bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

A conversion from slow to fast memory in response to passive motion

Mousa Javidialsaadi[1], Scott T. Albert[2], Jinsung Wang[1*]

[1]Department of Kinesiology, University of Wisconsin – Milwaukee, Milwaukee, WI, 53201
[2]Depertment of Biomedical Engineering, Johns Hopkins University – Baltimore, MD 21205

Mousa Javidialsaadi and Scott Albert have contributed equally to this work

Correspondence: Jinsung Wang, 492 Enderis Hall, University of Wisconsin – Milwaukee, WI 53201, USA. Email wang34@uwm.edu. Phone: 414-229-2645

Acknowledgements: This work was supported by a grant from the National Institutes of Health (F32NS095706). We dedicate this article to Dr. Fatemeh Pasand and Dr. Majid Chahardah Cheric for all their academic efforts and teachings. They passed away on 10 April 2018 and 26 June 2020, respectively.

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Abstract

When the same perturbation is experienced consecutively, learning is accelerated on the second attempt. This savings is a central property of sensorimotor adaptation. Current models suggest that these improvements in learning are due to changes in the brain's sensitivity to error. Here, we tested whether these increases in error sensitivity could be facilitated by passive movement experiences. In each experimental group, the robot moved the arm passively in the direction that solved the upcoming rotation, but no visual feedback was provided. Then, following a break in time, participants adapted to a visuomotor rotation. Prior passive movements substantially improved motor learning, increasing total compensation in each group by approximately 30%. Similar to savings, a state-space model suggested that this improvement in learning was due to an increase in error sensitivity, but not memory retention. Thus, passive memories appeared to increase the motor learning system's sensitivity to error. However, some features in the observed behavior were not captured by this model, nor by similar empirical models, which assumed that learning was due a single exponential process. When we considered the possibility that learning was supported by parallel fast and slow adaptive processes, a striking pattern emerged; whereas initial improvements in learning were driven by a slower adaptive state, increases in error sensitivity gradually transferred to a faster learning system with the passage of time.

Introduction

In visuomotor rotation experiments, participants actively move a cursor towards an intended target, but the cursor's path is perturbed by a visual rotation (Mazzoni & Krakauer, 2006; Taylor et al., 2014). With training, participants adapt to the visual error, rotating their reach angle in the opposite direction. Like many types of sensorimotor learning, visuomotor adaptation exhibits savings (Haith et al., 2015; Kitago et al., 2013; Morehead et al., 2015; Huberdeau et al., 2015; Huberdeau et al., 2019); participants adapt to a perturbation more rapidly when it has been experienced in the past. On the other hand, when two consecutive perturbations oppose one another, learning during the second period is impaired due to anterograde interference (Brashers-Krug, Shadmehr, & Bizzi, 1996; Sing & Smith, 2010; Tong & Flanagan, 2003; Wigmore, Tong, & Flanagan, 2002). Current models have suggested that these history-dependent changes in learning rate are mediated by one's sensitivity to error (Herzfeld et al., 2014; Albert et al., 2020). When two consecutive perturbations are similar, a given error causes more learning, resulting in savings. However, when two consecutive perturbations are dissimilar, error sensitivity is suppressed, resulting in slower learning (Lerner & Albert et al., 2020). Do these history-dependent changes in error sensitivity require active movement, or can they be evoked by passive experience?

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Recent studies have suggested that passively experiencing a visuomotor perturbation results in learning which transfers to active movement (Lei et al., 2016; Bao et al., 2017; Lei et al., 2017; Tays et al., 2020). That is, even the passive experience of a sensorimotor perturbation might be effective in altering subsequent motor skills. For example, recent studies using robot-assisted motor experiences suggest that passive robotic interventions can facilitate the acquisition of novel motor skills (Reinkensmeyer and Patton, 2009; Bara and Gentaz, 2011; Basteris et al., 2012; Beets et al., 2012) and might also improve motor function in hemiparetic stroke patients (Aisen et al., 1997; Krebs et al., 1998; Riener et al., 2005; Kahn et al., 2006; Vergaro et al., 2010). Yet, while passive experience may help to facilitate motor recovery (Sakamoto et al., 2012; Tays et al., 2020), little is known regarding how these passive experiences cause learning, and how this learning is expressed during active movement.

Current state-space models of learning (Smith et al., 2006; McDougle et al., 2015; Albert et al., 2018) posit that adaption is due to two opposing forces: error-based learning and trial-to-trial forgetting. In principle, passive training could enhance learning either by strengthening a motor memory's retention, or by increasing one's sensitivity to error. However, changes in learning parameters such as error sensitivity are thought to be driven by sensory prediction errors (Popa & Ebner, 2019; Shadmehr et al., 2010) that accompany active movements; the brain predicts the sensory consequences of its motor plan via a forward model and then compares this to the observed sensory feedback. Repeated exposure to these consistent prediction errors appears to upregulate sensitivity to those errors (Gonzalez-Castro et al., 2014; Herzfeld et al., 2014; Leow et al., 2016; Albert et al., 2020). But in a more general sense, prediction errors do not necessarily require movement. For example, in classical conditioning, these errors are driven directly by unexpected sensory stimuli (Ohmae & Medina, 2015; Kim et al., 2020; Ito, 2007; Sears & Steinmetz, 1991; Rasmussen et al, 2008). Here, we wondered if passive movements could generate prediction errors in a similar manner, and if consistent exposure to these errors might increase sensitivity to error during active motor learning.

To test this, we passively moved the hand to an unexpected location in the absence of visual feedback, prior to exposure to a visuomotor rotation. This passive movement resulted in a proprioceptive mismatch between the hand and the visual target. In addition, though this robotic intervention created proprioceptive errors during the passive period, the ultimate hand position provided the solution to the upcoming visual rotation. As in earlier studies, we observed that this manipulation facilitated active motor learning (Lei et al., 2016; Bao et al., 2017; Lei et al., 2017; Tays et al., 2020). When we applied a standard single-module state-space model to these data, the model predicted that improvements in learning were driven by changes in error sensitivity, not retention rates. Yet, some features in the observed behavior

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

were not captured by this model, nor by similar empirical models, which assumed that learning was due a single exponential process.

On the contrary, motor learning appears to be supported by at least two parallel systems: a slow system that responds little to error but retains its adaptation over time, and a fast system that responds strongly to error but decays rapidly (Smith et al., 2006; Sing & Smith, 2010; Albert et al., 2018; Coltman et al., 2019; Orozco et al., 2020). When we applied this model to the measured data, the model suggested that improvements in learning were driven by a slower adaptive state. However, when we extended the time between the passive training and active motor learning (to 24 hr), improvements in the slow state of adaptation appeared to transfer to a faster learning process. Interestingly, these changes in learning were also accompanied with biases in reach angles that appeared prior to perturbation onset. Thus, passive errors engaged both motor control and motor learning systems, but the resulting behavioral patterns migrated between slow and fast adaptive circuits as the passive memory consolidated.

Methods

Here we tested how passively experiencing an error alters the process of motor adaptation. Participants were divided into several groups. Each group experienced a passive movement period, a break in time, and then an active adaptation period. By varying the duration of the break between passive and active movement periods, we measured how memories created by passive errors consolidated over time.

Participants

Twenty-eight healthy volunteers (17 males, 11 females; aged: 18-35) participated in this study. All subjects were right-handed as assessed by the Edinburgh handedness inventory (Oldfield, 1971). Each subject signed a consent form that was approved by the University of Wisconsin-Milwaukee Institutional Review Board. Participants were randomly assigned to one of three experimental groups or a control group.

Apparatus

Participants were seated in a robotic exoskeleton (KIMARM, BKIN Technologies Ltd, Kingston, ON, Canada) that provided gravitational support to both arms. The exoskeleton was positioned so that the participant's arm was hidden underneath a horizontal display (Fig. 1A). To track the hand's position, a small cursor was projected onto the display, over the participant's index fingertip. During each trial, the KINARM projected visual stimuli (a start position and a target) onto the display, so that they appeared to be within the same plane as the arm. The visual stimuli consisted of a centrally located start circle (2 cm in diameter) and one

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

of four target circles (2cm in diameter) located 10 cm away from the start target (Fig. 1B). We sampled the hand's position in the x-y plane at 1000 Hz. Position data were low pass filtered at 15 Hz, and then differentiated to obtain velocity. All post-processing, analysis, and modeling was conducted in MATLAB R2018a (The MathWorks Inc., Natick, MA).

Experimental Design

Participants were assigned to one of three experimental groups (n=7/group). Each experimental group experienced three separate conditions: (1) a passive movement period, (2) a baseline reaching period, and (3) a visuomotor rotation period (Fig. 1C). To determine how passive movements altered reaching behavior (in the baseline and rotation periods), we compared behavior in the experimental groups to that of a control group (n=7) that did not experience the passive movement period prior to active reaching.

