

Practice makes perfect: a theoretical model of memory consolidation in the cerebellum

Summary:

- * Elucidated the consolidation process of motor memory in the cerebellum theoretically.
- * Provides a better understanding of the “Practice makes perfect” phenomenon in motor learning.
- * This work may be used to inform new learning methods and for building intelligent robots.

An international group of neuroscientists proposes a theory of cerebellar motor learning that elucidates how motor memory may be consolidated after training. This is a joint effort by Tadashi Yamazaki (Assistant Professor, Graduate School of Informatics and Engineering, The University of Electro-Communications, President Takashi Fukuda) with Soichi Nagao (RIKEN Brain Science Institute, Director Susumu Tonegawa), William Lennon (University of California, San Diego, President Mark G. Yudof), and Shigeru Tanaka (Brain Science Inspired Life Support Research Center, The University of Electro-Communications).

When we learn something new, learning a little bit day by day is more effective for forming a robust memory than learning it all at once. This phenomenon, known as the spacing effect, also applies to motor learning. Repeating shorter training sessions every day is more effective than one long training session in a day, even if the total training time is the same. Moreover, the learned memory is consolidated into long-term memory after training, but not during training. That is, while taking a rest after training, the brain continues to work to consolidate learned memory. What happens in the brain during the memory consolidation process, however, is not yet entirely clear.

The research group focused on a simple eye reflex known as the optokinetic response (OKR *1), and conducted a theoretical study of how the motor memory underlying this reflex is learned and consolidated. The cerebellum plays an important role in OKR adaptation (*2). Therefore, the researchers built a mathematical model of the cerebellar neural network and conducted computer simulations to mimic the learning process (Fig. 1). They found that after a 1-hour training, memory forms in the cerebellar cortex through synaptic plasticity (*3), and then the learned memory decays naturally after training. During the memory decay in the cortex, however, another form of synaptic plasticity is induced at the cerebellar nucleus, and the memory is consolidated there as if the learned memory was transferred from the cortex to the nucleus. The model is also able to reproduce the spacing effect and results from various pharmacological experiments, and it explains abnormal motor learning capabilities seen in genetically manipulated animals.

By assuming multiple plasticity mechanisms within the cerebellum, this new theoretical framework can accommodate seemingly contradictory experimental results. This work may inform the development of efficient learning methods and intelligent robots that acquire new movements through experience.

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Background

The cerebellum plays an essential role in motor learning and control. When the cerebellum is damaged, motor performance is degraded and adaptation capability is lost. Learning in the cerebellum is thought to be implemented by the decrease of transmission efficacy of neural signals (long-term depression) at junctions between neurons called synapses in the cerebellar cortex, specifically those between parallel fibers and Purkinje cells. The Marr-Albus-Ito theory (*4), which was proposed in the early 1970s, states that the cerebellum dynamically controls the amplitude and

timing of movements based on this synaptic plasticity. During the past 45 years since the theory was proposed, however, several experimental results that seem contradictory to the theory have been reported. The current consensus is that in addition to the plasticity at parallel fiber–Purkinje cell synapses, another type of plasticity at mossy fiber–cerebellar nuclear cell synapses is also involved. Specifically, the cerebellar cortex forms short-term memories that are learned immediately through training but disappear naturally after training, whereas the cerebellar nucleus forms long-term memories that are consolidated gradually day by day. To elucidate the neural mechanisms experimentally, a very long recording period of hours and days would be necessary, but is not practical.

Methods and Results

This study focused on an oculomotor reflex known as OKR adaptation. In OKR adaptation, eye movements increase over the course of training. The research group studied theoretically how information about eye movement amplitude is formed and consolidated in the cerebellum. The cerebellum has a regular anatomical structure, is composed of a relatively small number of types of neurons, and has rich experimental data, which allowed us to build a biologically plausible theoretical model. The group derived a set of three equations that describe the neural process of OKR adaptation. In the model, 1-hour training forms memory of the eye movement amplitude in the cerebellar cortex by long-term depression of parallel fibers. The memory, however, decays naturally within 24 hours after training. During the decay, another form of plasticity in the cerebellar nucleus is induced, which consolidates the memory in the nucleus after the training. That is, the short-term memory formed within the cerebellar cortex is “transferred” to the cerebellar nucleus after training. The model closely reproduced the OKR adaptation process seen in animal experiments.

The post-training memory consolidation suggests that repeating training several times with a rest between the training forms more robust memory than a single training, even if the total training time is the same, which is known as the spacing effect. The present model reproduced the spacing effect in OKR adaptation, similarly to that shown in animal experiments. The model also explained several pharmacological experimental results and behavioral results from studies using genetically manipulated animals.

