

Long thought to be solely  
the **BRAIN'S COORDINATOR** of body movement,  
**THE CEREBELLUM** is now known to be active during  
a wide variety of cognitive and perceptual activities

# Rethinking the “*Lesser Brain*”

By James M. Bower and Lawrence M. Parsons

“In the back of our skulls, perched upon the brain stem under the overarching mantle of the great hemispheres of the cerebrum, is a baseball-sized, bean-shaped lump of gray and white brain tissue. This is the cerebellum, the ‘lesser brain.’”

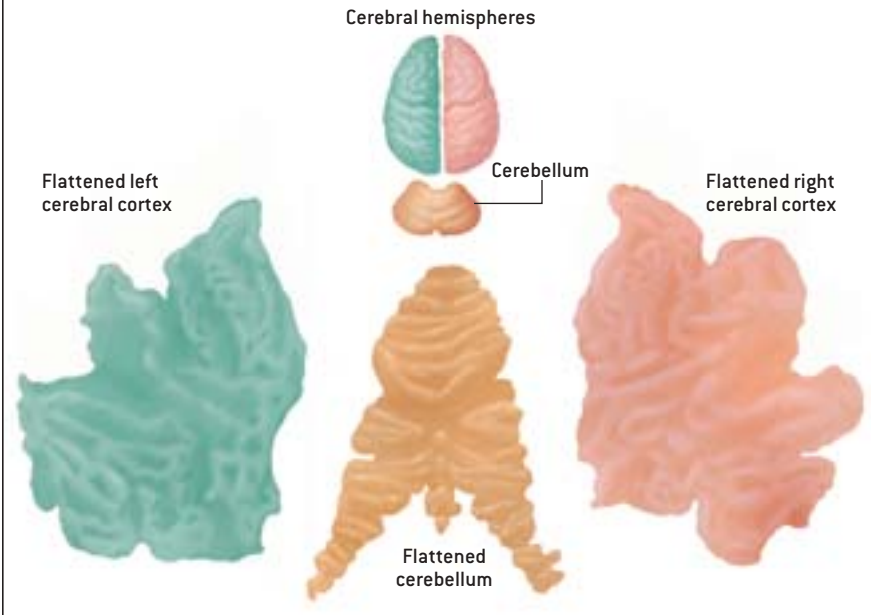
So began, somewhat modestly, the article that in 1958 introduced the cerebellum to the readers of *Scientific American*. Written by Ray S. Snider of Northwestern University, the introduction continued, “In contrast to the cerebrum, where men have sought and found the centers of so many vital mental activities, the cerebellum remains a region of subtle and tantalizing mystery, its function hidden from investigators.” But by the time the second *Scientific American* article on the cerebellum appeared 17 years later, author Rodolfo R. Llinás (currently at New York University Medical Center) confidently stated, “There is no longer any doubt that the cerebellum is a central control point for the organization of movement.”

Recently, however, the cerebellum’s function has again become a subject of debate. In particular, cognitive neuroscientists using powerful new tools of brain imaging have found that the

human cerebellum is active during a wide range of activities that are not directly related to movement. Sophisticated cognitive studies have also revealed that damage to specific areas of the cerebellum can cause unanticipated impairments in nonmotor processes, especially in how quickly and accurately people perceive sensory information. Other findings indicate that the cerebellum may play important roles in short-term memory, attention, impulse control, emotion, higher cognition, the ability to schedule and plan tasks, and possibly even in conditions such as schizophrenia and autism. Additional neurobiological experiments—both on the pattern of sensory inputs to the cerebellum and on the ways in which the cerebellum processes that information—also suggest a need to substantially revise current thinking about the function of this organ. The cerebellum has once again become an area of “tantalizing mystery.”

## LARGER THAN YOU'D THINK

FLATTENING the outer layer, or cortex, of the two human cerebral hemispheres and the cerebellum illustrates that the cerebellum has roughly the same surface area as a single cerebral hemisphere, even though when folded it takes up much less space. The size and complexity of the cerebellum indicate that it must play a crucial function.



