

Cerebellar function: **Coordination, learning or timing?**

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Theories of cerebellar function have largely involved three ideas: movement coordination, motor learning or timing. New evidence indicates these distinctions are not particularly meaningful, as the cerebellum influences movement execution by feedforward use of sensory information via temporally specific learning.

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Theories of cerebellar function have been inspired by the clear motor impairments that result from cerebellar lesions, as well as the characteristic synaptic organization of the cerebellum. On the basis largely of the properties of cerebellar afferent and efferent projections, the cerebellum is generally thought to integrate motor commands and sensory information to help coordinate movements. But the detailed cerebellar circuit diagram provided by the seminal work of Eccles, Ito, Szentégotai and others [1] makes it possible to consider more concrete ideas about cerebellar processing.

One of the earliest ideas, proposed by Braitenberg [2], invoked the long length and slow conduction velocity of the parallel fibers in the cerebellar cortex as the basis for the notion that the cerebellum is a biological clock, with the parallel fibers acting as ‘delay lines’ to provide timed signals. While not necessarily based on the parallel fibers as delay lines, many recent ideas suppose the cerebellum to be some sort of general purpose timing system [3]. Beginning in 1969 with the groundbreaking paper by Marr [4], ideas about the cerebellum have also focused on its role in motor learning [5]. There has thus been continued debate as to whether the cerebellum is for motor coordination (the execution of movements), motor learning or timing.

Recent evidence, converging from a number of directions, indicates that these three ideas are not mutually exclusive. We shall review the new evidence that the cerebellum contributes to the proper execution of movements via motor learning that displays temporal specificity.

Temporal specificity of cerebellar motor learning

Evidence that the cerebellum is capable of motor learning has come largely from analysis of eyelid conditioning [5,6], eye movement systems [7] and simple movements in primates. These findings have been described in a number of excellent reviews, and will be outlined here only

briefly. The temporal specificity of cerebellar motor learning has been revealed most clearly from analysis of eyelid conditioning and analysis of the vestibulo-ocular reflex (which keeps the retinal image stable when the head moves) [5]. For convenience, we will focus on eyelid conditioning studies.

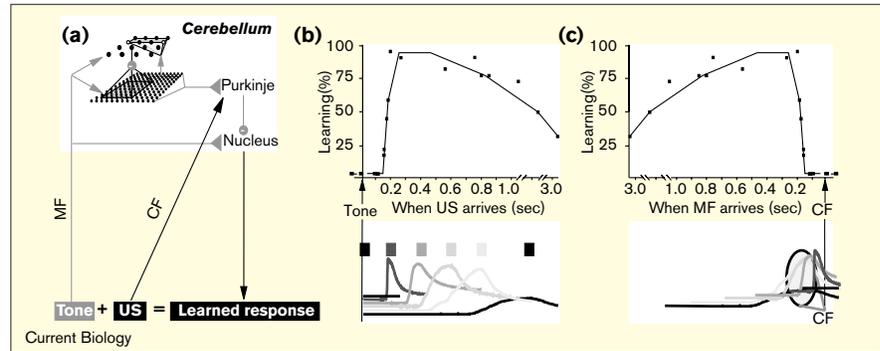
Eyelid conditioning provides a relatively direct look at the temporal specificity of cerebellar learning [6]. In short, training involves a relatively neutral stimulus such as a tone and a reinforcing stimulus such as stimulation around the eye. The latter, ‘unconditioned’ stimulus elicits a reflex eyelid response. Repeated pairing of the tone and unconditioned stimulus promotes the acquisition of a conditioned response: the eyelids close in response to the tone. Work from many groups has revealed that the tone and unconditioned stimulus are conveyed to the cerebellum via mossy fiber and climbing fiber inputs, respectively [6] (Figure 1a). Similarly, output of the cerebellum is responsible for expression of the conditioned responses. As the basic properties of the mossy fiber and climbing fiber activities elicited by the tone and the unconditioned stimulus are known, the temporal properties of cerebellar learning can be inferred from the temporal properties of eyelid conditioning.

In this regard, the key behavioral feature of eyelid conditioning is its dependence on the delay between the onsets of the tone and the unconditioned stimulus (Figure 1b). There is no learning with delays less than 100 milliseconds; learning occurs best with delays between 150 and 500 milliseconds; and learning gradually declines as the delay increases beyond 500 milliseconds. When learning occurs, the responses are precisely timed to peak at the time of the unconditioned stimulus. The results show that this represents true timing and does not simply reflect the fact that strong responses are fast and weaker responses slower. Recent evidence indicates that cerebellum-dependent adaptation of the vestibulo-ocular reflex displays similar temporal specificity [5].

