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A common task structure links together the fate of different types of memories

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Summary

Our memories frequently have features in common. For example, a learnt sequence of words or actions can follow a common rule, which determines their serial order, despite being composed of very different events [1, 2]. This common abstract structure might link the fates of memories together. We tested this idea by creating different types of memory task: a sequence of words or actions, which either did or did not have a common structure. Participants learnt one of these memory tasks, and then they learnt another type of memory task six hours later, either with or without the same structure. We then tested the newly formed memory's susceptibility to interference. We found that the newly formed memory was protected from interference when it shared a common structure with the earlier memory. Specifically, learning a sequence of words protected a subsequent sequence of actions learnt hours later from interference, and conversely, learning a sequence of actions protected a subsequent sequence of words learnt hours later from interference provided the sequences shared a common structure. Yet, this protection of the newly formed memory came at a cost. The earlier memory had disrupted recall when it had the same, rather than a different structure to the newly formed and protected memory. Thus, a common structure can determine what is retained (i.e., protected) and what is modified (i.e., disrupted). Our work reveals that a shared common structure links the fate of otherwise different types of memories together, and identifies a novel mechanism for memory modification.

Results & Discussion

We created memory tasks with or without the same structure. Each task contained different types of knowledge (actions or words). We mapped each of the four movements (designated 1 to 4) within the motor sequence onto one of the four semantic categories (transport, vegetable, animal, furniture) within the word-list (Figure 1). Using the mapping, we replaced each of the four elements of a 12-item motor sequence with a semantic category, and selected one of the three words from that category to appear once to create a 12-item word-list [2]. Without a consistent mapping between sequence element and semantic category, the motor sequence and word-list did not have a shared common structure. Thus, we created different types of memory task (actions or words) that either did or did not have a shared abstract structure (Figure 1).

Shared structure protects from interference

In the first set of experiments, participants initially learnt a motor sequence and had their skill tested (Experiment 1; Figure 2a, interference). Skill was the response time advantage to visual cues presented in a repeating sequence of positions compared to when the cue position was random. An increase in this response time difference demonstrated an increase in skill. Six hours after learning the motor sequence, participants learnt a word-list and had their recall tested (recall$_1$), which we sought to disrupt by having participants immediately learn another word-list. We then asked participants to recall again the first word-list (recall$_2$). The change in free recall (recall$_2$-recall$_1$) provided a measure of word-list interference. Participants were randomly allocated to a group in which the memory tasks did or did not have the same structure.

We found a significant decrease in total recall of the word-list, regardless of whether the word-list had the same or a different structure from the earlier skill-learning task (recall$_1$ *(mean±sem)* vs. recall$_2$, 10.4±0.4 vs. 8.7±0.4 words (same); 9.9±0.5 vs. 6.6±0.7 words (different); both groups; paired t-tests, $t(17) > 5.1$, $p<0.001$; Figure 2b). However, this change differed significantly depending on whether the learning tasks had the same or different structures (interaction term, performance change X group; mixed design ANOVA, $F(1,34) = 5.781$, $p = 0.022$; 17±3% decrease (same) vs. 34±6% decrease (different); Figure 2b). Disruption to the recall of the word-list was less when it shared a common structure with the earlier skill-learning task. The initial total recall did not differ significantly between the groups (unpaired t-test, t(34) = 0.8863, p = 0.381; Figure 2b). Thus, sharing a common structure with a skill acquired earlier protected the word-list from subsequent interference.

We next tested the critical importance of skill learning in protecting the word-list from interference. In an additional group of participants, we examined the susceptibility of a word-list to interference without any earlier skill learning. We found a significant decrease in total word recall (10.1±0.4 words vs. 6.7±0.9 words; paired t-test, t(12) = 4.985, p<0.001; Figure 2c), which was significantly greater than when participants had earlier learnt a motor skill with the same common structure as the word-list (comparing the size of the decrease, one-tailed, unpaired t-test, t(29) = 2.35, p = 0.013). There was no significant difference in total recall at initial testing between these two groups (unpaired t-test, t(29) = 0.545, p = 0.590; Figure 2b & 2c). In these groups, the word-list and interfering list were identical: the only difference between them was the presence or absence of the skill-learning task. When comparing these two groups with the group in which the memory tasks had different structures, we still found a significant difference in the change in total word recall across the groups (interaction term, performance change X group; mixed design ANOVA, F(2,46) = 3.324, p = 0.045) without any significant difference across the groups at initial testing (one way ANOVA, F(2,46) = 0.423, p = 0.657). Overall, sharing a common structure with a motor skill protects a subsequently learnt word-list from interference.

Only the total recall was protected from interference. The change in the proportion of the word-list recalled in the correct order (serial recall) did not differ significantly depending upon whether the word-list and earlier motor skill had the same or a different structure (interaction term, performance change X group; mixed design ANOVA, F(1,34) = 0.177, p = 0.677). Within each of these groups, there was no significant change in serial recall (74±5 vs. 76±6% (same); 77±4 vs. 82±6% (different); both groups; paired t-tests, t(17) < 0.8, p>0.48; Figure 2b). Similarly, in the group without any prior skill learning there was no significant change in serial recall (76±6% vs. 85±4%; paired t-test, t(12) = 1.83, p = 0.09; Figure 2c). Thus, serial recall was not susceptible to interference, and so could not express, or did not require, any protection from interference.

We also tested whether a common structure allows word-list learning to protect subsequent skill learning from interference. In these experiments, participants initially learnt a word-list and six hours later they learnt a motor sequence (Experiment 2; Figure 3a, interference). We then measured their skill (skill_1), which we sought to disrupt by immediately having the participants learn another motor sequence, and then we measured their skill again (skill_2). The change in skill (skill_2-skill_1) provided a measure of skill interference. Participants were randomly allocated to a group in which the memory tasks did or did not have the same structure.