In retrospect, it is perhaps not surprising that the cerebellum acts as more than just a simple controller of movement. Its great bulk and intricate structure imply that it has a more pervasive and complex role. It is second in size only to the cerebral cortex, the wrinkled surface of the brain's two large hemispheres, which is known to be the seat of many critical brain functions. Like the human cerebral cortex, the cerebellum packs a prodigious amount of circuitry into a small space by folding in on itself numerous times. Indeed, the human cerebellum is much more folded than the cerebral

cortex; in various mammals, it is the sole folded brain structure. Flattening out the human cerebellum yields a sheet with an average area of 1,128 square centimeters—slightly larger than a record album cover. That is more than half the 1,900 square centimeters of the surface area of the two cerebral cortices added together.

The cerebellum clearly has an important job, because it has persisted—and become larger—during the course of evolution. Although biologists often consider the growth of the cerebral cortex to be the defining characteristic of human brain evolution, the cerebellum has also

enlarged significantly, increasing in size at least three times during the past million years of human history, according to fossilized skulls. Perhaps the cerebellum's most remarkable feature, however, is that it contains more individual nerve cells, or neurons, than the rest of the brain combined. Furthermore, the way those neurons are wired together has remained essentially constant over more than 400 million years of vertebrate evolution [see box on opposite page]. Thus, a shark's cerebellum has neurons that are organized into circuits nearly identical to those of a person's.

### More than Movement

THE HYPOTHESIS that the cerebellum controls movement was first proposed by medical physiologists in the middle of the 19th century, who observed that removing the cerebellum could result in immediate difficulties in coordinating movement. During World War I, English neurologist Gordon Holmes added great detail to these early findings by going from tent to tent on the front lines of battle and documenting the lack of motor coordination in soldiers who had suffered gunshot or shrapnel wounds to the cerebellum.

In the past 15 years, however, more refined testing techniques have made the story more complicated. In 1989 Richard B. Ivry and Steven W. Keele of the University of Oregon observed that patients with cerebellar injuries cannot accurately judge the duration of a particular sound or the amount of time that elapses between two sounds. In the early 1990s researchers led by Julie A. Fiez of Washington University observed that patients with damage to the cerebellum were more error-prone than others in performing certain verbal tasks. One such individual, for instance, required additional time to think of an appropriate verb, such as “to shave,” when shown a picture of a razor, for example. He came up with a descriptor such as “sharp” more readily.

In more recent studies, the two of us demonstrated that patients who have neurodegenerative diseases that specifically shrink the cerebellum are often less accurate than others in judging fine differences between the pitch of two tones.

