

Simultaneous sensorimotor adaptation and sequence learning

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Abstract Sensorimotor adaptation and sequence learning have often been treated as distinct forms of motor learning. But frequently the motor system must acquire both types of experience simultaneously. Here, we investigated the interaction of these two forms of motor learning by having subjects adapt to predictable forces imposed by a robotic manipulandum while simultaneously reaching to an implicit sequence of targets. We show that adaptation to novel dynamics and learning of a sequence of movements can occur simultaneously and without significant interference or facilitation. When both conditions were presented simultaneously to subjects, their trajectory error and reaction time decreased to the same extent as those of subjects who experienced the force field or sequence independently.

Keywords Motor · Movement · Learning · Sequence · Memory

Introduction

Two aspects of motor learning are the ability to adapt one's force output and the ability to learn a sequence of movements. These aspects of learning are not necessarily dissociated in real behaviors. For instance, when learning to play the piano, people memorize both a sequence of keystrokes and the appropriate force to apply within each musical phrase. In the laboratory, a form of sensorimotor adaptation that is commonly studied is the straightening of whole-arm reach trajectories by subjects experiencing predictable, dynamic (force) perturbations (Shadmehr and Mussa-Ivaldi 1994). Sequence learning, in contrast, is frequently demonstrated by a reduction in reaction time for individual movements in finger tapping tasks (Nissen and Bullemer 1987).

Here, we introduce a paradigm for studying sensorimotor and sequence learning, simultaneously. We gauged their degree of interaction with a 2×2 design, by which we had subjects reach in a force field applied by a manipulandum (or otherwise in null forces), to targets that were implicitly sequenced (or else randomly ordered). We expected that participants given a force field would exhibit transient trajectory deviations relative to subjects given a null field, and that participants given a target sequence would develop lower reaction times than would subjects given random targets. As for subjects given both a sequence and a force field, we adopted the null hypothesis that they would simultaneously exhibit both of the trends described above, without interference or facilitation.

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Materials and methods

Subjects

The 48 right-handed, college-age participants (21.3 ± 1.0 years old, mean \pm SD; 15 males) gave informed consent and were screened for history of neurological illness, epilepsy, seizures, head injuries, and use of psychoactive medications. Ethical approval was obtained through the MIT committee on the use of humans as experimental subjects.

Groups

Subjects were randomly assigned to four groups (each $n = 12$) defined by the combination of Null forces and Random targets (NR), Null forces and Sequenced targets (NS), clockwise Forces and Random targets (FR), or clockwise Forces and Sequenced targets (FS).

Task

The targets were white 1-cm-wide squares appearing on a black background, shown on a vertical monitor above the manipulandum. The handle was represented on the screen as a 0.8-cm-wide red crosshair. Subjects had to complete each 10-cm reach within 1 s of target appearance, and once at the target observe a further 0.5-s hold time. Trial success or failure was indicated by a change in the target color from white to green or red. Subjects performed epochs of 180 baseline trials, 360 test trials, and 180 washout trials. Epochs were separated by 5 min. Care was taken not to refer to any temporal order (either random or sequenced) of the targets.

Targets

Targets were presented at six peripheral locations spaced hexagonally around a seventh, central location. Following each trial the target became the origin for movement to the subsequent target, whose location was restricted according to the arrows shown in Fig. 1b.

Forces

All subjects experienced null (0 N s/m) forces in the baseline and washout epochs, and NR and NS participants received null forces in the test epoch. During the test epochs of FR and FS subjects, the motors generated a

velocity-dependent clockwise force field of 10 N s/m (Fig. 1a). Forces were calculated on-line as $f = B\dot{x}$, where

$$B = \begin{bmatrix} 0 & 10 \\ -10 & 0 \end{bmatrix} \text{ and } \dot{x} \text{ was the velocity.}$$

Sequence

All subjects experienced pseudorandom targets in the baseline and washout epochs, and NR and FR participants received pseudorandom targets in the test epoch. During the test epochs of NS and FS subjects, the targets were ordered according to 20 repetitions of the same 18-target sequence (Fig. 1b), with no interruptions between repetitions.

