博士論文

The Influence of Habituation to Visual Feedback Delay on Motor Learning, Current Hand-State Estimation, and Mass Perception

（時間遅れへの適応が運動学習・手の状態推定・
質量知覚に与える影響に関する研究）

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Chapter 1

General Research Question

We receive environmental information through body sensors such as the eyes, ears, skin, nose, and tongue and respond to that information using the musculoskeletal system. One function of the nervous system is to integrate information between these sensors and effectors. Information from the sensors is decoded (e.g., determining whether an object seen is something needed; if so, determining precisely where it is and how to procure it in the present environment,) and output is sent to the effectors as motor commands (e.g., how strongly and when the numerous muscles should contract for reaching and grasping the object). The central nervous system (CNS) processes this information.

The nervous system has limitations in its signal processing: noise and delay. Nervous system delay is studied through the field of control mechanics, while the noise of the nervous system is studied in the field of statistics or probability theory. My main focus throughout this thesis is delay: how the nervous system compensates for delay and adapts to the environment.

In this chapter, I introduce features of neurons and the nervous system from the viewpoint of a system with delay and clarify the issue I will engage in this study.

1.1 Neural information transmission and processing delay

A neuron is an information-processing element consisting of a soma, axon, and dendrites (Figure 1.1). Dendrites collect electric signals from numerous other neurons and transmit them to the soma. The soma accumulates these signals and sends an output to the axon. The axon forms branches and the tip of each branch connects to the dendrite of another neuron. The connection is called a synapse. A neuron in the cortex typically receives more than 1000 inputs. More surprisingly, a Purkinje cell in the cerebellum, which plays a significant role in motor learning, receives more than 100 000 inputs.

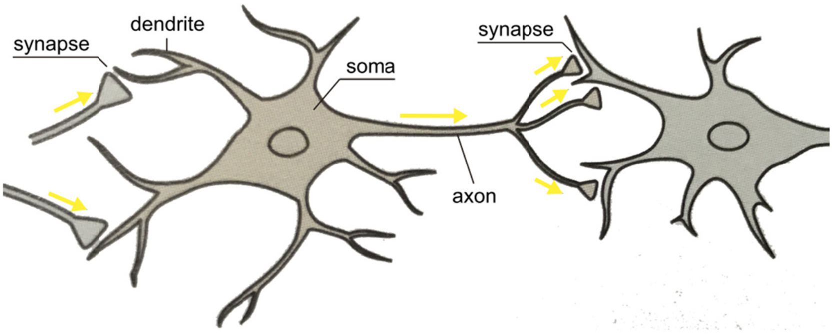


Figure 1.1 Structure of a neuron. Simplified from Kandel et al.[1], p.22.

Although nerve cells have a special ability to communicate with one another rapidly with tremendous precision over great distances, as from the brain to the tip of the toe, we cannot overlook a certain amount of delay in processing. One of the factors for the delay is in the signal processing mechanism of a neuron. Unlike the way an electric current flows in an electric line, the neural signal processing depends on the voltage change evoked by ion passing through the membrane. This causes an axon larger delay than electric current. Another factor is the signal processing delay between neurons. Communication between neurons is not processed electrically but done chemically for the most part (chemical types of synapses). Here, the electrical signal has to be replaced by emission of chemical substances, and the post-synaptic neuron has to receive them and convert them into an electrical signal. This process necessitates extra time in general [1]. Considering these factors, we can conclude that delay on the order of milliseconds is inevitable in signal transmission from one neuron to another. In addition, it takes at least several tens of milliseconds for the nervous system to transmit a signal from the sensor to the brain or from the brain to muscles through the neurons.

Consider the case when a subject needs to perform a saccadic eye movement to a visual target. It takes approximately 50 ms for the visual signal information of the target to be sent from the retina to visual cortex [7], and as long as 100 ms to its receptive field such as lateral intraparietal area [12,13]. After receiving this information, the CNS needs some time to produce a motor command and transmit it to ocular muscles through efferent nerves. There is also a time lag between the muscles receiving efferent signal and the motion initiation. Given these lags, it is estimated that the oculomotor control system has approximately 130 ms of feedback delay [7]. A more complicated visuomotor control system necessitates more than 200 ms [10], and it takes more than 110 ms for proprioceptive control systems to work [14].

As seen above, biological bodies have various afferent and efferent delays in each system or modality. If these delays were left uncontrolled, they would do fatal harm to our lives. Let me think of the temporal gap between visual and auditory afferent delays, for example. When light reaches the retina and a sound vibrates the eardrum at the same time, the brain activity invoked by the sound is observed 30-50 ms earlier than that invoked by the light [15]. In addition, the physical transmission speed of light and sound is different. This means that the arrival time of light on the retina and sound to the eardrum should differ depending on the location of the object which produces the light and sound. These biological and physical transmission discrepancies make it difficult for a human to identify the object. When a man is talking with another person, for instance, the visual information of his mouth motion and the auditory information of his speech are not processed concurrently in the CNS. The moment the CNS "sees" the person's mouth motion is not the moment it "hears" his voice. Notwithstanding the existence of these difficulties, our CNS is able to associate these two signals skillfully and properly. This mechanism is interpreted and understood in the framework of multi-sensory calibration [6] (Figure 1.2).

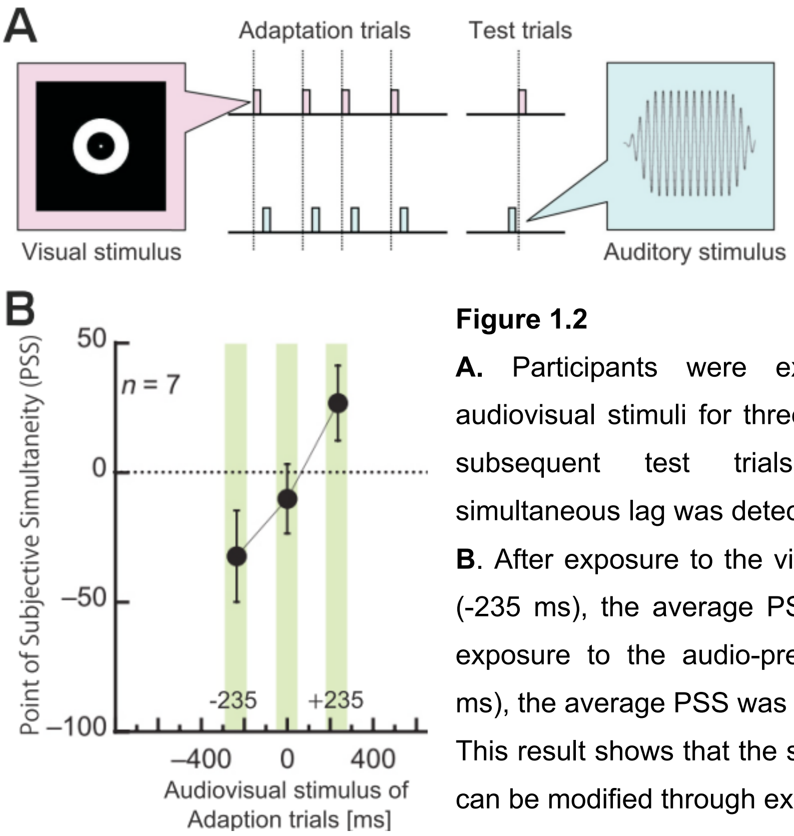


Figure 1.2

A. Participants were exposed to lag-fixed audiovisual stimuli for three minutes, and in the subsequent test trials, their subjective simultaneous lag was detected.

B. After exposure to the vision-preceding stimuli (-235 ms), the average PSS was -32 ms. After exposure to the audio-preceding stimuli (+235 ms), the average PSS was +27 ms.

This result shows that the subjective simultaneity can be modified through experience.

Adapted from Fujisaki et al. [6].

Another example I want to introduce here is the case in which we stretch out our hand to a book on a bookshelf. I believe you have had the experience where after reaching for a book without checking its precise location, you notice that you are reaching for the wrong book and quickly correct your reach for the desired one. Now the CNS has to produce a corrective motor command, which moves our hand from the present location toward the desired book. Estimating the present location is not such an easy task here. There is at least a 110 ms delay in a proprioceptive feedback loop [14]. (When the motor system depends on visual feedback, the delay is more than 200 ms [10].) Therefore, the CNS would make a corrective motor command depending on the hand location 110 ms before. If the hand moves at the speed of 30 cm/s, the hand location 110 ms before is 3.3 cm behind its present (real) location. This 3.3 cm discrepancy would lead to a larger separation between the hand and the desired book at the end of reaching if the reaching duration after the correction is too short to correct again. This means that our quick motor correction would not work properly and we could not reach the desired book with a quick correction. In reality, however, we empirically know that we can achieve this kind of correction quickly and precisely. Also, it has been experimentally reported that reaching correction is quick and precise even when a target is suddenly displaced during reaching [10,16] (Figure 1.3).

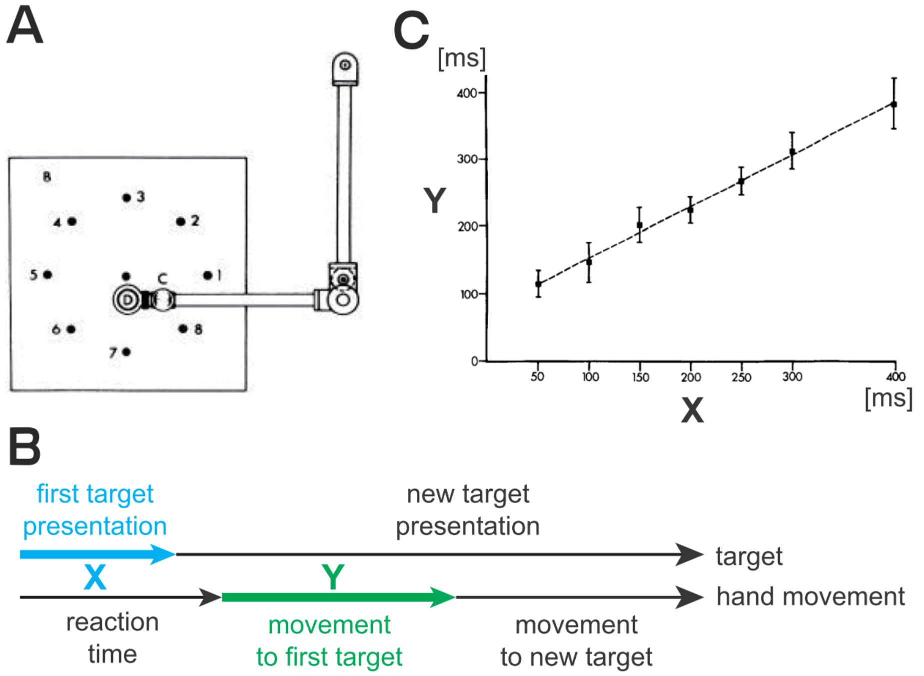


Figure 1.3

A. Three rhesus monkeys were trained to reach a target on the screen with the manipulandum quickly. The target locations were chosen from 1 to 8 in the illustration. **B**. After the first target appeared for a while (X = 50~400 ms), it went out and a new target appeared (the upper timeline). The monkeys had to try to correct their reaching toward the new target as quickly as possible (the bottom timeline). **C**. The average reaction time to the first target in this setup was more than 200 ms. If the CNS begins to prepare for reaching the new target after the initiation of the first reaching, the swift reaction to the new target is impossible (the small amount of Y). This result shows that the CNS can use sensory input and modify the motor command flexibly even during movement preparation as well as during movement. Adapted and modified from Georgopoulos et al. [10].

Let me introduce the last and most complicated example. Imagine the scene where you are walking with a friend in a crowd while talking. Here our brain continuously gives off various kinds of motor commands for walking, talking, and looking, etc. At the same time, many different sensory afferent signals are sent into the brain ceaselessly. Your right arm may be sometimes moved by a hit from a person in the crowd. Your friend's arm may continually touch your left arm. When you pat your left arm with your right hand in this situation, there are some efferent and afferent signals occurring at different times: the motor command to the right arm and hand, the proprioceptive feedback of the right arm and hand, the tactile feedback of the left arm, and the tactile feedback of the right hand. If there were no feedback loop delay, what the CNS has to do here would be somewhat easy. Your CNS could easily distinguish the proprioceptive and tactile feedbacks caused by others from those invoked by yourself simply by associating all afferent signals being input at the same time with the discharge of motor command with yourself. The reality, however, is not so simple. There is more than 100 ms of delay between the discharge of a motor command to the right arm and the arrival of its proprioceptive feedback. When you move your right arm relatively slowly, it takes more than one second for the tactile feedback of your right hand and left arm to arrive at the CNS. It is such a difficult task to properly judge the afferent feedbacks caused by you as your own, which are delayed and mixed up with other afferent signals caused by others. Patients with a kind of cognitive disease called “delusion of control” cannot accurately judge afferent signals [17]. They cannot recognize their motion (proprioceptive feedback with the delay of only approximately 100 ms) as their own. Then, how can healthy people perform this difficult task to achieve an appropriate recognition? This is still a controversial topic.

As demonstrated in the examples above, it is no exaggeration to say that creatures cannot live without delay compensation and must be equipped with such a mechanism. Many studies have been reported on the delay compensation in multi-sensory perception exemplified by the first example. On the contrary, the studies on the delay compensation in sensorimotor systems exemplified by the second and third examples are more complicated and less evidence has been accumulated. This is still an open question [18]. In this thesis, I will mainly focus on the delay compensation mechanism of sensorimotor systems. In the next section, I will overview the motor control studies, which provide a basic framework from which we can discuss delay compensation mechanisms.

1.2 Motor control studies

A simple feedforward model

Norbert Wiener proposed an interdisciplinary approach to understanding the regulatory system of human and animals, which is now called cybernetics [19,20]. He paid much attention to the similarities between a servo-mechanism and cerebellar reflex emphasizing the negative feedback. A system with feedback mechanism at times falls into oscillation, which is also observed in the movement of cerebellar patients. This fact led him to infer that the cerebellum has a feedback function in motor control. However, the feedback mechanism alone does not achieve a quick and coordinated movement because the innate nervous transmission delay exists in the biological system. Therefore, feedforward control is necessary. A feedforward control system is illustrated simply in Figure 1.4 In the 1970s, Polit and Bizzi proposed the Equilibrium-point control hypothesis as the simplest feedforward model [21]. They hypothesized that muscles are springs whose stiffness can be controlled on a voluntary basis. Once the stiffness of antagonistic muscles is determined, the joint controlled by these muscles can move automatically to the angle at which the stiffness of the antagonistic muscles becomes equivalent (equilibrium-point). What the motor area in the brain has to do before the initiation of a movement is to give off signals to determine the stiffness of each muscle. After this, arms and legs can move automatically. A continuous motor command output and afferent feedback are unnecessary on this control theory. Only two components are necessary: a propriospinal reflex loop which keeps a muscle's stiffness at a target level and sufficient stiffness. After the proposal of the equilibrium-point control hypothesis, many experimental studies denying this hypothesis have been reported. One of the most important studies of them was reported by Gomi and Kawato [22]. They proved that the stiffness of muscles is not so high enough to support the hypothesis. Another study reported the fact that a patient who lacks proprioception and cannot keep muscle stiffness constant is still able to perform reaching movements [23]. These studies completely denied the hypothesis.

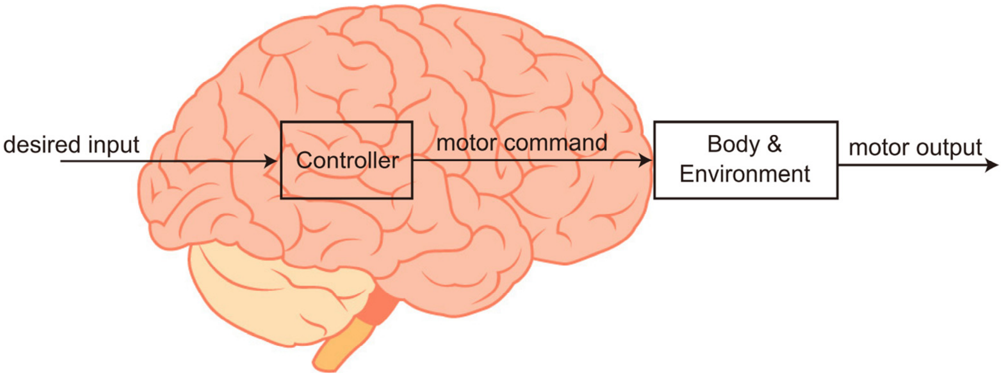


Figure 1.4 A simple illustration of feedforward control system.

The importance of afferent (sensory) and internal (efferent) feedbacks

During the 1980s, it had become clear that motor control is not as simple as the equilibrium-point control hypothesis insisted. Some studies reported that when a target location changes during reaching, the reaching movement can be modified in accordance with the extent of the displacement [10,16] (Figure 1.3). The change of cortical motor activity, namely the output of a new motor command from the brain to muscles, was also observed during reaching correction [24]. Trajectory related activity in the motor cortex observed 150 ms before the initiation of the movement was also observed during reaching [25]. These results demonstrate that trajectory determination and the related motor command output continue after the initiation of a movement. In addition, the fact that the use of visual and proprioceptive feedback during pointing task improves the accuracy suggests the contribution of the online correction with sensory feedbacks to motor control [26].

Surprisingly, this continuous trajectory correction occurs even when external (sensory) feedback cannot be used. This sensory feedback-free control was originally studied for eye movements. We all know empirically that the repetition of saccades never makes us feel the world moving. We can correctly distinguish the retinal displacement caused by our own eye movement from that produced by external causes. As a hypothesis to explain this, “efferent copy” was proposed [27]. This hypothesis assumes that a copy of motor command is used to predict the result of the movement and the prediction is compared to the actual outcome when its afferent feedback is input. Many studies have been conducted to prove this hypothesis. For example, Duhamel et al. revealed that the neural activities in the lateral intraparietal (LIP) area of the cortex are flexibly modulated: the visual receptive field in the cortex corresponding to the retinal information can change its activity before the saccade predicting the retinal information after the saccade [12]. There is an appreciable interval between the time that the decision to move the eyes is made and the moment at which the eye muscles are activated (termed “saccadic latency”; about 200 ms in this experiment). During this interval, a neuron could hold both current and future retinal information. Here, the future retinal information means the new retinal input after the intended saccade. Parietal cortex contributes to a continuously accurate representation of visual space by predicting the retinal information (Figure 1.5). The similar control operation is reported to work for arms control. Higgins and Angel required their experiment participants to reach for a target vertically stepping from one position to another in the environment where their horizontal lever manipulation was converted into vertical cursor motion [28]. The participants sometimes mistook their manipulation in this unusual environment. The latency after the mistaken motion to the initiation of their corrective motion was 83 – 122 ms. This duration was significantly shorter than the proprioceptive reaction time (108 - 169 ms) observed in the same experimental setup. This result means that reaching correction depends not only on sensory feedback but also on a certain signal processed faster than afferent feedbacks. The rapid trajectory correction during reaching movement has been reported since then [29,30]. These results suggest that internal feedback-loops of central origin also contribute to the corrective process of arm movement.

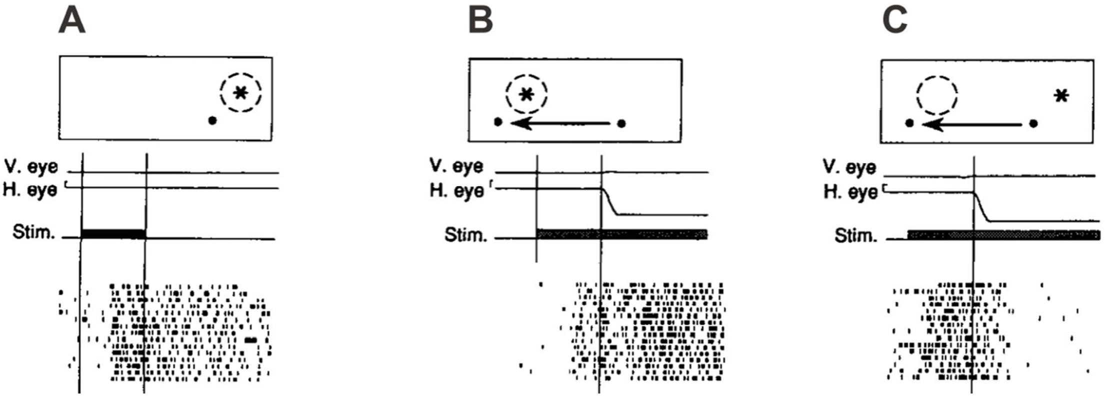


Figure 1.5 Visual activities in a single sample neuron in the lateral intraparietal (LIP) area. The dot in each panel is the fixation point. The star is the visual stimulus. The dashed circle is the location of the receptive field at the end of a trial. The arrow is the saccadic eye movement. Timelines below ("V. eye" and "H. eye") show vertical and horizontal eye position. "Stim." shows the onset and offset of the visual stimulus. Raster plots display the results of 16 trials. **A.** While the monkey fixates, a stimulus appears in the receptive field. And this neuron is activated approximately 70 ms after the onset. The neuron activity remains even after the offset of the stimulus. **B.** In a saccade task, the monkey moves the eye to a new target when it appears on the screen. The onset of the visual stimulus is at the same time with the target appearance. The data are aligned with the initiation of the saccade. If there were no predictive mechanism, this neuron would respond to the stimulus 70 ms after the end of a saccade. However, the neural activity to the stimulus in the receptive field is actually seen even before the initiation of the eye movement. **C.** Neural activity when the visual stimulus leaves away from the receptive field by saccade. In this case, a swift disappearance of activity is observed compared to the slow disappearance of activity after stimulus offset shown in **A**. Adapted and modified from Duhamel et al. [12].

The above results that motor control is based on the integration of afferent and efferent feedbacks are now formulated in the framework of the “forward model.” This model receives a copy of an efferent signal and predicts the outcome of its input into a plant (Body & Environment in Figure 1.6). The forward model must acquire and store the characteristics of the plant in order to predict the result properly. Researchers think that the forward model, as well as the controller, is learned through experience. Note that the controller converts the desired input into a proper motor command (Figure 1.6). Shadmehr and Mussa-Ivaldi provided a good example to support this idea [4]. The participants of their experiment were required to reach for one of 8 targets equally distributed around the starting position by manipulating a lever while they could not see their own hand. The reaching movements in the baseline session were natural with straight trajectories and bell-shaped speed profiles (Figure 1.7 A). In the adaptation session, they had to perform the same reaching movement in an unusual force field. The force distorted their reaching trajectories, and they could not reach for a target naturally at first (Figure 1.7 B). In the repetition of trials, they adapted to the force field and showed normal straight movements with bell-shaped speed profiles again (Figure 1.7 C). Sudden removal of the force field at this moment caused distorted trajectory again, whose direction was the opposite of the distortions observed at the beginning of the adaptation session (Figure 1.7 D). The authors interpreted this result as the controller and forward model acquiring this unusual force field through the process of trial and error. This process is called “motor learning.” Now I can modify the control system illustrated in Figure 1.4 with the evidence of internal and external feedback loops (Figure 1.6).

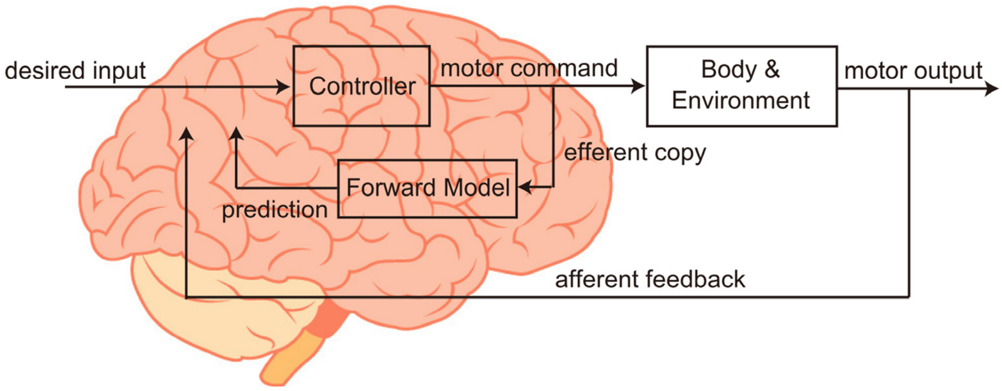


Figure 1.6 A motor control system with feedback loops.

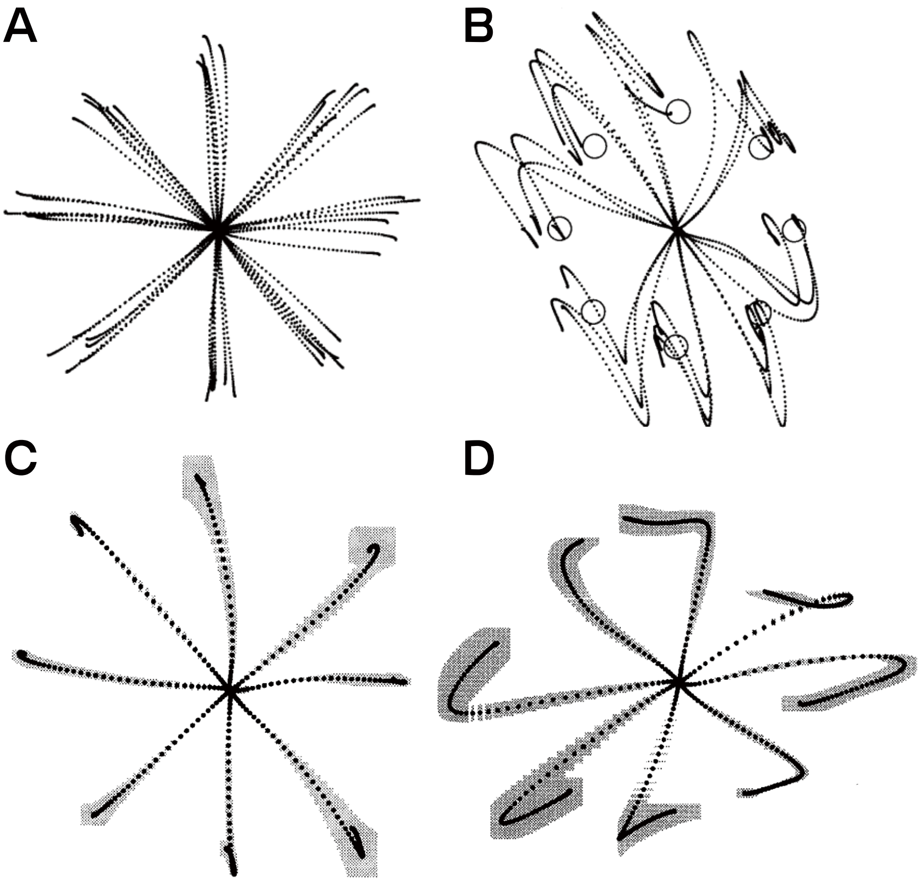


Figure 1.7

A. Baseline trials. **B.** Initial performance in the adaptation condition. **C.** The final performance in the adaptation condition. The average of the last 250 trials in 1000 adaptation trials. **D.** Aftereffect. This performance is the opposite of the initial performance of the adaptation condition (**B**). Adapted from Shadmehr and Mussa-Ivaldi [4].

The integration of the feedbacks

When a motor system achieves a perfect control, the prediction of the forward model coincides with the real outcome observation conveyed through an afferent feedback loop. This is the ideal scenario. Practically, however, the prediction error is inevitable even when the control itself is almost perfect because the prediction made by the forward model cannot be perfect due to the discrepancy between the model and the real plant. A more important factor is the imperfect reliability of afferent feedback signals with innate noise and delay. This fact leads to one notable question: how are these feedbacks integrated to estimate the current state of the motor apparatus? An important study on this topic was reported in the 1990s. Wolpert et al. asked their experimental participants to stretch their arm in conditions where they could not see their own hand and to estimate the hand location at the end of each movement. The movement duration had some variation (0.5 – 2.5 ms) causing the hand locations at the end of each movement to be distributed widely. They prepared for three experimental conditions: null, assistive, and resistive force field. The estimated hand location exhibited bias (displacement from the real hand position) and variance in accordance with the conditions and the movement durations (Figure 1.8 A and B). These bias and variances could not be reasonably explained if the CNS depends on either internal feedback (prediction) or afferent feedback. This result demonstrated that the participants used both feedbacks to estimate their hand location. More interestingly, their mathematical simulation explicated how these feedbacks are integrated: the CNS compares the reliability of these feedbacks and puts more weight on more reliable information to improve the precision of current state estimation (Figure 1.8 C and D). In the early stage of a movement, CNS refers more to the prediction of the forward model, and in the later stage, it refers more to the afferent feedback because here the precision of the prediction is not as high as that of the earlier stage. I call this hypothetical domain “state estimator” in this thesis.

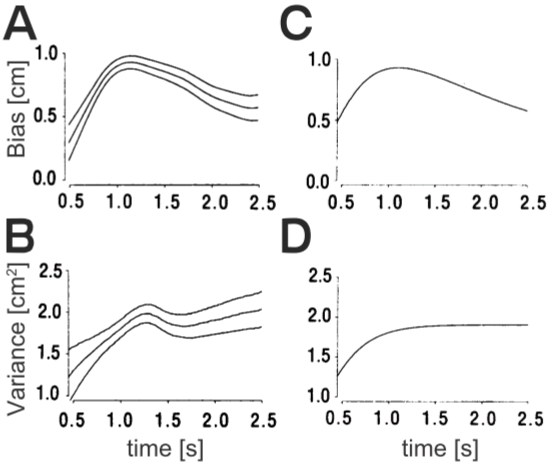


Figure 1.8 Experimental results (**A** and **B**) and Simulation results with the Kalman filter (**C** and **D**). The estimation bias was at its peak when trial duration was 1 s and declined as the duration became longer in all three conditions (**A**), while the estimation variance did not change when trial duration was longer than around 1 s (**B**). These results were well explained by the estimation mechanism with the Kalman filter (**C** and **D**). Adapted from Wolpert et al. [9].