In the passive movement period, the KINARM moved the participant's right arm along a straight 10 cm minimum jerk trajectory. On each trial, a visual target was displayed, but the robot passively moved the arm along a path that was rotated 30° clockwise (CW) to the visual target (Fig. 1B, left). Critically, this CW rotation served as the "solution" to a counterclockwise (CCW) visuomotor rotation that participants had not yet experienced (see below). Participants were told to relax their arm and not resist the passive motion. The passive period consisted of 30 cycles (4 trials in a cycle, 1 to each target in a pseudorandom order). No visual feedback was provided on these trials. Thus, participants received only proprioceptive information about the error between their arm's path and the visual target. The passive movement period terminated with a time-delay which distinguished each experimental group: 5-min delay (n=7), 1 hr delay (n=7), or 24 hr delay (n=7). Once the delay concluded, an active baseline reaching period began.

In the baseline period, participants moved their arm to each target over a 10-cycle (experimental groups) or 15-cycle (control group) reaching period. On each trial, continuous visual feedback was provided via a cursor over the index fingertip. Participants were instructed to move rapidly and accurately to the target location. The trial ended 1.5 sec after the target was presented. To begin the next trial, the participant had to move their hand back to the central start position.

The experiment ended with an active visuomotor rotation period that lasted 20 cycles (80 trials total). On rotation trials, the cursor was rotated 30° CCW to the hand path (Fig. 1B, right). As noted above, the "solution" to this rotation would be to counter-rotate the reach path by 30° CW relative to the target. Critically, this CW rotation would coincide with the movement path experienced during the passive period. Thus, participants in each experimental had been given the proprioceptive experience of this "solution", though this was never explicitly revealed to each participant. Participants in the control group, however,

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

had never experienced the passive movement period. Thus, there was no prior memory to draw upon during the baseline and rotation periods.

Empirical Data Analysis

Data analysis was performed using MATLAB (Mathworks, Natick, MA). The pointing angle at the reaching movement's midpoint (5 cm displacement) was used as our performance measure, calculated as the hand's angular position relative to the line segment connecting the start and target positions. Data were then averaged within each 4-trial cycle. Only cycled data were used in our analyses.

Here we considered how the passive movement period altered reaching behavior during both the baseline and rotation periods. To investigate the baseline reach period, we averaged the reach angle over the initial 10 cycles of the baseline period. To assess the rotation period, we considered both early and late adaptation measures. To quantify early adaptation, we isolated the reach angle on the first rotation cycle and second rotation cycle. To quantify late adaptation, we averaged the reach angle over the last 10 rotation cycles. Lastly, we also computed each subject's overall learning rate via an exponential function that tracked how reach angle (y) changed over each rotation cycle (t, starting at 0):

$$y^{(t)} = \alpha e^{-\beta t} + c \tag{1}$$

Here α and c determine the initial reach angle and asymptotic reach angle. The parameter β represents the participant's learning rate during the adaptation period. We fit this exponential function to each participant's data in the least-squares sense using *fmincon* in MATLAB R2018a. We repeated the fitting procedure 20 times, each time varying the initial parameter guess that seeded the algorithm. We selected the model parameters which minimized squared error over all 20 repetitions.

State-space learning model: one-state

Although the exponential function closely approximates the decay of motor error during adaptation to a perturbation, its learning rate parameter reflects a mixture of cycle-by-cycle forgetting and error-based learning (Lerner & Albert, et al. 2020). Thus, to better understand the adaptation process, we used a state-space model (Smith et al., 2006). The state-space model posits that learning consists of cycle-to-cycle error-based learning as well as cycle-by-cycle memory retention (i.e., forgetting). The forgetting process is controlled by a retention factor (a) which specifies how much adaptation is retained from one cycle to the next. The learning process is controlled by the participant's error sensitivity (b), which specifies how much is learned from a given error (e). These processes together determine how the participant's internal state (x) changes over time, in the presence of internal state noise (ε_x, normal with zero mean, SD=σ_x):

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

$$x^{(t+1)} = ax^{(t)} + be^{(t)} + \varepsilon_x^{(t)} \tag{2}$$

Eq. (2) allows us to ascribe any differences in performance during the adaptation period to meaningful quantities: retention (*a*) and error sensitivity (*b*).

Note however, that the internal state (*x*) is not a measurable quantity. Rather, on each cycle, the motor output (reach angle) is measured. This reach angle (*y*) directly reflects the subject's internal state, but is corrupted by execution noise (ε_x, normal with zero mean, SD=σ_y) according to:

$$y^{(t)} = x^{(t)} + \varepsilon_y^{(t)} \tag{3}$$

Thus, Eqs. (2) and (3) represent a single module state-space model. We fit this model to each participant's reach angles during the adaptation period using the Expectation-Maximization (EM) algorithm (Albert & Shadmehr, 2018). EM is an algorithm the conducts maximum likelihood estimation in an iterative process. We used EM to identify the model parameters {a, b, x_1, σ_x, σ_y, σ_1} that maximized the likelihood of observing the data (note that x_1 and σ_1 represent the participant's initial state and variance, respectively). We conducted 10 iterations, each time changing the initial parameter guess that seeded the algorithm. We selected the parameter set that maximized the likelihood function across all 10 iterations.

State-space learning model: two-state

The single-module state-space model describes learning as a single adaptive process. Motor adaptation, however, is believed to be comprised of multiple states, each with different timescales of learning. These states appear to be accurately summarized as a parallel two-state system, with adaptation supported by a slow adaptive process and a fast adaptive process (Smith et al., 2006; McDougle et al., 2015; Albert & Shadmehr, 2018; Coltman et al., 2019). The slow process exhibits slower error-based learning, but strong retention over time. The fast process exhibits faster error-based learning, but higher rates of forgetting. We wondered how these adaptive states may contribute to the consolidation of passive motor memory.

To answer this question, we fit a standard two-state model of learning to individual participant behavior. In this model, slow state and fast state adaptation are controlled by slow state and fast state retention factors (a_s and a_f, respectively), as well as slow state and fast state error sensitivities (b_s and b_f, respectively). As in Eq. (1), both internal states exhibit cycle-by-cycle learning and forgetting, in the presence of internal state noise ($\varepsilon_{x,s}$ and $\varepsilon_{x,f}$, normal with zero mean, SD=σ_x):

$$\begin{aligned} x_s^{(t+1)} &= a_s x^{(t)} + b_s e^{(t)} + \varepsilon_{x,s}^{(t)} \\ x_f^{(t+1)} &= a_f x^{(t)} + b_f e^{(t)} + \varepsilon_{x,f}^{(t)} \end{aligned} \tag{4}$$

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

To enforce the traditional two-state dynamics (slow state has higher retention, fast state has higher error sensitivity), retention factors and error sensitivities in Eq. (4) are constrained such that $a_s > a_f$ and $b_f > b_s$. As with the single-module state-space model, the two adaptive are not directly measurable. But together, they sum to produce the overall adapted reach angle, which is also corrupted by execution noise:

$$y^{(t)} = x_s^{(t)} + x_f^{(t)} + \varepsilon_y^{(t)} \tag{5}$$

Together, Eqs. (4) and (5) with the inequality constraints relating a_s, a_f, b_s, and b_f constitute the two-state model of learning. The full parameter set consists of: $\{a_s, a_f, b_s, b_f, x_{s,1}, x_{f,1}, \sigma_x, \sigma_y, \sigma_1\}$. Note that $x_{s,1}$, and $x_{f,1}$ are the initial slow and fast state magnitudes, which are also estimated by the model.

We fit this model to individual participant data, using the EM algorithm (Albert & Shadmehr, 2018). Note that one's ability to fit the two-state model greatly benefits from multiple trial conditions, such as set breaks, error-clamp periods, washout periods, and perturbation reversals (Albert & Shadmehr, 2018). However, the current experiment consisted of only perturbation trials with one orientation. Therefore, to improve our ability to robustly recover the two-state model parameters, we used a two-tiered fitting procedure (described below).

In our single-state model, we found that error sensitivity varied across experimental and control groups, but not retention. Therefore, to improve our ability to recover slow and fast error sensitivity, we started by constraining the model's retention factors (hypothesizing that these were not impacted by the passive movement period). To do this, we started by fitting the model to mean behavior in the 5 min, 1 hr, 24 hr, and control groups. Then we calculated the midpoint in the range spanned by slow and fast retention factors identified in each group. Lastly, we then fit the two-state model to individual participant behavior in each group, after fixing the slow and fast retention factors to these values.

When fitting the two-state model to either group behavior or individual participant behavior, we performed 10 iterations of the EM algorithm, each time varying the initial parameter guess that seeds the algorithm. We then selected the parameter set computed by EM with the greatest likelihood.

Statistics

Statistical tests such as one-way ANOVA were carried in MATLAB R2018a. For post-hoc testing following ANOVA, we used Dunnett's test to assess whether the mean behavior in the 5 min, 1 hr, and 24 hr differed from the control group. When testing for differences in slow and fast error sensitivities in our two-state model, we used the Kruskal-Wallis test to evaluate difference in medians. This test was used over one-way ANOVA due to the presence of a slow state error sensitivity outlier in the 1 hr group, and the small

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

group sizes used in each group. For post-hoc testing following Kruskal-Wallis, we used Dunn's test in IBM SPSS 25 to test for difference in median error sensitivity in the 5 min, 1 hr, and 24 hr groups against control.

