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Distinct contribution of the cortico-striatal and cortico-cerebellar systems to motor skill learning

Julien Doyon [a,c,*], Virginia Penhune [b], Leslie G. Ungerleider [c]

[a] *Department of Psychology, University of Montreal, P.O. Box 6128, Downtown Station, Montreal, Que., Canada H3C3J7*
[b] *Department of Psychology, Concordia University, 7141 Sherbrooke West, Montreal, Que., Canada H4BIR6*
[c] *Laboratory of Brain and Cognition, NIMH, NIH, Bethesda, MD, USA*

Abstract

This review paper focuses on studies in healthy human subjects that examined the functional neuroanatomy and cerebral plasticity associated with the learning, consolidation and retention phases of motor skilled behaviors using modern brain imaging techniques. Evidence in support of a recent model proposed by Doyon and Ungerleider [Functional Anatomy of Motor Skill Learning. In: Squire LR, Schacter DL, editors. Neuropsychology of Memory. New York: Guilford Press, 2002.] is also discussed. The latter suggests that experience-dependent changes in the brain depend not only on the stage of learning, but also on whether subjects are required to learn a new sequence of movements (motor sequence learning) or learn to adapt to environmental perturbations (motor adaptation). This model proposes that the cortico-striatal and cortico-cerebellar systems contribute differentially to motor sequence learning and motor adaptation, respectively, and that this is most apparent during the slow learning phase (i.e. automatization) when subjects achieve asymptotic performance, as well as during reactivation of the new skilled behavior in the retention phase.

Keywords: Cortico-striatal systems; Cortico-cerebellar systems; Motor skill learning; Motor required learning; Motor adaptation; PET; EURI

1. Introduction

In everyday life, we go about activities using a variety of motor skills that have been acquired gradually through practice and interactions with our environment. These include, for example, the use of smooth co-articulation of finger movements into a specific sequence (e.g. when playing a musical instrument like the piano), of regular multi-joint movement synergies (e.g. during reaching and grasping of small objects), and of a smoothly executed eye-body coordinated action (e.g. in playing sports such as golf). To study the time course, the biomechanics, the learning mechanisms (e.g. implicit versus explicit) and the neural substrates mediating our ability to learn such skilled behaviors in the laboratory, investigators have used experimental paradigms that fall into two categories: the first measures the incremental acquisition of movements into a well-executed behavior (motor sequence learning), whereas the second tests our capacity to compensate for environmental changes (motor adaptation) (e.g. [8,11,15,18,31,32,57,58]). Operationally defined, these two forms of motor skill learning refer to the process by which movements, either produced alone or in a sequence, come to be performed effortlessly through repeated practice [68].

In both animals and humans, motor skill learning is usually measured by a reduction in reaction time and the number of errors, and/or by a change in movement synergy and kinematics (e.g. [5–7,24,30,57,60] for reviews). For some skills, such as learning to play a new melody on a musical instrument, early learning can be facilitated using explicit knowledge (i.e. requiring thought). For most motor skills, however, motor performance is ultimately over-learned to a point where it can be performed implicitly (i.e. without conscious recollection). As opposed to other forms of memory (e.g. episodic memory), these changes in performance are known to evolve slowly, requiring many repetitions over several training sessions [30,60]. Indeed, psychophysical studies have demonstrated that the incremental acquisition of motor skills follows two distinct stages: first, an early, fast learning stage in which considerable improvement in performance can be seen within a single training session; and second, a later, slow stage in which further gains can be observed across several sessions (and even weeks) of practice [4,32,42]. In addition to these two stages, an intermediate phase corresponding to a consolidation period of the motor routine has recently been proposed, as gains in performance have been reported following a latent period of

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* Corresponding author. Tel.: +1-514-343-6502; fax: +1-514-343-5787.
E-mail address: julien.doyon@umontreal.ca (J. Doyon).

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more than 6 h after the first training session without additional practice on the task (e.g. [26,33]). Additionally, there is little or no interference from a competing task, provided it is administered beyond a critical time window of about 4–6 h [4,49,57]. Finally, with extended practice, the skilled behavior is thought to become resistant both to interference and to the simple passage of time [45]. Once over-learned, a motor skill can thus be readily retrieved with reasonable performance despite long periods without practice.

Based on animal and human work, several brain structures, including the striatum, cerebellum, and motor cortical regions of the frontal lobe have been thought to be critical for the acquisition and/or retention of motor skilled behaviors (e.g. [2,5,9,10,14,19,30,53,62,64,65] for reviews). Anatomical studies have demonstrated that these structures form two distinct cortical-subcortical circuits: a cortico-basal ganglia-thalamo-cortical loop and a cortico-cerebello-thalamo-cortical loop [37,46,61] (see Fig. 1). Evidence supporting the role of these cortical-subcortical systems in motor skill learning has come from impairments found in patients with striatal dysfunction (e.g. in Parkinson's or Huntington's disease), with damage to the cerebellum, or with a circumscribed lesion involving the frontal motor areas (e.g. [1,6,7,13,22,44,52,69]). Further support has come from neurophysiological studies (e.g. [21,42,61]), as well as from lesion experiments in rodents (e.g. [36,67] for a review) and non-human primates (e.g. [35,38]). More recently, modern brain imaging techniques have allowed us to confirm not only the functional contribution of both cortico-striatal and cortico-cerebellar systems in motor skill learning, but also to identify in vivo the neural substrates mediating this type of memory and the functional dynamic changes that occur over the entire course of the acquisition process (e.g. see [5,9,10,30,64,65] for reviews).

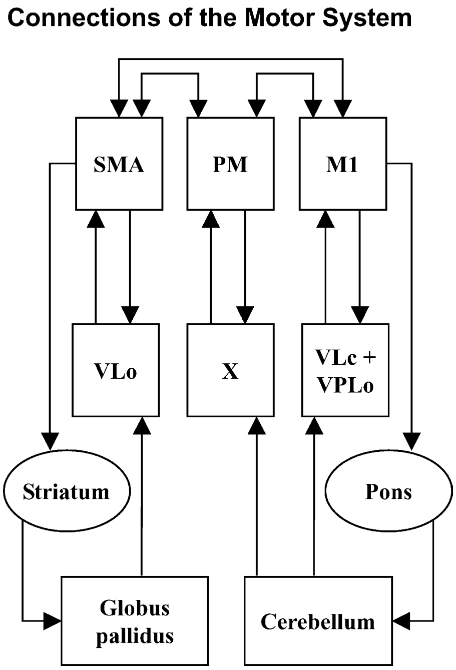

Fig. 1. Diagram illustrating the major cortical and subcortical structures involved in motor skill learning, and their interconnections. These structures are organized into two main circuits: a cortico-striato-thalamo-cortical loop and a cortico-cerebello-thalamo-cortical loop. Dynamic changes within these loops occur during motor sequence learning and motor adaptation (see text for more details): SMA, supplementary motor area; PM, premotor cortex; M1, primary motor cortex; Vlo, ventrolateral nucleus, oral division; X, area X; VLc, ventrolateral nucleus, caudal division; VPLo, ventralposterior nucleus, oral division.

