

Complementary roles of basal ganglia and cerebellum in learning and motor control

Kenji Doya

The classical notion that the basal ganglia and the cerebellum are dedicated to motor control has been challenged by the accumulation of evidence revealing their involvement in non-motor, cognitive functions. From a computational viewpoint, it has been suggested that the cerebellum, the basal ganglia, and the cerebral cortex are specialized for different types of learning: namely, supervised learning, reinforcement learning and unsupervised learning, respectively. This idea of learning-oriented specialization is helpful in understanding the complementary roles of the basal ganglia and the cerebellum in motor control and cognitive functions.

Addresses

Information Sciences Division, ATR International and CREST, Japan Science and Technology Corporation, 2-2-2 Hikaridai, Seika, Soraku, Kyoto 619-0288, Japan; e-mail: doya@isd.atr.co.jp

Current Opinion in Neurobiology 2000, **10**:732–739

0959-4388/00/\$ – see front matter

© 2000 Elsevier Science Ltd. All rights reserved.

Abbreviations

GP	globus pallidus
LTD	long-term depression
RL	reinforcement learning
SMA	supplementary motor area
SNc	substantia nigra pars compacta
SNr	substantia nigra pars reticulata
TD	temporal difference
VTA	ventral tegmental area

Introduction

The basal ganglia and the cerebellum have long been known to be involved in motor control because of the marked motor deficits associated with their damage. However, the exact aspects of motor control that they are involved in under normal conditions has not been clear. Traditionally, the cerebellum was supposed to be involved in real-time fine tuning of movement [1,2], whereas the basal ganglia were thought to be involved in the selection and inhibition of action commands [3]. However, these distinctions were by no means clear-cut [4]. Furthermore, an ever-increasing number of brain-imaging studies show that the basal ganglia and the cerebellum are involved in non-motor tasks, such as mental imagery [5,6], sensory processing [7–9], planning [10,11,12], attention [13], and language [14–17].

Both the basal ganglia and the cerebellum have recurrent connections with the cerebral cortex [1,3]. Anatomical studies using transneuronally transported viruses [18–20,21••] have clearly shown that the projections from the basal ganglia and the cerebellum through the thalamus to the cortex constitute multiple ‘parallel’ channels. The

diversity of the target cortical areas — not only the motor and premotor cortices but also the prefrontal [18], temporal [22], and parietal cortices [19] — is in agreement with their involvement in diverse functions. However, the neural activity tuning and the lesion effects of a subsection of the basal ganglia or the cerebellum tend to be similar to those of the cortical area to which it projects [21••]. This makes it difficult to distinguish the specific roles of the basal ganglia and the cerebellum simply from recording or lesion results.

Is it then impossible to characterize the specific information processing in the basal ganglia and the cerebellum? Despite their diverse, overlapping target cortical areas, the basal ganglia and the cerebellum have unique local circuit architectures and synaptic mechanisms. This strongly suggests that each structure is specialized for a particular type of information processing [23]. In this review, a novel view is introduced in which the basal ganglia and the cerebellum are specialized for different types of learning algorithms: reward-based learning in the basal ganglia and error-based learning in the cerebellum [24••]. Recent experimental as well as modeling studies on the basal ganglia and the cerebellum are reviewed from this viewpoint of learning-oriented specialization.

Learning-oriented specialization

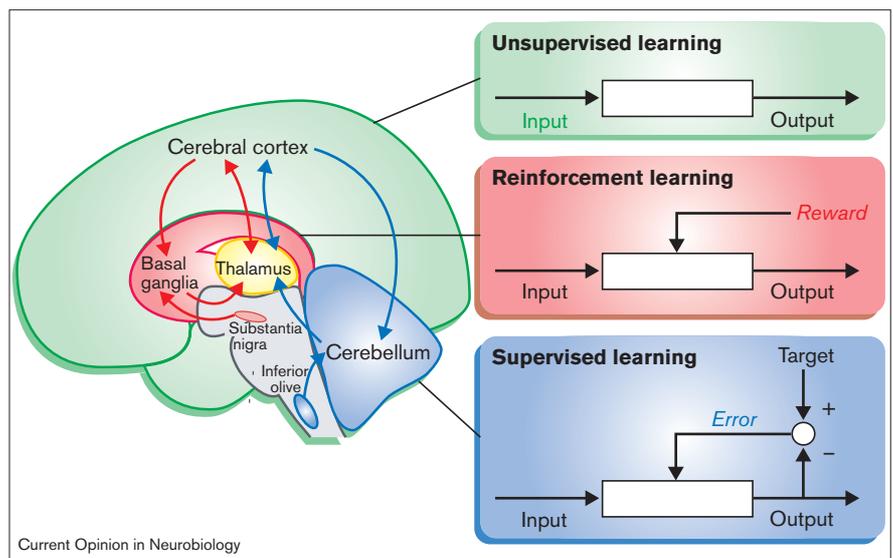
Theoretical models of learning in different parts of the brain suggest that the cerebellum, the basal ganglia, and the cerebral cortex are specialized for different types of learning [23,24••], as summarized in Figure 1. The cerebellum is specialized for supervised learning based on the error signal encoded in the climbing fibers [2,25–27]. The basal ganglia are specialized for reinforcement learning (RL) based on the reward signal encoded in the dopaminergic fibers from the substantia nigra [28–30]. The cerebral cortex is specialized for unsupervised learning based on Hebbian plasticity and reciprocal connections within and between cortical areas [31–34].