Test for explicit awareness

Immediately after the experiment, we questioned subjects as to any patterns among the targets. Five participants, all in the NS group, reported feeling that they could anticipate the next target, but only two of these referred this experience to the test epoch. Moreover, none of the participants could reproduce any part of the sequence except for two subjects who drew a sub-sequence of three or four movements that corresponded to part of the 18-target sequence. Whether or not this level of recall satisfies the criterion for sequence “awareness” on the standard 12-item serial reaction time task (Willingham and Goedert-Eschmann 1999), it does suggest a low level of explicit awareness in both the NS and FS groups.

Trajectory error

We defined trajectory error (Caithness et al. 2004) as the total area enclosed by the trajectory plus a straight line joining the centers of the origin and target squares (Fig. 1c).

Reaction time

We defined reaction time using a relative speed threshold (cf. Donchin et al. 2002), specifically the time at which a subject reached 20% of their peak speed (Fig. 1d).

Data reduction

We rejected any trial in which the cursor speed at the time of target appearance had already reached 20% of peak

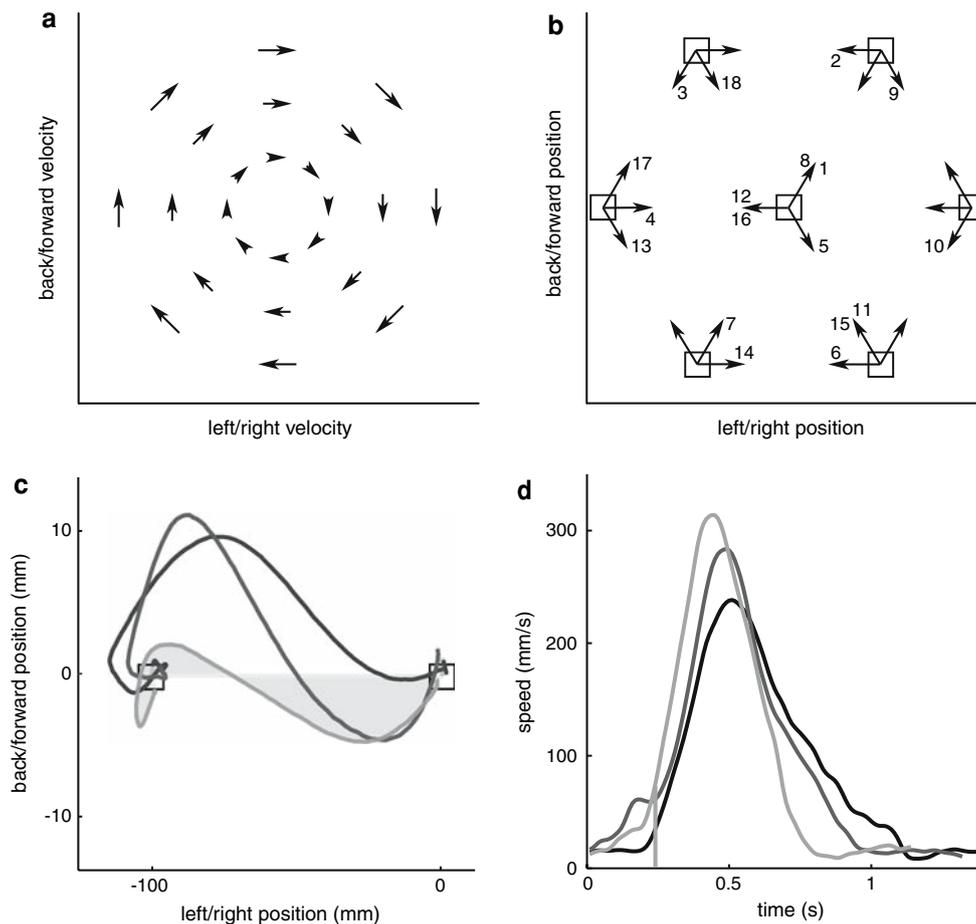


Fig. 1 Sensorimotor adaptation and sequence learning were manipulated independently. **a** Some subjects experienced forces that were proportional to the speed, and perpendicular to the direction, of their movement. **b** Some subjects were presented with a repeating, 18-target sequence in the order shown. Four groups were defined by the combination of a null (N) or force (F) field and a random (R) or sequenced (S) target presentation in the test epoch. **c** As can be seen in the leftward-directed trajectories of this sample FR subject, paths were deviated in the direction of the field but more so at the beginning

of the epoch (black) than at the end (gray). We measured such sensorimotor adaptation using the area enclosed by the trajectory and a straight line joining the origin and target. **d** As can be seen in the speed profiles recorded in one direction of movement from this sample NS subject, movements early in the epoch (black) were more delayed than those late in the epoch (gray). We measured such sequence learning using the time at which subjects reached 20% of their peak velocity

