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Long-term retention and reconsolidation of a visuomotor memory

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Abstract:

Visuomotor adaptation is a form of motor learning that enables accurate limb movements in the presence of altered environmental or internal conditions. It requires updating the mapping between visual input and motor output, and can occur when learning a new device/tool or during rehabilitation after neurological injury. In either case, it is desirable to stabilize, or consolidate, this visuomotor memory for long-term usage. However, reactivation of a consolidated memory, whether it is motor-based or not, is thought to render it temporarily fragile again, and thus susceptible to interference or modification. Here, we determined if visuomotor memories demonstrate long-term retention but are fragile once reactivated. We used prism lenses to create a novel visuomotor mapping, which participants learned while having to walk and step to the center of targets. We re-tested this memory after one week and one year. We found that the mapping is retained for at least one year, regardless of whether participants were exposed to an interfering (i.e., opposing) mapping in the first session. We also found that presenting an opposing mapping in a block of trials following reactivation of the memory one year later did not disrupt subsequent performance when we re-tested the original memory. Our results suggest that these visuomotor memories are stored for extended periods of time and have limited fragility. Taken together, our results highlight the robustness of visuomotor memories associated with walking.

Keywords = motor learning; motor memory; locomotion; reconsolidation

Introduction:

Once a novel motor skill is acquired, people can often retain performance for extended periods of time despite varying frequencies of practice. The memory of some motor skills, for instance, riding a bicycle, throwing a ball, or manipulating a fork to eat, may also last a lifetime. Research on such long-term motor memory is scarce, though several studies describe robust retention across a select few skills after months and even up to 8 years following initial learning (Draganski, Gaser, Busch, Schuierer, Bogdahn, & May, 2004; Hill, 1934, 1957; Park, Dijkstra, & Stenard, 2013; Swift, 1910). However, skill acquisition is only one form of motor learning (Kitago & Krakauer, 2013). In sensorimotor adaptation, the nervous system must learn to move in response to altered body or environmental conditions. This may occur following neurological injury or when first discovering how to use a new interactive electronic device.

Most research in this area uses a force field, visuomotor rotation, or prism goggle paradigm to disrupt the normal mapping between a perceived target location and the necessary motor command to move the limb to it. Studies in both reaching (Bock, Schneider, & Bloomberg, 2001; Brashers-Krug, Shadmehr, & Bizzi, 1996; Huberdeau, Haith, Mazzoni, & Krakauer, 2015; Klassen, Tong, & Flanagan, 2005; Krakauer, Ghez, & Ghilardi, 2005) and walking (Fortin, Blanchette, McFadyen, & Bouyer, 2009; Hussain, Hanson, Tseng, & Morton, 2013; Maeda, McGee, & Marigold, 2017; Malone, Vasudevan, & Bastian, 2011; McGowan, Gunn, Vorobeychik, & Marigold, 2017) demonstrate short-term retention of the new mapping in the neighborhood of days or weeks, often in the form of faster relearning, or savings. Three studies with the upper extremity, however, suggest that these short-term motor memories are retained for extended periods of time, that is, between five months and one year (Shadmehr & Brashers-Krug, 1997; Landi, Baguear, & Della-Maggiore, 2011; Yamamoto, Hoffman, & Strick,

2006). In two previous studies, we showed that the motor memory acquired after learning a novel visuomotor mapping in a precision walking paradigm is retained for at least one week (Maeda et al., 2017; McGowan et al., 2017). Here, we first asked whether this motor memory also shows long-term (i.e., one year) retention.

When a novel task is first learned, the motor memory of it is considered fragile (Brashers-Krug et al., 1996; Censor, Sagi, & Cohen, 2012). Time is required for neurons to produce new proteins, and for changes in overall synaptic efficacy (Dudai, 2004; Nader & Hardt, 2009). During this time, the motor memory is subject to interference. For instance, after learning a novel mapping, immediate exposure to an opposing mapping can interfere with recall of this initial mapping, reflected by a reduction in savings; this is referred to as retrograde interference (Krakauer et al., 2005; Maeda et al., 2017). If sufficient time separates initial learning and learning of the opposite mapping, then this interference is reduced or eliminated (Brashers-Krug et al., 1996; Walker, Brakefield, Hobson, & Strickgold, 2003). In this case, the motor memory is thought to have progressed from a fragile short-term memory into a stable long-term memory, a process known as consolidation. Several studies have shown that the motor memory related to novel force fields or visuomotor rotations consolidates (e.g., Brashers-Krug et al., 1996; Krakauer et al., 2005), though others have cast doubt (Caithness, Osu, Bays, Chase, Klassen, Kawato, Wolpert, & Flanagan, 2004). Interestingly, we recently found minimal interference of an opposing mapping on relearning in a walking paradigm that required individuals to adapt to a novel mapping caused by prism lenses (Maeda et al., 2017). Whether this opposing mapping affects the long-term retention of the initially learned mapping is unclear.

Similar to abundant research in animals (Lee, 2009; Nader, Schafe, & Le Doux, 2000; Nader & Hardt, 2009), recent human work demonstrates that re-exposure to a motor memory can

render it fragile again and in need of re-stabilization through a reconsolidation process (de Beukelaar, Woolley, & Wenderoth, 2014; de Beukelaar, Woolley, Alaerts, Swinnen, & Wenderoth, 2016; Censor, Dimyan, & Cohen, 2010; Walker et al., 2003). The typical paradigm to study this phenomenon is to have participants learn a new motor task on one day; reactivate the memory on a second day, followed by some interference procedure; and then re-test the original memory (reflected by motor performance) on the next day. To-date, the motor tasks studied are limited to finger-based movements.

Consolidation and reconsolidation assume that memories are fragile and that an interference procedure can disrupt subsequent performance. However, not all research supports this notion. For instance, Hardwicke, Taqi, & Shanks (2016) were unable to show interference of a reactivated motor sequence memory—in contrast to previous work using a similar paradigm (Walker et al., 2003). Furthermore, interference can be prevented by longer reactivation blocks of trials (de Beukelaar et al., 2014), anticipated monetary reward associated with a learned motor sequence (Fischer & Born, 2009), overlearning (Shibata, et al., 2017), and with probabilistic sequence learning (Kóbor, Janacsek, Takács, & Nemeth, 2017). Disrupting certain brain areas (the motor cortex, for example) via transcranial magnetic stimulation can also prevent interference (Cohen & Robertson, 2011).