Reward-based learning in the basal ganglia

A breakthrough in elucidating the function of the basal ganglia came from a series of experiments by Schultz and colleagues on the activity of midbrain dopamine neurons in primates [35,36]. In a conditioned reaching task, dopamine neurons initially respond to the liquid reward after successful trials. However, as the animal learns the task, dopamine neurons start to respond to the conditioned visual stimulus and cease to respond to actual reward delivery. This means that the activity of dopamine neurons does not just encode present reward, but prediction of future reward. Incidentally, prediction of future reward has been

Figure 1

Specialization of the cerebellum, the basal ganglia, and the cerebral cortex for different types of learning [24••]. The cerebellum is specialized for supervised learning, which is guided by the error signal encoded in the climbing fiber input from the inferior olive. The basal ganglia are specialized for reinforcement learning, which is guided by the reward signal encoded in the dopaminergic input from the substantia nigra. The cerebral cortex is specialized for unsupervised learning, which is guided by the statistical properties of the input signal itself, but may also be regulated by the ascending neuromodulatory inputs [80].



Current Opinion in Neurobiology

the main issue in the computational theory of RL [37,38]. In the RL theory, a policy (sensory–motor mapping) is sought so that the expected sum of future reward

$$V(t) = E[r(t+1) + r(t+2) + \dots]$$

is maximized. Here, $r(t)$ denotes the reward acquired at time t and $V(t)$ represents the ‘value’ of the present state. RL generally involves two issues: prediction of cumulative future reward and improvement of state–action mapping to maximize the cumulative future reward. A so-called ‘temporal difference’ (TD) signal $\delta(t)$

$$\delta(t) = r(t) + V(t) - V(t-1),$$

takes dual roles as the error signal for reward prediction and the reinforcement signal for sensory–motor mapping [37].

The reward-predicting response of dopamine neurons was a big surprise because it was exactly how the TD signal would respond in reward-prediction learning — initially responding to the reward itself [$\delta(t) = r(t)$], and later to the change in the predicted reward [$\delta(t) = V(t) - V(t-1)$] even without a reward. Dopamine was also well known to have the role of behavioral reinforcer. Accordingly, a number of models of the basal ganglia as a RL system have been proposed in which the nigrostriatal dopamine neurons represent the TD signal [28–30,39,40,41•].

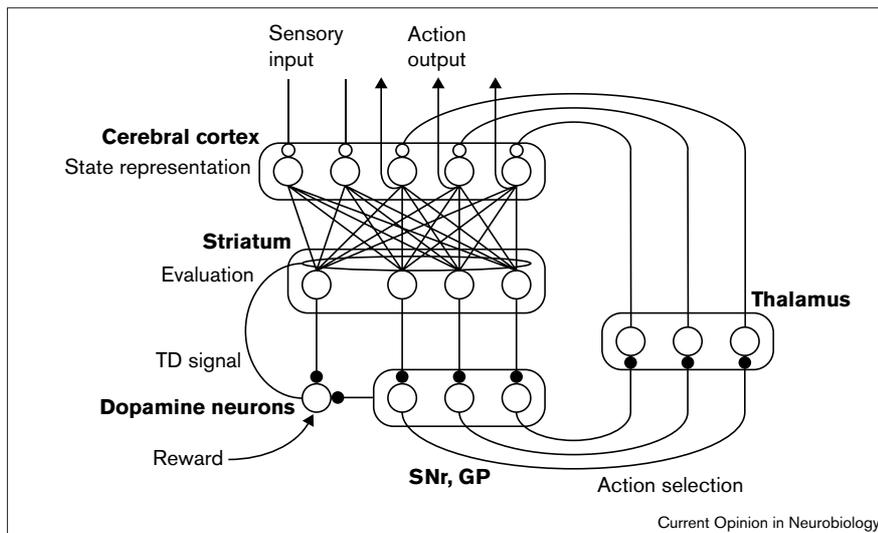
Figure 2 summarizes the outline of an RL-based model. The input site of the basal ganglia, the striatum, comprises two compartments: the striosome, which projects to the dopamine neurons in the substantia nigra pars compacta (SNc), and the matrix, which projects to the output site of the basal ganglia, the substantia nigra pars reticulata (SNr) and the globus pallidus (GP). In the RL model, the striosome is responsible for

predicting the future reward from the present sensory state whereas the matrix is responsible for predicting future rewards associated with different candidate actions.

Through a competition of the matrix outputs, the motor action with the highest expected future reward is selected in SNr/GP and sent to the motor nuclei in the brain stem as well as thalamo-cortical circuits. The TD error is computed in SNc, based on the limbic input coding the present reward and the striatal input coding the future reward. The nigrostriatal dopaminergic projection, which terminates at the cortico-striatal synaptic spines, modulates the synaptic plasticity and serves as the error signal in the striosome prediction network and the reinforcement signal for the matrix action network. Such models have successfully replicated the learning of conditioning tasks as well as sequence learning tasks [39,40,41•].

However, there still remain several issues to be clarified in the RL hypothesis of the basal ganglia. First, it is not clear how the ‘temporal difference’ of expected future reward is calculated in the circuit leading to the substantia nigra, although a few possible mechanisms have been suggested [28,29,40,42]. A recent review by Joel and Weiner [43••] provides a comprehensive picture of the connections to and from the dopaminergic neurons in SNc and the ventral tegmental area (VTA). According to their view, there are two major pathways from the striatum to the SNc dopamine neurons: direct inhibition by striosome neurons through slow GABA_B-type synapses, and indirect disinhibition by matrix neurons through inhibition of GABA_A-type synaptic inputs from SNr neurons [44]. Thus it is possible that the fast disinhibition by the matrix and the slow inhibition by the striosome provide the temporal difference component $V(t) - V(t-1)$.

