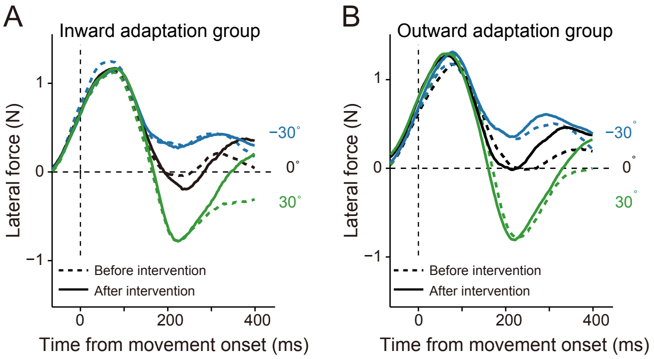

Figure 2.9: **Online Movement Corrections of Force Output in Experiment 3. A.B.** The x-component of the force output exerted on the handle before (broken lines) and after (solid lines) distortion of the visuomotor map are shown for the inward (**A**) and outward (**B**) adaptation groups from movement onset.

sual rotations to the cursor when reaching to 2 targets. After inward visual rotations were imposed when the participants aimed at two different targets located at ±30°, the actual movement direction became closer (Figure 2.3A) and the visuomotor map around at 0° became flatter (Figure 2.3C); the participant performed almost the same straight-ahead movement even when trying to reach peripheral targets (inward adaptation group). In contrast, the change in movement direction was more exaggerated after the participants experienced outward visual rotations (outward adaptation group) (Figure 2.3B,C). Importantly, these procedures did not change the reaching movement to the central target located at 0° (Figure 2.3C). Thus, the changes in online and/or offline movement corrections for movement toward this target can be attributable to the distortion of the visuomotor map around 0°. It should be noted that all participants were unaware of the presence of visual rotation throughout the experiment, because the degree of visual rotation was increased so gradually. Adherence to this procedure is critical to distort the visuomotor map effectively; if visual rotation is imposed abruptly the participants might intentionally aim askew of the target position, as part of an explicit strategy (Taylor et al., 2014). In contrast, if the participants happen to adapt to visual rotation by developing a strategy of moving the handle straight forward to the cursor located ±30°, then the adaptation does not necessarily result from an alteration of the visuomotor map, but rather from changing their aim.

Consistent with this hypothesis, I found that the degree of online and offline movement correction was altered according to the shape of the distorted visuomotor map. More specifically, in the inward (or outward) adaptation group, the degree of correction was reduced (or increased). These results indicate that the feedback controller and motor adaptation system refer to the visuomotor map that is used for feedforward control, suggesting a new perspective on the relation between feedforward control, feedback control, and motor adaptation.

Factors influencing the feedback response It is important to note that there are several other factors, besides the visuomotor map, that could potentially influence the feedback response. First, changes in the kinematics of the movement to the central target can induce different responses (Franklin et al., 2012). However, there were no statistically significant differences in the peak velocity of the handle during movement toward the central target, when the visual cursor was available, between groups (inward and outward groups) and periods (before and after interventions). Furthermore, these trajectories largely overlapped (Figure 2.6A,B). The lateral deviation at the peak velocity was slightly (0.2 cm) different before and after the intervention in the outward adaptation group; however, this effect was not observed in the inward group (Figure 2.6C). Therefore, differences in the kinematics of movement to the central target cannot fully explain the changes in the online movement correction, caused by distortion of the visuomotor map.

Second, the procedure used to distort the visuomotor map could also change the movement accuracy. For example, if the movements by the outward adaptation group became more inaccurate after the intervention (i.e., the cursor deviated from the target path more often), the participants would need to correct their movement more often. Such increased opportunities to correct movement can change the rapid feedback response. Indeed, Franklin and Wolpert (2008) reported that the online response to a cursor jump was enhanced after repeated exposure to cases in which perturbed cursor movement needed to be corrected to reach a target, and could similarly be suppressed by cases in which the cursor was perturbed but did not need correction. However, as shown in Figure 2.6D, movement accuracy was maintained in the outward adaptation group, even after intervention. In contrast, accuracy was deteriorated by the intervention in the inward group (Figure 2.6D), suggesting that these participants needed to correct their movement more often. Nevertheless, the online correction was decreased for the inward adaptation group (Figures 2.4 and 2.5), which opposes the prediction made by Franklin and Wolpert. Taken together, the changes in the online correction observed in the present study are most likely caused by distortion of the visuomotor map, rather than indirectly by changes in the kinematics and/or an increased opportunity to correct the movement deviations.

Relationship between feedforward and feedback control Recent several studies have shown a close link between feedforward and feedback controls. Wagner and Smith (2008) demonstrated that after reaching movements were adapted to a velocity-dependent curl force field, the lateral force response to the suddenly imposed increase/decrease in hand movement also changed (Wagner and Smith, 2008). In the visuomotor adaptation domain, Saijo and Gomi (2010) also reported the change in the feedback gain by adaptation to a visual rotation (Saijo and Gomi, 2010). These studies indicate that the feedback correction somehow reflected the acquired feedforward movement control. However, the muscle activity or movement direction of the hand for the probe trials differed before and after the motor adaptation, which makes interpretation of the feedback gain change before and after the adaptation difficult.

To overcome this possible criticism, Cluff and Scott (2013) developed a paradigm in which the kinematics and muscle activities during probe movement trials remained unchanged before and after the adaptation (Cluff and Scott, 2013). They demonstrated that the long-latency reflex induced by perturbation to an arm, which might reflect the gain of feedback control, was enhanced after adaptation to a novel dynamic environment and concluded that the changes in the long-latency reflex truly resulted from motor adaptation.

The present study took a similar strategy; the kinematics of the probe trials remained unchanged before and after distortion of the visuomotor map. Consistent with previous studies showing the close link between feedforward and feedback controls, my results indicated the shape of the visuomotor map for feedforward control constrained the online movement correction (feedback control gain) (Figures 2.4 and 2.5). Notably, I demonstrated that the feedback control gain could be enhanced or reduced according to the distortion of visuomotor map (Figures 2.4 and 2.5). The occurrence of both gain facilitation and reduction also indicates that changes in online movement correction were not merely due to habituation, sensitization, and/or fatigue effects caused by repetitive exposure to target jumps.

A recent prevailing optimal feedback control theory is a powerful scheme explaining many phenomena in voluntary movement control (Todorov and

Jordan, 2002; Liu and Todorov, 2007; Izawa et al., 2008; Nagengast et al., 2009). The optimal feedback control theory does not explicitly assume the separate presence of feedforward (inverse model) and feedback controllers. Rather, the controller is assumed to consist of a generic feedback controller with the help of the forward model and state estimator (Scott, 2004; Shadmehr and Krakauer, 2008). The results that the feedback and feedforward control were not completely separable are also consistent with this scheme.

Offline movement corrections were not influenced by the alteration of online movement correction in the preceding trial When I demonstrated that offline movement corrections were altered by the shape of the visuomotor map, I assumed that modifications of the offline movement correction occurred independently. However, if the online movement correction influenced the offline movement correction, as predicted by feedback-error learning (Kawato and Gomi, 1992), then alterations of the offline movement correction could be partly ascribed to the online movement correction in the preceding trial.

In order to exclude this possibility, I reduced the online feedback by setting the movement velocity in Experiment 3 to a faster speed than in Experiment 2. In addition, I instructed participants not to respond to the visual rotation of the cursor as this could suppress their response, although the earliest part of the responses remain unchanged by the instruction (Day and Lyon, 2000). In accordance with this, the online corrections were largely suppressed, as shown in the trajectories (Figure 2.8A-D). Although the force outputs for fast online corrections were still present, I did not observe alterations in the online corrections that were caused by distortion of the visuomotor map (Figure 2.9A,B). That distortion of the visuomotor map did not result in any modulations to the online corrections appear to be inconsistent with the results of Experiment 2. However, it is possible that instructing participants not to "respond," and/or differences in the characteristics of perturbation (perturbation was suddenly applied or gradually increased for target jumps or visual rotation, respectively), made the modification ambiguous and suppressed their response. Regardless, the data clearly indicated that modulation of the online movement correction did not cause the modulation of the offline movement correction in the subsequent trial.

Influence of shape of visuomotor map on motor adaptation Recently, the degree of adaptation has been shown to be modulated by a wide variety of factors including prior experiences of perturbation (Braun et al., 2009; Huang et al., 2011; Kobak and Mehring, 2012), training schedules (Orban de Xivry and Lefèvre, 2015; Takiyama et al., 2015), type of visual feedback (Kasuga et al., 2013), delay of visual feedback (Tanaka et al., 2011; Honda et al., 2012), and reward and/or punishment information (Galea et al., 2015).