The results thus show that, through mechanisms that are only partly understood, the cerebellum not only learns, but learns to change its output at the correct time. Eyelid conditioning reveals that, when a mossy fiber input repeatedly predicts a climbing fiber input, there will be an increase in cerebellar output timed to peak just prior to the arrival time of the climbing fiber input (Figure 1c). The cerebellum thus solves a temporal version of the credit assignment problem: that is, when there is a motor error — as signaled by the climbing fiber input — what

Figure 1

The temporally specific motor learning capacity of the cerebellum that is revealed by eyelid conditioning. (a) The temporal properties of cerebellar learning can be inferred from the relatively direct way in which eyelid conditioning engages the cerebellum. During training with a tone and reinforcing unconditioned stimulus (US), the tone is conveyed via mossy fiber (MF) inputs, the US by climbing fiber (CF) inputs, and cerebellar output drives the expression of the responses. The behavioral properties of eyelid conditioning thus reflect the input–output behavior of the cerebellum. Learning is thought to occur via changes in the strength of the excitatory synapses onto the Purkinje cells and onto the nucleus cells – each depicted by triangles. (b) Eyelid conditioning shows a systematic dependence on the time interval between the onsets of the tone and the US. The graph depicts the amount of learning produced for different delays between tone and US. Learning occurs only for a narrow range of intervals from about 0.2 seconds to 2–3 seconds. When an effective interval is used, the learned responses are precisely timed to peak near the US onset. The sample eyelid responses shown at the bottom – upward deflection means eye is closing – illustrate the timing of the responses that would be produced for six different tone–US delays. In each case, the rectangle



depicts the time at which the US is presented during training, which would produce the learned responses shown in the same shade. The short dark trace shows the lack of learning produced by simultaneous tone and US. Note how each learned response is timed to peak near the US. (c) The implications of these temporal properties are highlighted more clearly by plotting the same data aligned with respect to the climbing fiber input (US) rather than aligned to the mossy fiber input (tone) as in (b). This reveals that when a particular mossy fiber input repeatedly predicts the arrival of a climbing fiber-signaled motor error, the cerebellum learns to increase its output. The bottom panel shows the same timed eyelid

responses as in (b). The timing of the learned eyelid responses shows how the learned increases in cerebellar output are delayed to peak about 100 milliseconds before the arrival of the climbing fiber input. This time is shown by the gray oval that is superimposed on the eyelid responses. The arrival of a climbing fiber input at the time labeled 'CF' leads to increases in cerebellar output that are delayed with respect to the mossy fiber inputs to peak at the oval. As the errant movement that elicited the climbing fiber input was produced by motor commands near the oval, this timing capability ensures that the correct component of the movement is adjusted, as shown by how the responses are all timed to peak just before the error.

should be fixed? The solution is not just to alter cerebellar output, because that may not fix the appropriate movement component. Rather, the change in output is delayed — relative to the mossy fiber signals — so that it occurs about 100 milliseconds prior to the arrival of the climbing fiber signal. In this way, the change in output will influence the motor commands responsible for the error, so that subsequent performance will be improved [7] (Figure 1c).

Motor coordination through learning with timing

What are the implications of these findings for the debate about the cerebellum's functions in motor coordination, motor learning and timing? First, it seems clear that motor learning and timing are neither mutually exclusive nor even separate mechanisms. Rather, to alter movements properly requires the ability not only to adjust outputs, but to adjust output with the proper delays relative to the mossy fiber inputs. This should not be surprising, as controlling movements inherently involves activating motor units at the correct times. A motor learning mechanism without temporal specificity would be a poor one.

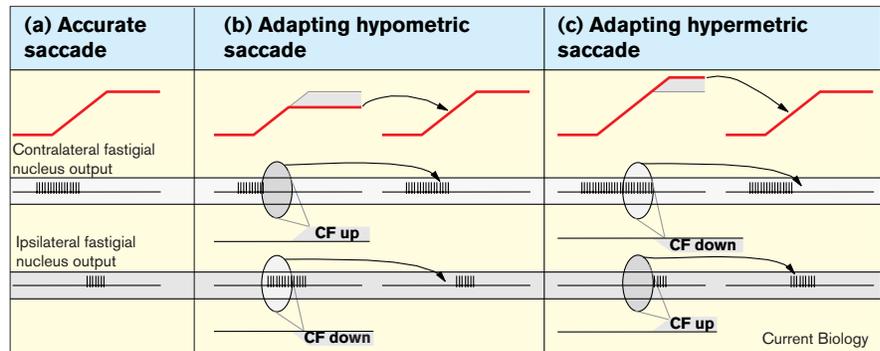
Similarly, the cerebellar functions of coordination through sensorimotor integration, and of motor learning, are also clearly intertwined. The learning capacity that eyelid conditioning reveals is consistent with a classic feedforward

use of sensory input to improve movement accuracy. Feedback use of sensory information is like a thermostat: sensory input (the thermometer in this analogy) is used during the execution of the movement (the heater) to produce accurate movement (the room stays at 70°). The utility of feedback control is inherently limited by its sluggishness and by its tendency to oscillate when forced to operate quickly. Feedforward control obviates this problem by using sensory information available prior to movement execution to make decisions about the motor commands.