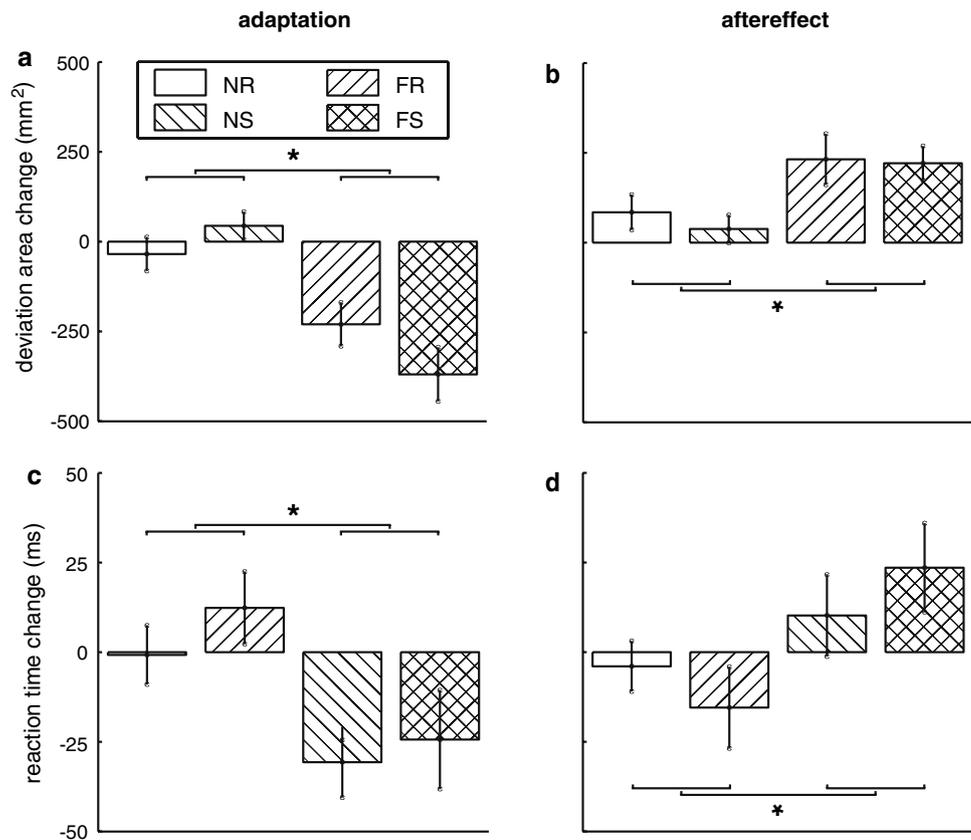
speed on the trial, or in which the combined reaction plus movement time was greater than 2 s. Trials in which the subject failed to reach the target in the allotted 1-s time limit were still included in the analysis.

Comparisons

We tested for changes in performance using two Force \times Sequence ANOVAs. The first ANOVA gauged learning between the beginning and end of the test epoch; the second measured aftereffects between the end of the test epoch and the beginning of the washout epoch. For both of these ANOVAs, we computed each subject's difference score,

taking the “beginning” or “end” of an epoch to be the set of trials including the first or last trial, respectively, along each unique path between origin and target squares. As there were 15 unique movement paths in the sequence (Fig. 1b), the difference score contrasted the average performance between two sets of 15 trials (cf. Shadmehr et al. 1998). This selection of trials allowed us to examine the effects of Force and Sequence on adaptation and after-effects without confounds of unbalanced movement origin and target frequency, which is important given the known variation of trajectory error and aftereffect magnitude with target direction and position (Shadmehr and Brashers-Krug 1997; Goedert and Willingham 2002). All significant effects (at $p < 0.01$) are reported.

Fig. 2 Sensorimotor adaptation and sequence learning occurred independently. **a** FR and FS subjects adapted to the force field, as shown by the difference in trajectory error between the beginning and end of the test epoch (mean \pm SEM). **b** These participants internalized the forces, as depicted by the difference in error between the end of the test epoch and the beginning of the washout epochs. **c** NS and FS subjects adapted to the sequence, as shown by the difference in reaction time over the test epoch. **d** These participants experienced sequence-specific procedural skill learning, as depicted by the difference in times between the test and washout epochs. (Note the reverse ordering of FR and NS in **c** and **d**.)