In the present study, we also asked whether a motor memory becomes fragile again even long after initial consolidation. Participants learned a novel visuomotor mapping created using prism lenses while they had to walk and step accurately on targets. We tested participants with a typical motor learning protocol and then reactivated the memory of the mapping one-year later to determine its fragility.

Materials and Methods:

Participants

This study included a total of seventeen healthy participants (7 male, 10 female, aged 21.7 ± 3.1 years; 14 right leg dominant as defined by the leg used to kick a soccer ball). These participants were part of a larger previous study (Maeda et al., 2017). Participants reported no history of visual, neurological, and/or musculoskeletal diseases but wore corrective lenses (glasses or contacts) when required (n = 11). The Office of Research Ethics at Simon Fraser University approved all experimental procedures, and participants provided written consent prior to the experiments.

Experimental task and procedures

To study visuomotor learning, we used a precision walking paradigm (Alexander, Flodin, & Marigold, 2011, 2013; Maeda et al., 2017; McGowan et al., 2017) whereby subjects had to walk, and without stopping, step with the right and left foot onto the center of two sequential targets (15 x 30 cm) (Fig. 1A). We placed the second target at a 30° counter-clockwise angle with respect to the plane of progression and at a distance equivalent to 90% of the height of the greater trochanter from the floor for each participant. During the task, subjects wore goggles that contained either flat lenses (normal vision) or 20-diopter wedge prism lenses that shifted the visual perception of a target to the left or right with respect to its actual location (see Fig. 1A, inset). The goggles were designed such that participants could only see through the lenses and not around them like regular prescription spectacles or sunglasses.

To begin a trial, participants waited for a verbal command to open their eyes and then immediately started walking. We instructed participants to walk at a quick and constant pace and

to step in the medial-lateral center of the targets. We also instructed participants to look at their foot when contacting the targets, and to not stop walking until taking at least one step after the second target. Participants walked with an average speed of 1.8 ± 0.2 m/s, and we confirmed on a trial-by-trial basis that the kinematic traces (position and velocity profiles) were smooth and absent of sudden changes. This indicated a lack of online corrections of limb trajectory to step onto the targets. After each trial, participants closed their eyes and an experimenter guided them back to the starting position. This prevented adaptation between trials. Participants started each trial at a random anterior-posterior location between 1.8- to 3-m from the first target to prevent them from learning a specific stepping sequence. In the first trial of each protocol (first adaptation trial), however, we always positioned participants at a fixed distance of 1.8 m, as described below. We provided participants with approximately five familiarization trials without prism lenses before the start of the first experimental session.

We used an Optotrak Certus motion capture camera (Northern Digital Inc., Waterloo, Ontario) to record, at a sampling frequency of 100 Hz, infrared-emitting diodes attached to the chest and bilaterally on each mid-foot over the lateral cuneiforms. We also used a Panasonic high-definition camcorder (model HDC-SD60) to record videos of each walking trial.

Protocols

Graphical representations of the protocols are shown in Fig. 1B. For each group, we randomly assigned each participant to either right or leftward mapping A prism shifts. Mapping B was always in the opposite direction. We tested the same participants in two different years. The average time interval between the sessions of year 1 and sessions of year 2 was 443.4 ± 53.3 days. Although this represents close to 15 months, there is no *a priori* reason to think a motor

memory improves or degrades between 12 and 15 months after initial learning and no subsequent practice. Therefore, we refer to this time gap as one year throughout for simplicity.

Eight participants experienced 30 baseline trials (with flat, 0 diopter lenses), 60 adaptation-phase trials (mapping A_1: 20 diopters or 11.4°), and 1 post-adaptation trial (with flat, 0 diopter lenses) in the first testing session, and then repeated the same 60 adaptation trials (mapping A_2) and 1 post-adaptation trial, 1 week later. This allowed us to assess short-term retention (A_1 versus A_2). Half of these participants (n = 4; A_1A_2-A_3BA_4 group; Fig. 1B, top) returned one year later and experienced 30 baseline trials (with flat, 0 diopter lenses), 60 adaptation-phase trials (mapping A_3), and 1 post-adaptation trial (with flat, 0 diopter lenses). Another 60 adaptation trials (mapping B: 20 diopter prism lenses of the opposite perturbation direction) and 1 post-adaptation trial followed. This group then returned one week later and experienced 60 adaptation trials of the original mapping again (A_4) and 1 post-adaptation trial. Thus, with this group, we assessed long-term retention (comparing A_2 and A_3) as well as whether reactivation of the mapping renders it fragile again and in need of reconsolidation (comparing A_3 and A_4). The other half of these participants (n = 4; A_1A_2-BA_3 group; Fig. 1B, middle) returned one year later and experienced 30 baseline trials, 60 adaptation phase trials with an opposite mapping (mapping B), and 1 post-adaptation trial. A week later, they experienced 60 adaptation trials of the original mapping (A_3) and 1 post-adaptation trial. With this group, we determined if the memory of mapping A is robust against interfering mappings after one year, provided that this original mapping is not reactivated first, or if contextual priming can destabilize and interfere with the memory. This latter argument is based, in part, on previous work (Caithness et al., 2004) that suggested the contextual cue of being exposed to a new visuomotor mapping (i.e., mapping B)

during the same task and in the same environment could destabilize and subsequently interfere with recall of mapping A.

Another group of participants (n = 9; $A_1B_1A_2$-$A_3B_2A_4$ group; Fig. 1B, bottom) first performed 30 baseline trials (with flat, 0 diopter lenses), 60 adaptation-phase trials (mapping A_1), and 1 post-adaptation trial (with flat, 0 diopter lenses). Immediately after these phases, participants performed 60 adaptation trials with the opposite mapping (mapping B_1: 20 diopter prism lenses of the opposite perturbation direction) and 1 post-adaptation trial. One week later, they experienced 60 adaptation trials of mapping A (A_2) and 1 post-adaptation trial. Participants repeated the same protocol one year later. Therefore, with this group, we determined (1) if exposure to an interfering mapping during initial learning affects long-term retention, and (2) if reactivation of the mapping renders it fragile again and in need of reconsolidation (similar to the A_1A_2-A_3BA_4 group).

