THE AUDITORY SYSTEM

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LEARNING OBJECTIVES

1. Learn the parameters of sound that are represented in perception and measured clinically.
2. Learn how auditory deficits arise and the nature of the major bilateral pathways that limit the usefulness of those deficits for the diagnosis of neurological lesions.
3. Learn and/or review structures, tonotopic projection patterns, and functions of the major elements in the primary auditory pathway.
4. Learn the two auditory pathway mechanisms used to localize sound sources.
5. Be able to apply the information you have learned to understand, diagnose, and/or treat clinical problems in the auditory system, and counsel patients who experience hearing impairment.

REFERENCES: Chapter 13 in Purves et al. *Neuroscience*, 4th edition.

OVERVIEW

Hearing loss is a highly prevalent neurological condition. For patients who acquire deficits after the development of speech, hearing loss can have serious negative effects on quality of life. Medical texts and courses in neuroscience focus great attention on the peripheral components of the auditory pathways for two reasons. 1.) Most hearing deficits arise as the result of damage within the cochlea, not from lesions in central nervous system pathways. At least 80% of those cases (about 20 million in the U.S.) stem from loss of hair cells. 2.) Decussations and bilateral projections are hallmarks of the central auditory pathways, beginning with the neurons that project from first synapses in the cochlear nuclei. In most cases of CNS lesions, the **bilateral redundancy** of information transmission in the auditory pathways that ascend to the cortex preserves auditory function, so specific deficits of hearing are seldom useful for neurological diagnosis.

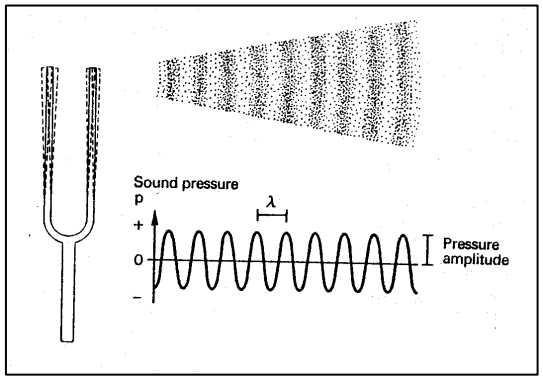
Therefore, we will not encourage you to become as intimately familiar with the neuroanatomical pathways of the central auditory system as we have for other brain systems. You should understand the functions of the peripheral auditory structures, understand how sound is perceived, and represented in terms of clinically measured parameters. You should also know the major centers in the primary auditory pathway and its major fiber tracts, and understand the concept of tonotopic representation and the two pathways that provide our capacity for sound localization.

Hearing loss

- Cochlear implants (and more on this later in the lecture).
- Age-related loss of sensory cells (a major cause of ***presbycusis***).
- Causes of sensorineural hearing loss (infections, acoustic overstimulation, aminoglycosides, cisplatin, head trauma, and unspecified causes with aging).
- Sensorineural vs conductive deficits.
- Potential for regenerative medicine.

Understanding the Clinical Representations of the Parameters of Sound:

- Sound waves are mechanical, dependent on molecular collisions.
- Sound speed is determined by the medium it travels through (**~340 meters/second or ~34 cm/millisecond in air**).
- Sounds waves are represented in terms of the following:
    - **Frequency** is the physical quantity that underlies our perception of the **pitch** of a sound (***f*** = cycles/second or Hertz (Hz) or thousands of cycles/sec = kilohertz (kHz))
    - **Wavelength** is the distance in space that is covered by one wave of the sound (λ = wavelength, usually measured in meters or centimeters).
    - In air, λ = 340 meters divided by the sound frequency in Hertz.

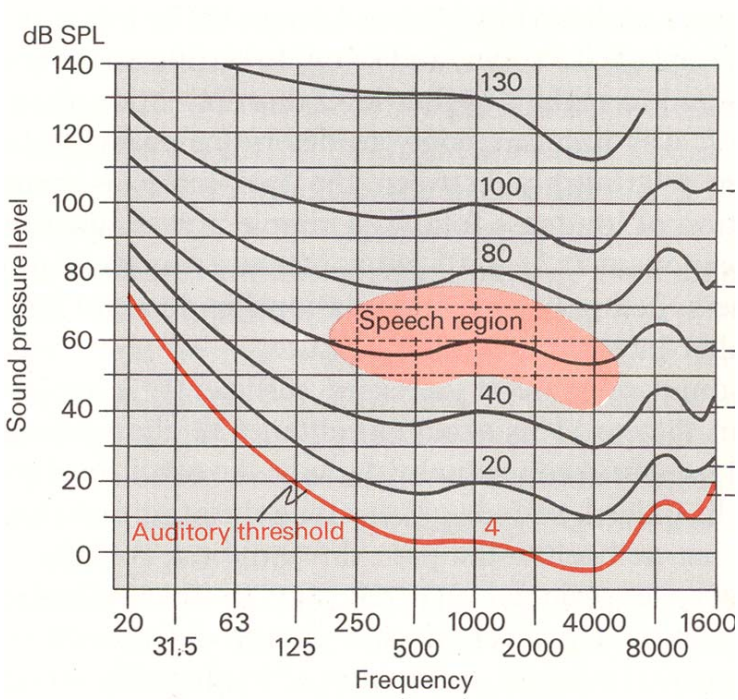


Vowels and Consonants:

- Speech is a combination of "tonal" vowels and "noisy" consonants.
- Vowels are somewhat tonal and typically lower in frequency.
- Tones are combinations of sine waves (a single frequency or a limited combination of frequencies).
- Consonants contain frequency transitions, “noisy” stops, and clicks. Clicks are brief, abrupt transitions and always contain many frequencies.
- Noise is comprised of many frequencies, typically occurring randomly.
- The high frequencies associated with consonants carry much of the information content of speech.
- High frequency hearing loss is the most common form. Patients who experience this often say they can hear, but they complain of reduced ability to understand speech.
- High frequency hearing loss impacts the ability to distinguish the consonant sound in spoken words, though the vowel sounds are adequately detected. Examples: bat, that, sat, hat, cat, fat, mat, rat, gnat.

Frequency Sensitivity:

- Normal young adults can hear sounds ranging from **20 Hz to 20,000 Hz (20 kHz)**. With aging the range of *normal* hearing becomes 20 HZ to 16 kHZ.
- Our perception of the frequency of a sound as called **pitch perception**.
- Sensitivity between ~200 to ~6,000 Hz is critical for understanding speech.



