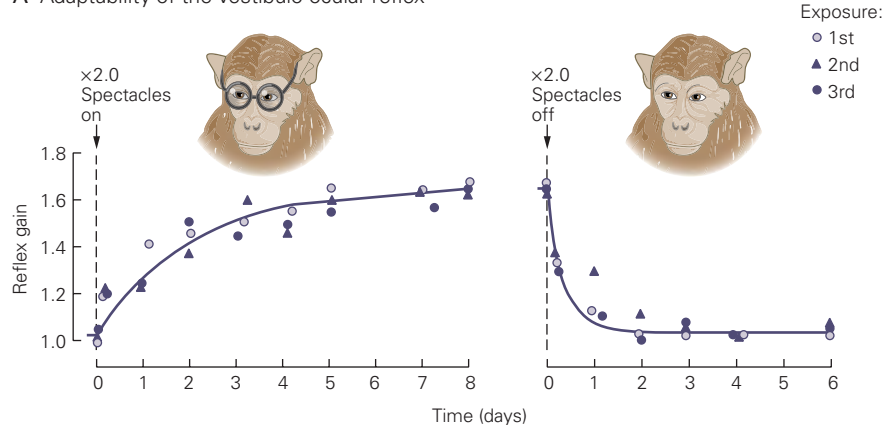


A Adaptability of the vestibulo-ocular reflex



B Sites of adaptive learning

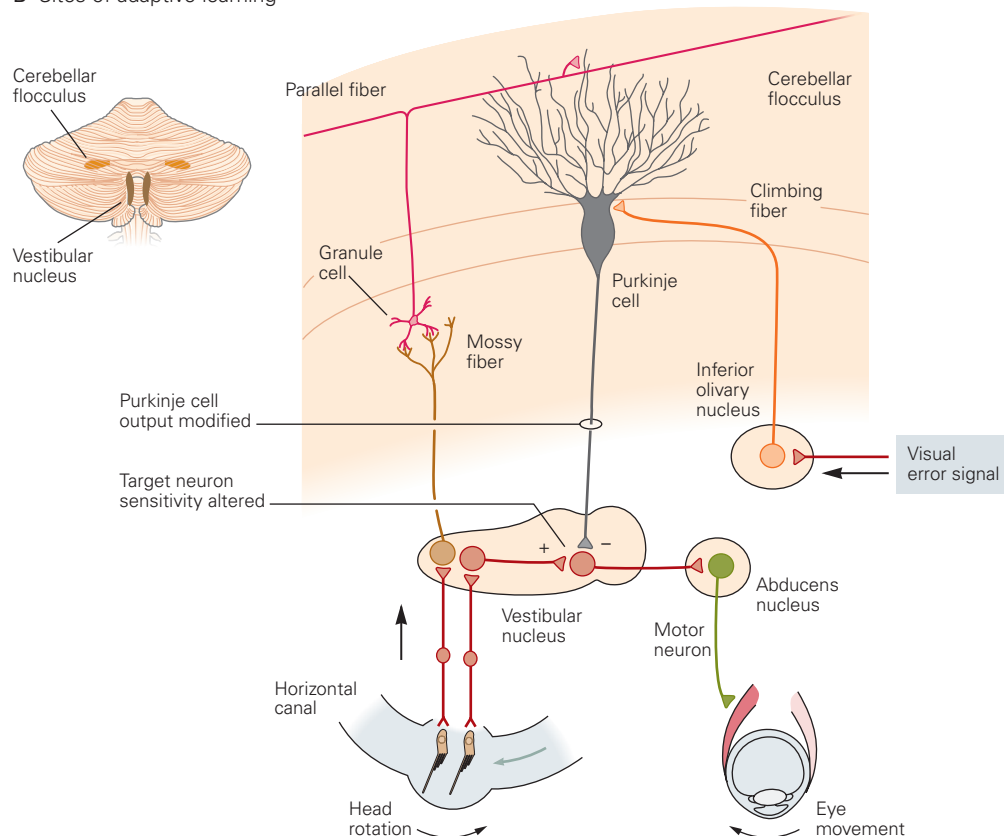


Figure 27–13 The vestibulo-ocular reflex is adaptable.