Data and statistical analysis

We used MATLAB (The Mathworks, Natick, MA) to analyze our data. We filtered the kinematic data with a fourth-order low-pass Butterworth filter (cut-off frequency of 6 Hz). Next, we determined on a trial-by-trial basis the moment of foot contact on the ground with respect to the targets, defined as the time point at which the foot marker's anterior-posterior velocity and acceleration profiles stabilized to zero. The medial-lateral distance (or error) between the position marker on the foot when it was in contact with the ground and the center of the target served to quantify performance. We flipped the sign of the errors during leftward prism shifts to positive for our analyses. Thus, positive values represent errors in the direction of the prism shift, regardless of whether it was a rightward or leftward shift.

We quantified two measures: foot-placement error for the first adaptation trial and the mean foot-placement error across trials 2 to 8 in the adaptation phase (i.e., early adaptation error; see Fig. 1C). The first adaptation trial error can provide an indication of how much of the mapping is recalled. This assumes, however, that the participant is aware that they are being exposed to the identical mapping, which is not the case in our study. This measure is also more susceptible to carry-over effects (i.e., anterograde interference) from the previous novel mapping. In addition, the brain likely requires experience with the mapping (i.e., the first adaptation trial) as a contextual cue to remember and set the proper mapping for the task. For these reasons, we separate out this trial's error, like many others (e.g., Krakauer et al., 2005; Krakauer, 2009; Maeda et al., 2017; Malone et al., 2011). The early adaptation error measure quantifies the large rapid reduction in error early in the adaptation phase and serves as our primary measure of retention and consolidation (Maeda et al., 2017). Nonetheless, the first adaptation trial error measure does provide an indication as to how participants treat the initial exposure to the altered mapping.

We used paired t-tests to compare specific mapping conditions within the different groups and to address several questions. We analyzed each target separately, but we focus our analyses only on the results of the step to target 1 in this report. We used JMP 13 software (SAS, Cary, NC) for all statistical analyses and an alpha level of 0.01 as a conservative approach due to the number of statistical tests.

Results:

Short-term (one-week) retention of a novel visuomotor mapping

Participants learned a novel visuomotor mapping while having to accurately step on the center of two consecutive targets with the right and left foot as they walked. We subsequently re-tested them with the same mapping one week and one year later. Participants showed large foot placement errors in the direction of the visual shift upon initial adaptation, but they quickly learned to reduce the errors to baseline levels over several walking trials (for example: Fig. 2). In addition, participants showed large negative aftereffects (i.e., missed the targets in the opposite direction) when probed with a single post adaptation trial without the prism shift.

We first asked whether participants could retain this novel visuomotor mapping over a 1-week period. To confirm short-term (i.e., one-week) retention, we compared performance on A_1 with performance on A_2 (A_1A_2-A_3BA_4 and A_1A_2-BA_3 groups combined). Note that these groups performed identical protocols in the first year and, in fact, formed one group in our original study (Maeda et al., 2017). As previously reported (Maeda et al., 2017), we found a reduction in first adaptation trial foot-placement error related to target 1 (paired t test: $t_7 = -6.9$, $p = 0.0002$) and a reduction in the mean foot-placement error early in adaptation (paired t test: $t_7 = -5.1$, $p = 0.001$) between A_1 and A_2 (Fig. 2). This replication included 8 of the 10 original study's participants.

Long-term (one-year) retention of a novel visuomotor mapping

To determine long-term (i.e., one-year) retention, we compared the performance on A_2 with that of A_3 for the A_1A_2-A_3BA_4 group. We found that the reduction in first adaptation trial foot-placement error (paired t test: $t_3 = 1.6$, $p = 0.204$) and in the mean foot-placement error early in adaptation (paired t test: $t_3 = 1.3$, $p = 0.277$) after one week also persisted after a one-year

period (A_2-A_3) (Fig. 3A). These results indicate that participants can retain novel visuomotor mappings in a precision walking task for at least one year.

To determine the robustness of the motor memory, a group of participants experienced an opposing mapping after one year and then the original mapping one-week later (A_1A_2-BA_3 group). Since the original learned mapping is not reactivated, one prediction is that the memory is still retained. An alternative prediction is that the contextual cue of being exposed to a new visuomotor mapping (i.e., mapping B) is sufficient to destabilize and interfere with recall of the originally learned mapping. We compared the performance between blocks A_2 and A_3 and found no statistical difference in the first adaptation trial foot-placement error (paired t test: $t_3 = 3.0$, $p = 0.056$) and in the mean foot-placement error early in adaptation (paired t test: $t_3 = 3.1$, $p = 0.054$) despite noticeable increases in error during A_3 for both measures (Fig. 3B). Nonetheless, these trends suggest that there is some degree of interference. However, we found a significant reduction in the early adaptation error of A_3 compared to A_1 (paired t test: $t_3 = -8.1$, $p = 0.004$), showing that performance is still better than during initial learning.

We next tested if the learning of an opposite mapping during the precision walking task in the first year causes retrograde interference, and whether any short-term interference affects the formation of long-term motor memories. To test for short-term interference, we compared the performance in blocks A_1 and A_2 from the $A_1B_1A_2$-$A_3B_2A_4$ group (Fig. 4A,B). Although foot-placement error in the first adaptation trial persisted (paired t test: $t_8 = -1.2$, $p = 0.277$), we found reduced mean foot-placement error early in adaptation in A_2 (paired t test: $t_8 = -3.6$, $p = 0.007$) (Fig. 4B). Interestingly, early adaptation foot-placement error was further reduced in A_3 compared to A_2 (paired t test: $t_8 = -10.3$, $p < 0.0001$) despite no intervening practice over the

course of the year (Fig. 4C). We also found a reduction in first adaptation trial foot-placement error in A_3 compared to A_2 (paired t test: $t_8 = -4.7$, $p = 0.002$).