In this review paper, we will discuss the results of studies in healthy human subjects that examined the functional anatomy and the cerebral plasticity associated with the learning, consolidation and retention phases of motor skilled behaviors using brain imaging technology, such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). Previous literature reviews have often pointed out the heterogeneity in the results obtained with this methodological approach [5,10,15,65]. However, Doyon and Ungerleider [10] have recently proposed that much of the variability in the pattern of results across studies can be accounted for if one considers the type of motor task and the learning phase at which subjects are scanned. The latter model suggests that the cortico-striatal and cortico-cerebellar systems contribute differentially to motor sequence learning and motor adaptation, respectively, and that this is most apparent during the slow learning phase (i.e. automatization) when subjects achieve asymptotic performance, as well as during reactivation of the new skilled behavior in the retention phase. In support of this model, we will put emphasis on the results of our own series of experiments with tasks designed to investigate the neural substrate mediating motor sequence learning, and will also describe in more detail some of the studies that focused on the neuronal system involved in motor adaptation.

2. Neural correlates of motor sequence learning

In brain imaging investigations designed to better understand the neuroanatomy of motor skill learning, subjects are typically required to produce a sequence of movements that they know explicitly before scanning [9,31,32,54,56], to discover a particular sequence by trial and error [27–29,50,63], or to follow the display of visual stimuli appearing sequentially on a screen [6,9,15,23,47,48]. The motor responses in those tasks involve finger-to-thumb opposition movements (e.g. [31,32,56]), finger presses on response boxes (e.g. [15,47,48]) or movements of the whole arm (e.g. [8,16]). However, other sequence tasks, including rotor pursuit [17,18], the tracing of cut-out mazes [66], and the practice of repeating two-dimensional trajectorial movements [55] have also been employed in previous brain imaging studies to examine this form of motor learning.

Using such paradigms, changes in activity in both cortico-striatal and cortico-cerebellar circuits have been reported. For example, activity in the striatum and the cerebellum has been associated with both the encoding of motor sequence programs (e.g. [8,15,27,28,47,54,56,63]) and the retrieval of learned sequences of movements [3,27,28]. On the few occasions in which learning-related activation in the cerebellum has not been observed [15,17,47], the negative findings have been thought to result from the limited field of view of the PET camera, thereby precluding full visualization of the inferior potions of the cerebellum [5,65]. Either or both the striatum and cerebellum, in concert with motor cortical regions, have also been shown to be activated during implicit learning [8,15,47,48], when subjects are practicing a motor sequence for which they have complete explicit knowledge [9,15,54,56,63], and during tasks in which subjects need to utilize problem-solving strategies to find a repeating sequence of finger movements [27,28,63].

Changes in activity in both the striatum and cerebellum have also been observed at different stages of the acquisition process of motor sequence learning. Numerous studies have demonstrated that the cerebellum is active during the fast learning phase [8,9,27], but that this activity decreases with practice and may become undetectable when the sequential movements are well learned [9,12,18,28,55,63]. Some investigators have also reported striatal activations in the early acquisition phase of motor sequence learning, when subjects have to rely more strongly on the use of cognitive strategies and working memory [27,28,63]. However, the results of other studies have shown that the striatum is significantly more activated when subjects have reached asymptotic performance on the task than when they are at the beginning of the acquisition process (e.g. [8,18,28]). Furthermore, unlike the pattern of activity changes in the cerebellum (see next section), no decrease in striatal activity is observed with extended practice. Together, the latter findings suggest that the striatum (and motor cortical areas discussed below) may be critical for the long-term storage of well-learned sequences of movements.

Evidence to support the role of the cortico-striatal system in memory storage comes from a PET study by Grafton et al. [18], who scanned subjects on two separate occasions: (1) on day 1, while they were learning to keep a stylus on a rotating disk (rotor pursuit task); and (2) on day 2, after they had completed an extensive practice session on the task. On day 1, learning-dependent changes were observed in the ipsilateral anterior cerebellum and parasagittal vermal area. Additional activations were seen in the primary motor cortex (M1) contralaterally, in the supplemental motor area (SMA) bilaterally, and in the cingulate and inferior parietal regions. By contrast, on day 2, after the subjects had received additional practice and achieved an asymptotic level of performance, activations were observed in the putamen bilaterally, as well as in parietal cortex bilaterally and the left inferior premotor area, but not in the cerebellum.

Other evidence supporting the role of the cortico-striatal system in storing well-learned behaviors come from our recent fMRI study [9]. Subjects were scanned during motor sequence learning using a version of the serial reaction time task, in which they were required to press as quickly as possible one of four buttons corresponding to the location of a red circle that appeared on a screen (Fig. 2a). The stimuli were either presented in an unpredictable order (random condition [R]) or followed a repeating 10-item sequence of movements that was taught to each subject prior to scanning (explicit learning condition [L]). Subjects were scanned over three separate sessions with intervening periods of practice of the 10-item sequence administered just prior to the second and third scan session.

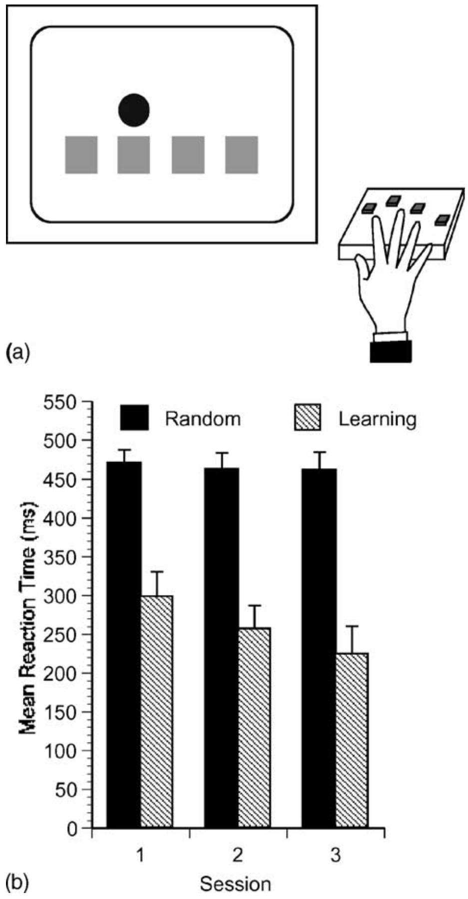

Fig. 2. (a) Materials and stimuli used in the motor sequence learning task [41]. The stimuli consisted of four blue boxes that were aligned in a horizontal row, and of a red circle that appeared above one of the boxes on each trial. These stimuli were projected on a screen located in front of the subject, and were reflected through a mirror embedded within the head coil. Subjects made responses using an optical-fiber device; (b) subjects' mean reaction time in both Random and Explicit Learning conditions across the three scanning sessions.