Structural learning is a recent influential idea (Braun et al., 2009; Kobak and Mehring, 2012) in which the sensorimotor system comprehends a perturbation structure by experiencing a randomly changing perturbations. This knowledge increases the adaptation speed when a constant perturbation is later imposed. In other words, the sensorimotor system learns to learn through experience (Braun et al., 2010). This notion is similar to my study, because my results indicate that the visuomotor map tells the sensorimotor system how the movements should be adapted. However, their scheme cannot explain my results, because both of my participant groups experienced the same visual rotations when they reached to the central target. Furthermore, the inward adaptation group demonstrated a reduction in aftereffect, implying that the adaptation speed could not necessarily be increased, but could be decreased. My experimental results thus indicate a novel aspect of motor adaptation.

It would be also interesting to consider my results from the perspective of model free learning; Huang et al. (2011) have reported that repeated successful movements to a particular direction, even after the effect was washed out, made subsequent visuomotor adaptation in this movement direction significantly faster. Thus, the repetitive movement direction worked as an attractor for adaptation (Huang et al., 2011). In the inward adaptation group, the forward movements could become an attractor, because this movement was repeated after the intervention. Thus, the movement to the central target could hardly escape from the forward movement, which might contribute to reducing the aftereffect. However, I interpreted that the decrement of aftereffect was likely to be caused by the distortion of visuomotor map rather than by the repetition of the movements. If the repetition of the movements was a main factor, it was hard to explain the result in the outward adaptation group that the aftereffect became greater after the intervention, because the movement to the central target was not repeated in this group. I assumed that the distortion of visuomotor map contributed to make the movement to the central target more escapable. However, future studies are necessary to provide mechanistic or theoretic explanations for how the repetition of movements could influence motor adaptation by examining the relationship between my scheme, structural learning, and model free learning.

Significance of establishing visuomotor map In my scheme, the motor system cannot correct movement appropriately if a visuomotor map has not been established. Consider an example in which a player practices by swinging a baseball bat at a ball thrown in a constant place. Even if the player acquires skill, it does not directly indicate that she/he will do well in the real situation. Without establishing the appropriate map between the positions of ball and bat, the player cannot correct the trajectory of the swing when the ball unexpectedly moves to a different place (e.g., split-fingered fastball). Furthermore, after the swing is deviated, it cannot be appropriately corrected in the next trial. In order to establish the appropriate map, the player might need to practice swinging a bat to a ball thrown to various places. This idea is similar to the schema theory proposed in the field of sports psychology (Schmidt, 1975). Recently, Wu et al. (2014) demonstrated that motor variability enhances the motor learning speed. Greater variability (or greater exploratory movement) should increase the opportunity of limbs to move toward various locations (Wu et al., 2014); it could be helpful to establish the visuomotor map in the vicinity of the movement.

Taken together, my results demonstrate that both online and offline movement corrections reflect the shape of the visuomotor map and suggest a close link between feedforward control, feedback control, and motor adaptation. Motor adaptation modifies the feedforward controller (i.e., visuomotor map), but my results indicate the influence of motor adaptation on visuomotor map is not unidirectional, because the shape of the visuomotor map also influenced motor adaptation. Such bidirectional interaction between the feedforward controller and motor adaptation reveals novel dynamic aspects of motor learning.

Chapter 3

Reorganization of Motor Primitives

3.1 Introduction

The sensorimotor system is capable of adapting movements to novel environments (Wolpert et al., 2011; Wolpert and Flanagan, 2016). Previous studies investigating motor learning have relied on visuomotor transformation experiments, such as visual rotation tasks, in which cursor movement is deviated clockwise (CW) or counter-clockwise (CCW) from the direction of hand movement.

In Chapter 2, I demonstrated that the degrees of motor learning are associated with the shape of the visuomotor map, which transforms visual information of the target into the movement execution (Hayashi et al., 2016). In the previously described experiment, participants of the inward adaptation group adapted to CW and CCW visual rotation when reaching to

CW and CCW targets, respectively, which resulted in inward hand movements. In contrast, participants of the outward adaptation group adapted to the opposite directions of visual rotation, which resulted in outward hand movements. Although the experimental procedures differentially altered the visuomotor map (Figure 2.3), the reaching movement toward the central target remained unchanged. I found that, according to the shape of visuomotor map distortion, the sizes of aftereffects induced by visual rotation decreased when reaching to the central target after the characteristic shape of the visuomotor map had been acquired in the inward adaptation group, while such aftereffects increased in the outward adaptation group. These results highlighted that motor learning influences not only how we move (the shape of the visuomotor map) but also how we learn to move (i.e., meta-learning of motor learning).

The conventional neural network model suggests that motor learning is accomplished by the flexible combination of outputs from the motor primitives (Figure 3.1) (Thoroughman and Shadmehr, 2000; Takiyama et al., 2015). The model assumes that the motor command ($x_t = W_t g$) is determined by the weighted sum ($W = [w_1, w_2, w_3, ..., w_N]$) of activities of activity in the motor primitives ($g = [g_1, g_2, g_3, ..., g_N]^T$) tuned with the target direction (θ). If a movement error ($e_t = x_t + p_t$) is produced by the a perturbation (p), the weight is updated corresponding to the activity of the motor primitives trial by trial (t). Learning dynamics ($W_{t+1} = \alpha W_t - \beta^W e_t g^T$) are determined by the retention rate (α) and learning rate (β^W). From this equation, I can obtain $x_{t+1} = \alpha x_t - \beta^W e_t g^T g$, indicating that the amount of movement correction (sizes of the aftereffects ($-\beta^W e_t g^T g$)) depends on the learning rate and motor primitive activity. In other words, as long as the activities of motor primitives remains unchanged, the conventional model predicts that the amount of movement correction is always constant, even after deformation of the visuomotor map. Thus, it is unlikely that the conventional model could reproduce the results presented in Chapter 2 (Hayashi et al., 2016).

As mentioned in Chapter 1, the neural substrates of the motor primitives remain uncertain. However, considering that neuronal activity in motor-related brain areas such as the primary motor cortex (M1), premotor cortex, and supplementary motor cortex changes during motor learning, the activity of the motor primitives may reflect levels of activity in these areas. For example, levels of activity in M1 are known to be sinusoidally tuned with the direction of movement, a phenomenon referred to as “cosine tuning” (Georgopoulos et al., 1982; Scott, 2004). The tuning properties can be characterized by the preferred direction (PD) in which the level of activity is maximized. Interestingly, research has indicated that motor adaptations to force fields and visuomotor rotation alter the PD (Alexander and Crutcher, 1990; Shen and Alexander, 1997a; Shen and Alexander, 1997b; Gandolfo et al., 2000; Li et al., 2001; Crutcher et al., 2004; Eisenberg et al., 2010; Eisenberg et al., 2011; Haar et al., 2015). For example, Li et al. (2001) investigated single neural activity in the primate M1 before and after adaptation to a velocity-dependent force field. They observed that most of the PDs rotated in the direction of the perturbation. PD rotation in motor-related cortices has been broadly observed: Both kinematic (i.e., visual rotation) (Alexander and Crutcher, 1990; Shen and Alexander, 1997a; Shen and Alexander, 1997b; Crutcher et al., 2004; Eisenberg et al., 2010; Eisenberg et al., 2011;

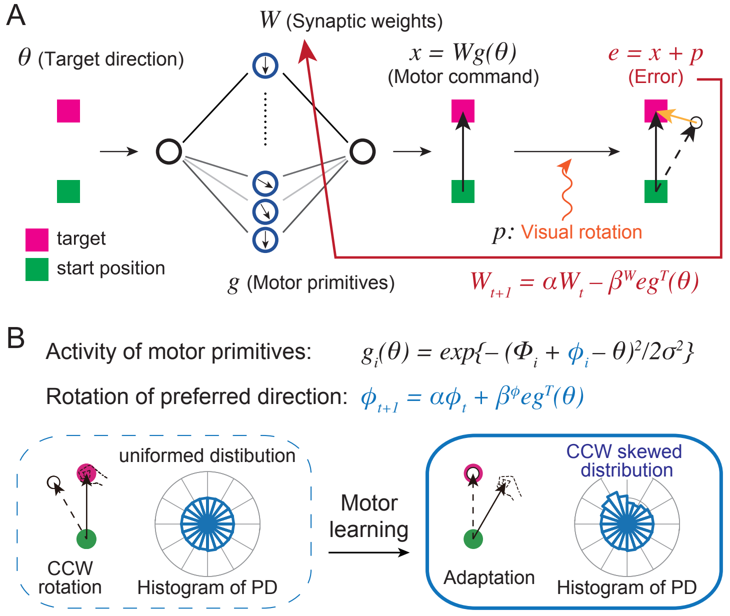

Figure 3.1: **Neural Network Model and Rotation of Preferred Direction. A.** The neural network model for motor learning. **B.** The new assumption: Rotation of preferred direction. Activity of the motor primitives was determined using a Gaussian function with differences between the preferred and target directions. The preferred direction was rotated trial by trial in the direction of perturbation based on previous neurophysiological studies (Shen and Alexander 1997a; Li et al., 2001).

Haar et al., 2015) and dynamic perturbations (i.e., force field) (Gandolfo et al., 2000; Li et al., 2001) have been reported in the brains of humans and non-human primates. However, this aspect has not been incorporated into the conventional state-space model for motor adaptation.

