Can We Teach the Cerebellum New Tricks?

Eliot Hazeltine and Richard B. Ivry

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man-made origin, using tools and insight of our own creation.

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PERSPECTIVES: NEUROSCIENCE

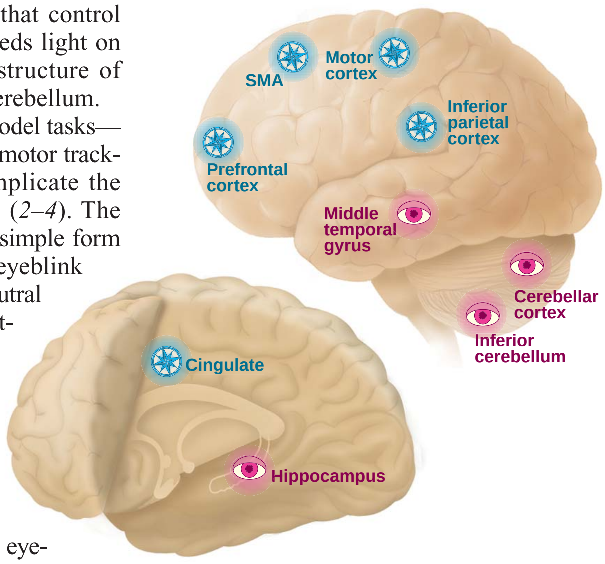
Can We Teach the Cerebellum New Tricks?

Eliot Hazeltine and Richard B. Ivry

Motor learning, the ability to learn a complex sequence of movements, is an essential feature of human behavior. Our brains continually encode new representations of incoming sensory information and translate them into motor commands that enable the execution of coordinated, even graceful, movements. A distributed network of neural structures contributes to this ability, but how these structures collaborate to produce goal-oriented actions is still unclear (see the figure). On page 2043 of this issue, Seidler *et al.* (*1*) present a new strategy for investigating the neural structures that control motor learning. Their work sheds light on the long-time favorite brain structure of motor learning theorists, the cerebellum.

Many studies that involve model tasks—such as prism adaptation, visuomotor tracking, and tool acquisition—implicate the cerebellum in motor learning (*2*–*4*). The best studied of these tasks is a simple form of Pavlovian learning called eyeblink conditioning. In this task, a neutral stimulus such as a tone is repeatedly paired with an airpuff to the eye (*5*). Over time, the animal learns to produce an eyeblink in response to the tone. Lesions to the cerebellum both abolish this conditioned response and prevent the acquisition of the predictive eyeblink in naïve animals. Importantly, the eyeblink elicited by the airpuff itself remains largely intact in decerebellate animals, indicating that the deficit is not one of motor production but rather is one of learning. Converging evidence from systems, cellular, and molecular neuroscience research provides a compelling case that the cerebellum is essential for acquisition of this conditioned response.

There remains, however, considerable debate as to whether the cerebellum plays a general role in motor learning. The computations required to learn that a tone predicts an airpuff are quite different from those needed by a master pianist to perform Rachmaninoff's Piano Concerto No. 3. One obstacle to progress on this question is that individuals with cerebellar damage show deficits in motor execution, performing poorly on movement tasks that they had learned before cerebellar injury. It is essential to distinguish between poor motor performance due to difficulties with encoding new representations and that resulting from problems with expressing this knowledge.



In the blink of an eye. Sagittal section of the human brain showing the neural structures that become activated during learning in the SRT task (compass), which is primarily spatial, or the eyeblink conditioning task (eye), which is primarily temporal. In the SRT task, the brain areas showing learning-related activity are the inferior parietal cortex, motor cortex, supplementary motor cortex (SMA), prefrontal cortex, and cingulate. In the eyeblink conditioning task, the brain areas showing learning-related activity are the inferior cerebellum, cerebellar cortex, hippocampus, and middle temporal gyrus (*14*).

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To address this question, Seidler *et al.* adopted the serial reaction time (SRT) task. Individuals performing the task are presented with a series of visual stimuli that indicate particular keypress responses (for example, left light indicates left keypress). The stimuli, and therefore the responses, appear either randomly or in a fixed sequence. Learning is indicated by a decreased response time on trials where the stimuli are in sequence compared with those where the stimuli are random. The inclusion of a distractor task (such as tone counting) is frequently used to prevent awareness of the sequence. Under such dual-task conditions, the expression of sequence learning is reduced, even though subsequent tests without the distractor task reveal that significant learning has taken place.

Taking advantage of this behavioral phenomenon, Seidler *et al.* asked subjects first to perform the SRT task concomitantly with the distractor task. With functional magnetic resonance imaging (fMRI), they measured brain activation as learning was taking place but not yet being expressed. Then they rescanned the participants in the absence of the distractor task, at a point when the learned sequence could be expressed. Their principal finding is that sequence-related activation in the cerebellum appears only when the distractor task is removed. This result suggests that the cerebellar contribution to the SRT task is restricted to the expression of a learned sequence of movements but not to the initial acquisition or learning of the sequence. These results challenge the commonly held assumption that the cerebellum is essential for motor skill acquisition. In so doing, the study offers a new interpretation of why patients with cerebellar lesions fail to learn the SRT task (*6*–*8*). Studies of the SRT task in patients have not included a distractor task. Thus, measures of learning and performance are conflated, and a performance deficit may be misinterpreted as a learning impairment.