As a group, the subjects showed consistent improvement in executing the sequence of finger movements across scanning sessions (Fig. 2b). The results revealed that subjects were faster to respond in the L than in the R condition. The results of the contrast between the L and R conditions across sessions revealed the existence of dynamic changes in activation within the cerebellum and other motor-related structures. First, a significant activation in Lobule V and Crus1 of

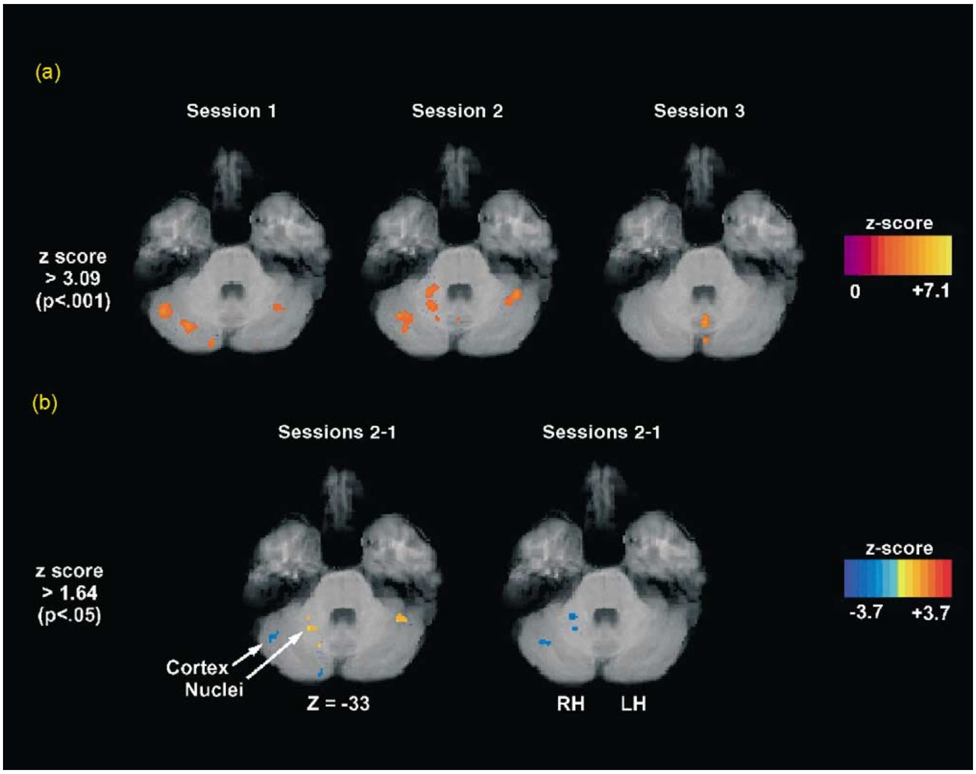

Fig. 3. Merged fMRI-MRI horizontal sections through the cerebellum ($z = -33$) illustrating the results of the multiple regression analysis averaged over 9 subjects. The results are shown as *z*-score maps and reveal both increases (orange) and decreases (blue) in BOLD signal over the three scanning sessions, and are displayed overlaid on a co-planar, high resolution MRI scan of a single subject. In the horizontal sections, the *z*-coordinate represents the position of the section relative to the anterior–posterior commissure line. The subject's right cerebellar hemisphere is on the left: (a) significant increases and decreases of activation (*z*-score >3.09, $P < 0.001$) in both the cerebellar cortex (Lobule V and Crus1) and deep nuclei across sessions; (b) results of the subtraction analysis comparing the *z*-score maps obtained in Sessions 2 vs. 1, and in Sessions 3 vs. 2.

the cerebellar cortex, mainly on the right, was seen in both Sessions 1 and 2, but not in Session 3 (Fig. 3a). Furthermore, comparisons between sessions demonstrated that the extent of the area activated in the cerebellar cortex declined significantly from Session 1 to 2, and again from Session 2 to 3 (Fig. 3b). By contrast, activations in the deep cerebellar nuclei, and in the right dentate nucleus in particular, were observed in Session 2 only (Fig. 3a), thereby yielding a significant increase in activation from Session 1 to Session 2, followed by a significant decline in activation in Session 3 (Fig. 3b). Thus, while the cerebellar cortex was activated at the beginning of learning, involvement of the dentate nucleus was seen only later in the acquisition process, suggesting that the contributions of the cerebellar cortex and deep nuclei differ in time as a function of the amount of motor sequence practice.

In addition to the experience-dependent shifts of activation in the cerebellum, plastic changes across sessions were also seen in the cerebral cortex and striatum, another subcortical structure frequently associated with motor sequence learning (e.g. [5,20,29,39,48,51]). From Session 1 to Session 2, increases in BOLD signal were observed in anterior cingulate and dorsal premotor cortex, with the activated regions located predominantly on the right (Fig. 4a). A complex pattern of change was seen in the right inferior parietal cortex when Sessions 1 and 2 were compared directly, with some voxels showing an increase in signal but others showing a decrease. Activations within both the right anterior cingulate and premotor regions subsequently declined in Session 3, whereas a further increase in activation was observed in the right inferior parietal region; this activation was located in a slightly more superior region than the one found in the subtraction between Sessions 2 and 1. Thus, changes in activation within the anterior cingulate and dorsal premotor cortex followed the same temporal pattern during learning as found in the dentate nucleus. This suggests that, like the cerebellum, these frontal regions participate in the formation of motor routines mediating the implicit learning associated with practice of an explicitly known sequence of movements.

The drop in activation in the anterior cingulate and dorsal premotor regions in Session 3 was accompanied by increased activation in the striatum (in particular, the putamen), supplementary motor area (SMA), precuneus, and ventrolateral prefrontal cortex in the right hemisphere (Fig. 4b). Increases in activation from Session1 to Session 2, and from Session 2 to Session 3 were also observed in the inferior parietal cortex (Fig. 4a). The latter findings suggest that when a sequence of movements is well learned and its execution has