Figure 2



A schematic diagram of the cortico-basal ganglia loop and the possible roles of its components in a reinforcement learning model. The neurons in the striatum predict the future reward for the current state and the candidate actions. The error in the prediction of future reward, the TD error, is encoded in the activity of dopamine neurons and is used for learning at the cortico-striatal synapses. One of the candidate actions is selected in SNr and GP as a result of competition of predicted future rewards. The direct and indirect pathways within the globus pallidus are omitted for simplicity. The filled and open circles denote inhibitory and excitatory synapses, respectively.

Another open issue in TD-based models is the plasticity of cortico-striatal synapses. The above RL model predicts that there should be different plastic mechanisms for the striosome and the matrix, which are respectively involved in the evaluation of current state and possible actions. Although it has been shown that cortico-striatal synaptic plasticity is strongly modulated by dopamine [45,46,47], it remains to be clarified whether there are different plastic mechanisms in different compartments.

Reward-related activities have also been found in frontal cortices, including dorsolateral prefrontal cortex [48], orbitofrontal cortex [49], and cingulate cortex [50]. Dopaminergic neurons in the VTA project to those cortical areas. What is the difference between reward processing in the cerebral cortex and that in the basal ganglia? A systematic comparison of the reward-related activities in the orbitofrontal cortex, the striatum, and the dopamine neurons revealed the following characteristics [51]: the cortical neurons retain more information about sensory input; the striatal neurons show a richer variety of activation in relation to task progress; and, the dopamine neurons respond mainly to unpredicted reward or sensory stimuli. This suggests that the cortex is responsible for analyzing sensory input, the striatum is involved in the production of actions, and the dopamine neurons are particularly responsible for learning new behaviors.

Error-based learning in the cerebellum

The idea that the cerebellum is a supervised learning system dates back to the hypotheses of Marr [25] and Albus [26]. It was shown by Ito in vestibulo-ocular reflex (VOR) adaptation experiments [2,52] that long-term depression (LTD) of the Purkinje cell synapses dependent on the climbing fiber input is the neural substrate of such error-driven learning (Figure 3). Although it is still controversial whether the LTD

in Purkinje cells is the only locus of plasticity and memory storage for the VOR [53], recent results are in accordance with the cerebellar error-based learning hypothesis.

During ocular following response movements, Kobayashi and colleagues [54] showed that the response tuning of complex spikes is the mirror image of that of simple spikes [55]. This is in agreement with the hypothesis that the simple spike responses of Purkinje cells are shaped by LTD of parallel fiber synapses with the error signal provided by the climbing fibers. These authors also showed that the modulation of simple spikes by complex spikes is too weak to be useful for real-time motor control.

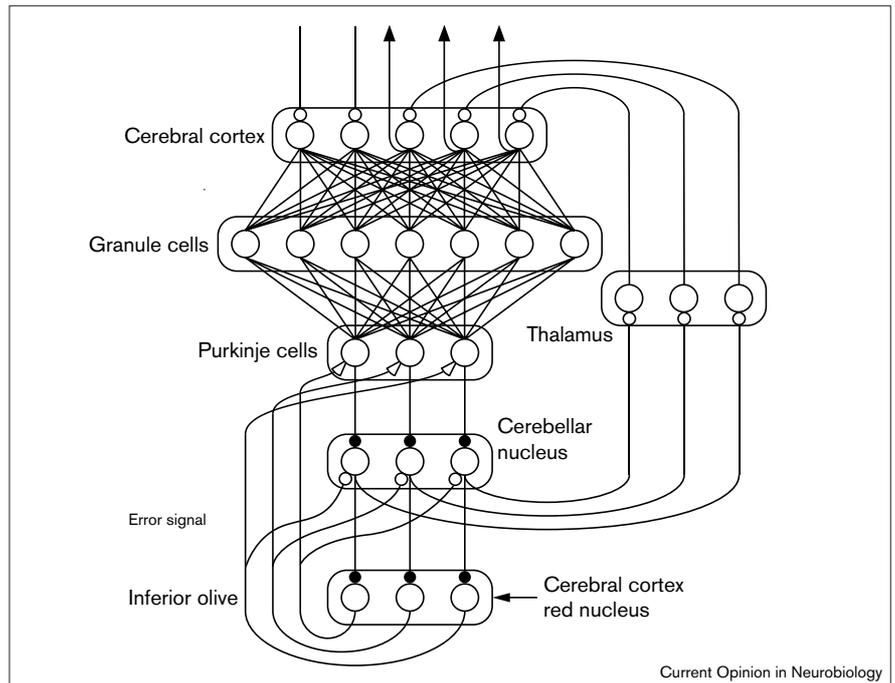
Kitazawa *et al.* [56] analyzed the information content of complex spikes in arm-reaching movement in monkeys. The results showed that complex spike firing carries information about the target direction in the early phase of the movement, whereas it carries information about the end-point error near the end of the movement. The coding of end-point error is consistent with the LTD hypothesis. What is the role of the target-related activity at the beginning of a movement? The low probability of firing of complex spikes near the beginning of a movement (less than one spike per trial) suggests that the signal may not be useful for on-line movement control. One possibility is that the spikes are potential error signals that could be used for further improvement of the performance should there be any preceding sensory cues that enable movement preparation.