## Overview/*The Cerebellum*

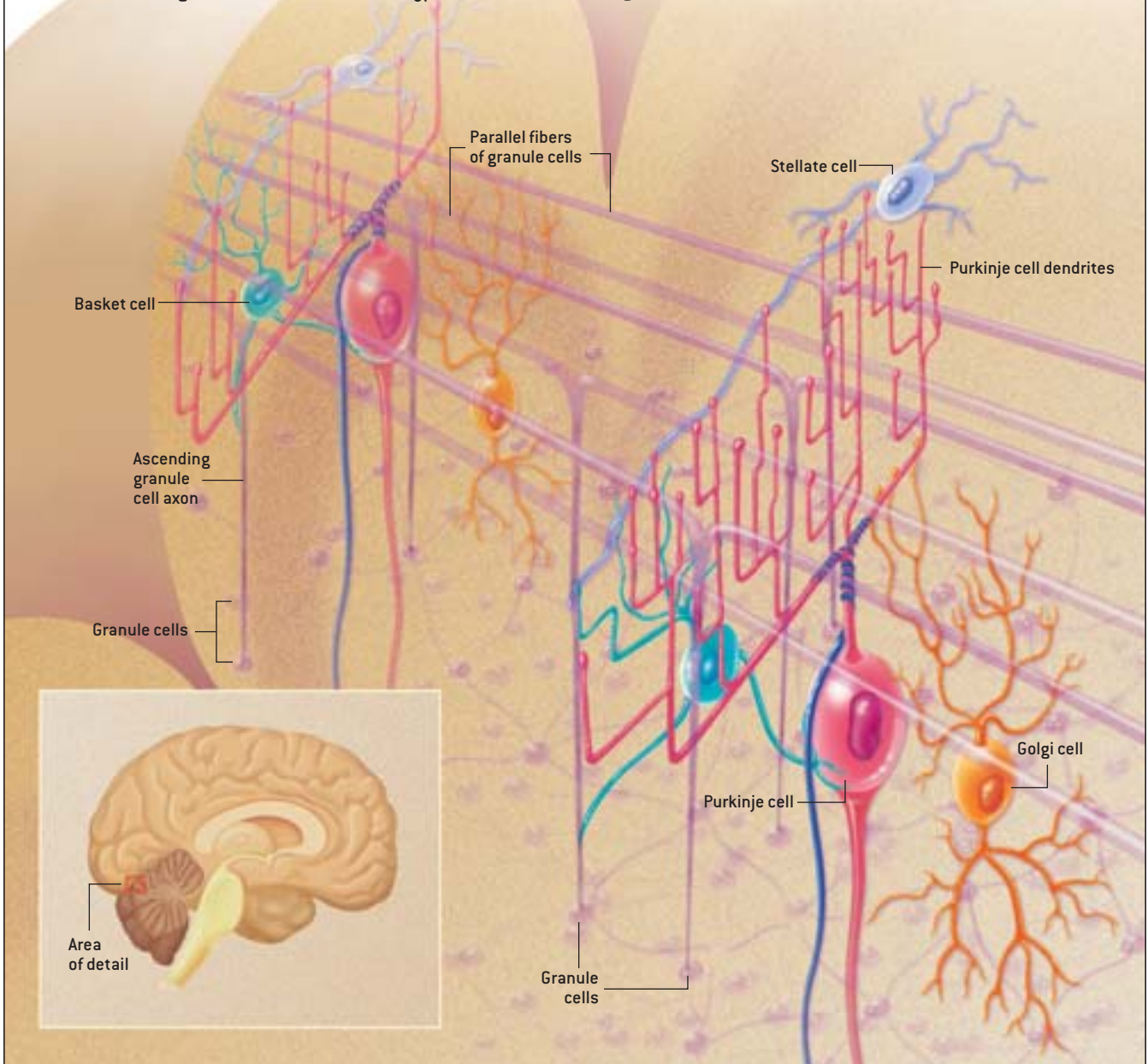
- The cerebellum sits at the base of the brain and has a complex neural circuitry that has remained virtually the same throughout the evolution of animals with backbones.
- The traditional notion that the cerebellum controls movement is being questioned by studies indicating that it is active during a wide variety of tasks. The cerebellum may be more involved in coordinating sensory input than in motor output.
- Removing the cerebellum from young individuals often causes few obvious behavioral difficulties, suggesting that the rest of the brain can learn to function without a cerebellum.

# HOW THE CEREBELLUM IS WIRED

**THE BASIC FEATURES** of cerebellar circuitry have been known since the seminal work of Spanish neuroanatomist Santiago Ramón y Cajal in the late 1800s. The central neuron is the Purkinje cell, named for Czech physiologist Johannes E. Purkinje, who identified it in 1837. The Purkinje cell provides the sole output of the cerebellar cortex and is one of the largest neurons in the nervous system, receiving an extraordinary 150,000 to 200,000 inputs (synapses)—an order of magnitude more than any single neuron in the cerebral cortex. These inputs spring principally from one of the smallest vertebrate neurons, the cerebellar granule cell. Granule cells are packed together at a density of six million per square millimeter, making them the most numerous type of neuron in

the brain. The axon, or main trunk line carrying the outgoing signal, of every granule cell rises vertically out of the granule cell layer, making multiple inputs with its overlying Purkinje cell. The axon then splits into two segments that stretch away in opposite directions. These segments align into parallel fibers that run through the arms, or dendrites, of a Purkinje cell like wires through an electrical pole, providing a single input to many hundreds of Purkinje cells. Granule cells also communicate with three other types of neurons—the stellate, basket and Golgi cells—which help to modulate the signals emitted by both the granule and Purkinje cells. This basic pattern occurs in every cerebellum, indicating that it must be integral to its function.