We also compared the performance in blocks B_1 and B_2 to test if the additional opposite mapping is also retained over a one-year period. As illustrated in Fig. 4D, the first adaptation trial foot-placement error persisted (paired t test: $t_8 = 1.5$, $p = 0.179$). However, the decrease in mean foot-placement error early in adaptation (paired t test: $t_8 = 10.9$, $p < 0.0001$) shows participants retained mapping B. Taken together, these results show that motor memories are robust over the course of one year and there is little evidence of short-term interference affecting this long-term retention.

Are motor memories fragile after one year?

We next asked whether mapping-based motor memories learned during visually guided walking are fragile and undergo reconsolidation. To address this question, after one year, we subjected participants to an opposite mapping (mapping B) immediately after reactivating mapping A. One week later, we tested mapping A again. If the motor memory is fragile, then foot-placement error should be larger in A_4 relative to A_3 because of interference. As shown in Fig. 5A, for the A_1A_2-A_3BA_4 group, there is no difference in the first adaptation trial (paired t test: $t_3 = -1.3$, $p = 0.272$) or the mean foot-placement error early in adaptation (paired t test: $t_3 = -0.5$, $p = 0.680$). For the $A_1B_1A_2$-$A_3B_2A_4$ group, foot-placement error in the first adaptation trial is actually reduced, though this reduction is not significant at our conservative alpha level of 0.01 (Fig. 5B; paired t test: $t_8 = -2.7$, $p = 0.029$). We also found no difference in early adaptation error between A_3 and A_4 for this group (paired t test: $t_8 = 0.7$, $p = 0.512$). In both groups, early

adaptation error is close to zero in A_4. These results suggest that when motor memories are reactivated one year later, they are stable and resistant to interference.

Discussion:

Here we investigated whether motor memories formed during a visually guided walking task show long-term retention but are fragile once reactivated. First, we found that a novel visuomotor mapping is retained for at least one year. This occurred regardless of whether we presented an opposing mapping in the first testing session. In fact, we found continued improvement in performance, reflected by faster relearning one year later. Interestingly, the opposing mapping is also learned and retained over this time period. Second, we found that the motor memory is relatively stable—that is, it is resistant to interference—following reactivation one year later. Taken together, our results highlight the robustness of sensorimotor mapping-based memories.

Long-term retention of a novel visuomotor mapping

Here we show that the motor memory associated with a novel visuomotor mapping experienced while walking is retained for at least one year. These results add to the growing upper extremity literature indicating that motor memories related to novel sensorimotor mappings are retained for extended periods of time (Shadmehr & Brashers-Krug, 1997; Landi et al., 2011; Yamamoto et al., 2006). Repetition may have contributed to the long-term retention of this motor memory in our study. Consistent with our previous work (Alexander et al., 2011, 2013; McGowan et al., 2017), participants reduced foot-placement error rapidly over the course

of relatively few walking trials. This provided them with a prolonged period of trials with which they were continually exposed to the same novel mapping but could produce the correct motor command to guide the foot to the target with minimal error. This was further reinforced in the A_2 block of trials. Based on the work of Huang, Haith, Mazzoni, & Krakauer (2011), there are two aspects of repetition that could explain our findings of faster relearning: (1) repetition of the newly acquired mapping to direct the foot to the target; and (2) an operant reinforcement process caused by repetition with successful foot placement. Although these authors argue that faster relearning due to this repetition occurs without the need for an internal model, it is still possible that prolonged exposure to the novel mapping simply serves to reinforce one. Since we did not design our experiment to tease out the precise mechanism for long-term retention, further research is warranted. Regardless, repeated exposure to the novel mapping following the initial rapid error reduction may engage the motor cortex to a greater extent (Orban de Xivry, Criscimagna-Hemminger, & Shadmehr, 2011). Structural changes in this region correlate with long-term retention of visuomotor memories (Landi et al., 2011).

The presentation of an interference block of trials immediately following initial learning did not prevent long-term retention. This is clearly evident in Fig. 4A,C. It is important to acknowledge that we did not observe interference in the A_2 block one-week after initial learning. The lack of interference from the introduction of an opposing perturbation is similar to other walking studies (Malone et al., 2011) but in contrast to many reaching studies (Caithness et al., 2004; Krakauer et al., 2005). Interestingly, we found that participants retained not only the original mapping but also the opposing mapping. This is reflected in the faster relearning of mapping B one-year later. Similarly, previous work has demonstrated the ability to learn multiple mappings, a so-called dual adaptation (McGonigle & Flook, 1978; van Dam, Hawellek,

& Ernst, 2013; Welch, Bridgeman, Anand, & Browman, 1993). Unlike our study, however, this required multiple, alternating practice with both mappings. It is important to note that the error in the first adaptation trial did not differ between B_1 and B_2; we only observed reduced early adaptation error (Fig. 4D). This suggests that the brain may require some initial context (i.e., experience with the induced error due to mapping B) before it can engage the correct mapping. This also applies to the first adaptation trial error for mapping A in all groups, and as discussed in the methods, is why we argue that the early adaptation error measure is the best reflection of memory retention in this paradigm. Nonetheless, our results indicate that motor memories formed during visually guided walking are robust and long lasting.

There is increasing evidence suggesting that many distinct neural structures are involved in the retention of a new sensorimotor mapping. Shadmehr & Holcomb (1997) first showed with neuroimaging that neural activity shifts from the prefrontal cortex to premotor cortex, posterior parietal cortex, and cerebellum within six hours of adapting to a novel force field. Furthermore, Della-Maggiore, Villalta, Kovacevic, & McIntosh (2017) recently reported an incremental change in functional connectivity of a network involving the motor cortex, premotor cortex, posterior parietal cortex, cerebellum, and putamen over the course of six hours after learning a novel visuomotor rotation. Interestingly, this change in functional connectivity correlated positively with 24-hr retention but not with short-term (immediate) retention. Additional studies also support a role of the cerebellum in the 12- to 24-hr retention of visuomotor and force-field-based memories (Debas, Carrier, Orban, Barakat, Lungu, Vanderwalle, et al., 2010; Herzfeld, Pastor, Haith, Rossetti, Shadmehr, & O'Shea, 2014).