The Seidler *et al.* strategy is a clever way to separate learning and performance

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and offers a new method for testing the cerebellar learning hypothesis. However, available data from both behavioral and neuroimaging experiments suggest alternative explanations for the pattern of cerebellar activation. First, the inclusion of the distractor task during the initial acquisition phase may alter the neural landscape for learning. Previous imaging of the SRT task showed that learning-related changes under conditions of attentional distraction were associated with motor and parietal cortex, the two areas associated with learning in the current study (*9*, *10*) (see the figure). However, previous work also indicated that a different learning network is engaged when acquisition occurs without such distraction. This suggests that the cerebellum may be recruited only during the encoding of movement sequences when the distractor task is absent.

Second, learning in the SRT task, at least under low levels of practice, is fairly abstract and not linked to particular muscles or movements. Finger movement sequences learned during practice are largely preserved following transfer to a task where responses are made with arm movements or through vocalization (*11*). The cerebellum may not be designed for the development of abstract representations; rather, its contribution to motor control may be intimately linked to the coordination of patterns of specific muscle activities (*12*). For example, the repeated pairing of a tone and airpuff leads to a conditioned response of the muscles protecting the eye. Should that airpuff be redirected at a finger (or paw), one would not expect to see transfer in the form of flexion or extension of the finger.

The contrast between the SRT and eyeblink conditioning tasks underscores the difficulty in succinctly characterizing the part played by the cerebellum in motor learning (see the figure). In this regard, it is instructive to examine the computational requirements of the two tasks. It is possible that the cerebellum is essential for eyeblink conditioning because the animal not only learns to associate two contiguous events, but also must extract the temporal relationship between the tone and airpuff (*13*). This precise timing is what makes the conditioned response adaptive, protecting the eye from the adverse stimulus, with the cerebellum forming these temporal representations. It is unlikely that precise timing is essential for learning in the SRT task. At least during the initial stages, learning involves the formation of associations between a series of spatial locations, each presented and responded to as a chain of discrete events. The repeated finding that activity of the parietal cortex correlates with SRT learning is consistent with the hypothesis that such learning is primarily spatial.

Seidler *et al*. provide an instructive challenge to theorists and empiricists who have championed the cerebellum as the key instigator of motor learning. Just as important, their work reveals the murky waters we face when attempting to understand brain function in terms of general task descriptions such as "motor learning." Complex skills are supported by multiple representations, each of which can be the target of learning. Moreover, it is difficult to define the boundary between "motor" activity and neural activity that lies beyond the motor system. The ability of a World Cup soccer player to score requires not only coordination of the muscles to generate a powerful kick, but also identification and anticipation of the locations of the defenders. As is typical of many debates in science, we will need to move away from binary questions such as "Does the cerebellum contribute to motor learning?" toward more complex questions such as "How does the cerebellum contribute to motor learning?"

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PERSPECTIVES: OCEANOGRAPHY

Small Critters—Big Effects

André Morel and David Antoine

The tiny unicellular algae inhabiting the upper well-lit ocean, collectively called phytoplankton, are the prime producers and the first link in the marine food chain. Their capacity for synthesizing organic matter (their net primary productivity, NPP) is therefore of great interest, particularly for the purpose of managing fisheries in a sustainable manner (*1*, *2*).

The NPP is also important in the context of the biogeochemical cycling of carbon and other elements. Through the photosynthetic activity of phytoplankton, inorganic carbon is fixed, organic matter is formed, and particulate matter is created, resulting in a vertical flux of sinking materials in the sea. As CO_2 concentrations increase in the atmosphere, the NPP of phytoplankton and the mechanisms of oceanic carbon storage are receiving increasing attention (*3*).

A number of ingredients are needed to calculate NPP. The two most important factors are the biomass in a given part of the ocean, and the rate at which this biomass takes up carbon. Paradoxically, the best way to obtain these data is from space, at a distance some 10^{12} times the size of the organisms involved.

Because photosynthesis results in simultaneous O_2 production and CO_2 uptake, the first estimates of oceanic primary production were based on local determinations of O_2 evolution or (after 1950) ^{14}C uptake, both of which can be measured during bottle incubations aboard ship. Such measurements give access to a rate (per unit of biomass); for estimates of NPP, they must be combined with the algal biomass distribution. Thanks to cruises carried out in various (but not all) parts of the ocean, the spatial distribution of phytoplankton, depicted by the chlorophyll concentration, has been progressively clarified. The extension of these unavoidably limited observations to the world ocean has, however, remained problematic. This is reflected in global estimates of NPP published from 1950 to 1980, which range from 20 to 126 Pg (1 Pg = 10^{15} g) of carbon fixed per year.

The situation changed dramatically in the 1980s, when ocean-color data obtained by the satellite-borne sensor CZCS (*4*) provided the first detailed chlorophyll concentration map of the entire ocean. Today, the spatial and temporal variability of algal biomass is documented on interannual scales with unprecedented accuracy with new sensors such as SeaWiFS, MODIS, and MERIS (*4*).

The phytoplankton biomass term can thus now be considered well constrained (*5*). But is the rate of carbon fixation (the incorporation of carbon into the biomass

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