Our results show that the change in skill between testing and retesting differed significantly depending upon whether the word-list and subsequent motor skill had the same or different structures (interaction term, performance change X group; mixed design ANOVA, F(1,39) = 6.249, p = 0.0169). We found that there was a significant decrease in skill when the learning tasks had different abstract structures (62±14ms vs. 42±12ms, -32±8%; paired t-test, t(19) = 3.815, p = 0.001; Figure 3b). By contrast, there was no significant change in skill when the tasks shared the same abstract structure (56±5ms vs. 60±8ms, +7±15%; paired t-test, t(20) = 0.506, p=0.619; Figure 3b). The initial skill did not differ significantly between these groups (unpaired t-test, t(39) = 0.456, p = 0.650; Figure 3b). Thus, sharing a common structure with a word-list protects a subsequently acquired motor skill from interference.

We next tested the critical importance of word-list learning in protecting the motor skill from interference. In this additional group, we examined the susceptibility of the motor skill to interference without earlier word-list learning. We found a significant decrease of the motor skill between testing and retesting (64±12ms vs. 37±8ms, -42±13%; paired t-test, t(14) = 2.352, p = 0.034; Figure 3c), which was significantly greater than when participants had previously learnt a word-list that shared a common structure with the subsequent motor skill (comparing the size of the decrease, one-tailed, unpaired t-test, t(34) = 2.3113, p = 0.014). Skill at initial testing did not differ significantly between these groups (unpaired t-test, t(34) = 0.7196, p = 0.4767; Figure 3b & 3c). In both groups, the motor skill and interfering skill were identical: the only difference between the groups was the presence or absence of the word-list learning task. When comparing these two groups with the group in which the memory tasks had different structures, we still found a significant difference in the change in motor skill across the groups (interaction term, performance change X group; mixed design ANOVA, F(2,53) = 4.121, p = 0.022) without any significant skill difference across the groups at initial testing (one-way ANOVA, F(2,53) = 0.176, p = 0.839). Thus, word-list learning is critical for protecting a subsequent motor skill from interference. Overall, our results show that a common structure enables established memories to affect the fate of recently formed memories, protecting them from interference.

Shared structure disrupts retention

We next examined the retention of the initial learning task by retesting performance 12 hours after initial learning (Figures 2a & 3a). In the first set of experiments; we retested (skill$_2$) participants 12 hours after they had been initially tested (skill$_1$) on the motor sequence (Experiment 1;Figure 2a). The skill change (skill$_2$-skill$_1$) provided a measure of skill retention.

We found a significant difference in the change in motor skill depending upon whether the motor sequence and word-list had the same or different structures (interaction term, performance change X group; mixed design ANOVA, F(1,34) = 4.88, p = 0.034). When the tasks had different structures, significant offline improvements developed between the initial testing and subsequent retesting 12 hours later (60±7ms vs. 80±7ms, +33±16%; paired t-test, t(17) = 2.48, p = 0.024; Figure 2d). Previous studies have described similar offline improvements, in which, skill is enhanced between practice sessions [2-7]. By contrast, when the motor sequence and word-list shared a common structure, there was no significant change in motor skill (62±5ms vs. 61±5ms, -1±8%; paired t-test, t(17) = 0.16, p = 0.873; Figure 2d). At initial skill testing there was no significant difference between the groups (skill$_1$, unpaired t-test, t(34) = 0.208, p = 0.836; Figure 2d). Rather than being enhanced between testing and retesting, skill was instead, only maintained, which made skill retention less than expected (by ~34%) when the skill and newly formed word-list memory shared a common structure.

In the second set of experiments, we retested (recall$_2$) participants 12 hours after their initial recall (recall$_1$) of the word-list (Experiment 2; Figure 3a). The change in recall (recall$_2$-recall$_1$) provided a measure of word retention.

We found that the change in total recall did not differ significantly between when the memory tasks had the same or different structures (interaction term, performance change X group; mixed design ANOVA, F(1,39) = 0.681, p = 0.4143). Both groups showed a significant decrease in total recall (10.2±0.3 vs. 9.4±0.4 words, a -8±3% (same); 10.3±0.3 vs. 9.2±0.6 words, a -11±3% (different); both groups; paired t-tests, t>2.2, p<0.035), and there was no significant difference in total recall between the groups at initial testing (unpaired t-test, t(39) = 0.234, p = 0.816; Figure 3d). The decrease in total recall within both groups may have been due to a variety of factors, including, that testing and subsequent retesting took place at different times of the day (circadian factors; [8]). Together, these results suggest that the structure of the learning tasks had little effect on the total recall of the word-list.

However, the common structural feature of the learning tasks was the serial order of their items. We found that the change in serial recall differed significantly depending upon whether the memory tasks had the same or different structures (interaction term, performance change X group; mixed design ANOVA, F(1,39) = 5.139, p = 0.029). There was a significant decrease in serial recall when the word-list and motor sequence shared a common structure (77.1±4% vs. 70.3±4%, paired t-test, t(20) = 2.66, p =

0.0149; Figure 3d). By contrast, there was no significant decrease in serial recall when the memory tasks had different structures (79.8±4% vs. 83.2±4%, paired t-test, t(19) = 0.89, p = 0.38; Figure 3d). At initial testing, there was no significant difference in serial recall between the groups (unpaired t-test, t(39) = 0.457, p = 0.650; Figure 3d). Thus, disruption of the word-list only occurred when the tasks shared a common structure, and it was a specific attribute, the serial structure of the word-list, that was disrupted; the same attribute that the word-list shared with the skill task. Overall, a common structure enables newly formed memories to affect the retention of established memories acquired many hours earlier.

Our work reveals that sharing a common structure links the fate of otherwise different memories together, and identifies a novel mechanism of memory modification. By sharing a common structure, an earlier memory protected a newly formed memory from interference. Yet, this protection of the newly formed memory came at a cost. The retention of the earlier memory was disrupted: expressed either as an absence in the skill enhancement that develops offline between testing and retesting, or as impaired serial word recall. By sharing a common structure, the newly formed memory, while being protected from interference, modified and disrupted the retention of the earlier memory. There was a reciprocal link with existing memories protecting newly formed memories, and newly formed memories modifying the retention of existing memories. This link was present even though the memories were of different types (actions vs. words), and so, memory organization goes beyond content to connect memories based upon their structure. Thus, a common structure enables a reciprocal communication between different types of memories; their fates become linked together, providing a mechanism for memory modification.