Collaboration of learning modules

In the above framework of learning-orientated specialization, each organization is not specialized in what to do, but in how to learn it. Specific behaviors or functions can be realized by a combination of multiple learning modules

Figure 3

A schematic diagram of the cortico-cerebellar loop. In a supervised learning model of the cerebellum, the climbing fibers from the inferior olive provide the error signal for the Purkinje cells. Coincident inputs from the inferior olive and the granule cells result in LTD of the granule-to-Purkinje synapses. The filled and open circles denote inhibitory and excitatory synapses, respectively.



Current Opinion in Neurobiology

distributed among the basal ganglia, the cerebellum, and the cerebral cortex [23,24**].

The use of internal models of the body and the environment can improve the performance of motor control [57,58*]. Such internal models could be acquired by supervised learning with the motor command as the input and the sensory outcome as the teacher signal. Furthermore, for supervised or reinforcement learning, it is often helpful to use unsupervised learning algorithms to extract the essential information in the raw sensory input. Such methods of combination of different learning modules could be helpful in exploring possible collaborations of the cerebellum, the basal ganglia, and the cerebral cortex [24**]. Table 1 summarizes possible roles of the learning modules in these three areas.

In many brain-imaging experiments, different parts of the cerebellum, the basal ganglia and the cerebral cortex are activated simultaneously. The above hypotheses concerning the specialization of these areas for the different frameworks of learning can provide us with a helpful hint as to the different roles of simultaneously activated brain areas. Below, we review recent studies from the viewpoint of this learning-oriented specialization.

Eye movements

Recent experiments on saccadic eye movements have shown separate gain adaptation for different types of saccades, such as visually guided and memory-guided [59,60]. Such input-dependent adaptation of eye movement is naturally expected from supervised learning models of the

cerebellum: only the synaptic weights for the inputs that are associated with the retinal error signal are modified [61].

Neurons in the caudate nucleus are known to be activated during memory-guided saccades toward a certain preferred direction [62,63*]. Recently, Kawagoe and colleagues performed delayed-saccade experiments in which reward was given in only one of four possible saccade directions [64]. Surprisingly, the direction tuning of caudate neurons was strongly modulated by the reward condition. In some neurons, direction tuning was enhanced when the preferred direction coincided with the rewarded direction. In others, the preferred direction changed with the reward direction [64]. These data suggest that the striatal neurons do not simply represent motor action itself, but the reward associated with the state and actions. In reference to the above reinforcement learning model, it is tempting to speculate that the reward-following neurons are in the striosome and the reward-modulated neurons are in the matrix [65] and that the change in their behaviors is based on the dopamine-dependent plasticity of cortico-striatal synapses [63*]. However, it remains to be tested if such a change in the striatal response tuning is solely due to the plasticity within the striatum or also due to the reward-dependent responses of the cortical neurons [48–50,51**].

Arm reaching

It has been shown in arm-reaching studies in monkeys that the cerebellum is involved in externally driven (e.g. visually guided) movement, whereas the basal ganglia are involved in internally generated (e.g. memory-guided) movement [66]. Recent recording and inactivation studies

Table 1

Possible roles of different learning modules.**Cerebellum: supervised learning**

Internal models of the body and the environment.
Replication of arbitrary input–output mapping that was learned elsewhere in the brain.

Basal ganglia: reinforcement learning

Evaluation of current situation by prediction of reward.
Selection of appropriate action by evaluation of candidate actions.

Cerebral cortex: unsupervised learning

Concise representation of sensory state, context, and action.
Finding appropriate modular architecture for a given task.

of motor thalamus [67*,68*] further confirmed this contrasting involvement. In the part of the thalamus that receives input from the cerebellum and projects to the ventral premotor cortex, the majority of neurons are selectively activated during visually triggered movements. On the other hand, in the part of the thalamus that receives input from the basal ganglia and projects to the prefrontal cortex, the majority of neurons are selective for internally generated movements.

What is the reason for such differential involvement? During visually guided movements, the most critical computation is the coordinate transformation of visual input to corresponding motor output. Such mapping could be learned in a form of supervised learning in the cerebellum. During memory-guided or internally generated movements, what is most critical is the selection of an appropriate action and the suppression of unnecessary actions, both of which require prediction of reward value.

Sequence learning

It has been shown by trial-and-error learning of sequential movement that cortico-basal ganglia loops are differentially involved in early and late stages of learning. Brain areas in the prefrontal loop (prefrontal cortex, preSMA [supplementary motor area], caudate head) are involved in the learning of new sequences, whereas those in the motor loop (SMA, putamen body) are involved in the execution of well-learned movements [69,70]. Why should the information about the sequence learned initially in the prefrontal loop be copied to the motor loop? We hypothesized that the two cortico-basal ganglia loops learn a sequence using different representations: visuospatial coordinates in the prefrontal loop and motor coordinates in the motor loop [41*,71**]. A RL model of sequence learning based on this hypothesis could replicate many experimental findings — for example, the time course of learning, the performance for modified sequences, and the results of lesion experiments [41*]. In a recent psychophysical experiment motivated by this hypothesis, it was confirmed in a sequential key-press task that human subjects depend increasingly on body-specific representation than on visual representation with the progress of learning [72*].

Timing and rhythm

In a series of imaging studies by Sakai and colleagues [73,74*], it was shown that the memory of simple rhythms involves the anterior cerebellum, whereas the memory of complex rhythms and the adjustment of movement timing in response to irregular external triggers involve the posterior cerebellum. A possible reason for such differential involvement is the use of different representations [71**]. The anterior cerebellum can provide internal models of body dynamics, which can be helpful in the prediction of regular timing as well as in the control of detailed movement parameters. The posterior cerebellum may provide internal models for prediction of sensory events, which may be useful in timing perception and adjustment.