A. For several days, the monkey continuously wears magnifying spectacles that double the speed of the retinal-image motion evoked by head movement. Each day, the gain of the vestibulo-ocular reflex—the amount the eyes move for a given head movement—is tested in the dark so that the monkey cannot use retinal motion as a clue to modify the reflex. Over a period of 4 days, the gain increases gradually (*left*). It quickly returns to normal when the spectacles are removed (*right*). (Adapted, with permission, from Miles and Eighmy 1980.)

B. Adaptation of the vestibulo-ocular reflex occurs in cerebellar and brain stem circuits. A visual error signal, triggered by motion of the retinal image during head movement, reaches the inferior olivary nucleus. The climbing fiber transmits this error signal to the Purkinje cell, affecting the parallel fiber–Purkinje cell synapse. The Purkinje cell transmits changed information to the floccular target cell in the vestibular nucleus, changing its sensitivity to the vestibular input. After the reflex has been adapted, the Purkinje cell input is no longer necessary.

The Thalamus and Cortex Use Vestibular Signals for Spatial Memory and Cognitive and Perceptual Functions

For decades, vestibular function has been studied primarily in relation to reflexes, both vestibulo-ocular and vestibulospinal. Yet, in the past decade, it has become increasingly clear that the function of the vestibular system is as important for cognitive processes as for reflexes. The difficulty in understanding the vestibular system's role in spatial cognition stems from the fact that these functions are inherently multisensory, arising through convergence of vestibular, visual, somatosensory, and motor cues, following principles that remain poorly understood. Some of these perceptual functions of the vestibular system include tilt perception, visual-vertical perception, and visuospatial constancy.

Tilt perception. Vestibular information is critical for spatial orientation—the perception of how our head and body are positioned relative to the outside world. Nearly all species orient themselves using gravity, which provides a global, external reference. Thus, spatial awareness is governed by our orientation relative to gravity, collectively typically referred to as tilt.

Visual-vertical perception. We commonly experience the visual scene as perceptually oriented relative to earth-vertical orientation, regardless of our spatial orientation in the world. This ability has been studied psychophysically in humans and monkeys using tasks in which a subject is turned ear-down in the dark and asked to orient a dimly lit bar vertically in space (to align it with gravity). The results suggest that the neural representation of the visual scene is modified by static vestibular and proprioceptive signals that indicate the orientation of the head and body.

Visuospatial constancy. Vestibular signals are also important for the perception of a stable visual world despite constantly changing retinal images caused by movement of the eyes, head, and body. The projection of the scene onto the retina continuously changes because of these movements. Despite the changing retinal image, the percept of the scene as a whole remains stable; this stability is critical not only for vision but also for sensorimotor transformations (eg, to update the motor goal of an eye or arm movement).

Vestibular Information Is Present in the Thalamus

Vestibular projections to the thalamus are complicated and overall less clear, partly because of the strong multisensory nature of the responses in these cells and the difficulty in comparing thalamic regions and

nomenclature across studies and species. Some neurons in all vestibular nuclei and likely the fastigial cerebellar nuclei project bilaterally to the thalamus, but most fibers terminate in the contralateral thalamic nuclei (Figure 27–9).

Several major thalamic regions receive vestibular projections, including the ventral posterolateral and ventral lateral thalamic nuclei and, to a lesser extent, the ventral posteroinferior nuclei, the posterior group, and the anterior pulvinar. These nuclei are traditionally thought to also receive somatosensory input and project to the primary and secondary somatosensory cortices, as well as the posterior parietal cortex (areas 5 and 7) and the insula of the temporal cortex.