Loudness and Sound pressure level (SPL):

- We perceive sound pressure increases as increases in **loudness**.
- Sound pressure at the just detectable level, **the auditory threshold**, is extremely low for a tone at ~1 kHz: **0.0002 dynes per square cm** (also referred to as 20 microPascal, 20 µPa).
- Clinical measures of sound pressure are typically expressed in reference to that level. The notation is: ***x*** **dB SPL**. (see section below).
- Sound pressure is a measure of the rapidly varying pressure differences between minute peaks and valleys in pressure that are superimposed on the much larger average atmospheric pressure. (The static atmospheric pressure is over one million dynes per square cm at 760 torr).

The Dynamic Range of Hearing:

- The dynamic range of hearing is the span of sound magnitudes from the weakest to the strongest sounds throughout a range where **differences in loudness** can be detected by our auditory system.
- The normal dynamic range of hearing extends from threshold (= 0 dB SPL for a normal young person) to a sound pressure that is one million times greater (= 120 dB SPL).

Decibels:

- Sound pressure is expressed in logarithmically scaled **decibel (dB)** units in reference to a standard sound pressure.
- The most common reference for a clinical acoustic dB scale is 0.0002 dynes per square cm. Those units are called "dB SPL" (standing for Sound Pressure Level), but other references are sometimes used.

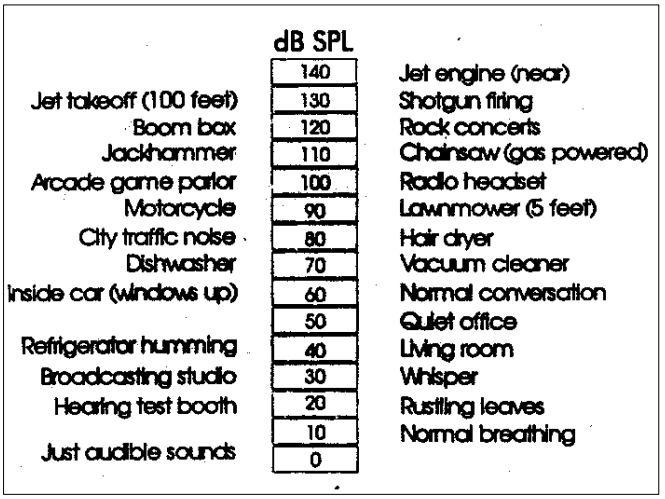
- The equation that relates a sound pressure to its value in dB relative to a reference is:

  ***x* dB = 20 log (observed sound pressure/reference sound pressure)**

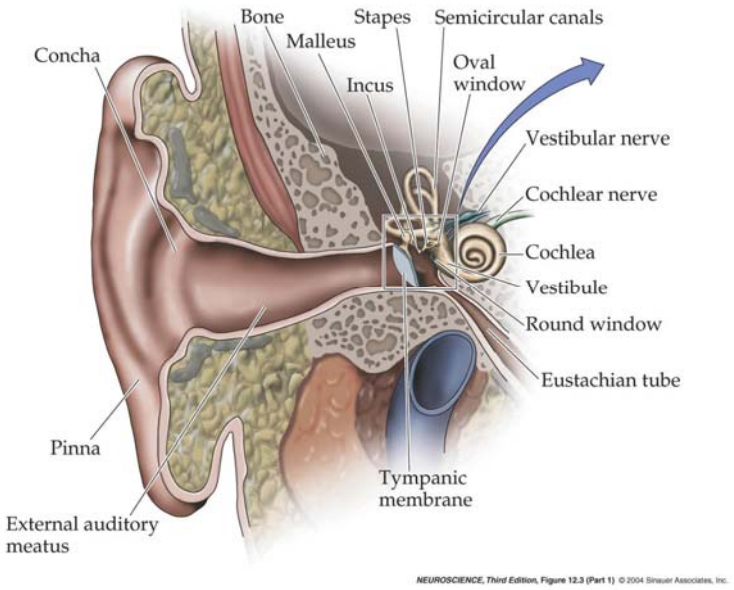
  where *x* is the number of dB units and log is the base-10 logarithm of the result of dividing the observed sound pressure by the reference pressure.

Examples:

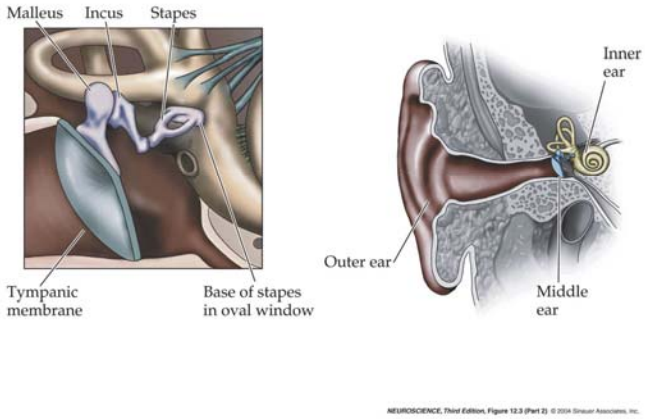
- A sound that has 10 times the pressure of the reference is 20 dB greater relative to that reference, because the log of 10=1.
- A sound that has 100 times the pressure of the reference is 40 dB, because the log of 100=2.
- A sound that has 1 million times the pressure is 120 dB.
- A sound of 120 dB SPL would be at the upper limit of our perception of loudness growth and just a few dB below the sound pressure that causes the perception of pain.



The Anatomy of the Ear *(A Quick Review)*:



- Middle ear ossicles: **malleus, incus, and stapes**.



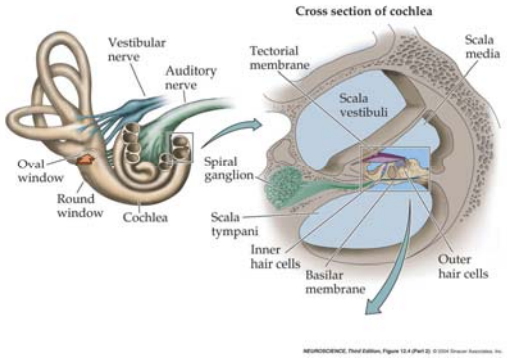
The Functions of the Middle Ear:
The middle ear transforms acoustic variations in air pressure into vibrational displacements that can pass into the cochlear fluids at the oval window.

The **Eustachian tube** allows equalization of static pressure differences across the tympanum. (When the Eustachian tube opens that nulls out any **<u>static</u> difference** between the pressure inside the middle ear and the outside atmospheric pressure).

The **acoustic middle ear reflex** reduces sound transmission to the cochlea <u>for sounds that are 75-85 dB SPL or greater</u>.