The primary motor cortex has also been proposed to play an important role in the retention of motor memories. Recently, Ramanathan, Gulati, & Ganguly (2015) recorded from an array of

motor cortex neurons in an experiment in which rats learned to reach-to-grasp a pellet with their forelimb. They found that reactivation of task-related patterns of synchronized neural activity during non-rapid eye movement sleep—the same neural ensembles as activated during learning—correlated with improvements in motor performance. At the synaptic level in the mouse, repetitive activation of the motor cortex due to motor skill learning leads to an increase in new, clustered dendritic spines and elimination of pre-existing spines, thus resulting in a rapid re-wiring of cortical circuits (Fu, Yu, Lu, & Zuo, 2012; Xu, Yu, Perlik, Tobin, Zweig, Tennant, et al., 2009; Yang, Pan, & Gan, 2009). The maintenance of these new dendritic spines is associated with long-term motor memories (Yang et al., 2009; Xu et al., 2009). Whether these synaptic changes occur in relation to sensorimotor adaptation is unclear, but motor cortex excitability is known to change throughout prism adaptation in humans (Bracco, Mangano, Turriziani, Smirni, & Oliveri, 2017). Furthermore, Landi et al. (2011) showed that adapting to visuomotor perturbations resulted in structural changes in the motor cortex that predicted faster relearning one-year later. Given the increase in activity of neurons in the motor cortex, posterior parietal cortex, and cerebellum when having to precisely guide foot placement (Beloozerova & Sirota, 1993, 2003; Drew & Marigold, 2015; Marple-Horvat & Criado, 1999), it is likely that these same regions are involved in the adaptation and retention observed in our study.

Reconsolidation of a visuomotor mapping after one year

Reconsolidation is the process of re-stabilizing a memory after reactivation of it has made it fragile again (Alberini, 2011; de Beukelaar et al., 2014, 2016; Lee, 2009; Nader et al., 2000). The role of memory reconsolidation is still under debate, though two theories are relevant to our discussion. The destabilization theory suggests that to modify or strengthen a memory, that

memory must first be rendered labile through destabilization and then subsequently re-stabilized (de Beukelaar et al., 2014, 2016; Lee, 2009). In contrast, the updating theory suggests that modification can occur after reactivation of a memory within a certain time window but that destabilization is not required (de Beukelaar et al., 2014, 2016; Lee, 2009). An important distinction between these two theories is that the former predicts memory loss (or impaired motor performance) if some form of interference is administered following memory reactivation, whereas the latter does not. In the present study, we found that reactivation of the motor memory, followed by an interference block of trials in the form of an opposing visuomotor mapping, did not disrupt performance when we re-tested the originally memory. In fact, there is evidence to suggest that motor performance improved after reactivation. These results seem to favour the predictions of the updating theory, and are more similar to the results of Hardwicke et al. (2016) for motor sequence learning.

It is interesting that, although it did not reach statistical significance, we found a trend for greater foot-placement error in block A_3 compared to A_2 in the A_1A_2-BA_3 group when mapping A was not reactivated before introducing mapping B. Thus, there is some degree of interference present with no prior reactivation after one year. This is in contrast to when memory A was reactivated first (Fig. 5). The results of the A_1A_2-BA_3 group, which should be interpreted with caution due to the small sample size, may have resulted from the effects of contextual priming (Caithness et al., 2004). According to this argument, the contextual cue of performing mapping B in the same task and in the same environment can destabilize and then interfere with retrieval of mapping A through anterograde mechanisms, because the brain may not distinguish between the opposing mappings. These results suggest a possible distinction between the effects of retrograde

and anterograde interference on reconsolidation that warrants further study; anterograde interference may persist (to some extent) but retrograde interference does not in this paradigm.

Why do we observe a lack of interference following reactivation in our study? The answer may relate to so-called boundary conditions (Lee, 2009), which constrain the extent that experimental manipulations can interfere with a memory. Here we provide several factors that may have contributed to our results. First, the age of the memory matters. We reactivated the visuomotor mapping memory after one year; this is a not a typical duration. Older memories appear more stable in that they are less susceptible to interference when reactivated (Alberini, 2011; Milekic & Alberini, 2002). In rats trained on an inhibitory avoidance task, for instance, administration of the protein synthesis inhibitor, anisomycin, after reactivation led to decreased retention of 2- and 7-day-old memories but not 14- and 28-day-old memories (Milekic & Alberini, 2002). Second, we exposed our participants to the mapping twice in the first year. In rats, repetition of the contextual fear memory can strengthen it through a reconsolidation process (Lee, 2008). In humans, Wymbs, Bastian, & Celnik (2016) found that after reactivating memory, if they gave the same task but with greater variability, it strengthened the memory (reflected in better performance) on next day testing. Third, the length of the reactivation block of trials can have a profound effect. Specifically, longer periods of reactivation make motor memories less susceptible to interference (de Beukelaar et al., 2014). At this stage, it is not clear whether the sixty trials used in this study represents a short or long reactivation period. Fourth, the time between reactivation and exposure to the interference manipulation can also dictate whether performance degrades, where shorter intervals result in greater interference (de Beukelaar et al., 2016). In contrast, however, we presented our interference manipulation immediately after the

reactivation phase and failed to see performance declines upon re-testing. Taken together, many of these temporal boundary conditions could provide at least a partial explanation for our results.

Several aspects of our task may have also played a role. For instance, there may be differences in the way visuomotor mappings and motor sequences are consolidated. Debas et al. (2010) found that the former is associated with the corticocerebellar system, whereas the latter is associated with the corticostriatal system. Alternatively, the opposing mapping may have had less of an effect since it was the second time it was presented. Indeed, we found reduced early adaptation error in B_2 one year later. However, even the group that did not experience this mapping in the first year showed similar findings (that is, a lack of interference after reactivation). Perhaps our results are because memory formation is more robust in a walking paradigm, as the consequences of degraded performance (especially outside of a lab) could cause injury. Interestingly, interference effects are less detrimental when a walking task is used to study motor learning compared to a reaching task (Brashers-Krug et al., 1996; Krakauer et al., 2005; Maeda et al., 2017; Malone et al., 2011). Regardless, understanding the factors that affect the formation and stability of long-term motor memories will be important for the design of more effective motor learning strategies, particularly following neurological injury. Our visually guided walking paradigm may facilitate this process.