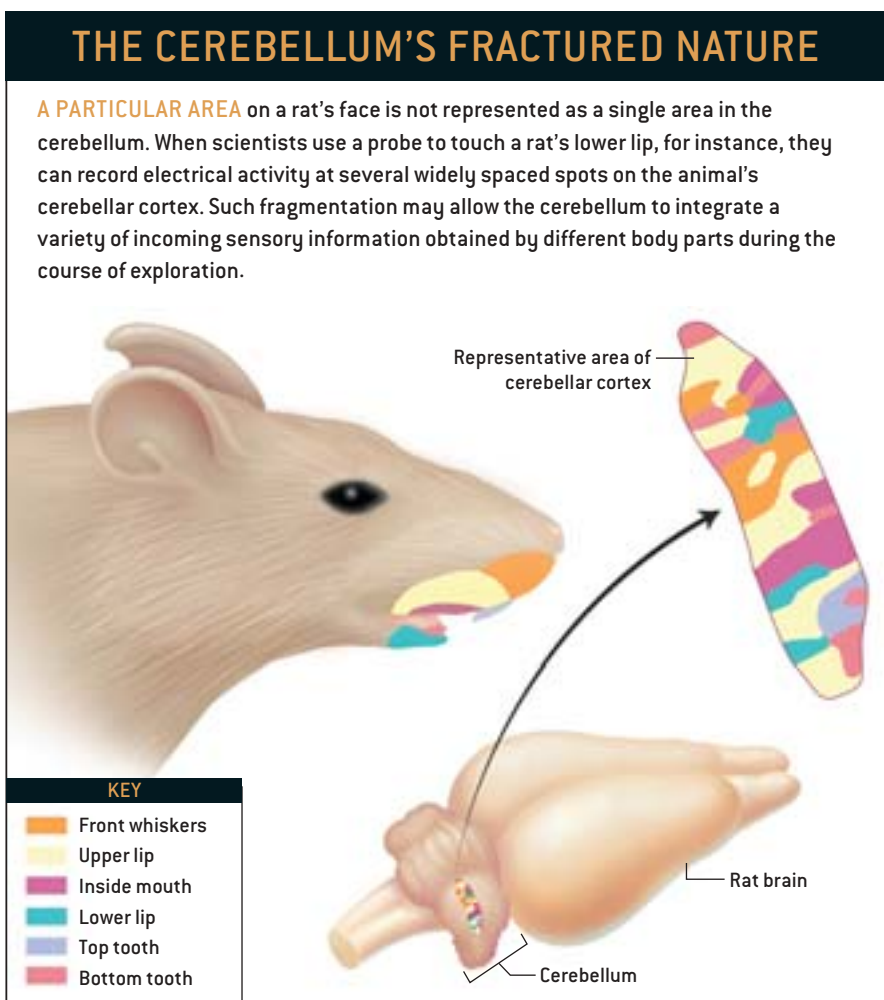
—J.M.B. and L.M.P.



Similarly, Peter Thier of the University of Tübingen in Germany and his co-workers found that people with damage to, or shrinkage of, part or all of the cerebellum are prone to make errors in tests in which they are asked to detect the presence, speed and direction of moving patterns. In addition, Hermann Ackermann and his collaborators, also at Tübingen, observed that patients with degenerated cerebellums are less able than healthy persons to discriminate between the similar-sounding words “rabbit” and “rapid.”

The impairments experienced by people with cerebellar damage can extend beyond language, vision and hearing. Jeremy D. Schmahmann of Massachusetts General Hospital reported that adult and child cerebellar patients have difficulty modulating their emotions: they either fail to react to or overreact to a stimulus that elicits a more moderate response from most people. Other researchers have demonstrated that adults with cerebellar damage show delays and tend to make mistakes in spatial reasoning tests, such as determining whether the shapes of objects seen from different views match. Some scientists have also tied the cerebellum to dyslexia. Rod I. Nicolson and his colleagues at the University of Sheffield in England, for instance, found that people with dyslexia and those with cerebellar damage have similar deficits in learning ability and that dyslexics have reduced cerebellar activity during certain tasks.