- **Trigeminal nerve > Tensor tympani > Malleus**
- **Facial nerve > Stapedius > Stapes**
- This reflex is important for:
  1. preventing damage due to overstimulation.
  2. increasing the dynamic range of hearing, by reducing the middle ear efficiency in transmitting sound energy in the 75 dB to 120 dB SPL range.
  3. reducing masking of high frequencies by low frequency sounds, because it happens that this reflex has its greatest effect below 2,000 Hz.

The Anatomy of the Cochlea *(Quick Review)*:

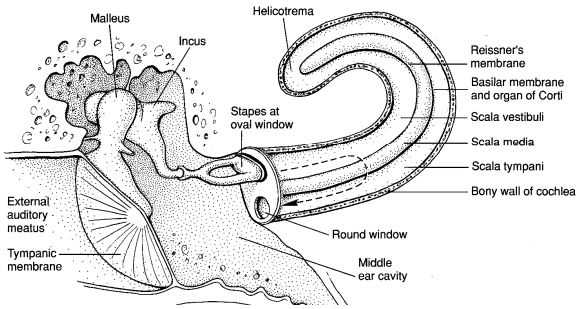


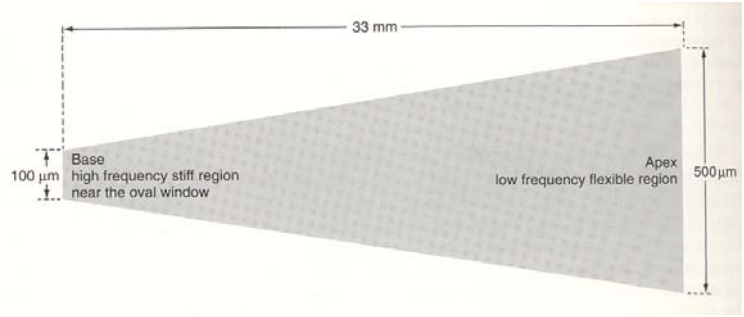
- Oval window, scala vestibuli, scala media (cochlear duct), scala tympani, round window, helicotrema.

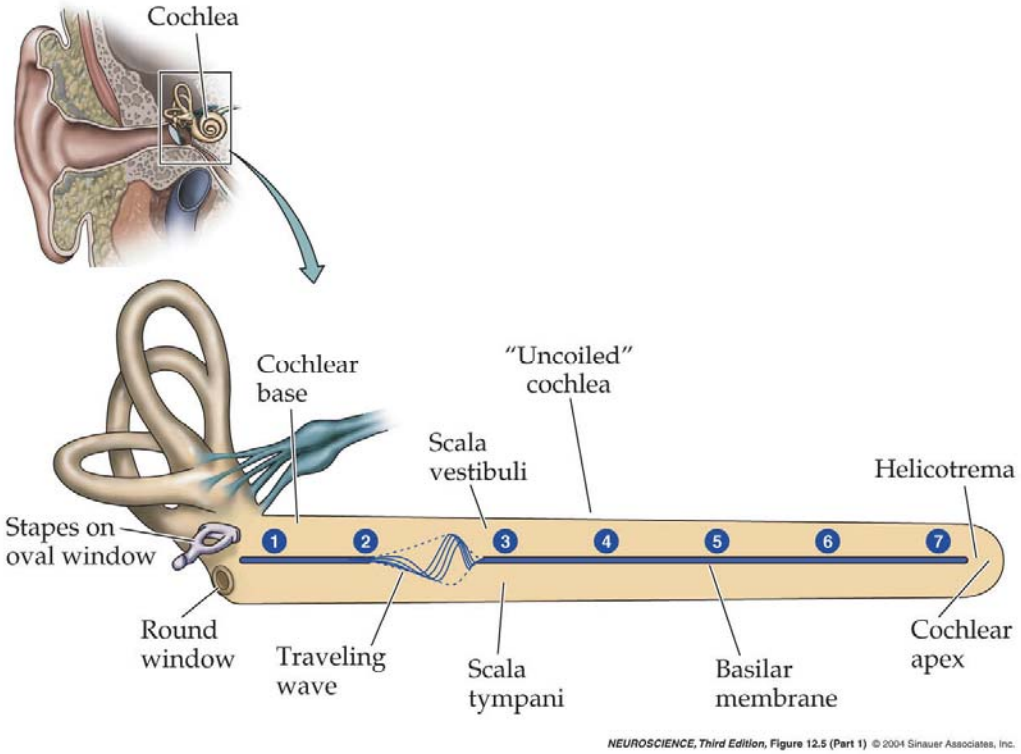
- Perilymph (high Na^+, low K^+), endolymph (high K^+, low Na^+) and with a maintained +80 mV endocochlear potential in the scala media

The Place Code

- The mechanical resonance properties of the basilar membrane change progressively along its length.

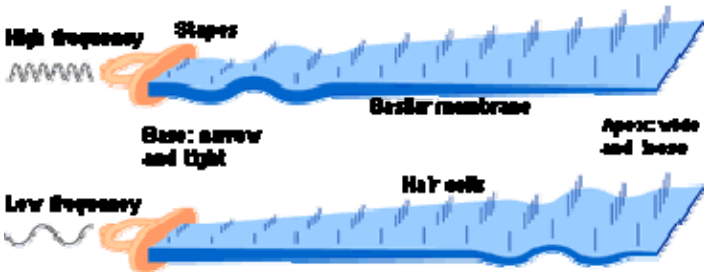




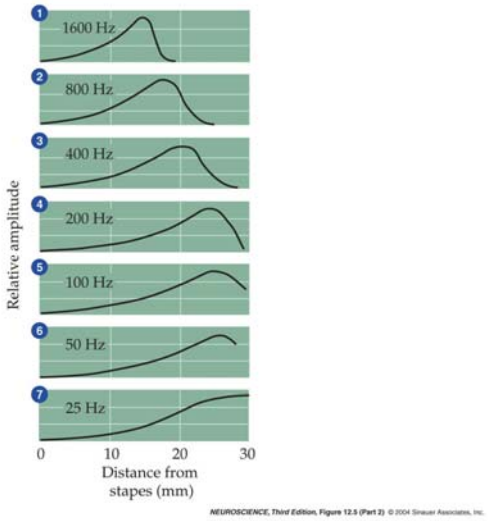


- The vibrations of the basilar membrane progress dynamically as traveling waves that run from its oval window end in towards its helicotrema end.