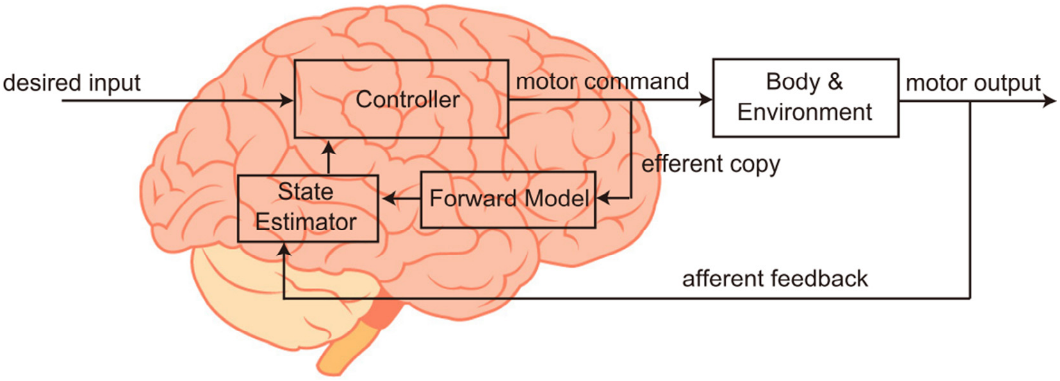


Figure 1.9 An illustration of the basic framework of motor control from which I discuss the delay compensation of sensorimotor systems in this thesis.

To sum up the studies on motor control, researchers understand and discuss the motor control mechanism in the model illustrated in Figure 1.9. Researchers examine each part in more detail depending on their interest. For example, the "Controller" has been continuously and enthusiastically researched for a long time. They discuss the control theory on which the controller determines movement trajectories or motor commands. There are numerous experimental and theoretical studies on the theory. In this thesis, the important components for the study of delay compensation are the two feedback loops: afferent and efferent feedback loops.

1.3 Delay compensation theories

In the previous section, I overviewed the motor control studies and reached the basic framework in which the delay compensation in sensorimotor systems should be discussed (Figure 1.9). The noticeable point for my study, here, is the existence of inevitable delay in afferent feedback: afferent feedbacks arrive at the CNS significantly later than the prediction of the forward model. As I already pointed out in the first section, this delay has to be compensated and is actually done so somehow. Then, how is it achieved? I will introduce some important delay compensation theories studied in the field of sensorimotor control.

Kalman Filter

The statistical process I referred to in the previous section, which enhances estimation precision by weighting according to the reliability (or uncertainty) of the information sources, is summarized in the Bayesian theory. On this theory, the probability distribution of the true value is produced not only by one noisy observation but also by integrating the observation with a prior statistical distribution (historical evidence). What offers an algorithm to predict the next state by comparing the internal feedback (prediction from the forward model) and the afferent feedback based on the Bayesian theory is well known as the Kalman filter (Figure 1.10). The Kalman gain is determined in accordance with the uncertainty of the internal feedback compared to that of afferent feedback. A large gain means greater reliance on the afferent feedback.

The theory of observer design for systems with delay has been rigorously investigated, in which the Kalman filter has played an important role as a filter insusceptible to time delays and low sampling rate [31-33]. Wolpert and Ghahramani have proposed that the sensorimotor control system adopts a Kalman filter-like mechanism to compensate for sensorimotor delays and reduce the estimation uncertainty occurring due to inherent noise by combining the sensory prediction produced by forward models and actual sensory feedback [34]. The sensory feedback is delayed and contaminated by noise, which makes the sensorimotor system unstable [7]. In contrast, the forward models can provide a quicker and more accurate estimate of possible sensory information, although it cannot deal with unexpected events. Combining these different types of information according to the Kalman gain (Figure 1.10) can improve the current state estimate and makes the sensorimotor system stable. The Kalman gain is determined in accordance with the uncertainty of the internal feedback compared to that of afferent feedback. In a situation where the uncertainty of the afferent feedback is assessed as high because of a problem in the environment or a sensory organ, the system decreases the gain and relies more on the prediction of the forward model.

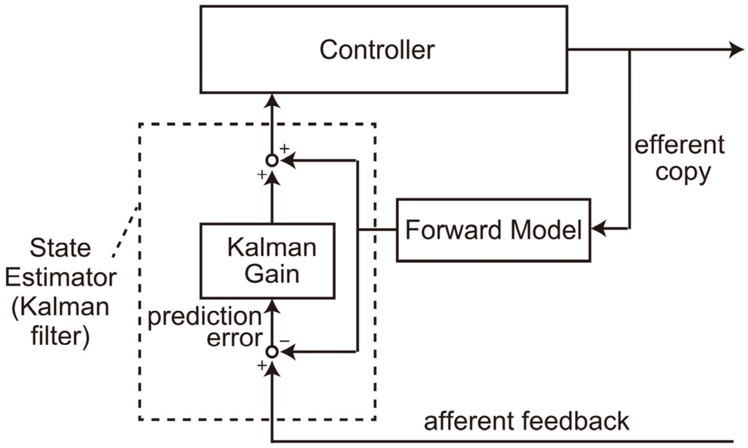


Figure 1.10 An illustration of the Kalman filter. Only the state estimator is depicted in more detail than the illustration in Figure 1.9.

The experimental result shown in Figure 1.8 is one of the examples demonstrating Kalman filter-like mechanism is working in the sensorimotor control system. Körding et al. provided another evidence that the Kalman filter works in motor control [5]. They required their participants to place a cursor on a target in the environment in which they could not see their own hand. The cursor was visible only at the end of trials and halfway to the target briefly. The cursor position did not indicate the hand position but shifted laterally. In each trial, a fixed amount of shift was chosen randomly from a Gaussian probability distribution (mean 1 cm, SD 0.5 cm). Therefore, the participants learned this distribution through experience. This prior information made them try to reach the point which is 1 cm away from the target leftward at the beginning of a trial. On the way to the point, the participants observed true cursor position briefly and corrected their prediction. As a result, the end point of each trial is the combination of both the prediction and the visual feedback. The authors expected that the correction would be large when the visual feedback is certain (Figure 1.11 A, blue path) and that the correction would be small when the visual feedback is uncertain (Figure 1.11 A, green path). The result showed that the certainty of the visual feedback affected the extent how much the motion executed based on the prediction was corrected (Figure 1.11 B). This result indicates that the Kalman filter contributes to motor control.

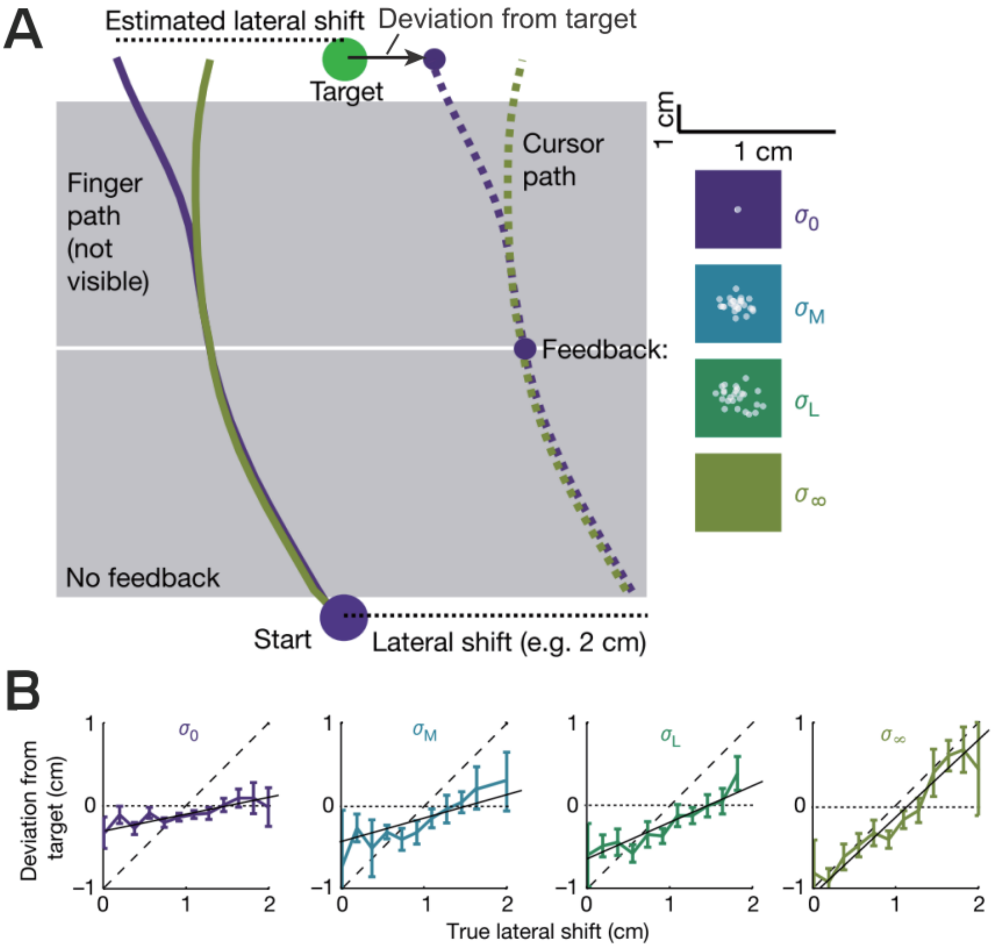


Figure 1.11

A. Setup and the four types of visual feedback.

B. Experimental result. When the visual feedback was certain (σ_0), the deviation from the target was small. This means that the CNS utilized the feedback information strongly. On the contrary, When the feedback was uncertain (σ_∞), no correction was observed. The extent to which the CNS utilizes the feedback depends on its certainty. Adapted from Körding et al. [5].

Smith Predictor

In the 1950s, Smith proposed a control system to enhance the productivity of a factory in which the transportation of products or parts takes a long time [35]. This idea has been generalized and applied to other fields. The basic concept of this idea is very simple. There is a large temporal gap between the prediction of a current state (the amount of products conveyed to a section in a factory, for instance) and the feedback signal from the plan. In order to overcome this temporal gap, he inserted a delay estimator in the prediction. This delay estimator prevents a wrong control caused by comparison of temporally discrepant signals (e.g., the above story of a shower with control delay). Figure 1.12 demonstrates a diagram where this delay estimator is applied to the CNS.

Miall insisted that the CNS utilizes the Smith Predictor to overcome its transmission delay. Miall et al. examined how the performance of a visual tracking task by primates was influenced when a delay was artificially added to the visual feedback [8]. They trained a rhesus monkey to track a sinusoidally moving target with a cursor manipulated with a joystick (Figure 1.13). When there was no cursor delay, the tracking behavior was relatively stable (Figure 1.13 A). However, when there was 300-ms cursor delay, the behavior became unstable (Figure 1.13 B). One possible solution of non-negligible delay in afferent feedback without using the Smith Predictor is to decrease the output of a controller. This solution can prevent control instability. However, this cannot achieve the optimal control overcoming the delay sufficiently (Figure 1.14A). After showing this fact in a simple mathematical simulation, they introduced a simulation with the Smith Predictor as a better solution (Figure 1.14B). They further insisted that this model is the best to explain the experiment results in a visually guided tracking task with cursor delay [36,37,8,7].

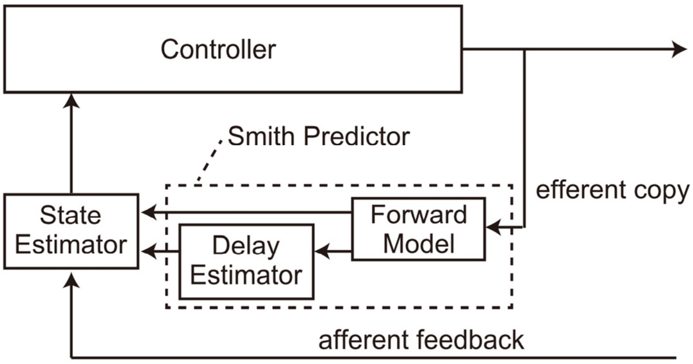


Figure 1.12 A diagram of a control system with a delay estimator (Smith Predictor). The CNS is able to use the quick information from the forward model and the temporally precise comparison between the prediction and the afferent feedback.

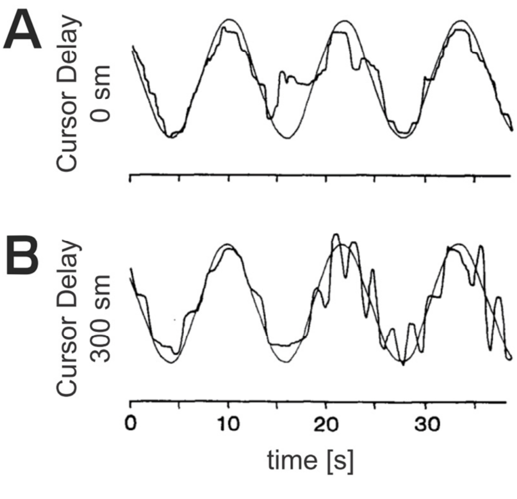


Figure 1.13

A part of the result in tracking experiment by a rhesus monkey. The thin smooth curves illustrate the target motion, and the thick zigzagging ones the position of a joystick manipulated by a monkey. **A.** No-delay condition, in which there was no delay between a joystick and its visual feedback. **B.** 300-ms delay condition. In this case, the joystick motion was more unstable than that in no-delay condition. Adapted from Miall et al. [8].

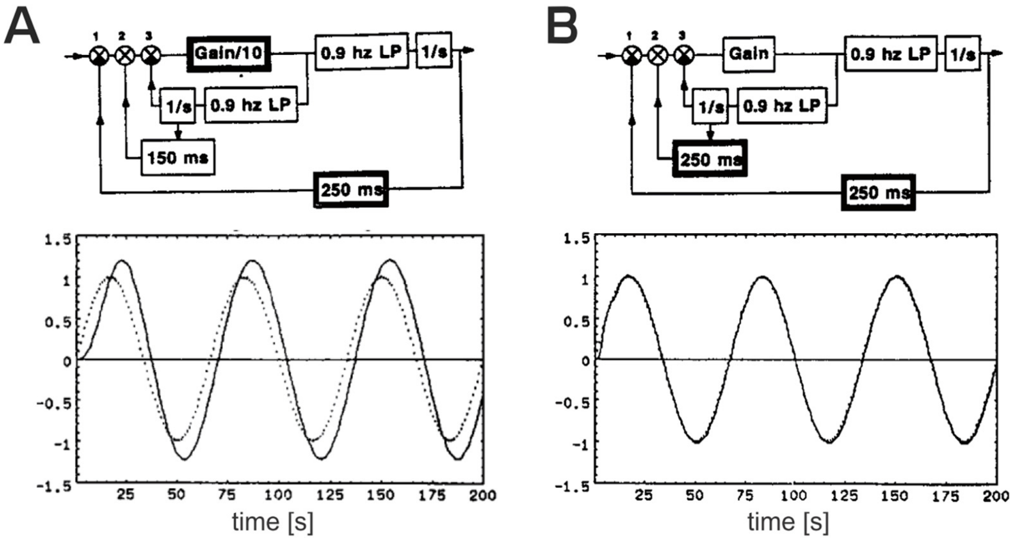


Figure 1.14

A. Even if the delay estimation (150 ms) differs from the true afferent delay (250 ms), the gain reduction approach works to prevent the tracking performance from unstable. **B.** When the delay estimation is correct, the tracking performance is similar to that with no afferent delay, even if there is much amount of afferent delay (250 ms). Adapted from Miall et al. [7].

Sensory Prediction

In the field of motor control, the phrase "sensory prediction" is a synonym of "motor prediction" (the prediction of the forward model). Here, I use this phrase "sensory prediction" as referring to a predictive mechanism independent of efferent copy. This might sound strange because in the previous cases of the *Kalman Filter* and the *Smith Predictor*, the forward model whose transmission delay is much smaller than that of the afferent feedback, plays an important role in prediction. How can a system predict a future state depending only on the delayed afferent feedback? Crevecoeur and Scott experimentally proved the existence of such a mechanism [2]. They put perturbations with various force profiles on their subjects' arms while they were at rest, and examined their stability and response to the perturbations (Figure 1.15A). They hypothesized that their subjects could learn a force profile after experiencing one type of perturbation profile repeatedly. If this learning occurs, they postulated, the sensory input of the perturbation triggers the CNS to refer to the learned force profile. This reference makes it possible to predict a future force perturbation (Figure 1.15B). When a perturbation with an unexpected force profile was put on their arms, the reference to the learned profile caused a wrong response to the perturbation (e.g., overestimate or underestimate). Figure 1.15C illustrates an example of overestimation. The authors experimentally demonstrated this phenomenon and proposed the "sensory prediction model" (Figure 1.15D). This model suggests that the delayed afferent feedback itself can also be used predictively in motor control.

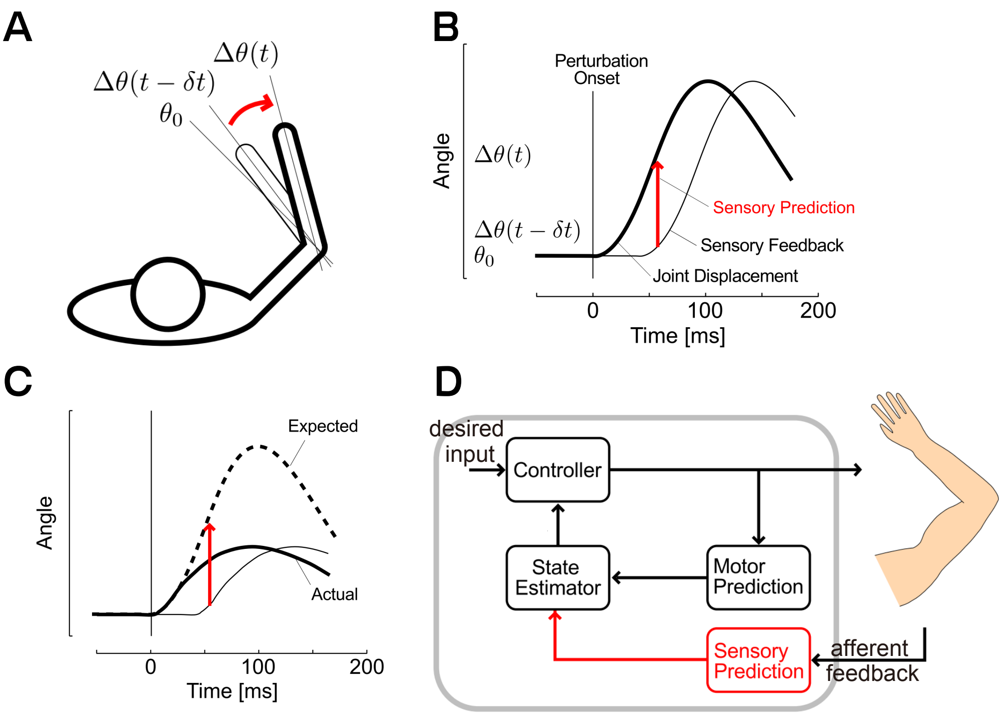


Figure 1.15 The outline of the sensory prediction, applied from Crevecoeur and Scott [2]. **A.** Experimental set up. The elbow angle before and at the beginning of the perturbation is θ_0. δt is the amount of delay in proprioceptive afferent input. **B.** The joint displacement and its sensory feedback have a temporal gap by δt. When the feedback reaches the CNS at time δt, it refers to the learned profile (Sensory Prediction: red arrow). **C.** An unexpectedly small perturbation (thin solid line) causes overestimation. **D.** A diagram of a motor control system with "Sensory Prediction."

Which model among them is correct? Or, is the CNS equipped with all of them? Are there any other possible models? The studies of delay compensation are now in progress. Each theory above has its advantages and disadvantages. The Kalman filter, for example, is efficient in noise canceling and prevents a feedback delay from making the motor control unstable. However, this theory does not provide the method to adapt or learn a new amount of delay. What this theory achieves is to change the reliance on delayed feedback. The Smith predictor theory, on the other hand, provides a system which can adapt and learn a novel amount of delay by adjusting its delay-predictive parameters. This theory looks to be most reasonable theoretically. However, this theory also has its disadvantages: the implementation of this mechanism in the CNS is still a mystery. For instance, Miall et al. who proposed that the CNS has the Smith Predictor in it based on the results of a visually guided manual tracking task [7], have become skeptical about its existence following the result of another experiment [38]. Although sensory prediction is a new and intriguing theory, it does not treat the amount of delay itself. It just connects a certain feedback input with the most probable experience in order to respond to a stimulus quickly. We cannot expect as much adaptability from this theory as the Kalman filter or Smith predictor provides. We have to wait more for the elucidation of the whole picture of a delay compensation mechanism in sensorimotor systems.

Adaptability has not been examined experimentally and theoretically so much in the studies of delay compensation mechanisms in sensorimotor systems regardless of its importance [18]. Therefore, adding new findings on the adaptability will heavily contribute to the study of delay compensation mechanisms in sensorimotor systems, and consequently to all studies in motor control. The key research questions in this thesis are as follows:

> Is a motor control system able to learn and adapt to a novel delay like it can do to a novel environment (e.g., force field, prism adaptation, visuomotor rotation, and so on)?

If it is possible, how can we observe such learning effects?

How does the delay adaptation in the motor control level relate to that in the perceptuomotor level?

(I will show examples of these adaptations in the motor control and perceptuomotor levels in the next section.)

Here, I have to note that I will call the adaptation to delay “habituation” in this thesis in order to distinguish it from the adaptation to a novel environment such as visuomotor rotation (motor learning).

1.4 Studies on delay habituation

Delay habituation in the perceptuomotor level

Sensorimotor delay habituation could be observed by various methods. There are many reports on delay habituation in the perceptuomotor level [39-42,11]. In these perceptuomotor experiments, researchers require their subjects to perform a small movement, which triggers visual or auditory feedback with some time lag. They are also asked to answer their perceptual judgment (e.g., which occurred earlier, the movement or the feedback?) Stetson et al., for example, required their subjects to push a button as early as possible when they heard a beep, which was an initiation signal for each trial [11]. In 60% of all trials, the time lag between button push and a flash was artificially injected by 100 ms (injected lag condition). In the other 40% of trials, the flash was not actually triggered by a button push but automatically lit with various time lags after the beep. After each trial, the subjects had to answer which they felt occurred earlier, their button push or the flash. Sorting their perceptual judgment according to the flash timing with respect to the button push (Δt), they calculated the ratio of "button push before flash." Furthermore, the point of subjective equivalent (PSE) was calculated by fitting a psychophysical curve for each subject. The average PSE in the injected lag condition (Figure 1.16A Red curve) was compared with that in the control condition (Figure 1.16A Blue curve), where the 60% of trials were done without lag injection. The result shows that the PSE shifts backward by 44 ms in the injected lag condition. This shift indicates the habituation effect of the 100 ms injected lag. The authors interpreted this effect as perceptual calibration (Figure 1.16B). They also discovered that this calibration does not happen without a voluntary movement. In their experiment, they tested the case where the button moved to the subjects' hands and the flash lit. Here, the same calibration did not occur. These results mean that the information from the forward model is crucial in delay habituation in the perceptuomotor level.

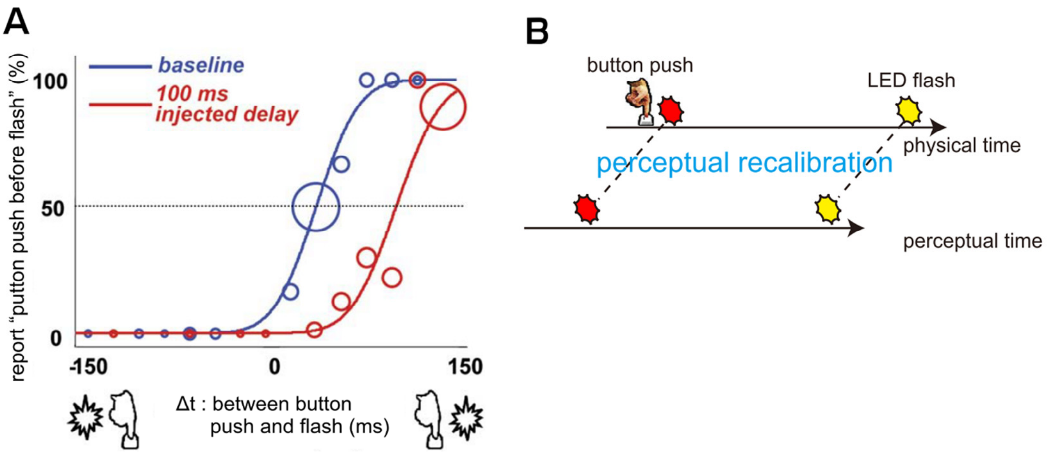


Figure 1.16 A. The PSE shift with injected delay (Red curve v.s. Blue curve). Applied from Stetson et al. [11]. **B.** An illustration of the concept of perceptual recalibration. After the recalibration, the LED flash lit 100 ms after the button push (yellow) is perceived earlier than its physical timing. More interestingly, the LED flash lit just after the push is perceived earlier than the push, though in reality the flash was lit by the push.

Delay habituation in the motor control level

Can this kind of phenomenon be observed in motor control? Namely, can delayed feedback information be used just like no-delay feedback information in motor control by habituating the delay? Before investigating this, I will introduce an important study which examined the effect of feedback delay on motor control systems. Kitazawa et al. examined the relationship between motor learning and visual feedback delay through a prism adaptation task [3]. In their experiment, the moment the subjects began reaching toward a target on a computer screen and took their finger off the starting plate, they were blinded by a shutter. When they touched the screen (the end of reaching), the shutter was opened, and they could observe the visual feedback (0 ms delay condition). The lag between the end of reaching and the shutter opening was constant throughout the experiment. Each condition had its amount of lag: 0 – 10000 ms. They found that motor learning performance significantly degraded with only a small amount of feedback delay (50 ms injected delay). Figure 1.17 shows the average motor learning rates as a function of the delay period. The average motor learning rate at 0 ms injected delay is standardized into 1 here. This result is interpreted from the viewpoint of the importance of temporal association on motor control/learning. Sensory feedback invoked by a movement is strongly associated with the movement when the temporal gap between them is small. On the other hand, sensory feedback is not associated with its causal movement when the temporal gap between them is large.

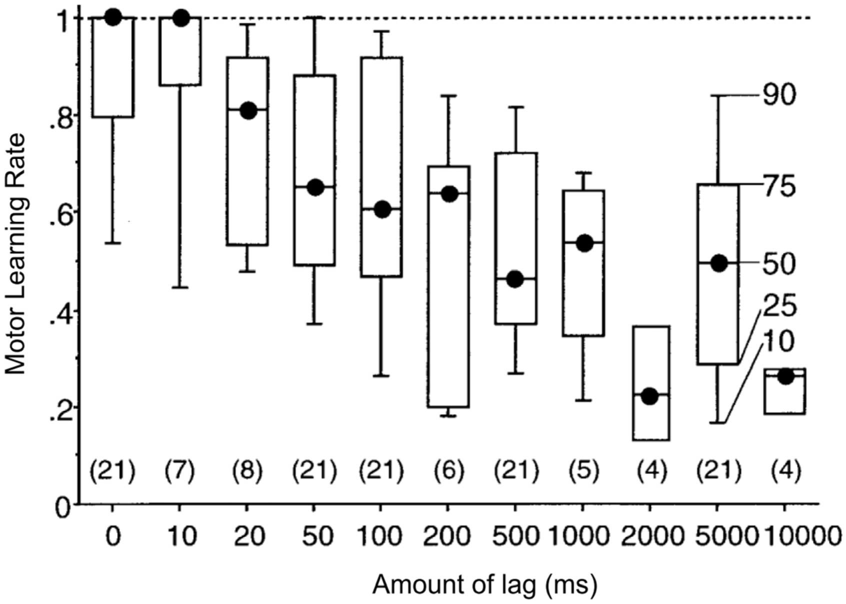


Figure 1.17 The average standardized motor learning rate with respect to the amount of lag between the end of reaching and the shatter removal. Applied from Stetson et al. [3]. Each boxplot indicates 10, 25, 50, 75, and 90 percentiles. The motor learning rates with 50 ms injected delay and more are significantly degraded compared to the rate with 0 ms injected delay.

Assuming that the delay habituation observed in the perceptuomotor level (Figure 1.16) is related to that of the motor control level, one experimental hypothesis is possible: the degraded motor learning rate caused by feedback delay (Figure 1.17) could be alleviated by exposure to the delay before the motor learning task. The observation of this alleviation indicates the existence of delay habituation in the motor control level. Tanaka et al. tested this hypothesis [43]. They used the same experimental setup as Kitazawa's: prism adaptation task with a blinding shatter. The important feature of their experiment was the 60 baseline trials before the prism adaptation (motor learning) task with 100 ms delay injection. In a delay exposure condition, the baseline trials were executed with the same amount of injected delay (100 ms). On the other hand, the baseline trials without feedback delay injection were conducted in a no delay exposure condition. The authors could not observe any conditional difference in the learning rate, suggesting that the exposure to the delay beforehand did not contribute to the alleviation of degraded motor learning. They also tested their subjects' perceptual duration between the end of reaching and the removal of the shutter with a temporal order judgment task. They found that the exposure to the 100 ms injected delay shortened their perceptual duration by 40 ms. This result is consistent with that of the experiment of Stetson et al. [11] shown in Figure 1.16. These results let the authors conclude that the exposure to a delay cannot easily lead to delay habituation in the motor control level even when it causes delay habituation in the perceptuomotor level. I have to note that they did not deny the possibility of delay habituation in the motor control level, but affirmed the difficulty of its observation.

As I overviewed in this chapter, a delay compensation mechanism is necessary not only for the percepuomotor level but also for the motor control level. Considering the ingeniousness and adaptability of the motor control system (e.g., a skillful performance of using a tool which has some time lag such as a fencing sword), a delay compensation mechanism should be incorporated into the motor control system. However, only a few studies have been reported about this mechanism in motor control probably because of its experimental difficulty compared to perceptual experiments as Tanaka et al. indicated [43]. I think that observing delay habituation in the unconscious motor control level is so important for the progress of delay habituation studies. A successful observation will broaden and deepen the study area about delay compensation, providing new study possibilities such as anatomical research related to delay compensation in motor control or the relationship between the two habituations in the motor control and perceptuomotor levels.

The same motivation initiated the study in Chapter 2 as Tanaka et al. While they manipulated static endpoint feedback delay by blinding their subjects during reaching, I showed the whole process of reaching to my subjects with feedback delay injection. To prevent the awareness of the environment change which is inevitable in the prism adaptation task, I used a gradual cursor rotation task. After observing the alleviation of degraded motor learning successfully, I examined how the habituation to 200 ms delay affects performance with other amounts of delay (Chapter 3). To investigate "what" changes by delay habituation more specifically, a target jump task was designed, in which I found that the hand state estimation is distorted by feedback delay and the distortion is alleviated by habituation to the delay (Chapter 4). In Chapter 5, the relationship between feedback delay and mass perception was investigated in the same experimental setup with that in Chapters 2-4. I successfully added a finding on the relationship between motor control and perception.

