NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

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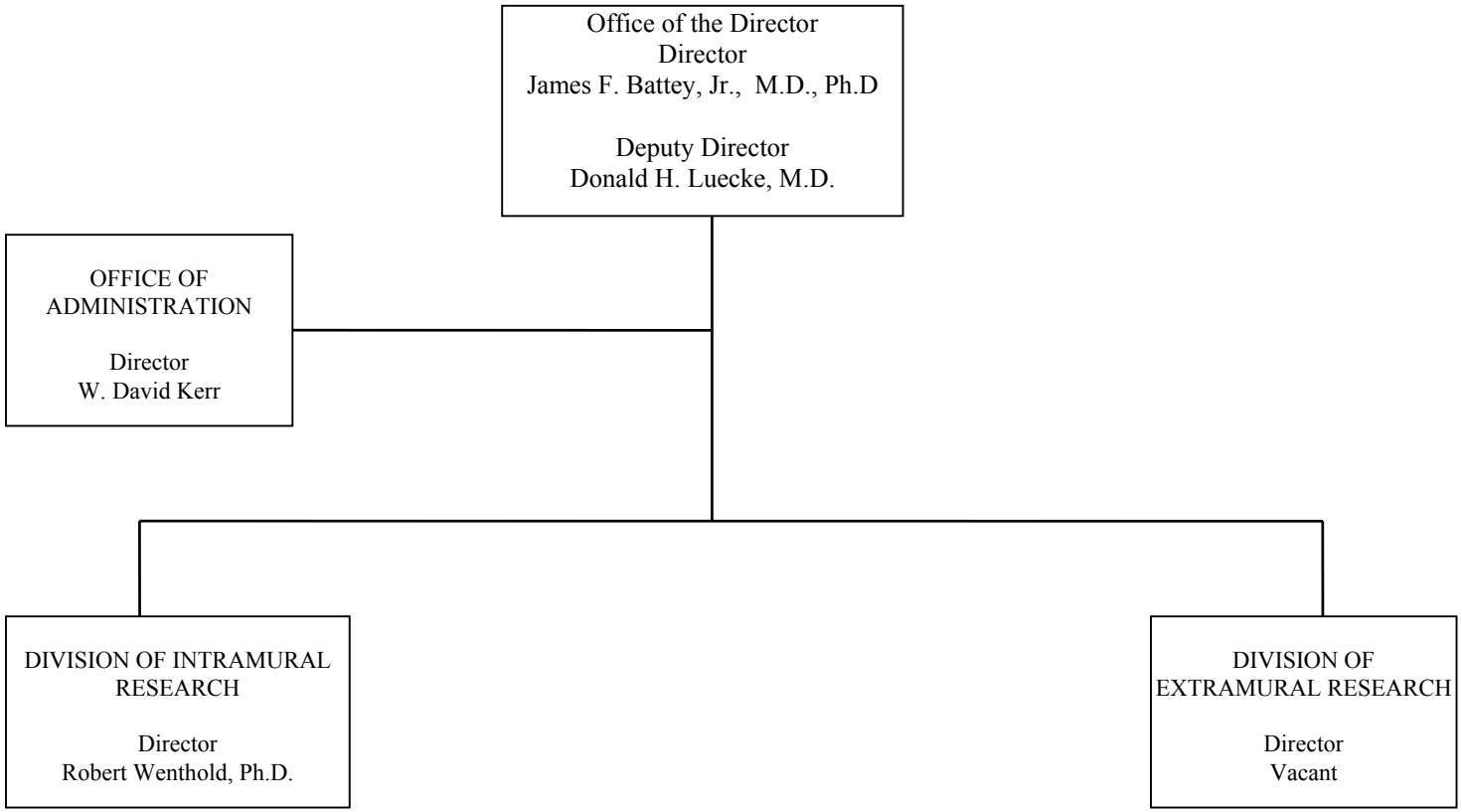

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

For carrying out section 301 and title IV of the Public Health Service Act with respect to deafness and other communication disorders, $380,377,000.

National Institutes of Health
National Institute on Deafness and Other Communication Disorders

Amounts Available for Obligation 1/

Source of Funding	FY 2002 Actual	FY 2003 Amended President's Budget	FY 2004 Estimate
Appropriation	$342,072,000	$365,929,000	$380,377,000
Enacted Rescissions	(397,000)	(0)	---
Subtotal, Adjusted Appropriation	341,675,000	365,929,000	380,377,000
Real transfer to:			
Other HHS Agencies through Secretary's one-percent transfer authority	(369,000)	(0)	(0)
Comparative transfer from:			
Fogarty International Center for International Services Branch	14,000	14,000	0
Comparative transfer to:			
Office of the Director for program changes	(194,000)	(209,000)	(0)
National Institute of Biomedical Imaging and Bioengineering	(0)	(0)	(0)
Subtotal, adjusted budget authority	341,126,000	365,734,000	380,377,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	341,126,000	365,734,000	380,377,000
Unobligated balance lapsing	(46,000)	---	---
Total obligations	341,080,000	365,734,000	380,377,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2002 - $1,967,000 FY 2003 - $2,000,000 FY 2004 - $2,000,000
Excludes $ 22,790 in FY 2002 and $58,470 in FY 2003 for royalties.