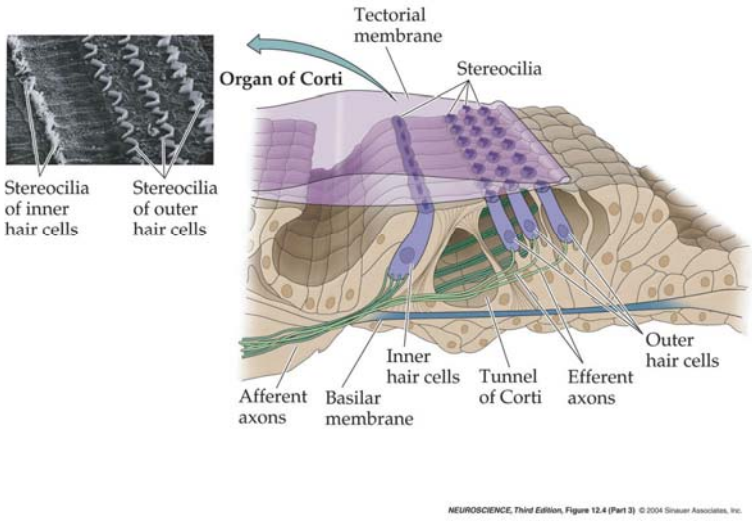
- High frequency sounds give rise to high frequency vibrations of the basilar membrane that travel along its length only a short distance before peaking and dying out without reaching the regions that are farther along the membrane.



- Low frequency vibrations travel far along the basilar membrane before gradually building up to a peak in the amplitude of their alternating up and down movements of the membrane. The illustration below just shows the envelope (essentially an average of the peaks) of the basilar membrane's upward vibrations.

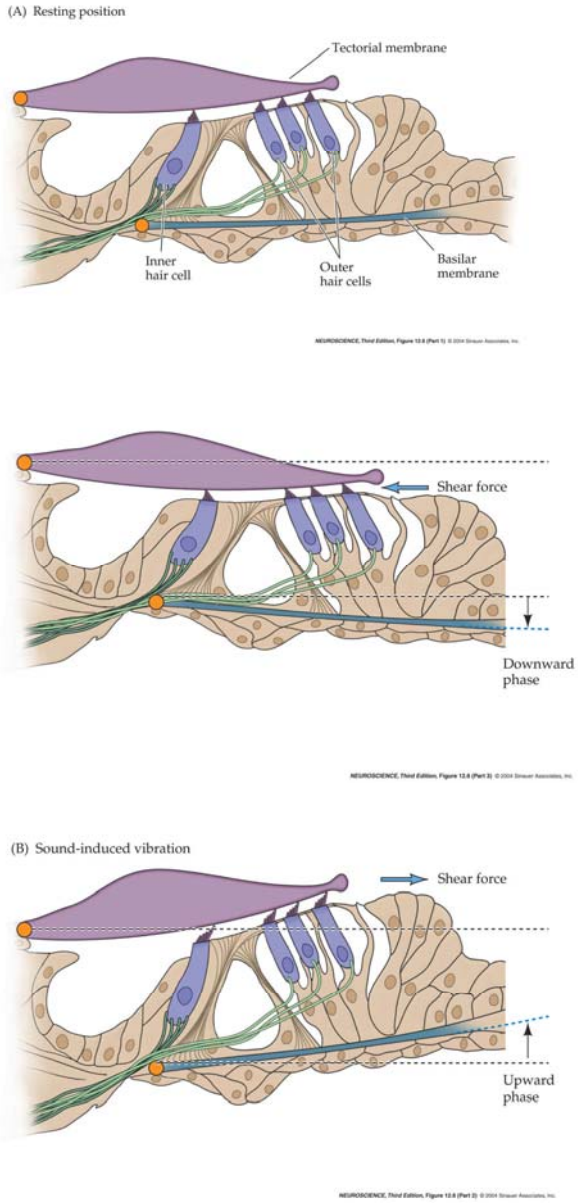


The Structure of the organ of Corti *(Quick Review)*:



- **Inner hair cells** (about 4,000 cells in a single-file row that runs ~33 mm).
- **Outer hair cells** (three or four rows containing about 12,000 cells), so that there are about **16,000 hair cells** in our cochlea.
- Several types of specialized supporting cells, and nerve terminals make up the remainder of the organ of Corti, and the acellular secreted matrix of proteins called the **tectorial membrane** rests above the hair cells.

A Brief Review of How Hair Cells are Stimulated:

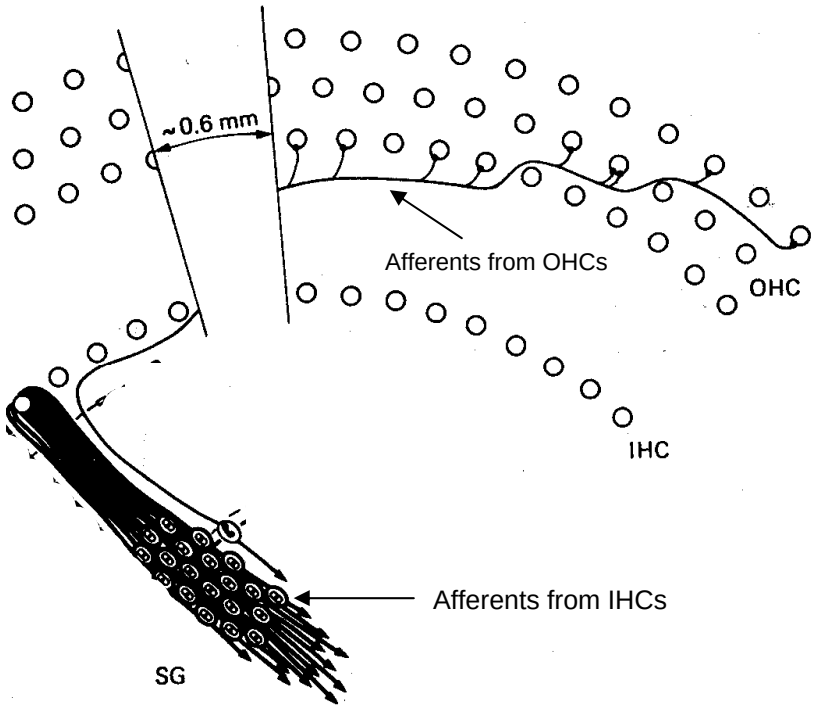


- The different levels of the pivot points for the tectorial membrane and basilar membrane convert the alternating upward and downward vibrations into radially directed deflections of the hair bundles.
- Hair bundle polarity (observed in the staircase-like array of actin-filled stereocilia). (During early development these hair bundles also have one eccentrically located kinocilium containing a 9+2 arrangement of microtubules, but that disappears during fetal development of the cochlea).