Vestibular Information Is Widespread in the Cortex

A number of cortical areas receiving short-latency vestibular signals either alone or more commonly in concert with proprioceptive, tactile, oculomotor, visual, and auditory signals have been identified (Figure 27–14). Although vestibular signals are widely distributed to a number of cortical regions, all such regions are multimodal and none seems to represent a purely vestibular cortex, similar to other modalities such as vision, proprioception, and audition.

Vestibular modulation has been established in the lateral sulcus (parietoinsular vestibular cortex), somatosensory cortex (areas 3a and 2v), oculomotor cortex (frontal and supplementary eye fields), extrastriate visual motion cortex (dorsal medial superior temporal area), and parietal cortex (ventral intraparietal area and area 7a). In the primary somatosensory cortex, area 2v lies at the base of the intraparietal sulcus just posterior to the areas of the postcentral gyrus representing the hand and mouth. Electrical stimulation of area 2v in humans produces sensations of whole-body motion. Area 3a lies at the base of the central sulcus, adjacent to the motor cortex. Many cells in the parietoinsular vestibular cortex are multisensory, responding to body motion, somatosensory, proprioceptive, and visual motion stimuli. Patients with lesions in this region report episodes of vertigo, unsteadiness, and a loss of perception for visual vertical. Neurons in the medial intraparietal and medial superior temporal areas respond to both visual (optic flow) and vestibular signals. These cells utilize multisensory cue integration (Bayesian) frameworks to assist in the cognitive perception of motion through space.

Imaging studies reveal an even larger portion of cerebral cortex involved in processing vestibular information, including the temporoparietal cortex and the insula, the superior parietal lobe, the

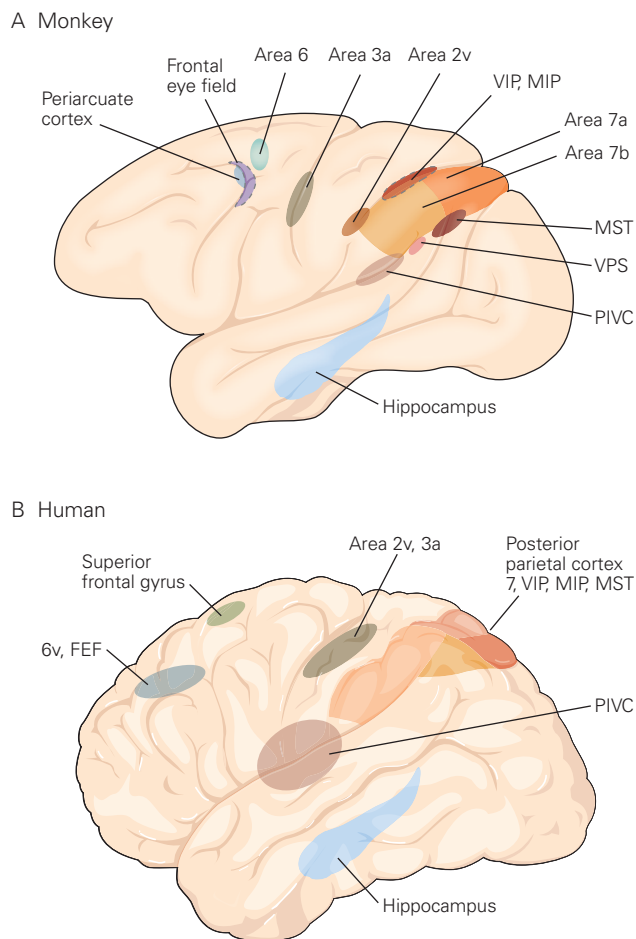


Figure 27-14 The vestibular cortex.

A. This lateral view of a monkey's brain shows the areas of cerebral cortex in which vestibular responses have been recorded. Areas in monkey cortex include periarculate cortex, area 6, frontal eye fields, areas 3a and 2v, ventral intraparietal area (VIP), medial intraparietal area (MIP), area 7, visual posterior sylvian area (VPS), medial superior temporal area (MST), parieto-insular vestibular cortex (PIVC), and the hippocampal formation.

