

Space/Time Interactions in Biological Motor Learning

Master of Science Thesis in Biomedical Engineering

Ali Farshchiansadegh

Department of Signals and Systems
Division of Biomedical Engineering
CHALMERS UNIVERSITY OF TECHNOLOGY
Göteborg, Sweden, 2012
Report No. EX084/2012

Master of Science Thesis
Ali Farshchiansadegh
Department of Signal & Systems
Chalmers University of Technology, 2012

Thesis Supervisor: Ferdinando (Sandro) Mussa-Ivaldi

Professor, Department of Biomedical Engineering
Department of Physical Medicine and Rehabilitation
Department of Physiology
Northwestern University
Founder and Director, Robotics Laboratory
Rehabilitation Institute of Chicago, United States

Examiner: Yngve Hamnerius

Professor, Department of Signals and Systems
Chalmers University of Technology
SE-412 96
Goteborg, Sweden

ACKNOWLEDGMENTS

Many thanks to Dr. Sandro Mussa-Ivaldi for his guidance, Dr. Yngve Hamnerius and fellow lab members for their assistance and encouragement, my wife and parents for their love and support.

Funding for this research comes from NINDS grant NS35673 and BSF grant 2007195.

Table of Contents

Chapter One	1
Abstract.....	1
1.1 Introduction	2
1.2 Methods	3
1.3 Experimental Protocols	4
1.4 Data Analysis.....	6
1.5 Results	8
1.6 Discussion.....	13
Chapter Two	17
Abstract.....	17
2.1 Introduction	18
2.2 Methods	20
2.2.1 Subjects	20
2.2.2 Apparatus	20
2.3 Procedure	21
2.3.1 First experiment: learning in presence of delay.....	21
2.3.2 Second experiment: spatial generalization of the learning	24
2.4 Data analysis.....	27
2.4.1 Statistical analysis.....	28
2.5 Computational Model.....	28
2.5.1 Learning in Allocentric space.....	28
2.5.2 Learning in Egocentric space	29
2.6 Results	31
2.6.1 First experiment: learning in presence of delay.....	31
2.6.2 Second experiment: generalization of the learning	34
2.6.3 Results of the computational model.....	39
2.7 Discussion.....	40
References	44

Chapter One

Adaptation to visual feedback delay in a redundant motor task

Abstract

The goal of this study was to examine the reorganization of hand movements during adaptation to delayed visual feedback in a novel geometrical environment. Two groups of subjects tracked a target along predictable paths by wearing an instrumented data glove that recorded finger motions. The high dimensional glove signals controlled a cursor on a two-dimensional computer display. The experiment was performed on two consecutive days. On the first day, subjects practiced tracking movements without delay. Their ability to reduce the tracking error and to guide the cursor over increasingly rectilinear paths indicates that they learned an inverse model of the hand-to-screen transformation. On the second day the test group performed the tracking task with a visual feedback delay of 300 ms, while the control group continued practicing the non-delayed trials. Due to the inherent redundancy of the task there were two possible solutions to compensate for the delay: One was to capture the nature of the perturbation and modify the inverse model of the hand-to-screen mapping which is formed during the non-delayed trials and the other option is to form a new inverse map during adaptation. We report two findings. First, subjects showed a clear evidence of adaptation to visual feedback delay by reducing the tracking error and variability of their movements as well as increasing movement smoothness. Second, the baseline inverse map was robust to the perturbation and subjects relied on the coordination patterns during the baseline practice to compensate for the delay.

1.1 Introduction

Sensory – motor adaptation is an essential aspect of motor control since the mechanical properties of muscles and the response properties of the sensory organs change both over long and short time scales. To maintain a desired performance, the neural controller must be robust to these ongoing alterations. During the past two decades, several studies have demonstrated the ability of the sensory-motor system to adapt to different types of perturbations. These perturbations included force fields (Shadmehr and Mussa-Ivaldi 1994; Shadmehr et al. 1995), visuomotor transformations brought by wearing optical prisms (Redding and Wallace 1990; Redding et al. 2005) and rotation and scaling of visual feedback (Krakauer et al. 2000; Krakauer 2009; Braun et al. 2009).

Most of the earlier studies are concentrated on the alteration of spatial and force information, while temporal distortions have been less extensively probed (Miall and Jackson 2006; Foulkes and Miall 2000; Miall 1996; Miall et al. 1985). Pressman and colleagues (2008) revealed that in a haptic task, the presence of delays between hand position and reflected force causes systematic alterations of perceived object stiffness. The slow transmission rate of sensory information within the nervous system causes significant delays in the sensory motor loop. The delays are also variable depending on sensory pathways (e.g. proprioceptive, visual, acoustic etc.) To preserve correct haptic perception and motor control, the brain must compensate for the effects of variable delays. It is therefore plausible that the brain would be able to adapt also to an externally imposed delay in the sensory motor loop.

The task in the current study was characterized by a high degree of kinematic redundancy, with 19 signals mapped into two cursor coordinates. The most important goal in a remapping task is to learn how to embed the controlled space within the articulation space. The ability of the motor learning system to perform such remapping operation was investigated by Mosier and colleagues (2005) who asked subjects to control the position of a cursor by changing the configuration of their fingers to reach targets appeared randomly on the screen. Although the task did not explicitly specify any particular trajectory, subjects expressed a trend toward straighter paths of the controlled cursor. This trend suggested that subjects learned a motor representation of the Euclidean space over which finger movements were remapped. Using a same experimental approach, Liu and colleagues (2010) reported that the central nervous

system compensates in two different ways for distorted cursors position by either a rotation or scaling transformation; subjects developed a new coordination pattern in compensating for the rotation but relied on the patterns established during baseline practice to compensate for the scaling. In the current study, we instructed, subjects to track a target, which moved in different directions on the screen. This task specified not only the position to be reached by the cursor, but also the time in which each position needed attained. Therefore, the task allowed us to investigate how the introduction of a visual feedback delay affects the inverse hand-to-screen mapping. Subjects had two choices when a delay, was imposed on the cursor such that the new coordinates became $(x(t - \tau), y(t - \tau))$. One is to maintain unchanged the internal model of the map between hand configuration and cursor position. In this case, the brain must represent correctly that there is a shift in time – the delay – and compensate for it by predictive control. The alternative approach would be to learn a new map that associates the configuration of the hand at t , with the position of the cursor at the same time. Because of the inherent redundancy of the task both solutions are legitimate to perform the task.

1.2 Methods

14 neurologically intact right hand dominant subjects (mean age 26 ± 6 , 5 females) participated in the experiment and were randomly assigned to a test ($n=7$) or an aged matched control ($n=7$) group. All subjects were naive to the purposes of the study and provided written informed consent approved by Northwestern University’s Institutional Review Board. Each subject wore a right-handed cyber glove (Immersion, San Jose, CA). The cyber glove captures the movement of each finger joint: flexion of the phalangeal joints (proximal, middle, and distal), abduction of the thumb and fingers, and wrist flexion/extension and abduction/adduction, via 19 resistive sensors. Data from the glove were sampled at the rate of 50Hz.

The 19- dimensional vector of the sensor values was mapped on to the 2-dimensional (x,y) coordinates of a computer screen using a linear transformation. (Liu et al. 2010; Mosier et al. 2005)

$$\mathbf{P} = \begin{bmatrix} x \\ y \end{bmatrix} = \begin{bmatrix} a_{1,1} & a_{1,2} & \dots & a_{1,19} \\ a_{2,1} & a_{2,2} & \dots & a_{2,19} \end{bmatrix} \begin{bmatrix} h_1 \\ h_2 \\ \vdots \\ h_{19} \end{bmatrix} + \begin{bmatrix} x_0 \\ y_0 \end{bmatrix} = \mathbf{AH} + \mathbf{P}_0$$

Where $P = [x \ y]^T$ is the cursor location on the screen (Endpoint Space), $H = [h_1 \ \dots \ h_{19}]^T$ is the glove signal vector (the articulation space) and $A = [a_{i,j}]$ is a matrix of mapping coefficients (hand to screen map). $P_0 = [x_0 \ y_0]^T$ is a constant matrix that aligns the mean value of calibration points to the coordinates corresponding to the center of the screen.

Before starting the experiment, in order to determine the coefficients of the hand to screen map ($A_{2 \times 19}$) we asked subjects to move all their fingers in a free-form spontaneous pattern – an activity which we called ‘finger dance’ - until around three thousand samples were recorded. We used principal component analysis (PCA) to derive a set of orthonormal axes capturing the distribution of finger movement variance. Coefficients of the first and second PCs formed the hand to screen transformation for each individual subject: the first two PCs mapped the high dimensional articulation space into the vertical and horizontal axes of the screen respectively. Furthermore the coefficients of the matrix A were scaled to insure that every point within workspace could be comfortably reached. In this framework, each hand posture corresponds to a unique point on the screen, while each screen location can be mapped into a continuous subspace of “equivalent” hand postures.

1.3 Experimental Protocols

Subjects seated 0.5 m in front of a flat screen (1280×1024 pixel resolution), wearing a cyber-glove. Each participant attended two one-hour sessions held across two consecutive days. At the beginning of each trial, subjects were asked to maintain the cursor inside a circle with the diameter of 50 pixels. Hereinafter, this circle is referred to as the “Moving Target”. After the cursor was inside this target for about 2 s, the target started to move toward one of three stationary targets that appeared in a random order on the screen (Fig1.A). Subjects were instructed to maintain the cursor inside the moving target until it reached one of the stationary targets. Each trial started from the same initial position and subjects could rest anytime between trials. The first session consisted of 10 epochs, in each epoch subjects performed 30 center-out trials, 10 for every movement direction. Subjects gained a positive score if they succeeded maintaining the cursor inside the moving target.

Between every two epochs, subjects performed three additional trials without visual feedback of the cursor position. In this task without cursor feedback, the moving target

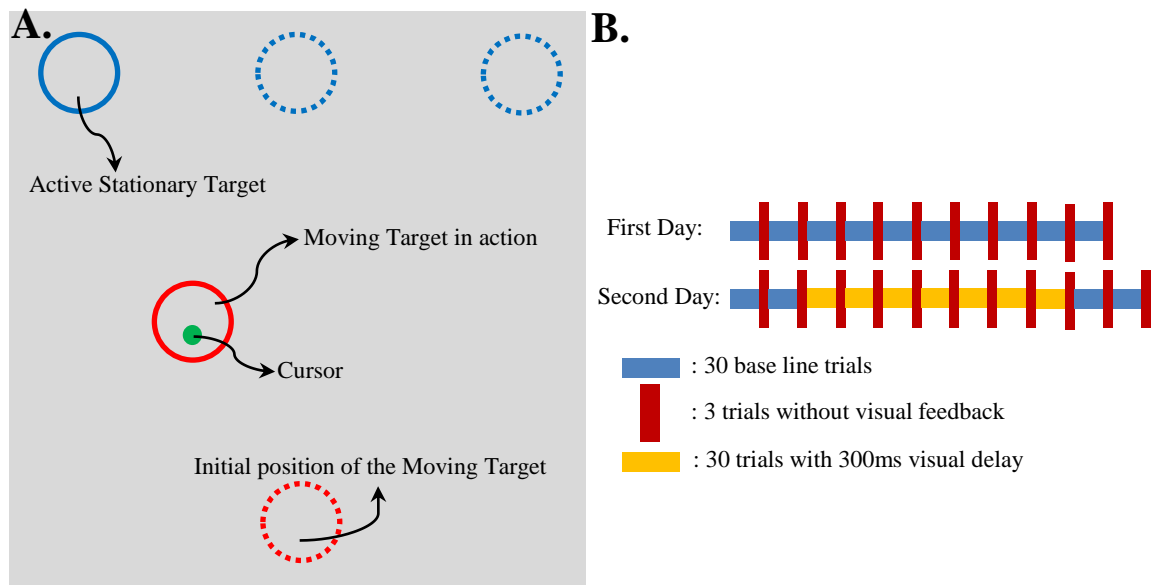


Figure 1: Schematic view of the experiment and protocol. **A.** After putting the cursor inside the moving target and holding it for 2s, the moving target started to move towards one of the stationary targets in random order. Subjects were instructed to keep the cursor inside the moving target until it reached the stationary target. **B.** In the first day, there were 10 epochs of 30 baseline (0 delay) trials and 3 trials without visual feedback after each epoch. In the second day there were 11 epochs with 7 epochs of adapting trials with visual delay for the test group.

was replaced by a variably sized red circle. The diameter of this circle was proportional to the Euclidean distance between the instantaneous cursor position and the center of the moving target at resting position (error), if this distance was less than the target radius, the error circle turned green indicating that the cursor was inside the moving target.

After the resting posture was held for about 2s, the stationary targets were presented in a random order. Subjects were instructed to start moving as soon as one of the stationary targets appeared and to stop moving whenever they believed they had reached the target. At the end of each movement, the feedback of the actual cursor position was presented for 1 s.

The second session consisted of 11 epochs. Control subjects followed the same protocol of the previous day. The test group had same configuration of the first session in the first two epochs in order to reinforce the learned baseline mapping of the previous day. The epochs 3 to 9 had delayed visual feedback. In these trials the representation of the cursor on the screen was 300ms delayed. The last two were the wash-out trials where the delay was removed (Fig1.B).

1.4 Data Analysis

Signals from 19 sensors of the cyber glove, the coordinates of the cursor, and center of the moving target were acquired during the experiment and used for further analysis. Six performance indicators were analyzed.

1) *Tracking error*: Tracking error was defined as the Euclidean distances between the cursor and the center of the moving target. Errors were then averaged across all 30 trials in a single epoch. The value obtained for all epochs from each subject were then normalized by the first epoch and averaged across all subjects in each group.

2) *Smoothness of the movements*: A widely used metric to measure the skilled, coordinated movements in goal directed reaching tasks is smoothness. Jerk or the second derivative of the speed profile is used in the literature as a standard measure to quantify smoothness (Flash and Hogan 1985). We calculated the jerk as in (Smith et al. 2000):

$$J = | \sum_{k=1}^n \ddot{x}(t_k) |$$

Here, t_k corresponds to discrete samples of a single trial. A 50 Hz Savitzky- Golay (1964) filter was used to smooth and attain the second derivative of the speed profile for each trial. We then averaged the jerk across all trials in a single epoch and all subjects in each group.