Other recent studies suggest that the cerebellum might be involved in working memory, attention, mental functions such as planning and scheduling, and impulse control. In 1992 Jordan Grafman and his co-workers at the National Institutes of Health observed, for instance, that indi-



viduals with an atrophied cerebellum had trouble with the planning and scheduling of steps required to solve the Tower of Hanoi problem, in which rings of different sizes must be arranged on a series of pegs according to specific rules. Two independent neuroimaging studies conducted in 1997 reported that the cerebellum of healthy volunteers became active when they were asked to recall a list of letters they had heard recited moments ear-

lier or when they were instructed to search a pattern for a specific image. In 2002 a brain imaging study by Xavier Castellanos, Judith L. Rapoport and their colleagues at the National Institute of Mental Health found that the cerebellum of children with attention-deficit hyperactivity disorder—which is characterized by a lack of impulse control—is reduced in size. Finally, brain imaging studies of healthy people and animals indicate that the cerebellum is normally active during sensory processes such as hearing, smell, thirst, need for food or air, awareness of body movement, and perception of pain.

### Touching, Feeling

WE ARE AMONG the researchers who have become convinced that the traditional motor-control theory of cerebellar function is inadequate to account for the new data. We came to this conclusion initially by intensively studying cerebellar re-

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gions that are active during touch. One of us (Bower) began such work while a graduate student more than 20 years ago in the laboratory of Wallace I. Welker at the University of Wisconsin–Madison. These investigations used a technique called micromapping to record the electrical activity of small patches of neurons in the brains of rats as they were touched lightly on various parts of their bodies.

in the cerebral cortex, where the spatial relations between areas of the body surface are retained in the cortical regions that respond to and send signals to those areas.

Although the fractured nature of the cerebellar maps is unusual, an even more surprising finding was that the rat cerebellum receives input primarily from the face of the animal. This was initially confusing because Snider had shown earlier that

a rat like the forepaws of a cat or the fingers of a monkey? The conclusion from the Wisconsin studies appeared to be that each structure is used by each animal to learn about its environment through touch. Anyone with a cat knows how much mischief its paws can cause, and anyone familiar with children recognizes how actively—and sometimes painfully—little fingers are used to gain information

## The cerebellum is more involved

in **SENSORY** than in **PURE MOTOR FUNCTION**.

Such tactile stimuli evoked activity across a large area of the cerebellum [see illustration on opposite page]. What is more, the map appeared fractured, with neighboring areas of the cerebellum often receiving inputs from disparate regions of the body and with areas that were far apart being represented next to one another in the cerebellum. Such a mapping plan is very different from that occurring

most of the tactile region of the cat cerebellum receives input from the forepaws and that the bulk of that region in monkeys is active when the fingers are touched.

### A Sensory Coordinator

GIVEN THE DIFFERENCES in the regions of the body surface represented in the cerebellum of various types of animals, the question became: How is the mouth of

about the youngsters' immediate world. But rats tend to get into trouble using their mouths. The fractured structure of the touch maps in the cerebellum supported the idea that the region was somehow comparing the sensory data coming from the multiple body parts used by each animal to explore its world. These maps seemed to be organized according to the use of the body parts rather than on their absolute proximity on the body surface. The idea that the rat cerebellum was somehow comparing the sensory information coming from different parts of the face was further supported by models and experiments examining how the cerebellum responded to these inputs. What emerged was a new hypothesis of cerebellar function suggesting that the cerebellum was specifically involved in coordinating the brain's acquisition of sensory data.