B. In the human cortex, areas recording vestibular activity include 6v, frontal eye fields (FEF), superior frontal gyrus, 2v, 3a, posterior parietal cortex, PIVC, and the hippocampal formation.

pre- and postcentral gyri, anterior cingulate and posterior middle temporal gyri, premotor and frontal cortices, inferior parietal lobule, putamen, and hippocampal regions. Using electrical stimulation of the vestibular nerve in patients activates the prefrontal lobe and anterior portion of the supplementary motor area at relatively short latencies. However, imaging and, to a lesser extent, single-cell recording studies may overstate the range of vestibular representations. In particular, vestibular stimuli often co-activate the

somatosensory and proprioceptive systems, as well as evoke postural and oculomotor responses, which might in turn result in increased cortical activations.

Vestibular Signals Are Essential for Spatial Orientation and Spatial Navigation

Our ability to move about depends on a stable directional orientation. Certain cells in the thalamus, hippocampal region, entorhinal cortex, and subiculum are involved in navigation tasks. Damage to these areas impairs a variety of spatial and directional abilities. At least six cell types contributing to spatial orientation have been identified, including place cells, grid cells, head direction cells, border cells, speed cells, and conjunctive cells. In the hippocampus, place cells discharge relative to the animal's location in the environment (Chapter 54). Head direction cells in the dorsal thalamus, parahippocampal regions, and several regions of the cortex indicate the animal's heading direction like a compass. Grid cells in the entorhinal cortex respond to multiple spatial locations in a unique triangular grid pattern. Border cells in the entorhinal cortex signal environmental boundaries, speed cells discharge in proportion to the animal's running speed, and conjunctive cells exhibit a combination of several of these properties.

These regions are intimately connected and appear to work together in a "navigation network" to provide for spatial orientation, spatial memory, and our ability to move through our surroundings. Think of walking through your house, driving to the store, or knowing which direction to go in a new city. Lesions of central vestibular networks disrupt head direction, place, and grid responses. Patients with disease or trauma to the vestibular system, hippocampus, and anterior thalamus regions often exhibit severe deficits in their ability to orient in familiar environments or even find their way home.

All of these cells depend on a functioning vestibular system to maintain their spatial orientation properties. The pathway by which vestibular signals reach the navigation network and the computational principles determining how vestibular cues influence these spatially tuned cells is not well understood. We know that there are at least three different influences: Semicircular canal signals contribute to the estimate of head direction; gravity signals influence the three-dimensional properties of head direction cells; and translation signals influence the estimate of linear speed, which controls both grid cell properties and the magnitude and frequency of theta oscillations in the hippocampal network. What is clear is that there is no evidence

linking vestibular nuclei response properties directly to head direction or other spatially tuned cell types, and no direct projections from the vestibular nuclei to the brain areas thought to house these spatially tuned neurons have been identified. Furthermore, vestibular nuclei responses are inappropriate for driving these spatially tuned cells, as these signals need to encompass the total head movement, rather than individual components during active or passive head movement.

It has long been recognized that proprioceptive and motor efference cues should participate, together with vestibular signals, to track head direction over time. It has been proposed that internally generated information from vestibular, proprioceptive, and motor efference cues can be utilized to keep track of changes in directional heading. More recent insights have started to shed light on how each of these cues contributes to the final self-motion estimate that can be precisely predicted and quantitatively estimated based on a Bayesian framework. Although as yet difficult to define, quantitative internal models govern the relationship of vestibular and other multisensory self-motion cues for computing the spatial properties of navigation circuit cells.

Clinical Syndromes Elucidate Normal Vestibular Function

As we have seen, rotation excites hair cells in the semi-circular canal whose hair bundles are oriented in the direction of motion and inhibits those in the canals oriented away from the motion direction. This imbalance in vestibular signals is responsible for the compensatory eye movements and the sensation of rotation that accompanies head movement. It can also originate from disease of one labyrinth or vestibular nerve, which results in a pattern of afferent vestibular signaling analogous to that stemming from rotation away from the side of the lesion, that is, more discharge from the intact side. There is accordingly a strong feeling of spinning, called vertigo.