Results

We first confirmed that sensorimotor adaptation and sequence learning could occur separately. Figure 1c, d demonstrates such trends for sample subjects who experienced either a force field or a sequence, but not both, during the test epoch. Among participants, given a force field and random targets (FR), sensorimotor adaptation was evident as a gradual decline in deviation area (Fig. 1c). Among subjects given null forces and sequenced targets (NS), sequence learning was evident as a reduction in reaction times (Fig. 1d).

In Figure 2 we present average performance changes for all four groups of subjects (NR, NS, FR, and FS). We found that application of a force field in the test epoch of the FR and FS group was associated with an initial increase in trajectory error that declined as both these groups adapted to the forces (Fig. 2a). We applied a Force \times Sequence ANOVA to the difference in all four groups' performance between the beginning and end of the epoch (see "Materials and methods"). Although the FS group appeared to adapt more than the FR subjects, the only significant effect was that of Force ($F_{(1,44)} = 28.37$, $p < 0.0001$). We estimated the degree to which the FR and FS subjects had actually internalized the forces by computing aftereffects (Shadmehr and Mussa-Ivaldi 1994), i.e., the change in

performance between the end of the test epoch and the beginning of the null-field washout epoch (Fig. 2b). FR and FS subjects displayed the only prominent aftereffects, as confirmed by a significant effect of Force ($F_{(1,44)} = 9.78$, $p < 0.01$). In neither the adaptation to the forces nor the aftereffects following removal of forces were there any significant effects of Sequence. Acquisition of a target sequence was not associated with any significant change in simultaneous sensorimotor adaptation.

Introduction of an implicit sequence in the test epoch of the NS and FS groups was associated with a gradual decrease in their reaction times (Fig. 2c). We applied a Force \times Sequence ANOVA to compare all four groups' change in reaction time between the beginning and end of the epoch. The only significant effect was that of Sequence ($F_{(1,44)} = 9.71$, $p < 0.01$). To gauge the degree of sequence-specific learning (Nissen and Bullemer 1987; Willingham et al. 1989), we computed the change in reaction time between the end of the test epoch and the beginning of the random-target washout epoch (Fig. 2d). The NS and FS groups displayed the only positive reaction time aftereffects. Although the aftereffect appeared to be greater for the FS than the NS group, statistically the only significant effect was that of Sequence ($F_{(1,44)} = 6.10$, $p < 0.01$). In neither the learning of the sequence nor the aftereffects following removal of sequenced targets were

there any significant effects of Force. Adaptation to a force field was not associated with any significant change in simultaneous sequence learning.

Discussion

Our paradigm allows for simultaneous, and independent, learning of novel sensorimotor mappings and sequences (Fig. 1). When both a dynamic perturbation and an implicit target sequence were presented to participants, they showed as much of a decline in trajectory error and reaction time as subjects who experienced the force field or sequence independently (Fig. 2a, c). After learning, trajectory error and reaction time aftereffects were evident among participants who had earlier experienced a force field or a sequence, respectively, and regardless of whether they had simultaneously experienced sequenced targets or forces (Fig. 2b, d).

The presence of aftereffects (Fig. 2b, d) suggests that sensorimotor adaptation and sequence learning lead to predictive motor commands, specifying required force output and movement direction, respectively. The observed independence of the two types of learning implies the independence of these two types of predictions. The fact that some brain areas such as the premotor cortex (Jenkins et al. 1994; Shadmehr and Holcomb 1997) and cerebellum (Ghilardi et al. 2000) can be modulated in both tasks may simply be due to common processing of, for example, sensory input that is required by, but not specific to, each prediction.

Indeed, different subsystems of motor memory have been proposed to underlie these phenomena (Hikosaka et al. 1999; Doyon et al. 2003). According to models and supporting evidence, acquisition and integration of sequence knowledge may depend on a frontal-subcortical network including nodes in the supplementary motor area, basal ganglia structures, and ventral anterior thalamus (e.g., Schendan et al. 2003; Shin and Ivry 2003; Lehéricy et al. 2005). In contrast, adaptation to a modified sensorimotor environment may rely more on a network including nodes in the premotor cortex, cerebellum and a different set of thalamic structures (e.g., Shadmehr and Holcomb 1997; Imamizu et al. 2000; Kassardjian et al. 2005).