Chapter 2

Habituation to visual feedback delay influences visuomotor learning

Considering the predictive system in the brain and its ability to construct a flexible perceptual binding between motor command and its consequent feedback [39,40](see section 4 in chapter 1), it can be hypothesized that the degradation of visuomotor learning caused by delayed visual feedback (Kitazawa et al. [3]) could be alleviated by prior exposure to the delay. Tanaka et al. recently examined this hypothesis by the same as Kitazawa's, but could not find any effect of prior repeated exposure to the delay in the motor control level [43].

In this chapter, I point out two factors why Tanaka et al. could not find any significant effect of prior exposure to delay in the motor control level, and propose a new experimental setup to examine the prior exposure effect. As a result, I have succeeded in indicating that the degradation of visuomotor learning caused by delayed visual feedback was alleviated by prior exposure to the delay.

2.1 Background

Appropriate associations between motor commands and their sensory consequences are important for motor learning. One of the challenges faced by the central nervous system in accomplishing this association is the feedback delay inherent in the sensorimotor loop. Physiological studies have shown that the cerebellum is equipped with a mechanism that compensates for this time delay [44]. Cerebellar long-term depression, which is one of the cellular basis of learning, is maximally induced when climbing fiber signals (i.e., sensory errors) are delayed by approximately 250 ms with respect to the parallel-fiber signals (i.e., motor commands) [45]. In accordance with this finding, a behavioral study showed that the rate of prism adaptation decreased in line with an artificially introduced increase in visual feedback delay [3]. These findings suggest that physical feedback delay in the sensorimotor loop is a crucial parameter in motor learning.

Given our perceptual ability to associate our own actions with their sensory consequences, it is possible that the central nervous system can overcome the negative effects of artificially introduced feedback delays on motor learning. Recent psychophysical studies have demonstrated that the perceived time between a voluntary action and its sensory consequence is not fixed, but modifiable [39,40]. When human participants were repeatedly exposed to an artificially introduced 250-ms delay between a key press and its consequent tone, the perceived time delay was decreased by approximately 100 ms. Specifically, intentional actions (i.e., a key press) are perceived as shifted forward in time towards their sensory consequences (i.e., a tone), while sensory consequences are perceived as shifted backwards in time towards their intentional actions. Such perceptual shifts have frequently been observed in auditory, visual, and tactile feedback tasks [41,42,11]. They are considered to reflect the causal binding between actions and their sensory consequences, to produce a coherent experience of our own actions.

Importantly, such perceptual binding is compatible with a recent theoretical framework of motor control, which involves a predictive model called the forward model [26,46,34]. In this framework, the efference copy of a motor command is processed to predict its sensory consequence, before actual sensory feedback is available. The motor control system uses this sensory prediction to correct the ongoing movement, without depending on delayed sensory feedback [29,47,48]. Additionally, it combines the prediction with actual sensory feedback [49-52], resulting in a reliable estimation of current movement states [9]. Accurate predictions from the forward model are crucial for fast and accurate movements. Thus, the brain evaluates the accuracy of the prediction by comparing it with the actual sensory feedback and by modifying the forward model according to the prediction error [53-55].

Perceptual binding occurs only when there are voluntary motor commands, and a reliable temporal relation between action and a sensory event [39,40]. Thus, perceptual binding is believed to result from recalibration of the feedback delay between motor commands and their sensory consequences in the predictive motor control process. I hypothesized that, if appropriate temporal associations between motor commands and their sensory consequences are created in the brain by the recalibration process, these associations may alleviate deficits of motor learning associated with delayed visual feedback.

To test this hypothesis, I examined the ability of human participants to adapt their reaching movements to a novel visuomotor environment with or without the presence of a delay between a movement and its visual feedback. A previous study [43], using a prism adaptation paradigm, examined the way in which repeated exposures to a delay in visual feedback influenced the subsequent prism adaptation during reaching. However, it failed to demonstrate a beneficial effect of the exposure. This may be attributed to 2 factors. Firstly, the study displayed only the endpoint error as visual feedback, and the participants did not see the entire hand path. Given the importance of continuous visual feedback for motor control and learning [56,57,52], it is possible that the beneficial effect of repeated delay exposure in motor learning is observed only when providing continuous visual feedback. Secondly, the sudden application of a prism perturbation made the participants aware of the discrepancy between the hand and target. This allowed them to engage some strategic processes during adaptation [58], which could influence the implicit motor learning process. Thus, it is important to ensure that the participants are not aware of the introduced perturbation. In this study, I introduced an artificial delay to a cursor that was continuously visible, and gradually increased the amount of visual rotation so that the participants were unaware of its presence.

2.2 Methods

Ethics Statement

This study was conducted according to the Declaration of Helsinki and the experimental procedures were approved by the ethics committee of the Graduate School of Education at the University of Tokyo. Written informed consent was obtained from all participants prior to the experiments.

Participants

Thirty-six volunteers (28 men and 8 women; age range, 19–28 yrs) participated in this study. Participants were randomly assigned to 1 of 3 experimental conditions, i.e., each group had 12 participants, and each participant completed only 1 experimental condition. Participants had no cognitive or motor disorders, and were naïve to the visuomotor adaptation task and to the purpose of the experiment. Their dominant hands were determined by the Edinburgh Handedness Inventory [59] : all participants were right handers. They were paid for their time.

Apparatus

Participants sat on a straight-backed chair, while grasping the handle of a robotic manipulandum with their right hand (Phantom Premium 1.5HF, Geomagic, USA). A spring simulated by the device (1.0 N/mm) generated a virtual horizontal plane, on which the handle movement was restricted. A projector was used to display the position of the handle by means of a cursor (8-mm diameter white circle) on a horizontal screen (45 cm × 60 cm), placed 13 cm above the virtual plane and 10–15 cm below shoulder level. Thus, the screen board prevented the participants from directly seeing their arm and the handle. Participants controlled the cursor from a start position (10-mm diameter yellow circle) to a target (10-mm diameter magenta circle), which were also displayed on the screen (Figure 2.1A). After completion of the reach, the device automatically returned the hand and handle to the start position, by applying a spring-like force toward the start position. During this automatic movement, the cursor was extinguished from the screen. Therefore, the participants could concentrate only on the reach toward the target in each trial. The start position was located approximately 25 cm in front of the body, and the distance between the start position and the target was 9 cm. In each trial, the target was randomly chosen from 6 equally spaced positions on a circumference. The start point was always visible. The position and velocity of the handle were recorded with a sampling frequency of 500 Hz for offline analysis.

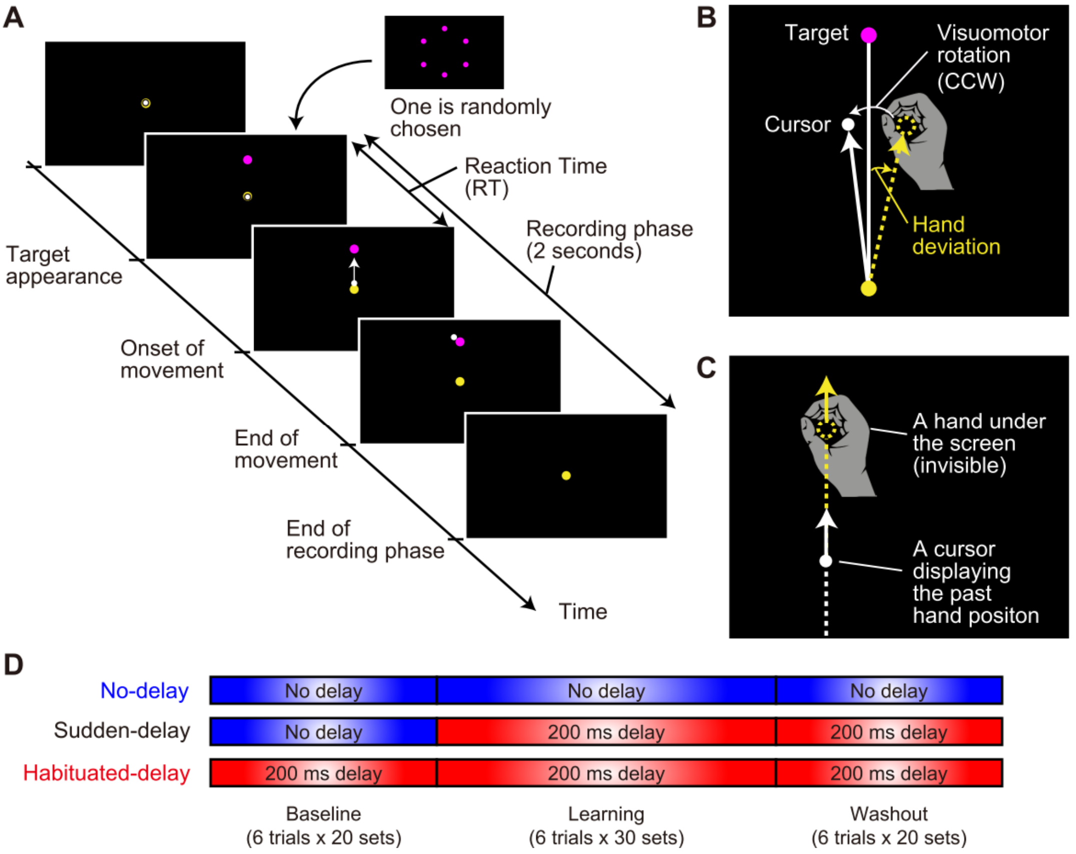


Figure 2.1 Experimental setting.

A. The sequence of events in a trial. **B.** As a visuomotor learning task, we used visuomotor rotation in which the direction of the cursor was rotated from the direction of the hand around the starting position. **C.** In the delayed cursor experiment, the cursor was displayed at the hand position immediately prior (200 ms ago). **D.** Three experimental conditions for the cursor display. In the no-delay condition, there was no artificial delay (cyan box) between the hand and cursor throughout the experiment. A 200 ms delay was artificially introduced (magenta box) for learning and washout sessions in the sudden-delay condition and throughout all sessions in the adapted-delay condition.

Procedures

Instructions. Participants were instructed to move the cursor from the start position to the target with a straight, fast, and uncorrected stroke [54,60], and to initiate the reaching movement as soon as the target was presented. The uncorrected stroke was requested to eliminate any effect of possible differences in online movement correction between the 3 experimental conditions, on motor adaptation performance. Participants were instructed to maintain the hand position where it stopped after each stroke, and not to correct this position, even if the cursor was not on the target.

General procedure. I arranged a series of 6 different target trials into 1 set. Within each set, the order of the 6 target trials was randomized. The entire experiment consisted of 70 sets (420 trials), and lasted for approximately 40 minutes. All participants performed the experiment without a rest break. The sets were organized into 3 sessions: 20-sets baseline session, 30-sets learning session, and 20-sets washout session. In the baseline and washout sessions, the direction of the cursor movement was the same as that of the hand movement. In the learning session, the direction of the cursor movement was rotated around the start position, counterclockwise from the direction of the hand movement (Figure 2.1B). During sets 21–40 (i.e., the first 20 sets in the learning session), this visual rotation angle was gradually increased from 0° to 20°. After the rotation angle reached 20°, it was kept constant for 10 sets until the end of the learning session. Aside from the visuomotor rotation, I inserted a 200-ms delay between the cursor and the hand position, i.e., the position of the cursor displayed the hand position that had occurred 200 ms previously (Figure 2.1C). Once the delay was inserted, it was not removed until the end of the experiment. The timing of the insertion differed according to the experimental conditions (Figure 2.1D).

Conditions. Figure 2.1D shows the time delay between the actual hand position (invisible) and the cursor position (visible) for the following 3 conditions: (1) the no-delay condition, in which the cursor moved synchronously with the hand throughout the experiment; (2) the sudden-delay condition, in which a 200-ms delay was artificially introduced between the hand position and the cursor position (Figure 2.1C) during the learning and washout sessions; and (3) the habituated-delay condition, in which the 200-ms delay was introduced at the start of the baseline session and maintained throughout the experiment; this allowed the participants to become accustomed to the delay before encountering the visual rotation. By comparing the 3 conditions, I was able to evaluate whether motor adaptation was affected either by the delay (no-delay vs. sudden-delay), or by exposure to the delay in baseline sessions (sudden-delay vs. habituated-delay).

It should be noted that, even in the no-delay condition, there was a physical delay between the handle movement and cursor position movement, because of the data processing time of the computer. To measure this delay, the handle and cursor positions were recorded by a high-speed video camera (EX-F1, Casio, Japan) with a sampling frequency of 1200 Hz, while the handle was moved randomly back and forth in a virtual one-dimensional channel. Cross-correlations were calculated between the handle and cursor velocities, and the lag at which the correlation was highest was determined as the physical delay. This physical delay was found to be 60 ms. Nevertheless, for clarity, I hereafter refer to this condition as the no-delay condition, in the sense that there is no delay other than the experimentally unavoidable delay. With respect to the 200-ms delay for the sudden-delay and habituated-delay conditions, the measured physical delay was 259.2 ms, indicating that the additional 200-ms delay was appropriately controlled.

Data analysis

The handle position data were low-pass filtered using a zero-lag fourth-order Butterworth filter (cutoff frequency, 5 Hz). The hand position at peak velocity (PV) was used to calculate the movement direction of the hand for each trial (Figure 2.1B). The clockwise deviation of the hand direction from the target was defined as positive, which reflected visuomotor adaptation (Figure 2.1B). The mean value of the deviations for the 6 target trials in each set was used as a measure of the degree of adaptation. The learning index was defined as the average level of adaptation evident through sets 41–50, where the visuomotor rotation was maintained at 20°. When the participants did not change the movement direction of the hand regardless of visual rotation, the learning index would be 0°. By contrast, if they adjusted their reaching direction clockwise so that the cursor reached the target correctly, the learning index would be close to 20°.

I also calculated the learning rate based on a state-space model:

$$x_{i+1} = x_i + k \cdot e_i + w_i \qquad (1)$$

$$e_i = -x_i + rot_i \qquad (2)$$

where x_i represents the internal state of the system indicating the hand direction at the i^{th} set; e_i represents the cursor error observed at the i^{th} set; k is a learning rate, representing how the internal state is updated according to error information; w represents Gaussian white noise with a mean of 0 and standard deviation of 1; and rot_i is an imposed visual rotation at the i^{th} set. To compare the present result directly with previously reported results, I did not consider the spontaneous memory loss (i.e., the constant coefficient before the term x_i is assumed to be 1; see Kitazawa et al. [3]). Although the learning rate could change across trials (e.g., if the participants gradually adapted to the sudden-delay condition), for simplicity, I assumed that it remained constant throughout the learning and washout sessions. Further, in order to make direct comparisons with previous studies [3,43], I did not include any other parameters (such as the slow and fast components introduced by Smith et al. [61]).

I used the time series of movement error and the hand direction data from sets 21–70 for each participant. The data for individual participants were noisy and often included outliers; hence, I used a 3-point moving average to reduce the effects of these factors. After preprocessing the data, I applied a system identification method to estimate the parameter k based on the state-space model. Given x_i and e_i, the prediction $\hat{x}_{i+1}$ can be calculated using Eq. (1), and the squared prediction error $\left(x_{i+1} - \hat{x}_{i+1}\right)^2$ can be determined. The parameter k was obtained to minimize the sum of the squared prediction error from sets 21–70, by using the prediction error identification method (pem) [62] function in the System Identification Toolbox of MATLAB software (MathWorks, Natick, MA, USA).

For each trial, the reaction time (RT) was calculated as the first time point at which the hand velocity exceeded 30 mm/s (approximately 5% of the peak velocity). The movement distance (MD) was calculated as the distance from the start point to the endpoint, defined as the position at which the hand velocity decreased to <30 mm/s. The movement time (MT) was defined as the time required to reach the endpoint from the RT.

On completion of the trials, I asked the participants verbally if they thought anything unnatural had occurred during the experiment. Even if participants did not mention the rotation or delay, I subsequently asked whether they had been aware of the rotation, or the delay, or both.

Simulation of motor learning

Using a model with identified learning rates for each condition [i.e., Eqs. (1) and (2)], I simulated the experimental task. I repeated the simulation 12 times, and calculated the average and standard deviation of the hand direction.

Statistical analysis

One-way ANOVAs were performed to test for any significant effects of the experimental conditions on the learning index and learning rate. For RT, PV, MD, and MT analysis, the mean ± SD values were calculated for all participants across each session, and two-way ANOVAs were performed to determine the within-subject (session; repeated factor) and between-subject (condition; non-repeated factor) effects. A post hoc Tukey's test was used for multiple comparisons in any analysis where a significant main effect was observed. The statistical significance threshold was set at $P < 0.05$.

2.3 Results

Figure 2.2A shows the data for mean hand deviations from the target (see *Data analysis* and Figure 2.1B for the definition) for the 3 consecutive sessions (baseline, learning, and washout) under each experimental condition (no-delay, sudden-delay, and habituated-delay). In the baseline session, the hand deviations were almost zero, indicating that the participants accurately moved their hands toward the targets. One-way ANOVA revealed no significant effect of experimental conditions on the hand deviations, averaged for the entire baseline session ($P = 0.756$).

I detected a significant effect of experimental conditions on the learning index (no-delay, 15.6 ± 1.6°; sudden-delay, 12.0 ± 2.3°; and habituated-delay, 14.2 ± 1.6°; $P = 0.0002$). A post hoc Tukey's test revealed that the learning index of the sudden-delay condition was significantly lower than that of the no-delay condition ($P = 0.0002$), and also than that of the habituated-delay condition ($P = 0.024$) (Figure 2.2B). These data indicate that the degradation of visuomotor learning caused by delayed visual feedback was alleviated by prior exposure to the delay.

I detected a significant effect of experimental conditions on the learning rate (no-delay, 0.128 ± 0.027; sudden-delay, 0.066 ± 0.020; and habituated-delay, 0.094 ± 0.018; $P < 0.0001$). A post hoc Tukey's test revealed significant differences in the learning rate between all experimental conditions (no-delay vs. sudden-delay, $P < 0.0001$; no-delay vs. habituated-delay, $P = 0.0031$; and sudden-delay vs. habituated-delay, $P = 0.0123$; Figure 2.2C).

Using a simulation based on the identified learning rate values, I successfully reproduced the experimental results (Figure 2.2D). During the first half of the learning session, I observed no clear difference between the experimental conditions, because of the relatively large noise for the small error inputs. However, the difference in hand directions between experimental conditions became more apparent during the second half of the learning session, indicating the validity of the learning index to evaluate variations in motor learning performance between conditions. The simulation model also reproduced the differences in error reduction during the washout session. For direct comparison with the experimental data, I used the simulation data to calculate the learning index, and obtained the following values: no-delay, 15.7 ± 2.1°; sudden-delay, 12.6 ± 2.6°; and habituated-delay, 14.7 ± 2.2°. Two-way ANOVA (condition × simulation/experiment) showed a significant main effect of condition ($P < 0.05$). By contrast, there was no significant main effect of simulation/experiment ($P > 0.05$), or significant interaction ($P > 0.05$), indicating that the behavioral data were well-described by the simulation model.

To eliminate any deliberate or explicit adaptation strategy arising from conscious awareness of the visuomotor perturbation, I imposed the visuomotor rotation not abruptly, but gradually. As anticipated, none of the participants was aware of the visuomotor rotation until the end of the learning session (set 50)—all participants believed that the movement direction of the cursor indicated that of the actual hand position. Three participants thought that a clockwise visuomotor rotation had suddenly been inserted at the beginning of the washout session, because the cursor largely deviated from the target in a clockwise direction. The remaining 33 participants were unaware of the visuomotor rotation throughout the experiment. Thus, I believe that my experimental design successfully eliminated any explicit adaptation strategy arising from conscious awareness of the visuomotor perturbation, at least until the end of the learning session.

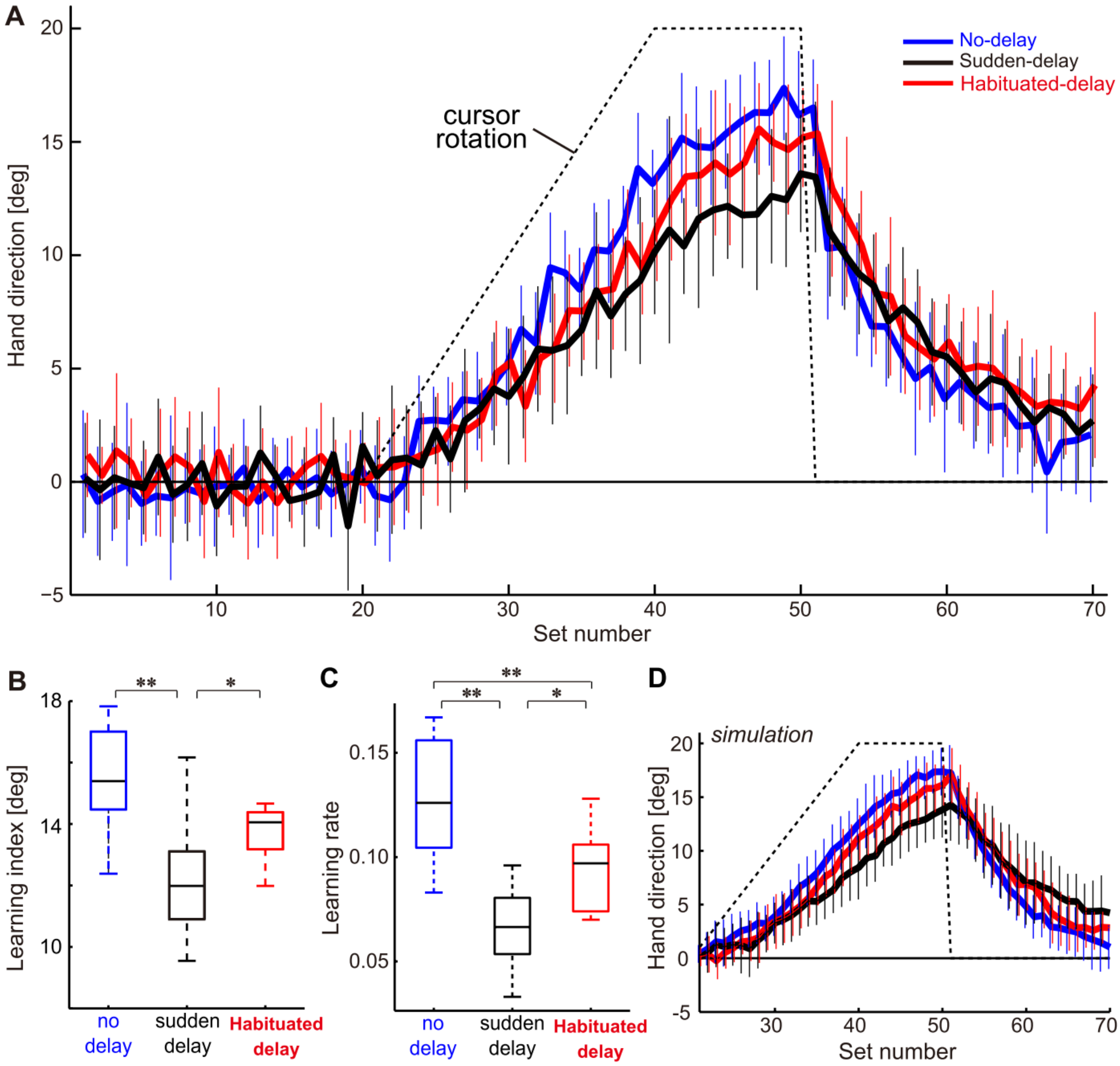
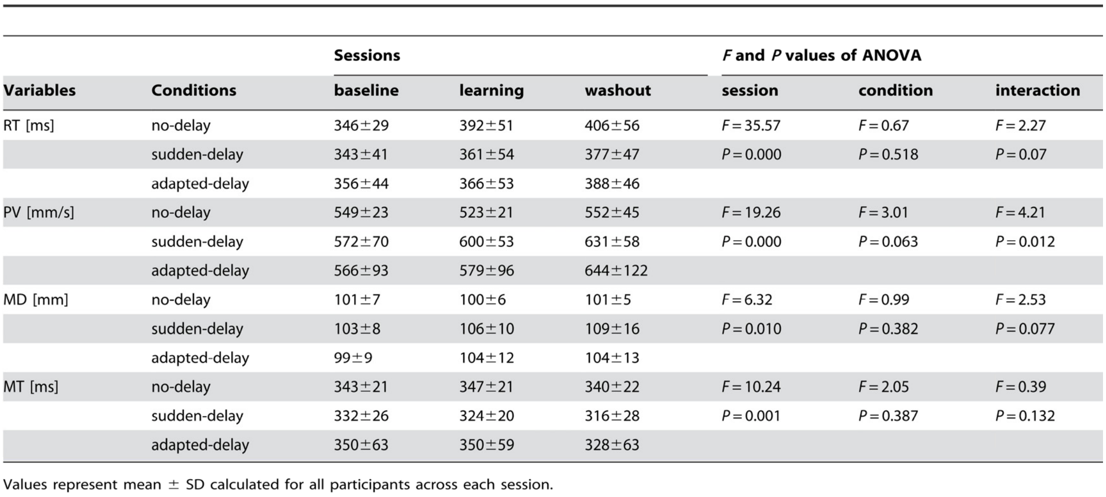


Figure 2.2 Experimental results.

A. Changes in hand directions averaged across all participants (blue, No-delay; black, Sudden-delay; red, Adapted-delay). The broken line indicates the imposed visuomotor rotation. The error bars are the SDs across participants. **B & C.** Learning indices (**B**) and learning rates (**C**) for 3 conditions. The vertical broken lines on the top and the bottom of the box plots represent the minimum and maximum values, the rectangles represent the first–third quartile, and the horizontal bars in the rectangles represent the median of each variable. The asterisks denote a significant difference (* P < 0.05, ** P < 0.01). **D.** The results of simulation with the identified state space model.

To validate the participants' compliance to the protocol requirement stating that they should not correct their reaching movements, I calculated the average reaching trajectories and velocity profiles for the 3 conditions in each session (Figure 2.3A, B). I obtained the reaching trajectories and velocity profiles by the following procedure: after normalizing all movements to a single movement direction and aligning the data with the RTs, I calculated the average of the position and velocity at every sampling time. I observed that the online corrections of reaching movement were small (Figure 2.3A). Indeed, the difference in the hand movement directions calculated at the endpoint and at the peak velocity was ~2°, even during the learning session. All of the velocity profiles were typically bell-shaped, although the PV and the time at the PV differed slightly between the experimental conditions (Figure 2.3B).

Table 1. The statistics of RT, PV, MD and MT.



		Sessions			***F* and *P* values of ANOVA**		
Variables	**Conditions**	**baseline**	**learning**	**washout**	**session**	**condition**	**interaction**
RT [ms]	no-delay	346±29	392±51	406±56	$F = 35.57$	$F = 0.67$	$F = 2.27$
	sudden-delay	343±41	361±54	377±47	$P = 0.000$	$P = 0.518$	$P = 0.07$
	adapted-delay	356±44	366±53	388±46			
PV [mm/s]	no-delay	549±23	523±21	552±45	$F = 19.26$	$F = 3.01$	$F = 4.21$
	sudden-delay	572±70	600±53	631±58	$P = 0.000$	$P = 0.063$	$P = 0.012$
	adapted-delay	566±93	579±96	644±122			
MD [mm]	no-delay	101±7	100±6	101±5	$F = 6.32$	$F = 0.99$	$F = 2.53$
	sudden-delay	103±8	106±10	109±16	$P = 0.010$	$P = 0.382$	$P = 0.077$
	adapted-delay	99±9	104±12	104±13			
MT [ms]	no-delay	343±21	347±21	340±22	$F = 10.24$	$F = 2.05$	$F = 0.39$
	sudden-delay	332±26	324±20	316±28	$P = 0.001$	$P = 0.387$	$P = 0.132$
	adapted-delay	350±63	350±59	328±63			

Values represent mean ± SD calculated for all participants across each session.

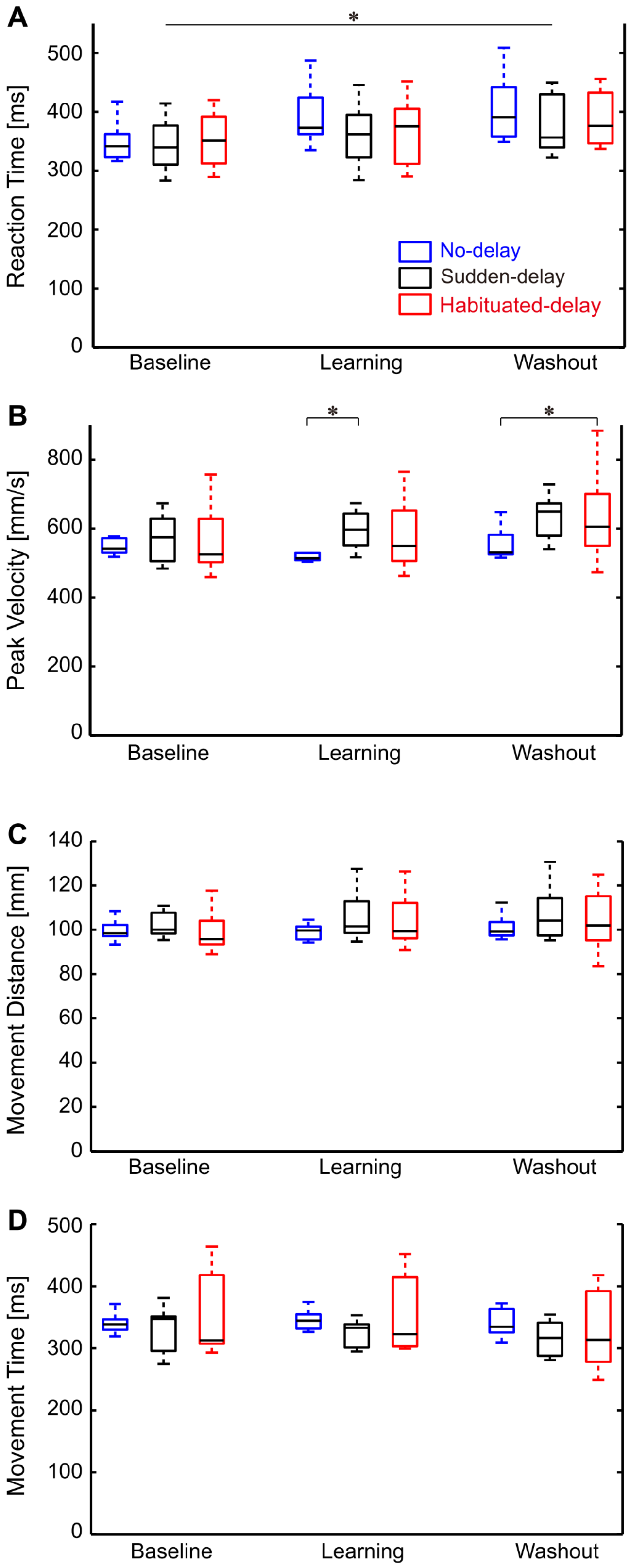


Figure 2.3 The movement parameters. **A.** Reaction time. **B.** Peak velocity. **C.** Endpoint distance. **D.** Reaching duration. The vertical broken lines on the top and the bottom of the box plots represent the minimum and maximum values, the rectangles represent the first–third quartile, and the horizontal bars in the rectangles represent the median of each variable. The asterisks indicate the significant difference (* $P < 0.05$).