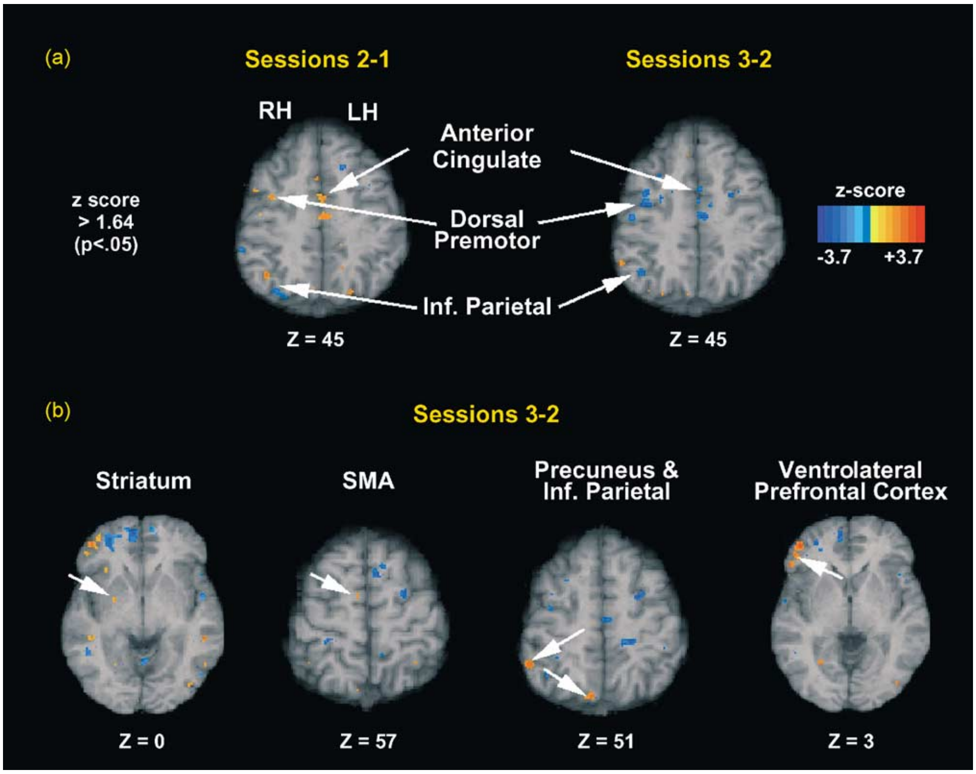

Fig. 4. Merged fMRI-MRI horizontal sections illustrating the results of the subtraction of z-score maps at the level of the cortex and striatum: (a) sessions 2–1: The results yielded an increase (z-score >1.64, $P < 0.05$) in BOLD signal from Session 1 to Session 2 in the right anterior cingulate ($x = 3$; $y = 2$, $z = 45$) and dorsal premotor region ($x = 38$; $y = 3$, $z = 45$). Both an increase and a decrease (z-score <-1.64, $P < 0.05$) in activation was also seen in the right inferior parietal cortex ($x = 40$; $y = -53$, $z = 45$). Sessions 3–2: by contrast, activations within both the right anterior cingulate and premotor regions subsequently declined (blue) in Session 3, while a further increase in activation was observed in the right inferior parietal region ($x = 56$; $y = -5$, $z = 45$); this activation was located in a slightly more superior region; (b) horizontal sections illustrate the significant increase in BOLD signal in the striatum ($x = 23$; $y = 0$, $z = 0$), SMA ($x = 9$; $y = -2$, $z = 57$), precuneus ($x = 9$; $y = -68$, $z = 51$), inferior parietal cortex ($x = 50$; $y = -45$, $z = 51$) and ventrolateral prefrontal cortex ($x = 45$; $y = 36$, $z = 3$).

become “automatic”, a distributed neural system composed of the striatum and related motor cortical regions, but not the cerebellum, may be sufficient to express and retain the learned behavior.

To examine the neural structures involved in long-term retention of a motor skill Penhune and Doyon [45] recently used PET to compare brain regions active during recall of a timed motor sequence with those active during learning of the same skill. Subjects were scanned during learning (LRN) and baseline (ISO) on 3 days: during early learning (day 1), after 5 days of practice (day 5) and after a 4-week delay with no additional practice (Recall). In this task, subjects were required to reproduce a complex timed motor sequence using a single key of the computer mouse. Stimuli were 10-element visual sequences made up of a series of white squares presented sequentially in the center of the computer screen (Fig. 5a). In the LRN condition, the sequences were made up of five long (750 msec) and five short (250 msec) elements with a constant ISI (500 msec). In the ISO condition, the sequences were made up of alternating sequences of either all long or all short elements. Subjects’ key-press and key-release durations were recorded and used to calculate three indices of learning: accuracy, response variance and response asynchrony.

On day 1 subjects were explicitly taught the LRN sequence to a criterion of three consecutive correct repetitions and then scanned during performance of one block of the LRN and ISO conditions. On days 2–4, subjects returned to the laboratory and practiced the LRN sequence without scanning. On day 5 and at Recall subjects were again scanned during performance of one block of the LRN and ISO conditions. Across the 5 days of learning, subjects performed 20 blocks (240 trials) of the LRN sequence and three blocks (36 trials) of the ISO sequences. Behavioral data (Fig. 5b) showed significant improvements in response variance and response asynchrony across the 5 days of learning. No significant differences were found between day 5 of learning and Recall, indicating that once learned the sequences were well retained.

The PET data revealed a network of cortical and subcortical structures that contribute differentially to the early and late phases of motor learning and to delayed recall. Overall, significant changes in activity were seen across days for the LRN condition, but not the ISO baseline. Day 1 results

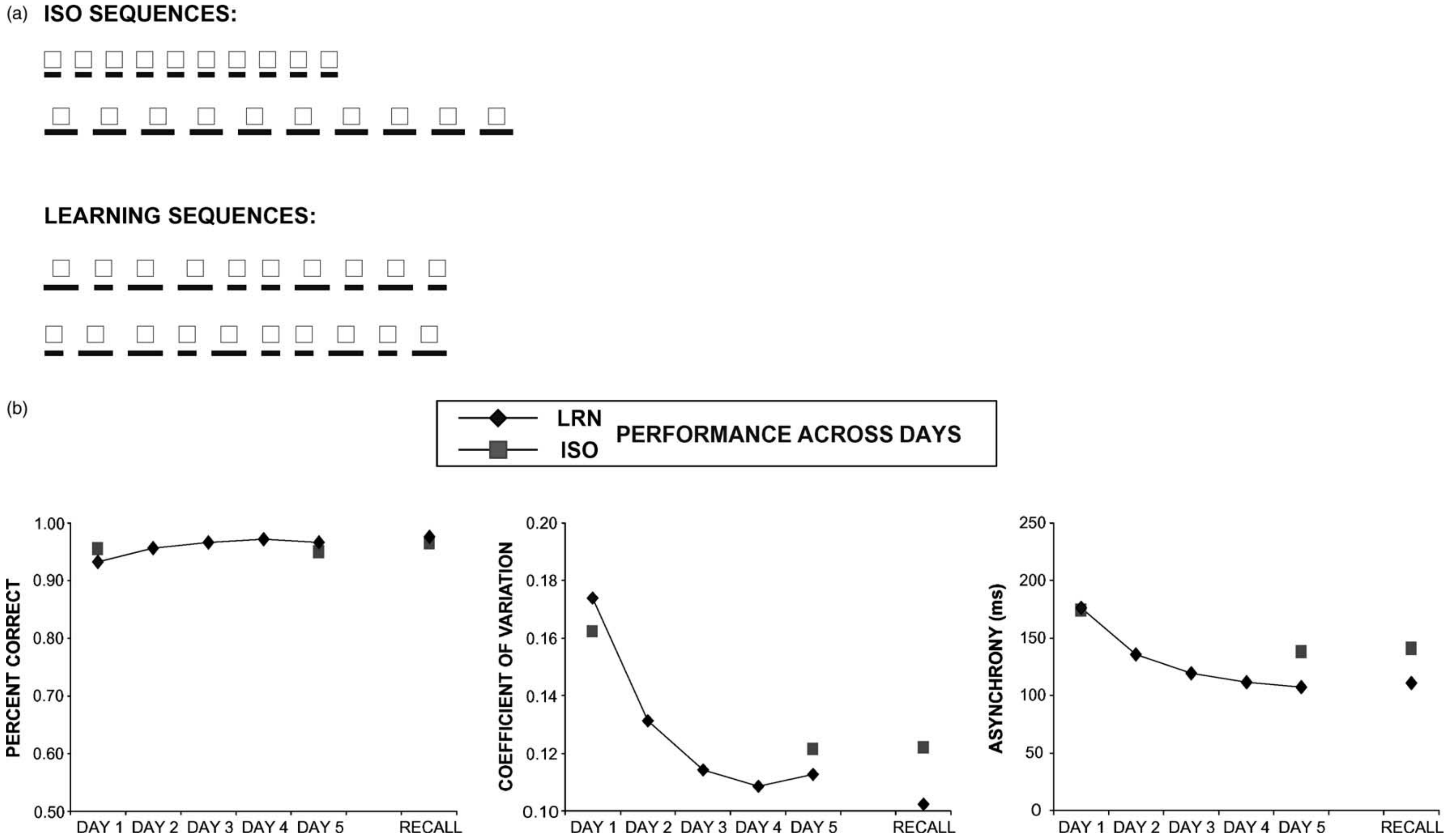

Fig. 5. (a) Illustrates the temporal structure of the isochronous and learned sequences used in the experiment by Penhune and Doyon [45]; (b) illustrates changes in performance for the learned sequences across days of scanning. The left graph shows the change in percent correct; the middle graph shows changes in the coefficient of variation and the right graph shows changes in response asynchrony. © Society for Neuroscience 2002.