Only a few, recent studies have investigated interactions between these two modes of learning. First, Seidler (2004) presented participants with a variety of consecutive visuomotor tasks and then a movement sequence, each involving center-out joystick movements. Subjects not only generalized their learning across the visuomotor perturbations, but also experienced a decline in reaction times on the sequence task that might have indicated a general

performance enhancement. But because this decline in reaction times was not specific to sequenced trials, and because the tasks were not simultaneous, Seidler (2004) neither supports nor addresses the possibility of direct interaction between sensorimotor adaptation and sequence learning.

Second, Watanabe et al. (2006) employed a task that did involve simultaneous sequence and sensorimotor learning, but did not investigate the relationship between these forms of learning. Instead of manipulating the presence of an (explicit) sequence and a sensorimotor perturbation (a visuomotor rotation), they divided their subjects according to putative awareness of the perturbation, and asked what effect this awareness had on sequence learning. Watanabe et al. (2006) found that sequence completion time decreased regardless of subjects' awareness of the perturbation. In contrast, we show that sequence reaction time decreased regardless of subjects' experience of a simultaneous perturbation.

Third, Waincott et al. (2005) also used a task involving simultaneous sensorimotor and sequence learning. Their subjects experienced forces dependent not only on reach direction but also on the serial order of the movement within a simple, explicit sequence of alternating "even" and "odd" movements. The authors developed a generalization function describing the transmission of error information from trial to trial as a function of movement direction and number. Their results suggest that two models of external forces can be acquired relatively independently of simultaneous sequential information about each movement. However, their experiment neither allowed the perturbation to be learned separately from the sequence, nor addressed the learning of the even-odd "sequence" per se. Nevertheless, their finding that serial order cues do not facilitate adaptation to multiple dynamical conditions is consistent with our evidence for no significant interaction between sensorimotor adaptation and sequence learning.

In this study we have not considered interactions between sensorimotor adaptation and sequence learning at the stage of motor consolidation. Studies of sensorimotor adaptation have defined consolidation as a resistance to retrograde interference (Brashers-Krug et al. 1996; Shadmehr and Brashers-Krug 1997) while investigations of sequence learning have conventionally defined it as off-line improvement in performance (Karni et al. 1998; Korman et al. 2003). There may be commonalities to these two phenomena. For instance, both dynamic and sequence learning appear to require a minimum of 2–6 h post acquisition to consolidate by the above definitions (Brashers-Krug et al. 1996; Press et al. 2005).

But as sensorimotor adaptation and sequence learning have traditionally been studied separately, the relation

between them at the level of motor consolidation remains largely unexplored (Robertson et al. 2004). Indeed, consolidation defined as offline improvement has only recently been reported in dynamic adaptation (Richardson et al. 2006) while consolidation defined as a resistance to interference has been inconsistently found in sequence learning tasks (Goedert and Willingham 2002; Walker et al. 2003). The present study not only demonstrates the ability of the motor system to simultaneously adapt to novel dynamics and to sequence its output, but provides an experimental paradigm for testing subsequent interactions between these forms of motor learning.