3) *Cursor Vector Direction*: following each epoch, there were three trials without a visual feedback. In these trials, the starting point was replaced by an error circle to prevent subjects to receive any information about the hand to screen transformation between trials. Subjects were instructed to stop moving whenever they believed that they had reached the target. Errors in blind trials were calculated for baseline epochs before introduction of the delay. The error was defined as the angular difference between the vector connecting the first sampled cursor position to the center of the stationary target and the cursor vector joining the start point and the end point of the movement. The error was calculated for trials without visual feedback and averaged across all subjects.

4) *Movement variability*: The joint articulation space had 19 degrees of freedom and cursor moved in a two dimensional space. Thus, there exist an infinite number of possible hand movements to capture targets. A unique feature of this task is the ability to clearly distinguish between the degrees of freedom that contribute to kinematic

performance and the degrees of freedom that do not. This is analogous – in simplified linear terms - to the concept of controlled and uncontrolled manifolds (Scholz and Schoner 1999). The Moore-Penrose pseudoinverse of A allows us to decompose the map into a “task space operator”, H_T and a “null-space operator”, H_N :

$$\begin{aligned} H_T &= A^+AH \\ H_N &= (I_{19} - A^+A)H \end{aligned}$$

Where $A^+ = A^T(AA^T)^{-1}$ and I_{19} is the 19-D identity matrix.

To calculate variability in the task and null space, glove signals corresponding to all ten trajectories toward each target in a single epoch (see experimental protocols) were divided into sets of ten hand postures, in which each set contained glove signals recorded at fixed time with respect to the initiation of the movement of the moving target. The variability of the projections of the hand postures in both the task and the null space were calculated for each set and then averaged across all sets and across all subjects in each group. Training during the delayed sets of trials influenced both the task and null space variability. One way, repeated measures ANOVA using a threshold for significance of $p \leq 0.05$ was performed to examine how training changed task and null space variability.

5) *Inverse map*: The metric we used to quantify the extent to which visual feedback delay induced change of the inverse hand-to-screen map is similar to the metric used by Liu and colleagues (2010). Let P denote a matrix containing the cursor locations on the screen in a certain epoch and H the corresponding glove signals, and then the inverse hand-to-screen map B_{est} is derived by the following equation:

$$B_{est} = P^T(PP^T)^{-1}H$$

We calculated the B_{est} for three epochs of the second session: the first two base line epochs (B_{BL1} and B_{BL2}) and the last delayed epoch (B_{adapt}). The cursor location was transformed during the delayed epoch. Therefore, to investigate whether the inverse map is completely changed or it is just modified to overcome the delay, we compute B_{adapt} by considering the actual coordinates (not a delayed representation) of the cursor. We evaluated the difference in magnitude between the two baseline epochs and the difference in magnitude between the inverse map obtained after adaptation (B_{adapt}) and inverse map at the end of baseline practice using the following equations:

$$\Delta B_{noise} = ||B_{BL1} - B_{BL2} ||$$

$$\Delta B_{adapt} = ||B_{adapt} - B_{BL2} ||$$

A difference magnitude ΔB_{adapt} significantly exceeding ΔB_{noise} would suggest that adaptation induced changes in the motor representation of the space.

6) *Euclidean distance between the null space components of the hand posturers:*

Examining the progression of the activities within the null space provides us with insight on how the central nervous system reorganizes patterns of coordination. For each trial, we calculated the null-space projections of the hand postures. The null-space component of each hand posture was a 17 dimensional vector. To limit the effects of noise on the calculation of the Euclidean distance in high dimensional data sets, we used PCA to compute for each trial an ordered set of orthogonal axes capturing the distribution of the variance of the movement in the null space.

Ten points on the cursor trajectory were selected based on their relative distance from the initial position: starting from 50 pixels and in increments of 50, to 500 pixels. For each epoch, the first two PCs of the null space components of the hand signals corresponding to each selected position were put into a single set and the mean of each set was then derived. The data of the first epoch of the second session was taken as reference, and the Euclidian distance of the mean null space components of the corresponding sets in the remaining epochs of the second session was calculated in reference to this epoch and averaged across all sets and across all subjects in each group. We also calculated the variance of the selected points from the cursor trajectory. It is important to note that this variance is different from the one we calculated in the task space: because in this metric the timing error is not factored into the calculations and we are calculating the variance of the cursor trajectory without taking in to account the time parameter. The variance of the cursor trajectory is calculated for each epoch and averaged across all subjects in each group.

1.5 Results

All subjects improved their performance with practice. Though training, subjects learned how to control the cursor and reduce the error (Fig.2). We ran repeated measures of ANOVA with two factors, i.e. practice and group, to compare the first set of trials with the epoch before introduction of the delay. While we found a significant effect of practice ($F(1,12) = 122.96, P < 0.001$), there was no group effect ($F(1,12) =$

0.18, $P = 0.68$). Being expected, when the delay was introduced the tracking error increased. Subsequently, subjects in the test group adapted to the perturbation and their performance converged toward the performance of the control group. One way repeated measures of ANOVA between early (epoch 4 of the second day) and late (epoch 9 of the second day) delayed epochs revealed that the performance significantly improved ($F(1,6) = 7.3, P = 0.036$). Learning of the kinematic mapping between hand configuration and object position progressed during the second session of the experiment as well. For control subjects the reduction of the tracking error during the time in which test subjects experienced the delay was significant ($F(1,6) = 11.59, P = 0.014$). However, at the end of the experiment the performance of the two groups was not significantly different (paired t-test: $p = 0.54$).

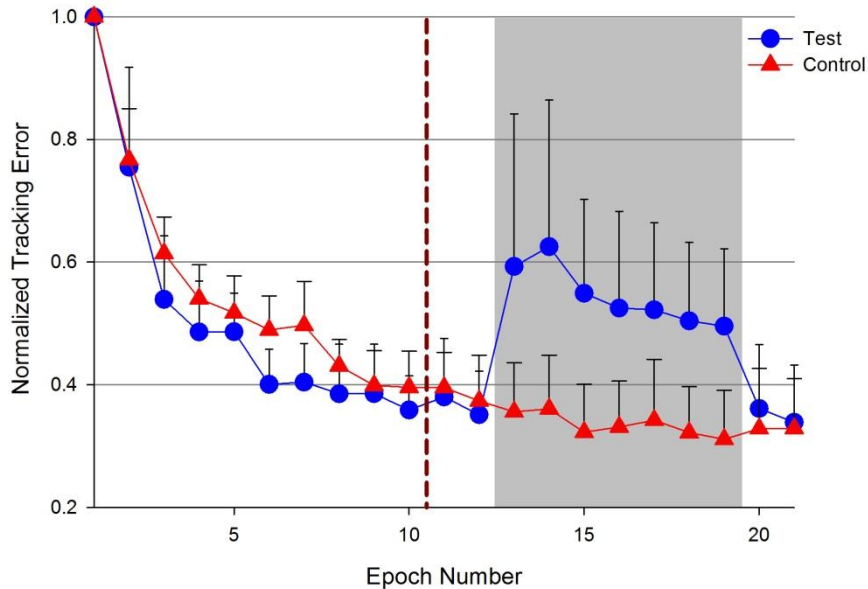


Figure 2: Normalized tracking Error. The dashed vertical line indicates separate days and the gray area includes epochs with the delay for the test group. Error bars represent 95% confidence intervals. The errors are calculated by summing Euclidean distances between cursor and center of the moving target during each trial and averaged across all trials in each epoch. The value obtained for all epochs of each subject were then normalized by the first epoch and averaged across all subjects in each group.

Subjects increased the smoothness of their movements with training. Two way repeated measures of ANOVA showed that the jerk index between the first set of trials and the epoch before introduction of the delay for both groups decreased significantly ($F(1,12) = 50.95, P < 0.001$) with practice and there was no group effect ($F(1,12) = 1.28, P = 0.28$). Jerks of movements increased drastically when delay was introduced and eventually subjects were able to regain smoothness ($F(1,6) = 22.8, P = 0.003$) (Fig 3.A). It is intuitive that the best strategy to do the task was to try to match the cursor's

velocity with the velocity of the target, which was moving at constant speed. Figure 3.B is derived by polynomial smoothing of the velocity profiles of a representative subject in three stages of the experiment: Before the delay, early delayed trial and late adaptation trial. It can be seen that starting from zero, the subject succeeded to preserve the velocity almost equal to the velocity of the moving target, which was 200 Pixel/S in the experiment. After introducing the delay this behavior interrupted and results show a disturbed velocity profile and finally in the last delayed trial, subject showed a clear adaptation to the delay since the velocity profile shows an almost steady tracking speed. The results from the tracking error and movement smoothness confirm that test subjects have adapted to 300 ms visual feedback delay.

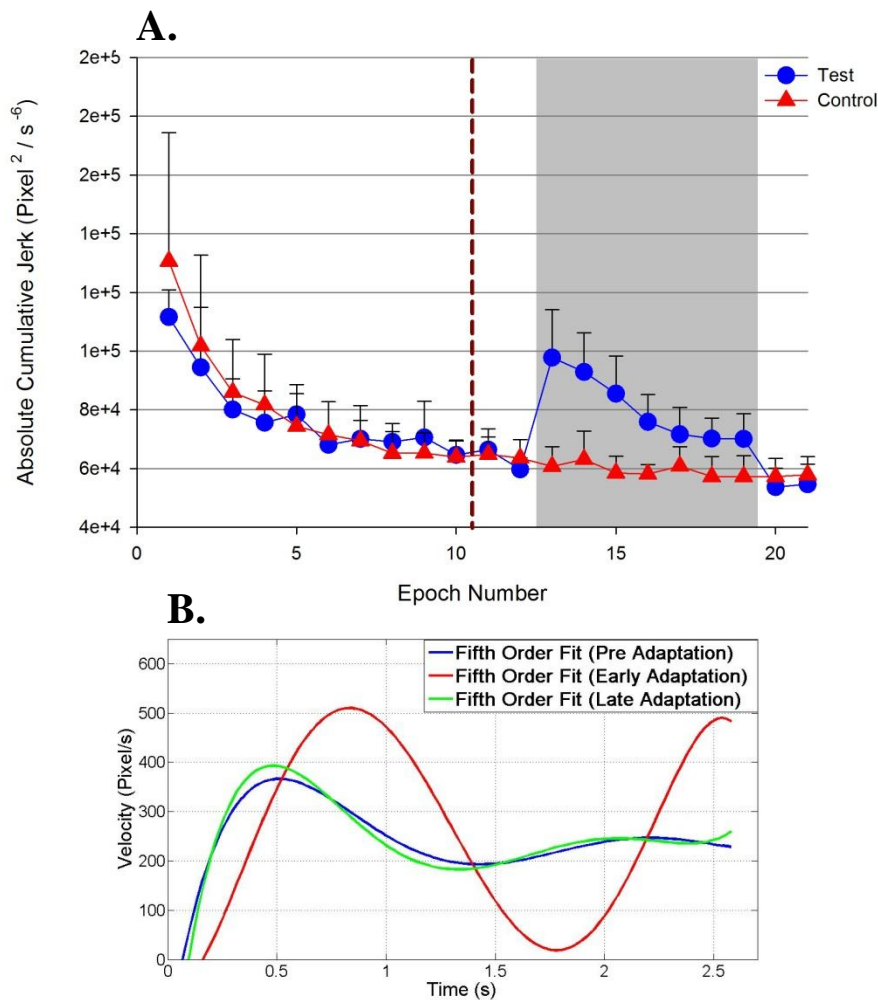


Figure 3: Analyzing smoothness of the movements. **A.** Absolute cumulative jerks, dashed line indicates separate days and gray area includes epochs with delay. Error bars represent 95% confidence intervals. Data is averaged across all trials in a single epoch and all subjects in each group. **B.** Fifth order polynomial fit to discrete velocity samples of a single trial of a representative test subject in 3 stages: Before the delay, early delayed trial and late adaptation trial.

We examined the extent to which delay distortions induce reorganization of the motor representation of the Euclidean space onto which finger movements are mapped. But

preliminary to this, it should be verified that subjects had built a forward model and they were aware of the sensory consequences of their motor commands. Therefore, angular differences between the cursor vector and desired movement vector were calculated for the trials without visual feedback. Through training subjects reduced the direction error (Fig 4.A). Figures 4.B and 4.C show the trajectory of a representative subject during trials without a visual feedback at the very beginning and after extensive training. This type of change suggests that participants have built a feed forward model and they were not purely relying on the visual feedback.

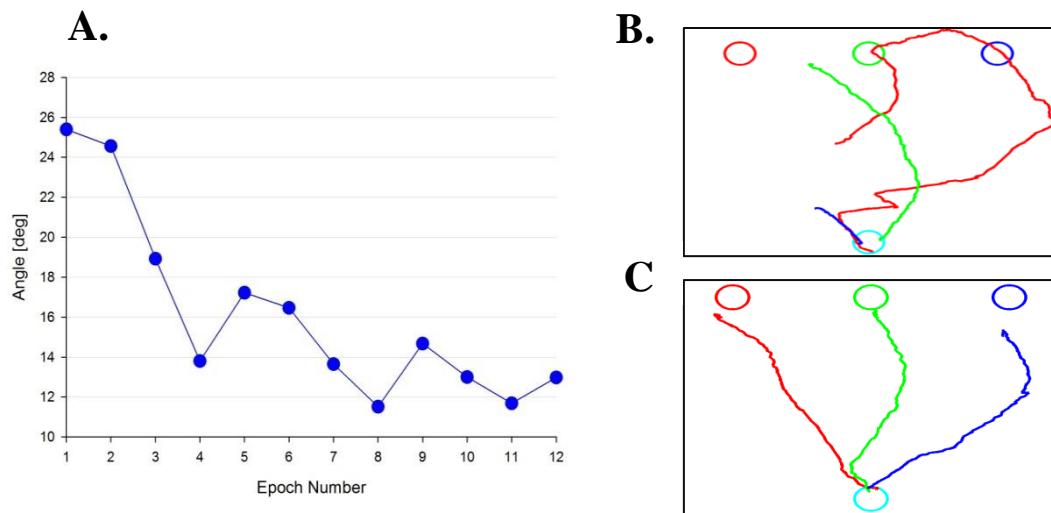


Figure 4: Evidence of building a forward model. A. Direction Error during base line trials: Angular difference between the vector joining the starting point to the center of the stationary target and the vector connecting the initial and last position of the cursor in trials without visual feedback. The data are averaged across three trials and across all subjects. B. Movement trajectory of a representative subject in the first set of trials without visual feedback. C. Movement trajectory of a representative subject in the last set of trials without visual feedback before delay adaptation trials.