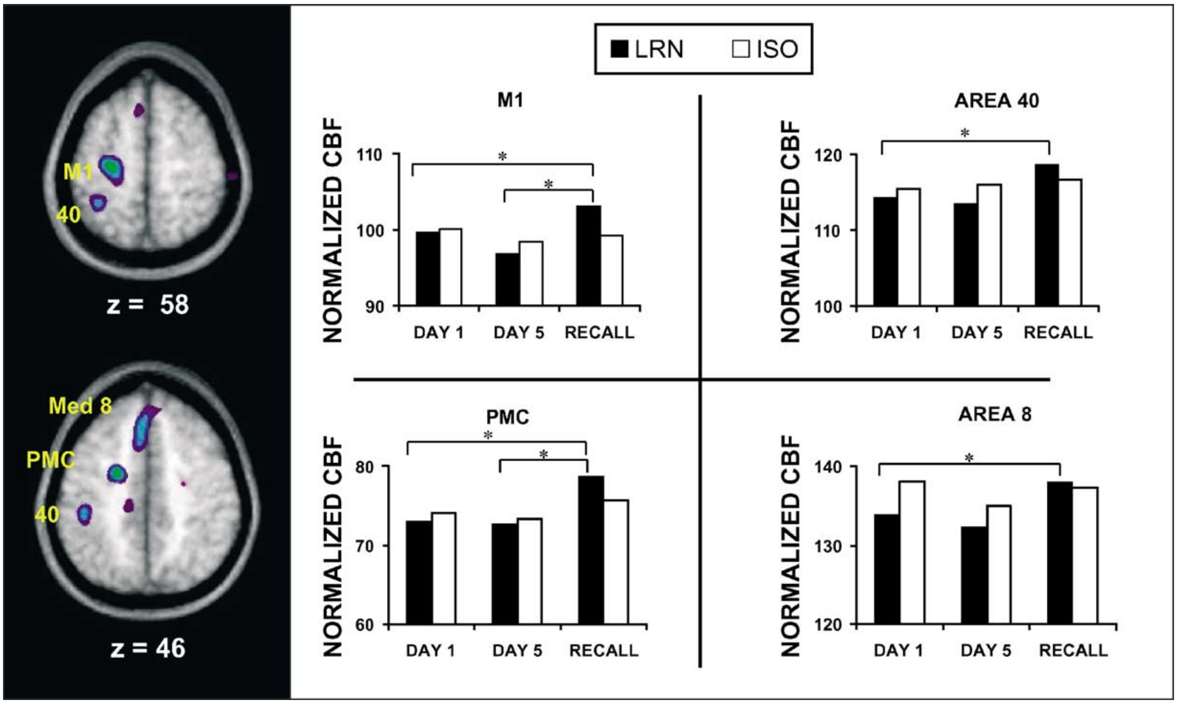

Fig. 6. PET results of the study by Penhune and Doyon [45]. The left panel presents *z*-statistic maps showing significant regions of activation in M1, PMC, parietal cortex and medial area 8 observed at Recall (REC-LRN2). PET data is co-registered with the average MRI of the nine subjects and slice levels are given in the standardized space of Talairach and Tournoux (*t*-value range: 2.5 to 4.8). The right panel graphs changes in nCBF values extracted from each VOI showing significant increases in activity between day 5 and Recall (significant differences are indicated with an asterisk). © Society for Neuroscience 2002.

revealed extensive activation in the cerebellum, including medial areas III/IV and V/VI, as well as lobules VI, VIIIA and VIIIB bilaterally. Day 5 results showed decreased cerebellar activity with increased activity in the basal ganglia (putamen/globus pallidus) and medial frontal lobe. At Recall, significantly greater activation was seen in M1, PMC and the parietal lobe, with no significant activity in the cerebellum or BG (Fig. 6). The results of the subtraction analyses were confirmed by changes in normalized CBF (nCBF). Across days of learning, nCBF in the cerebellum decreased, but increased in the BG between day 1 and day 5. No significant changes were observed across days for the isochronous condition. At Recall, nCBF for the learned sequences increased in M1, PMC and parietal cortex, but not for the isochronous baseline (Fig. 6).

These results are consistent with Doyon and Ungerleider's [10] hypothesis that the cerebellum is most actively involved in early sequence learning, with the BG and cortical regions more actively involved once the sequence is well-learned. During this early phase, cerebellar mechanisms may be involved in adjusting movement kinematics according to sensory input to produce accurate motor output. Once the sequence is well-learned these mechanisms are less actively required and the BG may be involved in the more automatic phase of performance. Finally, relative to learning, delayed recall of a motor sequence appears to be mediated by a predominantly cortical network including M1, the PMC and parietal cortex.

3. Neural correlates of motor adaptation

Several studies have examined the neural systems that are involved in motor adaptation. Tasks have included target reaching with the upper limb, in which the relationship between movements of a manipulandum and cursor on a monitor is reversed [11,25], and pointing to a target with a robotic arm to which different force fields are applied [34,58,59]. In these studies, subjects have been tested during both early in the fast learning process and later when they have achieved asymptotic performance on the task. In addition, in some studies, the relative changes in activation between sessions after variable time intervals have been considered in order to identify the cerebral structures mediating the memory consolidation [58] or the long-term retention [40] of the motor skilled behavior, as well as the ability to inhibit competing motor memories [59].

In a series of PET studies, Shadmehr and Holcomb [58,59] found that, at the beginning of the acquisition process, the capacity of subjects to adapt to a perturbing force field when reaching to randomly presented targets with a robotic arm was associated with increased activity in the left putamen and dorsolateral prefrontal cortex (DLPFC) bilaterally. Later in the fast learning phase of the first training session, when subjects failed to show further gains in performance, decreased activity in the putamen was seen. This pattern of findings in the striatum has been corroborated by Krebs et al. [34] who have used a similar force-field task with PET. In the latter study, early (fast) learning was associated with activations in the ventral striatum, as well as in the contralateral primary sensory cortex and bilateral parietal association areas. By contrast, when the skill was well learned and the subjects produced smooth reaching movements, there was a shift of activity from the striatum and parietal areas to the left motor and premotor regions and to the right cerebellar cortex, suggesting that the cortico-striatal circuit contributes more importantly during early motor adaptation learning, whereas the cortico-cerebellar circuit plays a more critical role during late adaptation learning.

The distinct contribution of the cerebellum to motor adaptation has also been studied by Imamizu et al. [25] and by Flament et al. [11] using fMRI technology, using tasks in which subjects are required to adjust to a change in their sensorimotor coordinate system. Both groups of researchers found an inverse relationship between the subjects' level of performance and the extent of cerebellar activation: better performance on the task was associated with decreased activity in the cerebellum, supporting the notion that this structure participates in the detection and correction of errors. In addition, however, these studies showed a sustained increase of activity in specific areas of the cerebellum with continued practice (i.e. in an area near the posterior superior fissure in Imamizu et al. [25] (Fig. 7), and possibly in the dentate nucleus in Flament et al. [11]), suggesting that these cerebellar regions may be part of the neuronal system engaged in the creation of a long-term representation of the skilled movements necessary to execute these motor adaptation tasks proficiently.