A memory following its formation is unstable and susceptible to interference [9]. However, here a newly formed memory was protected from interference due to earlier learning of a memory task with the same structure. Without that earlier experience – when the earlier memory task had a different structure to the subsequent task or when no earlier learning had occurred – the newly formed memory was disrupted and retention impaired. Initial experience of the shared structure provided an opportunity for the common feature to become stabilised during consolidation (6-hour interval; Figures 2a & 3a), which reduced the susceptibility of subsequent learning with that same structure to interference. Thus, by sharing a common structure an earlier memory can protect subsequent memories from interference.

Yet, sharing that common structure did not affect subsequent learning, which is only enhanced when the tasks are learnt in quick succession (Figures 2b & 3b; ([2, 10]; for reviews [11, 12]). An interval between tasks (6hrs, or 2hrs in earlier work) provides an opportunity for the memory to stabilize, which prevents performance transfer between the tasks, and enhanced learning [2, 9, 11]. Rather than enhancing learning, sharing a common structure with an earlier memory protected a subsequent memory from disruption.

However, the protection of the newly formed memory came at a cost. While the newly formed memory was protected from interference, the memory that it shared a common structure with, acquired many hours earlier, was disrupted. This change to the fate of the earlier memory – as shown by its decreased retention – occurred only when the earlier and newly formed memory shared a common structure. Typically, changing the fate of a memory requires it to be unstable and susceptible to interference [11, 13-16]. Yet, the memory had been acquired many hours ago when these types of memories have ceased to be susceptible to interference [6]. Rather than being due to memory instability, the modification of the earlier memory may have been because participants were being exposed again to the same common structure, but within the novel context of a different memory type (words vs. actions). This would impair the relationship between the original memory's content and its structure, preventing that original content being placed in the correct serial order, as defined by the structure, which is consistent with the serial recall of the word-list being impaired. Yet, the content itself would be preserved, which is consistent with the total recall of the word-list being retained. Thus, having a common structure enabled a newly formed memory to modify the retention of an earlier memory.

The abstract structure of a sequence may be processed by the prefrontal cortex (PFC), tuned to the structure of a movement sequence; rather than any specific movement ([17]; for a review [1]). Neurons may also be tuned to sequential patterns of (semantic) word categories. By contrast, the surface properties or content of the sequence, such as, the modality (auditory vs. visual) or type of information (actions vs. words) may be processed beyond the PFC. For example, the primary motor cortex (M1) is activated during motor sequence learning (for meta-analysis review; [18]). Thus, the link and ability to modify memories due to their shared structure may occur regardless of their content.

A similar network may be activated when experiencing the same abstract structure despite a change in content. Motor cortical areas, perhaps including M1, may be activated during word-list learning because the word-list shared a common structure with an earlier motor sequence. Alternatively, activation may be more specific (PFC only). Regardless, PFC activation may affect a large-scale brain network through low-frequency oscillations, which have been implicated in encoding the abstract structure of a word sequence (grammar), perhaps strengthening activity within those areas, making it less susceptible to interference [19]. This would explain how learning a memory task protects a subsequent memory task with the same structure from interference.

In this scenario, PFC activation is no longer uniquely associated with a specific content; instead, it is associated with both actions and words. This has the advantage that the abstract structure can be applied in these diverse circumstances. However, the association with any one circumstance is diminished; perhaps expressed, as a reduced connectivity between PFC and the circuits associated with the original sequence content. This would impair performance of the abstract structure with the original content explaining how forming a new memory disrupts retention of an earlier memory with the same structure but different content.

Sharing a common structure may impact every day life. Sentences can have a common structure (grammar), but contain different words; equally, musical tunes can have a common structure, but contain different notes. One tune might affect another because they share a common structure despite containing different notes, or being recalled in different ways (symbols vs. played). A sequence from any behavioral domain (language, music, or athletics) could through chance share a common structure with another within the same, or different domain, linking their fates together.

A memory was protected from interference by sharing a structure with an earlier memory (15% better retention). In everyday circumstances this protection may not be that important because there is sufficient redundancy in the information being conveyed, or opportunity to clarify. Yet, in high performance situations (athletic competitions, recitals), even a small change in performance could have a dramatic effect – determining the difference between success and failure. Thus, the importance of shared structured upon performance may depend upon context.

Overall, a common structure creates a reciprocal link between different types of memory. A recently formed memory is protected from interference by an earlier memory, and conversely, the earlier memory has its retention modified by the newly formed memory. Thus, a common structure links the fates of different memories together, and provides a mechanism for their modification.

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Author Contributions

Conceptualization, E.M.R.; Methodology, M.B. and E.M.R.; Formal Analysis, T.P.M. and E.M.R.; Investigation, T.P.M., M.B.; Writing – Original Draft, E.M.R.; Writing – Review & Editing, T.P.M., M.B., and E.M.R.; Visualization, E.M.R. and M.B.; Funding Acquisition, E.M.R.

Declaration of Interests

The authors declare no competing interests.

STAR Methods

Key Resource Table

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and Algorithms		
MATLAB 2015b	RRID: SCR_001622	https://www.mathworks.com
Psychtoolbox-3 [20]	RRID: SCR_002881	http://psychtoolbox.org/
Deposited Data		
Behavioural data	This paper; Mendeley Data	http://dx.doi.org/10.17632/nn3jvnttc4.1.

Contact for reagent and resource sharing

Further information and requests for resources should be directed to and will be fulfilled by the Lead Contact, Edwin Robertson (edwin.robertson@glasgow.ac.uk).

Experimental model and subject details

Experimental design

We tested the idea that sharing a common structure may link the fates of memories together. To do so, we created memory tasks that either did or did not share a common structure with one another. Across two sets of complementary experiments, we examined: (a) how the learning of one memory task might affect the susceptibility of a subsequent memory task to interference; and (b) how that newly formed memory affected the retention of the earlier memory. Only the abstract structure was shared between the tasks because each memory task had a different content (i.e., action vs.

word sequence). The two experiments had a similar design, and were approved and overseen by the local ethics committee.