The results of the RT, PV, MD, and MT measurements are summarized in Table 3.1 and Figure 2.3. With respect to RT, MD, and MT, two-way repeated-measures ANOVA revealed a significant main effect of session ($P < 0.05$), but no significant main effect of condition ($P > 0.05$) or interaction ($P > 0.05$). Multiple comparison analysis demonstrated a significant difference in RT ($P = 0.001$) (Figure 2.4A), but not in MD or MT ($P > 0.05$), between the baseline and washout sessions.

I observed a significant interaction (session × condition) on PV ($P = 0.012$). Thus, I conducted multiple comparisons between conditions for each session. In the baseline session, I detected no significant difference ($P > 0.05$) between any pair of conditions. In the learning session, there was a significant difference between the no-delay and sudden-delay conditions ($P = 0.017$) (Figure 2.4B) but not between any other pair. In the washout session, there was a significant difference between the no-delay and habituated-delay conditions ($P = 0.0278$) (Figure 2.4B), but not between any other pair. Conditional differences were observed in PV, but not between the sudden-delay and habituated-delay conditions.

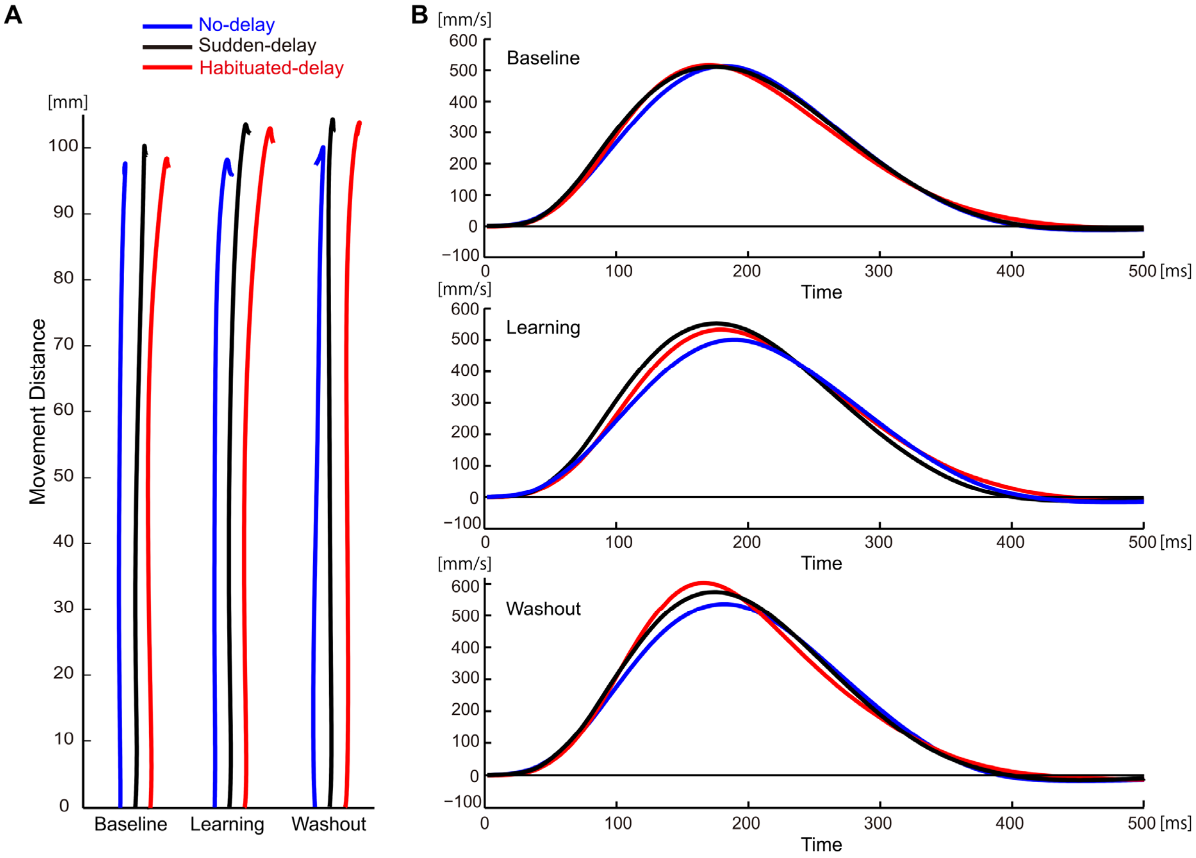


Figure 2.4 Average reaching trajectories and velocity profiles for 3 conditions in each session. **A.** Average reaching trajectories. **B.** Velocity profiles.

2.4 Discussion

Delayed visual feedback was previously shown to degrade prism adaptation [3,43]. Here, I replicated this finding using a gradual visuomotor rotation task. I observed that the learning index and learning rate degraded when a delay was artificially introduced between the hand and cursor positions (i.e., sudden-delay condition) (Figure 2.2). Although it is not clear whether the underlying mechanisms are similar between prism adaptation and adaptation to a visual rotation, the learning rate obtained in my present study (0.128) was similar to those derived previously (0.091 [3,43]). My findings therefore support the validity of the state-space model [Eqs.(1) and (2)]. The de-adaptation during the washout session appeared to be slightly slower for the sudden-delay condition than for the other two conditions (Figure 2.2A), as verified by the simulation result (Figure 2.2D). This finding partially supports my hypothesis that the constant learning rate, which is specific to each condition, persisted throughout the experiment.

Importantly, I also demonstrated that the degradation of motor learning associated with delayed feedback was partially alleviated by prior exposure to the delay (i.e., the learning index and learning rate in the habituated-delay condition were significantly higher than those in the sudden-delay condition; Figure 2.2B, C). Such learning alleviation associated with delayed visual feedback could not be explained by the changes in movement kinematics associated with conditions, because the PV, MD, and MT did not differ significantly between the 3 conditions (Figure 2.4; Table 1).

I considered the possibility that the difference in learning rate between the habituated-delay and sudden-delay conditions reflected the fact that, in the learning session of the habituated-delay condition, participants only had to adapt to the visual rotation, while in the sudden-delay condition, they had to adapt to the visual rotation and habituate to the delay (similar to a dual-task design). Therefore, an alternative interpretation is that when participants first habituated to the visual delay, the difficulty of adapting to the visuomotor rotation was reduced, because more attention was assigned to the rotation adaptation alone. In this case, however, I would expect the learning rate determined by Tanaka et al. [43] to be higher in the habituated-delay condition than in the sudden-delay condition. Given that Tanaka et al. [43] did not observe such a difference, it is unlikely that the dual-task nature was solely responsible for the differences in learning rate observed between my sudden-delay and habituated-delay conditions.

I conclude that motor learning was achieved implicitly at least until the 51st set because all the participants did not notice the gradual rotation. On the other hand, I can say that the cursor delay was explicit and participants in the SD condition noticed it at the 21st set. Recent studies clarified that explicit learning is faster and shows less target error than implicit learning, because explicitness invokes strategic behavior to offset target error [63,64]. If the explicit delay in the SD group had invoked strategic behavior for motor adaptation, it would have improved motor learning in the SD condition. If so, the introduction of gradual delay would probably lower the learning rate in SD and lead to a clearer result for this study. Therefore, the present results cannot be explained by a sudden introduction of cursor delay.

It is interesting to speculate what happens during the period of exposure to visual feedback delay. Psychophysical studies previously demonstrated that, when participants were repeatedly exposed to an artificially introduced 250-ms delay between voluntary actions and sensory consequences, they perceptually combined their voluntary actions with the sensory consequences, and perceived that the delay was shortened by approximately 100 ms [39,40]. Importantly, this finding is compatible with the theory of motor control based on the forward model. In this model, the efference copy of the motor command is processed to predict its sensory consequences. Such sensory prediction is continuously monitored and compared with the actual sensory feedback, and is used to maintain accurate predictions. Thus, perceptual binding has been considered to be caused by the formation of an appropriate temporal association between motor commands and sensory feedback (i.e., recalibration of the feedback delay in the sensorimotor loop). Based on the fact that appropriate associations between motor commands and sensory consequences are important for motor learning, I hypothesized that recalibration of the delay might alleviate the deficits of motor learning associated with delayed visual feedback. My data confirmed the validity of my hypothesis.

Tanaka et al. [43] also examined the effects of repetitive exposure to a visual feedback delay on the learning rate of prism adaptation. They demonstrated that repetitive exposure did not induce any positive effects to motor learning, although it did shorten the subjective experience of the delay. It was concluded that the physical delay, but not the subjective delay, determined the learning rate in prism adaptation.

In contrast, I observed that the learning rate was not fully determined by differences in the physical visual feedback delay. This contradiction can be explained by 2 factors. Firstly, in my study, the cursor and target locations were continuously displayed during movement. By contrast, Tanaka et al. [43] eliminated visual feedback during movement, and allowed participants to view the target and final static position of the hand only after completion of the reach. Continuous feedback and feedback after movement were previously shown to result in considerably different outcomes of motor learning; continuous feedback facilitated visuomotor learning to a visual rotation [65-67]. Furthermore, according to the optimal feedback control theory [52], the central nervous system continuously estimates the current location of the hand, by combining sensory feedback signals with predicted signals from the forward model [9]. It uses this estimate repeatedly to correct ongoing movements [50,51]. Thus, when continuous visual feedback is available, as in the present experiment, the central nervous system has the opportunity to compare sensory predictions with actual feedback at every time point during movement. This may facilitate the remapping of appropriate temporal associations between motor commands and sensory consequences during the exposure to the delay, eventually contributing to facilitation of visuomotor learning. Using a gradual visuomotor rotation task, Izawa and Shadmehr [68] demonstrated that, when the cursor was continuously displayed, participants perceived that the hand position at the end of the reach was at the cursor position. Conversely, when the cursor trajectory was not displayed, the perceived hand position at the end of the reach remained near the actual hand position. This finding indicates that continuous feedback is important for associating the hand movement with the cursor movement.

Secondly, in my study, I gradually increased the cursor rotation throughout the experiment. By contrast, Tanaka et al. [43] used a prism that necessarily imposed an abrupt visual perturbation. Motor adaptation is known to be achieved through at least 2 processes—a high-level strategic process and a low-level implicit process [54,58]. In the previous prism experiment [43], the prism caused an abrupt perturbation, participants could not help but explicitly notice the error during the first trial of the learning session, making it difficult entirely to exclude the effect of the strategic process. By contrast, in the present study, I succeeded in eliminating the strategic process, such that none of the participants were aware of the visuomotor rotation until the end of learning session (set 50). The small change (~25 ms) in the RT from the baseline to the learning session (Table 3.1) likely rules out the possibility of an explicit strategy, because Saijo et al. [69] reported a significantly longer reaction time (~ 100 ms) for an abrupt visual rotation than for a gradual visual rotation. They concluded that awareness of the presence of a visual rotation or discrepancy between the hand and cursor led to an increase in the reaction time.

It is important to note that the neural basis of learning in response to abrupt and gradual perturbations is most likely distinct. Gradual introduction of either visual or force perturbations was previously shown to result in larger aftereffects [70] and enhanced retention [71,72] following learning. The generalized pattern of adaptation differed according to whether the perturbations were introduced abruptly or gradually [73,74]. Surprisingly, cerebellar patients were able to adapt to a force field, even when it was gradually introduced [75]. Thus, I appear to have evaluated different aspects of motor learning from those investigated by Tanaka et al. [43]. This may further explain the observed discrepancies in results between the 2 studies.

Conventionally, theories of motor learning have assumed that learning proceeds in proportion to error [76,77]. Recently, however, an increasing number of studies have suggested that learning depends on the task relevance of error, and on the strength of the internal association between actions and their sensory feedback [78,79,60,80-84]. When perturbations are either too large or very transient, the central nervous system regards these errors as irrelevant to our own actions, and weakly adapts to them [78,81,83,84]. In a previous study of bimanual movements, Kasuga et al. revealed that motor learning was affected by the strength of the association between each limb's feed-forward movement controller (i.e., internal model) and visual feedback, and that this could be manipulated by varying the location of the visual feedback [80]. In addition to these findings in the *spatial* domain, *temporal* associations between actions and sensory feedback have also been shown to be important. The attenuated adaptation to visuomotor rotation observed in rhythmic movements as compared to discrete movements was reported to be caused by an erroneous association of error information with irrelevant motor commands, which are temporally close to relevant motor commands [79,60]. In the present study, I observed that visuomotor adaptation under delayed feedback conditions was alleviated by prior temporal binding between actions and their sensory feedback, thus further indicating the importance of appropriate temporal associations. However, this effect may be limited, because prior habituation to delayed visual feedback only partially resolved the deficit of motor learning (Figure 2.2C). In future studies, I aim to elucidate whether complete habituation to the delay is able fully to resolve the deficit, or whether the absence of delay in visual feedback is particularly beneficial to motor learning.

Chapter 3

Habituation to feedback delay restores degraded visuomotor adaptation by altering both sensory prediction error and the sensitivity of adaptation to the error

The experiment in chapter 2 revealed that the degradation of visuomotor learning caused by delayed visual feedback was alleviated by prior exposure to the delay. This result indicates that the temporal association between the motor plan and its consequence is important, and the association could be obtained through prior exposure in the previous study. This result is consistent with the perceptual binding between motor command and its consequent feedback (Figure 1.14) [39,40].

I argued in the Discussion session in the last chapter that repeated exposure to the delayed cursor could have increased the association with sensory feedback like intentional binding. However, the previous result could also be explained by the sensory prediction hypothesis, in which the sensory prediction (smith predictor) changed through exposure to a delay.

In this chapter, I conducted an experiment, in which these two hypotheses lead different results. And the result illustrates that both of them contribute to the alleviation.

3.1 Background

How the brain associates an action with its sensory consequence is crucial to sensorimotor learning. It is widely accepted that the brain predicts the sensory consequence of a motor command using a predictive model of the motor apparatus (i.e., internal forward model) before the actual sensory feedback signals become available [82,9]. The forward model is considered to play an important role in achieving fast and accurate control of movement without depending on delayed sensory feedback[49,29,48,47]. To maintain accurate prediction by the forward model, the brain must update the forward model according to the sensory prediction error between the predicted and actual sensory consequences [55,54,53].

In this motor adaptation scheme, the temporal relationship between actions and their sensory consequences is important to evaluate the sensory prediction error accurately [79]. Kitazawa et al. (1995), by using prism adaptation during reaching movements, showed that motor adaptation is degraded when the location of the reaching endpoint is displayed with an artificial delay [3]. However, we have the ability to perform motor actions even in the presence of a feedback delay that may change due to several factors (e.g., body growth or manipulating tool). Furthermore, recent psychophysical studies have demonstrated that when subjects experienced a constant delay between an action and its sensory consequence, the delayed sensory consequences came to be perceived as shifted backwards in time towards their actions [39,40,11,41,42]. Considering these points, it is reasonable to assume that the sensorimotor system can also habituate to a wide variety of delays.

Indeed, I showed in chapter 2 that, when visual feedback of the hand position is provided by a cursor throughout an entire reaching trajectory, the decreased rate of motor adaptation to a visual rotation caused by delayed feedback is alleviated by prior repeated exposure to the delayed cursor [85]. This result suggests that the ability of visuomotor adaptation can be influenced by habituation to the delayed feedback.

What kind of mechanism underlies this result, then? As we all know, the motor learning process is not such a simple one, and various mechanisms operate to achieve any type of learning. Recent computational studies have suggested that when a certain amount of sensory prediction error is experienced, the motor command for the subsequent trial is corrected in proportion to the amount of this sensory prediction error [46]. Thus, one possible factor for the alleviation is that repeated exposure to the delayed cursor increases the proportional coefficient, or the sensitivity (association) of adaptation to the sensory prediction error, as I demonstrated in my previous study [85].

However, habituation to the delayed-cursor condition can alter not only the sensitivity but also the degree of the sensory prediction error itself. Figure 3.1A-D illustrates the positions of the actual hand and cursor when the predicted hand position reaches the middle position. Before habituation to the delayed-cursor condition, the predicted hand is located at almost the same position as the actual hand (Figure 3.1A, B). Here, in order to explain the possible changes in the sensory prediction error with the cursor delay, I assume that when visual rotation is imposed, the sensory prediction error is a lateral deviation from the predicted hand position to the cursor. If the cursor is suddenly delayed (i.e., before habituation), the sensory prediction error caused by the visual rotation should be smaller than that of the *no-delay condition* (Figure 3.1B vs. Figure 3.1A). On the other hand, after habituation to the delay, the predicted hand position is shifted toward the past hand position (Figure 3.1C, D). This shift could recover the amount of sensory prediction error for the delayed cursor condition (Figure 3.1D vs. Figure 3.1B). At the same time, however, the sensory prediction error could be larger than reality if the delay is removed suddenly (Figure 3.1C vs. Figure 3.1D).

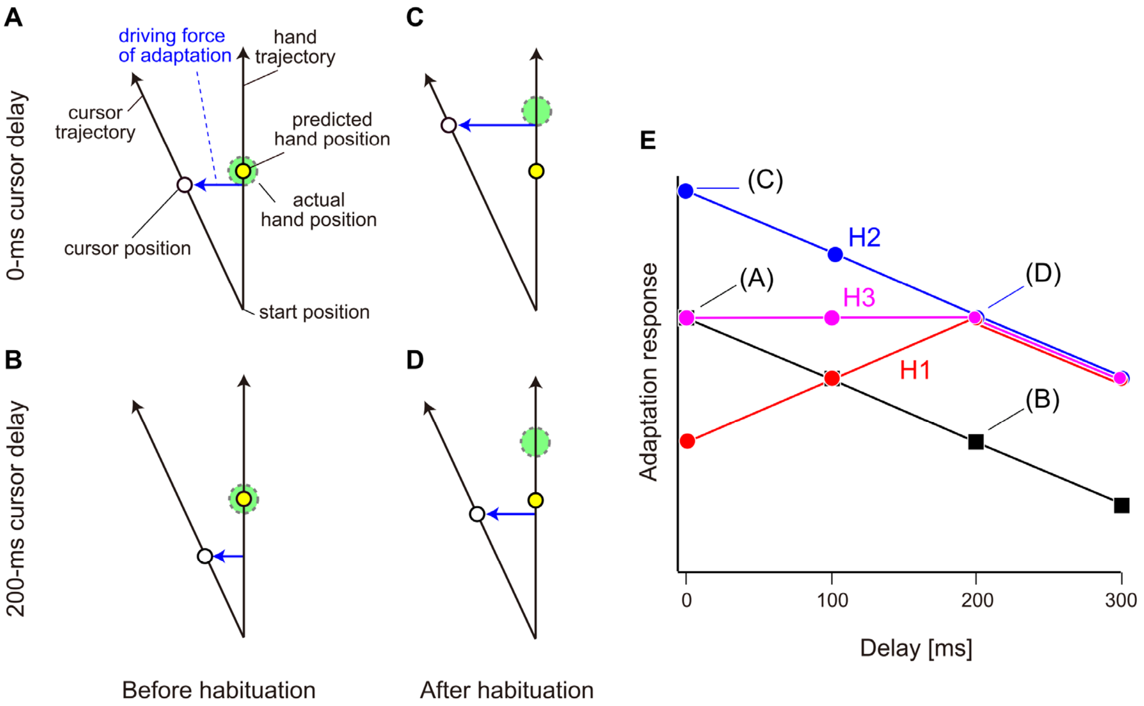


Figure 3.1 Schematic representation of the hypotheses.

A. We assume that the sensory prediction error represented by lateral deviation from the hand position predicted by the forward model to the cursor is a driving force of adaptation to a visual rotation. **B.** The sensory prediction error decreases when a cursor delay of 200-ms is introduced. In **A** and **B**, the predicted hand position (broken circle) is identical to the actual hand position (continuous circle). However, if the habituation to delayed cursor of 200-ms shifts the predicted hand position to the delayed position (**C** and **D**), the amount of sensory prediction error is restored when the cursor is displayed with the same 200-ms delay (**D**) and it rather increases when the cursor is displayed with no-delay (**C**).

E. When no visual feedback delay is introduced, the adaptation response to the visual rotation provided with a certain delay should gradually decrease with the increase in delay. Three hypotheses predict different patterns of adaptation response after habituation to a visual feedback delay of 200-ms. Hypothesis H1 predicts the response is maximal at 200-ms delay (red), while the H2 predicts the response has a monotonically decreasing function (blue), and H3 predicts an intermediate response of H1 and H2 (magenta).

Thus, I have 3 alternative hypotheses, namely, increase in the sensitivity (hypothesis H1), shift of the predicted hand position (hypothesis H2), or both (hypothesis H3). To test these hypotheses, I systematically examined the adaptation response of reaching movements to visual rotation applied with varying delays after repeated exposure to 0-ms (*no-delay condition*) or 200-ms delayed cursor (*delay condition*). In the *no-delay condition*, as shown in previous studies [85,3], all 3 hypotheses predicted the same outcome: the adaptation response should gradually decrease with the delay time (Figure 3.1E; black). In the *delay condition*, however, the 3 hypotheses predicted different patterns. Hypothesis H1 predicted that the adaptation response is the maximum when visual perturbation is applied at a 200-ms delay, and the response to the 0-ms, 100-ms, and 300-ms delay becomes minor, because the sensitivity of visuomotor adaptation is optimized to this delay (Figure 3.1E; red). Hypothesis H2 also predicted that after habituation to the delayed cursor, the adaptation response to the visual perturbation provided with a 200-ms delay is recovered (Figure 3.1E; blue) because the sensory prediction error is recovered (Figure 3.1D vs. Figure 3.1B). However, after the shift of the predicted hand position by habituation to the delay, the sensory prediction error is still greatest for the 0-ms delay (Figure 3.1C) and gradually decreases with increasing delay (Figure 3.1C and D). Therefore, I should observe a monotonic decrease in the adaptation response with increasing delay (Figure 3.1E; blue). Hypothesis H3 predicts an intermediate adaptation response (Figure 3.1E; magenta). I investigated which alternative hypothesis was likely to explain the data.

3.2 Methods

Participants

Twenty-seven volunteers (15 men and 12 women; age range, 19–30 years) participated in this study. Participants had no cognitive or motor disorders, and were naïve to the visuomotor rotation task and purpose of the experiment. Their dominant hands were determined by the Edinburgh Handedness Inventory [59]; all participants were right-handed. Further, they were paid for their time. This study was conducted in accordance with the Declaration of Helsinki and the experimental procedures were approved by the ethics committee of the Graduate School of Education at the University of Tokyo. Written informed consent was obtained from all participants prior to performing the experiments.

Apparatus and motor task

Participants sat on a straight-backed chair while grasping the handle of a robotic manipulandum with their right hand (Phantom Premium 1.5HF, Geomagic, USA). A spring simulated by the device (1.0 N/mm) generated a virtual horizontal plane on which the handle movement was restricted. A projector was used to display the position of the handle with a white circle cursor (diameter, 8 mm) on a horizontal screen (size, 45 cm × 60 cm) placed at 13 cm above the virtual plane and 10–15 cm below the shoulder level. Thus, the screen board prevented the participants from directly seeing their arm and the handle. Before each trial, participants were required to hold the cursor in its starting position (10-mm diameter, yellow circle; Figure 3.2A). After a 2-s holding time, a target (10-mm diameter, magenta circle) appeared at 30° counter-clockwise from straight ahead (only one target was used in this study), signaling the participant to initiate a reaching movement. The starting position was located approximately 25 cm in front of the body. The distance between the starting position and the target was 10 cm. Participants were required to move the handle with a peak velocity in the range between 350 to 550 mm/s. A warning message appeared on the screen if the movement velocity of the handle rose above ("Fast") or fell below ("Slow") this threshold value. After the completion of each trial (i.e., after the cursor stopped), the handle was automatically moved back to the starting position by the manipulandum; during this time, the cursor disappeared and remained invisible until the handle reached the starting position. Visual feedback of the cursor during the reaching movement was always provided, except in the probe trials. The starting position was always visible. The target was extinguished after the reaching movement was completed. The position and velocity of the handle were recorded with a sampling frequency of 500 Hz for offline analysis.

Instructions

Participants were instructed to move the cursor from the start position to the target with a straight and uncorrected stroke [54,60], and to initiate the reaching movement as soon as the target appeared. After each stroke, they were instructed to maintain the hand position where it stopped and not to correct the position even if the cursor was not on the target. Such uncorrected strokes were adopted to eliminate the possible effect of online correction of the current trial's movement to the adaptation response in the next trial (The absence of online correction was confirmed: I did not observe a significant amount of correction in the angular position of the hand relative to the starting position at its peak velocity and at the movement offset). No performance-based rewards such as money or sounds were provided after each trial.

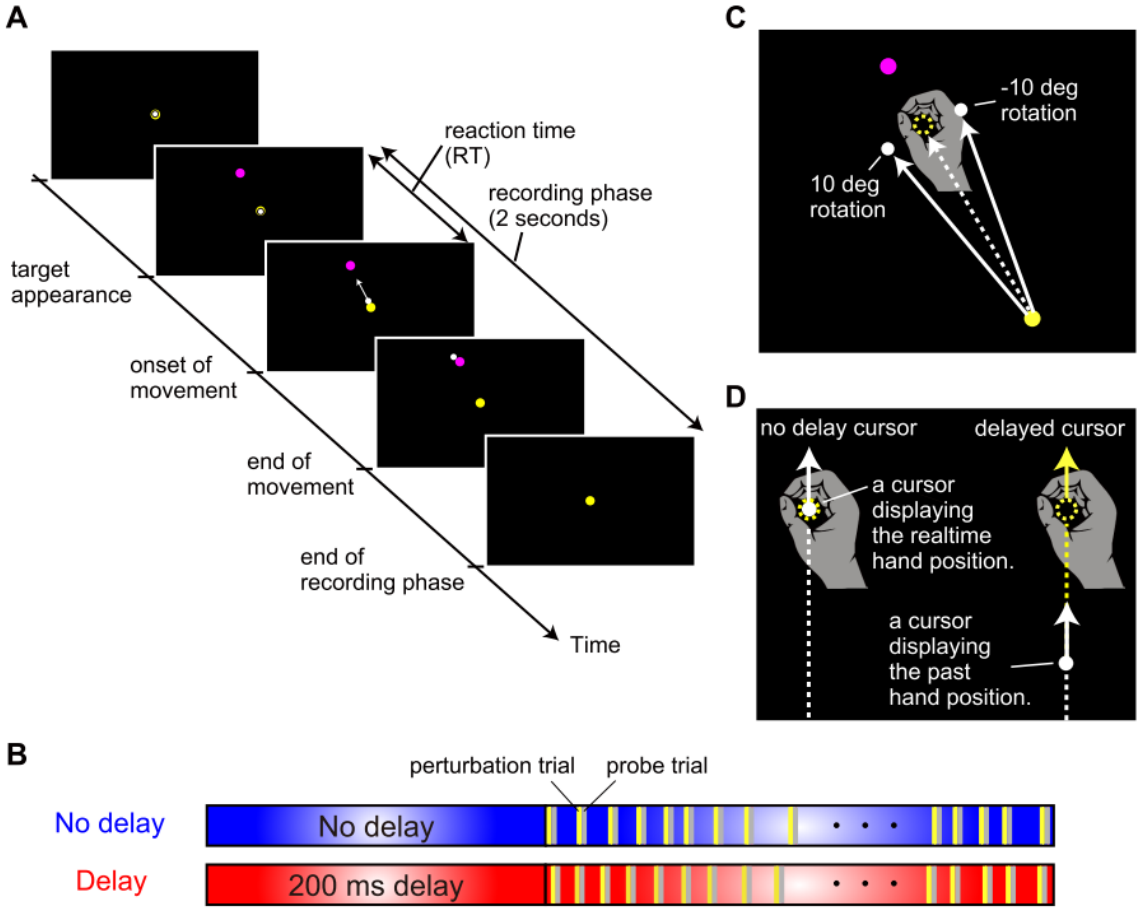


Figure 3.2 Experimental setting.

A. The sequence of events in a trial. **B.** Two experimental conditions for the cursor display. In the *no-delay condition*, there was no artificial delay (blue box) between the hand and cursor in the simple reaching task. In the *delay condition*, there was an artificial delay of 200 ms between the hand and cursor display of simple reaching. **C.** Visuomotor rotation. The direction of the cursor was rotated from the direction of the hand around the starting position clockwise or counterclockwise at 10°. **D.** Types of cursors. An artificial delay between the hand and cursor display was chosen from 0 ms, 100 ms, 200 ms, or 300 ms.

Experimental conditions

To examine the mechanism by which the motor learning system uses for the habituation to an artificially introduced delay, the present study systematically investigated the adaptation response to a visual perturbation applied with a varying delay in the *no-delay condition* and *delay condition* (Figure 3.2B).