Conclusions

In a visually guided walking task, the motor memory of a novel visuomotor mapping is retained for at least one year. This memory appears to have limited fragility, as it is not affected by interference following reactivation. Our results highlight the robustness of visuomotor

memories associated with walking. Future research should determine the mechanisms of this long-term retention and factors that facilitate it.

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FIGURE LEGENDS

Figure 1: Experimental task and protocols. A: schematic of the visually guided walking task. Participants walked and stepped onto two sequential targets on the ground. Inset: a simulated view of the target through the prism lenses and the perceived target shift for 20-diopter lenses. **B**: experimental protocols showing baseline (0-diopter prisms) and adaptation (20-diopter prisms) phases. **C**: graphical representation of the first adaptation trial error and early adaptation error measures used to quantify performance.

Figure 2: Short-term (one-week) retention of a visuomotor mapping. Group mean ± SE foot-placement error during the baseline and learning phases on day 1 and the relearning block of trials after one week (left side). Group mean ± SE foot-placement error for the first adaptation trial and early adaptation trials of target 1 across testing sessions (A_1 and A_2) are shown on the right side. The A_1A_2-A_3BA_4 and A_1A_2-BA_3 groups are combined in this panel since they experience the same protocol on these two days in the first year. Asterisk indicates testing days are significantly different from each other ($p < 0.01$).

Figure 3: Long-term (one-year) retention of a visuomotor mapping. A: group mean ± SE foot-placement error on day 2 of the first year (A_2) and day 1 a year later (A_3) for the A_1A_2-A_3BA_4 group (left side). Group mean ± SE foot-placement error for the first adaptation trial and early adaptation trials of target 1 across testing sessions (A_2 and A_3) for the A_1A_2-A_3BA_4 group (right side). **B**: group mean ± SE foot-placement error on day 2 of the first year (A_2) and day 1 a year later (A_3) after an opposing mapping for the A_1A_2-BA_3 group (left side). Group mean ± SE

foot-placement error for the first adaptation trial and early adaptation trials of target 1 across testing sessions (A_2 and A_3) for the A_1A_2-BA_3 group (right side).

Figure 4: The effects of an opposing mapping on one-week and one-year retention and consolidation. A: group mean ± SE foot-placement error across the different adaptation phases for the $A_1B_1A_2$-$A_3B_2A_4$ group. **B and C**: group mean ± SE foot-placement error for the first adaptation trial and early adaptation trials in relation to mapping A at different time points. **D**: group mean ± SE foot-placement error for the first adaptation trial and early adaptation trials in relation to the opposing mapping (mapping B). Asterisk indicates testing days are significantly different from each other ($p < 0.01$).

Figure 5: Stable motor memory upon reactivation one-year later. A: group mean ± SE foot-placement error during the first (A_3) and second (A_4) adaptation phases after one year for the A_1A_2-A_3BA_4 group (left side). Group mean ± SE foot-placement error for the first adaptation trial and early adaptation trials across testing sessions (A_3 and A_4) for the A_1A_2-A_3BA_4 group (right side). **B**: group mean ± SE foot-placement error during the first (A_3) and second (A_4) adaptation phases after one year for the $A_1B_1A_2$-$A_3B_2A_4$ group (left side). Group mean ± SE foot-placement error for the first adaptation trial and early adaptation trials across testing sessions (A_3 and A_4) for the $A_1B_1A_2$-$A_3B_2A_4$ group (right side).

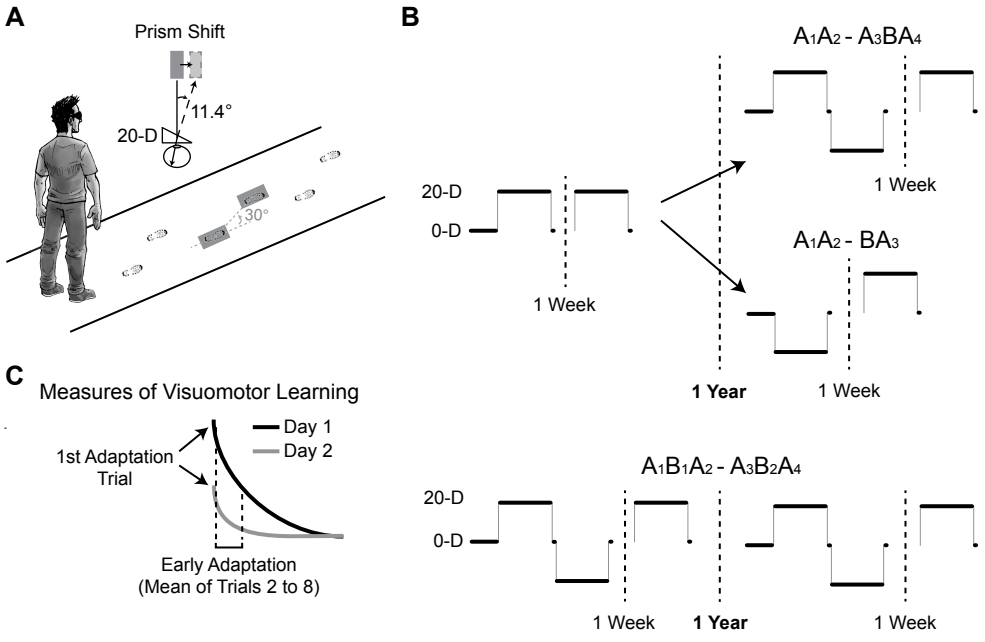
A
Prism Shift
11.4°
20-D
30°
B
A1A2 - A3BA4
20-D
0-D
1 Week
1 Week
A1A2 - BA3
1 Year
1 Week
A1B1A2 - A3B2A4
20-D
0-D
1 Week
1 Year
1 Week
C
Measures of Visuomotor Learning
1st Adaptation Trial
Day 1
Day 2
Early Adaptation
(Mean of Trials 2 to 8)