We have calculated the task and null space variability during the second day of the experiment (Fig. 5.A). One way repeated measures of ANOVA between two sets of trials before (epoch 2 of the second day) and after (epoch 4 of the second day) introduction of the visual feedback delay showed that test subjects exhibited a main effect of the training phase for the task space ($F(1,6) = 6.6, P = 0.042$) and no main effect of the training phase for the null space ($F(1,6) = 5.8, P = 0.052$). However, the P value is very close to the threshold. Increased variance in the task space simply shows subjects' errors in performing the task and indicates that during early adaptation, subjects failed to track the moving target appropriately. Furthermore, the cursor position at any particular time varied from trial to trial. In contrast, increased variance in the null space can have different interpretations. One interpretation is that the null space

contribution to command updating increased upon introduction of the delay suggesting that subjects were exploring the null space to build a new inverse model of the hand-to-screen mapping so as to compensate for the perturbation. Another possibility is based on the observation that, due to the physiological couplings between the articulations of the hand, it is not feasible for the brain to activate the degrees of freedom that are contributing to the task independently from the remaining degrees of freedom. In other words, the controlled space is embedded in the articulation space in such a way that it is impossible to increase the variance in task space without producing a similar effect in null-space.

Figure 5.B illustrates the extent to which B_{est} changed during the adaptation to the visual feedback delay. For the test subjects ΔB_{adapt} did not exceed ΔB_{noise} (repeated measures: $F(1,6) = 0.005, P = 0.94$) yielding an average within subject difference of 0.019 ± 0.014 glove signal unit (GSU) per pixel. Therefore, test subjects modified their baseline inverse map to compensate for the imposed temporal distortion.

A complementary approach is to investigate the null space components of the hand postures when the cursor is located at the certain position in the endpoint space before and after adaptation. If subjects applied an inverse transformation T^{-1} to the baseline inverse map, then once the actual position of the cursor (not the delayed representation) is located at a certain position in the endpoint space the null space components of the hand posture should be equal to the null space components of the hand posture at the same position in a baseline trial. On the contrary, if subjects created a new inverse map during adaptation then the null space components of the two hand postures would be different.

We have calculated the Euclidean distance between the null space components of the hand postures of the epochs 2:11 of the second day with respect to data of the first epoch of the same day (Fig 5.C). With the introduction of the delay the variance of the cursor trajectory significantly increased (Fig 5D). In the late adaptation epoch (epoch 9 of the second day) there is no significant effect of having trained with delay on the Euclidean distance (paired t-test: $p = 0.75$) between the test group and the control group. This suggests that the baseline inverse map was robust to the perturbation and subjects applied the inverse transformation T^{-1} to compensate for the visual feedback delay. In contrast, if test subjects had changed the inverse map, we would have expected the two curves to diverge. In early-perturbation trials the peak shows a deviation from the

baseline inverse map due to uncertainty but with practice subject tended to preserve the inverse map that they had acquired in the early baseline practice.

The variance of the cursor trajectory in each epoch significantly increased with the introduction of the delay (Fig 5.D, repeated measures between epochs 2 and 4 of the second day: $F(1,6) = 7.65, P = 0.033$).

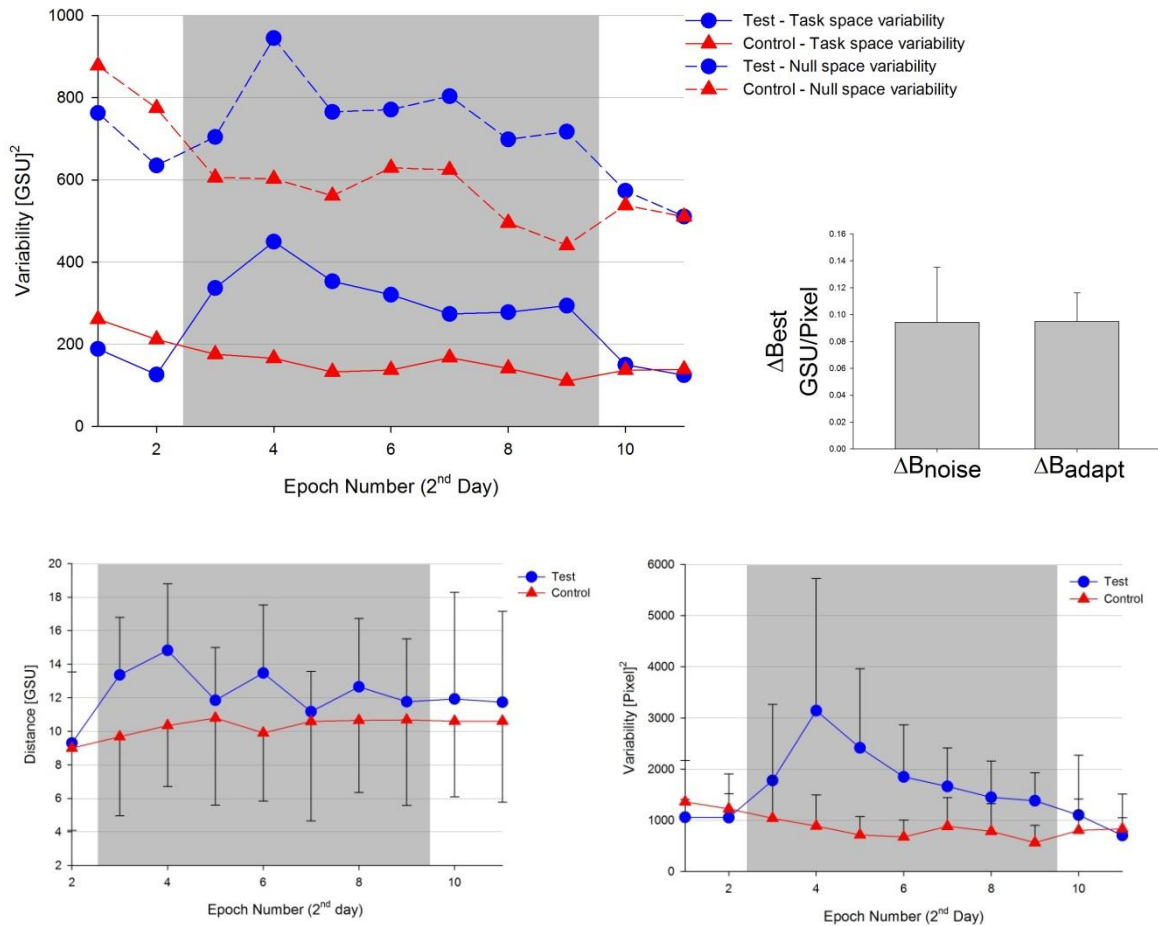


Figure 5: Analysis of kinematic performance during second session. A. Postural variability as a function of epoch number of the second day. Blue and red represent test and control groups respectively and dashed lines and solid lines represent the null space and the task space variance respectively. Grey area includes epochs with delay. The data of the first day of the experiment is not included for better visibility. B. ΔB_{est} the measure of reorganization within the articulation space before and after adaptation. C. The Euclidean distance between the null space components of the hand postures of the epochs 2:11 of the second session with respect to data of the first epoch of the same session. Grey area includes epochs with delay and error bars represent 95% confidence intervals. D. Variance of the cursor trajectory. Grey area includes epochs with delay. Error bars represent 95% confidence intervals.

1.6 Discussion

The objective of our study was to investigate how subjects compensate for the temporal visuomotor transformation corresponding to the introduction of a delay between the

motion of the hand and the display of a cursor controlled by this motion. We addressed this question in a remapping paradigm, where subjects controlled a cursor by moving their fingers. The map from the articulation space (the configuration of the finger captured by 19 data glove signals) to the task space (the 2 coordinates of the cursor on the computer monitor) had 2 key features:

- 1) It was a redundant map since a multitude of finger configurations – virtually infinite – correspond to a single position of the cursor. In order to move the cursor to a target, subjects needed to solve an inverse ill-posed problem (Bertero et al., 1988).
- 2) Because of its nature, the geometrical map was entirely novel for the subjects.

Therefore, the remapping paradigm offers a unique opportunity to investigate how the central nervous system learns to operate within a novel environment. Here, we considered specifically how the learning of a spatial map is affected by adapting to a temporal delay. We considered two possibilities:

- a) The temporal delay is learned as a transformation of space. In this case, subjects would learn to associate the instantaneous image of the cursor with their motor command. This would induce a new representation of the map between cursor positions and finger configurations.
- b) Alternatively, subjects would maintain the static map between cursor and finger position and would simply learn to cancel the temporal lag of the display by applying a corresponding lead to the finger configuration.

Our findings support the second hypothesis and refute the first. According to the first hypothesis, after training with delayed feedback, when we restored the baseline condition by suddenly removing the delay, we would expect to observe some after-effect with an increase on tracking error. In contrast, not only we failed to see such an after effect, but the analysis of the tracking error revealed that there were not significant differences either between the performances before and after the training or between the performance of the two groups. These observations are incompatible with the formation of a new map during the exposure to a delay, as this map would have likely interfered with the map previously acquired without a delay. These results confirm that subjects compensate the visual feedback delay by a temporal shift of their motor commands, without altering the representation of the hand-cursor map acquired by practicing without delay.

In an earlier remapping study, Liu and colleagues (2010) reported two different strategies adopted by subjects in response to rotation and scaling transformations of the cursor space. To compensate for a scaling, they maintained their baseline map and applied the inverse transformation. In contrast, to compensate for a rotation they created an entirely new inverse representation of the hand to cursor map.

Learning of the kinematic mapping between hand configuration and object position progressed promptly during the first day and resulted in decreased tracking error and increased smoothness of the movements. Subjects reduced complexity in the overall coordination of finger motions by presenting a strong and progressive decrease of variability in task space and null space. This is in agreement with the result obtained in similar studies (Liu et al., 2010; Casadio et al. 2010; Mosier et al., 2005). While our findings may be inconsistent with the idea that the motor system shifts its variance to the null space (Latash et al. 2001; Todorov and Jordan 2002a, 2002b) one should consider that those earlier studies didn't involve performing a task within a novel geometrical environment. An inexperienced subject first must learn a stable inverse map from desired behavior to motor commands. This requires, identifying the task-relevant and task-irrelevant components of a movement and also removing variability in the latter. Once this inverse map is formed, then the variability can be redirected toward the null space by effectively shifting the motor commands within a system of equivalent inverse maps (Wolpert and Kawato 1998).

We examined how the nervous system compensates for temporal perturbations by introducing 300 ms visual feedback delay during the second day of the experiment. The delay drastically increased the tracking error and decreased the smoothness of the movements. But eventually test subjects showed a clear adaptation. The increment of the jerk index indicates that during early adaptation subjects replaced rapid feedback adjustments with a prolonged “wait and see” approach. Subjects in this study used the same strategy to compensate for the delay as when subjects had been exposed to the scaling distortion in another experiment (Liu et al., 2010.) However, the adaptation to visual feedback delay was significantly slower than the adaptation to scaling perturbations. The adaptation to scaling, indeed, was almost completed within a set of 108 trials, whereas our findings show that subjects after 210 trials were not able to completely regain the level of performance in the non-delayed trials. This slower adaptation to temporal delays is in agreement with the findings of Foulkes and Miall (2000).

Time delay is a fundamental property of information processing in the central nervous system. By the time, a sensory apparatus reports an event, that event has already happened some time ago. This inherent delay in the sensorimotor loop can destabilize movements. If the motor system is capable of predicting the sensory consequences of the motor commands, instabilities resulting from the delay in measuring the state can be effectively removed (Miall and Wolpert 1996; Mehta and Schaal 2002). The central nervous system can rely on two types of feedback for state estimation: one type of feedback derives from different sensory modalities and another feedback arises from the “forward” models that predict the sensory consequences of motor commands. These two sources of information are likely to be weighted by the central nervous system in inverse proportion to the uncertainty of each source (Kording and Wolpert 2004; Todorov 2005; Izawa and Shadmehr 2008). By introducing a delay we increased the uncertainties in the subject’s estimate of the cursor position. Accordingly, during early adaptation, the variance of the cursor trajectory significantly increased. Rates of adaptation also depend on uncertainty of the feedback (Wei and Kording 2010): the nervous system appears to adapt more slowly when the sensory feedback is noisier. Therefore, the different adaptation rates observed in this study, in comparison with the scaling study, are mainly due to the greater uncertainty associated with the feedback.

Our results confirm that subjects adapt to visual feedback delay. We conclude that the space representation built during the baseline trials was robust to the delay perturbations and the process of adaptation to delay did not affect the learned spatial map.

Chapter Two

Spatial Warp Caused by Adapting to Temporal Visuomotor Delay

Abstract

An open question in neuroscience is the representation of time in the nervous system. In this study a more specific question is: does the brain represent and measure the flow of time to control our movements? Although there is not any dedicated sensor for time, the existence of temporal regularities implies that some process is dedicated to representing time. Dedicated timing could be result from operation of a specialized neural structure (internal clock) or could be an emergent property reflecting the fact that dynamic processes such as coordinating limbs for action occur in time. Therefore, there is a possibility that unlike classical physics, time and space are not separated in the central nervous system. Our hypothesis is that a key primitive of temporal information processing is the simultaneity of the sensory-motor events. This temporal primitive subject to adaptive changes and these adaptive changes result in predictable deformation in the space and state of the motion.

To test the validity of our hypothesis, we designed a 2D virtual pong experiment with visual, haptic and auditory feedback in which subjects repeatedly intercept a ball using a robotic manipulandum. Each interception was an event characterized by multiple stream of sensory information. After some baseline particle we delayed the whole environment. Pong trials were alternated with blind reaching trials. Subjects were trained and tested in two spatially separated workspaces to assess the generalization of the learning. The effect of temporal learning on proprioceptive space and the extent of generalization were evaluated by comparing the performance during pong and reaching tasks between the trained and untrained workspaces. We report three findings. 1) Learning a temporal delay result in predictable deformations in the central representation of the space, 2) Central nervous system compensates a temporal perturbation using state-dependent control policy and 3) Learning a delay is represented in an egocentric coordinate frame.