The proper use of such sensory information requires previous experience about what to do given the current circumstances. Specifically, it requires the type of learning capability revealed by eyelid conditioning. The cerebellar contribution to each movement is based on previous experience (learning) given particular patterns of mossy fiber input. If this motor learning capacity allows the cerebellum to adjust its output to meet the demands apparent under various circumstances, it follows that cerebellar damage should produce dysmetria (poorly measured movements). Thus, the ataxic and dysmetric movements characteristic of cerebellar pathology reflect the execution of movements without the calibrating benefits of previous experience accumulated through learning. A motor learning mechanism that ignored sensory input,

Figure 2

Cerebellar-mediated saccade adaptation mechanisms suggested by the eyelid conditioning studies. **(a)** Fuchs *et al.* [10] have shown that neurons in the contralateral fastigial nucleus fire pre-saccade bursts, the duration of which correlates with the amplitude of the saccade (represented by the red sweep), and that neurons in the ipsilateral fastigial nucleus fire bursts that precede the completion of the saccade by a relatively fixed interval. Panels **(b)** and **(c)** show how saccades of the wrong amplitude would engage the cerebellum in a way that leads to appropriate adaptation of subsequent saccade performance. **(b)** The red sweep depicts a saccade smaller than the target (shown in gray). This creates a motor error, represented by the stippled region between the sweeps. Recording studies during vestibulo-ocular reflex adaptation and during smooth pursuit eye movements suggest that this would increase climbing fiber activity for the contralateral cerebellum and decrease it for the ipsilateral cerebellum [12,13]. Eyelid conditioning suggests that the increase in climbing fiber activity (dark gray ovals) would



increase cerebellar output at that time whereas the decrease in climbing fiber activity (lighter gray ovals) would decrease cerebellar output. This would act to increase and prolong the contralateral burst as well as delay the ipsilateral burst, both of which would increase the duration and thus increase the amplitude of the saccade. **(c)** Eyelid conditioning suggests the opposite would occur for over-long (hypermetric) saccades. The decrease in

contralateral climbing fiber input would decrease and shorten the pre-saccade burst. The increase in climbing fiber input to the ipsilateral cerebellum would increase and make earlier the braking burst. Again, both of these changes would produce the appropriate decreases in saccade duration and amplitude. Thus, the temporal specificity suggested by eyelid conditioning ensures that cerebellar output is altered correctly.

or whose output was unable to influence ongoing movements, would also be a poor one [8].

Cerebellar contributions to saccades

The interrelations between sensorimotor coordination, learning and timing are illustrated by the recent work of Thier *et al.* [9], who evaluated cerebellar Purkinje cell responses during saccades — the rapid eye movements used to shift gaze from one location to another. Fuchs and colleagues [10] had shown previously that cerebellar output neurons in the fastigial nucleus display bursts of activity systematically related to saccades. They fire bursts prior to contralateral saccades, where the duration of the burst correlates with the duration and amplitude of the saccade. For ipsilateral saccades, the neurons fire bursts that precede the completion of saccades by a relatively fixed latency. These findings were interpreted as evidence that cerebellar output influences the accuracy of saccades, both by scaling the excitatory drive that initiates saccades and by properly timing a braking burst. This idea is supported by the effects of reversible lesions: inactivation of the fastigial nucleus causes contralateral saccades to be hypometric (too small), and ipsilateral saccades to be hypermetric (too large) [11].

Thier *et al.* [9] now report that, as a population (more so than as individuals), the duration of Purkinje cell responses predicts the duration or timing of saccades. As Purkinje cells in this region are known to project to the oculomotor region of the caudal fastigial nucleus, these results are also consistent with the work of Fuchs and colleagues [10,11].

Figure 2 shows how the motor learning capabilities suggested by eyelid conditioning could alter cerebellar output in a way consistent with these recording studies and consistent with a cerebellar control of saccade accuracy.

The new Purkinje cell data are interpreted by Thier *et al.* [9] as evidence leading “saccadic learning back to an optimization of a representation of time”. An alternative view is that the data again illustrate the importance of, and capability for, temporally specific learning. Here again, timing is embedded in the learning mechanism, and saccade accuracy is improved through feedforward use of sensory input that makes use of this learning. Perhaps theories of cerebellar motor learning or theories of saccade accuracy need not be forced to adopt either a timing explanation *or* a learning explanation. Instead, the data on saccade systems, adaptation of the vestibulo-ocular reflex and eyelid conditioning are all consistent with the view that a basic property of cerebellar processing is to use temporally specific learning to improve motor performance.

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