4. Changes in motor representations over the course of learning

A very limited number of imaging studies have investigated the changes in motor representation that occur in the brain over the entire course of motor learning [18,31,32,63]. Consequently, little is known about the neural circuitry mediating the acquisition of new motor skills that become fully mastered. Furthermore, the relative contribution of the cortico-striatal and cortico-cerebellar systems during the consolidation and long-term retention of motor skills remains largely unknown. Nevertheless, one indisputable finding emerging from the studies reviewed above is that practice of a motor task elicits plastic neuronal changes in both cortical and subcortical structures within these two circuits.

A few investigators have proposed that modifications in the representation of motor skills with learning occur within the same cerebral structures used to execute the task. Evidence supporting such a model of plasticity comes, for example, from a PET study by Grafton et al. [17] who showed that learning-dependent changes associated with performance of a rotor pursuit task were located in areas that were part of a more distributed network active during motor execution. Additional evidence stems from Karni et al. [31,32] who have reported the existence of experience-specific reorganization in the primary motor cortex (M1) after 4 weeks of practice on a sequence of finger movements. Finally, the results from Nudo and co-workers [42,43] using conventional intracortical microstimulation techniques in squirrel monkeys are also in accord with this view, inasmuch as the distal forelimb zone of M1 was found to undergo significant changes in cortical representation following extended practice on a reach-and-grasp task requiring skilled finger manipulations.

There is however evidence supporting an alternative view, namely, that the acquisition of motor skills produces representational changes in different cerebral structures over the course of learning (Fig. 8). This model of cerebral plasticity suggests that representational changes depend not only on the stage of learning, but also on whether subjects are required to learn a new sequence of movements (Motor sequence learning) or learn to adapt to environmental perturbations (Motor adaptation). We propose that, depending upon the nature of the cognitive processes (e.g. learning by trial and error, implicit learning, etc.) required during learning, both motor sequence and motor adaptation tasks recruit similar cerebral structures early in the learning phase: the striatum, cerebellum, motor cortical regions (e.g. premotor cortex, SMA, pre-SMA, anterior cingulate), as well as prefrontal and parietal areas. Dynamic interactions between these structures are likely to be critical for establishing the motor routines necessary to learn the skilled motor behavior. As learning progresses after consolidation in the slow learning phase, however, representational changes can be observed. For example, Krebs et al. [34] have demonstrated that learning to adapt to a force field first elicits activation in the striatum, which is followed by a change of activity in the cerebellum, whereas others (e.g. [9,18,45]) have shown that during motor sequence learning the cerebellar contribution to the task precedes that of the striatum. When a motor task is well learned and asymptotic performance is achieved in the automatization phase, the representation of the skill may be distributed in a network of structures that involves either the cortico-cerebellar or the cortico-striatal circuit, depending on the type of learning acquired. We suggest that, at this stage, for motor adaptation, the striatum is no longer necessary for the execution and retention of the acquired skill; increased activity in regions representing this skill will now be present in the cerebellum, parietal cortex and motor-related cortical regions. By contrast, a reverse pattern of plasticity is proposed to occur in motor sequence learning, such that with extended practice, the cerebellum becomes no longer essential, and the long-lasting retention of the skill will now involve representational changes (as

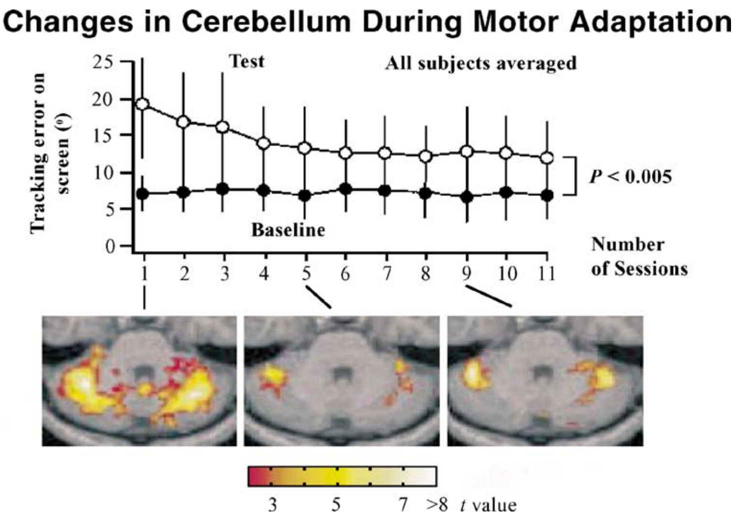

Fig. 7. Behavioral and neural changes associated with learning a motor adaptation task, during which subjects moved a cursor with a computer mouse to reach a randomly moving target on a screen. During the test period, the cursor appeared in a position rotated 120° around the center of the screen, whereas in the baseline period, the cursor was not rotated. Top: mean tracking errors over the training sessions; bottom: *t*-statistic maps showing two types of changes in learning-dependent activity within the cerebellum: one is spread over wide areas of the cerebellum, but decreases proportionally with the reduction in error signal that guides the acquisition of this skill, whereas the second is located in an area near the posterior superior fissure and remains stable even after subjects have reached asymptotic performance (see Session 9). Adapted from [25]. Copyright 2000 by Nature Publishing Group. Reprinted by permission.

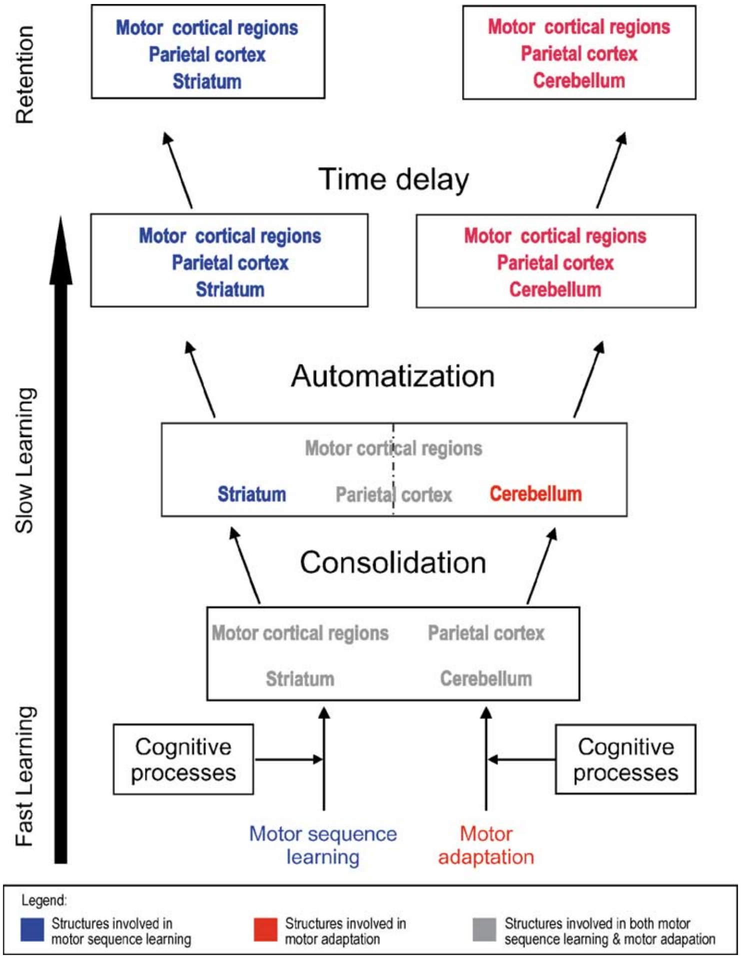

Fig. 8. Model of cerebral plasticity within the cortico-striatal and cortico-cerebellar systems over the course of learning a new sequence of movements (motor sequence learning) or to adapt to environmental perturbations (motor adaptation) (see text for more details) [10].