Cognitive processing

Involvement of the basal ganglia and the cerebellum in cognitive functions was once a controversial issue [14,75]. However, there are now abundant brain-imaging data showing their involvement in mental imagery [5,6], sensory discrimination [7–9], planning [10,11*,12], attention [13], and language [14–17]. Careful studies of patients with cerebellar and basal ganglia damage have also revealed that their impairments are not limited to motor control but also extend to cognitive functions [21**,76,77]. Lesion studies in rodents also suggest the involvement of the basal ganglia in rule-based learning [78] and spatial navigation [79].

In a recent positron emission tomography (PET) study using the Tower of London task, Dagher and colleagues found that the activity of the caudate nucleus, as well as the premotor and prefrontal cortices, is correlated with the task complexity [11*]. This suggests that the cortico-basal ganglia loops may be involved in multi-step planning of actions.

Conclusion

A new hypothesis concerning the specialization of brain structures for different learning paradigms provides helpful clues as to the differential roles of the basal ganglia and the cerebellum [24**]. Whereas the use of different learning algorithms is associated with differential involvement of the cerebellum, the basal ganglia and the cerebral cortex, the use of different representations is associated with differential involvement of the channels in cortico-basal ganglia loops and cortico-cerebellar loops.

The frontal cortex has been regarded as the site of high-level information processing because of its activity related to working memory, action planning, and decision making. However, what has been found in the cerebral cortex could be just the tip of an iceberg. The activities of the cortical neurons could be the result of the recurrent dynamics of the cortico-basal ganglia and cortico-cerebellar loops. An important role of the cerebral cortex is to provide common representations upon which both the basal ganglia and the cerebellum can work together.