In the first set of experiments, the initial memory task was a motor-sequence learning task, and the subsequent task was a word-list learning task (Figure 2a; Experiment 1; please see below, for task details). Participants initially learnt a motor sequence and had their skill tested (skill_1). Six hours later, they learnt a word-list, and recalled that word-list (recall_1). They then immediately learnt another word-list (an interfering word-list), before recalling the first word-list (recall_2). The change in word recall performance (i.e., $\text{recall}_2–\text{recall}_1$) between retesting and testing provided a measure of that newly formed memory's susceptibility to interference. Finally, 12 hours after initial testing, at 9pm, participants were retested on the motor sequence (skill_2). The change in performance (i.e., $\text{skill}_2–\text{skill}_1$) provided a measure of skill retention.

The design of the second set of experiments was almost identical to the first: except, we reversed the order of the tasks (Figure 3a; Experiment 2). Participants learnt a list of words and had their recall tested (recall_1). Then, six hours later, they learnt a motor sequence, had their skill tested (skill_1), and then immediately learnt another skill sequence (an interfering skill sequence), before having their skill on the initial sequence retested (skill_2). Finally, 12 hours after initial testing, participants recalled the word-list (recall_2). In this set of experiments, the susceptibility of the newly formed memory to interference was measured as a change in skill (i.e., $\text{skill}_2–\text{skill}_1$), while retention of the earlier memory was measured as a change in word recall (i.e., $\text{recall}_2–\text{recall}_1$).

We also measured interference without any prior learning. Participants learnt only one task either the word-list or motor skill, had their performance tested (recall_1 or skill_1, respectively), then immediately learnt a memory task of the same type (i.e., word-list or motor skill; interfering task) before having their performance retested on the initial memory task (recall_2 or skill_2, respectively). Susceptibility to interference was measured as a change in task performance (as in the main experiments; i.e., $\text{recall}_2–\text{recall}_1$ or $\text{skill}_2–$

$skill_1$; respectively). We used exactly the same word-list, motor skill and interfering tasks as in the main experiments when the tasks shared a common structure, and we also performed the tests at the same time of day. Thus, the design was identical to that within the main experiments, except there was no prior learning. It allowed us to test the importance of prior learning upon the subsequent susceptibility to interference of a memory task with the same structure. A difference in the susceptibility of the task to interference in these experiments, compared to those of the main experiment, where there had been prior learning, would be attributable to that prior learning.

Participants

We recruited 137 right-handed (as defined by the Edinburgh handedness questionnaire [21]), healthy participants, 18-35 years of age, with no medical, neurological or psychiatric history, and with either normal or corrected-to-normal vision. All participants provided informed consent for the study, which was approved by the local institutional ethics committee. Some participants showed little, or no, evidence of learning the motor sequence task (n = 9) because their response times remained greater during the sequential trials than during the subsequent random trials (i.e., at initial testing; $skill_1 < 0$). We exclude those participants from further analysis, and those who could verbally recall more than four items of the motor sequence (n = 23). This amount of recall can prevent the development of motor skill improvements between testing and retesting (i.e., offline improvements [3, 22]). Other earlier studies have shown that excluding participants with such a recall ensures that this motor sequence task retains its ability to develop improvements [3, 4, 6, 23]. As a consequence, we removed those participants with a recall of > 4-items to ensure that recall did not prevent the development of offline improvements, which would alter motor skill retention. Approximately the same proportion of participants was removed from analysis as in earlier studies (i.e., 20-30%; for example, [3, 24]).

The remaining 105 participants (32 male, 23.3±4.1 years, *mean±std*) were randomly distributed between the two experiments. We randomly assigned 49 participants to the first set of experiments (Experiment 1; see Figure 2). In this experiment, 18 participants were assigned to those groups where the tasks had the same, or different structures, and the remaining 13 participants assigned to the group with no prior motor learning (i.e., word-list learning only). This number of participants (n=18) within the main experimental groups was based upon the need to detect an offline improvement between testing and retesting 12 hours later. We recruited a greater number of participants than earlier work, which had successfully detected offline improvements, to ensure that even a change in the proportion of the offline improvements could be detected [2, 3, 6, 23]. The number of participants (n=13; no prior learning) recruited to the control group was based upon the need to detect impaired recall of a word-list due to immediately learning another word, which is a robust, well documented observation that has been reported with even a limited number of participants [9]. The other 56 participants were randomly allocated to the second set of experiments (Experiment 2; see Figure 3). In this experiment, 21 participants were assigned to the group that had the same task structures, 20 participants were assigned to the group that had different task structures, and the remaining 15 participants were assigned to the group that underwent no prior word-list learning. The number of participants (n = 21 or 20) recruited to the experimental groups was based upon seeking to detect a change in word recall. There was little prior work to guide how large an effect would be observed. However, in contrast, to the motor skill task, the word-list task does not show an offline improvement. As a consequence, the dynamic range available for a disruption to be expressed would be less than for the skill task that shows such improvements (i.e., in the first set of experiments), which lead us to recruit a greater number of participants to this set of experiments. The number of participants (n=15; no prior learning) recruited to the control group was based upon the need to detect impaired motor skill due to immediately learning another skill, which we estimated based in part on our own preliminary experiments, and upon earlier work, including work using different approaches (such as Transcranial Magnetic Stimulation) to disrupt other types of motor skill (for example; [25, 26]). All of these remaining participants (i.e., all 105 participants) were included in our analyses. Participants did not know the group to which they were assigned. For those assigned to groups with an interval between the training, testing and retesting sessions, participants engaged in normal daily activities and refrained from napping.

Method Details

Motor sequence learning task

We used a modified version of the serial reaction time task (SRTT; [27, 28]). This is an established and widely used task, which has provided important insights into a diverse array of behaviours that rely upon implicit processing from skill learning, to acquiring grammar, to intuition [28, 29]. It is also a task in which offline improvements develop over time between initial testing and subsequent resting during wakefulness [2-5, 30, 31]. These offline improvements contrast with, and complement the retention of knowledge seen between testing and retesting in the other task (i.e., the word-list task) we selected for this study (i.e., enhancement vs. maintenance; see below). Offline improvements are, however, prevented from developing when participants can correctly verbally recall more than four consecutive items of the sequence [6, 23, 32]. We identified those participants by administering a free recall test (see below), and removed them from subsequent analysis to ensure that any change in offline improvement, was attributable to having the same or different structure to the word-list, rather than due to having explicit knowledge of the sequence (i.e., recall>4-items). We used this same *a priori* criterion throughout the study so that the same implicit task was used within both experiments.

