

Central mechanisms of motor skill learning

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Recent studies have shown that frontoparietal cortices and interconnecting regions in the basal ganglia and the cerebellum are related to motor skill learning. We propose that motor skill learning occurs independently and in different coordinates in two sets of loop circuits: cortex–basal ganglia and cortex–cerebellum. This architecture accounts for the seemingly diverse features of motor learning.

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Abbreviations

BG	basal ganglia
CB	cerebellum
DA	dopamine
M1	primary motor cortex
preSMA	presupplementary motor area
SEF	supplementary eye field
SMA	supplementary motor area

Introduction

Neuroscience has evolved from the study of simple behaviors to examinations of complex behaviors. In particular, we are beginning to learn more about complex motor behaviors. We are usually unaware of how intricately our tongue moves during conversation and how elaborate our finger movements are during typing. Such awesome but implicit complexities had discouraged scientific approaches to skilled behaviors until recently.

A major breakthrough occurred when human imaging studies were developed. Recent imaging studies have addressed complex motor learning in human subjects. Their remarkable results have promoted neural theories of motor learning and have also renewed interest in studies of motor control on animal subjects.

In this review, we integrate diverse data obtained recently on the motor control of complex behaviors and provide a common ground for researchers working on motor skill learning. Due to space limitations, we leave out several important topics in motor learning, including visuomotor

associations, sensorimotor adaptations, cellular mechanisms of neural plasticity, and motor learning in birds.

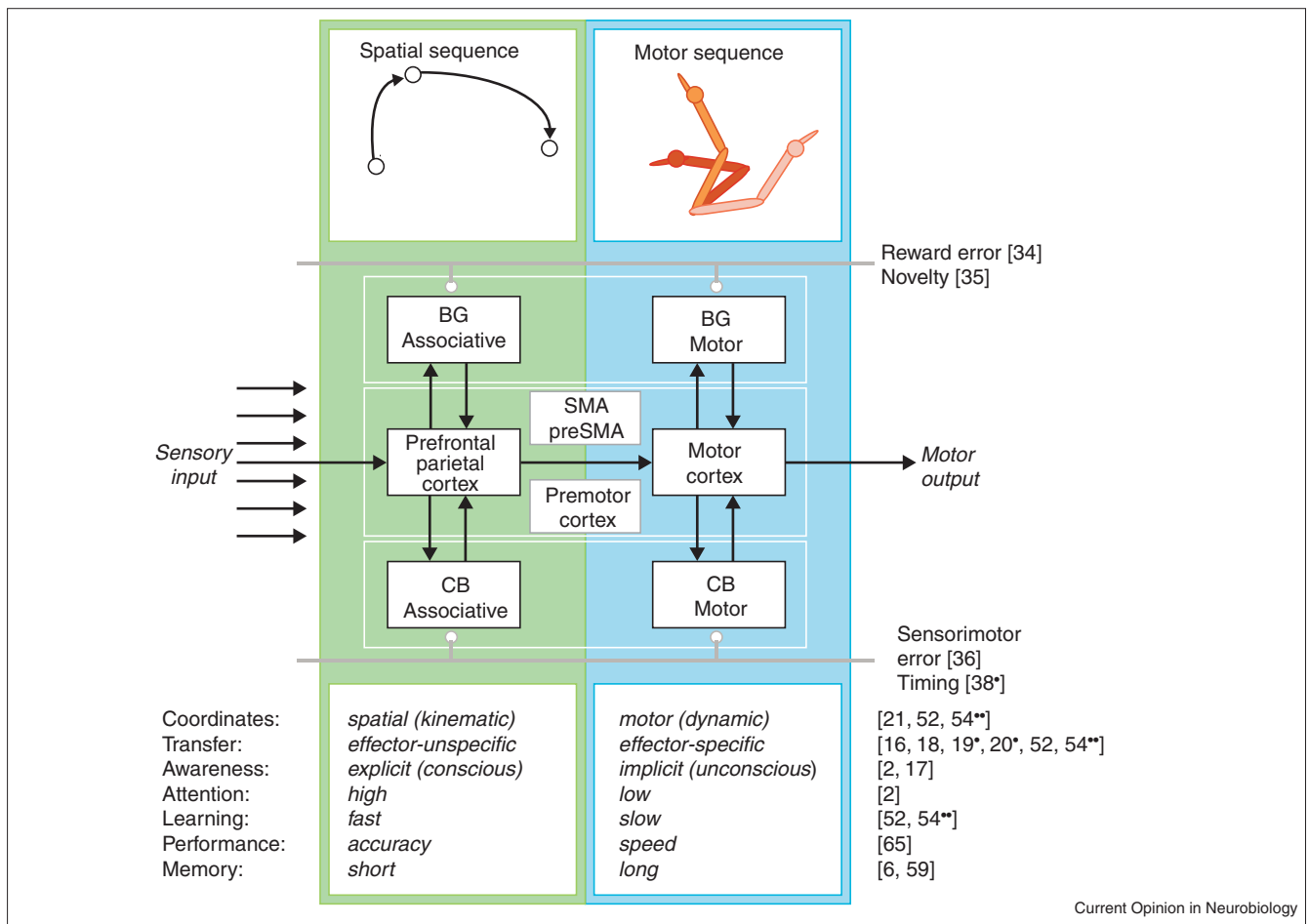
Multiple neural mechanisms for motor skill learning