Although proposing novel ideas of brain function is easy, having the ideas accepted in a field that had decided in the 1850s that the cerebellum was a motor structure is a different story. In this case, the task was made even harder by the fact that there is clearly an extremely close linkage between sensory and motor systems in the brain, especially those involving touch. To make sure that we were seeing the effects of only sensory—and not motor—activity, we needed to study people, who, unlike rats, can follow explicit instructions about when to move and when not to. It was at this point that the partnership between the two of us began. In collaboration with Peter T. Fox of the University of Texas



**RUDOLF VAN'T HOFF** of Howard County, Maryland, has cerebellar damage caused by type 1 spinocerebellar atrophy, a rare genetic disease that usually manifests itself in middle age. The disorder has affected van't Hoff's balance, speech, and coordination and has also impaired his ability to discriminate between some sounds. He steadies his body with a bungee cord when sitting on his tractor.

CHRIS HARTLOVE

## PROBING CEREBELLAR FUNCTION

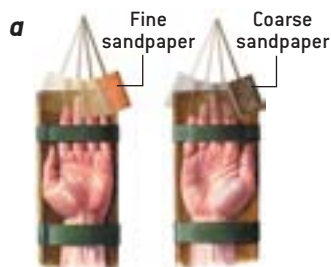
**TO DISCRIMINATE BETWEEN** the cerebellum's possible roles in coordinating movement and integrating sensory input, we devised a four-part experiment. We used a technique called functional magnetic resonance imaging to reveal brain activity in the cerebellum of six healthy people while they were either sensing a stimulus on their fingers without moving them or picking up and dropping small objects. In the first scenario, we immobilized a subject's hands and rubbed pieces of sandpaper gently across their fingertips (*a*). Sometimes they were asked to compare the coarseness of two different types of sandpaper (*b*). Both were purely sensory tasks, but the latter one required each person to discriminate between what they were feeling on each hand.

The second scenario involved both sensory and motor aspects. A volunteer placed his or her hands into separate bags that contained small wooden balls of different shapes and textures. In the first task (*c*), the person was told to randomly pick up and drop the balls, paying little heed to their shapes. In the second task (*d*), the individual was asked to compare the shape and feel of two balls every time he or she picked one up in each hand.

The cerebellum showed very little activity during the task that simply required picking up and dropping balls (*c*). In general, it was most active when the subjects were evaluating what they were sensing, either while moving (*d*) or still (*b*). These findings and others support our hypothesis that the cerebellum's main role is in processing sensory information rather than in controlling movement. —*J.M.B. and L.M.P.*

### PASSIVE SENSING

No movement



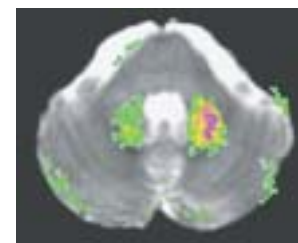
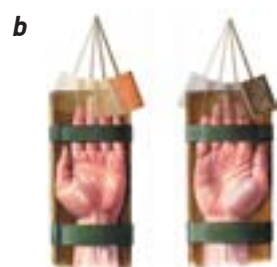
Cerebellum Active area

Movement

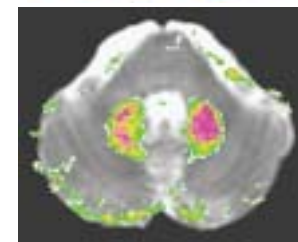


### ACTIVE SENSORY COMPARISON

No movement



Movement



Health Science Center in San Antonio, we designed a neuroimaging study to compare the amount of cerebellar activity induced when volunteers were instructed to use their fingers for a sensory touch discrimination task or told just to pick up and drop small objects. Under all previous theories of cerebellar function, the fine finger motor control required in picking up and dropping the small objects would be predicted to induce large amounts of cerebellar activity in the area associated with touch. Instead we found very little cerebellar activity in that region

during the pick-up-and-drop task, whereas sensory exploration using the fingers caused an intense cerebellar response [see box above]. This observation added support to our idea that the cerebellum is more involved in sensory than pure motor function and in particular that it is highly active during the process of acquiring sensory data.

### Life without a Cerebellum

OUR SENSORY-ACQUISITION hypothesis is but one of several new theories arising as a consequence of the growing evi-

dence for cerebellar involvement in more than just motor control. In many cases, the new data have been accommodated by simply broadening existing motor theories to account for nonmotor results. Ivry, for instance, has advocated a “generalized timing” hypothesis of cerebellar function that suggests that the cerebellum controls the timing of body movements (such as coordinating changes in joint angles) to allow individuals to time the duration of sensory inputs such as sights and sounds.