In the *no-delay condition*, participants performed normal reaching movements in which no delay was introduced between the actual hand and cursor movements. After the initial 100 trials for habituation to the no-delay cursor, visual perturbation trials were randomly interleaved once for every 5–6 trials during the subsequent 180 trials (see yellow bars in Figure 3.2B). In the perturbation trials (24 trials), the cursor's movement direction from the start position was rotated by 10° clockwise (12 trials) or counterclockwise (12 trials) from the hand's movement direction (Figure 3.2C). In the perturbation trials, visual feedback delay was also manipulated with a delay of 0-, 100-, 200-, or 300-ms that was artificially introduced between the cursor and the hand position, i.e., the position of the cursor displayed the hand position that had occurred 0, 100, 200, or 300 ms before, respectively (Figure 3.2D). Thus, the 24 perturbation trials consisted of 3 trials for each of the 8 cursor manipulations (2 rotation directions × 4 cursor delays). If this visual perturbation induced adaptation, then participants would move the handle in the opposite direction (i.e., aftereffect) in the next trial (probe trial; see gray bars in Figure 3.2B). I quantified the aftereffects by measuring the movement direction during the probe trials (see the data analysis section below). Further, during the probe trials, no visual feedback of the cursor was provided to remove the effect of online visual feedback. The experimental settings of the trials other than the perturbation and probe trials (blue area in Figure 3.2B) were the same as those of the initial 100 trials.

In the *delay condition*, the participants performed a normal reaching task in which a 200-ms delay was introduced between the hand and cursor movements. After the initial 100 trials for habituation to the 200-ms delayed cursor, visual perturbation trials were randomly interleaved in the same manner as that during the *no-delay condition*. The perturbation and probe trials were the same as those observed during the *no-delay condition*. The experimental settings of the trials other than the perturbation and probe trials (red area in Figure 3.2B) were the same as those for the initial 100 trials of the *delay condition.*

All participants were tested in both the *no-delay* and *delay conditions*. Participants were randomly assigned to 2 groups. The first group (14 participants) performed the *no-delay condition* first, whereas the second group (13 participants) performed the *delay condition* first. They performed each condition within approximately 25 min without a break. Between the 2 conditions, participants took a rest for 10–20 min according to their fatigue.

It should be noted that, even in the *no-delay condition* (Figure 3.2D left), there was actually a 60 ms system delay between the handle movement and cursor position movement because of the data processing time of the computer (see chapter 2.3 Methods). Nevertheless, for clarity, I refer to this cursor as the *no-delay condition* in the sense that there is no additional delay other than the experimentally unavoidable delay, and the delay values of 100, 200, and 300 ms represented the additional delays (e.g., 100 ms indicated 160-ms delay).

Data analysis

As a performance measure, I calculated the hand movement direction for each trial as the direction from the starting position to the actual hand position at the peak velocity during the reaching movement. Baseline of the movement direction was calculated for each participant and for each condition by averaging the movement directions of 10 trials from 90th to 100th trial (the last 10 trials of the habituation trials).

I quantified the adaptation response to visual perturbation by measuring the aftereffect in the probe trial. The magnitude of aftereffect was calculated as the movement direction in the probe trial subtracted by the baseline value. The sign of the aftereffect was defined positive if the movement direction was opposite to the visual perturbation: the compensatory direction for the observed error. The data for the 2 perturbation directions was pooled. In cases when the reaching in the previous perturbation trial was “FAST,” “SLOW,” or deviated more than 10° from the target direction, I excluded the probe trial from data analysis. On an average, 21.2 ± 2.2 trials out of 24 (approximately 90%) in each *delay* or *no-delay condition* (6 trials × 4 amount of delay) satisfied the criteria.

In addition to the movement direction, the visual perturbation may also affect other movement parameters such as reaction time (RT) and peak velocity (PV) in the next probe trial. The RT and PV were also calculated for each probe trial. The RT was calculated as the first time point at which the hand velocity exceeded 5% of the peak velocity of that trial.

Statistical analysis

Two-way repeated measures analysis of variance (ANOVA) was performed on the aftereffect, RT, and PV to examine the effects of cursor delay and condition. Ryan's multiple comparison tests and one-way repeated measures ANOVA were used for post-hoc analyses. The statistically significance threshold was set at $P < 0.05$.

3.3 Results

Figure 3.3 shows the adaptation responses (i.e., the aftereffect in the probe trials) to the perturbations applied with the 4 types of delays (i.e., 0-, 100-, 200-, and 300-ms delay) under the 2 experimental conditions (blue, *no-delay condition*; red, *delayed conditions*). Two-way ANOVA with repeated measures revealed a significant interaction (condition × cursor delay, P = 0.006, F(3,78) = 4.483), indicating that the effect of delay on adaptation response depended on whether subjects were habituated to 0- or 200-ms delay in advance.

The results of the *no-delay condition* showed that the aftereffect was the largest when the perturbation was applied with a 0-ms delay and gradually decreased as the delay increased (blue squares in 3.3). Statistical analysis confirmed this observation; one-way repeated measures ANOVA showed a significant effect of delay (P = 0.004, F(3,156) = 4.586), and the post-hoc multiple comparison test showed significant differences between the 0- and 200-ms delays (P = 0.003) and between the 0- and 300-ms delays (P = 0.009) (Figure 3.3).

How were these adaptation responses influenced when they were measured after habituation to the 200-ms delay? If the sensitivity of adaptation to a sensory prediction error is increased after habituation to the 200-ms delay and only this factor affects the aftereffect (i.e., H1), then the adaptation response should be recovered during a 200-ms delay and peak when visual rotation is applied with the habituated 200-ms delay (Figure 3.1; red). On the other hand, if the sensory prediction error itself is increased after habituation and only this factor affects the aftereffect (i.e., H2), then the adaptation responses should be recovered in the 200-ms delay, and the feature that the adaptation responses gradually decays with increasing delay (i.e., they are largest for 0-ms delay) should remain.

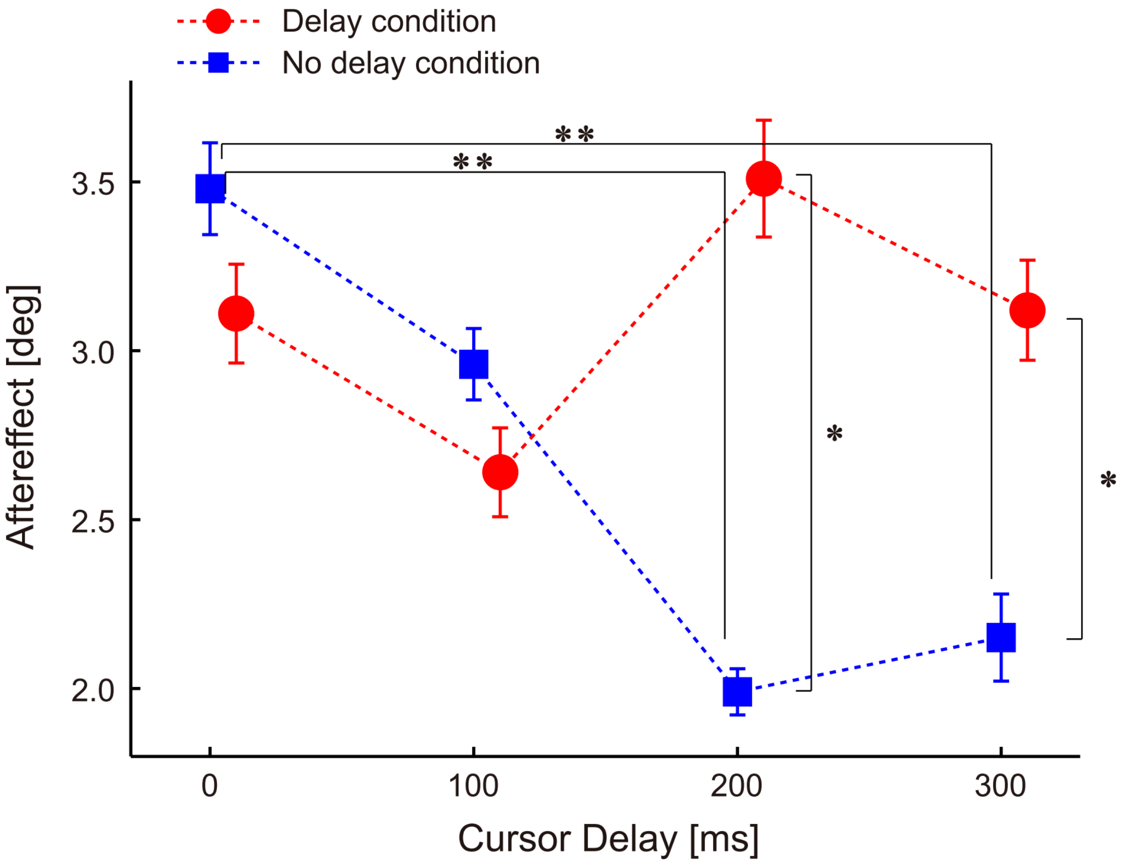


Figure 3.3 Aftereffect of 10 or -10 deg visuomotor rotation.

Data are sorted according to the cursor delay in their previous perturbation trials. The double asterisks illustrate the significant difference between cursor delays revealed by Ryan's multiple comparison test conducted for the aftereffects in the *no-delay condition*. The single asterisks illustrate the significant main effect of condition revealed by one-way repeated measures ANOVA conducted for each cursor delay. Error bars indicate standard error.

Although the aftereffect for the 200-ms delay was larger in the *delay condition* than in the *no-delay condition* ($P = 0.001$, $F(1,104) = 11.286$) as both hypotheses predicted (Figure 3.3), the results were not completely compatible with these hypotheses. There was no significant difference in the aftereffect for the 0-ms delay between the conditions ($P = 0.418$, $F(1,104) = 0.661$) (red circles in Figure 3.3), which was contrary to ideas that the aftereffect should peak at the 200-ms delay (i.e., H1) and that the aftereffect should be largest at the 0-ms delay (i.e., H2). The results of one-way repeated measure ANOVAs also contradicted both hypotheses; the results of the analyses showed no significant effect of delay after habituation to the *delay condition* ($P = 0.322$, $F(3,156) = 1.174$), indicating that there was no significant peak at the habituated 200-ms delay.

In my experiment, each participant performed the *delay* and *no-delay condition* successively. The effect of the condition order was unlikely to affect the results. To examine the effect, I analyzed the aftereffect of *no-delay condition* obtained from those who performed *no-delay condition* first ($N = 14$) and that of *delay condition* obtained from those who performed the *delay condition* first ($N = 13$). The pattern of the relationship between the aftereffect and the level of the delay was similar to the pattern obtained from the data combined (Figure 3.3). The aftereffect for the 200-ms delay was significantly larger for the *delay condition* than for the *no-delay condition* ($P < 0.001$, $F(1,100) = 14.427$), but no significant effect of delay was observed for the *delay condition* ($P = 0.0659$, $F(3,75) = 2.501$).

Visual perturbations might also affect other movement parameters such as RT and PV in subsequent probe trials. Two-way ANOVA with repeated measures on RT showed a significant main effect of cursor delay ($P < 0.001$, $F(3,78) = 6.899$), but no significant main effect of condition ($P = 0.618$, $F(1,26) = 0.256$) or interaction (condition × cursor delay, $P = 0.462$, $F(3,78) = 0.866$). The multiple comparisons across cursor delays showed a significant difference between the no-delay and the 300-ms delay (P = 0.042; the double asterisk in Figure 3.4A), indicating that visual perturbation applied with a 300-ms delay made the next movement take more time to initiate.

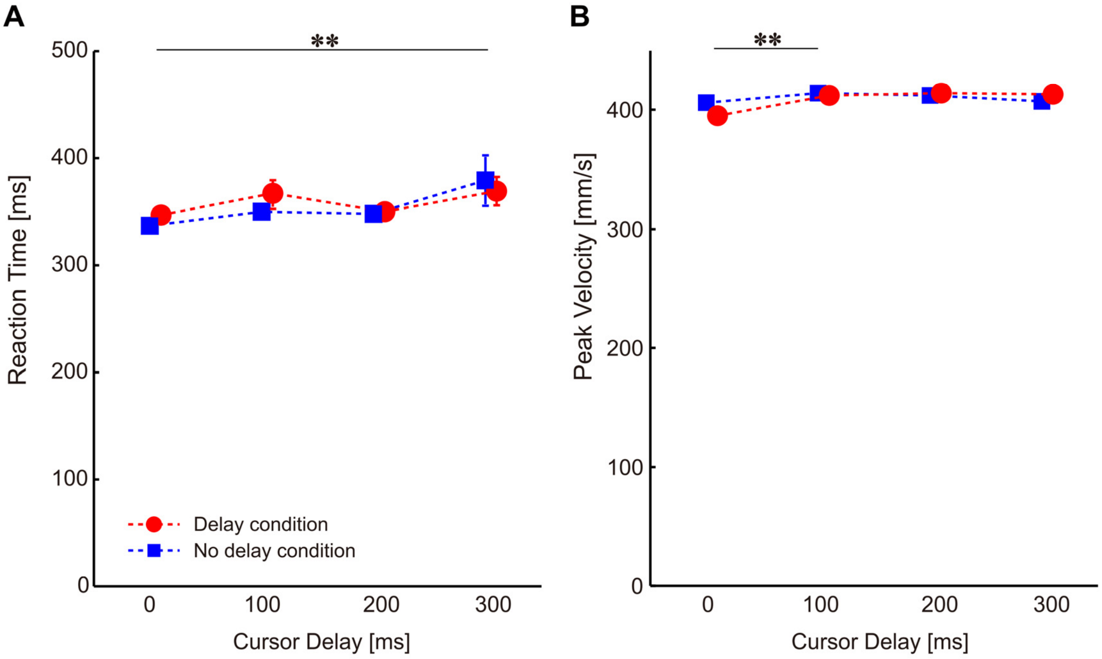


Figure 3.4 Changes in the movement parameters throughout the experiments. **A.** Reaction time. **B.** Peak velocity. Data are sorted according to the cursor delay in the previous perturbation trials. The double asterisks illustrate the significant difference between cursor delays revealed by Ryan's multiple comparison tests. Error bars indicate standard error.

Two-way ANOVA with repeated measures on PV revealed a significant main effect of cursor delay (P = 0.007, F(3,78) = 4.360), but no significant main effect of condition (P = 0.744, F(1,26) = 0.109) or interaction (condition × cursor delay, P = 0.092, F(3,78) = 2.222). The multiple comparison across cursor delay showed a significant difference between the no-delay and the 100-ms delay (P = 0.0498; the double asterisk in Figure 3.4B), indicating that visual perturbation applied with a short delay made the next movement faster.

These changes in RT and PV (gaps of less than 40 ms and 20 mm/s) were very small when compared with the large difference in RT (approximately 200 ms) and PV (approximately 50 mm/s) observed when visuomotor rotation was abruptly applied [69]. I conclude that the RT and PV differences according to the cursor delay were not sufficient to explain the visuomotor aftereffect shown in Figure 3.3.

I also noted the reaching duration in the baseline trials under each condition, namely, 462 ± 24 ms for the *no-delay*, 476 ± 25 ms for the *delay condition*. For each of calculation, the reaching duration was calculated as the time until the hand velocity exceeded 5 % of the peak velocity of that trial. In 200-ms or 300-ms delayed cursor trials, a reaching duration shorter than 500 ms showed that the cursor was still moving halfway even when the reaching finished.

3.4 Discussion

When a novel environment causes a discrepancy between the sensory prediction and actual sensory consequence, the sensory prediction error is used to correct the forward model [46]. Thus, in this motor learning scheme, the temporal relationship between the predicted and actual sensory consequences is important to accurately evaluate the sensory prediction error [79]. As represented in tool manipulation, temporal relationships may vary, raising the suggestion that the brain can manage variable delays during motor learning. Contrary to this expectation, Tanaka et al. (2011) showed that even after participants habituated to a situation in which the endpoint of a reaching movement is visually provided with a certain amount of delay, the degradation of motor adaptation caused by feedback delay (see Kitazawa et al. 1995 [3]) was never restored. I presumed that the absence of a beneficial effect was due to the method of displaying the movement error. A recent study [68] showed that sensory prediction is not completely altered when only the endpoint is displayed (i.e., the forward model is not updated); rather, it is altered when the feedback of the entire movement path is provided. In accordance with this presumption, I recently succeeded in showing that after repeated exposure to the delayed cursor, the degraded motor adaptation of reaching movements is recovered [85], which indicates the ability of the motor learning system to adjust to the feedback delay variability.

Nevertheless, there are still several possibilities to explain this alleviation of visuomotor adaptation. As described in the Introduction, I raised 3 alternative hypotheses (H1, H2, and H3). This study was designed to examine which hypothesis could explain the data most appropriately. I systematically investigated how the adaptation response to visual rotation during reaching movements was dependent upon the amount of visual feedback delay after participants were habituated to either the 0-ms (*no-delay condition*) or the 200-ms delay (*delay condition*). In the *no-delay condition*, the adaptation response (the aftereffect in the probe trial subsequent to the visual perturbation trial) should gradually decrease with increasing visual feedback delay as shown in previous studies [85,3,43]. This was confirmed by the data in the *no-delay condition* of the present study (Figure 3.3).

In the *delay condition*, the 3 hypotheses predict different patterns of the dependence of the adaptation response on the amount of visual feedback delay. Hypothesis H1 assumes that repeated exposure to a certain amount of feedback delay increases the sensitivity of the visuomotor adaptation to a certain amount of error. In this case, the adaptation response should be maximal when the feedback delay is the same as the habituation period (i.e., 200-ms delay in the red; Figure 3.1E). Conversely, hypothesis H2 predicts that the repeated exposure to a certain amount of feedback delay simply shifts the predicted hand position by forming an internal model of feedback delay much like a mechanism of Smith predictor [7]. This shift contributes to the recovery of the degraded adaptation response to the visual feedback provided with 200-ms delay, because a larger sensory prediction error is experienced during the movement (Figure 3.1A vs. 3.1D). However, since the sensory prediction error experienced during the movement should be larger as the feedback delay is smaller (Figure 3.1C vs. 3.1D), I should observe a monotonic decrease in the adaptation response with the increase in delay (Figure 3.1E; blue). The hypothesis H3 that both mechanisms of H1 and H2 are involved predicts the pattern of the adaptation response that is the intermediate of that of H1 and H2 (Figure 3.1E; magenta).

The results of the present study demonstrate that the adaptation response to the visual rotation imposed with 200-ms delay increased in the *delay condition* as compared to that of the *no-delay condition* (Figure 3.3), which is consistent with the results of my previous study [85]. On the other hand, there was no statistically significant difference in the adaptation response among the 0-, 100-, 200-, and 300-ms delays (Figure 3.3), suggesting that neither H1 nor H2 was likely to be supported by these results. Rather, hypothesis H3 was a more likely explanation of the results.

Thus, my interpretation of the results include the following: (a) habituation to delayed feedback shifts the predicted hand position toward the delayed cursor position, (b) the shift of the predicted hand position not only helps the brain quantify the sensory prediction error accurately, but also increases the sensitivity of the adaptation to a certain amount of error between the predicted and actual sensory consequences (i.e., sensory prediction error), and (c) these factors ultimately affect the degree to which the brain uses a sensory prediction error to correct a motor command in a subsequent trial through modifying the forward model. However, these changes do not necessarily indicate that the shift in predicted hand position is a phenomenon separate from the increase in the sensitivity of the adaptation. The adaptation response to a visual perturbation is not proportional to the amount of perturbation, but when the perturbation is large, the adaptation response tends to saturate or fall off [83]. In other words, the proportional coefficient decreases with the amount of the perturbation (or sensory prediction error), implying that a large sensory prediction error is tightly coupled with a reduction in sensitivity to the adaptation to a certain amount of sensory prediction error. Note that I did not directly test the correlation between sensitivity modification and current state estimation change, and this is still a future research challenge.

A fundamental question is how the habituation to a *delay condition* contributes to the shift in the predicted hand position. It is still controversial that the brain constructs an internal model of the feedback delay itself [7]. However, considering the ability of the brain to construct internal models of various dynamical systems [86] and that delay in a system can be approximated by the continuous dynamical system [87], the brain might be able to form an internal model of the feedback delay. Further studies are required to clarify the validity of this hypothesis.

Chapter 4

Visual feedback delay and current hand-state estimation

In the previous two chapters, I showed that the degradation of visuomotor learning caused by visual feedback delay was alleviated by previous exposure to the delay, and that this alleviation was brought about by increases in both the association with sensory feedback such as intentional binding and sensory prediction change. In the last chapter, I assumed that the predicted hand position changed during reaching by delay habituation without examining it empirically.

In this chapter, I focus on how the sensory prediction changes with habituation to delay. If the sensory prediction (e.g., Smith predictor) changes by habituation to delay, current hand-state estimation during reaching could change as I assumed in Chapter 3. To examine this possibility, I conducted an experiment called a "target-jump task." In this task, a target jumped from its original point to another and participants were required to correct their reaching toward the new point as quickly as possible. This correction motor command should be based on current-hand state estimation, and the trajectory correction should reflect the change of estimation.

Here, I tried to examine how the current hand-state estimation changed through exposure to feedback delay. I also demonstrated that a modified optimal feedback model, which includes a flexible delay-estimation parameter, explains the experimental results.

4.1 Background

Our central nervous system has inevitable noise; consequently, our motions have a degree of variety or inaccuracy, even if we try to achieve the same motion. To correct for this deviation, the central nervous system must estimate the current hand-state during reaching based on sensory feedback and must then make a corrective motor command [52,88]. However, the central nervous system also has signal transmission delay and the feedback signal comes with some delay as well. Theoretically, too much reliance on the delayed feedback signal makes the system unstable, and feedback gain has to be controlled moderately using a predictive system [9,7] called the forward model.

The amount of feedback delay depends on the sensory system; visual feedback takes longer than does auditory feedback, and the delay in tactile feedback differs according to body position. Furthermore, when we use tools, the feedback delay depends on the tool characteristics. In the practice of fencing, for example, the tip motion of the sword is delayed from the hand motion, and the central nervous system or forward model has to flexibly habituate to the additional delay to obtain the correct feedback error signal and to manipulate the sword accordingly. Miall et al. reported the effects of transcranial magnetic stimulation (TMS) over the ipsilateral cerebellum while healthy humans were made to interrupt a slow voluntary movement to rapidly reach towards a visually-defined target. Errors in the initial direction and in the final finger position of this reach-to-target movement were significantly higher for cerebellum stimulation condition than in control conditions [44]. This study displayed that the dynamic current-state estimation error (the effect of forward model disruption) could be observed through the trajectory correction task.

Typical visuomotor rotation tasks focus on static endpoint deviation, where spatial prediction error could be correctly calculated even if temporal mis-estimation occurred in the forward model because “when” information does not matter for this static feedback [56]. My previous studies in chapter 2 and 3 demonstrate that habituation to cursor delay in advance alleviated visuomotor learning degradation is caused by feedback delay. In these studies, I considered that the forward model had been modified through habituation to the visual feedback delay and that the prediction error was different even if the amount of deviation at the endpoint is spatially equivalent [85,89]. This result led to the hypothesis that the forward model is able to habituate to a particular temporal delay flexibly with the exposure.

In this study, I was interested in ⅰ) whether visual feedback delay affects the dynamic current-state estimation, similar to the way in which visuomotor rotation modifies the static current-state estimation at the endpoint, and ⅱ) whether the forward model can adapt its temporal delay estimation flexibly. I investigated these questions using a target jump task, in which a target jumped from its original point to another during reaching, and participants were required to correct their reaching toward a new point as quickly as possible.

4.2 Methods

Subjects

Fifteen volunteers (10 males and 5 females; age range, 19–26 yrs) participated in this study. Participants had no cognitive or motor disorders and were naive to the experiment purpose. Their dominant hand was determined using the Edinburgh Handedness Inventory [59]: all participants were right-handed. They were paid for their time. This study was conducted according to the Declaration of Helsinki, and the experimental procedures were approved by the ethics committee of the Graduate School of Education at the University of Tokyo. Written informed consent was obtained from all participants before the experiments.

Apparatus

Participants sat on a straight-backed chair while grasping the handle of a robotic manipulandum with their right hand (Phantom Premium 1.5HF, Geomagic, USA). A spring simulated by the device (1.0 N/mm) generated a virtual horizontal plane on which the handle movement was restricted. A projector was used to display the position of the handle with a white circular cursor (diameter, 8 mm) on a horizontal screen (45 cm × 60 cm) placed 13 cm above the virtual plane and 10–15 cm below shoulder level. Thus, the screen board prevented the participants from directly seeing their arm and the handle. Participants controlled the cursor from a start position (10-mm diameter yellow circle) to a target (10-mm diameter magenta circle), which were also displayed on the screen. After completion of the reach, the device returned the handle to the start position; therefore participants could concentrate only on the reach toward the target in each trial. The start position was located approximately 25 cm in front of the body, and the distance between the start position and the target was 15 cm. The start point was always visible. The position and velocity of the handle were recorded with a sampling frequency of 500 Hz for offline analysis.

Procedure and conditions

To examine the influence of visual feedback, two types of cursors were used in this experiment: a no-delay cursor and a delayed cursor (Figure 4.1A). I set two experiment conditions, both of which included 40 target jump trials and 200 non-jump trials (Figure 4.1B). In the no delay condition, all 200 of the non-jump trials were carried out using the no-delay cursor. In the delay condition, all 200 of the non-jump trials were carried out using the delayed cursor. The purpose of these 200 non-jump trials was to habituate the participants to the amount of cursor delay set for each condition. The first 40 trials in each condition were non-jump; therefore, jump trials were interspersed once in each five trials, in random order. In both types of trials, the target first appeared in the forward direction at 15 cm away from the start position. Figure 4.1C illustrates the experiment sequence. All participants executed two experimental conditions with approximately ten-minute interval between the conditions.

The focus of this experiment is the data from the target jump trials, the only data analyzed in this study. In these trials, the target was rotated 20 or −20 degrees just after the initiation of the reaching (20 trials for each direction). Ten of the 20 trials were carried out using a no-delay cursor, while the other 10 used a delayed cursor. Therefore, of the total 40 target-jump trials in each condition, 10 trials met each of the following sets of conditions: a 20-degree rotation with a no-delay cursor, a 20-degree rotation with a delayed cursor, a −20-degree rotation with a no-delay cursor, and a −20-degree rotation with a delayed cursor.

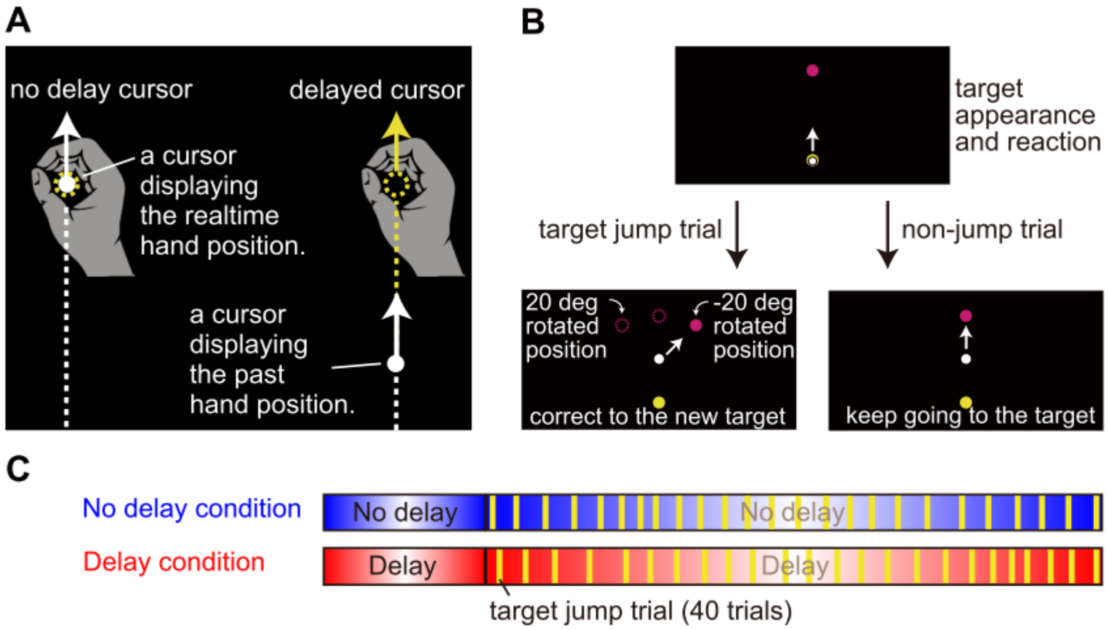


Figure 4.1 Experimental setting.

A. Two types of cursors used in this experiment. In the delayed cursor trial, the cursor was displayed at the hand position immediately prior (200 ms ago). **B.** Trial types. Basically, the experiment consisted of non-jump trials for the participants' exposure to no-delay or delayed cursor depending on the experiment condition. In 40 target jump trials interleaved randomly in 240 trials, the participants had to correct their reaching direction toward a new target immediately after getting aware of the jump. **C.** Protocol of the experiments. In no-delay condition, after the participants performed non-jump trials without delay, the target jump trials were randomly interleaved. In delay condition, the delay was provided to the cursor for both non-jump and target jump trials.

Instructions

Participants were instructed to move the cursor from the start position to the target and to initiate the reaching movement as soon as the target was presented. They were also instructed to keep the reaching peak velocity within 300‐420 mm/s range. If the reaching velocity was above this range, a "FAST" warning was immediately displayed on the screen; similarly, a "SLOW" warning was displayed if the velocity was too slow. In the target-jump trials, the participants had to correct their reaching direction toward the new target as soon as possible after they became aware of the jump.

Data analysis

Target-jump-trial data were used for the analysis. The trials for which the peak velocity was out of the 300‑420 mm/s range were excluded from the analysis. The reaction time (RT) for each trial was calculated as the first time point at which the hand velocity exceeded 5% of the peak velocity of that trial. The forward direction peak velocity (PV) and lateral-direction reaction time (LRT) were also calculated for comparison between conditions. No significant difference in PV and LRT between the conditions guarantees that any trajectory difference between conditions comes from the correction motor command after observing the new target. The forward position at the lateral-direction peak velocity was used as the criterion for comparing the trajectory difference. Data are reported as the mean ± SD calculated for all participants. One-way ANOVA was performed to test for any significant effect of the experimental condition on the performance measure. In addition, a post hoc Ryan's test was used for multiple comparisons. The threshold for statistical significance was set at $P < 0.05$.