A complex motor skill is often composed of a fixed sequence of movements [1,2]. It has been suggested that the supplementary motor area (SMA) plays an important role in sequential movements [3]. By training monkeys to perform different movements in specific orders, Shima and Tanji [4•] found that many neurons in the SMA become active specifically at particular transitions, not in response to particular movements. Neurons in the presupplementary motor area (preSMA), a cortical area anterior to the SMA, may be active specifically at certain rank orders in a sequence. On the basis of these results, Tanji proposed that the SMA and the preSMA work together to produce sequential movements correctly [5••].

How are such motor sequences acquired in the brain? To address this question, Hikosaka *et al.* [6] devised a sequential button press task, called the 2×5 task, in which the subject (either monkey or human) learned to press buttons in the correct order, by trial and error. This task enables the testing of an infinite number of different sequences and the effect of well-learned motor skills simultaneously on the same subject. Using this task, Nakamura *et al.* showed that the preSMA, rather than the SMA, is crucial for learning new sequences. Many neurons in the preSMA were activated during learning of new sequences, but not during the performance of learned sequences [7]. Furthermore, functional blockade of the preSMA led to selective deficits in learning new sequences [8]. The anterior cingulate cortex, ventral to the preSMA, may also contribute new sequence learning [9•]. As well as higher premotor areas, the primary motor cortex (M1) has been implicated in motor learning. Functional [10•,11•] and structural [12] changes occur in M1 during simple motor learning.

Consistent with these observations, functional neuroimaging studies on human subjects revealed that motor skill learning is associated with activation of many brain areas in the frontoparietal cortices. Researchers have begun asking how these areas contribute to motor learning. By applying the 2×5 task to human subjects (in a 2×10 version), Sakai *et al.* [13] demonstrated learning-related transition of activation from frontal to parietal areas. By using functional magnetic resonance imaging, they showed that the dorso-lateral prefrontal cortex and the preSMA were activated during early stages of learning, whereas more parietal areas — the intraparietal sulcus and the precuneus — were activated at later stages. Toni *et al.* [14] and Petersen *et al.* [15] also reported dynamic changes in human cortical activation during motor learning. Furthermore, a change in motor

Figure 1



Scheme of motor skill learning. We propose that motor skill learning operates as the interaction of two orthogonal connections: intracortical serial connections (horizontal arrows) and cortico–BG/cortico–CB loop circuits (vertical arrows). A sequence of movements is represented in two ways –spatial sequence and motor sequence. The left side of the figure is characteristic of the spatial sequence, the right side is characteristic of the motor sequence. The frontoparietal cortices form loop circuits with the associative region of the BG and CB, whereas the motor cortices form loop circuits with the motor region of the BG and CB. At the beginning of learning, movements are executed individually through the spatiomotor conversion process (horizontal connections). After learning, the movement sequence is represented by at least two networks in different coordinates: a spatial sequence supported by the parietal–prefrontal cortical loops and a motor sequence supported by the motor cortical loops (vertical connections). Spatial sequences are effector-unspecific (unless coding of space is effector-centered), are usually processed explicitly and therefore quickly acquired (as they may be accompanied by spatial attention or working memory), but require maximum attention. Motor sequences are effector-specific (as different effectors may perform different sequences), are usually processed implicitly and therefore slowly acquired, but require minimum attention. Performance on the