Figure 1

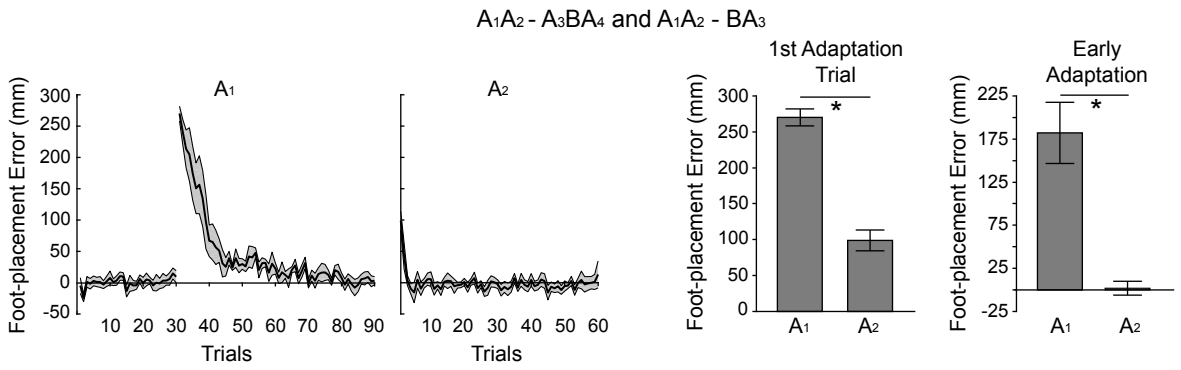
A1A2 - A3BA4 and A1A2 - BA3
A1
A2
Foot-placement Error (mm)
300
250
200
150
100
50
0
-50
10 20 30 40 50 60 70 80 90
Trials
10 20 30 40 50 60
Trials
1st Adaptation Trial
Foot-placement Error (mm)
300
250
200
150
100
50
0
*
A1
A2
Early Adaptation
Foot-placement Error (mm)
225
175
125
75
25
-25
*
A1
A2

Figure 2

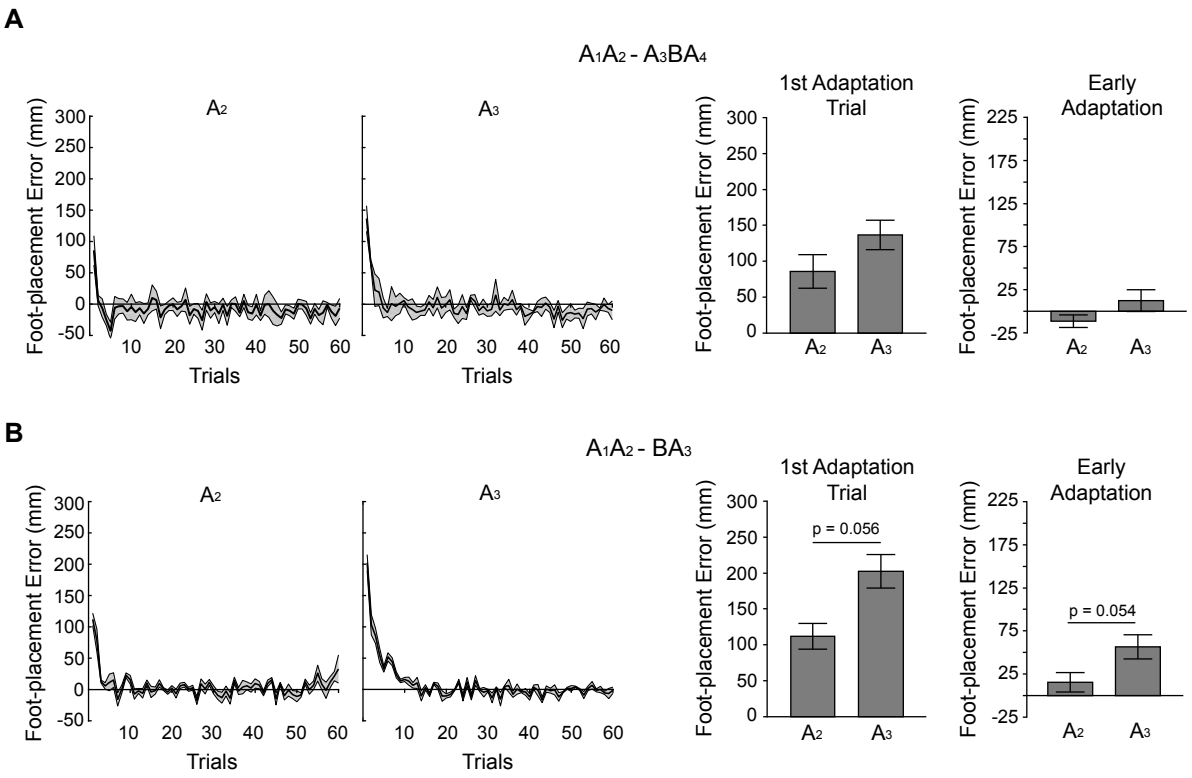
A
A1A2 - A3BA4
A2
A3
Foot-placement Error (mm)
Trials
1st Adaptation Trial
Early Adaptation
B
A1A2 - BA3
p = 0.056
p = 0.054