Computational models and predictions

I used stochastic optimal feedback control (OFC) to model this reaching task [52,88]. In this framework, the trajectory of a reach is determined by three components: an optimal controller that generates motor commands (G_c in Figure 1.9), an internal forward model that predicts the sensory consequences of those commands ($\hat{G}_p$ in Figure 1.9), and a delay estimator for the sensory feedback delay (e^{-Ls} in Figure 1.9). The motor signal in this model is made based on the estimated current state $\hat{x}_t$ at time t. And this estimated current state is updated recursively by the Kalman filter [9].

$$\hat{x}_{t+1} = A\hat{x}_t + Bu_t + K_t(y_t - H\hat{x}_t)$$

$\hat{x}_t$ includes position, velocity, acceleration, and force at time t. $A, B,$ and H are system dynamics and observation matrices. K_t is Kalman filter gain matrices at time t and u_t is the control signal at time t. The derivations are shown in Todorov's work [88]. Theoretically, the internal forward model uses an efference copy to predict the sensory feedback ($H\hat{x}_t$; this is equivalent to $\hat{y}(t)$ in Figure 1.9) and compare it with the actual feedback (y_t). Our nervous system, however, has inevitable delay (Δ), which means that the efference copy has to be pooled to wait for the delayed sensory feedback ($y_{t-\Delta}$). Such a wait is not easy to achieve in the nervous system, and how it is done is still controversial. Previous studies of OFC did not consider this innate delay in the nervous system [51,52,9].

Here I introduce the delay parameter estimated for the internal model (Δ_{est}) and modify the OFC model to reproduce the target-jump experiment (Figure 4.2A). OFC was first proposed to reproduce a simple, straight reaching, where the feedback gain and Kalman gain throughout the reaching are calculated in advance at a start point according to the given duration of the reaching and the present hand state. In the target-jump trials, the feedback gain and Kalman gain have to be recalculated when the participants notice the target jump because a new reaching plan based on the present state (such as hand position or velocity) toward the new target must be created. Thus, the corrective motor command and its consequent reaching trajectory to the new target strongly depend on the estimated current state ($\hat{x}_t$).

Figure 4.2B illustrates the characteristics of my model in the target-jump trial. The vertical axis is the forward direction distance from the start position when the lateral velocity is at its peak, which indicates the degree of overshoot or undershoot against the new target. I calculated this value by averaging 20 trials of reaching for each parameter setting, the cursor delay (Δ), and the estimation error ($\Delta - \Delta_{est}$). Figure 4.2B displays the strong influence of the temporal estimation error ($\Delta - \Delta_{est}$) on the trajectory. When the estimation error is zero, the trajectories are not biased, regardless of the extent of cursor delay (Δ), and never show overshooting or undershooting on average. On the other hand, the trajectory tends to overshoot against the target when the temporal estimation error is positively large, and undershoot when the estimation negatively large.

I put three hypothetical models according to Δ_{est} as follows, and the other parameters were the same among models. Limitations of my models are follows: ⅰ) I did not consider the proprioceptive feedback, and ⅱ) I assumed the estimated delay (Δ_{est}) is consistent throughout an experiment, especially from the 41st trial to the end, where the data analyzed were obtained (see Figure 4.1C).

Model 1. Naive estimation. In this model, for estimating the current state $\hat{x}_t$, the internal model ignores the visual feedback information. $\hat{x}_{t+1} = A\hat{x}_t + Bu_t$ Here, I cannot observe any trajectory difference among conditions and cursors (Figure 4.2C).

Model 2. Sensorimotor integration without delay habituation. In this model, for estimating the current state $\hat{x}_t$, visual feedback information is used: $\hat{x}_{t+1} = A\hat{x}_t + Bu_t + K_{t-\Delta_{est}}(y_{t-\Delta} - H\hat{x}_{t-\Delta_{est}})$ where Δ_{est} cannot change even after exposure to the delayed cursor. Thus, the conditional difference cannot be observed. In this model, a trajectory difference is only present between the two types of cursors delays (Figure 4.2D).

Model 3. Sensorimotor integration with delay habituation. In this model, the estimation is made in the same way as in model 2. However, here Δ_{est} can habituate to the cursor delay after repetitive exposures. The difference in trajectory is then observed between both conditions and cursor delays.

More importantly, the trajectory with the no-delay cursor in the no delay condition and that with the delayed cursor in the delay condition are nearly the same (solid blue line and dotted red line in figure 4.2E). This result indicates that the estimation Δ_{est} comes close to the real delay Δ after exposure to the delayed cursor, and the correct hand state can be estimated with the delayed cursor.

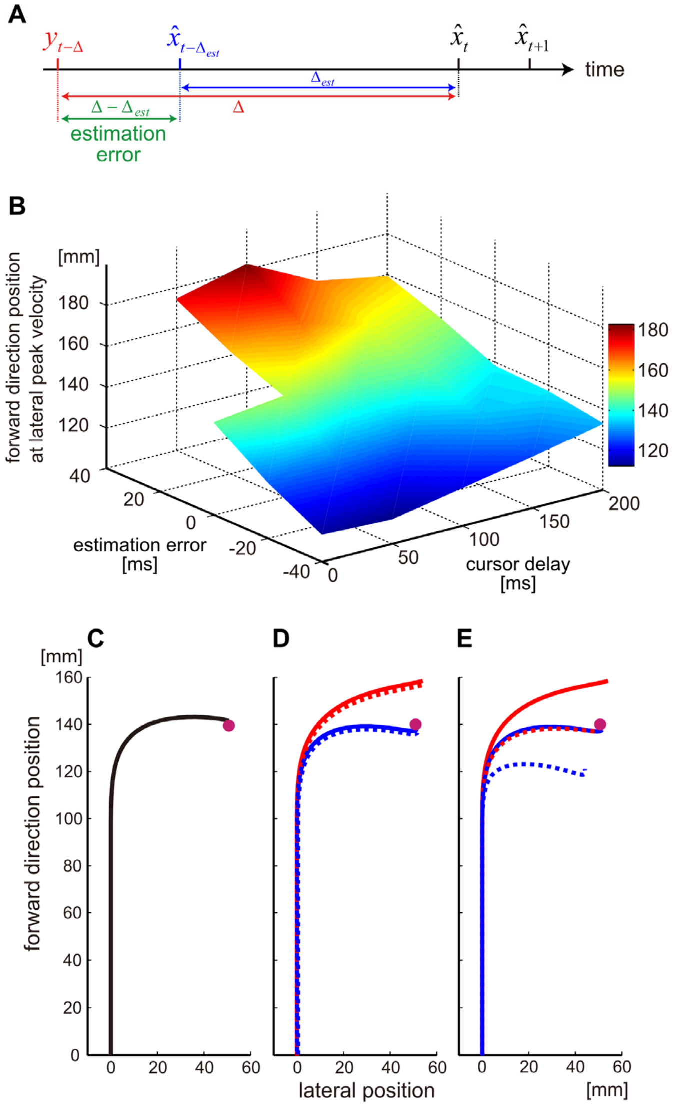


Figure 4.2 The modification, characteristics and predictions in our model.

A. We introduced the estimated delay parameter (Δ_{est}) to OFC. When calculating the state estimation error, $y - H\hat{x}$, our model cannot necessarily match the correct estimation in the memory, where the temporal "estimation error ($\Delta - \Delta_{est}$)" exists. **B.** The forward direction position at lateral peak velocity with respect to cursor delay (Δ) and estimation error ($\Delta - \Delta_{est}$). This figure indicates that the estimation error affects the trajectory much more than the cursor delay. Even with delayed cursor, the trajectory should be almost the same as that with no delay cursor if the estimation is correct. **C.** Naïve estimation, where the visual feedback does not affect the current hand state estimation, and then the trajectory does not differ between conditions and cursors. **D.** Sensorimotor integration without delay habituation, where the visual feedback does affect the current hand state estimation but no habituation occurs even after the exposure to the delayed cursor. Here the trajectory difference only depends on the cursors; no delay or delayed cursor. **E.** Sensorimotor integration with delay habituation, where the visual feedback does affect the current hand state estimation and habituation occurs after the exposure to the delayed cursor. Here the trajectory difference depends both on the conditions and the cursors.

4.3 Results

Figure 4.3A and B illustrate a typical subject's trajectories in the no delay and delay conditions, respectively. The trajectory correction occurred near the end of each reaching. This result is primarily of the low ratio of target jump trials: once in five trials randomly after the 41st trial. This city lowered the participants' expectation for the possibility that the target might jump. Although the curve points have some variance, there are features that clearly depend on the condition and cursor delay. In both conditions, the reaching with the delayed cursor goes further from the start position than that with the no-delay cursor. The forward direction positions at the lateral peak velocity in the delay condition (Figure 4.3A) were closer than those in the no-delay condition (Figure 4.3B). The average reaching trajectories and velocity profiles of all participants are illustrated in Figure 4.3C and D, respectively. The velocity profiles were calculated by combining the data for reaching toward 20 degree and －20 degree rotated targets for each condition because there was no clear difference between the two directions (Figure 4.4). The two graphs shown in Figure 4.4 A-D demonstrate the average reaching to the 20 degree rotated target (left) and to the －20 degree garget. Figure 4.4A, B, and C illustrate that there were no significant differences between the four trajectories in RT (P = 0.864 for the left reaching; P = 0.983 for the right reaching), PV (P = 0.339 for the left reaching; P= 0.175 for the right reaching), or LRT (P = 0.215 for the left reaching; P= 0.112 for the right reaching).

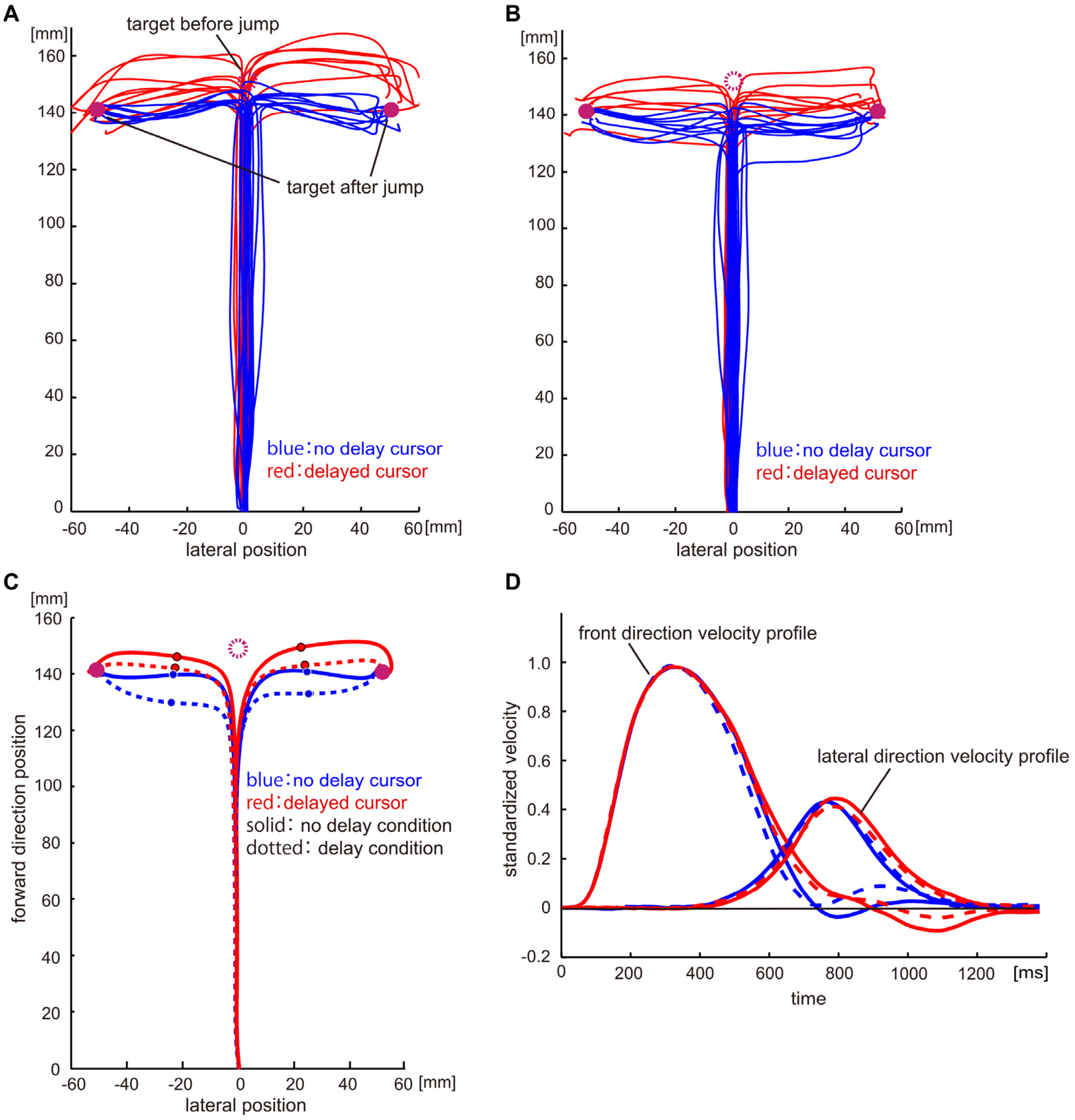


Figure 4.3 The experiment results. **A & B.** Typical single-participant's trajectories in no delay and delay conditions respectively. **C & D.** The averaged reaching trajectories and velocity profiles of all participants respectively. The blue means the reaching with no delay cursor and the red with delayed cursor. The line type depends on the conditions; the solid line means the no delay condition and the dotted line means the delay condition. The velocity start points were arranged and the velocity was standardized in accordance with the forward direction peak velocities of each.

In contrast, Figure 4.4D illustrates that there were significant differences in the forward direction position at the lateral peak velocities between the four trajectories ($P < 0.001$ for the left reaching, $P < 0.001$ for the right reaching). For the left reaching, a post hoc Tukey's test shows significant difference between no-delay cursor in no delay condition (NN) and delayed cursor in no delay condition (DN) ($P = 0.027$), DN and no-delay cursor in delay condition (ND) ($P < 0.001$), ND and delayed cursor in delay condition (DD) ($P < 0.001$), NN and ND ($P = 0.016$), but no significant difference between NN and DD ($P = 0.555$), DN and DD ($P = 0.400$). For the right reaching, a post hoc Tukey's test shows significant difference between NN and DN ($P = 0.001$), DN and ND ($P < 0.001$), ND and DD ($P < 0.001$), NN and ND ($P = 0.025$), DN and DD ($P = 0.036$); the only non-significance was between NN and DD ($P = 0.520$). While there was a slight difference between left and right reaching, both had the same tendency, and the non-significant difference between NN and DD was seen in both. These results support model 3 (*Sensorimotor integration with delay habituation*), where the visual feedback affects the current hand state estimation and the estimation Δ_{est} is adjustable to the exposed visual feedback.

The dots on the midpoint of each trajectory in Figure 4.3C show the points where the lateral peak velocity was reached: approximately 800 ms after the initiation of reaching (see Figure 4.3D). Until this point, there is little difference between the four lateral direction velocities. In addition, forward direction recorrections, such as reacceleration (dotted blue line) or recovery negative velocity (solid red line) observed around the new target, did not occur. This observation indicates that the initial part of the movement before the lateral peak velocity was strongly dependent on the estimation during the forward reaching. The late part of the movement around the new target (after the lateral peak velocity) was affected by the online visual feedback of the lateral cursor motion. I do not consider this part of the movement so much in this study because my interest here was on the current hand estimation difference during forward reaching, where the reaching behaviors themselves were nearly the same as those shown in Figure 4.4A, B and C.

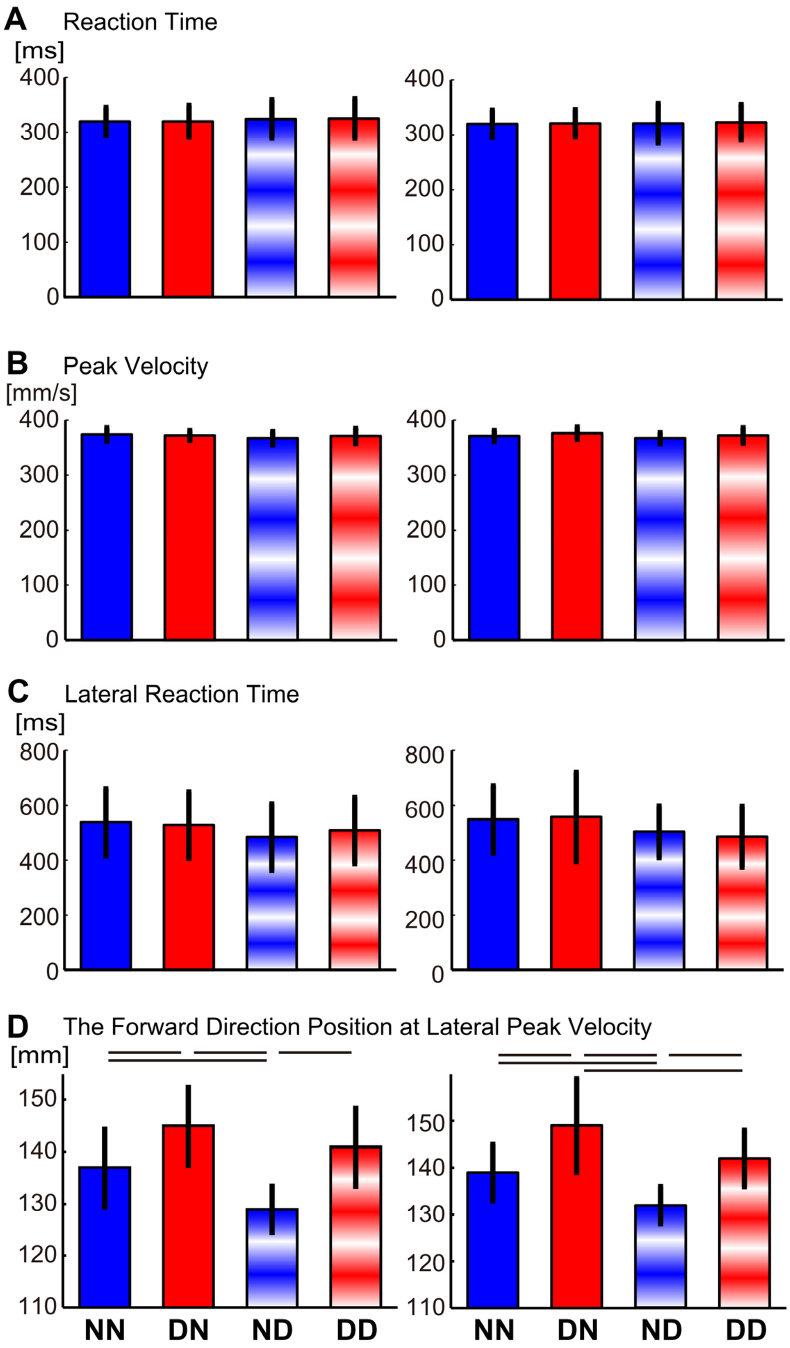


Figure 4.4 The bars illustrate the means of 15 participants and the error bars the SDs. **A.** Reaction time. **B.** Peak velocity. **C.** Lateral reaction time. **D.** The forward direction position at lateral peak velocity. Each has two graphs; the left is the reaching data to the 20 deg rotated target and the right is to the -20 deg.

4.4 Discussion

Before discussing the main findings of this study I note that the average reaction time to a new target in my (approximately 400 ms; see Figure 4.3D lateral velocity profile) study were slower than those in other “automatic pilot” studies, which examined the mechanism of quick (automatic) reaching correction [90,91]. The experimental setup of these studies was not so different from mine: the probabilities of target jumps were within 20-30%, and the visual angles of the target jumps were within 3-9°. A chief distinction of the automatic pilot studies were the existence of misreaching and disallowed correction, while my subjects executed all hundred trials without misreaching. This means that the automatic pilot studies were interested in the quick reaction to a new target and strongly instructed their subjects to react quickly. On the other hand, I did not emphasize quick reactions so much, though I required them to correct their reaching as soon as they became aware of a target jump, probably causing them to focus more on correct reaching.

The observed significant trajectory difference according to cursor delay denied model 1 (*Naive estimation,* Figure 4.2C). In both conditions, the trajectories with the delayed cursor were longer than those with the no-delay cursor (solid blue vs. solid red, dotted blue vs. dotted red in Figure 4.3C). There was no significant difference between the cursor delay and conditions in RT, PV, or LRT (Figure 4.4A-C). On the other hand, the trajectories toward the new target differed significantly between the conditions. These results indicate that the trajectory difference was derived from the corrective motor command, which must have been calculated to reduce the displacement between the estimated hand position and the new target. If the estimated hand position lags behind the actual position, the direction of the motor command will be more toward the forward direction than the direction from the real hand position to the new target; consequently, the trajectory would be further than in the case where the hand position was correctly estimated. On the other hand, if the central nervous system estimates the hand position ahead of the real position, a more lateral-directional motor command is made, and the trajectory is nearer. While the position, velocity, and acceleration should all be correlate with the new motor command toward the new target, here I address only the position for simplicity.

Wolpert et al. investigated the relationship between reaching duration and hand position estimation variance and showed that the estimation variance became larger as the reaching duration increased, but the variance had a limitation at a certain value that was clearly explained by the model combining efference copy and sensory feedback according to the signal accuracy [9]. Todorov and Jordan constructed an optimal feedback control model to explain how the central nervous system optimizes motor commands based on the estimation model suggested by Wolpert et al. [52,88]. My present model is a simple modification of the optimal feedback control model, where the temporal estimation error ($\Delta - \Delta_{est}$) was present (Figure 4.2A). In my model, I inserted this temporal estimation error into the position and velocity information of the optimal feedback control model and predicted the experiment results. I also explained the trajectory difference according to the cursor delay. As a result, I clarified that the visual feedback affected the current hand-state estimation in the central nervous system. The temporal estimation accuracy in the predictive system is critical.

Interestingly, after the exposure to the 200-ms constant delay in the delay condition, the reaching with the delayed cursor (DD) came close to the reaching with the no-delay cursor in the no delay condition (NN), indicating that the current-state estimations were almost identical between these two conditions (dotted red lines and solid blue lines, Figure 4.3C). Although this result cannot be explained by Model 1 or 2, it does not necessarily support Model 3. Remember the Kalman filtering system in the CNS, which can control information reference levels. This filtering can also explain DD by lowering the reference level of the delayed visual feedback, depending more on prediction (and/or proprioception). In this case, the reaching trajectories with no-delay cursor in delay condition (ND) should be almost the same as DD trajectories, because of the ignorance of visual feedback. However, this is not the case: ND shifted by the influence of the visual feedback (shift from solid red lines to dotted red lines and from solid blue lines to dotted blue lines, Figure 4.3C). Kalman filter cannot explain this result, while Model 3 (*Sensorimotor integration with delay habituation*) predicts this result (Figure 4.2E). In addition, the results shown in Chapter 2 and 3 cannot be explained by the Kalman filter either but can be explained by Model 3 (see Discussion in Chapter 3).

Note that I focused on the current state estimation during forward reaching by observing the corrective trajectory toward the new target. I did not refer to the trajectories after the lateral peak velocity because these trajectories reflect not only the current-state estimation during the forward reaching but also other error-correction behavior (see the trajectory variance around the new target, Figure 4.3A and B).

In the case of visuomotor rotation learning, the central nervous system updates the forward model after observing the visual error at the endpoint, such that the prediction becomes closer to the cursor position. As a result, the estimated hand position after visuomotor learning comes near to the visual feedback rather than to the actual hand position [56]. Using a delayed cursor means that the spatially displaced visual feedback behind the real hand position is observed during reaching. If habituation occurred in the same manner as visuomotor learning, the estimated hand position would come close to the visual feedback after exposure to the delayed cursor, and the trajectory would go much further than that before exposure. However, my experiment showed the opposite result; after exposure to the delayed cursor, the participants were able to reach the jumped target along nearly the same trajectory with the no-delay cursor (solid blue line, Figure 4.3C), even using the delayed cursor (dotted red line, Figure 4.3C). This result is predicted by model 3 (*Sensorimotor integration with delay habituation*, Figure 4.2E), indicating that the estimated hand state in the delay condition became closer to actual through habituation rather than visual feedback.

Krakauer et al. compared the time course of adaptation with two types of screen cursor transformation [92]. The first was a gain change that induced extent errors and required subjects to learn a new scaling factor. The second was a screen cursor rotation that induced directional errors and required subjects to learn new reference axes. They showed the gain adaptation learning curve was similar to the rotation adaptation learning curve, which implied that the state estimation was shifted to the cursor during adaptation. If this kind of gain adaptation occurred in my delay habituation task, the estimated hand position would come close to the visual feedback after exposure to the delayed cursor, and the trajectory would go much further than that before exposure, which was denied by my experiment (Figure 4.3C). Thus, I can conclude that the delay habituation and gain adaptation are distinct even though the cursor motion in the first half of the reaching is similar: the cursor behind the hand.

The spatial prediction errors of delay habituation and gain adaptation are not saliently distinct. Spatially, the cursor goes behind the real hand position in both adaptation and habituation during reaching. In case of adaptation with screen cursor transformation such as gain change or directional rotation, the spatial prediction error at the endpoint of reaching is a strong driving force in motor learning. On the contrary, the spatial prediction error at the endpoint does not provide important information in case of visual feedback delay; the endpoint spatial error should be the same regardless of the amount of delay. What then gives a salient difference between these two types of adaptations? I want to point out the information about cursor motion. The cursor velocity profile, for instance, has a clear difference. The cursor velocity profile during reaching in gain adaptation is almost the same as that of the hand, with a slight difference in its scale. Notably, the timing of initiation and finish of cursor motion is completely the same as that of hand motion. The cursor velocity profile in delay habituation, on the other hand, has a clear temporal shift, and we know that the visual system can perceive motion independently from location. Therefore, examining how the brain processes the prediction error regarding motion is very important to elucidate the mechanism of delay habituation.

In the present study, I introduced temporal delay information directly into my computational model to predict the experimental results, although it remains unclear how the central nervous system encodes the temporal delay information. The question “Is the cerebellum a Smith Predictor?” is still in controversial [7]. Because our knowledge of how the delay is recalibrated in the brain is limited both computationally and physiologically [38], it is unclear whether the cerebellum indeed forms 2 separate internal models: the forward model of motor apparatus and the model of feedback delay. And this remains for the future studies.

Chapter 5

Feedback delay and mass perception

Mass or weight is one of the useful perceptions when I examine the brain processing of motional information. Mass perception is not spatial information; where an object exists now does not contribute to the mass perception. It is empirically and experimentally known that delayed feedback makes us feel the manipulating object heavier than its actual mass or weight. For instance, some participants in my previous experiment in chapter 2, 3, and 4 reported that they felt the manipulandum lever became heavier when I inserted feedback delay though most of them were not aware of temporal delay itself.

This means that the brain could extract some kind of change about the feedback (physically it is delay), and attributed it not to visual delay but to mass perception. I think this issue is worthwhile being investigated to find a clue to understand how the brain process dynamical information obtained through visual feedback.

In this chapter, I examined i) whether feedback delay in reaching task really increased perceived mass, and ii) whether the perceived mass increment could vanish by delay habituation.

5.1 Background

While performing an action, information on the timing of the sensory feedback has a crucial role in detecting the causal link between the action and its consequence [93,94,85,3,43,89]. For example, when the visual feedback is delayed, a self-generated visual motion is perceived as generated by someone else [93,94]. Furthermore, the motor learning process is also disrupted in such situations, possibly due to the failure of accurately linking the feedback information with one's own action [85,3,43,89]. It has been suggested that the central nervous system (CNS) uses a forward model to predict the sensory consequence of an action (e.g., the position of the hand at a certain time point) by using a copy of the motor command [95,9,44]. In such a scenario, the amount of prediction error, which is the difference between the predicted and the actual sensory feedback, contributes to detecting whether the sensory input is actually generated by the person.

The feedback timing information is not only used for linking the action and the consequence but can also contribute to the perception of the external environment. For example, the perception of a somatosensory event induced by self-touch is modified when a delay is imposed between the action and the touch [93]. Likewise, it has been shown that delaying the visual feedback of an action while carrying an object makes people feel that the mass of that object is greater [96]. Such evidence suggests that delay in the sensory feedback of an action may violate the authorship of the sensory consequence and, at the same time, change the quality of perception of that sensory event. In this study, I focus on the influence of feedback timing on the perceptual quality of the object's mass. Similar to the violation of authorship induced by the prediction error, in this case, the difference in the visually predicted hand position and the actual visual feedback (prediction error) may also contribute to such an overestimation of the object's mass. However, it is not yet clear whether the prediction error or the actual delay itself plays the major role in causing this phenomenon.

To test these two possibilities, I set up a reaching experiment where participants made a straight reaching movement while holding a manipulandum. The movement of the manipulandum was presented as a cursor movement on a monitor, which allowed us to impose various delays between the actual hand movement and the visual cursor movement. In Experiment 1, I examined the relationship between the amount of delay and the illusory increase of mass. Since the authorship of the sensory consequence is violated with a longer imposed delay between the action and the consequence [94], I predict that the mass of the manipulandum will be perceived as heavier for a shorter delay but not for a longer delay.

In Experiment 2, I investigated the effect of delay habituation on the perceived mass. If the prediction error were the cause of the increase in perceived mass, reducing the prediction error by habituating to the delay would alleviate the overestimation of the mass. On the other hand, if the actual delay were the cause, the mass would be overestimated irrespective of the habituation.

5.2 Methods

Participants

A total of 24 neurologically normal right-handed [59] volunteers (22 males and 2 females; age range, 20–44 years) participated. The study was approved by the Ethics Committee of the Advanced Telecommunications Research Institute. Written informed consent was obtained from all participants prior to performing the experiments.

Apparatus

Participants sat on an adjustable chair while grasping the handle of a twin visuomotor and haptic interface system (TVINS) (Figure 5.1). The participant's forearm was secured to a support beam on the horizontal plane. TVINS consists of two parallel-linked, direct-drive floating manipulanda using air magnets. Thus, the experiment can be conducted either by using only one manipulandum or by using both at the same time. Each manipulandum was powered by two DC direct-drive motors controlled at 2000 Hz. TVINS yielded a virtual mass (M) according to the equation of motion: $M = F / a$. Here F is a resistance force generated by TVINS in proportion to the handle acceleration (a). I confirmed that the accuracy in online measurement of the acceleration was ±0.04 m/s^2 even at the peak acceleration. I also confirmed by measuring the resistance force with a spring scale that TVINS could generate a target force with the precision of 0.1 Kgf. The position of the manipulandum was measured using optical joint position sensors (4,800,000 pulse/rev). The position of the hand (handle of the manipulandum) was projected on a horizontal screen placed above the mechanical plane and below shoulder level. The projector refresh rate was 75 Hz. The screen prevented the participants from directly seeing their arm.