In this task a solid circular visual cue (diameter 20mm, viewed from approximately 800mm; implemented in Psytoolbox-3; [20]) could appear at any one of four possible positions, designated 1 to 4, and arranged horizontally on a computer screen. Each of the four possible positions corresponded to one of the four buttons on a key-pad, upon which the participant’s fingers rested. When a target appeared, participants were instructed to respond by pressing the appropriate button on the pad. If the participant made an incorrect response, the stimulus remained until the correct button was selected. Once the correct response was made, the cue on the screen disappeared and was replaced by the next cue after a delay of 400ms. Response time was defined as the interval between presentation of a stimulus and selection of the correct response.

Participants were introduced to the task as a test of reaction time; however, the position of the visual cue followed a repeating 12-item sequence (for example, 2-3-1-4-3-2-4-1-3-4-2-1). Participants were not told about the 12-item sequence. The sequence was repeated multiple times within a block.

Each block had the same organization. Fifty random trials preceded and followed the sequential trials in each block (i.e., sequential trials were sandwiched between fifty random trials). Within these random trials, there were no item repeats (for example, -1-1- was illegal), and each item had approximately the same frequency of appearance. Each set of random trials in each block was unique, which minimized the chance that participants might become familiar with the random trials. There were no cues marking the introduction or removal of the sequential trials (i.e., the transition between sequential and random trials was not marked).

In the first set of experiments, we examined motor skill retention and how this was affected (or not) by subsequent learning (of a word-list) with the same or different abstract structure (Figure 2a). We trained participants on an initial, short training block that contained 15 repetitions of the motor sequence, and then on a longer training block that contained 25 repetitions of the sequence, and then on a test block that contained 15 repetitions of the sequence. Subsequently, participants learnt a word-list either with or without the same structure as the motor sequence. Later, participants completed a retest block that contained 15 repetitions of the motor sequence (Figure 2a). Skill retention was measured as the change in skill between retesting the initial test (i.e., $skill_2$–$skill_1$). We expected skill to increase, because using this same design; earlier work had shown that skill is enhanced in the hours (>6 hr) between initial testing and subsequent retesting [2-6, 30].

In the second set of experiments, we were interested in the susceptibility of the motor skill task to subsequent interference (Figure 3a). We tailored the amount of training to ensure that the task remained susceptible to interference from the immediate learning of another motor sequence (prolonged training can make a skill invulnerable to immediate interference; [11, 33]). Guided by this work, and by our own preliminary work, we provided sufficient training for participants to acquire a substantial level of skill without it leading to overtraining and to invulnerability to interference. We trained participants on a training block of 25 repetitions of the motor sequence and then on a test block that contained 15 repetitions of the sequence. We then asked participants to practice a different motor sequence (the interfering sequence), which consisted of: an initial block of 15 repetitions of the sequence, followed by a block of 25 repetitions of the sequence, and a final block of 15 repetitions of the sequence. Participants then completed a retest block that contained 15 repetitions of the original sequence. The change in skill between retesting and initial testing provided a measure of skill interference (i.e., $skill_2$–$skill_1$). Any substantial decrease demonstrated that the skill was susceptible to interference.

We administered a free recall test when participants had completed their final block (i.e., the retest block) of the task. Participants were asked if they had noticed a pattern to the visual cues of the task, and if so, to report verbally as many items of the sequence as possible [6, 34].

Word-list task

A single word, from a list of 12 words (drawn from the California Verbal Learning Task; implemented in Psytoolbox-3; [20]; please see below for specific word-lists), was presented on a computer screen for 2s. The word was then removed, and replaced by another word also drawn from the list of 12 words. This process continued until all 12 words had been presented. The same 12 words were presented individually and in the same order for five iterations for each participant. At the end of each of these presentations, participants were asked to verbally recall in order as many of the words as possible (i.e., a serial recall). Participants were not prompted for particular words, nor were they told those words, if any, which they had failed to recall. Following the fifth recall, there was a ten-minute interval after which participants were again asked to verbally recall in order as many of the words as possible. In the first set of experiments, this final recall occurred immediately after learning another distinct interfering word-list, which itself had also been learnt over five iterations with a subsequent recall ten-minutes later (Experiment 1; Figure 2). The change in recall provided a measure of interference. While in the second set of experiments, the final recall occurred 12 hours after learning the word-list (Experiment 2; Figure 3), and the change in recall provided a measure of retention. In contrast to the motor skill that is enhanced between testing and retesting, we expected the recall of the word-list to be maintained (i.e., enhanced vs. maintenance).

Motor sequence and word-list structure

Using a technique applied in earlier work, we created memory tasks that either did or did not share a common structure ([2]; Figure 1). The four elements (1, 2, 3, 4) of the motor sequence were mapped onto one of the four semantic categories of the word-list (for example, transport, vegetable, animal, furniture), and in turn each category was mapped onto three words. By using this technique, a 12-item motor sequence (2-3-1-4-3-2-4-1-3-4-2-1) was transformed into a 12-item word-list (carrot-plane-jacket-shelf-boat-spinach-table-shoe-truck-couch-lettuce-sweater), in which there was a consistent relationship between the sequence element and the semantic category of the word (Figure 1). For example, the sequence element 2 was mapped onto the semantic category of transport appearing in the word-list initially as truck, then subway and finally as boat. By contrast in another group, there was no consistent mapping between sequence elements and the semantic categories of the words, and so the two memory tasks did not share a common structure. Thus, the memory tasks did (or did not) share a common structure by having (or not) a consistent mapping between elements within different types of sequence (action elements to semantic categories).