- Those deflections **alternately** tense and relax the **tip-links** at the tops of the stereocilia bundles thereby opening and closing mechanically gated ionic transduction channels. Those positive and negative deflections from the resting potential alternately depolarize and hyperpolarize of the hair cell's transmembrane potential.
- When transduction channels open cations (+) are driven in by the combined electromotive force of the +**80 mV endocochlear potential** above the hair bundles and the -60 mV transmembrane resting potential inside the typical hair cell. (The average net driving force on positive ions is ~140 mV.)
- **Microphonic potentials** arise from summed receptor potentials of hair cells.
- Afferent chemical synapses that transmit signals from the hair cells to nerve terminals are **tonically releasing**.

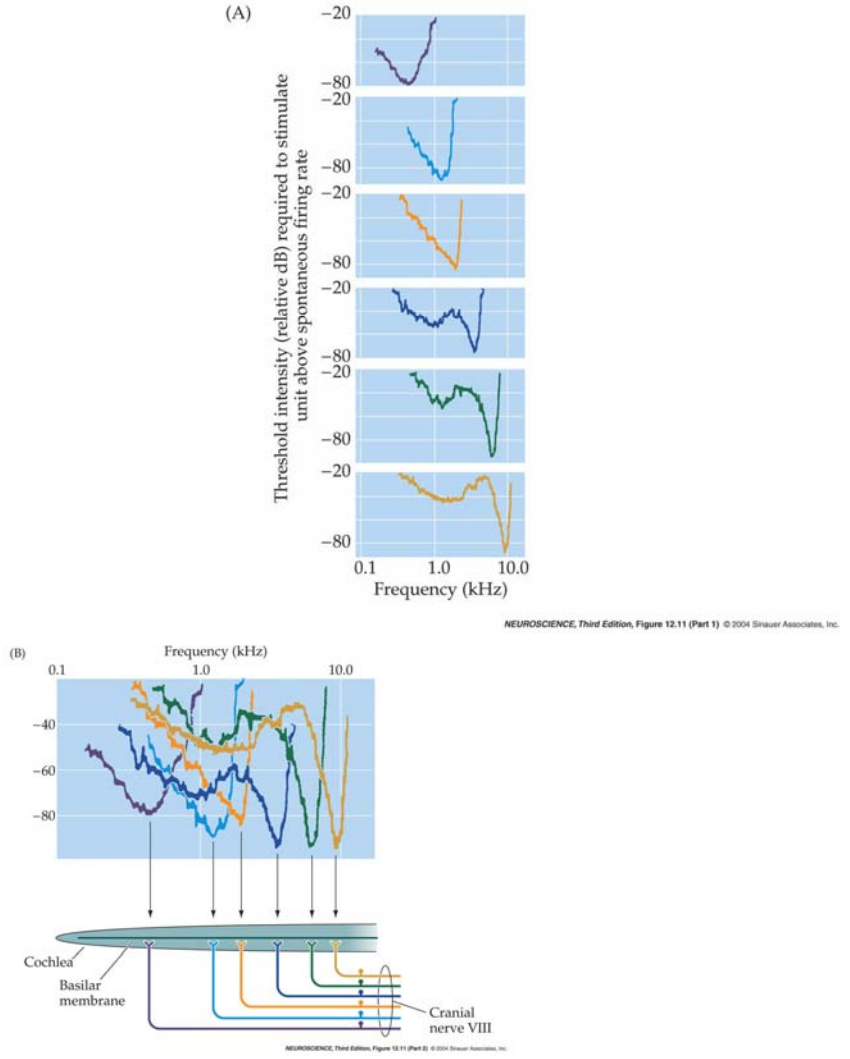
The Afferent Innervation of the Cochlea:

- The cell bodies of the afferent auditory neurons are in the **spiral ganglion**.
- There are two types of afferent neurons in the spiral ganglion, one type carries information from IHC's and the other from OHC's.
- Inner hair cells are contacted by approximately 95% of the afferent neurons that project from the cochlea to the brain.
- A spiral ganglion neuron contacts only one inner hair cell.
- But each inner hair cell may be contacted by several neurons as illustrated below.
- Outer hair cells are contacted by only about 5% of the afferent neurons and the individual spiral ganglion neurons that contact outer hair cells each innervate many outer hair cells.



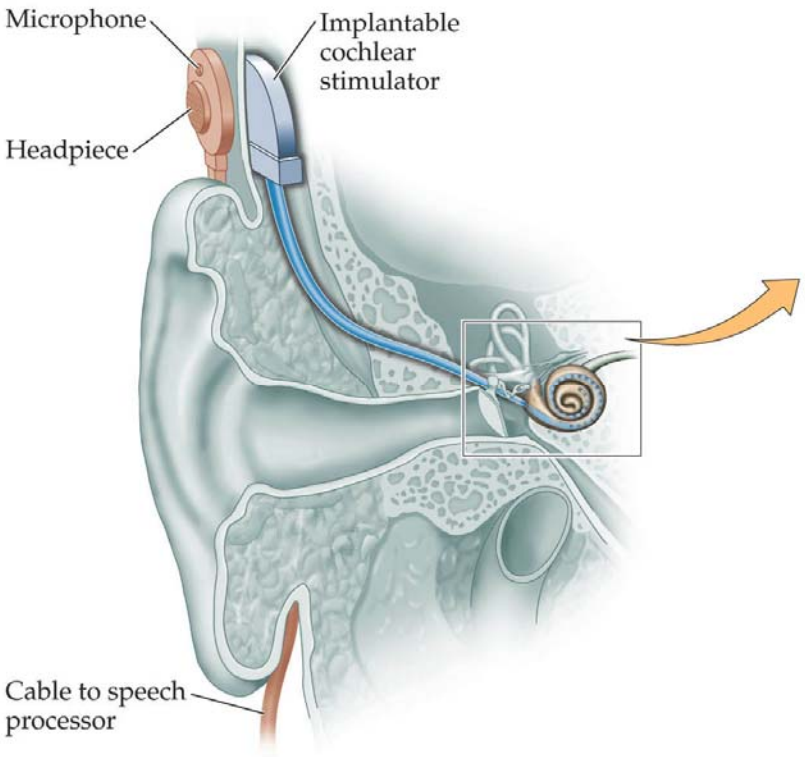
How Sound is Encoded in the Cochlear Nerve:

- The coding of sound frequencies in the cochlear nerve is the basis of the **place code** in the cochlea. Higher to progressively lower frequencies of sound-induced vibrations produce peaks in basilar membrane vibration at places that are progressively further along in the cochlea and the stimulation of those places is represented in the impulse activity that arises in the spatially ordered array of afferent neurons that contact the hair cells along the cochlea's length.