In summary, although there are many theoretical studies on memory acquisition, few have focused on memory consolidation. This study presents a theory of both memory acquisition and consolidation. Moreover, it supports the Marr-Albus-Ito theory stating that the learning starts from the synaptic plasticity in the cerebellar cortex, although multiple plasticity mechanisms work synergistically.

Future plan

By assuming multiple plasticity mechanisms within the cerebellum, this new theoretical framework can accommodate seemingly contradictory experimental results in cerebellar motor learning. A similar phenomenon — the change in location of memory storage during consolidation — has been observed for episodic memory and memory for location. The mechanisms, however, have remained unknown. The theoretical framework may be extended to this case. This study may be applied to the development of efficient motor training methods, rehabilitation, or the development of intelligent robots that acquire new movements through experience.

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Reference

Tadashi Yamazaki, Soichi Nagao, William Lennon, Shigeru Tanaka. Modeling memory consolidation during post-training periods in cerebellovestibular learning. *Proceeding of the National Academy of Sciences of the United States of America*, 2015, doi: 10.1073/pnas.1413798112

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Supporting information

(*1) OKR adaptation

When an oscillating checkerboard screen is moved slowly in front of an animal, the eye of the animal moves in the same direction as the screen rotation to stabilize the visual image on the retina. This is an oculomotor reflex known as optokinetic response (OKR). After the animal is exposed to the screen rotation for about 1 hour, the amplitude of the eye movement increases to further stabilize the retinal image. This is called OKR adaptation.

(*2) The cerebellum

A brain area located at the lower back of the brain. Although its size is 10 times smaller than the cerebrum in humans, the number of neurons inside the cerebellum is almost 50% of the entire brain. The cerebellum plays an important role in motor learning and control, and when the cerebellum is damaged, failure of motor control (ataxia) and impairment of motor adaptation are observed. Recent experiments have shown that the cerebellum is involved in cognitive functions as well.

(*3) Synaptic plasticity

In the brain, neurons are connected and transmit information at junctions called synapses. The signal transmission efficacy can change over time, which is called synaptic plasticity and is thought to be the basis for learning and memory in the brain.

(*4) The Marr-Albus-Ito theory

Around 1970, David Marr and James Albus proposed independently that the cerebellar cortex is a perceptron, a learning machine driven by supervised signals. Both predicted that the signal transmission efficacy of parallel fibers on Purkinje cells change and thereby store memory. This prediction was confirmed in 1982 by Masao Ito and his colleagues experimentally, in which paired activation of parallel fibers and a climbing fiber innervating the same Purkinje cell decreases the transmission efficacy (long-term depression). Now, the theory is called the Marr-Albus-Ito theory.