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References

- Brashers-Krug T, Shadmehr R, Bizzi E (1996) Consolidation in human motor memory. *Nature* 382:252–255
- Caithness G, Osu R, Bays P, Chase H, Klassen J, Kawato M, Wolpert DM, Flanagan JR (2004) Failure to consolidate the consolidation theory of learning for sensorimotor adaptation tasks. *J Neurosci* 24:8662–8671
- Donchin O, Sawaki L, Madupu G, Cohen LG, Shadmehr R (2002) Mechanisms influencing acquisition and recall of motor memories. *J Neurophysiol* 88:2114–2123
- Doyon J, Penhune V, Ungerleider LG (2003) Distinct contribution of the cortico-striatal and cortico-cerebellar systems to motor skill learning. *Neuropsychologia* 41:252–262
- Ghilardi M, Ghez C, Dhawan V, Moeller J, Mentis M, Nakamura T, Antonini A, Eidelberg D (2000) Patterns of regional brain activation associated with different forms of motor learning. *Brain Res* 871:127–145
- Goedert KM, Willingham DB (2002) Patterns of interference in sequence learning and prism adaptation inconsistent with the consolidation hypothesis. *Learn Mem* 9:279–292
- Hikosaka O, Nakahara H, Rand MK, Sakai K, Lu X, Nakamura K, Miyachi S, Doya K (1999) Parallel neural networks for learning sequential procedures. *Trends Neurosci* 22:464–471
- Imamizu H, Miyauchi S, Tamada T, Sasaki Y, Takino R, Putz B, Yoshioka T, Kawato M (2000) Human cerebellar activity reflecting an acquired internal model of a new tool. *Nature* 403:192–195
- Jenkins IH, Brooks DJ, Nixon PD, Frackowiak RS, Passingham RE (1994) Motor sequence learning: A study with positron emission tomography. *J Neurosci* 14:3775–3790
- Karni A, Meyer G, Rey-Hipolito C, Jezzard P, Adams MM, Turner R, Ungerleider LG (1998) The acquisition of skilled motor performance: fast and slow experience-driven changes in primary motor cortex. *Proc Natl Acad Sci USA* 95:861–868
- Kassardjian CD, Tan YF, Chung JY, Heskin R, Peterson MJ, Broussard DM (2005) The site of a motor memory shifts with consolidation. *J Neurosci* 25:7979–7985
- Korman M, Raz N, Flash T, Karni A (2003) Multiple shifts in the representation of a motor sequence during the acquisition of skilled performance. *Proc Natl Acad Sci USA* 100:12492–12497
- Lehéricy S, Benali H, Van de Moortele P-F, Péligrini-Issac M, Waechter T, Ugurbil K, Doyon J (2005) Distinct basal ganglia territories are engaged in early and advanced motor sequence learning. *Proc Natl Acad Sci USA* 102:12566–12571
- Nissen MJ, Bullemer PT (1987) Attentional requirements for learning: Evidence from performance measures. *Cognit Psychol* 19:1–32
- Press DZ, Casement MD, Pascual-Leone A, Robertson EM (2005) The time course of off-line motor sequence learning. *Brain Res Cogn Brain Res* 25:375–378
- Richardson AG, Overduin SA, Valero-Cabre A, Padoa-Schioppa C, Pascual-Leone A, Bizzi E, Press DZ (2006) Disruption of primary motor cortex before learning impairs memory of movement dynamics. *J Neurosci* 26:12466–12470
- Robertson EM, Pascual-Leone A, Miall RC (2004) Current concepts in procedural consolidation. *Nat Rev Neurosci* 5:1–7
- Schendan HE, Searl MM, Melrose RJ, Stern CE (2003) An fMRI study of the role of the medial temporal lobe in implicit and explicit sequence learning. *Neuron* 37:1013–1025
- Seidler RD (2004) Multiple motor learning experiences enhance motor adaptability. *J Cogn Neurosci* 16:65–73
- Shadmehr R, Brashers-Krug T (1997) Functional stages in the formation of human long-term motor memory. *J Neurosci* 17:409–419
- Shadmehr R, Holcomb HH (1997) Neural correlates of motor memory consolidation. *Science* 277:821–825
- Shadmehr R, Mussa-Ivaldi FA (1994) Adaptive representation of dynamics during learning of a motor task. *J Neurosci* 14:3208–3224
- Shadmehr R, Brandt J, Corkin S (1998) Time-dependent motor memory processes in amnesic subjects. *J Neurophysiol* 80:1590–1597
- Shin JC, Ivry RB (2003) Spatial and temporal sequence learning in patients with Parkinson's disease or cerebellar lesions. *J Cogn Neurosci* 15:1232–1243
- Wainscott SK, Donchin O, Shadmehr R (2005) Internal models and contextual cues: Encoding serial order and direction of movement. *J Neurophysiol* 93:786–800
- Walker MP, Brakefield T, Hobson JA, Stickgold R (2003) Dissociable stages of human memory consolidation and reconsolidation. *Nature* 425:616–620
- Watanabe K, Ikeda H, Hikosaka O (2006) Effects of explicit knowledge of workspace rotation in visuomotor sequence learning. *Exp Brain Res* 174:673–678
- Willingham DB, Goedert-Eschmann K (1999) The relation between implicit and explicit learning: Evidence for parallel development. *Psychol Sci* 10:531–534
- Willingham DB, Nissen MJ, Bullemer P (1989) On the development of procedural knowledge. *J Exp Psychol Learn Mem Cogn* 15:1047–1060