I speculated that the incorporating PD rotation into the model could reproduce our previous results. PD rotation due to motor adaptation indicates that the tuning functions of the motor primitives themselves also exhibit alterations. Thus, the inner product of $g^T g$ should be altered, which would then result in alteration in the amount of movement correction (i.e., aftereffect). In this chapter, I investigated whether the model including the PD rotation effect could reproduce the results discussed in Chapter 2 (Hayashi et al., 2016). In order to test this hypothesis, I formulated a computational framework of the PD rotation, which was tested using behavioral experiments and model selection.

3.2 Methods

Computational frameworks Motor learning has been described by the neural network model as follows (Figure 3.1A) (Thoroughman and Shadmehr, 2000; Takiyama et al., 2015):

$$x_t = W_t g(\theta) \tag{3.1}$$

$$e_t = x_t + p_t \tag{3.2}$$

$$W_{t+1} = \alpha W_t - \beta^W e_t g^T(\theta) \tag{3.3}$$

where the motor commands (x) in the trial t are determined by the weighted sum (W) of the activity of the motor primitives ($g(\theta)$). If the movement error (e) is induced by the exposure of the perturbation (p), the sensorimotor system updates the weight according to the movement error.

I assumed that the activity of the motor primitives is reflective of the activity of neural cells in the M1. As previously mentioned I described before (Figures 1.5 and 1.6), the PDs of the M1 neurons were exhibit dynamic rotation during motor learning (Alexander and Crutcher, 1990; Shen and Alexander, 1997b; Shen and Alexander, 1997a; Gandolfo et al., 2000; Li et al., 2001; Crutcher et al., 2004; Eisenberg et al., 2010; Eisenberg et al., 2011; Haar et al., 2015). Based on the findings of previous neurophysiological studies, I aimed to include the effect of PD rotation of the motor primitives into the conventional model (Figure 3.1B). I assumed that the activity of each motor primitive ($g_{i,t}^T$) was determined by a Gaussian function of the target direction (θ_t) around the PD ($\Phi_i + \phi_{i,t}$), as follows:

$$g_{i,t}(\theta) = \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left(-\frac{(\theta_t - \Phi_i - \phi_{i,t})^2}{2\sigma^2}\right) \tag{3.4}$$

where Φ_i and $\phi_{i,t}$ indicate fixed and rotated components of PD, respectively, and σ indicates tuning width of a Gaussian function. For simplicity, I assumed that the PDs were uniformly distributed prior to motor adaptation, and that the PD was rotated trial by trial according to the following rule:

$$\phi_{i,t+1} = \alpha\phi_{i,t} + \beta^{\phi} e g_{i,t}^T(\theta) \tag{3.5}$$

An important point of Eq. (3.5) is that PD rotation is directed in direction of error ($+\beta^{\phi} e g^T(\theta)$), according to previous neurophysiological studies. Notably this is the opposite direction of weight update ($-\beta^{W} e g^T(\theta)$). Therefore, after the participants adapt to CCW visual rotation, the PDs should rotate in the same CCW direction, which may result in make a skewed PD distribution being skewed (Figure 3.1B).

Fitting of the model to previous experimental results (Hayashi et al., 2016) I first aimed to determine model parameters by fitting the model to my previous results (Hayashi et al., 2016). In these experiments, participants of the inward adaptation group adapted to CW visual rotation for CW targets and CCW visual rotation for CCW targets, leading to more inward hand movements. In contrast, participants of the outward adaptation group adapted to the opposite direction of visual rotation, leading to more outward hand movements. The intervention distorted the shape of the visuomotor map, which became flatter and steeper around the central target, although movement to the central target remained unchanged because the adaptation effects were cancelled out at this target. I used the movement to the central target as probe trials to investigate the association between motor control (shapes of the visuomotor map) and motor learning (sizes of aftereffects). I observed that the sizes of aftereffects induced by constant visual rotation ($\pm 30^\circ$) decreased in the inward adaptation group and increased in the outward adaptation group.

By fitting both the conventional and my new models to the experimental results, I examined whether the proposed model can reproduce these results. The data of each participant were too variable to obtain reasonable parameters. Thus, averaged data was used (Smith et al., 2006; Ingram et al., 2013). Preliminary numerical simulations revealed that the learning curves and the sizes of the aftereffects before the intervention (Figures 2.2A,B and 2.7A) did not significantly depend on PD rotation. Hence, I fit the weight update parameters α and β^W to the data. Finally, I fit the model to the sizes of the aftereffects after the intervention to optimize the PD rotation parameter β^ϕ for the proposed model only. The fixed parameters were the number of the motor primitives ($N = 1000$) and tuning width ($\sigma = 0.4$ radian). I confirmed that the fixed parameters and condition did not substantially influence the results. The initial parameters of the retention rate and learning rate were arbitrarily determined at $\alpha = 0.975 \pm 0.025$, $\beta^W = 0.025 \pm 0.025$, and $\beta^\phi = 0.025 \pm 0.025$. The optimal values were searched using the MATLAB function "fminsearch".

Novel model prediction The proposed model predicted that even after participants adapted to a single visual rotation for a single target, the PD distribution should be skewed. For example, after adapting to CCW visual rotation, the density of the motor primitives increased in the CCW direction but decreased in the CW direction (Figure 3.1B). The skewness of the PD histogram may influence subsequent motor learning because the activity of motor primitives may influence the sizes of the aftereffects. To examine this possibility, I investigated whether aftereffects were differentially modulated by the CW and CCW target after participants had adapted to a visual rotation.

Participants Twenty healthy, right-handed participants were recruited to perform behavioral experiments (Ages 18-26, 14 men and 6 women). Written informed consent was obtained from all participants prior to experimental sessions. The protocol of the present study was approved by the ethics committee of the University of Tokyo.

Procedures Participants performed right-hand reaching movements while holding a KINARM robot (KINARM End-point Lab, BKIN Technologies, Kingston, ON, Canada). Participants were seated in front of a horizontal mirror that prevented the participants from directly viewing their own arm. Participants were presented with a display via the mirror and asked to manipulate a white cursor (diameter: 10 mm) representing the handle. Belts were fastened around the shoulders of each participant, and a wrist brace was used to constrain wrist movements in order to ensure that participants maintained a constant posture during the experiments, moving the handle only with the shoulder and elbow joints.

At the beginning of each trial, a green target (diameter: 14 mm) appeared 10 cm from the starting position (diameter: 14 mm). A few seconds later, the target's color changed to magenta, indicating "go." Participants were required to reach to the target as smoothly and straight as possible. A warning message about regarding movement velocity was displayed at the completion of each trial if the peak speed was below 350 mm/s ("slow") or above 450 mm/s ("fast"). In order to familiarize participants with the procedures, several practice trials for $0°, \pm 15°, \pm 30°, \pm 60°, \pm 90°$, and 180° targets were conducted prior to the main experiments.

The central target (0°) was used as an intervention target (Figure 3.2A). When reaching to the target, gradually increasing visual rotation was imposed to the cursor at a rate of 0.5° from 0° to 30° (61 trials). I used the data of 16 participants (CW visual rotation: n = 8, CCW visual rotation: n

= 8) who were not aware of the presence of the gradually increasing visual rotation. The data from the other four participants were not used for the analysis because they noticed the presence of the visual rotation, which may have resulted in the adoption of an explicit strategy for reaching the target.

The proposed model predicted that this intervention resulted in a skewed PD distribution, thereby resulting in target-dependent modulation of the sizes of the aftereffects. In order to test this prediction, the aftereffects were measured for various targets before and after the intervention. The participants iteratively performed blocks (Figure 3.2B) in which two null (before) or visual rotation (after the intervention) trials were followed by a perturbation trial (cursor clamp) and a probe trial (cursor off). In the perturbation trial, participants performed reaching movements toward a probe target with constant visual rotation (cursor clamp: Figure 3.2B) in which the cursor path was constrained at ±30° from the target direction regardless of hand movement direction. In the subsequent probe trial, participants performed reaching movements to the same target without cursor feedback (cursor off: Figure 3.2B) in order to assess the aftereffect induced by the perturbation trial. The perturbation and probe targets were located at $0^\circ, \pm 15^\circ, \pm 30^\circ, \pm 60^\circ, \pm 90^\circ$, or 180° from the intervention target. Eight blocks (four trials for +30° and −30° cursor clamping) were performed in each target direction (i.e., 320 trials in total) before and after the intervention. Participants were not to correct the hand movement direction within a trial, even when they detected movement errors, because differences in feedback movement correction may obscure motor learning (Kawato et al., 1987; Albert and Shadmehr, 2016).