Results

When people adapt to two similar perturbations consecutively, re-adaptation evokes a hallmark of sensorimotor adaptation called savings: more rapid learning during the second exposure to a perturbation (Smith et al., 2006; Zarahn et al., 2008; Leow et al., 2013; Haith et al., 2015; Day et al., 2018; Coltman et al., 2020; Yin & Wei, 2020). These changes in learning are thought to be mediated by error sensitivity (Gonzalez-Castro & Hadjiosif, 2014; Herzfeld et al., 2014; Coltman et al., 2020), whereby the trial-by-trial experience of consistent errors makes the brain more sensitive to those errors in the future (Herzfeld et al., 2014; Leow et al., 2016; Albert et al., 2020). Do these changes in the brain's learning systems require errors to be actively experienced, or can learning be improved by passive experiences as well?

Here we tested this possibility by exposing participants to a passive movement period, prior to exposing them to a visuomotor rotation (Fig. 1C). In the passive period, the robot moved the participant's arm towards a target, without any visual feedback (Fig. 1A; Fig. 1B, left). But rather than move the arm directly to the visual target, the robot deviated along a path rotated clockwise by 30°. Thus, consistent proprioceptive "errors" were passively delivered to the participant without them ever producing an active movement. Following a break in time (Fig. 1C, break; 5 min, 1 hr, or 24 hr) participants then returned and produced active movements to the same targets, first in a baseline condition (Fig. 1C, baseline), and then under the influence of a 30° CCW visuomotor rotation (Fig. 1B, right; Fig. 1C, rotation). The perturbation's orientation was chosen so that the passive movements provided the "solution" to the rotation that had not yet occurred. Is it possible that this passive memory could facilitate learning during active movement?

To answer this question, we compared reaching movements during the baseline and adaptation periods (Fig. 1D, black), to those of a control group that never experienced passive training (Fig. 1D, gray). By measuring how behavior changed with the time-delay between passive and active periods, we investigated how memory acquired passively was consolidated and expressed over time.

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

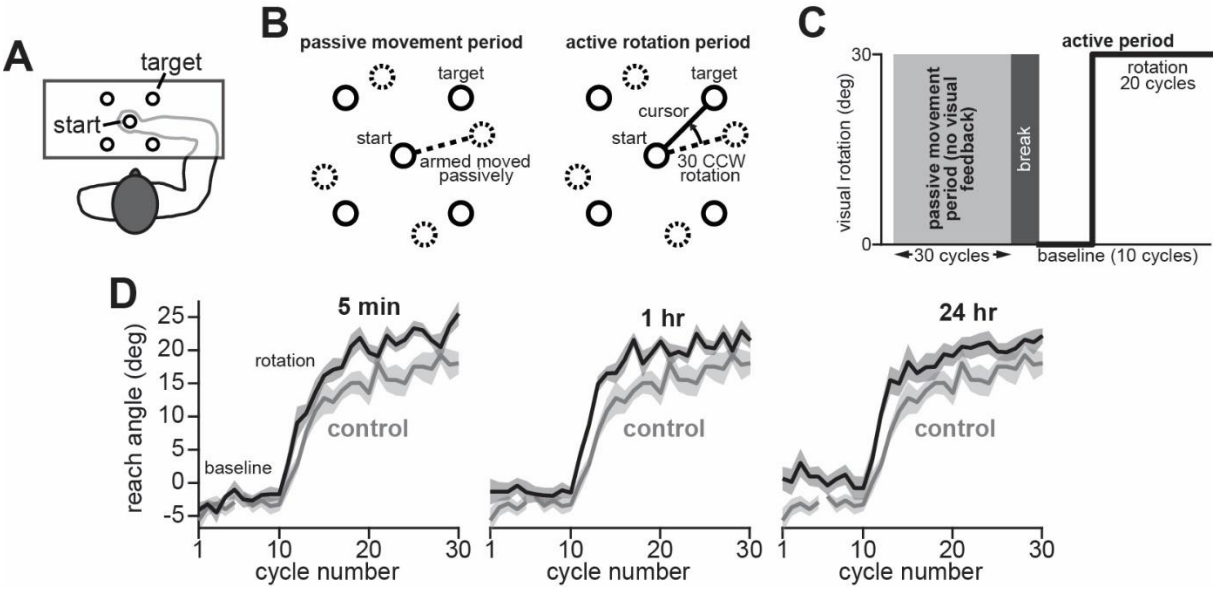

Figure 1. Passive and active motor paradigm. **A.** Participants (n=28) were seated in a KINARM exoskeleton which each arm supported against gravity. Their arm was placed underneath a horizontal display. **B.** During the passive movement period (left) participants were shown a target at either 45°, 135°, 225°, 315°, but the KINARM passively moved the hand along a path that was rotated 30° clockwise (CW) to the visual target. No visual feedback of hand position was provided. During the active learning period (right) participants reached to the same targets, but the cursor was rotated counterclockwise (CCW) by 30°. Thus, to solve this rotation, participants needed to move along the same path traversed during the passive manipulation (solution shown in dashed line. **C.** The experiment started with 30 cycles (4 trials to each target) of passive movements. Then participants took either a 5 min, 1 hr, or 24 hr break. When participants returned to the experiment, they completed 10 cycles of baseline reaching movements, followed by 20 visuomotor rotation cycles. **D.** We calculated the reach angle between the hand and the straight-line path between the start and target cursor. The reach angle was calculated at the movement's midpoint (5 cm displacement). Reach angles for the control group (no passive training) are shown in gray. Reach angles for the 5 min group (left), 1 hr group (middle), and 24 hr group (right) are shown in black. Error bars show mean ± SEM.

Consolidating passive movement experiences biases reaching commands

Active movement periods in the experimental and control groups began with a series of baseline reaching movements where participants reached with veridical visual feedback (Fig. 1D, baseline). Were these initial baseline movements altered by the passive experience of proprioceptive error?

To answer this question, we isolated baseline reaching behavior in each group (Fig. 2A). Without any prior exposure to passive movements, the control group exhibited a counterclockwise (negative) bias in baseline reach angle, which was likely caused by the inertial properties of the arm and robotic apparatus (Fig. 2B, control; one-sample t-test, $t(6)=-5.38$, $p=0.002$). Remarkably, this bias was gradually lifted in the experimental groups (Fig. 2B; one-way ANOVA, $F(3,24)=3.2$, $p=0.0415$), with the 24 hr group showing a statistically significant reduction in bias relative to the control group (post-hoc Dunnett's test, 24 hr vs. control, $p=0.019$).

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Critically, this change in baseline reach angle was directed towards past locations where the arm had been passively moved (i.e., "rotation solution" in Fig. 2). In other words, whereas subjects without passive training produced reaching movements that deviated slightly CCW, subjects with passive training where the robot moved their arm CW, exhibited biases that were shifted in that direction. Because this change in reach angle was only present in the 24 hr group, it appeared that this shift in baseline reach angle required long-term consolidation. Moreover, the data suggested a clear trend (Fig. 2B) where changes in baseline reach angle gradually strengthened with increased time-delay between passive and active periods (though with our small group sizes, we did not have enough power to statistically confirm these gradual changes).

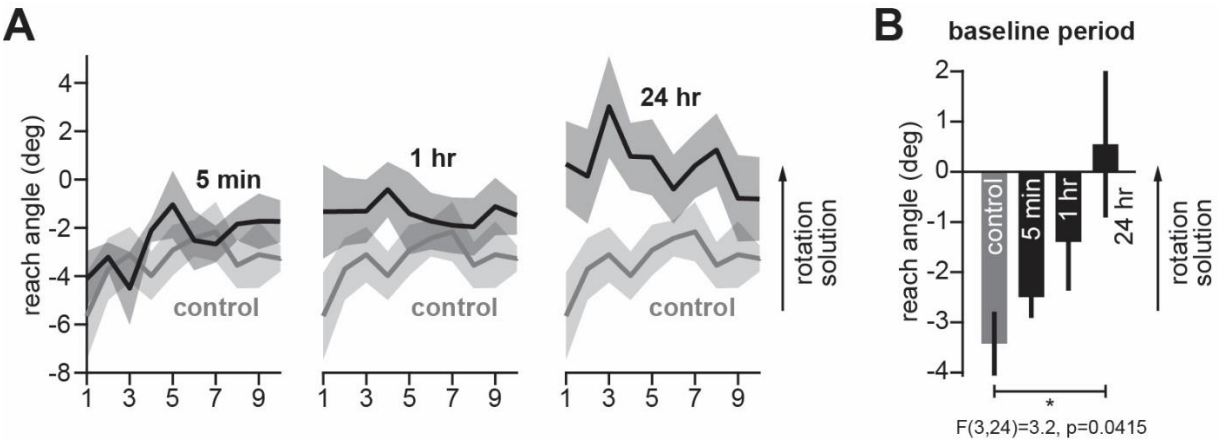

Figure 2. Passive training evoked a time-dependent bias in initial reach angle. **A.** Here we show reach angles during the 10 baseline cycles in the active movement period. The control group (no passive training) is shown in gray. The experimental groups (5 min, 1 hr, and 24 hr) are shown in black. Note that the control group exhibited a slight negative (counterclockwise) bias in reach angle at the movement's midpoint. This was likely due to the inertial properties of the arm and robotic system. However, this bias appeared to change in the experimental groups. The direction of this shift (upwards in the graph) is directed towards the solution of the upcoming rotation (which is also the direction along which the hand was passively moved during the preceding passive movement period). **B.** We calculated the mean reach angle during the baseline period. Statistics show post-hoc Tukey's test following one-way ANOVA (* indicates $p<0.05$). Error bars show mean ± SEM.