Acknowledgements

The author is grateful to Mitsuo Kawato and Hiroyuki Nakahara for their helpful comments on the manuscript.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Allen GI, Tsukahara N: **Cerebro cerebellar communication systems.** *Physiol Rev* 1974, **54**:957-1006.
 2. Ito M: *The Cerebellum and Neural Control.* New York: Raven Press; 1984.
 3. Alexander GE, Crutcher MD: **Functional architecture of basal ganglia circuits: neural substrates of parallel processing.** *Trends Neurosci* 1990, **13**:266-271.
 4. Thach WT, Mink JW, Goodkin HP, Keating JG: **Combining versus gating motor programs: differential roles for cerebellum and basal ganglia?** In *Roles of Cerebellum and Basal Ganglia in Voluntary Movement.* Edited by Mano M, Hamada I, DeLong MR. Amsterdam: Elsevier; 1993:235-245.
 5. Parsons LM, Fox PT, Downs JH, Glass T, Hirsch TB, Martin CC, Jerabek PA, Lancaster JL: **Use of implicit motor imagery for visual shape discrimination as revealed by PET.** *Nature* 1995, **375**:54-58.
 6. Lotze M, Montoya P, Erb M, Hulsmann E, Flor H, Klose U, Birbaumer N, Grodd W: **Activation of cortical and cerebellar motor areas during executed and imagined hand movements: an fMRI study.** *J Cogn Neurosci* 1999, **11**:491-501.
 7. Gao JH, Parsons LM, Bower JM, Xiong J, Li J, Fox PT: **Cerebellum implicated in sensory acquisition and discrimination rather than motor control.** *Science* 1996, **272**:545-547.
 8. Poldrack RA, Prabhakaran V, Seger CA, Gabrieli JD: **Striatal activation during acquisition of a cognitive skill.** *Neuropsychology* 1999, **13**:564-574.
 9. Parsons LM, Denton D, Egan G, McKinley M, Shade R, Lancaster J, Fox PT: **Neuroimaging evidence implicating cerebellum in support of sensory/cognitive processes associated with thirst.** *Proc Natl Acad Sci USA* 2000, **97**:2332-2336.
 10. Kim S-G, Ugurbil K, Strick PL: **Activation of a cerebellar output nucleus during cognitive processing.** *Science* 1994, **265**:949-951.
 11. Dagher A, Owen AM, Boecker H, Brooks DJ: **Mapping the network for planning: a correlational PET activation study with the Tower of London task.** *Brain* 1999, **122**:1973-1987.
- In this positron emission tomography (PET) study, the authors used not only the subtraction between the test and control conditions, but also the correlation with the complexity of the task (in this case, the number of steps needed to solve a puzzle), to identify the areas that are involved in multi-step action planning. These areas include lateral premotor, rostral anterior cingulate, and dorsolateral prefrontal cortices, as well as dorsal caudate nucleus.
12. Weder BJ, Leenders KL, Vontobel P, Nienhusmeier M, Keel A, Zaunbauer W, Vonesch T, Ludin HP: **Impaired somatosensory discrimination of shape in Parkinson's disease: association with caudate nucleus dopaminergic function.** *Hum Brain Mapp* 1999, **8**:1-12.
 13. Allen G, Buxton RB, Wong EC, Courchesne E: **Attentional activation of the cerebellum independent of motor involvement.** *Science* 1997, **275**:1940-1943.
 14. Leiner JC, Leiner AL, Dow RS: **Cognitive and language functions of the cerebellum.** *Trends Neurosci* 1993, **16**:444-447.
 15. Kim JJ, Andreasen NC, O'Leary DS, Wiser AK, Ponto LL, Watkins GL, Hichwa RD: **Direct comparison of the neural substrates of recognition memory for words and faces.** *Brain* 1999, **122**:1069-1083.
 16. Price CJ, Green DW, von Studnitz R: **A functional imaging study of translation and language switching.** *Brain* 1999, **122**:2221-2235.
 17. Dong Y, Fukuyama H, Honda M, Okada T, Hanakawa T, Nakamura K, Nagahama Y, Nagamine T, Konishi J, Shibasaki H: **Essential role of the right superior parietal cortex in Japanese kana mirror reading: an fMRI study.** *Brain* 2000, **123**:790-799.
 18. Middleton FA, Strick PL: **Anatomical evidence for cerebellar and basal ganglia involvement in higher cognitive function.** *Science* 1994, **266**:458-461.
 19. Middleton FA, Strick PL: **Cerebellar output: motor and cognitive channels.** *Trends Cogn Sci* 1998, **2**:348-354.
 20. Hoover JE, Strick PL: **The organization of cerebellar and basal ganglia outputs to primary motor cortex as revealed by retrograde transneuronal transport of herpes simplex virus type 1.** *J Neurosci* 1999, **19**:1446-1463.
 21. Middleton FA, Strick PL: **Basal ganglia and cerebellar loops: motor and cognitive circuits.** *Brain Res Brain Res Rev* 2000, **31**:236-250.
- A thorough review of the anatomy of the outputs of the basal ganglia and cerebellum to the cerebral cortex. Multiple output channels that target different cortical areas are revealed by the group's studies using transneuronally transported herpes virus. The paper also includes a comprehensive review of the physiology and the pathology of the basal ganglia and the cerebellum in motor control and cognitive functions.
22. Middleton FA, Strick PL: **The temporal lobe is a target of output from the basal ganglia.** *Proc Natl Acad Sci USA* 1996, **93**:8683-8687.
 23. Houk JC, Wise SP: **Distributed modular architectures linking basal ganglia, cerebellum, and cerebral cortex: their role in planning and controlling action.** *Cereb Cortex* 1995, **2**:95-110.
 24. Doya K: **What are the computations of the cerebellum, the basal ganglia, and the cerebral cortex.** *Neural Networks* 1999, **12**:961-974.
- This paper presents a novel view that the cerebellum, the basal ganglia, and the cerebral cortex are specialized for different types of learning: namely, supervised, reinforcement and unsupervised learning, respectively. The paper reviews basic algorithms for three learning paradigms and presents the way in which they could be implemented in the neural circuits. Possible control architectures that combine different learning modules are also considered.
25. Marr D: **A theory of cerebellar cortex.** *J Physiol* 1969, **202**:437-470.
 26. Albus JS: **A theory of cerebellar function.** *Math Biosci* 1971, **10**:25-61.
 27. Kawato M, Gomi H: **A computational model of four regions of the cerebellum based on feedback-error learning.** *Biol Cybern* 1992, **68**:95-103.
 28. Houk JC, Adams JL, Barto AG: **A model of how the basal ganglia generate and use neural signals that predict reinforcement.** In *Models of Information Processing in the Basal Ganglia.* Edited by Houk JC, Davis JL, Beiser DG. Cambridge, MA: MIT Press; 1995:249-270.
 29. Montague PR, Dayan P, Sejnowski TJ: **A framework for mesencephalic dopamine systems based on predictive Hebbian learning.** *J Neurosci* 1996, **16**:1936-1947.
 30. Schultz W, Dayan P, Montague PR: **A neural substrate of prediction and reward.** *Nature* 1997, **275**:1593-1599.
 31. Malsburg CVD: **Self-organization of orientation sensitive cells in the striate cortex.** *Kybernetik* 1973, **14**:85-100.
 32. Amari S, Takeuchi A: **Mathematical theory on formation of category detecting nerve cells.** *Biol Cybern* 1978, **29**:127-136.
 33. Sanger TD: **Optimal unsupervised learning in a single-layer linear feedforward neural network.** *Neural Networks* 1989, **2**:459-473.
 34. Olshausen BA, Field DJ: **Emergence of simple-cell receptive field properties by learning sparse code for natural images.** *Nature* 1996, **381**:607-609.
 35. Schultz W, Apicella P, Ljungberg T: **Responses of monkey dopamine neurons to reward and conditioned stimuli during successive steps of learning a delayed response task.** *J Neurosci* 1993, **13**:900-913.
 36. Schultz W: **Predictive reward signal of dopamine neurons.** *J Neurophysiol* 1998, **80**:1-27.
 37. Barto AG: **Adaptive critics and the basal ganglia.** In *Models of Information Processing in the Basal Ganglia.* Edited by Houk JC, Davis JL, Beiser DG. Cambridge, MA: MIT Press; 1995:215-232.
 38. Sutton RS, Barto AG: *Reinforcement Learning.* Cambridge, MA: MIT Press; 1998.
 39. Suri RE, Schultz W: **Learning of sequential movements by neural network model with dopamine-like reinforcement signal.** *Exp Brain Res* 1998, **121**:350-354.
 40. Berns GS, Sejnowski TJ: **A computational model of how the basal ganglia produce sequences.** *J Cogn Neurosci* 1998, **10**:108-121.