Caloric Irrigation as a Vestibular Diagnostic Tool

Nystagmus can be used as a diagnostic indicator of vestibular system integrity. In patients complaining of dizziness or vertigo, the function of the vestibular labyrinth is typically assessed by a caloric test (Figure 27–15). Either warm (44°C) or cold (30°C) water is introduced into the external auditory canal. In normal persons, warm water induces nystagmus that beats toward the ear into which the water has been

introduced, whereas cold water induces nystagmus that beats away from the ear into which the water has been introduced. This relationship is encapsulated in the mnemonic COWS: Cold water produces nystagmus beating to the Opposite side; Warm water produces nystagmus beating to the Same side. In normal persons, the two ears give equal responses. If there is a unilateral lesion in the vestibular pathway, however, nystagmus will be induced and directed toward the side opposite the lesion.

The vertigo and nystagmus resulting from an acute vestibular lesion typically subside over several days, even if peripheral function does not recover. This is because central compensatory mechanisms restore the balance in vestibular signals in the brain stem, even when peripheral input is permanently lost or unbalanced.

The loss of input from one labyrinth also means that all vestibular reflexes must be driven by a single labyrinth. For the VOR, this condition is quite effective at low speeds because the intact labyrinth can be both excited and inhibited. However, during rapid, high-frequency rotations, inhibition is not sufficient, such that the gain of the reflex is reduced when the head rotates toward the lesioned side. This is the basis of an important clinical test of canal function, the head-impulse test. In this test, the head is moved rapidly one time along the axis of rotation of a single canal. If there is a significant decrease in gain owing to canal dysfunction, the movement of the eyes will lag behind that of the head, and there will be a visible catch-up saccade.

Bilateral Vestibular Hypofunction Interferes With Normal Vision

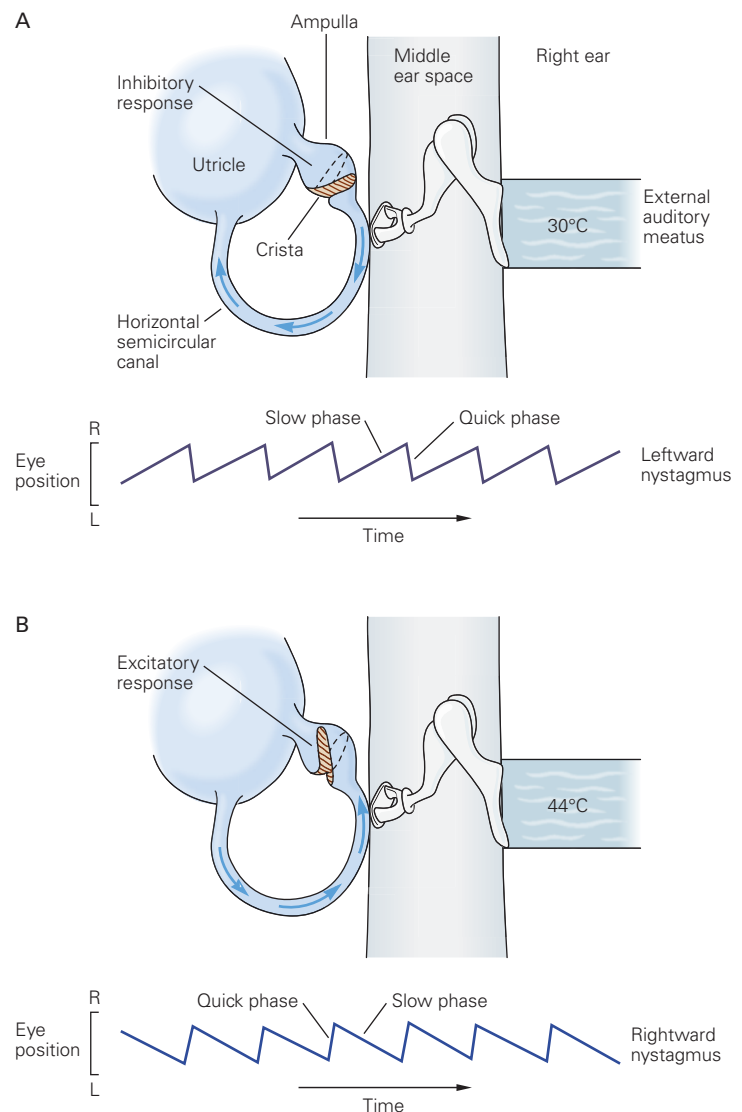
Vestibular function is sometimes lost simultaneously on both sides, for example, from ototoxicity owing to aminoglycoside antibiotics such as gentamicin or cancer treatment medications such as cisplatin. The symptoms of bilateral vestibular hypofunction are different from those of unilateral loss. First, vertigo is absent because there is no imbalance in vestibular signals; input is reduced equally from both sides. For the same reason, there is no spontaneous nystagmus. In fact, these patients may have no symptoms when they are at rest and the head is still.