In summary, the naïve assumption might be that the reach system produces commands which are heavily dependent on visual stimuli. Surprisingly however, it appears that when the hand is passively moved to a location, this proprioceptive experience gets paired with visual targets; later, the reach commands actively produced to move towards the target, are computed via some weighting between the target's visual location and the past proprioceptive memory. This proprioceptive weighting appears to

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

require consolidation, arising only after long periods of delay. Next, we investigated whether this consolidated proprioceptive memory alters the process of motor adaptation.

Passive movement experiences enhance motor adaptation

Following the baseline reaching period, all participants were abruptly exposed to a 30° CCW rotation (Fig. 1C, rotation). The perturbation's orientation was selected such that rotation's "solution" (counter-rotate clockwise) mirrored the passive movement direction participants had experienced in the past (Fig. 1B, right). Did this passive experience somehow facilitate or obstruct the process of motor learning?

Fig. 3A shows the rotation period reach angle in the experimental and control groups (positive values denote greater adaptation). Remarkably, passive training appeared to greatly facilitate adaptation in all three experimental groups (Fig. 3B, mean reach angle; one-way ANOVA, $F(3,24)=3.98$, $p=0.02$; post-hoc Dunnett's test against control, 5 min: $p=0.021$, 1 hr: $p=0.021$, 24 hr: $p=0.038$), increasing average compensation by approximately 30%.

At what point did this improvement appear? To answer this question, we analyzed the reach angle on the first two cycles. Though the reach angle on the first cycle appeared slightly larger in the experimental groups (Fig. 3C), this trend was not statistically significant (one-way ANOVA $F(3,24)=1.38$, $p=0.274$) and could have been biased by lingering differences in baseline reach behavior (Fig. 2). However, by the second reaching cycle (Fig. 3D) adaptation in each group surpassed that of the control group (one-way ANOVA, $F(3,24)=4.59$, $p=0.011$; post-hoc Dunnett's test against control, 5 min: $p=0.027$, 1 hr: $p=0.039$, 24 hr: $p=0.006$). This analysis suggested that enhancements in learning developed quite rapidly, and unlike changes in baseline behavior (Fig. 2), did not require long-term consolidation of the passive training period (considering the improvement was present even in the 5 min group).

All evidence pointed towards the possibility that passive training increased the rate of learning during the rotation period. To mathematically test this idea, we fit an exponential curve (Eq. (1)) to the adaptation period reach angles (dashed lines in Fig. 3A). Indeed, the exponential model suggested that passive training increased the rate of learning during the rotation (Fig. 3E, one-way ANOVA, $F(3,24)=3.48$, $p=0.031$). Surprisingly however, this increased rate was not exhibited by each group; only the 24 hr group showed a statistically significant increase in learning rate over the control group (post-hoc Dunnett's test against control: 5 min: $p=0.99$, 1 hr: $p=0.3$, 24 hr: $p=0.046$).

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

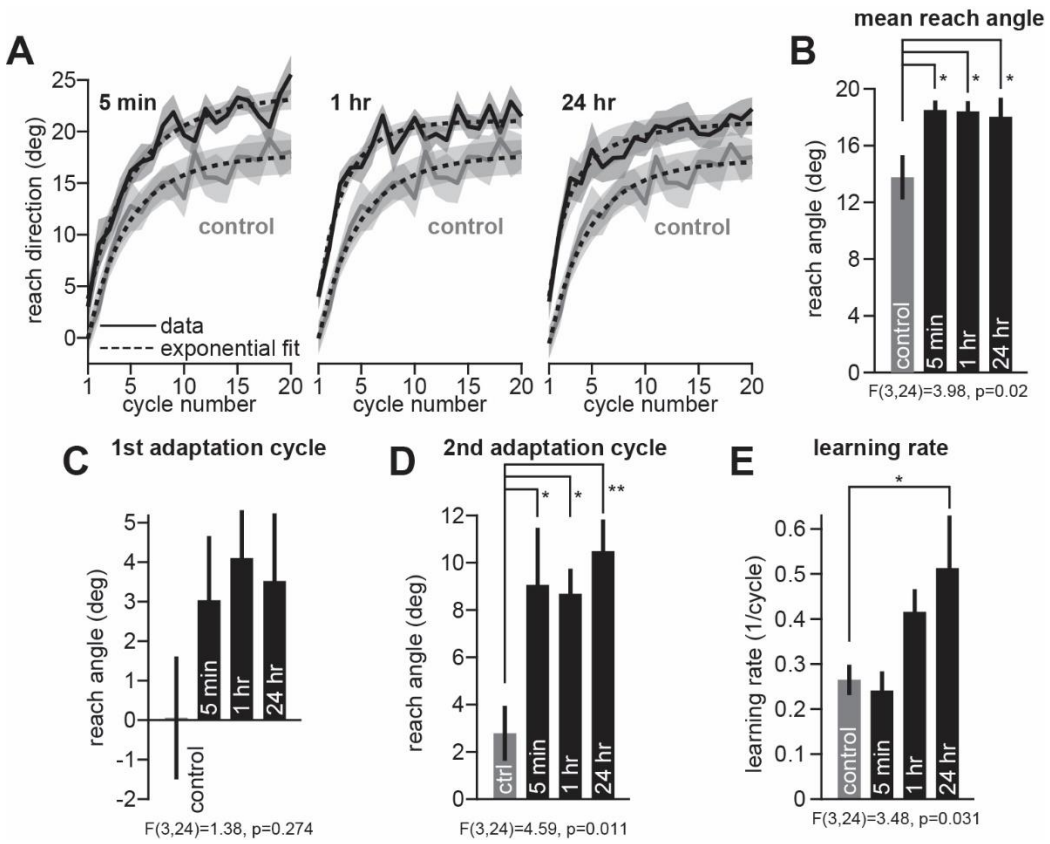

Figure 3. Passive training enhances active motor learning. **A.** Here we show reach angles during the active rotation learning cycles. The control group (no passive training) is shown in gray. The experimental groups (5 min, 1 hr, and 24 hr) are shown in black. Dashed black lines show an exponential fit to the data (mean across individual subjects). **B.** We quantified the mean reach angle across the 20 rotation cycles. All experimental groups showed greater adaptation than the control group. **C.** We measured the reach angle on the initial adaptation cycle. **D.** We measured the reach angle on the second adaptation cycle. All experimental groups showed greater adaptation than the control group on this cycle. **E.** We quantified each participant's learning rate with a 3-paremeter exponential model. In each panel, statistics show post-hoc Tukey's test following one-way ANOVA (* indicates $p<0.05$, ** indicates $p<0.01$). Error bars show mean ± SEM.

Thus, our analysis presented a puzzle. On one hand, passive training improved overall adaptation (Fig. 3B), with improvements evident even on the second rotation cycle (Fig. 3D) in each group. Therefore, this facilitation did not appear to require long-term consolidation. However, the rate of learning (assessed via an exponential curve) was only enhanced in the 24 hr group (Fig. 3E) suggesting that the improvement in learning did in fact require long-term consolidation. How are we to rectify this contradiction? One idea is that there are in fact improvements in learning across all experimental groups, but this improvement is only partially captured by a model-free exponential curve.

Passive movement experiences enhance sensitivity to error, but not retention

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

One issue with the exponential model, is that is does not parse behavior into interpretable physiologic processes. That is, motor adaptation is known to be governed by at least two critical processes: error-based learning and trial-by-trial forgetting. While these two processes are mixed together within an exponential curve, they are more easily recovered by a state-space model of learning. The state-space model of learning (Eqs. (2) & (3)) posits that adaptation is due to learning and forgetting events, which are controlled by one's sensitivity to error (*b*) and retention (*a*), respectively. Might passive training alter one (or both) of these properties, thus producing the facilitation in adaptation noted in Fig. 3?