2.1 Introduction

The flow of time intrigued philosophers and scientists from Zeno of Elea to Albert Einstein. In modern neuroscience, we ask how the brain addresses the flow of time, and more specifically, we ask about perception and representation of time. We know the difference between ten minutes and one hour and some studies have suggested the existence of biological clocks (Ivry 1996; Spencer, Zelaznik et al. 2003; Buhusi and Meck 2005). However, does our brain measure and represent the flow of time for controlling movements? There are a number of early and current studies that suggest otherwise (Conditt and Mussa-Ivaldi 1999; Karniel and Mussa-Ivaldi 2003). As motor actions develop over fractions of a second, we cannot find evidence for processes that are capable to estimate time in any reliable way over such intervals. Our brains unlike computers do not have clock base frequencies of mega- or giga- Hz. A temporal concept that may be more critical than the duration of an interval is the simultaneity of sensory-motor events. In this study, we challenge and explore the consequences of a radical hypothesis. This is the hypothesis that *over short intervals of time, the key primitive of temporal information processing is the simultaneity of perceived sensory-motor events, this temporal primitive is subject to adaptive changes and these adaptive changes result in predictable deformations in the central representation of space and state of motion.* A key element in this study is also the quantitative identification of what is to be intended as “short interval of time”. This question is addressed by evaluating how deformations of space and state are affected by temporal sensory-motor delays.

A cardinal principle of classical physics lies in the possibility to separate space and time. Space is a three-dimensional timeless container of events, and the flow of events is captured by the ticks of a clock along the oriented one-dimensional time line (Arnold 1989). We know today, from relativistic mechanics, that this separate treatment for space and time is not always possible. However, we are reassured that problems of space-time entanglement only appear at speeds close to the speed of light. Is it really so? On a closer look, the separability of space and time rests upon the unequivocal definition of simultaneous events. Starting from the concept of a four-dimensional affine space-time, what we call ordinarily “space” is the three dimensional subspace of events that are simultaneous to a given event. This construct is made viable by the possibility to apply the notion of simultaneity across the spatial domain, and this is what we can do when measuring quantities in our daily non-relativistic domain. However, the

concept of simultaneity is rather elusive when it comes to our brains. There, signals issued simultaneously in the external world propagate with different velocities. Consider, for example, the simple act of knocking on a door. As our knuckles hit the door a sound is produced, our retinas register the image of the contact and the tactile organs detect the mechanical impulse. Furthermore, the very motor commands that drive our hand, together with the proprioceptive organs in our joints and muscles, carry the information of an expected impact. While these various sensory-motor signals originate from the same instantaneous event – the act of knocking – because of a difference in transmission rates they are likely to reach any integrative brain center with a substantial temporal scatter. Therefore, the fact that we perceive these sensory events as happening “at the same time” must be the outcome of active reconstruction processes that effectively remove the temporal scatter of multi-modal information based on the prior assumption that different sensory streams share a common cause (Fujisaki, Shimojo et al. 2004; Vogels 2004; Miyazaki, Yamamoto et al. 2006; Vroomen and Keetels 2010). In this study, we consider the hypothesis that the neural processing of simultaneity is not only relevant to temporal processing. Instead, we suggest that it tampers our sense of space, and in particular, its proprioceptive representation. According to this hypothesis, if the processing of simultaneity was altered, then our proprioceptive representation of space would also be altered in a corresponding way.

Based on the background, we are ready to formulate a solid set of hypotheses about the interaction between time, space and state representations, elaborating our basic assertions that:

- (a) The brain uses state and not time representations to control movements, and
- (b) Neural simultaneity has a direct impact upon the representation of space.

One classical methods of studying the role of time in motor control has been introducing a fixed delay between action execution and the sensory feedback associated to that action in a motor task (Miall and Jackson 2006; Foulkes and Miall 2000; Miall 1996; Miall et al. 1985) or virtual driving (Welch et al. 1996)

To address these question we performed a task in which subjects had to play to a virtual video game inspired by the classical PONG game, when a large delay (150 ms) was introduced between the movements and all the sensory information constituting the sensory feedback (i.e. visual, auditory and tactile feedback). We assessed the ability to adapt to such a temporal deformation and the pattern of the generalization of such

learning across the workspace. Moreover, we investigated how such adaptation modified the proprioceptive representation of space by asking subjects to perform reaching movements before and after delay training.

The results both of the learning and of the generalization are consistent with subjects not actually learning the temporal distortion, but rather a state-space approximation of such a deformation. Moreover, the prolonged exposure to altered simultaneity between action and sensory consequences seems to lead to a modification in the representation of space, producing a significant change in the subjects' reaching pattern.

2.2 Methods

2.2.1 Subjects

12 right-handed subjects (mean age 25 ± 4 , 4 females) participated in the first experiment (Learning). 18 right-handed subjects (mean age 28 ± 6 , 8 females) participated in the second experiment (Generalization). All subjects were healthy, with normal or corrected to normal vision, and did not present any neurological, muscular or cognitive disorder. All participants gave written consent prior to testing by signing the informed consent form approved by Northwestern's university Institutional Review Board.

2.2.2 Apparatus

Subjects played a virtual 2-D pong game by driving a virtual paddle on the screen by moving the handle of a robotic manipulandum (Fig. 6). The robotic manipulandum was a 2-degrees-of-freedom lightweight, low friction planar manipulandum with a large elliptical workspace. The apparatus included a projector, which projected the video game image on a screen mounted horizontally above the hand working space of the subjects. This was used to display the position of the robot's handle and give targets for reaching movements. Both hand position and velocity were determined from digital encoders mounted on each axis of the manipulandum and also recorded for further analysis. Two torque motors operating independently on each joint were programmed to apply controlled force perturbations to the hand of the subject. Software environment was based on Matlab and Simulink (for further details about the robotic manipulandum see Shadmehr and Mussa Ivaldi 1994). An opaque fabric was used to cover all visible parts of the body, so that the only visual information about the hand position could be derived by the visual cursor on the screen. Before each experiment a custom 9 points

calibration procedure was performed to match the visual cursor on the horizontal screen with the manipulandum handle, with a precision of about 1 mm.

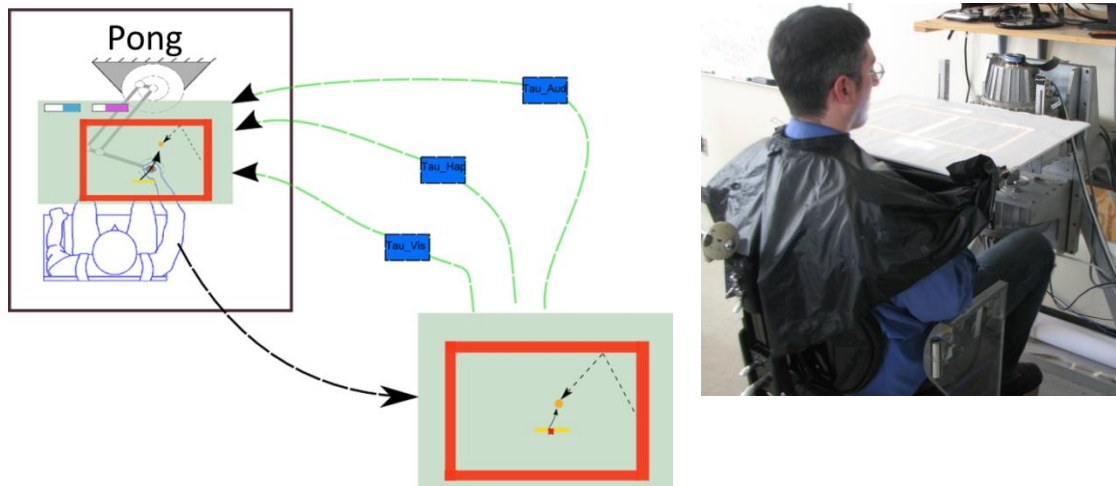


Figure 6: Experiment setup. Subjects played a 2-D virtual Pong with visual, auditory and haptic feedback using a robotic manipulandum, after some baseline practice, the whole environment was delayed and subjects played in this delayed environment.

2.3 Procedure

Two experiments were conducted on two separate groups of subjects. The first (Learning Experiment) was aimed at investigating the ability to adapt to a significant delay (100 ms) during the execution of a complex task and the consequences of such adaptation on the representation of proprioceptive space. The second (Generalization Experiment) investigated the generalization properties of such learning across space and across different directions, to assess the structure of the learned model and the consequent deformations of the proprioceptive space. All experiments were composed of two tasks: the pong game and the blind reaching.

2.3.1 First experiment: learning in presence of delay

Pong game

During the pong game subjects observed the scene illustrated in Fig. 7.A. The light gray rectangle indicates the border of the global pong arena. Subjects were instructed to hit the ball (a red circle) with a paddle (a horizontal red bar) whose position corresponded with the hand location, to make it bounce against the top wall. Once the subject hit the ball, it reversed its movement direction and a haptic pulse was delivered to the robotic handle, accompanied by a tapping sound produced by the manipulandum motor. The

velocity at which the subject hit the ball determined the reflection velocity of the ball through the equation:

$$V_{ball}^+ = -(V_{Ball}^- - 0.6 \cdot V_{Hand}) \cdot 0.7$$

Where V_{ball}^- and V_{ball}^+ are the ball velocities before and after the collision, respectively, and V_{Hand} is the hand velocity at impact.

The ball could bounce against all the four walls, but when it hit the top wall a random jitter was introduced in the reflection, to make the task more challenging. However, to limit the unpredictable behavior of the ball, its velocity was characterized by a deceleration profile. Because of inherent delay in the system a Kalman predictor (Kalman 1960) was implemented to compensate the delay.

Each pong trial lasted one minute. Subjects' goal was to increase as much as possible their hit rate (i.e. the number of hits per minute). This requirement implied that they had to play as fast as possible as long as they could successfully control the ball and that they had to avoid letting the ball bounce on the bottom wall behind the paddle (miss).

A timer (a cyan horizontal bar in the top left corner of the workspace, Fig. 6) continuously provided information about the elapsed time, while at the end of each trial the current number of hits was shown to the subjects. Subjects were allowed to decide when to restart the game, by driving the paddle into a specific area of the screen (starting zone), below the bottom right corner of the right court.

During certain part of the protocol a delay of 100 ms was introduced in the virtual environment (see Protocol). This delay produced a discrepancy between hand position and the paddle position on the screen and, at the moment of hit, also the haptic and auditory information of impact resulted delayed (Figure 6).

Reaching task

During the reaching task, the scene turned black and a yellow small disk was displayed as a target. The subjects were asked to reach and stop at the target, with a one-shot movement (i.e. with no corrections during the motion). As the movement stopped (hand velocity lower than a 0.03 m/s) the target disappeared, to avoid any further movement adjustment. After a brief pause following the reach, the robot brought the hand to the initial position and a new target was presented. The targets were 3 in total and were located at a distance of 14 cm with respect to the relative starting position (Fig.7.B) Note that subjects were given no visual feedback on the position of their hand. The

reaching was guided only by the subject's proprioceptive representation of the hand location in relation to the visual target.

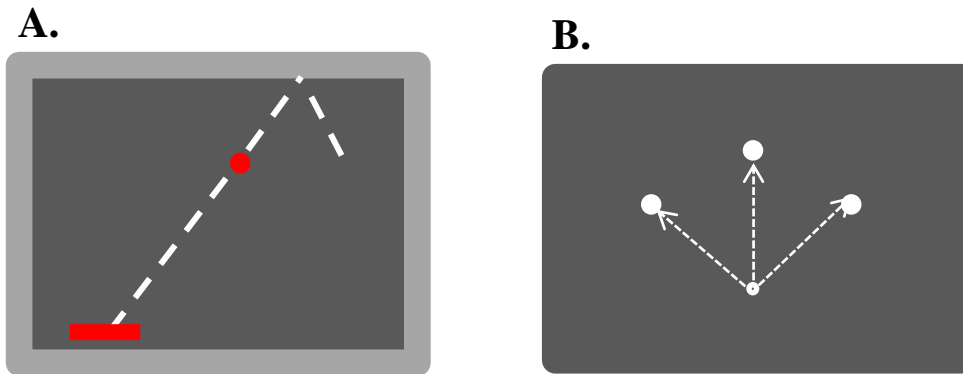


Figure 7: Schematic view of the training experiment. **A. Pong game:** During pong game subjects repeatedly intercept a ball. Horizontal bar represents the paddle and circle represents the ball. **B. Reaching movement:** During reaching movement the robot brought the hand to the starting position, one of target appeared randomly on the screen and subjects were instructed to reach the target without visual feedback.

Protocol

Subjects in the Learning group followed the protocol depicted in Fig 8. At the beginning of the experiment subjects played the pong game with no delay for about 4 minutes (± 0.4 (SE); *Baseline*). Subsequently they were presented with 48 reaching trials (*Pre Reaching*) toward the 3 targets (16 repetitions for each target reach). The order of target presentation in each block of trials was randomized. This set of reaching trial was performed to measure the natural subjective biases in a blind reaching task toward the specified targets. After the reaching phase, subjects started training with the delay (*Train*). Pong was played with a delay of 100 ms for about 40 minutes (39.3 ± 1.7 (SE) minutes). Immediately after the end of the training, a second reaching session was conducted (*Post Reaching*), identical to the previous ones (48 trials). This measure was performed to evaluate whether any change in the reaching pattern was occurred due to the prolonged exposure to the delayed pong game. After the reaching, subjects were presented with one pong trial with no delay (*Post Train*). The latter pong trials were performed to evaluate whether any after effect was associated to the delay learning.

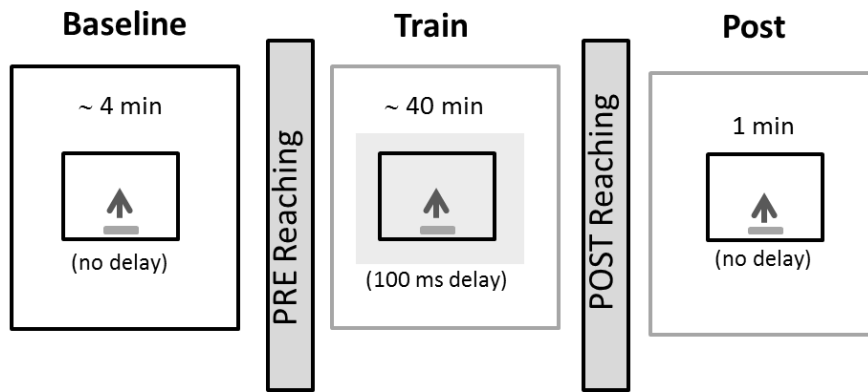


Figure 8: Training Experiment Protocol

Control experiment

5 subjects of the Learning group performed, on a separate day, the same exact protocol, but without any delay. This task was executed to ascertain whether any deformation of the proprioceptive space could be a byproduct of interacting with the robot for a long time rather than by the delayed environment. The order in which the two subjects performed the main and the control experiment was randomized.