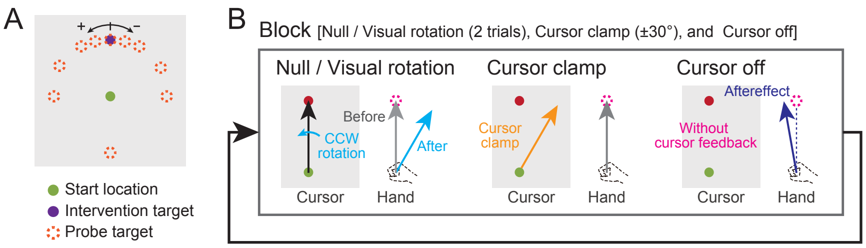

Figure 3.2: **Experimental Setup. A.** In the intervention trial, gradually increasing CW or CCW visual rotation was applied to the cursor when reaching from the start location (green) to a target located directly ahead (purple). Aftereffects were measured for targets located at various positions $(0^\circ, \pm15^\circ, \pm30^\circ, \pm60^\circ, \pm90^\circ$, or $180^\circ)$ relative to the intervention target. **B.** Before and after the intervention, participants iteratively performed blocks including four trials, which were composed of two null (before) or visual rotation (after the intervention) trials, one perturbation trial (cursor clamp), and one probe trial (cursor off). In perturbation trials, the cursor moved through predetermined paths that were ±30° from the probe target direction (cursor clamp). For the cursor clamp visual rotation, participants experienced the same visual error across all conditions. In the subsequent trial, participants again reached to the same probe target without cursor feedback.

Data Analysis The handle positions were smoothed using a 4th-ordered Butterworth filter with a cutoff frequency of 10 Hz. Hand movement directions at the peak velocities were calculated by subtracting the actual hand movements from the target direction. The latencies of the peak velocities were fast, and thus the hand movement direction at peak velocities may reflect the feedforward motor commands. In order to analyze data from the CCW and CW visual rotation intervention, data from CW visual rotation were reversed along the midline (i.e., 0°).

The aftereffect was measured by the subtracting hand movement in the perturbation trial from that in the probe trial (this value was positive when the change in the movement direction was opposite to the perturbation). In order to investigate the direction-dependent modulation of the aftereffects, a two-way repeated ANOVA (before and after the intervention, target direction) was performed. When significant interactions were identified, I tested simple main effects between aftereffects in each target direction before and after the intervention to see if the aftereffects statistically increased or decreased due to the intervention.

The conditions used to measure aftereffects before and after the intervention differed because the actual movement directions were altered due to the generalization effect of the intervention. Thus, I also examined whether the actual hand movement directions and actual target directions accounted for the sizes of the aftereffects. I pooled the complete dataset before and after the intervention and examined the angular-angular correlation with the sizes of the aftereffects (Fisher and Lee, 1983). I also examined whether the generalization, which was calculated by subtracting hand movements before the intervention from those after the intervention in perturbation trials, was correlated with the alteration of the aftereffects.

3.3 Results

In the present study, I investigated whether PD rotation of the motor primitives is involved in human motor learning. I proposed a neural network model in which the PD of each motor primitive is rotated during the visuomotor adaptation. First, I examined if the new model could reproduce my previous experimental results (Hayashi et al., 2016). Second, I investigated if the model's new prediction was consistent with the experimental results.

Fitting of the model to experimental results I previously illustrated that the shape of the visuomotor map is associated with the sizes of the aftereffects. Participants were divided into two groups. The groups adapted to different visual rotations, resulting in differential deformation of the visuomotor map. I further demonstrated that the sizes of the aftereffects increased or decreased according to the shape of the visuomotor map. First, I examined whether the proposed model can successfully reproduce these previous experimental results. Figure 3.3 depicts the results of model fitting with the optimal parameters. The deformation of the visuomotor map can be reproduced by both the conventional ($R^2 = 0.9929$, Figure 3.3A) and proposed models ($R^2 = 0.9942$, Figure 3.3C). However, the conventional model could not reproduce alterations in aftereffects (Figure 3.3B). In contrast, the proposed model could successfully reproduce the experimental results ($R^2 = 0.9426$, Figure 3.3D). In the proposed model, the PD distribution around the central target direction became less dense for the inward adaptation group, while such distribution became more dense for the outward adaptation group, because the PD was rotated in the direction of the visual rotation. Under this PD distribution, the total sizes of the motor primitive activities in the inward adaptation group decreased, contributing to decreases in aftereffect size, while those in the outward adaptation group increased, contributing to increases in aftereffect size. The parameters with the best fit were $\beta^W = 0.0017$ for the weight update, $\beta^\phi = 0.0345$ for the PD rotation, and $\alpha = 0.9832$, suggesting that PD rotation is relatively faster than weight update. I used these parameters to validate the proposed model by fitting to the additional behavioral tasks.

Novel model prediction The proposed model predicted that adaptation to a visual rotation rotates the PDs of motor primitives in the direction of visual rotation, resulting in higher PD density in the direction of visual rotation and lower PD density in the opposite direction. It should be noted that the number of recruited primitives determines the degree of movement correction in response to a visual error (i.e., aftereffect). Thus, with this skewed PD distribution, the aftereffect should become greater in one direction and smaller in another direction.

Figure 3.4 shows the sizes of the aftereffects induced by constant visual rotation (A-C: before the intervention, D-F: after the intervention). I found that, even before the intervention, the sizes of the aftereffects imposed by CW (A) and CCW (B) cursor clamps were dependent on the target direction. More specifically, the aftereffects were larger when reaching to the right and

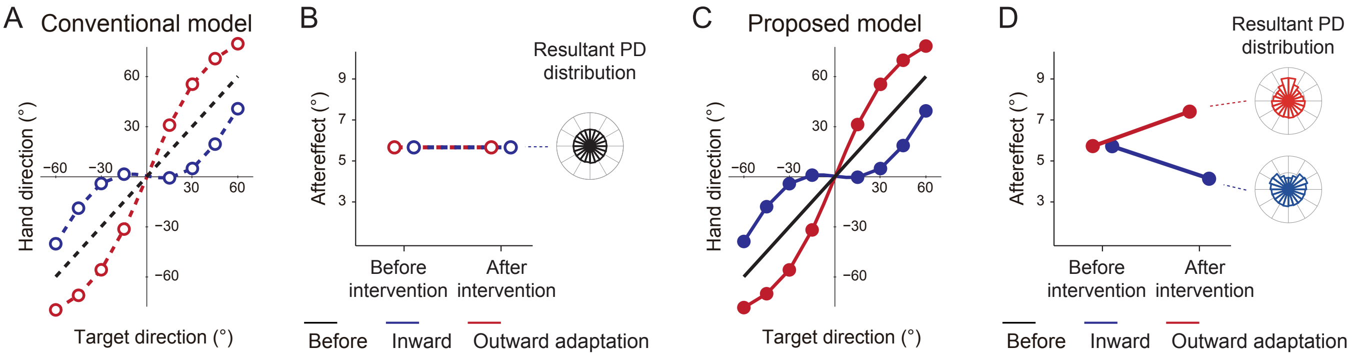

Figure 3.3: **Model Fitting to the Previous Results. A,C.** The deformation of the visuomotor map can be reproduced by both the conventional and proposed models. The conventional model could not reproduce the changes in the sizes of aftereffects (**B**), while the proposed model successfully reproduce the experimental results (**D**). In the proposed model, the PD distribution became less (more) dense for the inward (outward) adaptation group, because the PD was rotated in the direction of the visual rotation. Under this PD distribution, total sizes of the motor primitive activities decreased (increased), which contributed to decreases (increases) in aftereffect size.

left targets than reaching to the forward and backward targets (Fig.3.4C includes averaged data).

The conventional and proposed models provided different predictions regarding alterations in aftereffects following the intervention: The conventional model predicted no changes, while the proposed model predicted that changes in aftereffects are dependent on target direction (Fig. 3.5A). I observed that the experimental data were consistent with the prediction of the proposed model. The sizes of the aftereffects increased for the CCW target but decreased for the CW target (Figure 3.4), irrespective of CW and CCW cursor clamps. Two-way repeated ANOVA indicated that there is significant interaction between the aftereffects before and after the intervention and target directions ($F(1, 9) = 3.153, p = 0.0017$) (Figure 3.5B). Furthermore, statistically-significant simple main effects between the aftereffects before and after the intervention were obtained for the $-30°$ target ($F(1, 1) = 5.869, p = 0.0167$), for the $-15°$ target ($F(1, 9) = 14.57, p = 2.049 \times 10^{-4}$), and for the $15°$ target ($F(1, 9) = 5.143, p = 0.0249$). Alterations in aftereffect size predicted by the proposed model (Fig. 3.5A) was smaller than the actual values (Fig. 3.5B) maybe because the perturbation (cursor clamp) and probe trials (cursor off) were different from those in the pervious experiment in Chapter 2 (Hayashi et al., 2016).