To answer this question, we fit a single-module state-space model to individual participant reach angles in the experimental and control groups. The model (Fig. 4A, dashed lines) appeared to closely track each group's learning curve. Next, we isolated the retention factor (Fig. 4B) and error sensitivity (Fig. 4C) predicted by the state-space model. Interestingly, passive training did not appear to alter the retention processes in any experimental group (Fig. 4B, one-way ANOVA, $F(3,24)=2.19$, $p=0.115$). On the other hand, passive training clearly impacted error sensitivity (Fig. 4C, one-way ANOVA, $F(3,24)=3.81$, $p=0.023$), which appeared to grow with time-delay duration; though only the 24 hr group showed a statistically significant difference relative to the control condition (post-hoc Dunnett's tests against control, 5 min: $p=0.72$, 1 hr: $p=0.061$, 24 hr: $p=0.017$).

In summary, the state-space model suggested that the passive experience of proprioceptive error increased sensitivity to visual errors during the active movement period. These changes appeared quite similar to those observed in savings paradigms, where initial adaptation increases error sensitivity, but not retention (Herzfeld et al., 2014; Coltman et al., 2019). But the single-module state-space model still could not solve the puzzle that arose in our empirical analysis of behavior; why is error sensitivity only increased in the 24 hr group (Fig. 4C), when all the experimental groups show a facilitation in learning (Figs. 3B&D)?

Conversion from slow to fast memory states during passive training consolidation

Both our exponential model (Fig. 3E) and state-space model (Fig. 4C) suggested that changes in adaptation were specific to the 24 hr group, while the empirical data (Figs. 3B&D) showed clear improvements in adaptation across all groups (5 min, 1 hr, and 24 hr) exposed to passive errors. This discrepancy suggested that there were some features in the adaptation curve that were altered by passive training, which our models could not quite capture. Both the exponential and state-space models describe learning as a single adaptive process. Could it be that adaptation patterns were truly the result of multiple states of learning?

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

To investigate this possibility, we considered a standard two-state model of learning (Smith et al., 2006). The two-state model posits that adaptation is supported by multiple adaptive states: a slow state and a fast state which differ in their sensitivity to error and retention. The slow process learns less due to error, but retains its state strongly over time. The fast process learns more due to error, but is volatile and decays more rapidly over time. How do the changes in error sensitivity noted in our single-module state-space model relate to these two parallel adaptive processes?

To answer this question, we fit the two-state model (Eqs. (4) & (5)) to individual participant reach angles in the experimental and control groups. Using the resultant model parameters, we simulated the slow (Fig. 4D) and fast (Fig. 4F) states predicted by the model. These states showed a remarkable trend; immediately after the passive training period in the 5 min group, the slow state of learning was enhanced, but this facilitation diminished over time (Fig. 4D). On the other hand, the fast state of learning exhibited the opposite trend; as the time-delay following the passive training period increased, so too did activity in the fast adaptive process (Fig. 4F).

These changes in the slow and fast states were due to a striking pattern in error sensitivity. The slow state's error sensitivity increased nearly two-fold following the passive training period in the 5 min group (Fig. 4E, Kruskal-Wallis test, $X^2(27)=8.32$, $p=0.0398$) but gradually returned to control levels with the passage of time following the passive training period (post-hoc Dunn's tests against control, 5 min: $p=0.024$, 1 hr: $p=1$, 24 hr: $p=1$). On the other hand, the fast-state's error sensitivity increased by 50% (Fig. 4G, Kruskal-Wallis test, $X^2(27)=9.04$, $p=0.0288$) but only in the 24 hr group after the passage of time (post-hoc Dunn's tests against control, 5 min: $p=0.486$, 1 hr: $p=0.087$, 24 hr: $p=0.012$).

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

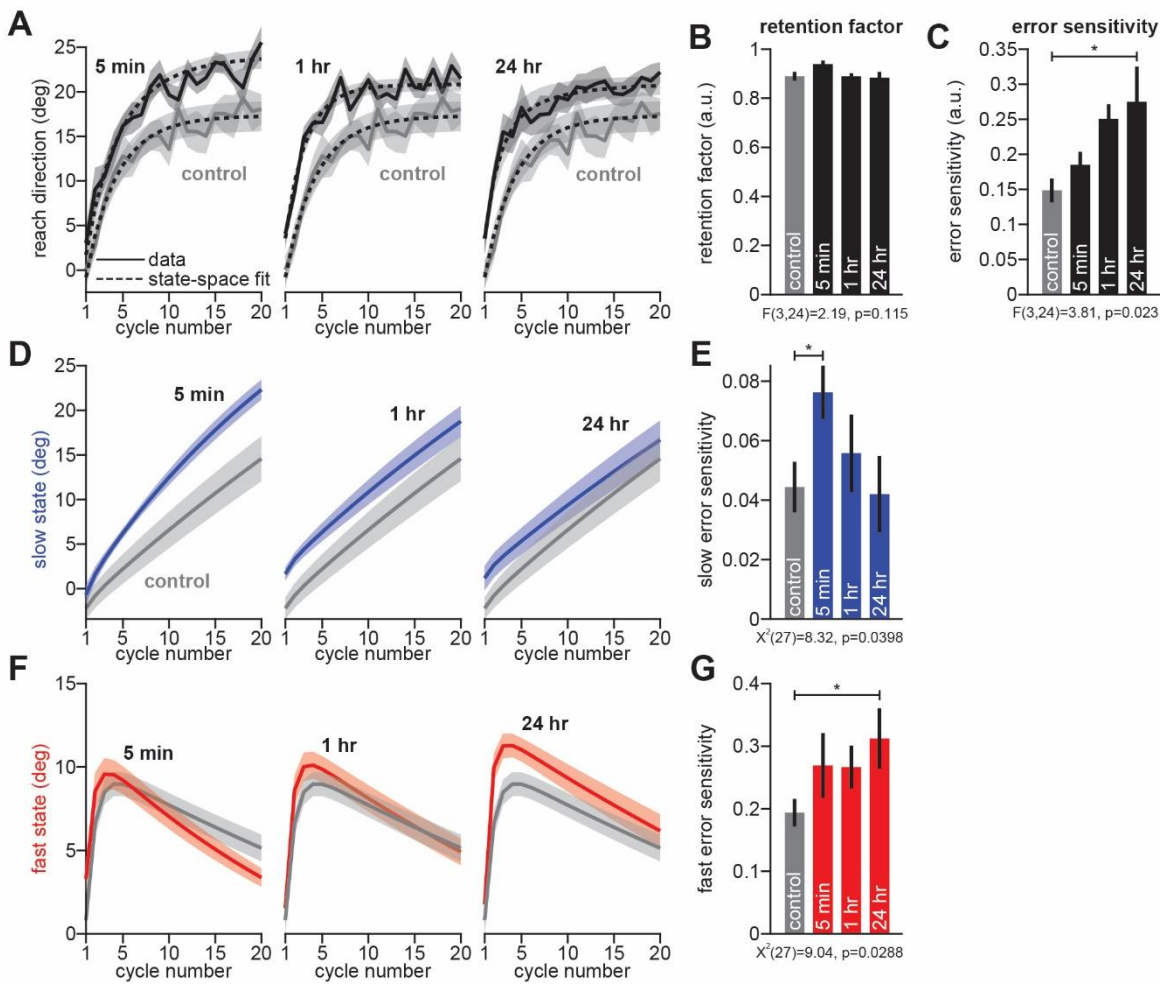

Figure 4. Passive training improves motor learning by increasing sensitivity to error. **A.** Here we show reach angles during the active rotation learning cycles. The control group (no passive training) is shown in gray. The experimental groups (5 min, 1 hr, and 24 hr) are shown in black. We fit the data with a single-module state-space model (dashed black line; mean across individual participants). The state-space model posited that adaptation was due to both error-based learning (controlled by error sensitivity) and trial-by-trial forgetting (controlled by retention factor). **B.** Here we show the retention factor predicted by the single-module state-space model. **C.** Here we show the error sensitivity predicted by the single-module state-space model. **D.** We fit a two-state model to individual participant behavior. The predicted slow state for the experimental groups (5 min, 1 hr, and 24 hr) are shown in blue; time-delay between passive and active training increases left-to-right. The predicted slow state in the control group is shown in gray. **E.** Here we provide the slow state error sensitivity predicted by the two-state model. **F.** Same as in **D**, but for the fast state of learning. **G.** Same as in **E** but for the fast state error sensitivity. In each panel, statistics show post-hoc Tukey's test (**C**) or Dunn's test (**G**) following one-way ANOVA (**C**) or Kruskal-Wallis (**E** and **G**). Statistics: * indicates $p<0.05$, ** indicates $p<0.01$). Error bars show mean ± SEM.

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

In summary, the two-state model made an intriguing prediction; adaptation in each experimental group was enhanced by the passive error experience, but the nature of this enhancement varied over time. Initially following the passive movement period, error sensitivity had increased in the slower adaptive process. But with the passage of time, this improvement transferred to the fast state of adaptation. Thus, as the passive memory consolidated, it appeared that its benefits were converted from slower learning processes, to faster learning processes.