2.3.2 Second experiment: spatial generalization of the learning

Pong game

The Pong game was similar to the one used in the first experiment. However, the direction of play was rotated by 90 degrees: subjects had to move horizontally the paddle and to make the ball bounce on the vertical walls (Fig.9.A). The area was divided in two different courts (left and right court) and on each trial subjects had to play just in one of the two areas (see Protocol for details). Before the beginning of the trial the current court was indicated by the presence of a green wall. Subjects were instructed to hit the ball to make it bounce against the green wall. As before, when the ball hit the target wall (i.e. the green wall) a random jitter was introduced in the reflection. During certain part of the protocol a delay of 150 ms was introduced in the virtual environment (see Protocol). All other game characteristics remained the same as in the first experiment.

Reaching task

In this second experiment the targets were 6 in total and were located a distance of 12 cm with respect to the relative starting position. Two starting positions were individuated, one for each court, at the same vertical distance from the bottom limit of

the workspace. Three targets were associated to the right starting position and the other 3 targets were symmetrically positioned in the left court and associated to the left starting position (Fig. 9B). The procedure was exactly the same described for experiment one.

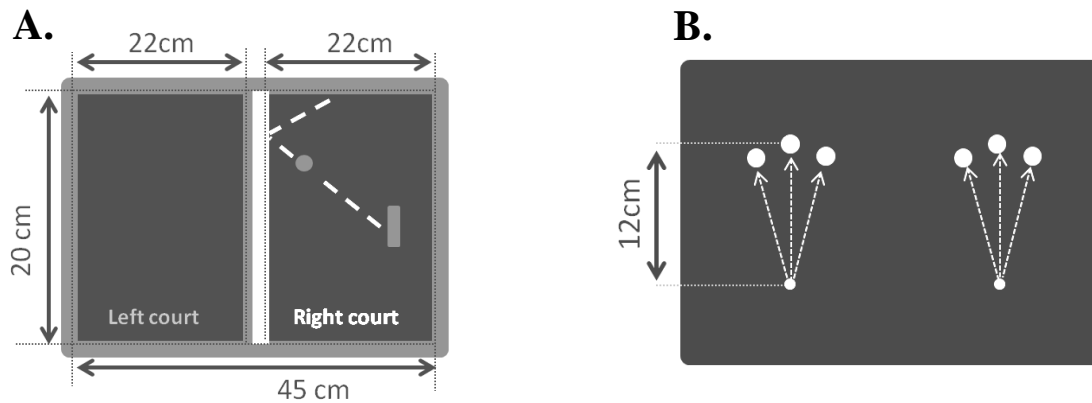


Figure 9: Schematic view of the generalization experiment. **A. Pong game:** Subjects adapted to the delay only in one court and the generalization is assessed in the other court. **B. Reaching movement:** Same pattern of targets in each court. In this experiment the direction of the reaching movements is orthogonal to the direction of playing pong

Protocol

Subjects were divided into two groups, with no overlap of subjects between the groups. One group (RIGHT_left Group) performed the training to the delay in the right court (9 subjects, 4 females), while the other group (LEFT_right Group) performed the training to the delay in the left court (9 subjects, 4 females).

Each group had to perform both the pong and the reaching tasks, which were interleaved throughout the experiment (Fig 10).

At the beginning of the experiment subjects played the pong game with no delay for 8 minutes (*Baseline*), alternating trials in the right and in the left court. Subsequently they were presented with 30 reaching trials (*Pre Reaching*) toward the 6 *long* targets from the corresponding starting positions (5 repetitions for each target reach). The order of target presentation in each block of trials was randomized. This set of reaching trial was performed to measure the natural subjective biases in a blind reaching task toward the specified targets. After the reaching phase, subjects started training with the delay (*Train 1*). Pong was played with a delay of 150 ms for 20 minutes in just one of the two courts (right for the RIGHT_left subjects, left for the LEFT_right group).

This training phase was followed by another reaching session (*Middle Reaching*), analogous to the previous one (30 trials). Afterwards, another delayed pong training

session followed (*Train 2*), identical to *Train 1* and, immediately after, the last reaching session was conducted (*Post Reaching*), identical to the previous ones (30 trials). This measure was performed to evaluate whether any change in the reaching pattern was occurred due to the prolonged exposure to the delayed pong game.

After the reaching, to eliminate any possible interaction that the reaching phase might have on delay learning, subjects were presented with three additional training trials (*End Train*), i.e. right for the RIGHT_left group, left for the LEFT_right Group, followed by three trials in the other court (*Generalization*), i.e left for the RIGHT_left group, right for the LEFT_right Group. The latter pong trials were performed to evaluate the degree of spatial generalization of the delay learning.

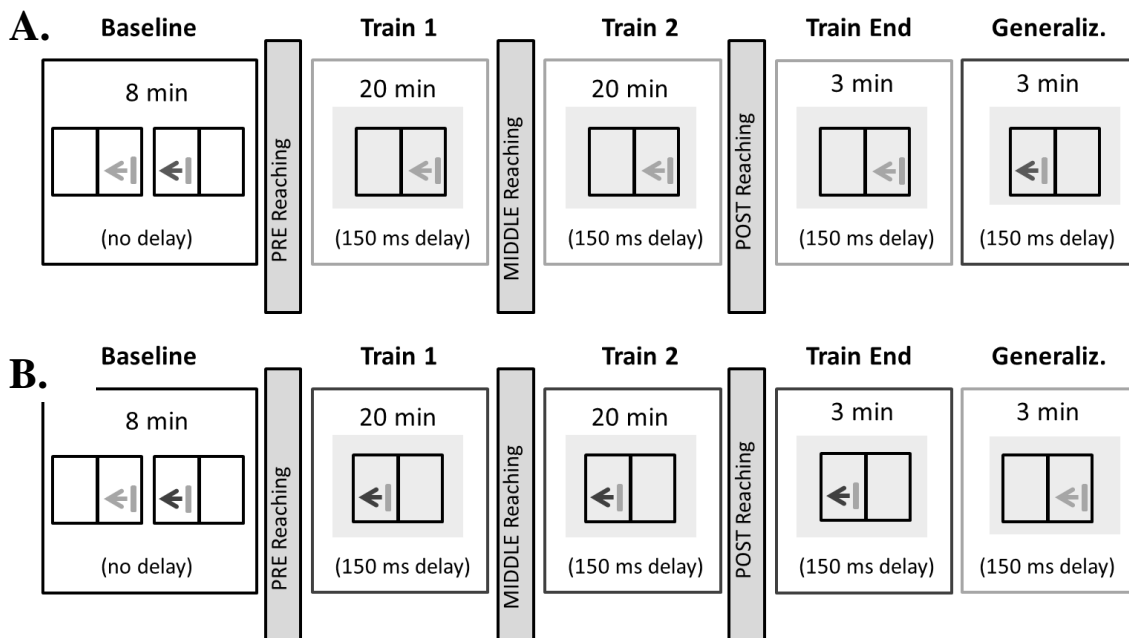


Figure 10: Generalization experiment protocol. A. RIGHT_left group. B. LEFT_right group.

Familiarization

Before starting the experiment, each subject was presented with a familiarization phase, in which he/she was asked to reach for all the reaching targets, first under continuous visual feedback (i.e. by moving a visual cursor on the screen with the manipulandum), then with a blind reaching (as in the reaching trials during the real experiment). This phase guaranteed that subjects had understood the instructions about the movements to be performed in the reaching phases.

2.4 Data analysis

Kinematic parameters were computed from the two dimensional hand, paddle and ball position collected in successive frames taken at 5 ms intervals. To compute hand velocity during the Pong game we differentiated the horizontal hand position data from the rightmost to the leftmost positions reached during the hitting movement and low-pass filtered it using a digital second-order zero phase lag Butterworth filter with a cutoff frequency of 20 Hz. The instant corresponding to the maximum value of the velocity trace was considered the time of hand peak velocity. In the Reaching task, the two dimensional hand velocity was evaluated.

For the Pong task we computed the following parameters:

- Hit rate. The number of hits performed by the subject on each one minute trial.
- Δ , the temporal difference between time of the hit and time of the paddle peak velocity. For each hit, we evaluated the temporal distance the instant at which the paddle achieved its peak horizontal velocity during the hitting movement and the moment of impact with the ball. This difference should be almost zero to transfer the maximum amount of kinetic energy from the hand- paddle to the ball and indeed it is almost zero in expert tennis players.

For the reaching task, for each trial we estimated movement start and ending position by individuating when the two- dimensional hand velocity became higher (and lower) than a fixed threshold. Then we estimated the following parameters:

- Reaching offset. The difference between the amplitude of the performed movement - evaluated in two-dimensions as the distance between starting and end handle position – and the amplitude of an ideal movement connecting the starting position with the target. Such offset was computed both before the adaptation to the delay (Pre Reaching) – yielding an estimate of individual blind reaching accuracy - and after the end of the training phase (Post Reaching). The difference in offset between the Post and the Pre reaching phases provides a measure of the modification in the motor planning of the reaching after adaptation to the sensorimotor delay.

Despite the familiarization phase, in the Generalization experiment two subjects (one per group) did not comply with the instructions given for the reaching protocol at least in one of the Reaching phases, by performing corrective movements during the reach or

by moving their hand into sight before moving. Therefore, their reaching data were excluded from all further analysis.

2.4.1 Statistical analysis

All aforementioned metrics followed a normal distribution, as confirmed by the Shapiro-Wilk test. To evaluate statistically the changes in the different phases of the experiment, these results were subjected to One-Way Repeated Measures ANOVAs, followed by Tukey post hoc tests or to one or two-tailed pair-sample t-tests (as specified in the text).

2.5 Computational Model

Three alternative generalization patterns have been taken into account in this work:

- Global learning in Allocentric space: the adaptation to the delay performed in one court generalizes everywhere in the workspace in end effector coordinates, i.e. producing the same results in all spaces
- Local learning in Allocentric space: the adaptation can be achieved in the trained space, but its effect decays with the distance from the trained court.
- Global learning in Egocentric space: the adaptation is achieved by learning the deformation with respect to egocentric frame of reference. That is, the position of hand and paddle are coded with respect to the subject's shoulder, in a polar coordinate system. Therefore, moving in different parts of the workspace could produce seemingly different behaviors, predictable only by an egocentric description of the learning.

2.5.1 Learning in Allocentric space

During the Pong game in presence of the delay, subjects had discrepant visual and proprioceptive information about the position of their hand. While hand and visual paddle were almost coincident when their movement was slow, their relative distance increased as a function of their movement speed. We propose that the recalibration occurred at relevant instants of the game, when proprioceptive and visual position information were sampled and used to recalibrate the perception of hand position. Such relevant instants in the game are the ones in which subjects need to evaluate the accomplishment of their task, which was hitting the ball. Therefore, we propose that the calibration events occurred when subjects received the feedback of a hit. In particular,

as the feedback arrives 150 ms after the real hit and in general the hand is moving near peak speed at hit (see Hit Time), the proprioceptive position of the hand will be much forward with respect to the apparent visual position at the moment of hit. As, on the contrary, at the beginning of the hitting movement, when speed is low, hand and paddle positions are almost coincident, this discrepancy could be interpreted as a visual compression: I have to travel a larger distance with my hand, to achieve a certain visual displacement of the paddle. Such compression can be described as follows:

$$(\underline{X}_{\text{HIT}} - \underline{X}_{\text{START}})_P = G * (\underline{X}_{\text{HIT}} - \underline{X}_{\text{START}})_V,$$

Where \underline{X} is the vector representing the (x,y) proprioceptive (subscript P) or visual (subscript V) estimation of hand position, at the moment of the feedback of the hit (subscript HIT) and at movement start (subscript START).

If this is the learning achieved during the exposure to the delay, in the reaching task subjects will plan their movements accordingly, executing longer hand movement with respect to the necessary visual movement amplitude. More precisely:

$$(\underline{X}_{\text{TARGET}} - \underline{X}_{\text{START}})_P = G (\underline{X}_{\text{TARGET}} - \underline{X}_{\text{START}})_V, \text{ where the starting position is proprioceptively sensed and considered coincident with its visual representation, as in the Pong task, at movement initiation and the visual target is shown.}$$

2.5.2 Learning in Egocentric space

By describing paddle and hand position in terms of distance ρ and angle θ with respect to the right shoulder (Fig 11), we will have a visual $(\rho, \theta)_V$ and a proprioceptive $(\rho, \theta)_P$ for each instant of play. In particular, at the beginning of the hitting movement they will be very similar, while when subjects receive the feedback of the hit hand and paddle positions will be quite different, thus being characterized also by different polar coordinates. We can describe such visuomotor discrepancy as a compression expressed in polar coordinates:

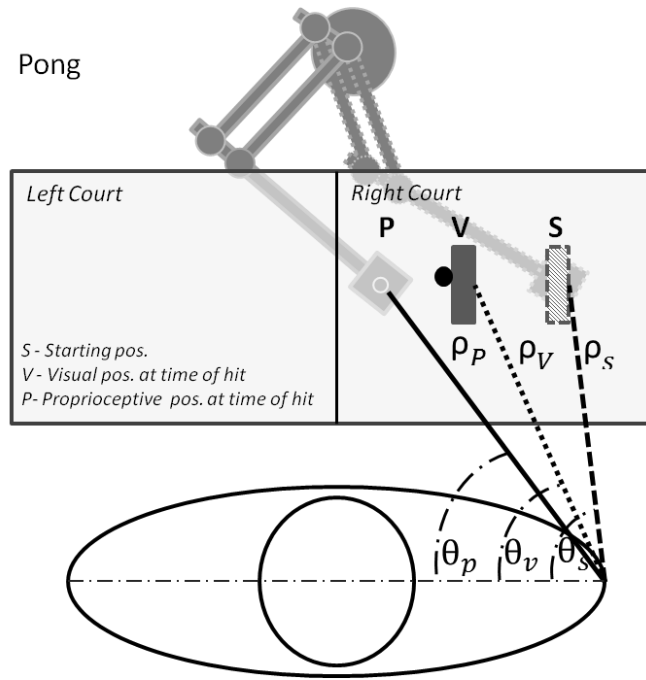


Figure 11: Learning in egocentric space.