I also observed that the modulation of the aftereffects could not be explained by the actual hand movement direction or the actual target direction. I sorted the sizes of the aftereffects with these directions (Figure 3.6A,B). Although there were significant correlations between them (hand movement direction: $r = 0.2009, p = 0.0016$, target direction: $r = 0.1689, p = 0.0104$), the

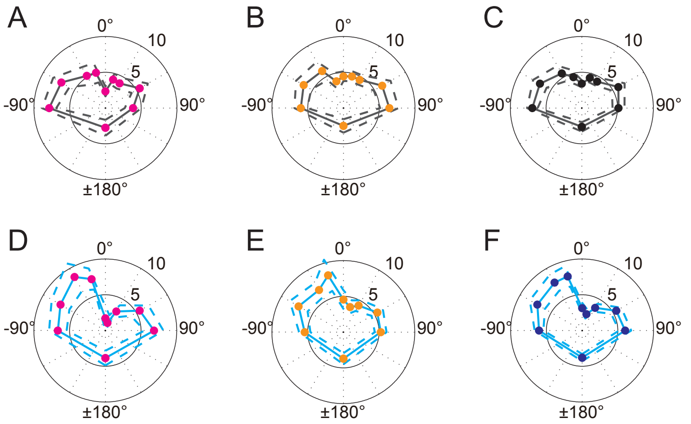

Figure 3.4: **Direction-Dependent Modulation of Motor-Learning Rates.** Aftereffects to the CW (left panels **A,D**) and CCW (middle panels **B,E**) cursor clamps and averaged aftereffect sizes (right panels **C,F**) before (top panels) and after intervention (bottom panels). The aftereffects increased for the CCW target but decreased for the CW target.

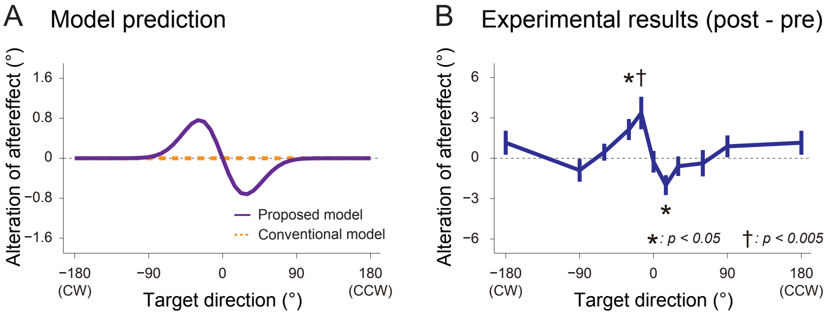

Figure 3.5: **Model Prediction and Modulation of Aftereffects. A.** With the numerical simulation, the conventional model suggested that the aftereffects remained constant, while the proposed model suggested that the aftereffects were directionally-tuned. **B.** Alterations in aftereffect sizes were reproduced by the proposed model only.

correlation coefficients were very small, suggesting that neither represented the main cause of alterations in aftereffect size. I also examined whether the sizes of the generalization were associated with the alterations in the sizes of aftereffects (Figure 3.6C). However, no significant correlations were observed ($r = 0.0703, p = 0.3890$), suggesting that the other possible factors cannot fully explain alterations in aftereffect size.

3.4 Discussion

The findings of the previous studies discussed in Chapter 2 suggested the possibility that the sensorimotor system rebuilds the knowledge of how to adjust motor commands in a novel environment during motor learning (Hayashi et al., 2016). However, current computational frameworks based on motor primitives are unable to reproduce these results (Thoroughman and Shadmehr, 2000). Our novel computational principle assumed that, when movement error occurs, the preferred directions (PD) of the motor primitives are rotated in the direction of error, based on previous neurophysiological findings (Shen and Alexander, 1997b; Li et al., 2001). This mechanism results in novel re-organization of motor primitives, which influences subsequent motor-learning rates. I observed that the proposed model can successfully reproduce the results discussed in Chapter 2 (Hayashi et al., 2016). Furthermore, the results of the present experiments support the model's prediction that rates of motor-learning change in a target-direction-specific manner. Taken together, these data suggest that our new scheme may represent fundamental mechanisms underlying human motor learning.

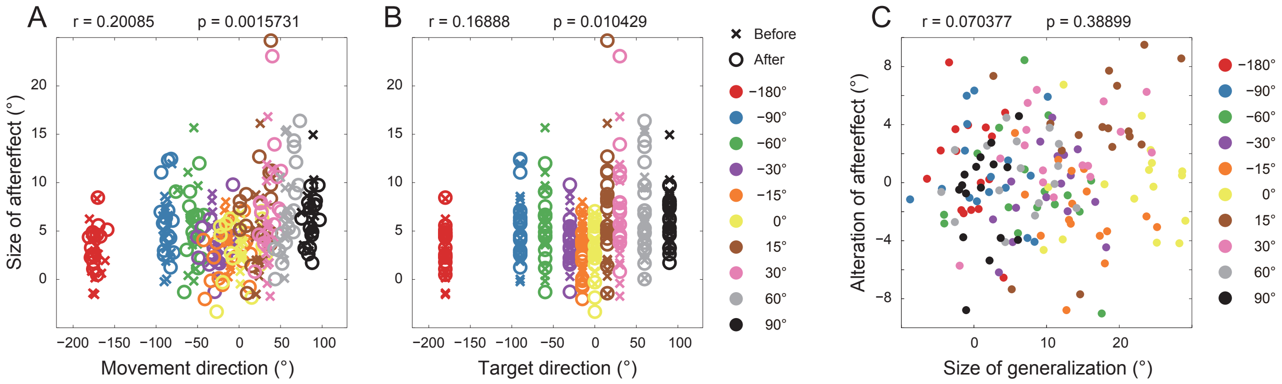

Figure 3.6: **Relationship of Movement Direction, Target Direction, and Generalization with Aftereffects.** The sizes of the aftereffects were significantly correlated with (**A**) movement direction or (**B**) target direction. However the correlation coefficients were very small. **C.** The alteration of the aftereffects was not significantly correlated with the sizes of generalization. Visual/mechanical information and adaptation index were unable to fully explain the results. Each color indicates a different target direction. Cross and circle markers indicate before and after the intervention, respectively.

Factors influencing the motor-learning rates Figure 3.4 shows that motor-learning rates differed among the target directions even before the intervention. The aftereffects were larger for reaching movements to leftward and rightward than to forward and backward targets (Figure 3.4). Such directional-dependent modulation of aftereffects may be due to both neural (e.g., nonuniformity of PD distribution) and biomechanical factors (e.g., movement kinematics, physical property of the arm, and manipulandum). Further studies are required in order to dissociate the contribution of each factor.

I also demonstrated that the intervention altered the sizes of the aftereffects depending on the target direction (Figure 3.5). More specifically, after the adaptation to CW (or CCW) visual rotation, the aftereffect was increased for the CW (CCW) target direction. Further analysis revealed that the movement and target directions did not account for the sizes of the aftereffects (Figure 3.6), suggesting that kinematics and dynamics of the limb and manipulandum are not main factors inducing the changes.

Previous studies have illustrated that rates of motor learning are determined by a wide variety of factors, including prior experience of the perturbation (Braun et al., 2009; Kobak and Mehring, 2012), history of movement errors (Herzfeld et al., 2014; Takiyama et al., 2015), repetition of successful movement (Huang et al., 2011; Orban de Xivry and Lefèvre, 2015), combination of visual feedback (Kasuga et al., 2013), delay of visual feedback (Tanaka et al., 2011; Honda et al., 2012), a balance of exploratory and exploited actions (Wu et al., 2014), and reward and/or punishment information (Galea et al., 2015). The reorganization of motor primitives via the rotation of PDs is a novel factor influencing motor-learning rates.

Comparison to the other computational principles Previous theoretical studies have assumed that other factors are involved in reproducing the results of previous behavioral experiments. For example, it has been suggested that repetition of a successful action makes the movement an attractor of subsequent motor tasks (model-free learning (Huang et al., 2011; Orban de Xivry and Lefèvre, 2015)). From the perspective of model-free learning, after adaptation to CW visual rotation, since the movement in CCW direction was repeated, it should become the new attractor for subsequent motor learning. Model-free learning therefore predicts that the sizes of the aftereffects will increase if movements are corrected toward the CCW direction. However, such modulation was not observed in our experiments, suggesting that model-free learning cannot account for the experimental results.

Other theoretical studies have suggested that the history of movement errors may modulate the rate of motor learning (Herzfeld et al., 2014; Takiyama et al., 2015). Computational models have suggested that motor-learning rates decrease when different perturbations are applied in alteration. From the model prediction, in our previous studies (Hayashi et al., 2016), participants in both the inward and outward adaptation groups had experienced the same degrees of visual rotation, meaning that the motor-learning rates should have decreased in both groups. However, the results were not consistent with this prediction, as the sizes of the aftereffects decreased in the inward adaptation group but increased in the outward adaptation group. Furthermore, the model tacitly assumes that the effects of the history of movement errors occur in the single target only. Thus, the model cannot reproduce that the sizes of the aftereffects for the central targets were changed by the intervention for the CW and CCW targets.

Neural substrate for PD rotation In this chapter, I have presented evidence that PD rotation is likely to be involved in human motor learning. Neurophysiological findings have further suggested that motor-related areas such as the primary motor cortex, premotor cortex, and supplemental motor cortex have a preferred reaching direction in which each neural cell is highly activated. Notably, the preferred direction remains constant but becomes rotated during motor learning. Previous neurophysiological studies assumed that PD rotation is reflective of motor output only. However, the present computational model illustrates that PD rotation influences subsequent motor learning, suggesting that PD rotation is also reflective of dynamic reorganization of the sensorimotor system during motor learning. In other words, meta-learning occurs along with PD rotation. Model fitting illustrated that PD rotation is faster than weight update processes. Since PD rotation can be regarded as meta-learning of subsequent motor learning, these data suggest that the sensorimotor system organizes the learning field for the environment in preparation for motor learning.