Discussion

When the same perturbation is experienced consecutively, learning is accelerated on the second attempt. This savings is a central property of sensorimotor adaptation which is observed across several motor effectors: the reaching system (Smith et al., 2006; Zarahn et al., 2008; Leow et al., 2013; Haith et al., 2015; Coltman et al., 2020; Yin & Wei, 2020), walking (Mawase et al., 2014; Day et al., 2018), and even the oculomotor system (Kojima et al., 2004). Current models have suggested that these improvements in learning are due to changes in the brain's sensitivity to error (Gonzalez-Castro & Hadjiosif, 2014; Herzfeld et al., 2014; Mawase et al., 2014; Coltman et al., 2020). Here, we tested whether these increases in error sensitivity could be facilitated by passive experiences, as opposed to active movements.

To do this, we used a state-space model to interpret how motor adaptation is altered due to passive proprioceptive memory. Consistent with earlier work (Lei et al., 2016; Bao et al., 2017; Lei et al., 2017; Tays et al., 2020) we observed that passive training facilitated active motor adaptation. In each experimental group, the robot moved the arm passively in the direction that solved the upcoming rotation, but no visual feedback was provided. Somehow, this passive proprioceptive experience substantially altered subsequent motor learning, increasing total compensation in each group by approximately 30%. Similar to savings, the state-space model suggested that this improvement in learning was due to an increase in error sensitivity. Thus, passive memories appeared to increase the motor learning system's sensitivity to error.

However, the state-space model's prediction exhibited a puzzle; whereas all experimental groups showed improvements in total compensation, only the 24 hr group showed a statistically significant increase in sensitivity to error (Fig. 4C). This peculiarity was also present when we fit an exponential curve to estimate participant learning rates (Fig. 1E). This suggested that these models were missing a key component: multiple adaptive states. That is, converging evidence suggests that sensorimotor learning is supported by parallel processes (Smith et al., 2006; Mawase et al., 2014; McDougle et al., 2015; Coltman et al., 2020). The parallel adaptive states are well-approximated as a two-state system: with one slow

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

state the learns slowly but is decay-resistant, and one fast state which learns rapidly but also forgets rapidly. When we applied this two-state model to our data (Albert & Shadmehr, 2018), a new pattern emerged; passive training initially facilitated improvements in the slow state's sensitivity to error (Fig. 4E) which gradually transferred to the fast state of adaptation over time (Fig. 4G). Thus, while proprioceptive memory immediately enhanced motor learning, these improvements appeared to gradually consolidate from a slower system, into a faster system.

This putative conversion between learning systems mirrored other changes in behavior exhibited during the baseline period. Prior to the rotation, participants reached towards each target without any visual perturbation. These reaches were their very first attempts to produce active movements with the robotic system. Curiously, previously acquired proprioceptive memory appeared to alter the motor system during this baseline period, pulling the arm towards the path it travelled during the passive movement period. This biasing in reach angle, however, was not present in the 5 min group or 1 hr group, and only emerged with time (in the 24 hr group). Thus, the consolidation of passive training led to time-dependent changes in both error sensitivity and initial reaching behavior, which may or may not have shared a common source.

This biasing in initial reaching direction appeared qualitatively similar to use-dependent learning (Wang et al., 2015; Bao et al., 2017; Lei et al., 2017; Verstynen & Sabes, 2011; Lei et al., 2016; Diedrichsen et al., 2010; Jax & Rosenbaum, 2007; Scheidt et al., 2005; Diedrichsen, 2007); with use dependent learning, active (Verstynen & Sabes, 2011) as well as passive (Diedrichsen et al., 2010) motion induces persistent biases in active movement towards past motor actions or proprioceptive states. But there is one substantial difference in the reaching patterns we measured and those exhibited in these earlier studies. Namely, use-dependent biases in motor commands are immediately precipitated by past active or passive motion: they do not require time to emerge. However, here we observed that when active movement quickly (5 min break) followed passive training, no use-dependent biases in reach angle occurred. On the other hand, once considerable time had elapsed (24 hr), passive training biased initial reach angles during active movement. Why were use dependent changes absent in the 5 min and 1 hr experimental groups? One possibility is that because the passive movements were uniformly spread across the unit circle (4 movement directions, with 90° spacing between them), movements produced a type of motor or proprioceptive averaging, qualitatively similar to the uniformly distributed reach condition studied by Verstynen & Sabes (2011). Thus, our data propose two possible ways that passive movements may bias active reaching: one through traditional use-dependent mechanisms, and another that involves some process of consolidation which emerges with time.

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Might these changes in initial reaching bias be linked to the changes in error sensitivity we measured during the rotation period? Both passive movements (Carel et al., 2000) and active motor learning (Della-Maggiore & McIntosh, 2005; Herzfeld et al., 2015; Popa et al., 2012; Izawa et al., 2012; Tseng et al., 2007; Gibo et al., 2013; Maschke et al., 2004) are known to involve both the primary motor cortex (M1) and the cerebellum. Might it be that interactions between these two areas lead to changes in error sensitivity and reaching biases? While we can only speculate, one possibility might be that prediction errors experienced during passive training cause changes in Purkinje cells (P-cells) in the cerebellar cortex, which rapidly transfer to slower and more robust learning units in the deep cerebellar nucleus (Herzfeld et al., 2020; Lisberger et al., 1994; McCormick & Thompson, 1984; Perret et al., 1993). Thus, interplay between P-cells and the deep nuclei, might be responsible for facilitating the changes in slow state error sensitivity observed early (5 min) after passive training. Next, with passage of time, these changes may somehow be transferred through an unidentified mechanism to, and consolidated within, M1. Perhaps it is these delayed changes in M1 that subsequently bias motor commands during baseline reaching movements, and facilitate the faster learning state observed in the 24 hr group.

But if this is true, what are the errors that engage the cerebellar cortex during passive movement? While normally it is thought that errors arise with the sensory outcome that follows an active movement (Herzfeld et al., 2015; Herzfeld et al., 2018), associative learning mechanisms such as eye-blink condition, lead to sensory-evoked complex spikes within the cerebellar cortex without any active movement at all (Ohmae & Medina, 2015; Kim et al., 2020; Ito, 201; Sears & Steinmetz, 1991; Rasmussen et al, 2008). Thus, it is interesting to wonder whether the discrepancy between the visual (target) and proprioceptive (arm position) state created by our passive intervention, might too have somehow engaged the cerebellar cortex with a prediction error (Popa & Ebner, 2019; Shadmehr et al., 2010). If true, the repeated experience of consistent prediction errors may have upregulated error sensitivity in the cerebellar cortex (Herzfeld et al., 2014; Albert et al., 2020), thus facilitating learning in the active condition. Alternatively, lingering changes in the somatosensory and motor cortices induced by passive movements may have indirectly altered cerebellar state throughout adaptation (as opposed to passive errors driving the cerebellar cortex directly). In either case, rTMS and tDCS over the cerebellum and M1 may provide a path to elucidating the various timescales of memory that are engaged by passive training.

Lastly, there is another dichotomy in motor adaptation, which also may relate to the conversion between slow and fast learning: implicit and explicit adaptation. Motor learning is known to be supported by two parallel learning systems: a strategic explicit system that can be guided by instruction (Taylor et al., 2014; Mazzoni & Krakauer, 2006; McDougle & Taylor, 2019), as well as an implicit system that adapts

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

without our conscious awareness (Avraham et al., 2020; Miyamoto et al., 2020; Javidialsaadi and Wang., 2020). Might interplay between these two systems relate to the time-dependent error sensitivity patterns observed during rotation learning? Because we did not measure implicit or explicit learning, we cannot know the answer to this question. However, we did observe that reaction time (Fig. S1A) appeared elevated after passive training in the experimental groups, which is known to commonly accompany cognitive operations (Fernandez-Ruiz et al., 2011; Sakamoto and Kondo, 2012; Anguera et al., 2010; Georgopoulos and Massey, 1987; McDougle et al., 2019; Albert et al., 2020).

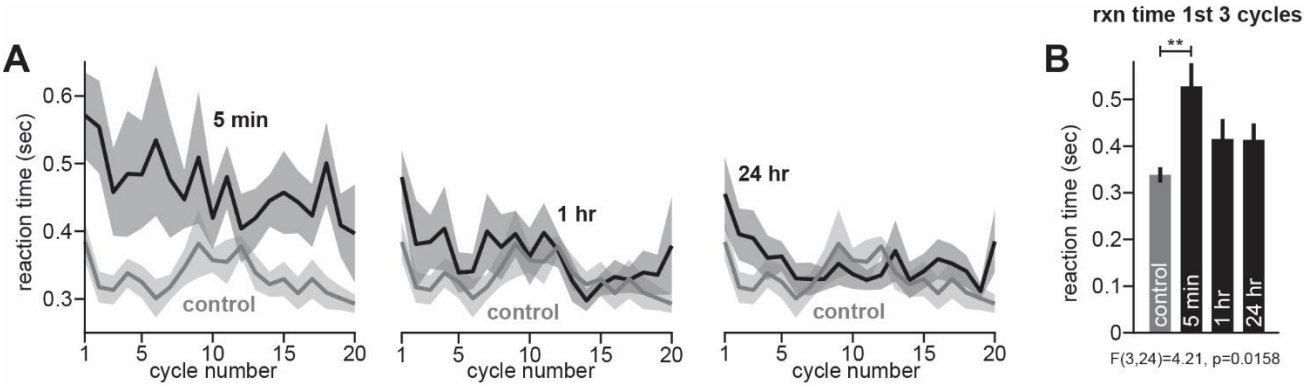

Figure S1. Changes in reaction time. **A.** We measured reaction time as the difference between target appearance and reach onset. Here we show reaction time during the perturbation period in the experimental (black) and control (gray) groups. **B.** We investigated early differences in reaction time by calculating the mean reaction time over the first three cycles. Statistics show post-hoc Tukey's test following one-way ANOVA (** indicates p<0.01). Error bars show mean ± SEM.