It should be noted that there was a slight time delay for the actual handle movement to be reflected as the cursor movement on the screen, due to the limitations of the computer's data processing speed. When the delay between the handle and the cursor movements was measured 10 times by a high-speed camera (600 Hz), it was found to be 42.5 ms (SD 2.4 ms) when around the handle position near the body (around the “starting position” in the experiments) and 41.8 ms (SD 2.4 ms) when at a distance from the body (around the “target position”). No significant difference between the positions ($t(18) = 2.11$, $p = 0.543$) was observed. Since this delay is comparable across positions, and my interest was in the difference between the conditions, I believe that this delay itself will not affect my results. In the following, I describe the delay from this “baseline delay” but note that an additional 42-ms delay always existed in all of the conditions.

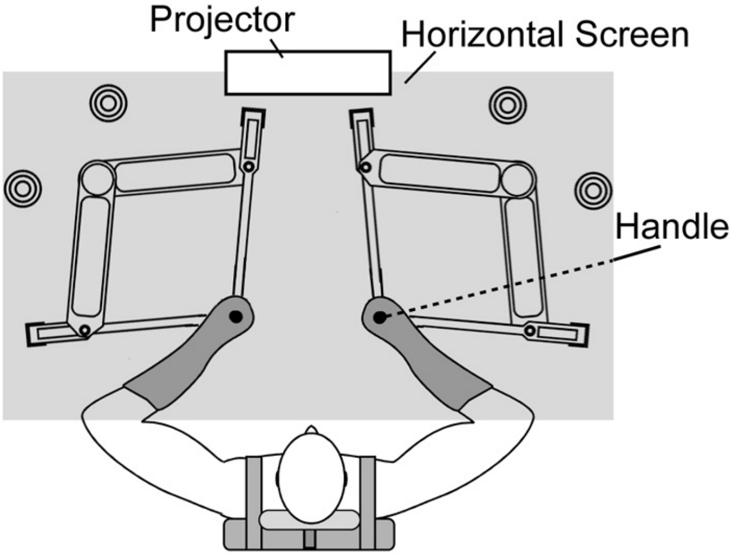


Figure 5.1 Top-down view of twin visuomotor and haptic interface system (TVINS). In Experiment 1, only the right-hand manipulandum was used. In Experiment 2, both manipulanda were used. The horizontal screen is illustrated as if it were transparent in order to show the manipulandum. In reality, it was opaque and reflected images generated by the projector installed above.

Experiment 1

I tested how the difference in imposed visual delay between the actual movement and the cursor feedback information influences the mass perception.

Task procedure

Fourteen volunteers participated. By making a reaching movement while grasping the manipulandum with their right hand, participants moved the cursor toward the target presented 10 cm from the starting point on the screen. After the reaching movement, the handle automatically moved back to the starting position. Participants judged the perceived mass of the manipulandum after each trial.

Three target locations were prepared. The middle target was straight ahead from the starting point, and the other two were 20-deg rotated clockwise or counterclockwise around the starting point from the middle target's path. The peak velocity of the reaching movement was required to be within the range of 300–450 mm/s. A warning message appeared on the screen if the movement velocity of the handle was faster ("Fast") or slower ("Slow") than the set velocity range. The mass of the manipulandum was varied from trial to trial by adding a resistive force against the movement of the hand (see above). Nine mass values were prepared: 1, 2, 3, 4, 5, 6, 7, 8, and 9 kg. Furthermore, a variable delay was imposed between the cursor movement and the actual movement of the hand in each trial, where this delay was chosen from five values: 0, 100, 200, 400, or 800 ms. The experiment investigated every combination between mass and delay (9 masses × 5 delays: 45 combinations). Each combination was repeated 15 times in random order. Consequently, each participant carried out a total of 675 trials. The experiment was divided into five 135-trial blocks, and the participants were allowed to take a break between the blocks. After each reaching movement, participants judged whether the mass of the manipulandum was greater or smaller than the average of all of the mass values presented in the previous trials. This is a version of the 'method of single stimuli,'[97] which requires participants to use their internal criterion for the judgment. The accuracy of this method is comparable to, and even more accurate than,[98] the method that always presents a standard stimulus as a comparison stimulus [99,100]. Moreover, this method enables us to increase the number of trials for a given period of time, which is crucial for reconstructing the psychometric function. The judgment ("lighter" or "heavier") was made by pressing one of two buttons with the left hand. Before the experiment, participants practiced and experienced each mass 30 times in order to familiarize themselves with the distribution of the input mass.

Data analysis

Participants' judgments of the masses were analyzed separately for five imposed delays. Logistic regression was used to relate the percentage of 'heavier' judgment to overall stimulus mass value for each participant. The form of the function was

$$y = \frac{1}{1 + e^{\left(\frac{x-\alpha}{\theta}\right)}},$$

where α is the mass value corresponding to the point of subjective equality (PSE, the 50% response level on the psychometric function) and θ provides an estimate of the mass discrimination sensitivity. To estimate the parameters, the logistic function was fitted to the judgment data of individual subjects by using a generalized linear mode as implemented in a MATLAB *glmfit* function (MathWorks, Natick, MA, USA). One-way analysis of variance (ANOVA) with repeated measures was used to test the effect of the delay value on both the PSE and the discrimination sensitivity. Ryan's multiple comparison tests were used to compare the 0-ms delay condition with the other delay conditions. The threshold for statistical significance was set at $p < 0.05$ throughout this study.

Experiment 2

In Experiment 1, I found that the perceived mass of the manipulandum significantly increases with the amount of imposed visual feedback delay when the delay is in the short range, but not when it is in the longer range (see Results). Next, I examined whether decreasing the prediction error for the feedback delay would change this delay-induced overestimation of the object's mass.

Task procedure

Ten volunteers participated. There were two conditions: *delay condition* and *no-delay condition*. In *delay condition*, participants were continuously exposed to the visual feedback delay when reaching to a target with the manipulandum, whereas delay was not imposed in *no-delay* condition (*simple reach* trials). Between these reaching trials, the participants' ability to perceptually recognize the delay (*delay awareness* trials) and their perception of the manipulandum mass (*mass comparison* trials) were measured.

The two conditions were performed by each participant on two separate days. The order of the conditions was randomly assigned to each participant: five of them performed *no-delay condition* first, while the others performed *delay condition* first. Each condition consisted of 404 trials, which were divided into four 101-trial blocks. Each block consisted of 87 *simple reach* trials, 5 *delay awareness* trials, and 9 *mass comparison* trials. Participants took short breaks between blocks. Note that the *delay awareness* and *mass comparison* trials were identical between conditions. Therefore, any conditional difference observed in these trials would be due to the pre-exposure to the feedback delay occurring in the *simple reach* trials. The details of these different trial types are explained below.

In *simple reach* trials, participants made a right-hand reaching movement by moving the manipulandum toward the target that appeared 15 cm from the starting position. The visual feedback was delayed for 200 ms in *delay condition*, whereas no delay was imposed in *no-delay condition*. The aim of *simple reach* trials was to allow participants to habituation to the 200-ms delay in *delay condition* (and the lack of delay in *no-delay condition*). To maintain participants' concentration, in one of 10 to 11 trials, the target jumped to the 20-deg clockwise-rotated position immediately after the onset of the reaching. The *simple reach* trials were distributed pseudo-randomly in a block, where more than one *simple reach* was conducted before *delay awareness* or *mass comparison* trials.

In *delay awareness* trials (sequence A in Figure 5.2), after making the right-hand reaching movement, participants were required to answer whether they felt any delay between their hand and the cursor movement. This trial was used to assess the change in perceptual sensitivity to the delay. Since I found in my pilot study that the delay of 200 ms was easily detectable, the cursor delay in *delay awareness* trials was set to 150 ms to avoid any ceiling effect.

Finally, in *mass comparison* trials (see sequence B in Figure 5.2), after making a right-hand reaching movement, participants were asked to make the same straight reaching movement with their left hand. Then, they were asked to judge whether the right hand was heavier or lighter than the left hand. The cursor delay was set to 200 ms for the right-hand movement, and there was no cursor presented for the left-hand movement. The mass value of all of the right-hand reaches was set to 3 kg (this was also the case for *simple reach* and *delay awareness*), while the mass was set to 1, 3, or 5 kg for left-hand reaches. This trial was used to evaluate the perception of mass under the delay of visual feedback, in the same manner used in Experiment 1. Since my aim was to extend my findings in Experiment 1, which was performed with the right hand, the left hand was used only to present the reference mass for the right hand.

Before *delay awareness* and *mass comparison* trials, participants were instructed about which type of trial they were going to perform (see 'announcement' in Figure 5.2).

Data analysis

For the *delay awareness* and the *mass comparison* trials, the probability of judging the trial as "delayed" and that of judging the mass of the right hand "heavier" were calculated. These values were compared between the *delay* and *no-delay conditions*.

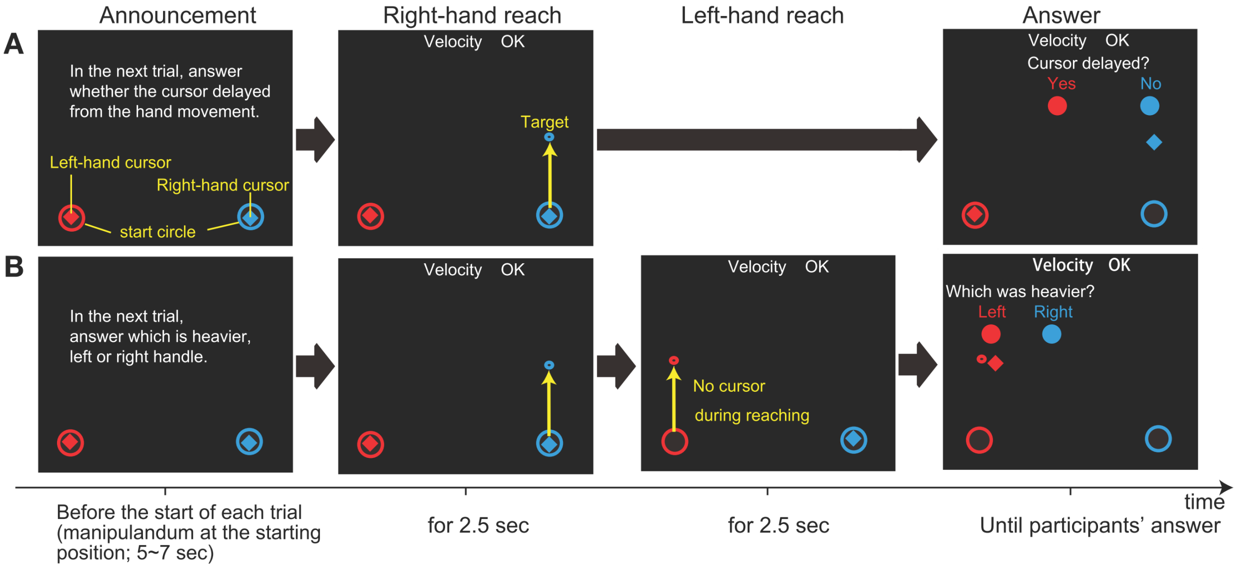


Figure 5.2 Two types of trials in Experiment 2. The horizontal flow is the sequence of each trial; **A**. *Delay awareness* trial in which subjects were asked if they felt any delay in cursor movements, and **B.** *mass comparison* trials in which subjects were asked to judge whether the right- or left-hand movement was heavier. The instruction was on the screen from the end of the last trial until the onset of the next trial (target appearance). The yellow letters and arrows are used to explain each display, but they are not shown on the screen during the actual experiment.

5.3 Results

Experiment 1

The psychometric function in Figures 5.3A and B describes the participants' judgment of mass as a function of actually delivered mass. Figure 5.3A shows the psychometric function constructed for different imposed delays (0, 100, 200, 400, or 800 ms) of a representative participant, while Figure 5.3B shows that of the data averaged across all participants. One-way ANOVA with repeated measures performed on the PSEs of different delay values showed a significant effect of delay on mass perception ($p = 0.024$, $F(4,52) = 3.082$). Figure 5.3C shows a shift in PSE for each delay from the case of 0-ms delay. The post hoc comparison performed from the 0-ms delay condition showed that the PSE significantly shifted toward the heavier side when the 200-ms delay ($p = 0.030$ after correction with Ryan's nominal significant level) or the 400-ms delay ($p = 0.038$ after the correction) was imposed, but not when the delay was 100 ms ($p = 0.175$ after the correction) or 800 ms ($p = 0.175$ after the correction). Moreover, one-way ANOVA with repeated measures performed on the discrimination sensitivity of different delay values showed no significant effect of delay ($p = 0.130$, $F(4,52) = 1.866$; mean sensitivity (±SD) was 0.97 ±0.09 for a 0-ms delay, 1.11 ±0.10 for a 100-ms delay, 1.02 ±0.10 for a 200-ms delay, 0.94 ±0.08 for a 400-ms delay, and 1.01 ±0.08 for a 800-ms delay). This indicates that sensitivity to the mass did not differ according to the delays. The results show that the visual feedback delay significantly modifies the mass perception of the manipulandum but failed to reach significance for a longer delay.

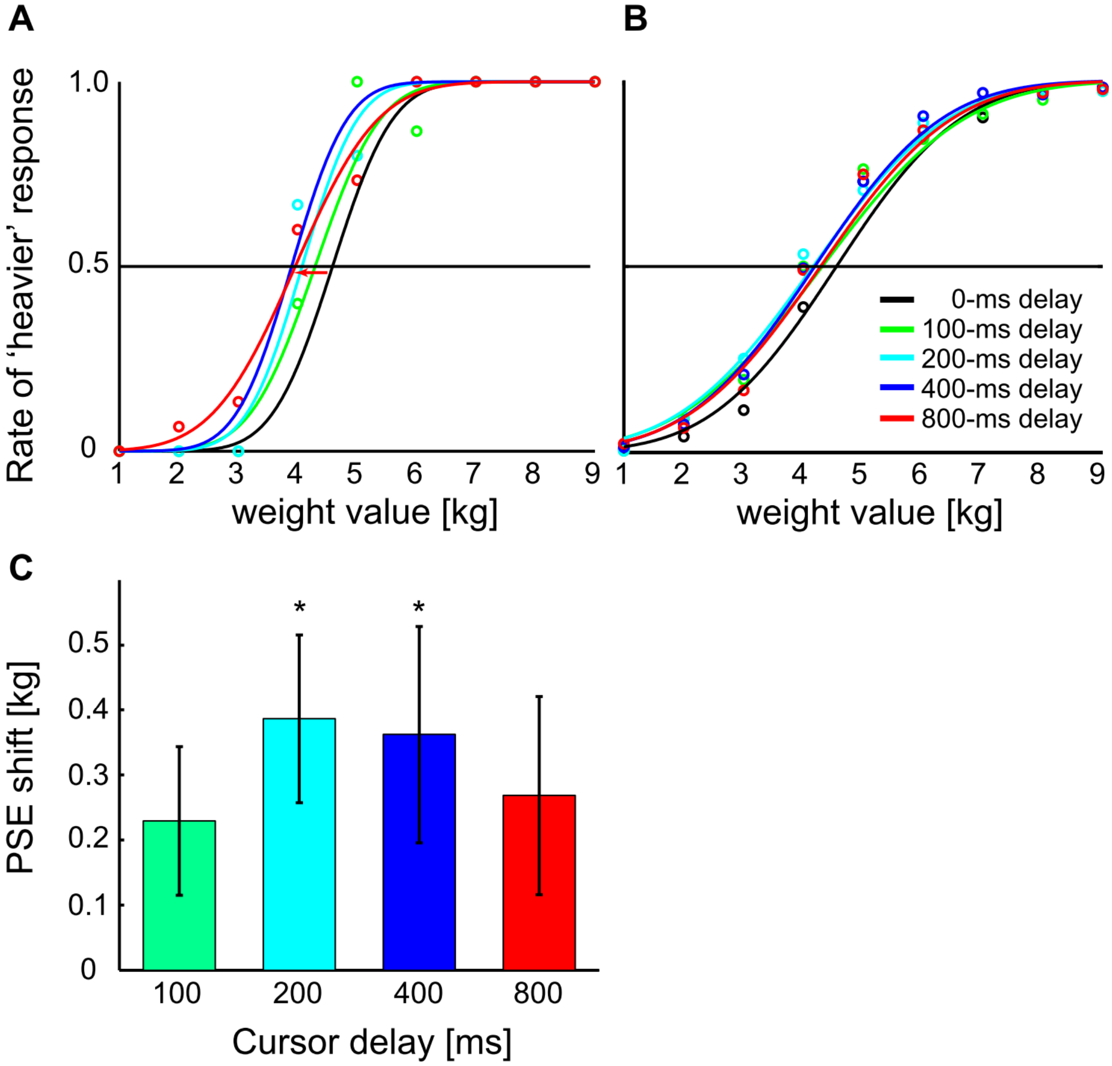


Figure 5.3 Results of Experiment 1.

A. Results are shown for a typical participant. The mass value at which each curve crosses the 0.5 line is PSE for each delay value. The red arrow indicates the shift of PSE for a 800-ms delay from that for a 0-ms delay (see Figure 3C). **B.** Psychometric functions are fitted to data averaged across participants. Average judgment rate across participants was calculated for each mass value, and sigmoid functions were fitted to the averaged rates. **C.** For each delay, the shift of PSE from that for a 0-ms delay is shown. Shifts were calculated for each cursor delay and averaged across participants. Error bars indicate standard error of measures across participants.

*: $p < 0.05$ according to Ryan's multiple (four) comparison tests for difference in PSE between 0-ms delay and the other delay conditions.

Experiment 2

One participant was excluded from the analysis based on his extremely slow reaction times, that is, initiation of the movement onset from the target appearance was more than 1000 ms on average, possibly due to a lack of concentration on the task.

For the *delay awareness* trials, the rate of delay awareness was significantly higher in the no-delay condition than in the delay condition according to the paired *t*-test ($p < 0.001$; $t(8) = 6.468$; Figure 5.4A). Namely, participants tended to more accurately perceive the imposed 150-ms delay in the *no-delay condition* compared to the *delay condition*. This indicates that repeated exposure to the delay in the simple *reach trials* made the participants less sensitive to the delay. The lower sensitivity to the delay after being exposed to the delay was already observed in the first block of trials, and it continued throughout the experiment (Figure 5.4B). When I analyzed the data with a two-way ANOVA, using the effect of block number along with the effect of condition (*delay* or *no-delay*), only a main effect of the condition ($p = 0.0001$, $F(1,8) = 47.059$) was observed, without any main effect of the block ($p = 0.102$, $F(3,24) = 2.313$) nor of the interaction between the two factors ($p = 0.592$, $F(3,24) = 0.649$). These results show that exposure to the delay seems to have an immediate impact on the delay sensitivity, and the effect was consistent throughout Experiment 2. Following this tendency, participants perceived the mass of the manipulandum as lighter in the mass comparison trials of the *delay condition* compared to that of the *no-delay condition* (Figure 5.4C). Two-way ANOVA with repeated measures showed significant main effects of the condition ($p = 0.002$, $F(1,8) = 19.139$) and the mass value ($p < 0.001$, $F(2,16) = 71.627$), without any significant effect of interaction ($p = 0.558$, $F(2,16) = 0.605$). This indicates that the habituation to the delay induced the insensitivity to the delay, and this was accompanied by the perception of smaller mass compared to when there was no habituation. In other words, the perceived delay may play a critical role in judging the mass of an object while making a movement.

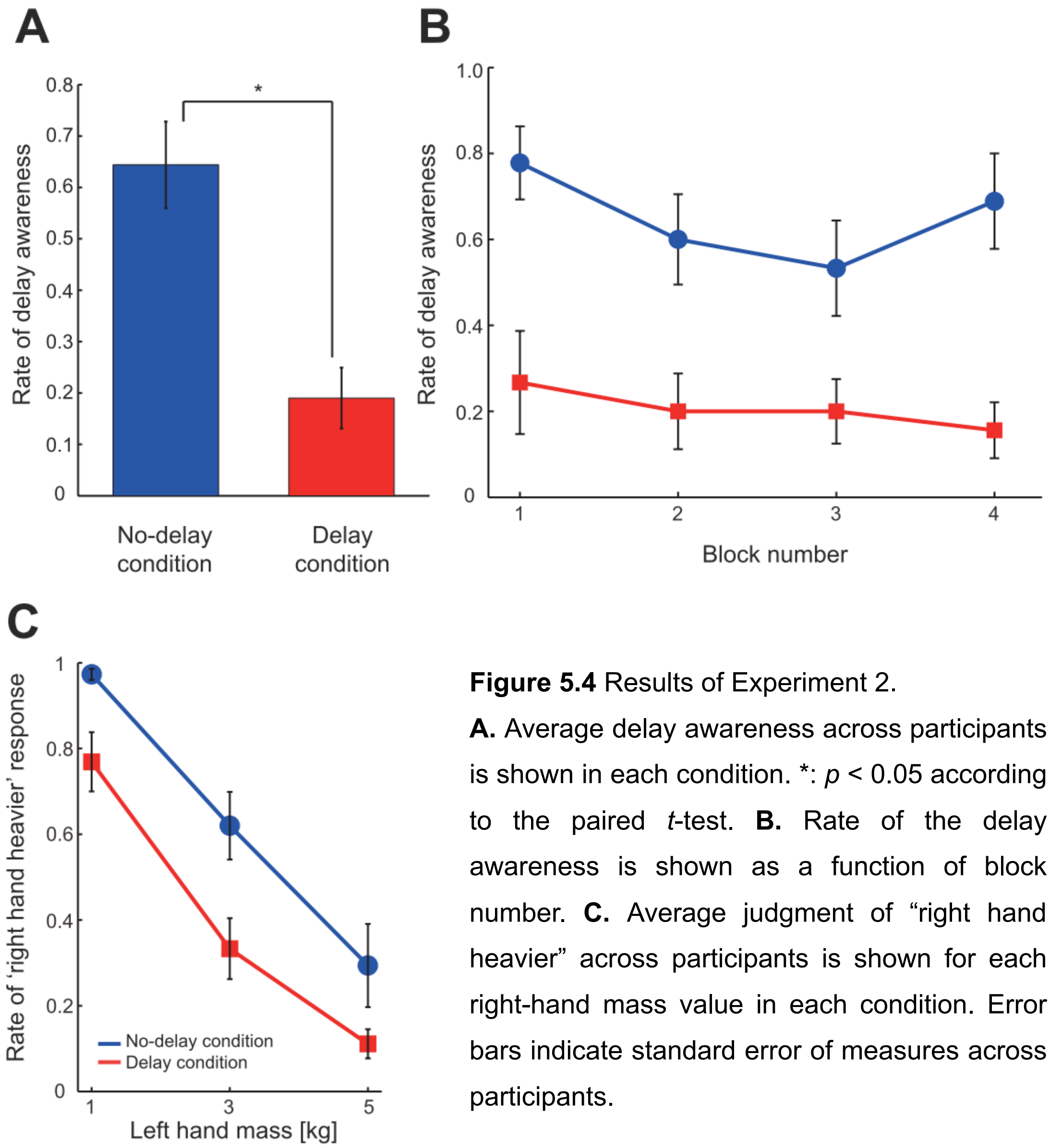


Figure 5.4 Results of Experiment 2.

A. Average delay awareness across participants is shown in each condition. *: $p < 0.05$ according to the paired *t*-test. **B.** Rate of the delay awareness is shown as a function of block number. **C.** Average judgment of "right hand heavier" across participants is shown for each right-hand mass value in each condition. Error bars indicate standard error of measures across participants.

5.4 Discussion

I examined how imposing a delay between an action and its visual feedback influences mass perception. In Experiment 1, participants felt that the manipulandum was heavier as the feedback delay increased to 400 ms, but this effect was less clear when the delay was 800 ms (Figure 5.3C). This indicates that mass perception modified by feedback delay is not solely related to the amount of delay. The results of Experiment 2 show that the mass overestimation was alleviated when the participants habituated to the delay, compared to when there was no habituation (Figure 5.4C). This suggests the sensory feedback prediction error may play an important role in inducing the overestimation of mass.

Delaying the visual feedback during manual actions causes a discrepancy between visual and proprioceptive positional estimates of the hand, or between expected and actual hand positions. This kind of discrepancy tends to be attributed to the mass perception, making the participants feel that the hand-held object is heavier than expected [96]. Within the range of the delay investigated in the previous study (0 - 200 ms), the perceived mass linearly increased as the delay increased. Note that Figure 5.3C shows the PSE “shift” meaning that the PSE with 0 ms of cursor delay is standardized at 0 kg for each participant. So I can say that the “three” PSEs (0, 100, and 200 ms cursor delays) are almost linear. However, this was not the case for much longer delays, which was specifically tested in my experiment (Figure 5.3C); when the delay was 800 ms, the effect of overestimating the mass became variable. This shows that longer feedback delay is processed differently from shorter delays. A previous study showed that delaying the timing of a sensory consequence of an action makes people feel that the time between an action and its sensory consequence is shorter than it actually is [40]. This binding effect was regarded as an implicit measure of whether the sensory input is actually processed as one's own action (authorship of the sensory event) [39,40]. Several studies have shown that the binding effect is modulated by temporal contiguity: When the feedback delay is large, the binding effect becomes weak [40,41]. Many studies have demonstrated that such binding does not occur if the delay is more than 200–300 ms [93,40,41]. In considering this evidence, the reason why the longer feedback delay (800 ms) was not reflected as an increase in mass may be due to the disruption of the association between an action and its sensory consequence: The longer delay may have violated the authorship of the sensory feedback information rather than being processed as the consequence of the action. Violation of action-authorship modifying the quality of the sensory perception may reflect findings in the literature showing that the participant's perceived intensity (amount of force) [101] or the quality (ticklishness) of a tactile input depends on the applied timing of the tactile stimulus in relation to the participant's own action [93].

In Experiment 2, when the participants were repeatedly exposed to the delay (*delay condition*), they became less sensitive to the delay compared to when not exposed to the delay (*no-delay condition*) (Figures 5.4A and B). Reduced sensitivity to the temporal delay shows that the participants were perceptually habituated to the feedback delay in the *delay condition*, as has been shown both in the perceptual domain [40,39] and in the motor control domain [85]. Accompanying this habituation effect, the illusory increase in mass was significantly alleviated in the *delay condition* in comparison to the *no-delay condition* (Figure 5.4C; red plots are significantly below blue ones). This result clearly shows that the mass overestimation accompanying feedback delay is not caused by the actual delay itself, since the actual delay is constant in the two conditions (Figure 5.4C). Furthermore, this suggests that the factors changing in accordance with the perceptual temporal habituation might be tightly linked to the alleviation of mass overestimation.

Two different types of adaptation may underlie the temporal adaptation observed between the action and the sensory input in this study. One is the adaptation between different sensory inputs, such as between vision and proprioception [102]. Feedback delay will lead to a discrepancy between the two, which may require calibration. The other possibility is the involvement of a motor command, providing prediction about the timing of the sensory reafference. In this case, adaptation may have occurred between the predicted and the actual timing of the incoming sensory input (prediction error). Either mechanism could have worked in my experiment. However, Stetson et al. [11] showed that the strength of calibration of perceived timing between pressing a button and a visual flash is much weaker when the button press was replaced by a passive button touch. Other studies on delay perception have also suggested that prediction in the sensorimotor system is critical for a change in temporal perception [39,11]. Therefore, I believe that the increase in mass perception dominantly involves motor-based prediction error. In any case, further study is necessary to clarify this point.

In conclusion, I propose that the misattribution of a visual delay to the increased mass perception is induced by the sensorimotor prediction error, and it seems to preferentially occur when the delay is within the range that can be attributed to the consequence of the action.

Chapter 6

General Discussion

6.1 Summary of findings

It is naturally important for all animals and humans to judge whether a piece of sensory information is relevant or irrelevant to its actions. When an animal hears a sound unrelated to its own step while walking in the woods, the possibility rises that another animal aims to prey on it from behind. In this case, it must flee from the enemy as soon as possible. If the nervous system had no processing delay, this judgment would be easy, because only sensory feedback occurring at the same time as actions would be relevant. However, the nervous system takes several tens to hundreds of milliseconds to convey information and cannot easily achieve such judgment.

Regardless of the inevitable feedback delay, we all know empirically that our judgment is not poor. Thus, our central nervous system is able to calculate its inevitable delay accurately. Moreover, when we consider the variation and change of delay in case of using tools, for example, we recognize that our central nervous system has much flexibility in the amount of delay. For instance, we can use both a solid sword and an elastic whip as weapons, even though they have completely different time lags after a hand swing. When a person grows in height as much as 20 cm per year during adolescence, she can still perceive the sensory feedback properly from the tip of her legs even though the delay is longer than before.

These daily experiences inspire the admiration of the CNS that can compensate for and habituate to various feedback delays. When I first began to work on this topic, I assumed it easy to experimentally demonstrate the flexibility of our CNS to feedback delay in the motor control level. However, I encountered a challenge. While some studies were showing the perceptual habituation to delay [39-42,11], I could not find any study finding such habituation to delay in the motor control level. Moreover, Tanaka et al. reported that the degradation of sensorimotor learning with feedback delay could not be alleviated by previous exposure to feedback delay, while the perceived feedback delay flexibly changed with previous exposure [43]. They concluded that the delay habituation in the perceptuomotor level is easily observed than that in the motor control level. Thus, I first started my work with the purpose of investigating the delay habituation in the motor control level.

In my first study, described in chapter 2, I investigated the ability of human participants to adapt their reaching movements in a visuomotor rotation task with three visual feedback conditions: no-delay, sudden-delay, and habituated-delay conditions. To introduce novelty into the trials, the cursor position, which originally indicated hand position in baseline trials, was rotated around the starting position. In contrast to the no-delay condition, a 200-ms delay was artificially introduced between the cursor and hand positions during the presence of visual rotation (sudden-delay condition) or before the application of visual rotation (habituated-delay condition). I compared the learning rate (representing how the movement error modifies the movement direction in the subsequent trial) between the three conditions. In comparison with the no-delay condition, the learning rate was significantly degraded for the sudden-delay condition. However, this degradation was significantly alleviated by previous exposure to the delay (sudden-delay vs. habituated-delay conditions in Figure 2.2C). In this study, I successfully proved that previous exposure to feedback delay alleviated the degradation of sensorimotor learning with feedback delay.