- The precise registry between a single-file line of inner hair cells along the basilar membrane and the afferent neurons provides the basis for our ability to discriminate sound frequencies, which is critical for understanding speech.

Cochlear Implants Capitalize on the Place Code and Stimulate Cochlear Afferents Directly:



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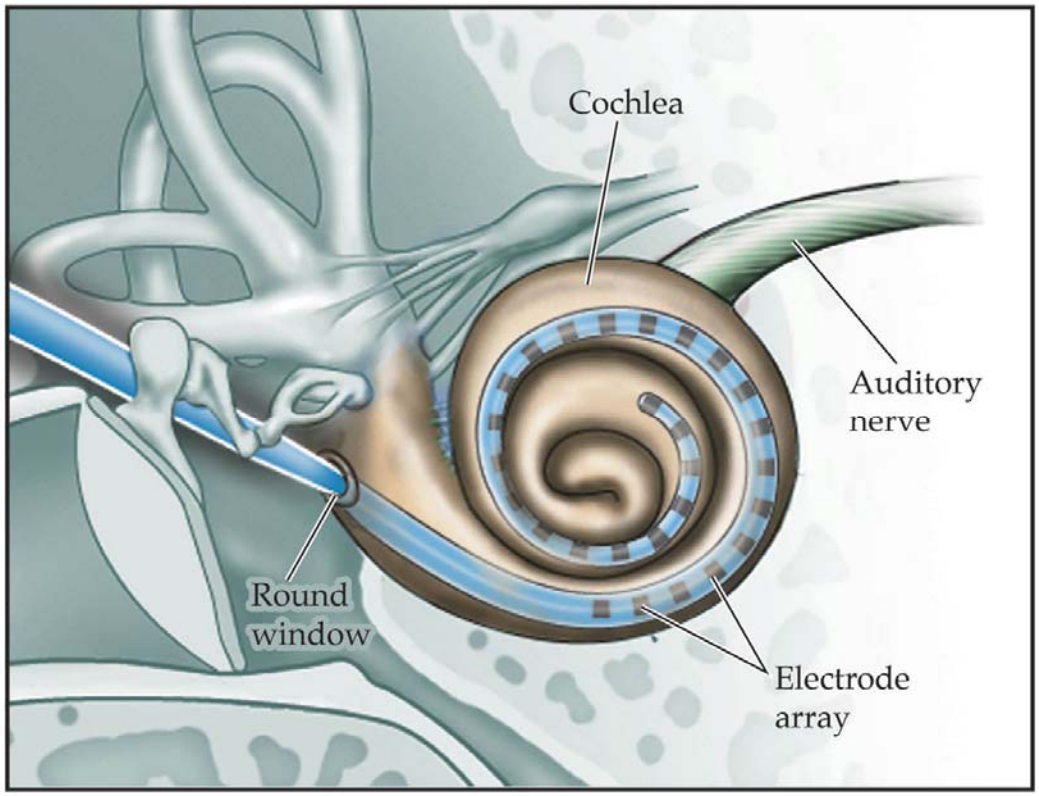

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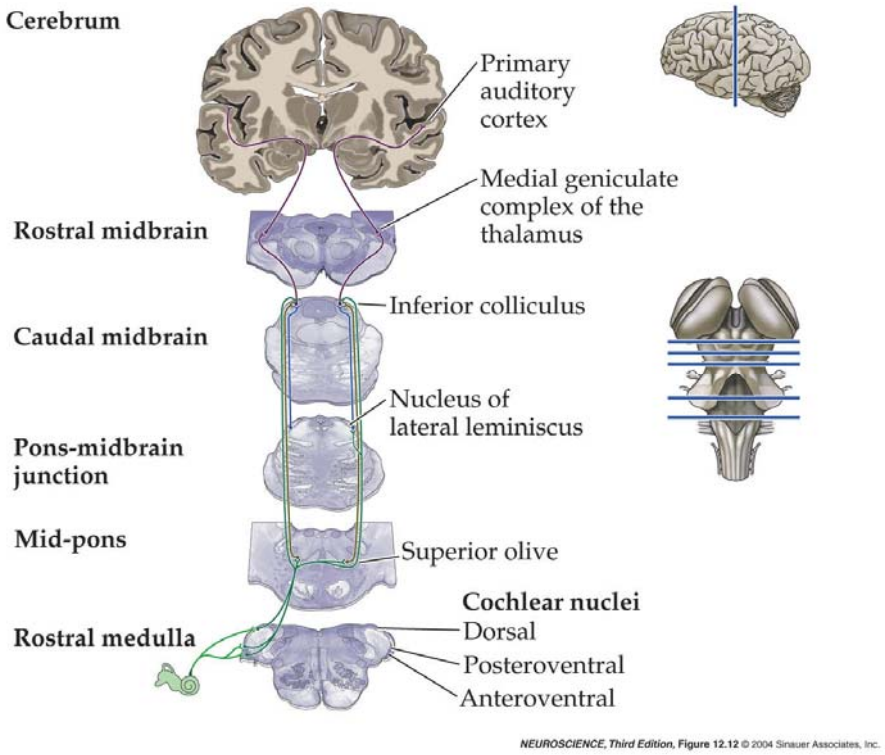
The Primary Central Auditory Pathway:



(You'll be expected to know the anatomical structures labeled on the right side of the figure above and a few more anatomical structures that are highlighted in bold or underlined in the sections below.)

Hallmarks of the Auditory CNS:

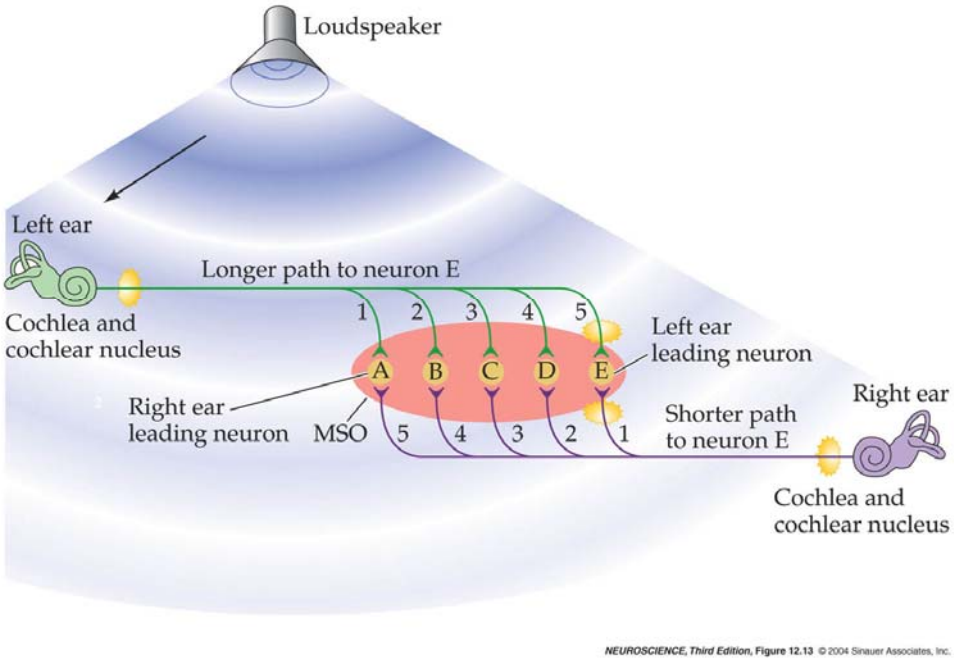
1. All the spiral ganglion neurons terminate in the dorsolateral brainstem within the **Ventral Cochlear Nucleus (VCN)** and **Dorsal Cochlear Nucleus (DCN)**.
2. **Decussations** and **bilateral projections** occur starting with the axons that arise from neurons in the cochlear nuclei, the second order neurons in the auditory pathway. This property of early bilateral projections is clinically important because it means that lesions in the auditory CNS pathways seldom provide hearing deficits that are useful for neurological diagnosis. Because of **bilateral redundancy,** lesions in the ascending pathways seldom if ever results in monaural hearing loss.
3. The auditory CNS is comprised of **multiple parallel pathways** that appear to underlie our capacity for perceiving different aspects of sound stimuli, but we will just focus on the so-called primary auditory pathway.
4. **"Tonotopic"** spatially ordered frequency representations are maintained throughout many but not all levels in the central auditory system.

How Brain Pathways Localize Sources of Sound:

- Two pathways provide our ability to localize sound source direction. One uses **Interaural Time detection (ITD)**; the other uses **Interaural Intensity detection (IID)**.

Interaural Time Detection (ITD): Uses time of arrival at the two ears.

- For sound frequencies of **3 kHz and lower** cochlear neurons can phase lock (i.e. their neural impulse patterns follow the pattern of sound wave cycles).
- Sources of those lower frequency sounds can be localized via neural circuitry that uses differences in the time of arrival of the sound at the two ears.
- Interaural delay time detection occurs in the **Medial Superior Olive (MSO).**
- The neurons in the **Anteroventral Cochlear Nucleus (AVCN)** project bilaterally to the MSOs.
- The neurons in the MSO are bipolar. Each has a lateral dendrite that receives inputs from the ipsilateral AVCN and a medial dendrite that receives inputs from the contralateral AVCN.
- **Both the ipsilateral and contralateral inputs to the the MSO are excitatory.**
- MSO neurons function as **coincidence detectors.** They respond maximally when the inputs from the ipsilateral and contralateral ears arrive on their two dendrites simultaneously.
- The different neurons in the MSO (labeled A, B, C…E in the illustration below) are "tuned" to different pairs of arrival times at the two ears.
- That comes about because the axons that project from the AVCN to the MSO differ systematically in length and act as **delay lines** (conduction times are proportional to axon lengths).
- The different lengths of the axons each compensate for one difference in the time of arrival of sound at the two ears so that the neural impulses running to MSO neurons will arrive at one particular MSO neuron simultaneously.
- The ordered pattern of delay line inputs from the two ears to each MSO, makes each MSO neuron especially sensitive to sounds originating from one direction relative to the two ears.



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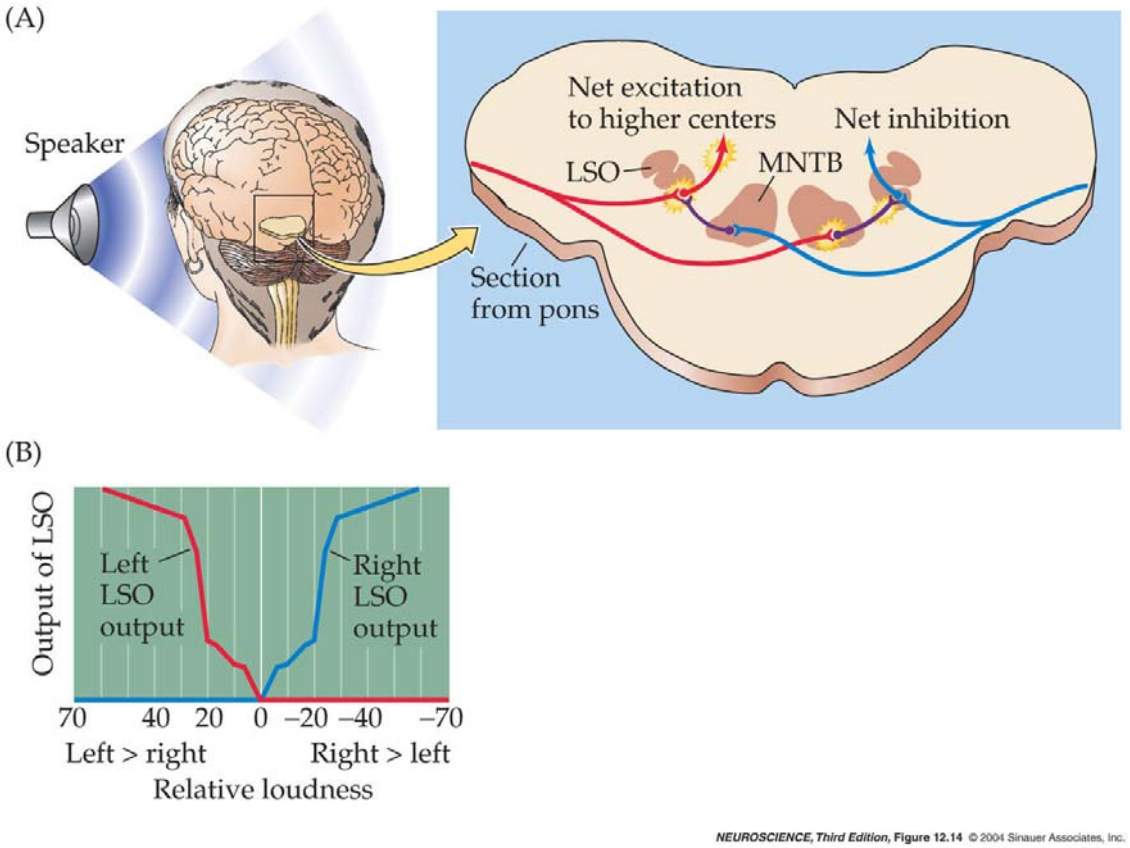
Interaural Intensity Detection (IID): Uses "loudness" differences at the two ears.