In the first set of experiments, the participants initially learnt a motor sequence (2-3-1-4-3-2-4-1-3-4-2-1; task A). Subsequently, they learnt a word-list that either did (carrot-plane-jacket-shelf-boat-spinach-table-shoe-truck-couch-lettuce-sweater) or did not (carrot-jacket-spinach-shelf-plane-shoe-desk-boat-lettuce-sweater-truck-couch; task B) share a common structure with the earlier motor sequence. They then learnt an interfering word-list (necklace-hammer-apple-earring-mountain-orange-shovel-river-bracelet-cherry-valley-scissors), which had a structure different from either of the other two possible prior word-lists, and were then retested on the initial word-list (i.e., task B). Finally, participants were later retested on the motor sequence (i.e. task A).

In the second set of experiments, the type of task was reversed. Participants initially learnt a word-list (carrot-plane-jacket-shelf-boat-spinach-desk-shoe-table-couch-lettuce-sweater; task A). They then learnt a motor sequence that either did (2-3-1-4-3-2-4-1-3-4-2-1) or did not (1-3-2-1-4-2-3-4-1-2-4-3; task B) share a common structure with the earlier word-list. Next, they learnt an interfering motor sequence (4-1-3-2-3-1-2-4-2-1-4-3), which had a structure different from either of the other two possible prior motor sequences, and were then retested on the initial motor sequence (i.e., task B). Finally, participants were later retested on the word-list (i.e., task A). Thus, we created memory tasks with the same or different structures by changing the order of the elements within the second memory task (i.e., task B).

Differences in the second memory task (i.e., differences between the groups in task B) might have been responsible for any difference in the susceptibility of the task to interference. To test this possibility, and more broadly, to test the importance of prior learning for modifying the susceptibility of a memory task to interference, we included an additional group within each experiment. In this group, participants did not learn the initial memory task (the 'no prior learning' group). Instead, they learnt either a word-list (Experiment 1) or a motor skill (Experiment 2), and immediately learnt an interfering memory task of the same type (a word-list or motor skill, respectively) before being retested on the initial memory task. Both the memory task and the interfering task were identical to that used in the other groups when the tasks shared a common structure (i.e., word-list; carrot-plane-jacket-shelf-boat-spinach-table-shoe-truck-couch-lettuce-sweater; and motor skill; 2-3-1-4-3-2-4-1-3-4-2-1). We expected the susceptibility of the task to interference would remain unchanged if it were due to the specific order of elements within the memory task. For example, the task might still be protected from interference due to some aspect of the element order (words or movements), which made it less prone to disruption. By contrast, a difference in the susceptibility (of task B) to interference due to it sharing a common abstract structure with an earlier learning task (task A) would no longer be present. Including this additional group within each experiment allowed us to compare the importance of the specific order of elements within a task against the importance of the abstract relationship between prior learning and subsequent learning for the susceptibility of that subsequent task to interference.

Behavioural data analysis

In the sequence learning task (i.e., the SRTT), response times were defined as the time to make a correct response. Any response time in the top one percentile (i.e., $\alpha = 0.01$) of a participant's data was identified using a Grubbs' Test and removed. We quantified the amount of skill learning by subtracting the average response time (RT) of the final 50 sequential trials from the average response time of the 50 random trials that immediately followed [27, 35]. The difference between random and sequential RT is a widely used learning measure, which is both sensitive and specific to learning of the motor sequence (for example; [27, 35, 36]; for review [28]). We did not use accuracy as a measure of motor skill because even with limited experience, error rates are extremely low (<2-4%, [3, 4, 35]). The free recall of the motor sequence was scored as the longest, continuous and accurate verbally recalled segment of the sequence that was at least three items long (i.e., a triplet or more; [23, 24, 37]).

For the word-list learning task, we analysed both the total number of words correctly recalled (i.e., total recall), and the order of recall (i.e., serial recall). The latter was calculated using the Levenshtein edit distance [38]. This provides a measure of the minimum number of changes (i.e., deletions, substitutions, or insertions) required for the recalled list to match the order of the words in the learnt target list. It ensures that all segments of the word-list that are recalled in the correct order are used to calculate a serial recall, as opposed to simply using the longest segment recalled in the correct order as a measure. For example, being able to recall 7 and subsequently 3 words in the correct order will achieve a better score than recalling a single segment of 7 words. A better score is a lower score because it indicates that fewer changes were necessary to achieve a match between the order of words in the recalled and learnt lists. By contrast, a high score (the highest being 12) would indicate poor serial recall with very little or no matching between the word order in the recalled and learnt word-list. For ease of interpretation, we calculated a modified Levenshtein edit distance: the difference between the maximum (i.e., highest) score and the Levenshtein edit distance (i.e., 12 – Levenshtein). An increase in this modified score indicates an increase in serial recall. We then divided this modified score by each individual participant’s total recall, which provided a specific measure of participants’ ability to place their own word-list knowledge into the correct serial order. Together, these two measures – total recall and serial recall – provided complementary measures of different aspects of the participants’ performance at recalling the word-list.

Quantification and Statistical Analysis

We explored graphically all of the data in MATLAB (2015b, The MathWorks, Inc., Natick, Massachusetts, United States). Specifically, we examined the distribution of the data using histograms, normal probability plots, and verified that the data followed a normal distribution using the Shapiro-Wilk test.

We used mixed design ANOVAs to test whether the susceptibility of a memory to interference differed across groups. This was achieved by comparing the word-list or motor skill performance immediately prior to and following the interfering task across the groups (i.e., recall_1 vs. recall_2 (Experiment 1) or skill_1 vs. skill_2 (Experiment 2) x group). The performance change had two levels (test vs. retest; within subject factor) and group was either two levels (same vs. different structure; between subject factor) or three levels when we also included the group in which there was no prior learning (same, different vs. no prior learning; between subject factor). Using a similar approach, we tested whether memory retention differed between groups. In this case, we compared the change in the motor skill or word-list performance at initial testing, against performance 12 hours later at subsequent retesting between the groups (i.e., skill_1 vs. skill_2 (Experiment 1) or recall_1 vs. recall_2 (Experiment 2) x group). In this case, performance change again had two levels (test vs. retest; within subject factor) and group had two levels (same vs. different structure; between subject factor). For all the mixed design ANOVAs, we provide the result of the interaction between performance change and group (performance change X group). Other subsequent tests were used to establish the pattern of the results. We used further ANOVAs, when appropriate, to compare across groups, and unpaired t-tests to better understand the differences between the groups. These tested for differences in initial task performance (i.e., skill_1 or recall_1) across groups, and for differences in performance decrease between groups. We used paired t-tests to determine the significance of changes within groups. All the statistical tests used in the analysis were two-tailed unless otherwise stated (when we were comparing the extent of a skill or word recall decrease (as opposed to simply a change) using a one-tailed test).