basis of the spatial sequence mechanism is accurate in space but slow (as its output must be converted to motor coordinates). Performance on the basis of the motor sequence mechanism is quick. Long-term retention of a motor skill is supported mainly by the motor sequence mechanism so that its speed is maintained even without awareness. Signals from the frontoparietal cortices and the motor cortices are sent to different functional divisions of the BG and CB (vertical arrows). In the BG, the signals are evaluated for their reward or likelihood values; in the CB, they are evaluated for their sensorimotor or timing errors (gray lines). Hence, the performance of the spatial and motor sequence mechanisms can be optimized independently. Note that the scheme may fail to account for the following kinds or aspects of motor learning. First, non-sequential motor skills: sequencing may not be important for some motor skills such as adaptation in a force field [59] and arbitrary visuomotor associations [60]. Second, non-spatial sequences: learning can occur for a sequence of objects or colors, for which the preSMA [61], but not the dorsolateral prefrontal cortex [62], is recruited. Third, abstract rules: learning can transfer to another sequence that shares the same global structure, not elements [63,64]. Fourth, temporal sequences: timing errors may be encoded in the cerebellar posterior lobe [38*], an important area for future research.

effector (finger versus arm) affects activation of sensorimotor cortex, but not parietal cortex [16]. Awareness of performance — explicit learning — is correlated with activation of the prefrontal cortex and preSMA, but not sensorimotor cortex [17].

Related behavioral studies also suggest that different brain areas control different aspects of motor learning. With practice, accuracy of performance was acquired earlier than speed of performance [6]. Accuracy was effector-unspecific, in the early learning stage, whereas the speed was

effector-specific [18,19•,20•]. Learning occurred independently for the kinematics — the spatial reference — of movements and for the dynamics — the load bearing — of movements [21]. The motor skill, once established, was maintained for a long time, mainly in the form of speed [6]. For a more extensive review on behavioral studies of motor skill learning, the reader is referred to Willingham [2], in which important concepts are described.

These results suggest that motor skill learning may be the integrative product of multiple neural mechanisms, each contributing to a different aspect of learning. How, then, do different neural mechanisms interact with each other to acquire and store motor skills efficiently? The basal ganglia and the cerebellum may play crucial roles.

Learning is optimized by the basal ganglia and the cerebellum

In addition to human functional imaging studies [22,23], several lines of evidence suggest that both the basal ganglia (BG) and the cerebellum (CB) are involved in motor sequence learning. Several studies implicate the BG. Activity of monkey caudate neurons is related to spatial sequence [24]. Dopamine depletion disrupts skilful performance of sequential movements [25]. Population activity of striatal neurons changes with long-term motor learning [26]. Reversible blockade of the anterior striatum (associative region) leads to deficits in learning new sequences, and blockade of the posterior striatum (motor region) leads to disruptions in the execution of learned sequences [27].

The CB also seems necessary for motor skill learning. Cerebellar blockade disrupts learning of complex goal-directed behaviors [28]. Cerebellar lesions impair motor sequence learning, but not conditional visuomotor learning or spatial working memory [29]. In contrast, blockade of the dorsal part of the dentate nucleus (which is connected with M1) does not affect learning new sequences, but disrupts the performance of learned sequences [30]. Long-term memories for motor skills may be stored in the CB [31•]. The conclusions of these studies seem inconsistent but may reflect anatomical and functional differentiation in the CB between motor and associative regions [32•].

What then is unique about the BG or the CB, compared with the cerebral cortex? Doya [33••] proposed that learning in the BG and the CB is guided by error signals, unlike in the cerebral cortex. This error signal may be mediated by midbrain dopamine (DA) neurons in the BG and by climbing fibers in the CB. DA neurons encode reward expectation error [34] and/or novelty [35], whereas climbing fibers encode sensorimotor error signals [36], which possibly include a timing error [37•,38•] (Figure 1). In the BG, cortical signals are integrated with reward error signals carried by DA neurons in striatal projection neurons: visual and memory responses of caudate neurons

were strongly modulated by reward expectation [39]. In the CB, cortical signals and sensorimotor error signals carried by the climbing fibers are integrated in Purkinje cells [40]. These signals would, at least partly, be relayed back to the cerebral cortex.