- $G_\rho = (\rho_{HIT} - \rho_{START})_P / (\rho_{HIT} - \rho_{START})_V$ that is the ratio between the change in the visual ρ from start to hit and the change in the proprioceptive ρ from start to hit.
- $G_\theta = (\theta_{HIT} - \theta_{START})_P / (\theta_{HIT} - \theta_{START})_V$ that is the ratio between the change in the visual θ from start to hit and the change in the proprioceptive θ from start to hit

If the effect of the sensory-motor delay experienced in the Pong game is approximated as a visuo-proprioceptive compression, as described, then we can formulate predictions about the performance during the reaching task. Indeed, subjects should plan –after training with delay – a larger hand movement than before to reach the target, to compensate for the compression they have learned. More precisely, when their hand is passively positioned in the starting position and they look at the visual target to be reached, they will be able to compute the visual distance to be covered (assuming, as in the Pong, almost the coincidence of visual and proprioceptive positions at start). In other words, the target proprioceptive position will be computed, in terms of its polar coordinates as follows (Fig.12):

- $(\rho_{TG} - \rho_{START})_P = G_\rho(\rho_{TG} - \rho_{START})_V$
- $(\theta_{TG} - \theta_{START})_P = G_\theta(\theta_{TG} - \theta_{START})_V$

Where the unknown are the proprioceptive position of the target $(\rho, \theta)_{TG,P}$, while the visual target position and the proprioceptive starting position is given. The visual

starting position is assumed coincident with the proprioceptive one, as the subject's hand is passively driven there, and subjects do not need to plan the movement and compensate for any putative compression before. G_ρ and G_θ are estimated during the Pong task as described before. By applying a similar principle subjects could estimate the proprioceptive position to be reached in order to reach the visual position individuated by the reaching target.

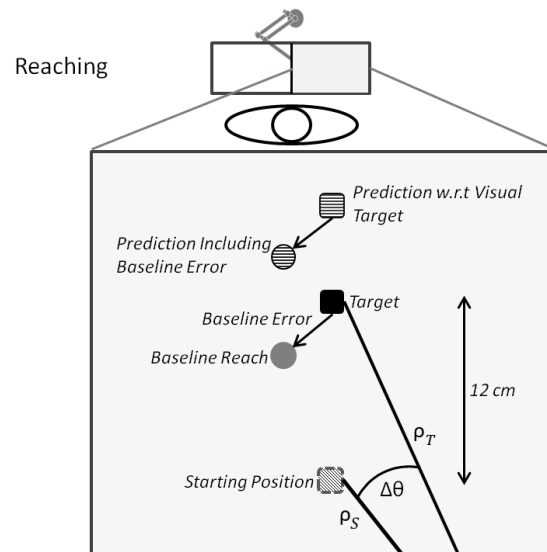


Figure 12: Predicting the end point of blind reaching movements after adaptation to the delay in an egocentric coordinate frame.

2.6 Results

2.6.1 First experiment: learning in presence of delay

In this experiment we confronted subject with a delayed sensory-motor feedback while they trying to hit a virtual ball by driving a paddle on the screen by moving a manipulandum with their unseen hand. We wanted to assess whether the delay could be compensated during the training and if the prolonged exposure to the delayed environment would affect the planning of reaching movements.

Hit rate

To evaluate subjects' performance in the Pong task, we measured the hit rate as the number of times the paddle hit the ball during each one minute trial. During the Baseline – when subjects play with no delay between hand movement and visual feedback – they show high performance rate, on average around one hit per second (58 ± 4 (SD) hit per minute, Fig. 13.A). With the introduction of the 100 ms delay the

performance decreases drastically, becoming on average 65.8% ($\pm 4\%$ SD) of the baseline hit rate. During the training subjects significantly improve their performance (final performance is significantly higher than initial hit rate, $t(11) = -2.65$, $p = 0.012$, one-tailed, pair-sample t-test), even though they never recover completely the hit rate obtained during the baseline. In fact, the hit rate at the end of the training session is on average just the 72.9% ($\pm 8.5\%$ SD) of the baseline hit rate. No after effects were present after the training. In fact, the removal of the delay in the very last Pong trial allowed subjects to immediately recover the performance exhibited during the baseline (performance during post not significantly different from baseline; $t(11) = -1.0822$, $p = 0.3$, two-tailed, pair-sample t-test), with the hit rate in the Post session analogous or slightly higher than that of the baseline (on average 104.9% $\pm 15.5\%$ SD of the baseline hit rate).

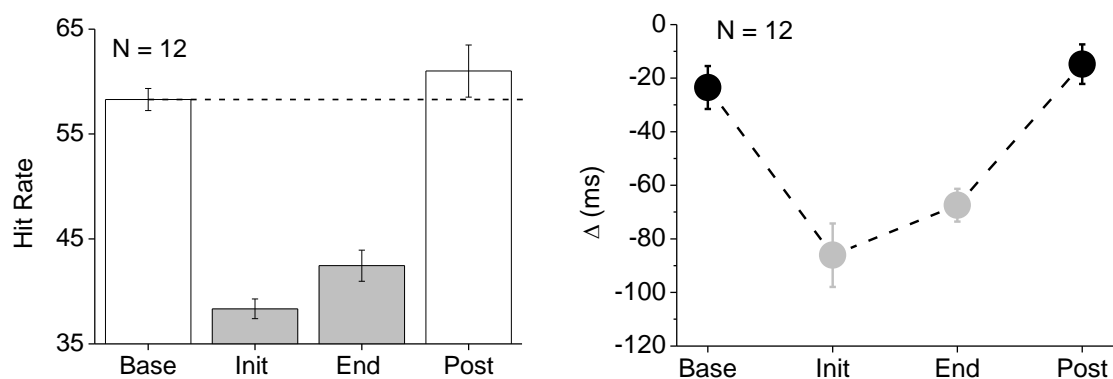


Figure 13: Performance metric. A. Number of interceptions per one minute trial. Data is averaged across all subjects. Error bars represent the standard error. Gray bars represent delayed trials. B. Time difference between interception and maximum paddle velocity. Data is averaged across all subjects. Error bars represent the standard error. Gray circles represent delayed trials.

Hit time

The same pattern of results is individuated by a temporal performance metric as Δ that is the temporal difference between paddle peak velocity and the moment of ball hit. During the baseline trials subjects tend to hit the ball when the paddle is approaching peak velocity (on average 23.5 ± 28 (SD) ms before reaching peak paddle velocity). During the first trials after the delay introduction, they show a negative jump in Δ , that is they hit the ball much earlier than reaching peak paddle velocity. This can be explained by them trying to hit with their invisible hand (rather than with the paddle) the visual representation of the ball, which is however delayed. Their hand will tend to hit the real ball much earlier than predicted, causing this non optimal behavior. The

introduction of the delay produces a modification in the timing of the hit, causing the collision to happen on average 80ms before paddle peak velocity (86 ± 41 ms (SD), Fig. 13.B). After the prolonged training with the delay, however, the timing significantly improves with Δ increasing toward 0 (Δ at the end of the training significantly smaller, in magnitude, than at the beginning: $t(11)=-1.96134$, $p=0.03782$; one-tailed, pair-sample t-test), although never reaching the baseline performance. Eliminating the delay an immediate recovery of the hit timing adopted during the baseline (no significant difference; $t(11)= -1.39$ $p =0.19$, two-tailed pair-sample t-test) with Δ becoming again very near to the moment of peak paddle velocity (on average 15 ± 25 ms before the time of the peak),

Reaching

Subjects were requested to perform several reaching actions toward three different targets both before and after the Pong training in presence of delay. The comparison between the reaching movements executed at the end of the training with those shown before training initiation was performed to measure whether the prolonged exposure to a delayed environment could modify the planning of actions in space.

Fig 14.A illustrates the arrival positions of the reaching movements in the Post phase with respect to the arrival positions in the Pre phase for each subject. As we are interested in the changes between reaching before and after the training, rather than in the subjective errors associated to the reaching per se, all data have been shifted to align, for each subject, the arrival of the Pre reaching movements to the targets. The figure 14.B shows an increase in the amplitude of the reaching movements after the delay training for all the targets considered. Indeed the reaching overshoot, i.e. the difference in amplitude between reaching before and after the delay training is significant larger than zero ($t(11) = 2.348$ $p=0.01931$; one-tailed pair-sample t-test). The results suggest that learning a temporal delay changes the central representation of space.

Control experiment

To make sure that the effect is not simply a byproduct of interacting with the robot for a long time we had a control experiment. During the control experiment, 5 subjects performed the same protocol (pong + reaching trials) but without any delay. Their Hit rate and Hit time did not change significantly during the task, with only a slight

improvement during the game. The reaching before and after the training did not show any significant change (Fig 14.B)

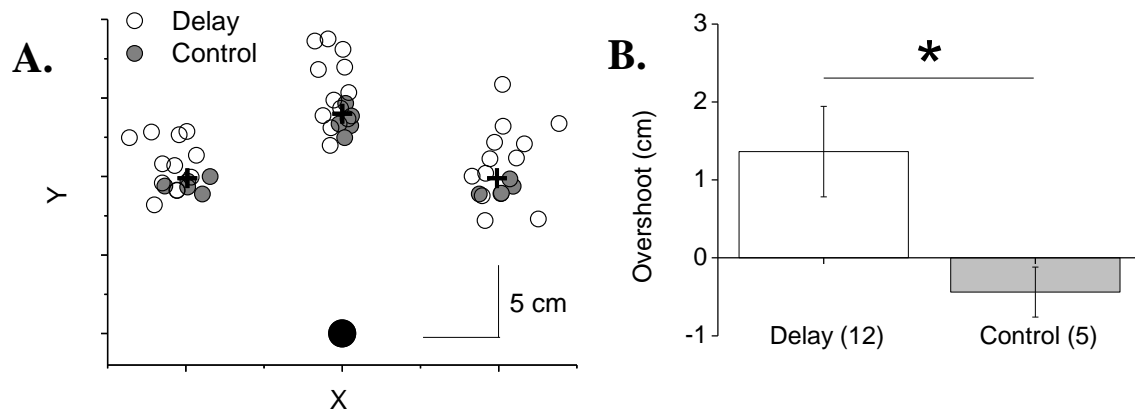


Figure 14: Results of the reaching movements after adaptation. **A.** Averaged end points of the reaching movements for training and control group. The results are shown as a relative difference between pre and post reaching movements, therefore eliminating the initial proprioceptive errors. **B.** Averaged magnitude of the overshoot for training and control group. Error bars represent the standard error.

2.6.2 Second experiment: generalization of the learning

The results of the first experiment have shown that people are able to adapt to a certain degree to the introduction of a sensory-motor delay in a complex task as playing a Pong video game. Moreover, they have indicated that such learning modifies proprioceptive space, provoking a change in the reaching behavior. Such proprioceptive space modification is specific to the delay and does not depend just on Pong training. In a second set of experiments we wanted to investigate the generalization pattern of this learning. This, in turn, allows also assessing also the nature of the proprioceptive deformation associated to such learning. To do so we divided subjects into two groups, the RIGHT and the LEFT group. The former were trained to the delay in just the right half of the workspace, while the latter only in the left side. All were then tested in the whole workspace; both in the pong and the reaching task (Fig 9). Differently from previous experiment, the pong game was played along the horizontal direction. The reaching movements, however, remained vertically oriented. This choice allowed us also to evaluate if the proprioceptive deformation generalized to untrained movement directions.

Hit rate

In the non-delayed baseline trials subjects in both the RIGHT and LEFT groups played with a rather high hit rate: on average around one hit per second (56 ± 10 (SD) hits per minute and 63 ± 10 (SD) for the RIGHT and the LEFT groups respectively). Importantly their performance is the same in the two courts ($t(8)=0.62311$, $p=0.55$ for the RIGHT group; $t(8)=-0.636$, $p=0.54$ for the LEFT group; two-tailed, pair-sample t-tests) which basically shows that the level of difficulty of playing Pong in the two courts were about the same. When a delay of 150 ms is inserted between each action and all its sensory consequences, the hit rate diminishes substantially, as it appears in Fig 15. Indeed, hit rate almost falls by half, becoming $55.1\% \pm 8.4\%$ (SD) of the baseline for the RIGHT group and $49.9\% \pm 5.4\%$ (SD) for the LEFT group. During the 40 minutes Training phase subjects in both groups significantly improve their performance (hit rate at the end higher than at the beginning: $t(8)=-5.38$, $p < 0.001$ for the RIGHT group, $t(8)=-5.53$, $p < 0.001$ for the LEFT group; one-tailed, pair-sample t-tests), reaching on average the 77.2% ($\pm 10.2\%$ SD) of the baseline hit rate for the RIGHT group and 72.2% ($\pm 8.9\%$ SD) for the LEFT group even if the recovery is not complete for neither group.

After the training to the delay in one part of the workspace, subjects were required to play for three further minutes in the opposite court, in the so-called Generalization phase. Interestingly, a difference appears in the performance of the two groups during this last phase (Fig 15). The RIGHT subjects, trained on the right court, show a significant decrease in the hit rate when playing in the left court in the Generalization trials, obtaining an average hit rate not different from the one shown at the very beginning of the exposure to the delay. A one way RM ANOVA ran on the hit rate during the initial training, the final training and generalization phases, followed by a post hoc Tukey test, confirmed a significant decrease of performance during generalization ($p = 0.001$) and a no significant difference between generalization performance and that of the initial exposure to delay. On the contrary, LEFT subjects, trained on the left court, maintain their performance unvaried when playing on the right court: they hit rate in the Generalization phase is significantly higher than the hit rate at the beginning of the training and not different from the level of performance they reached in the left court at the end of the learning ($p < 0.001$; One Way RM ANOVA, Tukey Post hoc test).