What causes PD rotation? Recent magnetic resonance imaging (MRI) studies may provide insight into this issue. Haar et al. (2015) investigated which cortical areas engaging in the motor task show movement and/or visually dependent activation patterns (Haar et al., 2015). Participants adapted to visual rotation in an MRI scanner, and the neural patterns were compared before and after adaptation using multivariate pattern analysis. The results of this study suggested that the visual cortex and superior parieto-occipital cortex encode visual information, while the primary motor cortex, premotor cortex, and supplementary motor cortex encode movement information. Notably, the medial intraparietal sulcus (parts of posterior parietal cortex: PPC) shows activities reflecting both movement and visual information. These results suggest that the PPC may engage in visuomotor transformation. Furthermore, inhibition to the PPC is associated with maladaptation to a novel environment (Della-Maggiore et al., 2004; Mutha et al., 2011). Given such findings, I speculate that the PPC plays a significant role in PD rotation in downstream areas such as the primary motor cortex, premotor cortex, and supplementary motor cortex.

I also observed that aftereffects in the CW direction increased, while those in the CCW direction decreased, after the intervention. Interestingly, increases in rates of motor learning in some contexts were always accompanied by decreases in such rates in different contexts, resulting in preservation of total motor-learning rate values. The feature resembles homeostatic stability (homeostatic plasticity) in the brain, indicating that total plasticity/activity is preserved in general (Turrigiano, 1999). The preservation of the total sizes of the motor-learning rates may seem to reflect the homeostatic stability of the brain.

Significance of reorganization of motor primitives Perfect adaptation is not always the best strategy for the brain. Consider the following scenario: You want to hit the golf ball into a certain position. The final position of the ball is the result obtained due to the combination of movement (club swing) and environmental conditions (wind). Thus, if you obtain the resultant error from the actual and desired ball positions, the movement might ought not to be corrected because the movement may contribute less to the resultant error. Previous studies have indicated that movement errors are only corrected by approximately 20% (Wei and Körding, 2009; Kasuga et al., 2013; Hayashi et al., 2016).

In my previous experiment, participants in the inward adaptation group adapted to CW visual rotation for CW targets and CCW visual rotation for CCW targets, resulted in more inward hand movement. I observed that the sizes of the aftereffects for the central target decreased after the intervention. However, if the the sizes of the aftereffects become too large, alterations in hand movement towards the central target would diminish adaptation effects for the CW and CCW targets. In other words, in order not to diminish the adaptation effects for CW and CCW targets, the brain actively decreases the motor-learning rates. In contrast, if the sizes of the aftereffects become too small in the outward adaptation group, adaptation effects for the CW and CCW targets diminished with natural decay, as in forgetting. My computational framework regarded PD rotation is the basis for precise modulation of motor learning, suggesting that the brain modulates the motor-learning rate to optimize motor learning abilities in individual environments. Gonzalez Castro et al. (2014) also suggested that the brain memorizes environmental consistency and modifies the motor-learning rate accordingly (Gonzalez Castro et al., 2014). This is similar to the notion presented here: The brain learns the features of the novel environment via reorganization of neural properties (i.e., PD histogram of the motor primitives) and utilizes this information to enhance subsequent motor learning in each environment.

In summary, my results indicate that a novel computational principle, PD rotation, is involved in human motor learning, further highlighting the dynamic aspect of this process: The PD of each motor primitive is rotated in the direction of movement error, following which alterations in the number of motor primitives recruited determine the motor-learning rates. Thus, PD reorganization allows the brain to learn and express the states of the environment, which may maximize learning ability in novel environments. In other words, the initial histogram of PD distribution indicates the optimal sets of neural substrate (or motor primitives) for the natural scene.

Chapter 4

General Discussion

Several studies have investigated the mechanisms of motor control and learning from psychophysical, neurophysiological, and theoretical perspectives. In particular, the computational explanation of motor control and learning has provided important insights for understanding brain function (Marr and Poggio, 1976; Marr, 1982). The computational framework for motor control suggests that the mechanism of movement control involves an internal model with feedforward and feedback controllers (Kawato et al., 1987). The computational framework for motor learning suggests that the learning is accomplished by the modification of weighting parameters of motor primitives according the movement errors (Thoroughman and Shadmehr, 2000; Smith et al., 2006; Takiyama et al., 2015).

The computational models of motor control and learning can reproduce a variety of movement features (see Chapter 1). However, previous studies have independently investigated motor control and learning, and thus it remains unclear how motor control and learning is interrelated. In a series of studies, I investigated the tripartite relationship of feedforward control, feedback control, and motor learning. In the current chapter, I summarize my findings and present my perspective. Finally, I discuss the practical implications of my findings for areas such as sports, rehabilitation, and education.

4.1 Summary of Findings

Visuomotor Map for Motor Control and Motor Learning

In Chapter 2, I tested the hypothesis that the visuomotor map is a common basis for feedforward and feedback control. I found that the inward adaptation group adapted to clockwise (CW) visual rotation for a CW target and to counter-clockwise (CCW) visual rotation for a CCW target, leading to inward hand movements (Figure 2.3A). In contrast, the outward adaptation group simultaneously adapted to CCW visual rotation for a CW target and to CW visual rotation for a CCW target, leading to an outward hand movements (Figure 2.3B). Consequently, the visuomotor map was flatter in the inward adaptation group and steeper in the outward adaptation group, indicating that feedforward motor commands for the actual hand movement direction became more insensitive and sensitive, respectively, to changes of the target direction (Figure 2.3C). I also found that feedback motor commands to the target jump became more insensitive and sensitive respectively in the inward and outward adaptation groups after distorting the visuomotor map (Figure 2.4AB).

I also tested whether the shape of the visuomotor map influences the subsequent motor-learning rates. I found that the sizes of the aftereffects induced by a ±30° visual rotation for 0° target decreased and increased, respectively, in the inward and outward adaptation groups (Figure 2.7). Thus, these results suggested that the visuomotor map can be regarded as the a common foundation for motor control and learning. Importantly, these results suggested that motor learning is more dynamic than ever envisaged; Motor learning changes the shape of the visuomotor map, which recursively influences the motor learning.

Reorganization of Preferred Direction of Motor Primitives

In Chapter 2, I found that the shape of the visuomotor map is associated with motor-learning rates. Previous theoretical studies suggested that motor primitive activities, which are related to the visuomotor map, influence motor-learning rates (Figure 3.1A). However, according to this conventional model, motor primitive activities should remain unchanged after deformation of the visuomotor map (Thoroughman and Shadmehr, 2000). Inspired by neurophysiological studies (Alexander and Crutcher, 1990; Shen and Alexander, 1997b; Shen and Alexander, 1997a; Gandolfo et al., 2000; Li et al., 2001; Paz et al., 2003; Paz and Vaadia, 2004; Crutcher et al., 2004; Arce et al., 2010a; Arce et al., 2010b; Eisenberg et al., 2011; Haar et al., 2015), I proposed a novel model that the preferred directions (PD) of the motor primitives rotated trial by trial (Figure 3.1B). This new model could successfully reproduce experimental results (Figure 3.3C,D).

According to this new model, the motor adaptation to visual rotation while reaching towards a target skews the distribution of the PD histogram (Figure 3.1B). For example, when CW visual rotation is imposed while reaching toward the front target, the PD distribution should be more dense and sparse for CW and CCW direction, respectively. Thus, when the reaching movement to CW (or CCW) targets is performed, more (or less) motor primitives should be recruited, causing an increase (or decrease) in the aftereffects. I tested this prediction with a behavioral experiment where I measured the sizes of the aftereffects for the various target directions before and after an intervention (Figures 3.4 and 3.5). The CCW visual rotation created skewed the CCW shape of the PD histogram. As the proposed model predicted, I found that the sizes of the aftereffects increased for the CCW targets and decreased for the CW targets, suggesting that the motor primitives (i.e., PD) are reorganized in the progress of motor learning and that this reorganization influences the subsequent motor-learning rates.

4.2 Perspective

4.2.1 Possible Neural Substrate

I demonstrated that a newly acquired visuomotor map not only influences feedforward control but also feedback control. Thus, the visuomotor map should be stored as a common process of feedforward and feedback control.

Previous neurophysiological studies have investigated the neural responses in several brain areas during feedforward control (Georgopoulos et al., 1982; Georgopoulos et al., 1986; Georgopoulos et al., 1989; Caminiti et al., 1991; Fu et al., 1995; Scott et al., 2001; Rizzolatti et al., 2001a; Rizzolatti et al., 2001b; Kakei et al., 1999; Kakei et al., 2001; Cisek and Kalaska, 2005) and feedback control (Desmurget et al., 2001; Seidler et al., 2004; Pruszynski and

Johansson, 2014; Omrani et al., 2016). Using positron emission tomography (PET), Desmurget et al. (2001) examined the brain activity associated with reaching movement correction toward a suddenly moved target (Desmurget et al., 2001). In their investigation, movements both with (i.e., feedback control) and without correction (i.e., feedforward control) were accompanied by activity within several brain areas, including the primary motor cortex, the dorsal premotor area, the primary somatosensory area, the parietal cortex, and the cerebellum. Thus, the neural architectures in these areas are engaged in common tasks for feedforward and feedback controls.