In humans, receptor and nerve fiber loss due to disease, trauma, or ototoxicity is permanent. However, in other animal classes such as amphibians, reptiles, and birds, spontaneous regeneration does occur over time. Although the differences in regeneration between animal groups is not yet understood, recent

Figure 27–15 Bithermal caloric test of the vestibulo-ocular reflex. The vestibular caloric test remains the primary test used today in clinics around the world to determine if there is system dysfunction. The head is elevated 30° to align the horizontal semicircular canals with gravity.

A. Cold water or air introduced into the right ear causes a downward convection current in the endolymph, producing an inhibitory response in the right ear hair cells and afferent fibers. The result is a leftward (opposite side) beating nystagmus (as determined by fast phase direction).

B. Warm water or air introduced into the right ear produces an upward endolymph movement, producing an excitatory response in the hair cells and afferents. The result is a rightward (same side) beating nystagmus.



research shows promise for the future development of regenerative treatments in humans.

For the present, the loss of vestibular reflexes is devastating. A physician who lost his vestibular hair cells because of a toxic reaction to streptomycin wrote a dramatic account of this loss. Immediately after the onset of streptomycin toxicity, he could not read without steadying his head to keep it motionless. Even after partial recovery, he could not read signs or recognize friends while walking in the street; he had to stop to see clearly. Some patients may even “see” their heartbeat if the VOR fails to compensate for the miniscule head movements that accompany each arterial pulse.

Highlights

1. The vestibular system provides the brain with a rapid estimate of head movement. Vestibular signals are used for balance, visual stability, spatial orientation, movement planning, and motion perception.
2. Vestibular receptor hair cells are mechanotransducers that sense rotational and linear accelerations. Through kinematic and neural processing mechanisms, movements are transformed into acceleration, velocity, and position signals. These signals are used throughout the brain efficiently and quickly to guide behavior and cognition.