Data and software availability

The dataset generated during this study is available at Mendeley Data http://dx.doi.org/10.17632/nn3jvnttc4.1. Further information is available upon request by contacting the Lead Contact, Edwin Robertson (edwin.robertson@glasgow.ac.uk).

Figure Legends

Figure 1, Creating a common structure for a sequence of actions and words (a) Each of the four elements within the sequence was mapped onto a semantic category, and in turn each category was mapped onto three words. **(b)** Using this mapping, we replaced each item of the 12-item motor sequence with a word. With four semantic categories, and three words within each category there was a total of 12-words, which allowed a complete mapping of the motor sequence. **(c)** Yet, when there was no consistent mapping between sequence element and semantic category, the motor sequence and word-list did not have a shared common structure.

Figure 2, A common structure protects a newly learnt word-list from interference; at the cost of disruption, to an earlier learnt motor skill. (a) Experimental Design (Experiment 1). Participants learnt and were tested ($skill_1$) on performing a sequence of actions (i.e., finger movements) that had the same (participant number per group; n = 18) or a different structure (n = 18) to that of a sequence of words (word-list), which was learnt six hours later. After learning the word-list, participants recalled it ($recall_1$), then immediately learnt another different (interfering) word-list, and then recalled the initial word-list ($recall_2$). Finally, 12 hours after their initial testing, participants were retested on the motor sequence ($skill_2$). **(b)** The word-list was protected from interference when it had the same structure as the earlier motor skill. The significant decrease in total word recall between testing and retesting (in both groups; paired t-tests, $t(17)>5.1$, $p<0.001$; bar plots display mean ± SEM) differed significantly between the groups depending on whether the learning tasks had the same or different structures (interaction term, performance change X group; mixed design, ANOVA, $F(1,34) = 5.78$, $p = 0.022$). **(c)** The protection of the word-list was dependent on the earlier motor skill having the same structure. There was a greater decrease in total word recall when there was no earlier skill learning compared to when a motor skill with the same structure had been learnt earlier (n =13; unpaired t-test, $t(29) = 2.35$, $p = 0.026$). The change in serial recall did no differ significantly across the groups (lower panels of (b) and (c)). **(d)** The retention of the motor skill was disrupted when it has the same structure as the word-list. The skill change between testing and retesting differed significantly between the groups depending upon whether the learning tasks had the same or a different structure (interaction term, performance change X group; mixed design, ANOVA, $F(1,34) = 4.88$, $p = 0.034$). Skill increased between testing and retesting when the learning tasks had different structures (paired t-test, $t(17) = 2.48$, $p = 0.023$); such a skill enhancement normally develops over wakefulness following implicit skill learning (for example, [2, 3, 39]). By contrast, skill did not change significantly when the learning tasks had the same structure (paired t-test, t(17) = 0.16, p = 0.873). s^* significant difference; ns, no significant difference.

Figure 3, A common structure protects a newly learnt motor skill from interference; at the cost of disruption, to an earlier learnt word-list. (a) Experimental Design (Experiment 2). Participants learnt and recalled (recall_1) a sequence of words (i.e., a word-list) that either had the same (n = 21) or a different serial structure (n = 20) to that of a sequence of finger movements, which was learnt 6 hours later. After learning the motor sequence, participants were tested on it (skill_1). They then immediately learnt another distinct motor sequence, and were subsequently retested on the initial motor sequence (skill_2). Finally, 12 hours after their initial learning, participants once again recalled (recall_2) the word-list. **(b)** The motor skill was protected from interference when it had the same structure as the earlier word-list. There was no significant decrease in motor skill between testing and retesting when the learning tasks had the same structure (paired t-test, t(20) = 0.506, p = 0.618); but a significant decrease when the learning tasks had different structures (paired t-test, t(19) = 3.815, p = 0.0012; bar plots display mean ± SEM). **(c)** The protection of the motor skill was dependent on the earlier word-list having the same structure. There was a greater decrease in motor skill when there was no earlier word-list learning compared to when a word-list with the same structure had been learnt earlier (n = 15; unpaired t-test, t(34) = 2.3113, p = 0.027). **(d)** The retention of the serial order of the word-list was disrupted when it shared the same sequential structure as the motor skill. There was a significant decrease in serial recall between testing and retesting when the learning tasks had the same structure (paired t-test, t(20) = 2.66, p = 0.0149); whereas, there was no significant change when the learning tasks had different structures (paired t-test, t(19) = 0.89, p = 0.38). A significant decrease in total recall was present in both groups (same and different structure; both paired t-tests, t>2.2, p<0.035), and did not differ significantly between those groups (interaction term, performance change X group; mixed design, ANOVA, F(1,39) = 0.681, p = 0.414). s^* significant difference; ns, no significant difference.