Figure 3

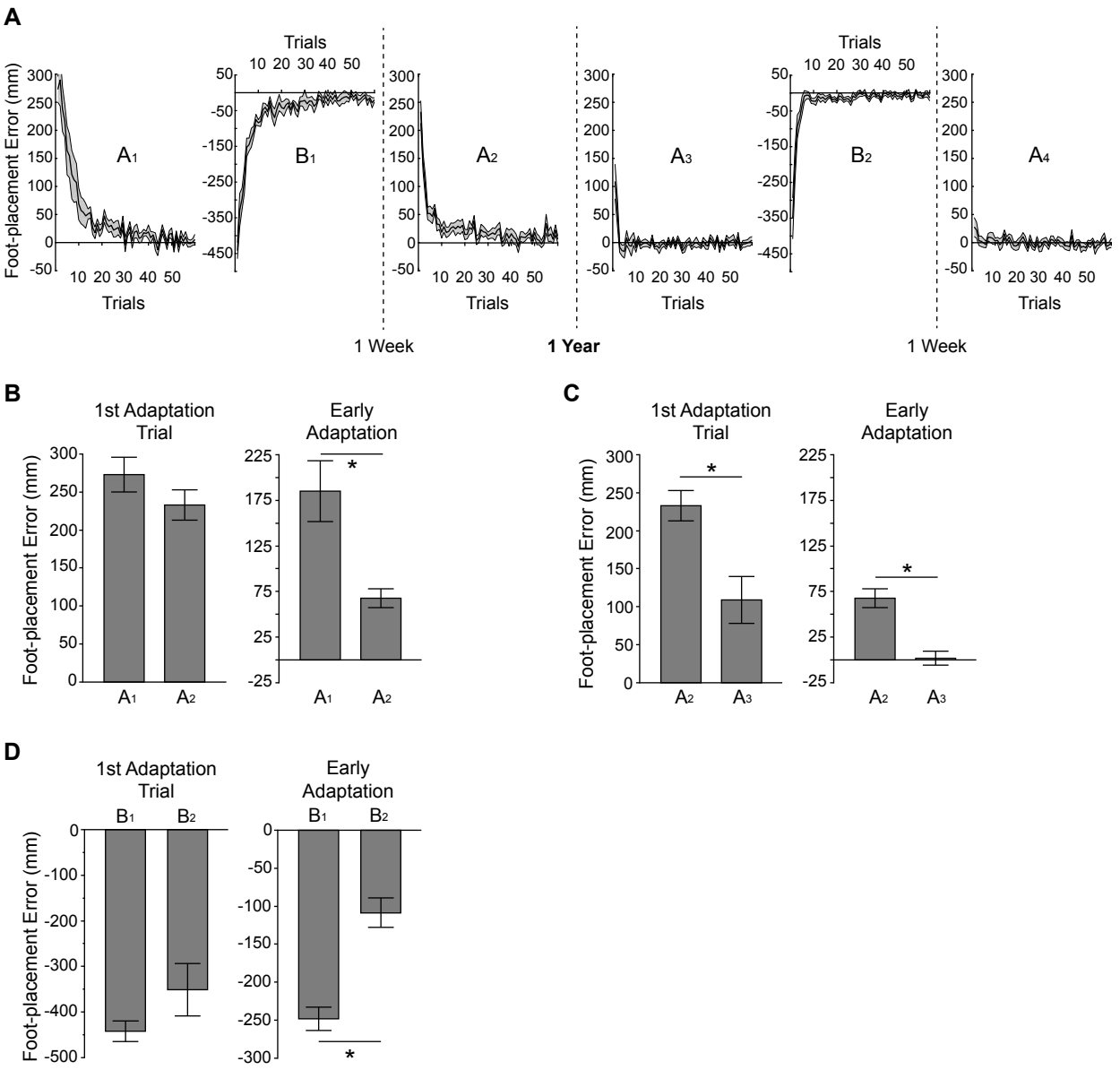
A
Foot-placement Error (mm)
Trials
A1
B1
A2
A3
B2
A4
1 Week
1 Year
1 Week
B
1st Adaptation Trial
Early Adaptation
C
D
B1
B2

Figure 4

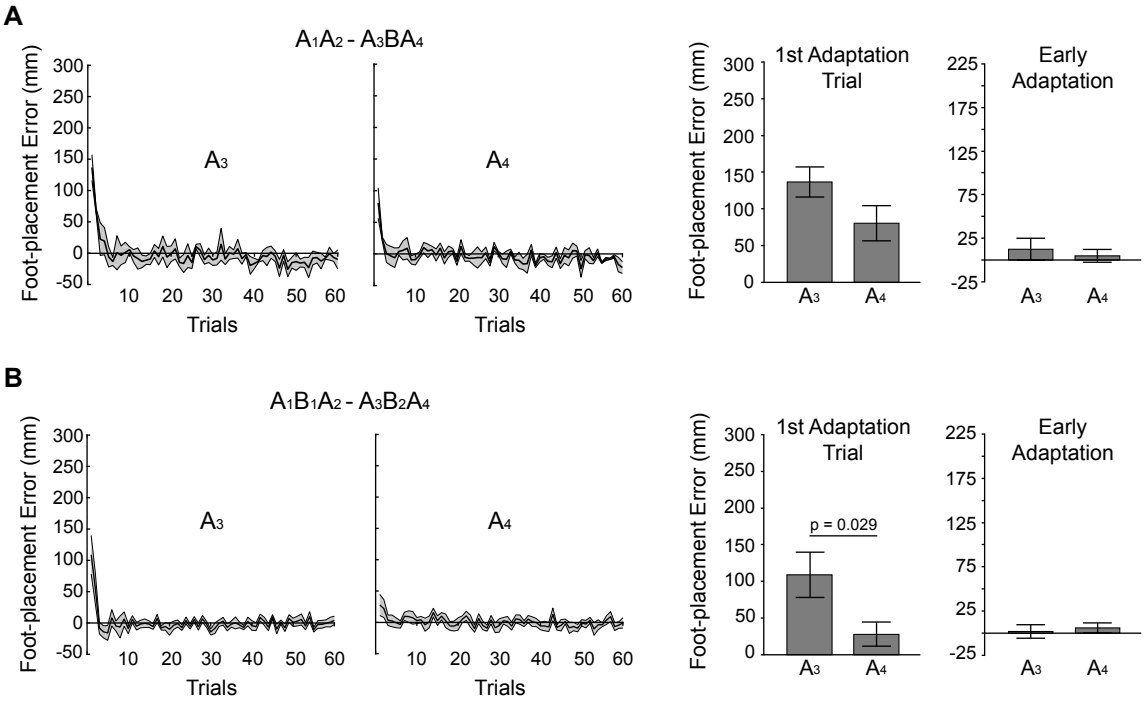
A
A1A2 - A3BA4
Foot-placement Error (mm)
A3
A4
Trials
1st Adaptation Trial
Early Adaptation
B
A1B1A2 - A3B2A4
p = 0.029

Figure 5