However, this trend was only statistically significant in the 5 min group (Fig. S1B) and appeared to dissipate quite rapidly in the 1 hr and 24 hr groups. If explicit strategies did contribute to increases in error sensitivity, it is also puzzling why reaction time was greatest in the 5 min group (Fig. S1B); this group was primarily enhanced by a slow learning state (Figs. 4D&E) which is believed to reflect implicit learning processes (McDougle et al., 2015). Nevertheless, the idea that passive training may evoke changes in both implicit and explicit processes is a fascinating possibility which remains to be formally tested.

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

References

Albert, S. T., & Shadmehr, R. (2018). Estimating properties of the fast and slow adaptive processes during sensorimotor adaptation. *Journal of neurophysiology*, *119*(4), 1367-1393.

Albert, Scott T., Jihoon Jang, Adrian M. Haith, Gonzalo Lerner, Valeria Della-Maggiore, John W. Krakauer, and Reza Shadmehr. "Competition between parallel sensorimotor learning systems." *bioRxiv* (2020).

Albert, S. T. (2020). *The role of error-based learning in movement and stillness* (Doctoral dissertation, Johns Hopkins University).

Aisen, M. L., Krebs, H. I., Hogan, N., McDowell, F., & Volpe, B. T. (1997). The effect of robot-assisted therapy and rehabilitative training on motor recovery following stroke. *Archives of neurology*, *54*(4), 443-446.

Anguera, J. A., Reuter-Lorenz, P. A., Willingham, D. T., & Seidler, R. D. (2010). Contributions of spatial working memory to visuomotor learning. *Journal of cognitive neuroscience*, *22*(9), 1917-1930.

Avraham, G., Morehead, J. R., Kim, H. E., & Ivry, R. B. (2021). Reexposure to a sensorimotor perturbation produces opposite effects on explicit and implicit learning processes. *PLoS biology*, *19*(3), e3001147.

Bao, S., Lei, Y., & Wang, J. (2017). Experiencing a reaching task passively with one arm while adapting to a visuomotor rotation with the other can lead to substantial transfer of motor learning across the arms. *Neuroscience letters*, *638*, 109-113.

Bara, F., & Gentaz, E. (2011). Haptics in teaching handwriting: The role of perceptual and visuo-motor skills. *Human movement science*, *30*(4), 745-759.

Basteris, A., Bracco, L., & Sanguineti, V. (2012). Robot-assisted intermanual transfer of handwriting skills. *Human movement science*, *31*(5), 1175-1190.

Beets, I. A., Macé, M., Meesen, R. L., Cuypers, K., Levin, O., & Swinnen, S. P. (2012). Active versus passive training of a complex bimanual task: is prescriptive proprioceptive information sufficient for inducing motor learning?. *PLoS One*, *7*(5), e37687.

Brashers-Krug, T., Shadmehr, R., & Bizzi, E. (1996). Consolidation in human motor memory. *Nature*, *382*(6588), 252-255.

Carel, C., Loubinoux, I., Boulanouar, K., Manelfe, C., Rascol, O., Celsis, P., & Chollet, F. (2000). Neural substrate for the effects of passive training on sensorimotor cortical representation: a study with functional magnetic resonance imaging in healthy subjects. *Journal of Cerebral Blood Flow & Metabolism*, *20*(3), 478-484.

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Castro, L. N. G., Hadjiosif, A. M., Hemphill, M. A., & Smith, M. A. (2014). Environmental consistency determines the rate of motor adaptation. *Current Biology*, *24*(10), 1050-1061.

Coltman, S. K., Cashaback, J. G., & Gribble, P. L. (2019). Both fast and slow learning processes contribute to savings following sensorimotor adaptation. *Journal of neurophysiology*, *121*(4), 1575-1583.

Coltman, S. K., & Gribble, P. L. (2020). Time course of changes in the long-latency feedback response parallels the fast process of short-term motor adaptation. *Journal of Neurophysiology*, *124*(2), 388-399.

Day, K. A., Leech, K. A., Roemmich, R. T., & Bastian, A. J. (2018). Accelerating locomotor savings in learning: compressing four training days to one. *Journal of neurophysiology*, *119*(6), 2100-2113.

Della-Maggiore, V., & McIntosh, A. R. (2005). Time course of changes in brain activity and functional connectivity associated with long-term adaptation to a rotational transformation. *Journal of neurophysiology*, *93*(4), 2254-2262.

Diedrichsen, J., Shadmehr, R., & Ivry, R. B. (2010). The coordination of movement: optimal feedback control and beyond. *Trends in cognitive sciences*, *14*(1), 31-39.

Diedrichsen, J., Criscimagna-Hemminger, S. E., & Shadmehr, R. (2007). Dissociating timing and coordination as functions of the cerebellum. *Journal of Neuroscience*, *27*(23), 6291-6301.

Fernandez-Ruiz, J., Wong, W., Armstrong, I. T., & Flanagan, J. R. (2011). Relation between reaction time and reach errors during visuomotor adaptation. *Behavioural brain research*, *219*(1), 8-14.

Georgopoulos, A. P., & Massey, J. T. (1987). Cognitive spatial-motor processes. *Experimental brain research*, *65*(2), 361-370.

Gibo, T. L., Criscimagna-Hemminger, S. E., Okamura, A. M., & Bastian, A. J. (2013). Cerebellar motor learning: are environment dynamics more important than error size?. *Journal of neurophysiology*, *110*(2), 322-333.

Haith AM, Huberdeau DM, Krakauer JW. The influence of movement preparation time on the expression of visuomotor learning and savings. J Neurosci 35: 5109–5117, 2015.

Herzfeld, D. J., Hall, N. J., Tringides, M., & Lisberger, S. G. (2020). Principles of operation of a cerebellar learning circuit. *Elife*, *9*, e55217.

Herzfeld, D. J., Kojima, Y., Soetedjo, R., & Shadmehr, R. (2018). Encoding of error and learning to correct that error by the Purkinje cells of the cerebellum. *Nature neuroscience*, *21*(5), 736-743.

Herzfeld DJ, Vaswani PA, Marko MK, Shadmehr R. A memory of errors in sensorimotor learning. Science 345: 1349–1353, 2014.

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Herzfeld, D. J., Kojima, Y., Soetedjo, R., & Shadmehr, R. (2015). Encoding of action by the Purkinje cells of the cerebellum. *Nature*, *526*(7573), 439-442.

Huberdeau, D. M., Haith, A. M., & Krakauer, J. W. (2015). Formation of a long-term memory for visuomotor adaptation following only a few trials of practice. *Journal of neurophysiology*, *114*(2), 969-977.

Huberdeau, D. M., Krakauer, J. W., & Haith, A. M. (2019). Practice induces a qualitative change in the memory representation for visuomotor learning. *Journal of neurophysiology*, *122*(3), 1050-1059.

Ito, K., Doi, M., Kondo, T.: Feedforward Adaptation to a Varying Dynamical Environment during Reaching Movements, Journal of Robotics Mechatronics, 19, 4, 474–481 (2007).

Izawa, J., Criscimagna-Hemminger, S. E., & Shadmehr, R. (2012). Cerebellar contributions to reach adaptation and learning sensory consequences of action. *Journal of Neuroscience*, *32*(12), 4230-4239.

Javidialsaadi, M., & Wang, J. (2021). Lack of interlimb transfer following visuomotor adaptation in a person with congenital mirror movements despite the awareness of the visuomotor perturbation. *Brain and Cognition*, *147*, 105653.

Jax, S. A., & Rosenbaum, D. A. (2007). Hand path priming in manual obstacle avoidance: evidence that the dorsal stream does not only control visually guided actions in real time. *Journal of Experimental Psychology: Human Perception and Performance*, *33*(2), 425.

Kahn, L. E., Zygman, M. L., Rymer, W. Z., & Reinkensmeyer, D. J. (2006). Robot-assisted reaching exercise promotes arm movement recovery in chronic hemiparetic stroke: a randomized controlled pilot study. *Journal of neuroengineering and rehabilitation*, *3*(1), 1-13.