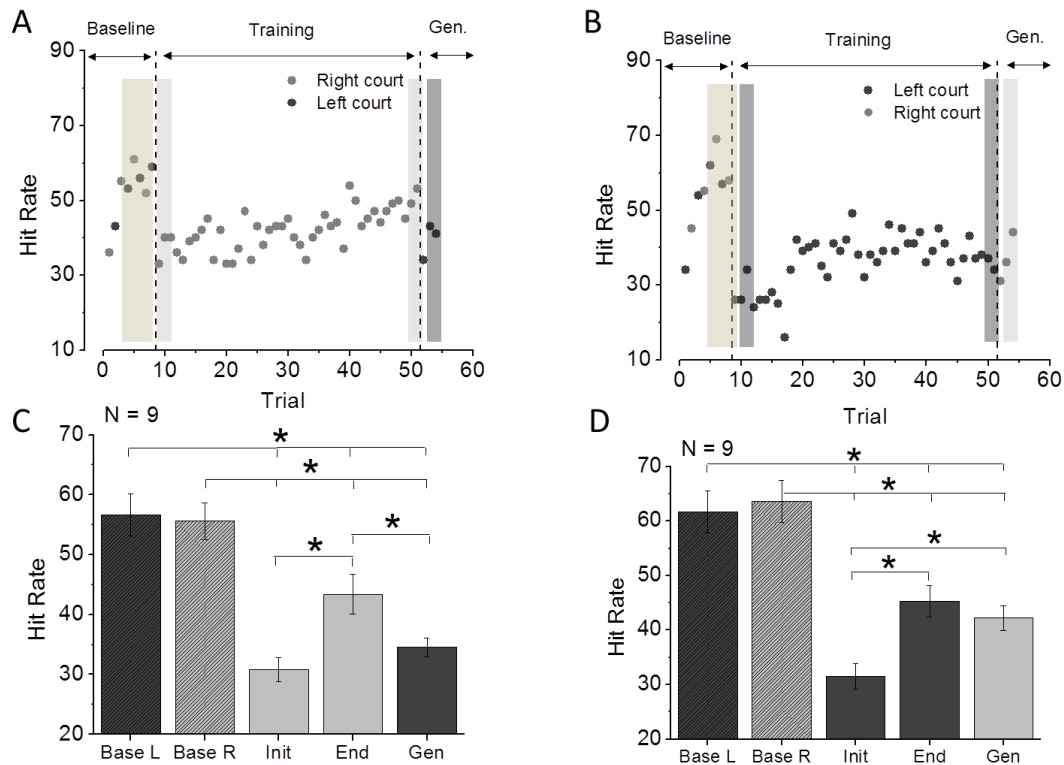


Figure 15: Performance metric: A. Hit rate of a representative subject in the RIGHT group (Training: right court, Generalization: left court). B. Hit rate of a representative subject in the LEFT group (Training: left court, Generalization: right court). C. Averaged hit rate of subjects in the RIGHT group. Error bars represent the standard error. D. Averaged hit rate of subjects in the LEFT group. Error bars represent the standard error.

Hit time

To evaluate the learning and generalization pattern during the training we measured also the timing of the hit with respect to the time of peak paddle velocity (Δ). During the baseline trials subject time their hits almost optimally, by hitting the ball in the proximity of the instant of paddle peak velocity in both courts (Δ on average -1 ± 20 ms (SD) for the RIGHT group and -17 ± 19 ms (SD) for the LEFT group) with Δ not significantly different between courts (Pair-sample t-tests, $t(8)=-1.968$, $p=0.08$ for the RIGHT group and $t(8)=-1.91$, $p=0.09$ for the LEFT group).

The introduction of the delay induces a big variability in subjects' behavior. Most subjects (6 of 9 in the RIGHT group and 8 of 9 in the LEFT group) in the very first delayed trials show a drastic anticipation in the hitting time, as if they were planning to hit the delayed ball with their unseen hand rather than with the delayed paddle. This attempt determines anticipation in the hit between the unseen hand and the unseen, non-delayed, ball, thus causing the hit between paddle and delayed ball to happen earlier

than at the instant of paddle peak velocity (highly negative Δ). The remaining subjects show instead a smaller change in the timing of their hits at the very beginning of the training. This is in general achieved by reducing the speed of the hitting actions, so that the spatial discrepancy between hand and delayed paddle was reduced. As they however progressively increase the speed to increment their hit rate their timing deteriorates, with the hit occurring too early with respect to the moment of paddle peak velocity. After about ten minutes of exercise all subjects show a similar behavior: they have reached a suboptimal timing, with the hit happening around 100 – 120 ms before paddle peak velocity (91 ± 18 ms (SD) for the RIGHT group and 128 ± 25 ms (SD) for the LEFT group). After training with the delay, the timing significantly improves for both groups, with Δ increasing toward 0 (Δ at the end of the training less negative than at the beginning of delay exposure: $t(8)=-2.48$, $p= 0.019$ for the RIGHT group and $t(8)= -9.49$, $p<0.001$ for the LEFT group; one-tailed, pair-sample t-test). As observed in the analysis of the hit rate, also the trend of Δ is different between the two groups in the Generalization phase (Fig 16). Indeed, when subjects in the RIGHT group move from the trained right court to the un-trained left court show a significant worsening of their timing, hitting too early with respect to the moment of paddle peak velocity. In fact their Δ becomes significantly more negative in the generalization phase than at the end of the training, returning similar to the timing they adopted at the beginning of the training on the right court ($p=0.03$; One Way RM ANOVA and Tukey post-hoc test on initial training, end training and generalization). On the contrary, LEFT subjects show, during their generalization phase a timing of the hits similar if not better than the one obtained at the end of the training, with a Δ significantly nearer to zero than the one measured at the beginning of the training ($p<0.001$; One Way RM ANOVA and Tukey post-hoc test on initial training, end training and generalization).

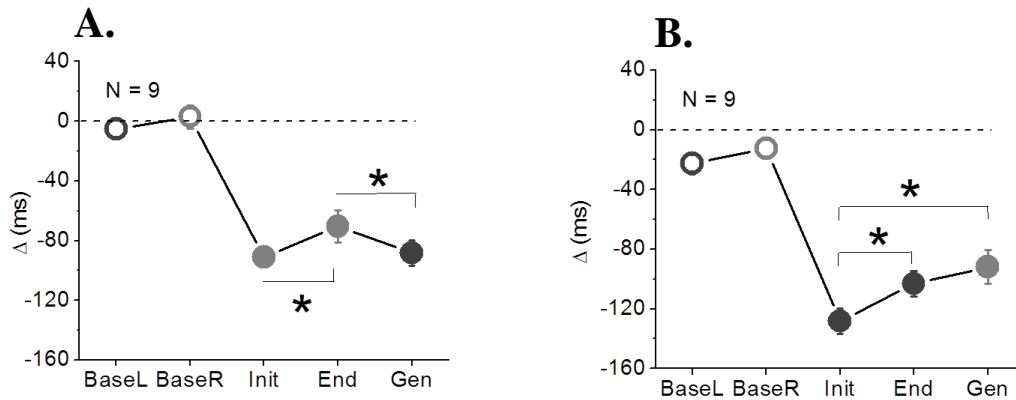


Figure 16: Time difference between interception and maximum paddle velocity. A. Averaged hit time of subjects in RIGHT group. B. Averaged hit time of subjects in LEFT group.

Reaching

Half of the reaching targets were situated in the trained workspace (right court), while the other three were symmetrically placed in the non-trained court – the one used at the end of the experiment to evaluate the generalization pattern of the Pong task (see Methods). These different localizations allowed us to evaluate whether also the deformations of the reaching movements depended on the workspace. Moreover, reaching movements were executed in the direction perpendicular to the training with Pong, thus providing us information about the generalization of the deformation of the proprioceptive space across movement directions. Subjects in the RIGHT group, after training with the delay, performed longer reaching movements in all workspace (Fig 17.A). However, the increase in amplitude in the right court is significantly larger than in the left court, as proved by a pair-sample t-test ($t(7) = -2.842$, $p = 0.025$; Fig 17.C). Considering the LEFT group, the reaching pattern is different: the increase in movement amplitude in the trained court (left) is significantly smaller than the one measured for the RIGHT group in the same court ($t(35.38) = -3.758$, $p < 0.001$; two-sided two-sample t-test, collapsing data from all targets; Fig 17.B). Moreover, such amplitude change is not significantly different between the two sides (Pair-sample t-test $t(7) = 0.0627$, $p = 0.95$; Fig 17.D).

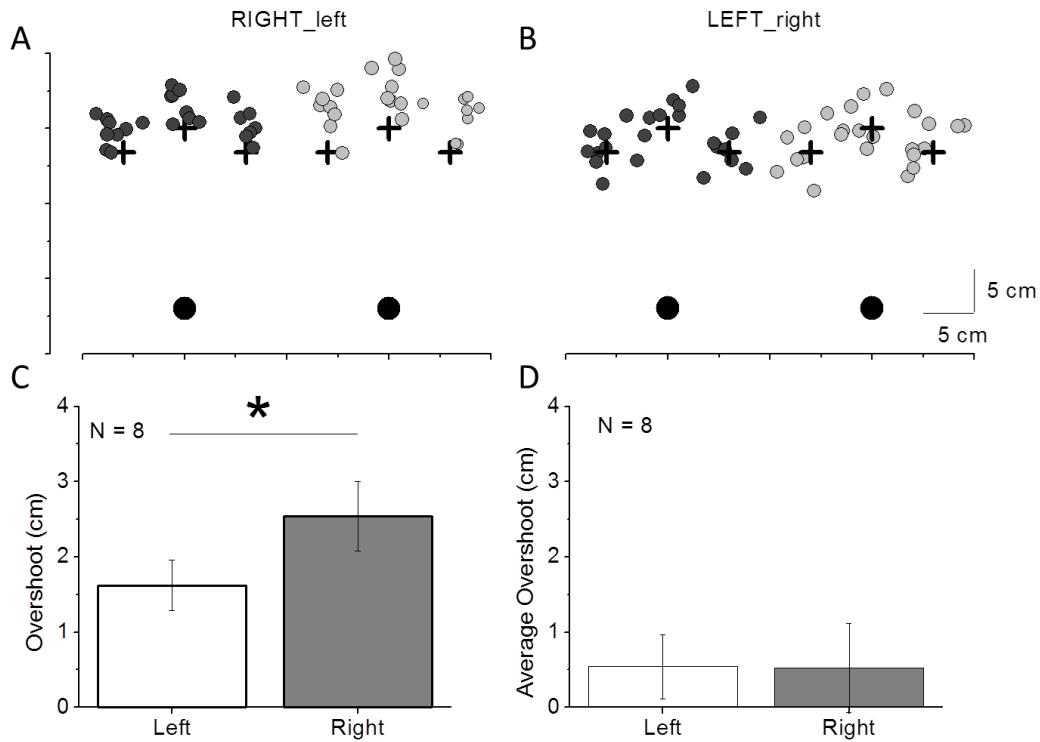


Figure 17: Results of the reaching movements after adaptation. The results are shown as a relative difference between pre and post reaching movements, therefore eliminating the initial proprioceptive errors. A. Averaged end points of the reaching movements for the RIGHT group (Training: right court, Generalization: left court) B. Averaged end points of the reaching movements for the LEFT group (Training: left court, Generalization: right court) C. Averaged magnitude of the overshoot for the RIGHT group. Error bars represent the standard error. D. Averaged magnitude of the overshoot for the LEFT group. Error bars represent the standard error.

2.6.3 Results of the computational model

From a perfectly symmetric task in the end effector coordinate frame we ended up having completely asymmetric results both in generalization performance and reaching movements. This suggests that learning delay is represented in an egocentric coordinate frame. Knowing this fact and the fact that the hypermetric generalizes also in different directions and therefore learning a delay provokes similar effects as learning a visuo-motor gain. We used a computational model described in (2.5) to predict the terminal positions of the reaching movements after adapting to the delay for the two groups. First we extracted the average starting position and average positions of hand and paddle at the time of hit from the pong data (Fig 11). Then we set the origin of a polar coordinate frame at the shoulder and calculated two separate gains for ρ and θ in this polar coordinate frame. We assumed that these are the two parameters that subjects brought with themselves from pong to the reaching. Having these two gains we

predicted, for each individual subject, what is going to be the results of the reaching movements after learning a delay by taking into account the baseline proprioceptive errors. Fig 18 illustrates model predictions and actual data of the subjects and it seems that the model can reasonably explain the data.

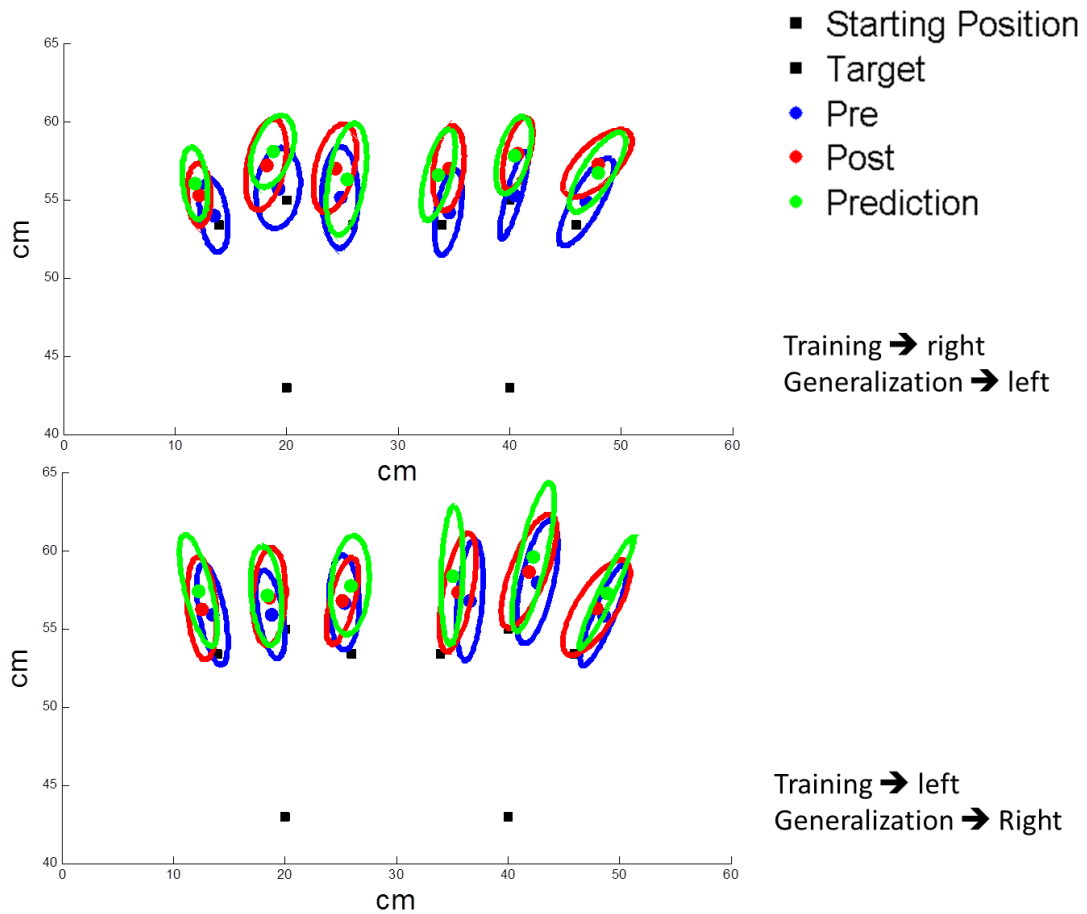


Figure 18: Predictions of the computational model. Black squares represent starting positions and target locations. Blue circles represent base line reaching movements. Red circles represent terminal reaching positions after adaptation. Green circles represent model predictions. Ellipses represent the standard error.