Motor learning largely reorganizes the neural processing in motor-related areas. For example, PD of the primary motor cortex (M1) is rotated during adaption to visual rotation and force field perturbation. Li et al. (2001) performed a neurophysiological experiment in which they recorded single neuron activities in M1 of macaque monkeys who adapted to a force field perturbation when reaching toward targets located at various directions (Li et al., 2001). Their investigation found that the PDs of most of the neural cells in M1 were systematically rotated in the direction of the force field (See Chapter 1, Figure 1.6). In both macaques (Shen and Alexander, 1997b; Shen and Alexander, 1997a; Crutcher et al., 2004) and humans (Eisenberg et al., 2010; Eisenberg et al., 2011; Haar et al., 2015), a rotation in the PD was observed when adapting to visual rotation. The PD of motor-related cortices is thought to be similar to that of the motor primitives of the neural network model. Thus, I speculated that preprocessing of the PD rotation should occur before neural processing in the motor-related cortices.

Previous magnetic resonance imaging (MRI) studies have examined whether each cortical area candidate shows visual-directional coding or movement-directional coding after motor learning (Eisenberg et al., 2010; Eisenberg et al., 2011; Haar et al., 2015). Participants in the Haar et al. (2015) study adapted to visual rotation in the MRI gantry. Haar et al. (2015) created a classifier using brain activities patterns before the visual rotation and decoded the patterns with the classifier after the visual rotation. The results showed that the movement direction could be decoded using the activity patterns of motor-related areas such as the primary motor cortex and the premotor cortex, while the cursor/target direction could be decoded using the activity patterns of visual-related areas such as the visual cortex and the superior parieto-occipital cortex. Most importantly, only the activity pattern of the medial intraparietal sulcus within the posterior parietal cortex (PPC) could be used to decode both movement and target/cursor directions. These results suggested that the PPC is involved in transforming visual information into motor commands. That is, the acquired visuomotor map is likely stored in the PPC. Previous studies also suggested that the inhibition of the PPC deteriorated both motor control (Desmurget et al., 1999) and learning (Della-Maggiore et al., 2004; Mutha et al., 2011), indicating that the PPC may have a fundamental role in visuomotor transformation.

Nonetheless, I have not directly identified the cortical areas that are associated with common functions of motor control and learning. Additional studies are necessary to investigate whether each neuron and/or neural unit show general processes related to visuomotor map transformation for feed-forward control, feedback control, and motor learning.

4.2.2 Modality of Perturbations and Behavioral Contexts

In the study described in Chapter 2, I used visuomotor adaptation in reaching movement (visual rotation) to modify the internal model (visuomotor map), and demonstrated that the internal model is utilized for feedforward control, feedback control, and motor learning. In order to expand my idea further, the most promising direction is the investigation of whether there is a "more general" internal model for motor control and learning with regard to "perturbations" and "contexts."

Modality of Perturbations

One of the most important and interesting future directions of my idea is whether the acquired internal model is utilized for different modalities of perturbations. Particularly, a comparison of the mechanical and visual perturbations may provide important insight into this issue.

A reaching movement is a single limb movement that is performed by coordinating the shoulder and elbow joints. For this movement, the sensorimotor system must coordinate the strength and timing of the contraction of each muscle. Recent studies on mechanical perturbations suggested that not only feedforward control but also feedback control shows very sophisticated coordination (Kurtzer et al., 2008; Pruszynski et al., 2011; Pruszynski and Scott, 2012). Kurtzer et al. (2008) performed elegant experiments on producing sudden flexion or extension of the elbow joint while the shoulder joint remained stationary by separately applying mechanical perturbations to the shoulder and elbow joints (Kurtzer et al., 2008). This investigation found that the fast feedback response of the shoulder joint approximately 70 ms after perturbation (called the “long latency reflex”) compensated for the perturbed elbow torques, suggesting that not only the feedforward controller but also the feedback controller uses an internal model of coordination for each joint. Indeed, a previous study by Cluff and Scott (2013) demonstrated that the long latency reflex induced by mechanical perturbation increased after the participants adapted to a dynamic environment (i.e., force field) (Cluff and Scott, 2013).

The study in Chapter 2 used only the kinematic intervention (i.e., visual rotation) and visual perturbation (i.e., target jumps). Thus, investigation of whether the internal model acquired by the kinematic (or dynamic) adaptation is utilized for the movement correction of mechanical (or visual) perturbation may answer the question on whether the acquired internal model can be utilized irrespective of perturbation type. Additionally, previous studies suggested that the mechanical and visual perturbations result in different neural processes and responses (Scott, 2012; Scott, 2016). Thus, this approach may also elucidate the general architecture of the internal model regarding how the model uses and integrates different modalities of neural information (i.e., visual and proprioceptive information).

Behavioral contexts

It has been shown that the internal models can be switched depending on the contexts (Nozaki et al., 2006; Nozaki and Scott, 2009; Howard et al., 2010; Yokoi et al., 2011; Yokoi et al., 2014). For example, different internal models are learned for identical reaching movements according to whether the opposite arm is stationary (i.e., unimanual movement) or moving (i.e., bimanual movement) (Nozaki et al., 2006; Yokoi et al., 2011). Future research should be directed at investigating how our new idea based on a visuomotor map as a common foundation is influenced by different contexts.

Previous studies demonstrated that the internal model for feedforward control is partially segregated between unimanual and bimanual movements (Nozaki et al., 2006; Nozaki and Scott, 2009), suggesting that the different shapes of the visuomotor maps for feedforward control (e.g., inward and outward visuomotor maps) can be learned between unimanual and bimanual movement simultaneously. If context changes influenced both feedback control and motor learning, the online and offline movement correction would increase and decrease depending on the shapes of the visuomotor map associated with the behavioral contexts of unimanual and bimanual movements, as seen in Figures 2.4 and 2.7.

Previous studies also suggested that bimanual coordination involves an asymmetric engagement of both arms' controllers and a task-dependent control policy (Johansson et al., 2006; Diedrichsen, 2007; Omrani et al., 2013). Diedrichsen (2007) demonstrated that the feedback responses of the right hand were not induced by left hand perturbation while the participant separately controlled two cursors with each hand (Figure 4.1A,B, left panels); however, they were induced when controlling a single cursor with both hands (Figure 4.1A,B, right panels). That is, the different contexts can be elicited according to the different task conditions (i.e., the single and double cursors conditions) in the same bimanual movements (Figure 4.1A). Bimanual responses specific to manipulating only one cursor with both arms were also observed for offline movement corrections. For example, Kasuga and Nozaki (2011) reported that when a cursor's movement is associated with one of the arms while performing bimanual reaching movement, visual perturbation to the cursor can also elicit offline movement correction for another arm that is not related to the cursor's movement (Kasuga and Nozaki, 2011). Thus, using similar methods as shown above, the utilization of an internal model according to different task conditions in the same behavioral contexts is testable.

These investigations will provide an important insight into understanding how a common internal model for feedforward control, feedback control, and motor learning is constructed according to different behavioral contexts (i.e., unimanual and bimanual conditions) and/or different task contexts (i.e., the single and double cursor conditions).

4.2.3 Skill Acquisition and Motor Adaptation

Regarding the study described in Chapter 3, I incorporated the rotation of the preferred direction of the motor primitives into the neural network model. An important issue in the motor primitive framework is whether the motor primitives are innate or acquired. I speculated that different motor learning mechanisms (skill acquisition and motor adaptation) correspond to different mechanisms between construction and reorganization of the motor primitives.

Motor learning is divided into two processes: skill acquisition and motor adaptation. Skill acquisition is the process of acquiring novel skills, such as

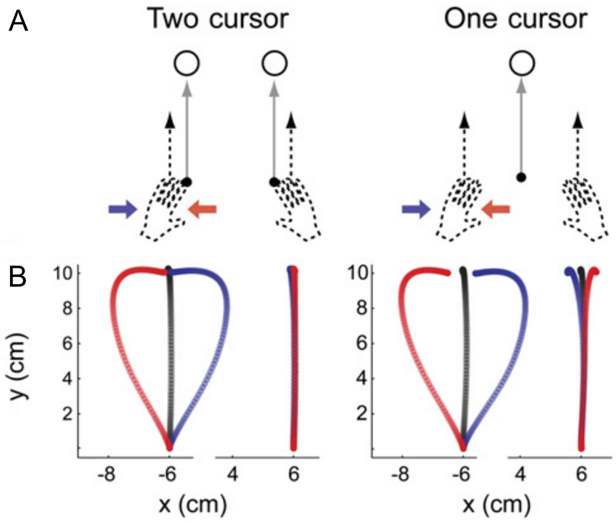

Figure 4.1: **Single and Double Cursors Manipulated by the Same Bimanual Movements A.** Participants performed bimanual reaching tasks while controlling double cursors representing the positions of each arm (left) or a single cursor located at an averaged position between them (right). They were required to perform the same bimanual movements between the tasks. **B.** During the movements, velocity-dependent force fields are suddenly applied to their left hand only, which induced right hand movement correction in the double cursor condition only. Adapted from Diedrichsen, 2007.

juggling and playing the piano. Once the motor skills are acquired, the motor memories do not conflict each other; the motor memories used for juggling do not deteriorate those for playing the piano. The sensorimotor system might separately stores the motor memories for different skills. In contrast, motor adaptation is the process of modifying existing motor memories to adapt to environmental changes. Shadmehr and Wise (2005) examined whether participants could adapt to two conflicting environments during one reaching movement (Hwang et al., 2003; Osu et al., 2004; Shadmehr and Wise, 2005; Hirashima and Nozaki, 2012). In their experiment, the participants reached towards the target with a CW and CCW force field in an alternating fashion. Although the participants understood which perturbation was applied in each trial, they showed no adaptation, suggesting that the sensorimotor system does not contain different motor memories for one motor skill regardless of whether a person has explicit knowledge of the perturbation.