Figures

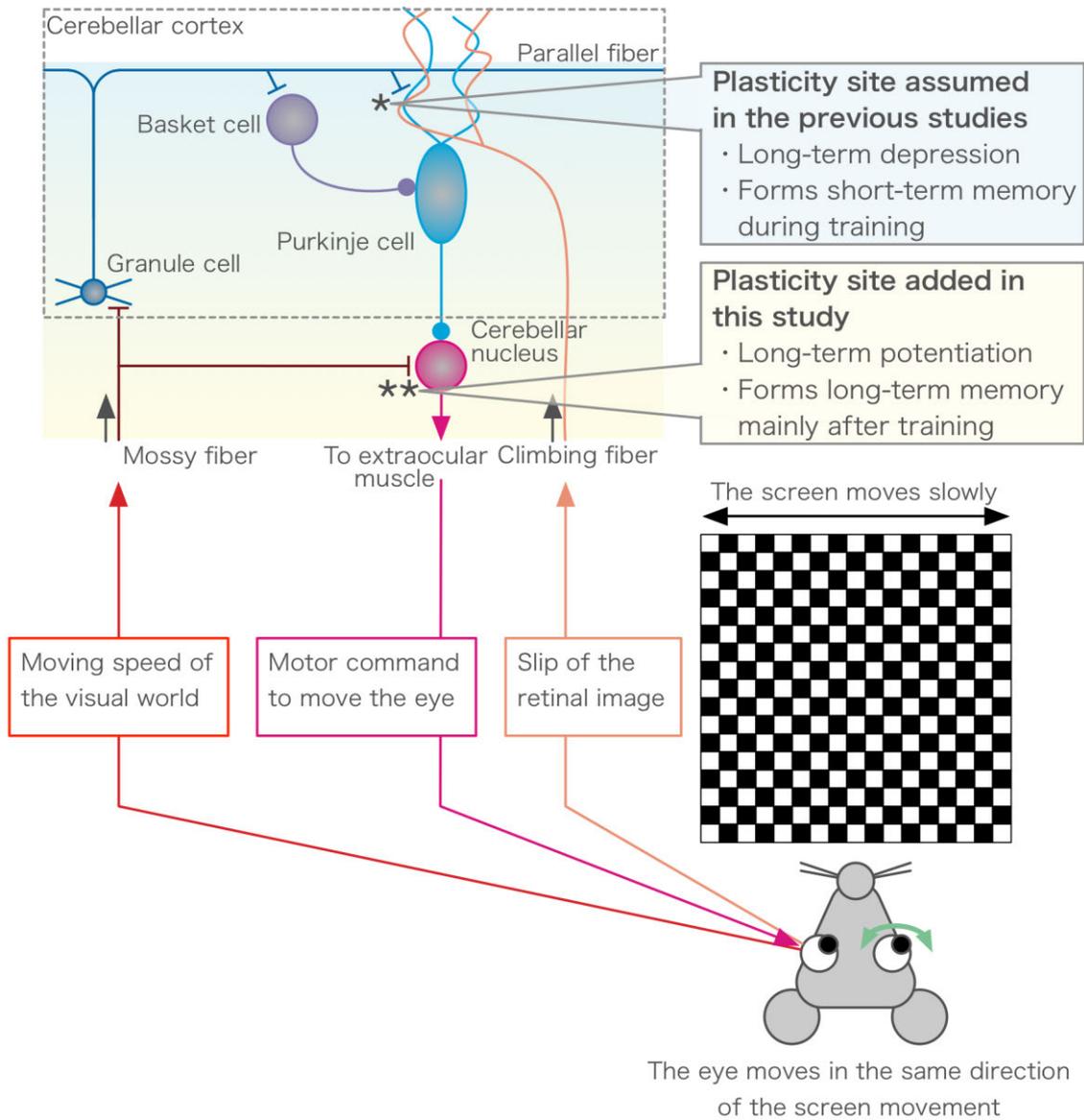


Figure 1. Schematic diagram of the cerebellum in OKR adaptation. Moving speed of the visual world and the slip of the retinal image are fed to the cerebellum via mossy fibers and climbing fibers, respectively. The cerebellar nucleus issues the motor command to move the eye. This study built a theoretical model that incorporates dual plasticity at parallel fiber-Purkinje cell synapses and mossy fiber-cerebellar nuclear cell synapses.

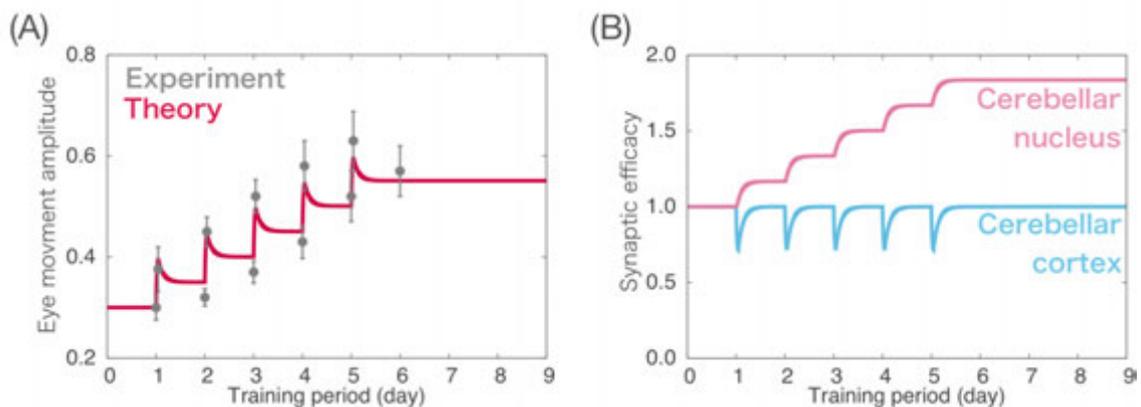


Figure 2. Results of computer simulation. (A) Comparison of mouse experiments and the model in OKR adaptation. The horizontal axis represents the training day, whereas the vertical axis the

amplitude of the eye movement. Animals are given daily 1-hour training followed by dark rearing for 23 hours. The amplitude increases by 1-hour training, and after that decays naturally. Meanwhile, the amplitude increases gradually day by day. Gray dots with error bars represent experimental data, whereas the red line plots the simulation result. (B) Transmission efficacy of signals at parallel fiber-Purkinje cell synapses (blue) and that at mossy fiber-cerebellar nuclear cell synapses (red) in the model. The former decreases quickly during training and returns slowly after training. The latter does not change during training and starts to increase after training.