3. Receptor cells are polarized to detect the direction of motion. Three semicircular canals in each inner ear detect rotational motion and work in bilateral synergistic pairs through convergent commissural pathways in the vestibular nuclei. Two otolith organs in each ear detect linear translations and tilts relative to gravity.
4. Vestibular nuclei neurons receive converging multisensory and motor signals from visual, proprioceptive, cerebellar, and cortical sources. The multisensory integration allows for discrimination between active and passive body motion, as well as appropriate motor responses for reactive or volitional behavior.
5. Projections from the vestibular nuclei to the oculomotor system allow eye muscles to compensate for head movement through the vestibulo-ocular reflex to hold the image of the external world motionless on the retina. Cortical projections to the vestibular and oculomotor nuclei allow volitional eye movements to be separated from reflex eye movements but work through a final common pathway. Motor learning through vestibulocerebellar networks provides compensatory changes in eye movement responses to changing visual conditions through the use of spectacles, disease, or aging.
6. Projections from the vestibular nuclei to motor areas and the spinal cord facilitate postural stability. Gaze stability coordinates eye and neck movements through the medial vestibulospinal pathway. Postural control is exerted through the lateral vestibulospinal pathway.
7. Projections from the vestibular nuclei to the rostral and caudal medulla nuclei are involved in regulation of blood pressure, heart rate, respiration, bone remodeling, and homeostasis.
8. Projections from the vestibular nuclei to thalamus and cortex ensure spatial orientation and influence spatial perception more generally.
9. Vestibular signals processed in the hippocampal regions are crucial for spatial location and navigation functions.
10. Vestibular signals are combined with visual signals in several cortical regions through Bayesian cue integration to provide motion perception.
11. Disease or trauma to the vestibular system can produce nausea, vertigo, dizziness, balance disorders, visual instability, and spatial confusion.
12. We are only beginning to appreciate the role of the vestibular system in cognition. However, it is clear that vestibular signals contribute to our perception of self, conception of body presence, and memory.
13. New approaches in computation and theory promise to provide the lapidary keys needed to unlock our understanding of how vestibular signals contribute to the essence of brain function.

J. David Dickman
Dora Angelaki

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Auditory Processing by the Central Nervous System

Sounds Convey Multiple Types of Information to Hearing Animals

The Neural Representation of Sound in Central Pathways Begins in the Cochlear Nuclei

The Cochlear Nerve Delivers Acoustic Information in Parallel Pathways to the Tonotopically Organized Cochlear Nuclei

The Ventral Cochlear Nucleus Extracts Temporal and Spectral Information About Sounds

The Dorsal Cochlear Nucleus Integrates Acoustic With Somatosensory Information in Making Use of Spectral Cues for Localizing Sounds

The Superior Olivary Complex in Mammals Contains Separate Circuits for Detecting Interaural Time and Intensity Differences

The Medial Superior Olive Generates a Map of Interaural Time Differences

The Lateral Superior Olive Detects Interaural Intensity Differences

The Superior Olivary Complex Provides Feedback to the Cochlea

Ventral and Dorsal Nuclei of the Lateral Lemniscus Shape Responses in the Inferior Colliculus With Inhibition

Afferent Auditory Pathways Converge in the Inferior Colliculus

Sound Location Information From the Inferior Colliculus Creates a Spatial Map of Sound in the Superior Colliculus

The Inferior Colliculus Transmits Auditory Information to the Cerebral Cortex

Stimulus Selectivity Progressively Increases Along the Ascending Pathway

The Auditory Cortex Maps Numerous Aspects of Sound

A Second Sound-Localization Pathway From the Inferior Colliculus Involves the Cerebral Cortex in Gaze Control

Auditory Circuits in the Cerebral Cortex Are Segregated Into Separate Processing Streams

The Cerebral Cortex Modulates Sensory Processing in Subcortical Auditory Areas

The Cerebral Cortex Forms Complex Sound Representations

The Auditory Cortex Uses Temporal and Rate Codes to Represent Time-Varying Sounds

Primates Have Specialized Cortical Neurons That Encode Pitch and Harmonics

Insectivorous Bats Have Cortical Areas Specialized for Behaviorally Relevant Features of Sound

The Auditory Cortex Is Involved in Processing Vocal Feedback During Speaking

Highlights

HEARING IS CRUCIAL FOR LOCALIZING and identifying sound; for humans, it is particularly important because of its role in the understanding and production of speech. The auditory system has several noteworthy features. Its subcortical pathway is longer than that of other sensory systems. Unlike the visual system, sounds can enter the auditory system from all directions, day and night, when we are asleep as well as when we are awake. The auditory system processes not only sounds emanating from outside the body (environmental sounds, sounds generated by others) but also self-generated sounds (vocalizations and chewing sounds). The location of sound stimuli in space is not conveyed by the spatial arrangement of

sensory afferent neurons but is instead computed by the auditory system from representations of the physical cues.