41. Nakahara H, Doya K, Hikosaka O: **Parallel cortico-basal ganglia mechanisms for acquisition and execution of visuo-motor sequences: a computational approach.** *J Cogn Neurosci* 2001, in press.
This paper explores how the prefrontal and motor cortico-basal ganglia loops can work together in order to realize quick acquisition and robust execution of sequential movement. The authors used a RL model of the cortico-basal ganglia loops to simulate the experiments of the '2 × 5 task' in monkeys [71**]. The model successfully replicated the time-course of short-term and long-term learning as well as the differential effects of lesions to the basal ganglia loops.
42. Brown J, Bullock D, Grossberg S: **How the basal ganglia use parallel excitatory and inhibitory learning pathways to selectively respond to unexpected rewarding cues.** *J Neurosci* 1999, **19**:10502-10511.
43. Joel D, Weiner I: **The connections of the dopaminergic system with striatum in rats and primates: an analysis with respect to the functional and compartmental organization of the striatum.** *Neuroscience* 2000, **96**:451-474.
This paper reviews the connections of the dopaminergic neurons in SNc and VTA to and from the striatum. In the authors' view, the motor striatum can affect the dopaminergic neurons in two opposite ways: striosome neurons directly inhibit SNc neurons through GABA_B-type receptors, while matrix neurons indirectly disinhibit SNc neurons by removing GABA_A-type inhibitory inputs from SNr neurons. They also postulate an open-interconnected loop organization of the basal ganglia circuit, rather than closed, segregated loops.
44. Tepper J, Martin LP, Anderson DR: **GABAA receptor-mediated inhibition of rat substantia nigra dopaminergic neurons by pars reticulata projection neurons.** *J Neurosci* 1995, **15**:3092-3103.
45. Wickens JR, Begg AJ, Arbuthnott GW: **Dopamine reverses the depression of rat corticostriatal synapses which normally follows high-frequency stimulation of cortex *in vitro*.** *Neuroscience* 1996, **70**:1-5.
46. Calabresi P, Pisani A, Mercuri NB, Bernardi G: **The corticostriatal projection: from synaptic plasticity to dysfunctions of the basal ganglia.** *Trends Neurosci* 1996, **19**:19-24.
47. Reynolds JNJ, Wickens JR: **Substantia nigra dopamine regulates synaptic plasticity and membrane potential fluctuations in the rat neostriatum, *in vivo*.** *Neuroscience* 2000, **99**:199-203.
It is shown in *in vivo* intracellular recording of rat striatal neurons that high-frequency stimulation of cortical input without nigral dopamine input results in LTD of the cortico-striatal synapse. This LTD is suppressed or reversed if the SNc is concurrently stimulated. The result reconfirms the authors' and others' previous results in *in vitro* experiments.
48. Watanabe M: **Reward expectancy in primate prefrontal neurons.** *Nature* 1996, **382**:629-632.
49. Hikosaka K, Watanabe M: **Delay activity of orbital and lateral prefrontal neurons of the monkey varying with different rewards.** *Cereb Cortex* 2000, **10**:263-271.
50. Shima K, Tanji J: **Role for cingulate motor area cells in voluntary movement selection based on reward.** *Science* 1998, **282**:1335-1338.
51. Schultz W, Tremblay L, Hollerman JR: **Reward processing in primate orbitofrontal cortex and basal ganglia.** *Cereb Cortex* 2000, **10**:272-284.
This paper summarizes the results of the authors' own studies on the activities of dopaminergic, striatal, and orbitofrontal neurons in goal-directed motor control and learning. All these neurons show reward-predictive activities, but the cortical neurons tend to retain specific sensory information, the striatal neurons show variety of temporal response profiles during a trial, and the dopaminergic neurons are activated only in response to unexpected rewards.
52. Ito M, Sakurai M, Tongroach P: **Climbing fibre induced depression of both mossy fibre responsiveness and glutamate sensitivity of cerebellar Purkinje cells.** *J Physiol* 1982, **324**:113-134.
53. Raymond JL, Lisberger SG, Mauk MD: **The cerebellum: a neuronal learning machine?** *Science* 1996, **272**:1126-1131.
54. Kobayashi Y, Kawano K, Takemura A, Inoue Y, Kitama T, Gomi H, Kawato M: **Temporal firing patterns of Purkinje cells in the cerebellar ventral paraflocculus during ocular following responses in monkeys. II. Complex spikes.** *J Neurophysiol* 1998, **80**:832-848.
55. Gomi H, Shidara M, Takemura A, Inoue Y, Kawano K, Kawato M: **Temporal firing patterns of Purkinje cells in the cerebellar ventral paraflocculus during ocular following responses in monkeys. I. Simple spikes.** *J Neurophysiol* 1998, **80**:818-831.
56. Kitazawa S, Kimura T, Yin P-B: **Cerebellar complex spikes encode both destinations and errors in arm movements.** *Nature* 1998, **392**:494-497.
57. Wolpert DM, Miall RC, Kawato M: **Internal models in the cerebellum.** *Trends Cogn Sci* 1998, **2**:338-347.
58. Kawato M: **Internal models for motor control and trajectory planning.** *Curr Opin Neurobiol* 1999, **9**:718-727.
This paper provides a comprehensive review of how the internal models of the body and the environment can be acquired in the cerebellum and how they can be used for feedforward control, trajectory planning, and selection of appropriate control modules.
59. Deubel H: **Separate adaptive mechanisms for the control of reactive and volitional saccadic eye movements.** *Vision Res* 1995, **35**:3529-3540.
60. Fujita, M, Amagai A, Minakawa F: **Selective and delayed adaptations of human saccades.** In *Proceedings of the International Joint Conference on Neural Networks*. Como, Italy; July 24–27, 2000. 5:460-463.
61. Gancarz G, Grossberg S: **A neural model of saccadic eye movement control explains task-specific adaptation.** *Vision Res* 1999, **39**:3123-3143.
62. Hikosaka O, Wurtz RH: **Visual and oculomotor functions of monkey *Macaca mulatta* substantia nigra pars reticulata.** *J Physiol* 1983, **49**:1230-1301.
63. Hikosaka O, Takikawa Y, Kawagoe R: **Role of the basal ganglia in the control of purposive saccadic eye movements.** *Physiol Rev* 2000, **80**:953-978.
This paper reviews the anatomy and physiology of the network linking the cortical areas, the basal ganglia, and the superior colliculus. In addition to the classical notion of inhibition and disinhibition of movement, the role of the basal ganglia in associating the sensory input from the cortex and the reward input from the dopamine neurons are stressed.
64. Kawagoe R, Takikawa Y, Hikosaka O: **Expectation of reward modulates cognitive signals in the basal ganglia.** *Nat Neurosci* 1998, **1**:411-416.
65. Trapenberg T, Nakahara H, Hikosaka O: **Modeling reward dependent activity pattern of caudate neurons.** In *Proceedings of the International Conference on Artificial Neural Networks*. Skövde, Sweden; Sept 21–24, 1998:973-978.
66. Mushiaki H, Strick PL: **Pallidal neuron activity during sequential arm movements.** *J Neurophysiol* 1995, **74**:2754-2758.
67. van Donkelaar P, Stein JF, Passingham RE, Miall RC: **Neuronal activity in the primate motor thalamus during visually triggered and internally generated limb movements.** *J Neurophysiol* 1999, **82**:934-945.
This and the subsequent paper [68*] compare the activities and the lesion effects of different parts of the thalamus during limb movements. While area X, which receives major input from the cerebellum, is specifically involved in visually guided movements, VApc (parvocellular portion of the ventral anterior nucleus), which receives major input from the basal ganglia, is involved in internally generated movements.
68. van Donkelaar P, Stein JF, Passingham RE, Miall RC: **Temporary inactivation in the primate motor thalamus during visually triggered and internally generated limb movements.** *J Neurophysiol* 2000, **83**:2780-2790.
See annotation to [67*].
69. Miyachi S, Hikosaka O, Miyashita K, Karadi Z, Rand MK: **Differential roles of monkey striatum in learning of sequential hand movement.** *Exp Brain Res* 1997, **151**:1-5.
70. Jueptner M, Frith CD, Brooks DJ, Frackowiak RSJ, Passingham RE: **Anatomy of motor learning. II. Subcortical structures and learning by trial and error.** *J Neurophysiol* 1997, **77**:1325-1337.
71. Hikosaka O, Nakahara H, Rand MK, Sakai K, Lu X, Nakamura K, Miyachi S, Doya K: **Parallel neural networks for learning sequential procedures.** *Trends Neurosci* 1999, **22**:464-471.
This paper summarizes this group's series of experiments using the '2 × 5 task' paradigm, in which sequential key-press movements are learned by trial and error. They propose a parallel learning mechanism by multiple cortico-basal ganglia loops. While the network linking the prefrontal cortex and the anterior part of the basal ganglia is specifically involved in acquisition of a new sequence with the use of visuospatial representation, the network linking the supplementary cortex and the posterior part of the basal ganglia is mainly involved in quick, robust execution of well-learned sequences with the use of somatosensory representations.