Kim, H. E., Avraham, G., & Ivry, R. B. (2020). The psychology of reaching: action selection, movement implementation, and sensorimotor learning. *Annual review of psychology*, *72*.

Kitago T, Ryan SL, Mazzoni P, Krakauer JW, Haith AM. Unlearning versus savings in visuomotor adaptation: comparing effects of washout, passage of time, and removal of errors on motor memory. Front Hum Neurosci 7: 307, 2013.

Kojima Y, Iwamoto Y, Yoshida K. Memory of learning facilitates saccadic adaptation in the monkey. *J Neurosci* 24: 7531–7539, 2004.

Krebs, H. I., Hogan, N., Aisen, M. L., & Volpe, B. T. (1998). Robot-aided neurorehabilitation. *IEEE transactions on rehabilitation engineering*, *6*(1), 75-87.

Lei, Y., Bao, S., & Wang, J. (2016). The combined effects of action observation and passive proprioceptive training on adaptive motor learning. *Neuroscience*, *331*, 91-98.

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Lei, Y., Bao, S., Perez, M. A., & Wang, J. (2017). Enhancing generalization of visuomotor adaptation by inducing use-dependent learning. *Neuroscience*, *366*, 184-195.

Leow LA, de Rugy A, Marinovic W, Riek S, Carroll TJ. Savings for visuomotor adaptation require prior history of error, not prior repetition of successful actions. *J Neurophysiol* 116: 1603–1614, 2016.

Leow, L. A., De Rugy, A., Loftus, A. M., & Hammond, G. (2013). Different mechanisms contributing to savings and anterograde interference are impaired in Parkinson's disease. *Frontiers in human neuroscience*, *7*, 55.

Lerner, G., Albert, S., Caffaro, P. A., Villalta, J. I., Jacobacci, F., Shadmehr, R., & Della-Maggiore, V. (2020). The origins of anterograde interference in visuomotor adaptation. *Cerebral Cortex*, *30*(7), 4000-4010.

Lisberger, S. G. (1994). Neural basis for motor learning in the vestibuloocular reflex of primates. III. Computational and behavioral analysis of the sites of learning. *Journal of Neurophysiology*, *72*(2), 974-998.

Maschke, M., Gomez, C. M., Ebner, T. J., & Konczak, J. (2004). Hereditary cerebellar ataxia progressively impairs force adaptation during goal-directed arm movements. *Journal of neurophysiology*, *91*(1), 230-238.

Mawase, F., Shmuelof, L., Bar-Haim, S., & Karniel, A. (2014). Savings in locomotor adaptation explained by changes in learning parameters following initial adaptation. *Journal of neurophysiology*, *111*(7), 1444-1454.

Mazzoni, P., & Krakauer, J. W., (2006). An implicit plan overrides an explicit strategy during visuomotor adaptation. Journal of neuroscience, 26(14), 3642-3645.

McCormick, D. A., & Thompson, R. F. (1984). Neuronal responses of the rabbit cerebellum during acquisition and performance of a classically conditioned nictitating membrane-eyelid response. *Journal of Neuroscience*, *4*(11), 2811-2822.

McDougle, S. D., Bond, K. M., & Taylor, J. A., (2015). Explicit and implicit processes constitute the fast and slow processes of sensorimotor learning. Journal of Neuroscience, 35(26), 9568-9579.

McDougle, S. D., & Taylor, J. A. (2019). Dissociable cognitive strategies for sensorimotor learning. *Nature communications*, *10*(1), 1-13.

Miyamoto, Y. R., Wang, S., & Smith, M. A. (2020). Implicit adaptation compensates for erratic explicit strategy in human motor learning. *Nature neuroscience*, *23*(3), 443-455.

Morehead, J. Ryan, Salman E. Qasim, Matthew J. Crossley, and Richard Ivry. "Savings upon re-aiming in visuomotor adaptation." *Journal of neuroscience* 35, no. 42 (2015): 14386-14396.

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Ohmae, S., & Medina, J. F. (2015). Climbing fibers encode a temporal-difference prediction error during cerebellar learning in mice. *Nature neuroscience*, *18*(12), 1798-1803.

Orozco, S. P., Albert, S. T., & Shadmehr, R. (2020). Spontaneous recovery and the multiple timescales of human motor memory. *bioRxiv*.

Perrett, S. P., Ruiz, B. P., & Mauk, M. D. (1993). Cerebellar cortex lesions disrupt learning-dependent timing of conditioned eyelid responses. *Journal of Neuroscience*, *13*(4), 1708-1718.

Popa, L. S., & Ebner, T. J. (2019). Cerebellum, predictions and errors. *Frontiers in cellular neuroscience*, *12*, 524.

Popa, L. S., Hewitt, A. L., & Ebner, T. J. (2012). Predictive and feedback performance errors are signaled in the simple spike discharge of individual Purkinje cells. *Journal of Neuroscience*, *32*(44), 15345-15358.

Reinkensmeyer, D. J., & Patton, J. L. (2009). Can robots help the learning of skilled actions?. *Exercise and sport sciences reviews*, *37*(1), 43.

Riener, R., Nef, T., & Colombo, G. (2005). Robot-aided neurorehabilitation of the upper extremities. *Medical and biological engineering and computing*, *43*(1), 2-10.

Rasmussen, A., Jirenhed, D. A., & Hesslow, G. (2008). Simple and complex spike firing patterns in Purkinje cells during classical conditioning. *The Cerebellum*, *7*(4), 563.

Sakamoto, T., & Kondo, T. (2012, November). Can passive arm movement affect adaptation to visuomotor rotation?. In *2012 IEEE International Conference on Development and Learning and Epigenetic Robotics (ICDL)* (pp. 1-6). IEEE.

Shadmehr, R., Smith, M. A., & Krakauer, J. W. (2010). Error correction, sensory prediction, and adaptation in motor control. *Annual review of neuroscience*, *33*, 89-108.

Scheidt, R. A., Conditt, M. A., Secco, E. L., & Mussa-Ivaldi, F. A. (2005). Interaction of visual and proprioceptive feedback during adaptation of human reaching movements. *Journal of neurophysiology*, *93*(6), 3200-3213.

Sing, G. C., & Smith, M. A. (2010). Reduction in learning rates associated with anterograde interference results from interactions between different timescales in motor adaptation. *PLoS Comput Biol*, *6*(8), e1000893.

Smith MA, Ghazizadeh A, Shadmehr R. Interacting adaptive processes with different timescales underlie short-term motor learning. *PLoS Biol* 4: e179, 2006.

bioRxiv preprint doi: https://doi.org/10.1101/2021.03.09.434594; this version posted March 17, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Steinmetz, J. E., Sears, L. L., Gabriel, M., Kubota, Y., & Poremba, A. (1991). Cerebellar interpositus nucleus lesions disrupt classical nictitating membrane conditioning but not discriminative avoidance learning in rabbits. *Behavioural brain research*, *45*(1), 71-80.

Taylor, J. A., Krakauer, J. W., & Ivry, R. B., (2014). Explicit and implicit contributions to learning in a sensorimotor adaptation task. Journal of Neuroscience, 34(8), 3023-3032.

Tays, G., Bao, S., Javidialsaadi, M., & Wang, J. (2020). Consolidation of use-dependent motor memories induced by passive movement training. *Neuroscience Letters*, *732*, 135080.

Tong, C., & Flanagan, J. R. (2003). Task-specific internal models for kinematic transformations. *Journal of Neurophysiology*, *90*(2), 578-585.

Tseng, Y. W., Diedrichsen, J., Krakauer, J. W., Shadmehr, R., & Bastian, A. J. (2007). Sensory prediction errors drive cerebellum-dependent adaptation of reaching. *Journal of neurophysiology*, *98*(1), 54-62.

Vergaro, E., Casadio, M., Squeri, V., Giannoni, P., Morasso, P., & Sanguineti, V. (2010). Self-adaptive robot training of stroke survivors for continuous tracking movements. *Journal of neuroengineering and rehabilitation*, *7*(1), 1-12.

Verstynen, T., & Sabes, P. N. (2011). How each movement changes the next: an experimental and theoretical study of fast adaptive priors in reaching. *Journal of Neuroscience*, *31*(27), 10050-10059.

Wang, J., & Lei, Y. (2015). Direct-effects and after-effects of visuomotor adaptation with one arm on subsequent performance with the other arm. *Journal of neurophysiology*, *114*(1), 468-473.

Wigmore, V., Tong, C., & Flanagan, J. R. (2002). Visuomotor rotations of varying size and direction compete for a single internal model in a motor working memory. *Journal of Experimental Psychology: Human Perception and Performance*, *28*(2), 447.

Yin, C., & Wei, K. (2020). Savings in sensorimotor adaptation without an explicit strategy. *Journal of neurophysiology*, *123*(3), 1180-1192.

Zarahn, E., Weston, G. D., Liang, J., Mazzoni, P., & Krakauer, J. W. (2008). Explaining savings for visuomotor adaptation: linear time-invariant state-space models are not sufficient. *Journal of neurophysiology*, *100*(5), 2537-2548.