Sounds Convey Multiple Types of Information to Hearing Animals

Hearing helps to alert animals to the presence of unseen dangers or opportunities and, in many species, also serves as a means for communication. Information about where sounds arise and what they mean must be extracted from the representations of the physical characteristics of sound at each of the ears. To understand how animals process sound, it is useful first to consider which cues are available.

Most vertebrates take advantage of having two ears for localizing sounds in the horizontal plane. Sound sources at different positions in that plane affect the two ears differentially: Sound arrives earlier and is more intense at the ear nearer the source (Figure 28–1A). Interaural time and intensity differences carry information about where sounds arise.

The size of the head determines how interaural time delays are related to the location of sound sources; the neuronal circuitry determines the precision with which time delays are resolved. Because air pressure waves travel at roughly 340 m/s in air, the maximal interaural delay in humans is approximately 600 μ s; in small birds, the greatest delay is only 35 μ s. Humans can resolve the location of a sound source directly ahead to within approximately 1 degree, corresponding to an interaural time difference of 10 μ s. Interaural time differences are particularly well conveyed by neurons that encode relatively low frequencies. These neurons can fire at the same position in every cycle of the sound and in this way encode the interaural time difference as an interaural phase difference. Sounds of high frequencies produce *sound shadows* or intensity differences between the two ears. For many mammals with small heads, high-frequency sounds provide the primary cue for localizing sound in the horizontal plane.

Mammals can localize sounds in the vertical plane and with a single ear using spectral filtering. High-frequency sounds, with wavelengths that are close to or smaller than the dimensions of the head, shoulders, and external ears, interact with those parts of the body to produce constructive and destructive interference, introducing broad spectral peaks and deep, narrow spectral notches whose frequency changes with the location of the sound (Figure 28–1B). High-frequency sounds from different origins are filtered differently

because in mammals the shape of the external ear differs back-to-front as well as top-to-bottom. Animals learn to use these spectral cues to locate sound sources. If the shape of the ear is experimentally altered, even adult humans can learn to make use of a new pattern of spectral cues. If animals lose hearing in one ear, they lose interaural timing and intensity cues and must depend completely on spectral cues for localizing sounds.

How do we make sense of the complex and changing sounds that we hear? Most natural sounds contain energy over a wide range of frequencies and change rapidly with time. The information used to recognize sounds varies among animal species, and depends on listening conditions and experience. Human speech, for example, can be understood in the midst of noise, over electronic devices that distort sounds, and even through cochlear implants. One reason for its robustness is that speech contains redundant cues: The vocal apparatus produces sounds in which multiple parameters covary. At the same time, this makes the task of understanding how animals recognize patterns a complicated one. It is not clear which cues are used by animals under various conditions.

Music is a source of pleasure to human beings. Musical instruments and human voices produce sounds that have energy at the fundamental frequency that corresponds to its perceived pitch, as well as at multiples of that frequency, giving sounds a quality that allows us, for example, to distinguish a flute from a violin when their pitch is the same. Musical pitches are largely in the low-frequency range in which auditory nerve fibers fire in phase with sounds. In music, sounds are combined simultaneously to produce chords and successively to produce melodies. Euphonious, pleasant chords elicit regular, periodic firing in cochlear nerve fibers. In dissonant sounds, there is less regularity both in the sound itself and in the firing of auditory nerve fibers; the component frequencies are so close that they interfere with one another instead of periodically reinforcing one another.

The Neural Representation of Sound in Central Pathways Begins in the Cochlear Nuclei

The neural pathways that process acoustic information extend from the ear to the brain stem, through the midbrain and thalamus, to the cerebral cortex (Figure 28–2). Acoustic information is conveyed from cells in the cochlear ganglion (see Figure 26–17) to the cochlear nuclei in the brain stem. There information is received by several different types of neurons, most of which are arranged tonotopically.