72. Bapi RS, Doya K, Harner AM: **Evidence for effector independent and dependent representations and their differential time course of acquisition during motor sequence learning.** *Exp Brain Res* 2000, **132**:149-162.

In order to test the above hypothesis [71**], the authors tested the generalization performance of sequential finger movement under two conditions: the same spatial targets pressed with different finger movement (visual condition) and altered spatial targets pressed with the same finger movement (motor condition). It was shown that after extended training, the response time was significantly shorter in the motor condition than in the visual condition, which is in accordance with the above hypothesis that the motor representation is established and used in the late stage of sequence learning.

73. Sakai K, Hikosaka O, Miyauchi S, Takino R, Tamada T, Iwata NK, Nielsen M: **Neural representation of a rhythm depends on its interval ratio.** *J Neurosci* 1999, **19**:10074-10081.
74. Sakai K, Hikosaka O, Takino R, Miyauchi S, Nielsen M, Tamada T: **What and when: parallel and convergent processing in motor control.** *J Neurosci* 2000, **20**:2691-2700.

The brain activity during a choice reaction-time task in four conditions (with and without response selection and timing adjustment) was measured using fMRI. While the preSMA was selectively active in response selection, the posterior cerebellum was selectively active in timing adjustment.

Furthermore, lateral premotor cortex was most active when both response selection and timing adjustment were required, suggesting its role in integrating the outputs of preSMA and the posterior cerebellum.

75. Ito M: **Movement and thought: identical control mechanisms by the cerebellum.** *Trends Neurosci* 1993, **16**:448-450.
76. Knowlton BJ, Mangels JA, Squire LR: **A neostriatal habit learning system in humans.** *Science* 1996, **273**:1399-1402.
77. Middleton FA, Strick PL: **Basal ganglia output and cognition: evidence from anatomical, behavioral, and clinical studies.** *Brain Cogn* 2000, **42**:183-200.
78. Van Golf Racht-Delatour B, El Massioui N: **Rule-based learning impairment in rats with lesions to the dorsal striatum.** *Neurobiol Learn Mem* 1999, **72**:47-61.
79. Devan BD, White NM: **Parallel information processing in the dorsal striatum: relation to hippocampal function.** *J Neurosci* 1999, **19**:2789-2798.
80. Doya K: **Metalearning, neuromodulation, and emotion.** In *Affective Minds*. Edited by Hatano G, Okada N, Tanabe H. Amsterdam: Elsevier; 2000:101-104.