2.7 Discussion

In this study we have shown that learning to cope with short to medium delays (100-150 ms) in complex visuomotor tasks such as playing a pong video game induces significant changes in the proprioceptive space. After a prolonged exposure to delay, subjects show a significant increase in the amplitude of blind reaching movements, suggesting that a change has occurred in their encoding of proprioceptive space. Investigating more in detail also the dynamics of the learning in presence of the delay, it emerges that the compensation is never complete, as the performance never reaches baseline levels.

Moreover, the generalization of the learning across space is not global or homogeneous, but rather strongly depends on the location of the learning workspace and seems to be encoded in an egocentric frame of reference. All these findings seem to point to the conclusion that learning to cope with a delayed feedback in a motor task is not achieved by means of a temporal adaptation (i.e. the use of an internal clock). On the contrary, it is obtained through a state-space approximation, where the spatial effects of the delay are interpreted as a function of body state (e.g. position and velocity) rather than as dependent on time.

When people are faced with a systematic temporal distortion, i.e. a change in simultaneity between action and sensory consequences, they have shown to be able to adapt to a certain degree. Usually, small delays between multiple modalities are introduced in simple tasks as visuo-auditory signals (e.g. Ventriloquist effects) in which a recalibration is obtained, with time perception in one modality being driven by the other modality. The insertion of a delay between action and sensory consequences in simple turn-on-a-light task actually recalibrates the natural timing between action execution and its consequences leading to also a more profound change in the sense of causality (Stetson et al. 2006). The acquisition of the ability to deal with delayed feedbacks in more complex motor tasks, ranging from the more traditional tracking (Miall and Jackson 2006; Foulkes and Miall 2000; Miall 1996; Miall et al. 1985) tasks to balancing (Mehta and Schaal 2002), driving (Welch et al. 1996), and – in our case – playing a quite complex 2D video game, appears to be more complex. In particular, learning appears to be quite slow, even if the experiment is protracted for multiple days and only rarely after effects have been shown. The compensation never seems to be complete, with subjects being able to recover the initial performance. All these evidence seem to suggest that subjects are not actually learning the real temporal deformation introduced by the task, but that they are coping with it by approximating it, trying to understand it as a spatial (or state-space) modification, rather than as a temporal one. A similar interpretation seems to be sustained by recent results by Sarlegna and colleagues (2010). These authors introduced a delay in a tracking task in which subjects had to move a small mass to track an oscillatory target. When a delay was introduced by the hand motion and the cursor, the pattern of the grip forces exercised on the mass showed a peculiar trend, which could be explained, in simulation, only assuming that subjects were modeling the cursor not as delayed, but rather as a dynamic system connected with a spring and a damper to the moving hand. Another

result which is against the idea of a temporal encoding of delay during motor control comes from the works by (Conditt and Mussa-Ivaldi 1999; Karniel and Mussa-Ivaldi 2003). In these studies of motor learning to compensate force fields, the encoding of the field is in state-dependent variables, even though its real nature is that of a temporal dependence. In this work we accumulate proofs of the non-use of a temporal coding in compensating for short to middle time delays (100-150 ms) during a motor task.

The adaptation to the delay leads to significant change in the reaching performance, that is it modifies the proprioceptive space of the movements. No temporal adaptation would explain such specific modification. The generalization of the learning is not global. If subjects simply learned to anticipate their action of 100-150 ms, it could be expected that such behavior would be applied similarly everywhere in the workspace. On the contrary, the generalization of the learning is strongly position-dependent and its pattern is consistent with an egocentric coding of the space (Scheidt and Ghez 2007; Ghez et al. 2007). The results of the second experiment disprove the simple idea of a spatial decay of the generalization of the learning. Although the spatial distance between courts is always the same (around 20 cm from center to center), moving from the right to the left court cancels the adaptation, while the opposite displacement allows for an almost complete generalization. The same asymmetry is evident in the reaching performances after the delay training: for subjects who have trained on the right, the reaching exhibits a much larger overshoot, which moreover is smaller in the left than in the right court.

These findings suggest that the learning to compensate for the delay has actually occurred as a function of subjective posture – i.e. in egocentric coordinates. Such assumption, in fact, would explain the observed pattern of asymmetries both in the reaching and during the pong game.

Our results comply with a body-centered description of the deformation to be learned. Indeed, the asymmetries in the generalization patterns of the reaching movements are in line with an adaptation to the visuomotor deformation in terms of a shoulder center reference frame. Such finding adds up to a bulk of research evidencing the relevance of a body – centered coordinate system – among multiple frames of references- in particular for blind reaching movements. The terminal position of reaching movements toward visual targets seems to be encoded (also) in body-centered coordinates, both toward a memorized or an actual target (Carrozzo et al. 1999; McIntyre et al. 1998). Also the pointing to kinesthetic targets show features consistent with a shoulder-

centered reference frame (Baud-Bovy and Viviani 1998). More recently Ghez et al (2007) have shown that also a new visuo-motor transformation as a rotation can be learned in egocentric coordinate frame (head/shoulder center).

References

- Arnold, V. I. (1989). *Mathematical methods of classical mechanics*, Springer-Verlag.
- Baud-Bovy, G., & Viviani, P. (1998). Pointing to kinesthetic targets in space. *The Journal of Neuroscience*, 18(4), 1528-1545.
- Bertero, M, Poggio T.A, Torre V (1988) Ill-posed problems in early vision, *Proceedings of the IEEE* , 76(8): 869-889.
- Braun DA, Aertsen A, Wolpert DM, Mehring C (2009) Motor task variation induces structural learning. *Curr Biol* 19:352-357.
- Buhusi, C. V. and W. H. Meck (2005) What makes us tick? Functional and neural mechanisms of interval timing. *Nature Reviews Neuroscience* 6(10): 755-765.
- Carrozzo, M., McIntyre, J., Zago, M., Lacquaniti, F. (1999). Viewer-centered and body-centered frames of reference in direct visuomotor transformations. *Experimental Brain Research*, 129(2), 201-210.
- Casadio M, Pressman A, Fishbach A, Danziger Z, Acosta S, Chen D, Tseng H, Mussa-Ivaldi FA (2010) Functional reorganization of upper-body movement after spinal cord injury. *Exp Brain Res* 207:233–247.
- Conditt, M. A. and F. A. Mussa-Ivaldi (1999) Central representation of time during motor learning. *Proceedings of the National Academy of Sciences of the United States of America* 96(20): 11625-11630.
- Flash T, Hogan N (1985) The coordination of arm movements: an experimentally confirmed mathematical model. *J Neurosci* 5:1688-1703.
- Foulkes AJ, Miall RC (2000) Adaptation to visual feedback delays in a human manual tracking task. *Exp Brain Res* 131:101–110.
- Fujisaki, W., S. Shimojo, M. Kashino and S. Nishida (2004). Recalibration of audiovisual simultaneity. *Nature neuroscience* 7(7): 773-778.
- Gibbon J, Churchwarren RM, Meck H (1984) Scalar timing in memory. *Annals of the New York Academy of Sciences*. 423:52-77.
- Ghez, C., Scheidt, R., & Heijink, H. (2007). Different learned coordinate frames for planning trajectories and final positions in reaching. *Journal of neurophysiology*, 98(6), 3614-3626.
- Ivry, R. B. (1996) The representation of temporal information in perception and motor Control. *Current Opinion in Neurobiology* 6(6): 851-857.
- Izawa J, Shadmehr R (2008) On-line processing of uncertain information in visuomotor control. *J Neurosci* 28(44): 11360-11368.
- Kalman, R. E. (1960). A new approach to linear filtering and prediction problems. *Journal of basic Engineering*, 82(1), 35-45.
- Karniel, A. and F. A. Mussa-Ivaldi (2003). Sequence, time, or state representation: how does the

- motor control system adapt to variable environments? *Biological Cybernetics* 89(1): 10-21.
- Kording KP, Wolpert DM (2004) Bayesian integration in sensorimotor learning. *Nature* 427: 244-247.
- Krakauer JW, Pine ZM, Ghilardi M-F, Ghez C (2000) Learning of visuomotor transformations for vectorial planning of reaching trajectories. *J Neurosci* 20:8916–8924.
- Krakauer JW (2009) Motor learning and consolidation: the case of visuomotor rotation. *Adv. Exp. Med. Biol.* 629:405–421.
- Latash ML, Scholz JF, Danion F, Schöner G (2001) Structure of motor variability in marginally redundant multifinger force production tasks. *Exp Brain Res* 141:153–165.
- Liu X, Mosier KM, Mussa-Ivaldi FA, Casadio M, Scheidt RA (2010) Reorganization of finger coordination patterns during adaptation to rotation and scaling of a newly learned sensorimotor transformation. *J Neurophysiol* 105:454-473.
- McIntyre, J., Stratta, F., & Lacquaniti, F. (1998). Short-term memory for reaching to visual targets: psychophysical evidence for body-centered reference frames. *The Journal of Neuroscience*, 18(20), 8423-8435.
- Mehta B, Schaal S (2002) Forward models in visuomotor control. *J Neurophysiol.* 88: 942-953.
- Miall RC, Weir DJ, Stein JF (1985) Visuomotor tracking with delayed visual feedback. *J Neurosci* 16:511–520.
- Miall RC (1996) Task-dependent changes in visual feedback control: a frequency analysis of human manual tracking. *J Mot Behav* 28:125–135.
- Miall RC, Wolpert DM (1996) Forward models for physiological motor control. *Neural Networks* 9:1265-1279.
- Miall RC, Jackson JK (2006) Adaptation to visual feedback delays in manual tracking: evidence against the Smith Predictor model of human visually guided action. *Exp Brain Res* 172:77–84.
- Miall RC, Weir DJ, Stein JF (1985) Visuomotor tracking with delayed visual feedback. *J Neurosci* 16:511–520.
- Miyazaki, M., S. Yamamoto, S. Uchida and S. Kitazawa (2006). Bayesian calibration of simultaneity in tactile temporal order judgment. *Nature neuroscience* 9(7): 875-877.
- Mosier KM, Scheidt RA, Acosta S, Mussa-Ivaldi FA (2005) Remapping hand movements in a novel geometrical environment. *Neurophysiol* 94:4362-4372.
- Pressman A, Nisky I, Karniel A, Mussa-Ivaldi FA (2008) Probing virtual boundaries and the perception of delayed stiffness. *Advanced Robotics* 22:119–140.
- Redding GM, Wallace B (1990) Effects on prism adaptation of duration and timing of visual feedback during pointing. *J Mot Behav* 22(2):209-24.
- Redding GM, Rossetti Y, Wallace B (2005) Applications of prism adaptation: a tutorial in theory and method. *Neuroscience & Biobehavioral Reviews* 29(3):431-444.

- Sarlegna, F. R., Baud-Bovy, G., & Danion, F. (2010). Delayed visual feedback affects both manual tracking and grip force control when transporting a handheld object. *Journal of neurophysiology*, 104(2), 641-653.
- Savitzky A, Golay MJE (1964) Smoothing and differentiation of data by simplified least squares procedures. *Anal. Chem.* 36(8):1627-1639.
- Scheidt, R. A., & Ghez, C. (2007). Separate adaptive mechanisms for controlling trajectory and final position in reaching. *Journal of neurophysiology*, 98(6), 3600-3613.
- Scholz JP, Schoner G. (1999) The uncontrolled manifold concept: identifying control variables for a functional task. *Exp Brain Res* 126:289–306.
- Shadmehr R, Mussa-Ivaldi FA (1994) Adaptive representation of dynamics during learning of a motor task. *J Neurosci* 14:3208-3224.
- Shadmehr R, Brashers-Krug T, Mussa-Ivaldi FA (1995) Interference in learning internal models of inverse dynamics in humans. In Tesauro G, Touretzky DS, Leen TK (eds) *Advances in neural information processing systems* 7:1117–1124.
- Smith MA, Brandt J, and Shadmehr R (2000) Motor disorder in Huntington's disease begins as an error feedback control. *Nature* 403:544-549.
- Spencer, R. M. C., H. N. Zelaznik, J. Diedrichsen and R. B. Ivry (2003) Disrupted timing of discontinuous but not continuous movements by cerebellar lesions. *Science* 300(5624):1437-1439.
- Stetson C, Cui X, Montague P.R, Eagleman D.M. Motor-Sensory Recalibration Leads to an Illusory Reversal of Action and Sensation, *Neuron*, 51(5): 651-659.
- Todorov E, Jordan M (2002a) A minimal intervention principle for coordinated movement. In S. Becker, S. Thrun, & K. Obermayer (Eds.), *Advances in neural information processing systems*, 15:27–34.
- Todorov E, Jordan M (2002b) Optimal feedback control as a theory of motor coordination. *Nature Neuroscience*, 5(11):1226-1235.
- Todorov E (2005) Stochastic optimal control and estimation methods adapted to the noise characteristics of the sensorimotor system. *Neural Computation*, 17(5): 1084-1108.
- Vogels, I. M. L. C. (2004). Detection of temporal delays in visual-haptic interfaces. *Human Factors* 46(1): 118-134.
- Vroomen, J. and M. Keetels (2010). Perception of intersensory synchrony: A tutorial review. *Attention Perception & Psychophysics* 72(4): 871-884.
- Wei K, Körding K (2010) Uncertainty of feedback and state estimation determines the speed of motor adaptation. *Front. Comput. Neurosci.* 4: 4:11.
- Welch R.B, Blackmon T.T, Liu A, Mellers, B.A Stark L.W (1996) The effects of pictorial realism, delay of visual feedback, and observer interactivity on the subjective sense of presence. *Presence: Teleoperators and Virtual Environments*. 5(3): 263-273.
- Wolpert D.M, Kawato M (1998) Multiple paired forward and inverse models for motor control. *Neural Networks*, 11(7-8) 1317-1329.