Shadmehr and Wise (2005) proposed that skill acquisition be defined as the "formation of new attractors in the neural networks to enhance sensorimotor system capability," and that motor adaptation be defined as an "alteration of existing attractors in the neural circuits" (Shadmehr and Wise, 2005). Moreover, they supposed that the attractors align, map, or control action, which is consistent with the concepts of the visuomotor map and the motor primitives.

Additional research is needed to test the hypothesis that skill acquisition is involved in the process of creating the motor primitives. In this case, investigating a reaching movement is not suitable because we can easily perform reaching movements; that is, the sensorimotor system already acquires the motor primitives for reaching movements. Rather, the study should involve more complex skills, such as sport movements and tool use, and investigate how acquired motor skills are organized in motor primitive framework and reorganized for the subsequent motor adaptation.

4.3 Implication

Motor control and learning are important human abilities. In particular, the accuracy and efficiency at which we can learn to move is important for athletes, musicians, and patients with motor disorders. My findings suggest that the construction of a visuomotor map through reorganizing motor primitives is significant for feedforward control, feedback control, and motor learning.

4.3.1 Implication for Sport Training

In the case of baseball hits, the player must practice swinging a bat at a ball coming from various angles. In other words, the player has to construct an accurate visuomotor map that transforms ball positions into bat swings. My findings suggest that the accurate visuomotor map is constructed and utilized for the feedback control (e.g., movement correction for a split-fingered fast ball) as well as the motor learning (e.g., movement correction at the next bat). In order to construct an accurate visuomotor map, the batter needs to learn the batting movement for a ball pitched to different locations and at different speeds. This type of skill training, called “variable practice,” is shown to be helpful to efficiently learn the motor skill (Schmidt and Lee, 2011). The conventional interpretation of this skill training is that the player learns the schema of the motor task (Schema theory) (Schmidt, 1975). Our idea based on the visuomotor map provide a more mechanistic view to this classical psychological concept: constructing the visuomotor map by performing variety of movements is significant for online and offline movement correction. Thus, constructing an accurate visuomotor map is necessary for any athlete.

As discussed in the previous section, the internal model can be influenced by behavioral contexts (e.g., unimanual vs bimanual movement) in which the motor task is performed. A psychological study by Smith and Glenberg (1978) demonstrated that the performance for memorizing a list of words improved when the memorizing task was performed in different environmental contexts (Smith et al., 1978). From this point of view, if the internal model is trained in different behavioral contexts, the motor performance can improve more. Indeed, I examined a study supporting this idea (Hayashi and Nozaki, 2016). I demonstrated that, even after unimanual motor skills are sufficiently learned, bimanual training in a new context can further improve unimanual motor skills. The participants adapted to velocity-dependent force fields only on the left arm without a reaching movement by the right arm (Figure 4.2A), in which unimanual performances reached a plateau at approximately 60% of the ideal levels (Figure 4.2B). Subsequently, the participants were divided into two groups: one group that adapted without the right arm reaching movement (i.e., same context, UT group), and the other group that adapted with the right arm reaching movement (i.e., different context, BT group) (Figure 4.2A). I found that although the UT group did not improve in the unimanual performance, the BT group, who did not unimanually train there-after, significantly improved in unimanual performance (Figure 4.1B). This investigation provides significant insight and shows that distributed movement contexts are important for the acquisition of an accurate internal model (i.e., visuomotor map) (Hayashi and Nozaki, 2016).

4.3.2 Implication for Functional Rehabilitation

One of the important challenges in the clinic is the creation of efficient methods for relearning motor skills (i.e., functional rehabilitation). Due to an increasing elderly population, the number of individuals affected with neural disorders such as stroke is increasing. Stroke typically impairs movement abilities, and the methods of functional rehabilitation involve the performance of organized and stereotyped behaviors, such as the training of gait, fingers dexterity, and limb movement. However, motor function does not fully recover for approximately 65% of all stroke patients (Dobkin, 2004; Han et al., 2008; Takiyama and Okada, 2012).

My results suggest that a well-organized visuomotor map (i.e., the motor primitives) increases efficacy not only for motor control but also for motor learning, which could be useful for functional rehabilitation. Thus, if a patient relearns a wide variety of motor skills despite the stereotyped method of functional rehabilitation, the patient can create an input-output mapping of almost all motor skills, which would improve future motor control and learning.

Many studies have shown that different types of neural disorders are associated with different types of motor control and learning malfunctions. For example, patients with cerebellar disorders show impaired motor adaptation

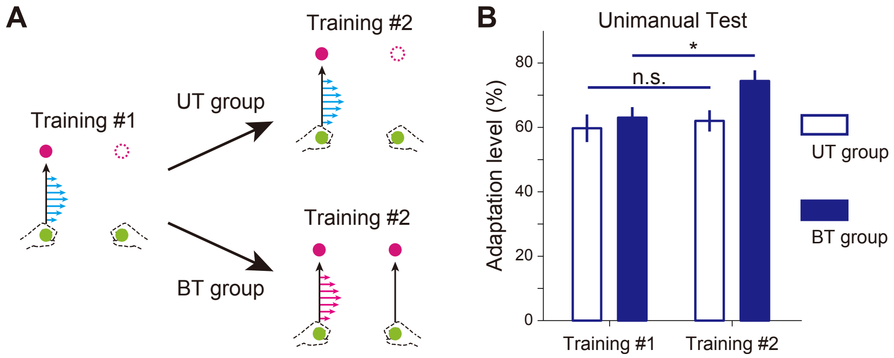

Figure 4.2: **Contexts of Unimanual and Bimanual Movements. A.** Participants sufficiently adapted to force fields on the left arm (left panel). Then, one group continues training in the same unimanual context (UT group, right-upper panel), while the other group trained with the right arm reaching movement (BT group, right-bottom panel). **B.** Unimanual motor performance reached a plateau at approximately 60% of the ideal levels in the UT group, but improved at approximately 80% of the ideal levels in the BT group. Adapted from Hayashi and Nozaki, 2016.

but an increase in the gain of feedback control compared to healthy control participants (Smith and Shadmehr, 2005; Tseng et al., 2007; Criscimagna-Hemminger et al., 2010; Izawa et al., 2012). In contrast, Huntington's disease is associated with decreased corrective motor feedback commands, but maintained motor learning abilities (Smith et al., 2000; Smith and Shadmehr, 2005). Parkinson's disease is associated with a superior motor learning ability compared to healthy control participants, but the inability of feedforward control (Semrau et al., 2014). In general, neural functions are distributed in various cortical areas. Thus, movement disorders due to an impairment of different cortical areas differently affect motor control and learning. My results suggest that the visuomotor map (i.e., the motor primitives) serves both motor control and learning.

4.3.3 Implication for Physical and Health Education

Physical and health education teaches an aging society how to improve and preserve health and the quality of life. Physical education is required to maximize movement skills, including strength, stamina, and dexterity. Importantly, the critical period for the acquisition of dexterity ends at approximately 12 years old (Viru et al., 1999; Stafford, 2005). Thus, the skill that is acquired during early childhood affects motor control and learning throughout life. In this regard, the results of my study may also be insightful. As aforementioned for functional rehabilitation, the acquisition of a broad range of input-output mappings (repertoires) improves motor control and learning ability. Thus, many kinds of motor repertoires should be learned during childhood to improve and preserve our health throughout life.

Health education, that is, teaching health preservation and improvement skills, should significantly involve physical education. Some studies have shown that motor performance is a predictor of health awareness, physical activity, and mental health (Taylor et al., 1985; Morrison et al., 2012; Blankevoort et al., 2013; Larsen et al., 2015). Again, these findings support the idea that the acquisition of a broad range of input-output mappings eventually lead to the acquisition of physically and mentally healthy behaviors, leading to a healthier society.

Future research should construct a computational model that accounts for all of the features and brain mechanisms of motor control and learning. With this knowledge, we can optimally identify methods for training students and athletes, which could compensate for the development of neural deficits and/or preserve a high quality of health and life.

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