Other researchers have posited that the cerebellum not only facilitates fine

movement but also “smooths” the processing of information related to mood and thought. Schmahmann expressed such a view in 1991, and in 1996 Nancy C. Andreasen of the University of Iowa adapted the hypothesis to schizophrenia. She maintains that cerebellar deficits could underlie the disordered mental function characteristic of the disease. Other scientists have proposed that the regions of the cerebellum that have expanded dramatically during human evolution provide computational support for psychological tasks that can be offloaded from the

Few cerebellar theories, including those based on motor control, have provided an explanation for this puzzling resilience. In our view, the ability of the brain to compensate for the cerebellum’s absence implies a general and subtle support function. Under the sensory coordination hypothesis we favor, the cerebellum is not responsible for any particular overt behavior or psychological process. Rather it functions as a support structure for the rest of the brain. That support involves monitoring incoming sensory data and making continuous, very fine adjust-

eration of a faulty cerebellum would have more serious consequences than its complete removal. Although other brain structures can compensate for the outright lack of sensory data control, ongoing faulty control would be expected to cause continuing dysfunction in other brain regions attempting to use bad data. This type of effect might explain the recent implications for cerebellar involvement in disorders such as autism, in which patients fail to respond to incoming sensory data.

Hypotheses such as ours carry a useful reminder for future research: the presence

## It is clear that how we think about this brain structure—and how we CONCEIVE OF THE BRAIN as a whole—is about to change.

cerebral cortex when it is overburdened.

As the number of conditions that involve changes in cerebellar activity has grown, researchers have attributed more and more functions to the cerebellum. But scientists must yet explain how a single brain structure whose neural circuitry is organized into a uniform, repetitive pattern can play such an integral role in so many disparate functions and behaviors.

What is even more confounding is that people can recover from cerebellar injury. Although total removal of the cerebellum initially disrupts movement coordination, individuals (particularly young ones) can, with sufficient time, regain normal function to a considerable degree. Such plasticity is a general characteristic of the brain, but similar damage to primary sensory or motor-control regions of the cerebral cortex usually leaves animals and humans severely and permanently impaired in specific functions.

The capacity to recover from removal of the cerebellum has led some researchers to propose facetiously that its function might be to compensate for its own absence. It is highly unlikely, however, that such a large and intricate structure as the cerebellum is functionless or vestigial. Instead cerebellar function appears to permit the rest of the brain to compensate to a considerable degree for its absence.

ments in how that information is acquired—the objective being to assure the highest possible quality of sensory input.

We predict that those adjustments take the form of extremely subtle changes in the positions of probing human fingers or rat whiskers or in the retina or the inner ear. As a support structure, the cerebellum would be expected to have some level of activity in a large number of conditions, especially those requiring careful control of incoming and perhaps remembered sensory data. Other brain systems can usually compensate for the lack of sensory data coordination through the use of alternative processing strategies if the cerebellum is damaged or removed.

Indeed, motor coordination studies suggest that people with cerebellar damage slow down and simplify their movements—reasonable strategies to compensate for a lack of high-quality sensory data. An interesting and important extension of this idea is that the continued op-

of activity in a brain area does not necessarily mean that it is directly involved in a particular behavior or psychological process. Most of the machinery under the hood of a car, by analogy, is there to support the function of the engine. One could generate all kinds of hypotheses about the role of the radiator in propulsion—by correlating increased temperature to miles per hour, for instance, or by observing that a car ceases to run if its radiator is removed. But the radiator is not the engine.

If the cerebellum is primarily a support structure, then it does not contribute directly to motor coordination, memory, perception, attention, spatial reasoning or any of the many other functions recently proposed. Although this theory is one of several competing to account for the new and surprising data about the cerebellum, it is clear that how we think about this brain structure—and therefore how we conceive of the brain as a whole—is about to change. SA

### MORE TO EXPLORE

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