References

1. Dehaene, S., Meyniel, F., Wacongne, C., Wang, L., and Pallier, C. (2015). The Neural Representation of Sequences: From Transition Probabilities to Algebraic Patterns and Linguistic Trees. Neuron *88*, 2-19.
2. Mosha, N., and Robertson, E.M. (2016). Unstable Memories Create a High-Level Representation that Enables Learning Transfer. Current biology : CB *26*, 100-105.
3. Robertson, E.M., Pascual-Leone, A., and Press, D.Z. (2004). Awareness modifies the skill-learning benefits of sleep. Current biology : CB *14*, 208-212.
4. Cohen, D.A., Pascual-Leone, A., Press, D.Z., and Robertson, E.M. (2005). Off-line learning of motor skill memory: A double dissociation of goal and movement. PNAS *102*, 18237-18241.
5. Spencer, R.M., Sunm, M., and Ivry, R.B. (2006). Sleep-dependent consolidation of contextual learning. Current biology : CB *16*, 1001-1005.
6. Brown, R.M., and Robertson, E.M. (2007). Off-Line Processing: Reciprocal Interactions between Declarative and Procedural Memories
10.1523/JNEUROSCI.2799-07.2007. J. Neurosci. *27*, 10468-10475.
7. Bonstrup, M., Iturrate, I., Thompson, R., Cruciani, G., Censor, N., and Cohen, L. (2019). A rapid form of offline consolidation in skill learning. Current biology : CB.
8. Folkard, S., and Monk, T.H. (1980). Circadian rhythms in human memory. British Journal of Psychology *71*, 295-307.
9. Robertson, E.M. (2012). New insights in human memory interference and consolidation. Current biology : CB *22*, R66-71.
10. Stockinger, C., Thurer, B., Focke, A., and Stein, T. (2015). Intermanual transfer characteristics of dynamic learning: direction, coordinate frame, and consolidation of interlimb generalization. Journal of neurophysiology *114*, 3166-3176.
11. Robertson, E.M. (2018). Memory instability as a gateway to generalization. PLoS biology *16*, e2004633.
12. Herszage, J., and Censor, N. (2018). Modulation of Learning and Memory: A Shared Framework for Interference and Generalization. Neuroscience *392*, 270-280.
13. Lee, J.L. (2008). Memory reconsolidation mediates the strengthening of memories by additional learning. Nature neuroscience *11*, 1264-1266.
14. Lee, J.L. (2009). Reconsolidation: maintaining memory relevance. Trends in neurosciences *32*, 413-420.
15. Hupbach, A., Gomez, R., Hardt, O., and Nadel, L. (2007). Reconsolidation of episodic memories: a subtle reminder triggers integration of new information. Learning & memory *14*, 47-53.
16. Cai, D.J., Aharoni, D., Shuman, T., Shobe, J., Biane, J., Song, W., Wei, B., Veshkini, M., La-Vu, M., Lou, J., et al. (2016). A shared neural

ensemble links distinct contextual memories encoded close in time. Nature *534*, 115-118.

17. Shima, K., Isoda, M., Mushiake, H., and Tanji, J. (2007). Categorization of behavioural sequences in the prefrontal cortex. Nature *445*, 315-318.
18. Hardwick, R.M., Rottschy, C., Miall, R.C., and Eickhoff, S.B. (2013). A quantitative meta-analysis and review of motor learning in the human brain. NeuroImage *67*, 283-297.
19. Martin, A.E., and Doumas, L.A. (2017). A mechanism for the cortical computation of hierarchical linguistic structure. PLoS biology *15*, e2000663.
20. Brainard, D.H. (1997). The Psychophysics Toolbox. Spatial vision *10*, 433-436.
21. Oldfield, R. (1971). The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia *9*, 97-113.
22. Robertson, E.M. (2009). From creation to consolidation: a novel framework for memory processing. PLoS biology *7*, e19.
23. Brown, R.M., and Robertson, E.M. (2007). Inducing motor skill improvements with a declarative task. Nature neuroscience *10*, 148-149.
24. Breton, J., and Robertson, E.M. (2017). Dual enhancement mechanisms for overnight motor memory consolidation. Nature human behaviour *1*.
25. Muellbacher, W., Ziemann, U., Wissel, J., Dang, N., Kofler, M., Facchini, S., Boroojerdi, B., Poewe, W., and Hallett, M. (2002). Early consolidation in human primary motor cortex. Nature *415*, 640-644.
26. Walker, M.P., Brakefield, T., Hobson, J.A., and Stickgold, R. (2003). Dissociable stages of human memory consolidation and reconsolidation. Nature *425*, 616-620.
27. Nissen, M.J., and Bullemer, P. (1987). Attentional requirements of learning: evidence from performance measures. Cognitive Psychology *19*, 1-32.
28. Robertson, E.M. (2007). The serial reaction time task: implicit motor skill learning? J Neurosci *27*, 10073-10075.
29. Chafee, M.V., and Ashe, J. (2007). Intelligence in action. Nature neuroscience *10*, 142-143.
30. Press, D.Z., Casement, M.D., Pascual-Leone, A., and Robertson, E.M. (2005). The time course of off-line motor sequence learning. Brain research. Cognitive brain research *25*, 375-378.
31. Robertson, E.M., Press, D.Z., and Pascual-Leone, A. (2005). Off-line learning and the primary motor cortex. J Neurosci *25*, 6372-6378.
32. Galea, J.M., Albert, N.B., Ditye, T., and Miall, R.C. (2010). Disruption of the dorsolateral prefrontal cortex facilitates the consolidation of procedural skills. Journal of cognitive neuroscience *22*, 1158-1164.
33. Shibata, K., Sasaki, Y., Bang, J.W., Walsh, E.G., Machizawa, M.G., Tamaki, M., Chang, L.H., and Watanabe, T. (2017). Overlearning hyperstabilizes a skill by rapidly making neurochemical processing inhibitory-dominant. Nature neuroscience *20*, 470-475.

34. Cohen, D.A., and Robertson, E.M. (2011). Preventing interference between different memory tasks. Nature neuroscience *14*, 953-955.
35. Willingham, D.B., Nissen, M.J., and Bullemer, P. (1989). On the development of procedural knowledge. J Exp Psychol Learn Mem Cogn *15*, 1047-1060.
36. Boyd, L.A., and Winstein, C.J. (2001). Implicit motor-sequence learning in humans following unilateral stroke: the impact of practice and explicit knowledge. Neurosci Lett *298*, 65-69.
37. Willingham, D.B., and Goedert-Eschmann, K. (1999). The relation between implicit and explicit learning: Evidence for parallel development. Psychological Science *10*, 531-534.
38. Levenshtein, V.I. (1965). Binary codes capable of correcting deletions, insertions, and reversals. Cybernetics and Control Theory *10*, 845-848.
39. Tunovic, S., Press, D.Z., and Robertson, E.M. (2014). A physiological signal that prevents motor skill improvements during consolidation. J Neurosci *34*, 5302-5310.