- For sounds **2 kHz and above** the wavelengths are so small that they do not diffract (i.e., bend) around the head. For those sounds the head casts an acoustic shadow, and the intensity of the sound will be greater in the ear that is nearer to the source of the sound.
- Interaural intensity differences are encoded in a pathway that involves the **Lateral Superior Olive (LSO)**, the **Medial Nucleus of the Trapezoid Body (MNTB)** and the **Trapezoid Body** (a major transverse auditory tract that can be found a short distance dorsal to the pyramidal tracts).
- Neurons in the AVCN project excitatory inputs to the ipsilateral LSO and excitatory inputs to the contralateral MNTB.
- Neurons in the MNTB project inhibitory inputs to the LSO on their side of the brain, so that each LSO is receiving excitatory stimulation from the ipsilateral ear and inhibitory inputs from the contralateral ear via the neurons in the MNTB.
- The balance of these excitatory and inhibitory inputs results in net excitation of the LSO on the same side as the sound source and no net excitation when the sound source is in the midline.



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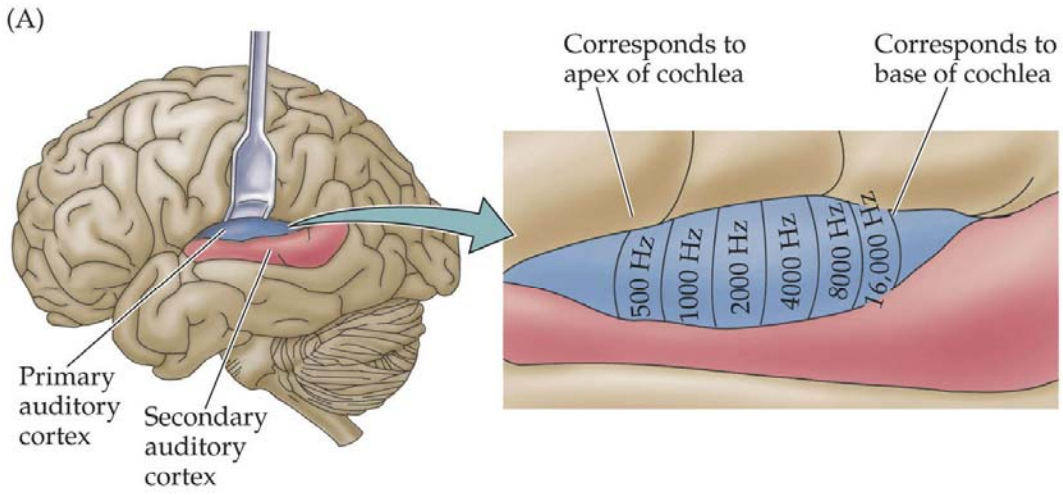
Other Brainstem Projections in the Primary Auditory Pathway:

- The MSO and LSO neurons both project to the **Inferior Colliculus (IC)** via the fiber tract called the **Lateral Lemniscus**.

- Some cochlear nucleus neurons project directly to the contralateral **Nucleus of the Lateral Lemniscus (nLL)**. Some evidence suggests that the neurons in the nLL contribute to the processing of temporal aspects of sound.
- Like the neurons in the MSO and LSO those in the nLL project to the **Inferior Colliculus (IC)** in the midbrain.
- In barn owls, which are champions at directional hearing, the neurons of the IC are organized in a topographical calculated map of auditory space. The neurons at particular points across the surface of the IC are sensitive to sounds (of almost any type) that arise from particular regions of space. It is suspected that the IC in mammals may be comparably organized to provide our spatially-referenced experience of the auditory world around us.

Cortical Projections

- The **Medial Geniculate Complex** is an obligatory thalamic relay nucleus for projections to the auditory cortex.
- **Tonotopic** order is maintained even in the cortical fields of the auditory pathway.
- In **Brodmann's area 41** (a.k.a. the **primary auditory cortex**) high frequencies are represented posterodorsally and low frequencies anteroventrally.



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- We have considered the primary auditory pathway and two pathways for sound localization, but the brain contains other "parallel pathways" that process other properties of the sounds we hear.

- Each division of the central auditory system also gives rise to descending components that may influence how the ascending pathways process sound information. Those descending pathways eventually lead to efferent nuclei that project back out to the cochlea itself.

Efferent innervation of the cochlea

- Efferent projections to the cochlea originate from neurons in the peri-olivary nuclei of the lower brainstem.
- One type of efferent terminal makes direct contacts on the bases of outer hair cells.
- The other type of efferent fiber runs to the inner hair cell region, but makes few direct contacts with inner hair cells; instead most of those efferents contact the dendrites of spiral ganglion cell afferents just beneath the inner hair cells.
- One function of the efferent innervation is improvement of the ability to distinguish sounds of interest when they occur together with background sounds, but researchers have yet to determine all their potential effects.

The Cochlear Amplifier and Infant Screening for Hearing Impairment:

- In the early 1980's Bill Brownell discovered that outer hair cells are motile. Outer hair cells slowly change shape when efferents are activated and they quickly shorten and elongate when activated by sound.

- In 1980 Bill Rhode conducted experiments that revealed that passive cochlear mechanics account for only part of the sharpness of frequency tuning in the living cochlea.

- The contribution of an active (living) mechanism to the sharp frequency tuning of basilar membrane vibrations is not fully understood, but is referred to as the "**Cochlear Amplifier**."

- In 1978 David Kemp discovered minute sounds emitted from the cochlea itself, which are now called Oto-Acoustic Emissions (OAEs). When outer hair cells are functioning normally their <u>motility</u> results in the production of OAEs. OAEs are measured by playing a probe tone into the ear and recording the resulting OAE via a specialized microphone placed in the ear canal.

- The clinical usefulness of OAE measurements stems from the fact that this objective measure correlates with normal hearing, can be measured quickly, and <u>does not depend on behavioral responses</u>.

- In the past 10 years most states have enacted legislation to require OAE screening of newborns so as to identify infants who are at risk for the effects of hearing impairment. Early screening and the availability of cochlear implants are bringing important medical benefits to many lives.

- Prior to the availability of OAE testing the average diagnosis of profound hearing impairment in children occurred at 30 months of age, well into the period for optimal development of language.