reflected through increased activity) in the striatum and its associated motor cortical regions, including the parietal and motor-related structures. Finally, when a well-learned motor behavior is elicited again, even after a long delay without practice, it is proposed that the same cortico-subcortical systems are reactivated. For motor sequence learning skills, it is expected that the long-term retention of this type of skill is dependent upon activity maintained in the cortico-striatal system, whereas for motor adaptation skills, the long lasting representation of this form of learning is mediated through the cortico-cerebellar system.

Interestingly, the model of cerebral plasticity during motor learning that we propose here makes predictions that can be tested experimentally. For example, based on the results from Shadmehr and Holcomb [58] who have shown that the cerebellum is critical for consolidating adaptation learning, and those from Imamizu et al. [25] who have demonstrated that this structure constitutes a storage site for this form of motor memory, one would expect that the striatum would play an equally important role in the consolidation of movement sequences, as this structure is known to contribute to the development and maintenance of the final representation of this skill. At present, however, this remains a working hypothesis, awaiting experimental investigation.

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References

[1] Ackermann H, Daum I, Schugens MM, Grodd W. Impaired procedural learning after damage to the left supplementary motor area (SMA). Journal of Neurology Neurosurgery Psychiatry 1996;60:94–7.

[2] Bloedel JR. Functional heterogeneity with structural homogeneity: how does the cerebellum operate? Behavioral and Brain Sciences 1992;15:666–78.

[3] Boecker H, Dagher A, Ceballos-Baumann AO, Passingham RE, Samuel M, Friston KJ, Poline J, et al. Role of the human rostral supplementary motor area and the basal ganglia in motor sequence control: investigations with H2 15O PET. Journal of Neurophysiology 1998;79:1070–80.

[4] Brashers-Krug T, Shadmehr R, Bizzi E. Consolidation in human motor memory. Nature 1996;382:252–5.

[5] Doyon J. Skill learning. In: Schmahmann J D, editor. The cerebellum and cognition. San Diego: Academic Press; 1997. p. 273–94.

[6] Doyon J, Gaudreau D, Laforce RJ, Castonguay M, Bedard PJ, Bedard F, et al. Role of the striatum, cerebellum, and frontal lobes in the learning of a visuomotor sequence. Brain and Cognition 1997;34:218–45.

[7] Doyon J, Laforce RJ, Bouchard JP, Gaudreau D, Roy J, Poirier M, et al. Role of the striatum, cerebellum and frontal lobes in the automatization of a repeated visuomotor sequence of movements. Neuropsychologia 1998;36:625–41.

[8] Doyon J, Owen AM, Petrides M, Sziklas V, Evans AC. Functional anatomy of visuomotor skill learning in human subjects examined with positron emission tomography. European Journal of Neuroscience 1996;8:637–48.

[9] Doyon J, Song AW, Karni A, Lalonde F, Adams MM, Ungerleider LG. Experience-dependent changes in cerebellar contributions to motor sequence learning. Proceedings National Academic Science USA 2002;99:1017–22.

[10] Doyon J, Ungerleider LG. Functional anatomy of motor skill learning. In: Squire LR, Schacter DL, editors. Neuropsychology of Memory. New York: Guilford Press; 2002.

[11] Flament D, Ellermann JM, Kim SG, Ugurbil K, Ebner TJ. Functional magnetic resonance imaging of cerebellar activation during the learning of a visuomotor dissociation task. Human Brain Mapping 1996;4:210–26.

[12] Friston KJ, Frith CD, Passingham RE, Liddle PF, Frackowiak RS. Motor practice and neurophysiological adaptation in the cerebellum: a positron tomography study. Proceedings of the Royal Society London B Biology Science 1992;248:223–8.

[13] Gabrieli JD, Stebbins GT, Singh J, Willingham DB, Goetz CG. Intact mirror-tracing and impaired rotary-pursuit skill learning in patients with Huntington's disease: evidence for dissociable memory systems in skill learning. Neuropsychology 1997;11:272–81.

[14] Georgopoulos AP. Neural aspects of cognitive motor control. Current Opinion on Neurobiology 2000;10:238–41.

[15] Grafton ST, Hazeltine E, Ivry R. Functional mapping of sequence learning in normal humans. Journal of Cognitive Neuroscience 1995;7:497–510.

[16] Grafton ST, Hazeltine E, Ivry RB. Abstract and effector-specific representations of motor sequences identified with PET. Journal of Neuroscience 1998;18:9420–8.

[17] Grafton ST, Mazziotta JC, Presty S, Friston KJ, Frackowiak RS, Phelps ME. Functional anatomy of human procedural learning determined with regional cerebral blood flow and PET. Journal of Neuroscience 1992;12:2542–8.

[18] Grafton ST, Woods RP, Mike T. Functional imaging of procedural motor learning: relating cerebral blood flow with individual subject performance. Human Brain Mapping 1994;1:221–34.

[19] Graybiel AM. Building action repertoires: memory and learning functions of the basal ganglia. Current Opinion on Neurobiology 1995;5:733–41.

[20] Graybiel AM. The basal ganglia. Current Biology 2000;10:R509–11.

[21] Graybiel AM, Aosaki T, Flaherty AW, Kimura M. The basal ganglia and adaptive motor control. Science 1994;265:1826–31.

[22] Harrington DL, Haaland KY, Yeo RA, Marder E. Procedural memory in Parkinson's disease: impaired motor but not visuoperceptual learning. Journal of Clinical Experiment Neuropsychology 1990;12:323–39.

[23] Hazeltine E, Grafton ST, Ivry R. Attention and stimulus characteristics determine the locus of motor-sequence encoding. A PET study. Brain 1997;120:123–40.

[24] Hikosaka O, Rand MK, Miyachi S, Miyashita K. Learning of sequential movements in the monkey: process of learning and retention of memory. Journal of Neurophysiology 1995;74:1652–61.

[25] Imamizu H, Miyauchi S, Tamada T, Sasaki Y, Takino R, Putz B, et al. Human cerebellar activity reflecting an acquired internal model of a new tool. Nature 2000;403:192–5.

[26] Jackson PL, Forget J, Soucy M-C, Leblanc M, Cantin J-F, Doyon J. Consolidation of visuomotor skills in humans: a psychophysical study. Society for Neuroscience Abstracts 1997;23:1052.

[27] Jenkins IH, Brooks DJ, Nixon PD, Frackowiak RS, Passingham RE. Motor sequence learning: a study with positron emission tomography. Journal of Neuroscience 1994;14:3775–90.