In my second study, described in chapter 3, I investigated how the motor learning system accomplishes this alleviation more precisely. I assumed two mechanisms work to achieve it during habituating to a certain amount of delay: the sensitivity shift to the habituated delay and the shift of the predicted hand position by habituation. I introduced an experimental setting in which these two mechanisms lead to different outcomes (Figure 3.1E). After the subjects habituated reaching movements using a 0-ms (no-delay condition) or 200-ms-delayed cursor (delay condition), visual rotation of 10 degrees was sometimes imposed on the cursor with various delays (0, 100, 200, or 300 ms). The aftereffect of the trials was quantified in their next trials to evaluate the adaptation response. After habituating to the 0-ms delayed cursor, the adaptation response was maximal when the visual feedback of the perturbation was provided with 0-ms delay and gradually decreased in proportion to the amount of cursor delay (blue line, Figure 3.3). On the other hand, habituation to the 200-ms delayed cursor alleviated the degraded adaptation response to the visual perturbation imposed during the 200-ms delay (red circle at 200-ms cursor delay, Figure 3.3). However, the habituation did not significantly degrade or super-alleviate the adaptation response to the visual perturbation with the 0-ms delay. Based on these observations, I conclude that habituation to delayed feedback not only shifts the predicted position of the hand but also increases the degree to which the CNS uses a certain amount of sensory prediction error to correct the motor command.

Although I hypothesized that the predicted hand position is modified by delay habituation, the study in Chapter 3 did not verify such modification directly. Then, I decided to test this possibility in my third study, described in chapter 4, by using a target-jump experiment (see Methods section, Chapter 4). The hand trajectories to the jumped target differed significantly between no-delay and delayed cursor trials (red vs. solid blue lines, Figure 4.3C), suggesting that current hand-state estimation is affected by visual feedback delay. Before habituation to the delay, the forward model does not know the cursor delay. Then the outcome of the combined motor efferent and sensory afferent signals (i.e., current-state estimation) was incorrect in delayed cursor trials. Interestingly, however, the trajectory with the delayed cursor after habituation was almost the same as that with the no-delay cursor, indicating that the current-state estimations were appropriately corrected (dotted red lines vs. solid blue lines, Figure 4.3C). This result cannot be explained by ignoring visual feedback delay (blue dotted lines in Figure 4.3C). These results indicate that the forward model can adjust its temporal delay prediction flexibly to allow for appropriate current-state estimation. The Smith predictor predicts these results.

In my fourth study, described in chapter 5, I first examined the relationship between the amount of delay and the illusory mass increase, and then investigated the effect of delay habituation on mass perception. Participants made a straight reaching movement while holding a manipulandum. The movement of the manipulandum was presented as a cursor movement on a horizontal monitor. In the first experiment of this study, various delays were imposed between the actual and the cursor movements. The participants' mass perception of the manipulandum increased in proportion to the amount of delay (0, 100, and 200 ms), and the PSE shift at 200 and 400 ms delay was significant. This result suggests the presence of a temporal tuning mechanism for incorporating the visual feedback into the perception of mass (Figure 5.3C). In the second experiment of this study, I examined whether the increase of mass perception was caused by the prediction error of the visual consequence of an action or by the actual/physical delay of the feedback. The result shows that, after habituating to the feedback delay, the mass perception of the object became lighter than that without habituation (Figure 5.4C). My interpretation of the result is that updating the temporal prediction model diminishes the overestimation of the object's mass. I propose that the misattribution of the visual delay into mass perception is induced by the sensorimotor prediction error, possibly when the amount of delay (error) is within the range that can reasonably include the consequence of an action.

6.2 Perspectives on findings

What happens in delay habituation in motor control?

Here, I will discuss the results from studies one to three (Chapters 2-4) and open questions for the future. At first, I will discuss the results of the third study (Chapter 4). This study revealed that the CNS can properly estimate hand position (state) ahead of a delayed cursor by habituating the delay (Figure 6.1A). This result was not derived from ignoring the delayed visual feedback (see Discussion in Chapter 4), which means that “a kind of habituation” occurred to the visual feedback delay. If this habituation is caused by the CNS learning the delay like the Smith Predictor, I can hypothesize that the CNS is able to properly estimate the current hand state by comparing a 200-ms delayed visual feedback with a motor prediction made 200 ms before. If the temporal and spatial processing is separated in the CNS as the Smith Predictor suggests, the proper state estimation should be achieved not only for a simple straight reach (Figure 6.1A) but also for more complicated motions. For example, imagine a tracking task where a target moves on a 2D screen unexpectedly. In this case, the hand trajectory is following the random motion of the target. Estimating the current hand state while observing a 200-ms delayed cursor in this setup (Figure 6.1B) is not as easy as doing so in a simple straight reach (Figure 6.1A). Even so, the Smith Predictor theory makes this estimation possible. The existence of the Smith Predictor in the CNS can be proven by observing the performance in such a complicated tracking task. Miall et al. conducted such a tracking task with 300 ms of cursor delay. Their participants’ performance did not show the expected improvement even after a 5-day training session [38]. They interpreted this result as denying the existence of the Smith Predictor in the CNS.

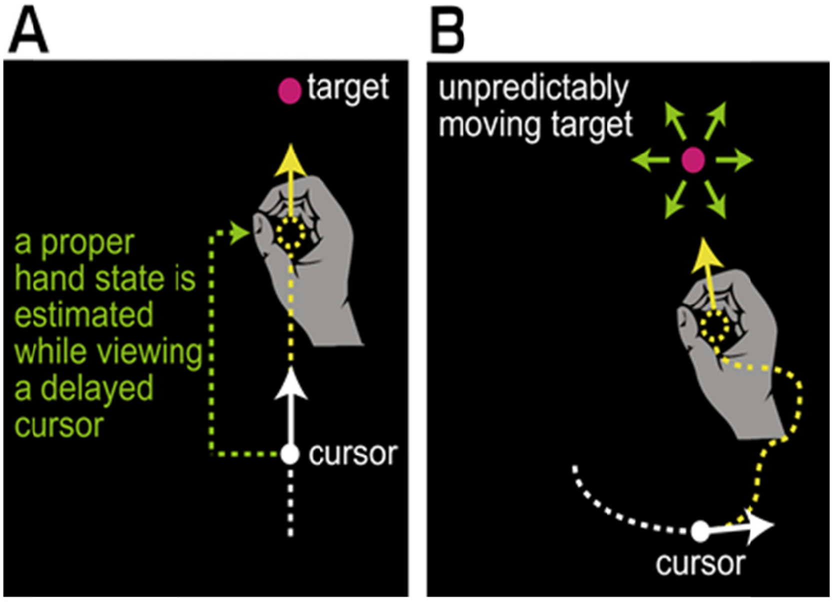


Figure 6.1 Illustration of a simple straight reaching task (A) and a 2D tracking task (B) with delayed cursors.

In the tracking task of Miall, the CNS was required to store the complicated 2D past state of hand for at least 300 ms, in order to achieve a proper estimation. Even if there is a mechanism like the Smith Predictor in the CNS, it does not work when the memory capacity of the CNS is insufficient for the task. If so, we may be able to observe the existence of the Smith Predictor by limiting the motion dimensions and reducing the cursor delay. Rohde et al. conducted such an experiment [103]. They used a one-dimensional moving target and 200 ms of cursor delay. There were two conditions: predictable and unpredictable (Figure 6.2). While the participants habituated to the cursor delay in the predictable condition (Figure 6.2A), they could not habituate to the delay in the unpredictable condition (Figure 6.2B).

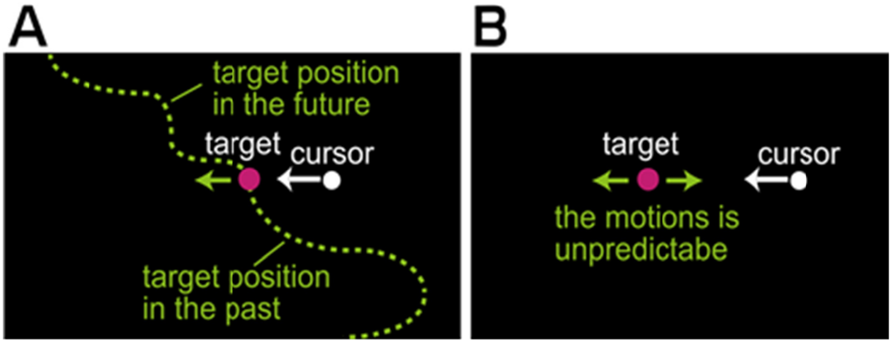


Figure 6.2 Simplified illustration of the setup of Rohde et al.
A. In the predictable condition, a visual display of future motion continually scrolled down, allowing the participants to prepare in advance. **B.** In the unpredictable condition, such a reference was not available and the participants had to follow the target without any hints for future movement.

I note that this simplified task (Figure 6.2B) could not observe delay habituation (the existence of the Smith Predictor) again. The CNS could not estimate the current state of the hand with the delayed cursor which moved rightward and leftward randomly. This result denies the existence of the Smith Predictor in the CNS (at least in the motor control level). Then, what underlies the delay habituation observed in my third study and the predictable condition of Rohde et al.? I postulate that the CNS identifies the cursor delay as a displacement between the hand and cursor in these studies. In my third study, the velocity profile of reaching was almost the same between trials. This means that the displacement profile produced by 200 ms of delay did not differ so much between trials. Therefore, the CNS could obtain an identical displacement profile through trials. This displacement hypothesis is enough to explain the result of my third study (Figure 4.3). In the predictable condition of Rohde et al., what the CNS had to do was not to estimate the current hand state with the delayed cursor (this was required in the unpredictable condition; Figure 6.2B) but to maintain a constant displacement between the hand and target by using the future target position information. This displacement hypothesis is consistent with a recent study reporting that delay is represented mechanically in human motor control systems [104]. Cursor delay cannot be identified as a simple displacement in the experiments shown in

Figure 6.1B and Figure 6.2B. This is why delay habituation was not observed here according to the displacement hypothesis.

How can the alleviation of degraded motor learning in the first and second studies be explained? Remember the study of Tanaka et al. [43]. They allowed their participants to see only endpoint errors, and their participants did not show alleviation of motor learning. On the other hand, I successfully observed alleviation in experiments where continuous feedback was displayed. This comparison leads us to hypothesize that the continuous feedback during movement contributed to the alleviation. As I observed in the third study and discussed in the previous paragraphs, continuous feedback allowed the CNS to estimate the current hand state properly with a delayed cursor after habituating to the delay. This current hand state estimation during movement possibly affected motor learning (Figure 6.3).

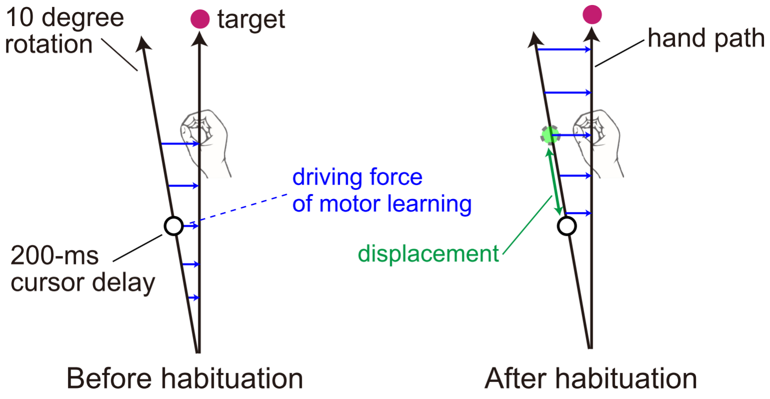


Figure 6.3 Schematic representation of the hypothesis. I assume that the sensory prediction error represented by lateral deviation from the cursor to the hand position predicted by the forward model is a driving force of adaptation to a visual rotation (before habituation). Following the displacement hypothesis, the CNS can estimate future cursor position (represented by the green spot) after habituation. As a result, the total driving force of adaptation during reaching (represented by the blue arrows) is larger after habituation.

Note that our third study (Figure 4.3C, the blue dotted paths) observed the change of hand state estimation predicted in Figure 3.1C. However, the motor learning effect did not show the positive influence of this estimation change (the result of my second study denied Hypothesis 2 in Figure 3.1E). Here I pick up following two factors as what we should study further in the future.

1) The association with a cursor moving before predicted time. After habituating to cursor delay, a cursor moving earlier than predicted time (Figure 3.3, 0 and 100 ms of delay in the *delay condition*) can be perceived as the motion the operator did not cause [11]. The break of a causal relationship with the cursor might have weakened the driving force for motor learning. This possibility is already mentioned in the Discussion in Chapter 3.

2) The relationship between the endpoint and continuous feedback. The endpoint error after each trial works as a driving force for motor learning, as the continuous feedback error does during movement, illustrated in Figure 6.3. The ways that these two kinds of driving force corroborate is still unclear. I conjecture that the result in the second study (Figure 3.3, the aftereffect with 0 ms of delay in the *delay condition*) reflects the corroboration of these two driving forces. Current motor control studies cannot fully explain this phenomenon, and this is an area of research for future studies.

Taylor et al. investigated explicit and implicit motor learning processes with a sudden 45-degree rotation which allowed their participants to notice the perturbation [64]. After noticing the cursor rotation, they started to explore a proper solution to set off the cursor error. One strategy they adopted was to change their aiming location. Taylor et al. set numbers around the start position at the same distance as the target (Figure 6.4, the left illustration). They asked the participants to say which number they were aiming at before beginning (Figure 6.4, the dotted arrow). This allowed them to know how much the participants changed their aiming location (Figure 6.4, the yellow area defined as explicit learning). As the participants repeated trials, their actual reaching direction began to displace from their aiming direction (Figure 6.4, the blue area defined as implicit learning). Taylor et al.

compared the contribution of explicit and implicit learning with continuous feedback to that with endpoint feedback. Their result showed that the contribution of implicit learning was greater in a continuous feedback task than that in an endpoint feedback task. This result is consistent with the finding from another study [105]. In the study of Taylor et al., explicit learning worked in both continuous and endpoint feedbacks. This is because the amount of initial visuomotor rotation (45 degrees) was large enough for the participants to notice. The setup of Tanaka et al. was a combination of a sudden rotation (prism adaptation) and endpoint feedback. Thus, explicit learning should have highly contributed in the early stages of motor learning [43]. The increase of reaction time in the first few trials in the adaptation section of Tanaka's experiment indicates the contribution of explicit learning [106,107]. On the other hand, my first study used a combination of a gradual rotation and continuous feedback. Here, the dominant process throughout the adaptation section was implicit learning. The difference of the dominant motor learning process (explicit or implicit) in these studies may have led to the distinct result that I observed delay habituation while Tanaka et al. did not. I will briefly summarize the findings on explicit and implicit learning in Figure 6.4.

What then is the neural basis for the explicit and implicit learning processes? The cerebellum and cerebellar-cortical loops have been thought most important in supervised error-based learning [108]. Motor learning experiments where a target and an error can be observed (e.g., prism adaptation, visuomotor rotation, force field) are typically thought to require the participants to engage in error-based learning because they must decrease the errors. Both explicit and implicit learning processes are supervised error-based ones by definition. However, researchers nowadays notice that explicit and implicit learning processes cannot be seen as homogeneous. The contribution of the cerebellum, for example, is different between these two processes. Taylor et al. revealed that patients with spinocerebellar ataxia were dependent on strategic (explicit) learning more than healthy controls [109], which means that the spinocerebellar area is strongly related to implicit learning and does not contribute directly to explicit learning. In addition, Izawa et al., through comparing motor adaptation in a gradual visuomotor rotation task of cerebellar patients (most of them with spinocerebellar ataxia) and healthy controls, reported that the cerebellum (esp. the spinocerebellar area) is important for the association between motor commands and sensory consequences (Forward Model in Figure 1.9) [110]. Keisler et al. examined the relationship between motor learning and declarative memory, which is generally thought irrelevant to motor control [111]. They inserted a declarative memory task in a motor task and found that fast motor learning was inhibited by the declarative memory task, while slow motor learning was not. This means that the fast learning process is dependent on declarative memory, for which the medial temporal cortex is thought to be important. They associated their findings with past functional imaging studies, which revealed the importance of attentional process [112] and working memory [113] in the early stage of a sudden perturbation task. They interpreted that the prefrontal regions contribute to fast (explicit) learning, so the activity of the prefrontal regions is high in the early stages of a sudden perturbation.

Considering these two facts that explicit and implicit learning depend on different neural basis, and that the alleviation of degraded motor learning with a feedback delay can be observed in an implicit learning task but not in an explicit task [85,89,43], I hypothesize that the brain regions and neural networks related to implicit learning strongly contribute to delay habituation. As I reviewed in the last paragraph, one of the areas which affect implicit learning rather than explicit learning is the spinocerebellar area. Roth et al. reported that cerebellar patients did not show a temporal recalibration in perceptual prediction for external sensory events, while healthy controls did [114], indicating that the cerebellum controls perceptual predictions. Note that they could not detect the particular region in the cerebellum relating to predictions because most lesions of the patients prevailed among the global cerebellar area. Although we need further studies to detect the neural basis contributing to delay habituation in sensorimotor systems, we can say that the role of the cerebellum is critically important.

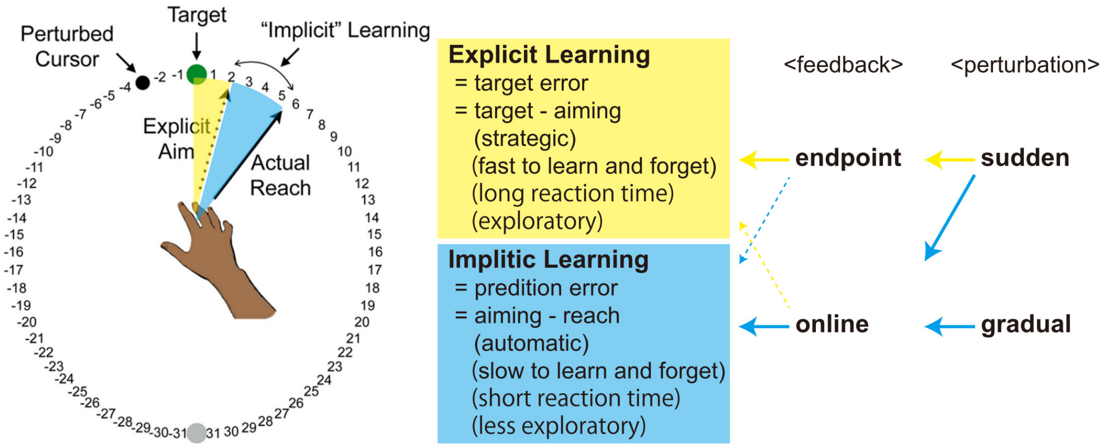


Figure 6.4 A summary of findings on explicit and implicit learning

Although it has been known that motor learning consists of several different processes [61], the differences have not been recognized qualitatively but quantitatively, because researchers have categorized all of them into the same category: supervised error-based learning [108]. However, researchers have come to see these processes to be qualitatively different as the motor control studies progress. One of the most important signs of progress was the development of a method to directly measure the explicit and implicit learning processes (the left illustration [64]). This method, for example, allowed researchers to show that fast and slow learning processes, having been recognized as qualitatively identical so far, are derived from qualitatively different (explicit and implicit learning) processes [63]. It has been known that the requirement of a rapid reaction degrades motor learning. Researchers have recently found that this is because the CNS cannot use an explicit learning process when required to react rapidly [107]. The explicit learning process shows more exploratory behavior [64], which is a feature of reinforcement learning rather than supervised error-based learning [68]. This means that an explicit learning process cannot be simply categorized into supervised error-based learning, despite appearing error-based. In the yellow and blue squares, I summarize the features of explicit and implicit learning. The right diagram indicates which experimental method invokes which learning process.

The impact of delay habituation on perception

To explain the results of the first, second and third studies, as well as previous related studies, I hypothesize that the CNS identifies feedback delay as spatial displacement rather than temporal delay after habituation. The fourth study found that this identification is related to perception. Visual feedback delay was perceived as mass increase before habituation (Figure 5.3). Interestingly, the increase of mass perception disappeared after habituating to the delay (Figure 5.4). The setup I used in this experiment was the same as that in the previous three studies, in which I observed delay habituation in the motor control level. Therefore, I can combine the result of the fourth study with the results of the previous three studies, and postulate that a common mechanism underlies the delay habituation in the perceptuomotor and motor control levels: a predictive mechanism and prediction error. I simply summarize the results of my studies in Table 6.1.

Table 6.1 A simple summary of my findings

	< Before habituation >	< After habituation >
delay	unexpected	expected
motor control (study 1-2)	degradation of motor learning	alleviation of the degradation
state (hand position) estimation (study 3)	biased to a delayed cursor	alleviation of the bias
delay perception (study 4)	sensitive	insensitive
mass perception (study 4)	mass increase	little influence

After the publication of my fourth study, a study against this interpretation was published. Takamuku et al. sought for a factor significantly related to the sense of resistance caused by cursor delay [115]. They found that the significant factor was not the prediction error of position, velocity, and acceleration caused by the delay but the acceleration of a delayed cursor. They concluded that the prediction error did not affect the sense of resistance (mass increase in my study). Importantly, however, this cannot explain the delay habituation in mass perception (Figure 5.4). If the findings from the study of Takamuku et al. applied to my study, the disappearance of the mass increase by habituation would not have occurred because the acceleration of the delayed cursor does not change. Then, how can we interpret these inconsistent results? It may be explainable by examining the setup differences between the studies: I used a reaching task, while Takamuku et al. a reciprocating motion task. In a simple reach, the prediction error is relatively easy to detect due to the amount of displacement between a predicted hand position and a cursor. On the other hand, in a reciprocating motion, the temporal delay or the spatial displacement cannot be easily detected because of the complicated motion of the hand and cursor. Here, identifying prediction error in a temporal or spatial domain is more difficult, and the CNS probably relies more on the inverse dynamics calculation. I believe that the difference of the dominant mechanism invoked by each setup led to the contradictory results.

As Rohde et al. pointed out, sensorimotor delay habituation mechanisms have received little scientific attention until recently [18], much less the relationship between these mechanisms and perception. The effect of sensorimotor systems on perception is biologically interesting and important for our daily lives. One of the most familiar examples is haptic devices such as smartphones. The comfortability the users feel has a great impact on the sale of a device, which affects the international market. Nowadays remote control technology using a network is widespread. In the fields of space development, where expensive devices are used, and medicine, which treats human life, even a slight operation error can be disastrous. Especially in the medical field, there is great motivation to develop a device that medical doctors can use without feeling any discomfort. The more precisely they can operate it, the more quickly and safely patients can recover from their diseases. I would be so glad if the findings of delay habituation and perception can contribute to decreasing human errors.

To close this section, I discuss the contributions and limitations of my studies in the field of temporal recalibration. Temporal recalibration is thought to necessitate the following three components: correspondence detection, bias detection, and error assignment [18].

1) Correspondence detection. The CNS has to detect the correspondence of one's own action as his/her own. When the amount of delay of consequent feedback is somewhat large (more than approximately 600 ms after motor action in a button push task [40,116]), it is difficult to identify agency of the delayed consequence. In the series of my studies, the amount of delay for habituation was 200 ms, which is not thought to break the correspondence detection. It may be difficult to expect the same level of habituation effect with a larger amount of delay for habituation.

2) Bias detection. Only when errors occur systematically, the recalibration against the errors is efficient similarly to spatial errors for motor learning. In the series of my studies, the amount of delay in habituation trials was constant. The probability that I observed the same level of habituation effect with a variable amount of delay for habituation is low [40].

3) Error assignment. The cause of errors has to be properly assigned to the origin of the bias. In other words, which parameters should be recalibrated? In spatiotemporal tasks, error assignment is difficult not only for participants but also for experimenters because of simultaneous spatial and temporal errors. The important parameter for the habituation in my studies might have been the temporal mismatch between hand and cursor motion at the beginning or end of the motion, the spatial offset between hand and cursor in the middle of the motion, or others. The precise detection of the cause to the habituation is necessary to generalize the findings in my thesis. Various

experimental setups will help to approach this purpose: partial blind of a cursor, reaching with variable velocity, curved paths, and so on. It is still unclear whether the habituation I observed in this thesis works in other motor control tasks, which involve different sensory-motor mapping (e.g., a force delay task [96]).

6.3 Implications

Implications for efficient training programs on manipulating devices with delay

Generally speaking, there are two ways to enhance the precision of operating a device. One is a technological approach: reducing possible obstacles like noise and delay to zero. This is what engineers are engaged in. If they can make a perfect device without any noise or delay, other struggles are unnecessary. However, this is impossible. Therefore, the other approach is a must. This is what neuroscientists are engaged in: improving the operating accuracy by understanding the sensorimotor control mechanisms of humans.

Afgin et al. investigated the relationship between perception and motor control when humans perform a telerobotic grasping task with transmission delay [117]. Their participants were required to manipulate a pair of Phantom Premium devices fitted with finger thimbles, which were connected to a robotic arm with two fingers. Their main task was to grasp various objects with the device. Both their motion and perception were recorded by the Phantom devices. The authors revealed that perception and motor control do not synchronize when manipulating a telerobotic hand with delay, while they do synchronize in natural grasping. This separation probably increases the risk of human error. Thus, elucidation of the mechanisms for the separation, and development of a solution are required.

My fourth study showed that delay habituation in motor control is related to perceptual change. Note that whether the delay habituation in sensorimotor control directly affected perception is not clear in my study, and that further studies are necessary to understand their causal relationship and detailed mechanisms. I expect the progress of these studies to develop effective training programs to cancel the gap between motor control and perception in the CNS when controlling a device with delay, and therefore enhance performance.

In the previous section, I introduced recent studies about two motor learning processes: explicit and implicit learning. According to these studies, memory learned implicitly can reproduce acquired motions stably for a long time, and is acquired and stored without perception, preventing undesirable effects on perceptuo-motor systems. Therefore, I expect that an implicit introduction of delay may progress delay habituation efficiently in both the perceptuomotor and motor control levels, though it takes more time than explicit ones. Avraham et al. compared the explicit and implicit introduction of a delay in a part of their study, in which they investigated whether the CNS copes with delay using a representation of the actual time delay [118]. The device they used was a manipulandum similar to that I used. In the habituation trials, the cursor shown on the horizontal screen was delayed. In the probe trials, the participants were required to reach a target without visual feedback, and the hand position at the end of reaching was evaluated. They reported that no significant difference of delay habituation was observed between the two conditions. Note that the delay exposure period (trial number) was long, possibly long enough to render implicit learning dominant by the end of the sudden introduction of delay. In this case, catch trials are necessary to strictly compare the effect of the two kinds of delay introduction. However, they did not, maybe because it was just an additional experiment. More importantly, the probe trials after the delay exposure were not set with the purpose of detecting the qualitative difference of delay habituation. I think that there is still a high possibility that the different effects of explicit and implicit delay habituation will be detected. Indeed, though the experiment of Avraham et al. did not find a significant difference, we can see the tendency that effects of delay habituation in implicit learning were greater than those in the explicit. In the same manner, as motor learning studies, which revealed the existence of qualitatively different learning processes with the advancement of the study, delay habituation studies will also progress and detect such mechanisms.

I expect such advancement to contribute to the development of more comfortable devices and fewer human errors in remote control tasks.

Implications for clinical neuroscience

It has been well known that certain psychiatric disorders are strongly related to motor dysfunction. For example, it is reported that 60-80 percent of schizophrenia patients have at least one kind of motor dysfunction [119]. Patients with autism spectrum disorder (ASD) are also known to show some motor dysfunction [120]. However, the motor dysfunction is not considered as a critical feature necessary for a diagnosis of these psychiatric disorders, because the relationship between certain motor abnormality, related neural basis and cognitive symptoms is complicated and not fully understood. Thus, the diagnosis deeply depends on the doctor's judgment causing the following problems. 1) The diagnosis precision depends on the doctor's experience and skill, and the diagnosis could be diverse among doctors. 2) The doctors cannot show an objective measure to the patients and their family members. 3) Finding the disease only through cognitive symptoms is difficult.

Nowadays, neurological soft signs (NSS), which represent neurological abnormalities in the domain of motor coordination, sensory integration, or motor sequencing, are spotlighted as a way to detect a psychiatric disorder in its early stages [121]. Motor coordination can be tested by the balance of gait, and sensory integration through multisensory tests such as audio-visual integration. If these unconscious motions or simple perception tests can precisely predict later psychiatric symptoms, they will help discover potential patients quickly and allow for early treatment. Thus, researchers are struggling [119]. The struggle to develop an objective assessment for ASD is also underway [122]. I believe that cognitive neuroscience can help develop more sophisticated assessments for patients with psychiatric disorders.

I want to introduce a study by Voss et al., which investigated the relationship between schizophrenia and perception [123]. They used the experimental setting introduced by Haggard et al. [39] to compare delay perception in schizophrenic patients with the perception in healthy people, and showed that temporal perception in schizophrenic patients differs from that of healthy people. Schizophrenic patients relied more on sensory information and less on motor prediction. This result shows that schizophrenia is related to the deficit of a predictive mechanism in the brain, which is consistent with the hypothesis Frith et al. suggested. They postulated that the failure of the forward model in schizophrenic patients causes abnormal motor perception [17].

My experiments (Chapter 2 to 4) indicate that motor command or motion per se includes delay-predictive information. This is a slight piece of findings on predictive mechanisms. If we carefully investigate and correlate these experimental findings with clinical findings in patients, we may be able to understand better both the disease and the neural basis of predictive mechanisms. Though my present studies cannot directly contribute to the clinical field, I hope the accumulation of these findings helps to improve precise screening, early disease discovery, better treatment, and improved rehabilitation for patients with psychiatric diseases.

6.4 Conclusions

Regardless of the importance of delay habituation, deserved attention has not been paid to it. Especially in motor control, difficulties in investigating delay habituation have prevented researchers from approaching it. A series of delay habituation studies in this thesis successfully vindicated the existence of such a mechanism from various viewpoints: motor learning and current state estimation (Chapter 2 to 4). Also, I clarified that delay habituation in motor control is strongly connected to delay and mass (or resistance) perception. These findings can contribute to the elucidation of the neural basis for delay habituation and the relationship between motor and perception.

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