Thus, signals originating from the cerebral cortex are optimized in terms of their reward value and sensorimotor accuracy, by going through the BG and cerebellar loop circuits, respectively. This feedback is likely to be a critical process for motor skill learning.

Rules, concepts, and models for motor learning

Having reviewed the literature on motor skill learning, we are struck by the diversity of brain structures and mechanisms that are supposedly responsible for motor skill learning. To understand the nature and mechanisms of motor skill learning, it is necessary to integrate such diversity of information into schemes or models [2,33••,41–45]. To make such attempts realistic, the concepts of coordinate transformation and loop circuits must be incorporated. For simple reaching to a visual target, for example, the target position is first coded in spatial coordinates — for example, centered around the eye, head or object — and then converted to motor coordinates — for example, joint angles or muscle forces. This coordinate transformation process may roughly correspond to the intracortical connections from the association cortices to the motor cortices [46•,47,48•] (horizontal connections in Figure 1). The frontoparietal cortices and the motor cortices form loop circuits with different regions in the BG and the CB (vertical connections in Figure 1) [49,50•,51].

The scheme shown in Figure 1 was derived from the above considerations [52,53]. According to this model, a motor sequence is learned by two sets of cortex–BG and cortex–CB loop circuits independently, but in different coordinates — spatial and motor. The scheme successfully accounts for various lines of experimental observations, including coordinate transformation, hand transfer, awareness, and attentional cost.

Nakahara *et al.* [54••] elaborated this scheme by formulating a neural network model and successfully replicated various experimental results of the 2'5 task in a unified manner. One problem foreseen with this neural network was that the spatial and motor mechanisms might produce different results because they work independently. Such 'between network error', which is inherent to any parallel network model, was solved in this model by a kind of conflict monitor, corresponding to the preSMA. The proposed architecture turned out to be robust. Even if one of the spatial or motor mechanisms was destroyed, the other mechanism could still learn the sequence, though not perfectly [54••]. Once a sequence is implemented as a motor sequence, the spatial sequence mechanism can work on other sequences so that eventually many sequences can be learned.

Conclusions and future directions

Motor skills emerge from our experience, not from knowledge, as they easily escape our consciousness. Naturally, we acquire many motor skills and execute them without awareness. Such ever-changing and hidden properties of motor skills have impeded analytical approaches. The discovery of synaptic plasticity in single neurons was revolutionary, but was far from sufficient to explain motor skills. Recent integrative and multidisciplinary approaches have begun to suggest that essential features of motor skills reside in dynamic interactions between multiple neural networks. Such networks are composed of loop circuits formed by the frontoparietal cortices, the BG, and the CB. These circuits acquire the same motor sequence in different coordinates, at diverse speeds, with varying robustness, and with different levels of attention and awareness. Their operation is likely optimized by learning mechanisms, each unique to the BG and CB. Such dynamic interactions of neural networks would thus create the emergent and ever-changing properties of motor skills.

However, such integrative approaches have just started and modeling attempts of motor learning mechanisms have created more questions. Let us raise one important issue: timing. At the most advanced stage of a motor skill, movements of different body parts are accurately coordinated in time [55•]. A key structure for such a timing function might be the CB [37•,38•,56]. Related to timing is a phenomenon called ‘chunking’ [57] or ‘rhythm’ [58]. After practice, a long sequence of movements is often grouped into a series of chunks [1]. From these chunks may emerge the hierarchical organization of learned behavior.

Update

Lu *et al.* [66••] have recently found that many neurons in the supplementary eye field (SEF) were active in specific learned sequences of saccadic eye movements. These data, together with the preceding data on the SMA and preSMA, suggest that the medial frontal cortex represents learned sequences of eye–hand movements. They further suggest that the relationship between the eye and hand mechanisms is flexible, being either independent or well-coordinated, depending on the context or the level of practice.

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Using an oculomotor version of the 2x5 task [6], these authors found that many neurons in the SEF became active with a specific target/distractor combination in a specific sequence. Other neurons were less specific to the sequence, but were more selective for saccadic output. The results suggest that the SEF contributes to the generation of saccades in many learned sequences.