[28] Jueptner M, Frith CD, Brooks DJ, Frackowiak RS, Passingham RE. Anatomy of motor learning. II. Subcortical structures and learning by trial and error. Journal of Neurophysiology 1997;77:1325–37.

[29] Jueptner M, Stephan KM, Frith CD, Brooks DJ, Frackowiak RS, Passingham RE. Anatomy of motor learning. Part I. frontal cortex and attention to action. Journal of Neurophysiology 1997;77:1313–24.

[30] Karni A. The acquisition of perceptual and motor skills: a memory system in the adult human cortex. Cognitive Brain Research 1996;5:39–48.

[31] Karni A, Meyer G, Jezzard P, Adams MM, Turner R, Ungerleider LG. Functional MRI evidence for adult motor cortex plasticity during motor skill learning. Nature 1995;377:155–8.

[32] Karni A, Meyer G, Rey-Hipolito C, Jezzard P, Adams MM, Turner R, et al. The acquisition of skilled motor performance: fast and slow experience-driven changes in primary motor cortex. Proceedings of the National Academic Science USA 1998;95:861–8.

[33] Karni A, Sagi D. The time course of learning a visual skill. Nature 1993;365:250–2.

[34] Krebs HI, Brashers-Krug T, Rauch SL, Savage CR, Hogan N, Rubin RH, et al. Robot-aided functional imaging: application to a motor learning study. Human Brain Mapping 1998;6:59–72.

[35] Lu X, Hikosaka O, Miyachi S. Role of monkey cerebellar nuclei in skill for sequential movement. Journal of Neurophysiology 1998;79:2245–54.

[36] McDonald R, White NM. A triple dissociation of memory systems: hippocampus, amygdala, and dorsal striatum. Behavioral Neuroscience 1993;107:3–22.

[37] Middleton FA, Strick PL. Cerebellar output channels. International Review of Neurobiology 1997;41:61–82.

[38] Milak MS, Shimansky Y, Bracha V, Bloedel JR. Effects of inactivating individual cerebellar nuclei on the performance and retention of an operantly conditioned forelimb movement. Journal of Neurophysiology 1997;78:939–59.

[39] Miyachi S, Hikosaka O, Miyashita K, Karadi Z, Rand MK. Differential roles of monkey striatum in learning of sequential hand movement. Experimental Brain Research 1997;115:1–5.

[40] Nezafat R, Shadmehr R, Holcomb HH. Long-term adaptation to dynamics of reaching movements: a PET study. Experimental Brain Research 2001;140:66–76.

[41] Nissen MJ, Bullemer P. Attentional requirements of learning: evidence from performance measures. Cognitive Psychology 1987;19:1–32.

[42] Nudo RJ, Milliken GW, Jenkins WM, Merzenich MM. Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys. Journal of Neuroscience 1996;16:785–807.

[43] Nudo RJ, Wise BM, SiFuentes F, Milliken GW. Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. Science 1996;272:1791–4.

[44] Pascual-Leone A, Grafman J, Clark K, Stewart M, Massaquoi S, Lou JS, et al. Procedural learning in Parkinson's disease and cerebellar degeneration. Annals of Neurology 1993;34:594–602.

[45] Penhune VB, Doyon J. Dynamic cortical and subcortical networks in learning and delayed recall of timed motor sequences. Journal of Neuroscience 2002;22:1397–406.

[46] Picard N, Strick PL. Motor areas of the medial wall: a review of their location and functional activation. Cerebral Cortex 1996;6:342–53.

[47] Rauch SL, Savage CR, Alpert NM, Brown HD, Curran T, Kendrick A, Fischman AJ, Kosslyn S. In: Proceedings of the First International Conference on Functional Mapping of the Human Brain on Functional Neuroanatomy of Implicit Sequence Learning Studied with PET. Human Brain Mapping 1995;409(Suppl.1).

[48] Rauch SL, Whalen PJ, Savage CR, Curran T, Kendrick A, Brown HD, et al. Striatal recruitment during an implicit sequence learning task as measured by functional magnetic resonance imaging. Human Brain Mapping 1997;5:124–32.

[49] Rey-Hipolito C, Adams MM, Ungerleider L, Karni A. When practice makes perfect: time dependent evolution of skilled motor performance. Society for Neuroscience Abstracts 1997;23:1052.

[50] Sakai K, Hikosaka O, Miyauchi S, Takino R, Sasaki Y, Putz B. Transition of Brain activation from frontal to parietal areas in visuomotor sequence learning. Journal of Neuroscience 1998;18:1827–40.

[51] Sanes JN. Motor cortex rules for learning and memory. Current Biology 2000;10:R495–7.

[52] Sanes JN, Dimitrov B, Hallett M. Motor learning in patients with cerebellar dysfunction. Brain 1990;113:103–20.

[53] Sanes JN, Donoghue JP. Plasticity and primary motor cortex. Annual Review of Neurosciences 2000;23:393–415.

[54] Schlaug G, Knorr U, Seitz R. Inter-subject variability of cerebral activations in acquiring a motor skill: a study with positron emission tomography. Experimental Brain Research 1994;98:523–34.

[55] Seitz RJ, Canavan AG, Yaguez L, Herzog H, Tellmann L, Knorr U, et al. Successive roles of the cerebellum and premotor cortices in trajectorial learning. NeuroReport 1994;5:2541–4.

[56] Seitz RJ, Roland E, Bohm C, Greitz T, Stone-Elander S. Motor learning in man: a positron emission tomographic study. NeuroReport 1990;1:57–60.

[57] Shadmehr R, Brashers-Krug T. Functional stages in the formation of human long-term motor memory. Journal of Neuroscience 1997;17:409–19.

[58] Shadmehr R, Holcomb HH. Neural correlates of motor memory consolidation. Science 1997;277:821–5.

[59] Shadmehr R, Holcomb HH. Inhibitory control of competing motor memories. Experimental Brain Research 1999;126:235–51.

[60] Squire LR. Declarative and nondeclarative memory: Multiple brain systems supporting learning and memory. Journal of Cognitive Neuroscience 1992;4:232–43.

[61] Tanji J. New concepts of the supplementary motor area. Current Opinion Neurobiology 1996;6:782–7.

[62] Thach WT. Context-response linkage. International Review Neurobiology 1997;41:599–611.

[63] Toni I, Krams M, Turner R, Passingham RE. The time course of changes during motor sequence learning: a whole-brain fMRI study. Neuroimage 1998;8:50–61.

[64] Ungerleider LG. Functional brain imaging studies of cortical mechanisms for memory. Science 1995;270:769–75.

[65] Van Mier H. Human learning. In: Toga A W, Mazziotta J C, editors. Brain mapping: the systems. San Diego: Academic Press; 2000. p. 605–20.

[66] Van Mier H, Tempel LW, Perlmutter JS, Raichle ME, Petersen SE. Changes in brain activity during motor learning measured with PET: effects of hand of performance and practice. Journal of Neurophysiology 1998;80:2177–99.

[67] White NM. Mnemonic functions of the basal ganglia. Current Opinion in Neurobiology 1997;7:164–9.

[68] Willingham DB. A neuropsychological theory of motor skill learning. Psychology Review 1998;105:558–84.

[69] Willingham DB, Koroshetz WJ. Evidence for dissociable motor skills in Huntington's disease patients. Psychobiology 1993;21:173–82.