Justification

National Institute on Deafness and Other Communication Disorders

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended. Reauthorizing legislation will be submitted.

Budget Authority: (dollars in thousands)

FY 2002 Actual		FY 2003 Estimate		FY 2004 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
156	$341,126,000	157	$365,734,000	154	$380,377,000	(3)	$14,643,000

This document provides justification for the Fiscal Year 2004 research activities of the National Institute on Deafness and Other Communication Disorders (NIDCD), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2004 HIV/AIDS activities can be found in the NIH section entitled Office of AIDS Research (OAR).

INTRODUCTION

What if Ludwig van Beethoven were able to reverse his deafness and regain his hearing again as he reached the climax of his career as a composer? Would the world have been blessed with even more of his music? What we do know is that scientific technology has advanced significantly since the 18th century and assistive devices are now available for restoring the perception of sound to individuals who are deaf. One such device, the cochlear implant, has provided hope to thousands of deaf individuals worldwide. The development of this neural prosthesis was in part due to years of research commitment from scientists supported by the National Institutes of Health.

Disorders of hearing, balance, smell, taste, voice, speech, and language exact a significant economic, social, and personal cost for many individuals. The National Institute on Deafness and Other Communication Disorders (NIDCD) supports and conducts research and research training in the normal processes and the disorders of human communication that affect many millions of Americans. Human communication research now has more potential for productive exploration than at any time in history. With substantive investigations conducted over the past decades and the advent of exciting new research tools, the NIDCD is pursuing a more complete understanding of the scientific mechanisms underlying normal communication and the etiology of human communication disorders. Results of this research investment will foster the development of more precise diagnostic techniques, novel intervention and prevention strategies, and more effective treatment methods.

Story of Discovery: Early Cochlear Implantation Yields Best Results to Restore Hearing

Since the beginning of the 19th century, scientists have attempted to stimulate hearing by delivering electrical currents to the ears of deaf individuals. The first published report of an experiment to excite the auditory nerve by directly applying an electrode was documented by two French scientists in 1957. This research eventually led the way to the cochlear implant, the only sensory neural prosthesis in widespread clinical use today. This device converts sound into electrical impulses on an array of electrodes surgically inserted into the inner ear, bypassing the damaged hair cells that normally converts sound into neural impulses, stimulating the auditory nerve directly and restoring the perception of sound to individuals who are deaf. Many adults who lose their hearing suddenly can use the telephone again after receiving a cochlear implant.

The NIH has played a significant and important role in sponsoring the development of cochlear implant technology. Two institutes have been particularly important in this development: the National Institute of Neurological Disorders and Stroke (NINDS) and the NIDCD. Cochlear implant research in the U.S. significantly increased after the NIH Neural Prosthesis Program (NPP) was established in 1970 and again when the NIDCD was established in 1988. Under the leadership of the NIH over the past three decades, support and funding of research grants to universities have built a community of scientists and led to the establishment of cochlear implant programs in the U.S. In addition, NIH support provided a forum for scientists to share information through NIH-sponsored conferences and workshops. The support of research on cochlear implants provided critical information that allowed for the acceptance of auditory prostheses. This eventually resulted in the issuance of regulations by the Food and Drug Administration that ensured pre-market approval for safety and effectiveness of a cochlear implant in 1984. To date, approximately 58,000 individuals have received cochlear implants worldwide, including 22,000 Americans, with about one-half of the recipients being children.

One of the anticipated benefits of implantation in children is the improved acquisition of spoken language. Recent data indicate that the improvements in speech perception and language production in deaf children with cochlear implants have also resulted in better language and reading performance. With many states screening newborn infants for hearing impairment before discharge from the hospital, many more infants with hearing impairment will be identified at an early age when appropriate intervention, such as a cochlear implant, can be started that will optimize their long-term speech and language skills.

When is the best time to implant a deaf child so that he or she will acquire a normal level of speech and language skills? The prevailing wisdom is before the effects of deafness substantially alter the brain's ability to adapt to the stimulus of sound introduced through a cochlear implant. However, the time line for adaptiveness (plasticity) in the central auditory nervous system of humans is not known. NIDCD-supported scientists are measuring electrical activity of the brain in response to sound in children who received an implant in early childhood and in late childhood and have found that the brain can survive up to 3.5 years of sound deprivation and still remain plastic, that is, can change quickly once sound is introduced through a cochlear implant. Immediately after young children are fitted with a cochlear implant, the brain's responses to sound resemble those of normal hearing newborns. Once sound stimulation is started with a cochlear implant, young children's brains develop at a very rapid rate. As a result of this rapid development or plasticity, young implanted children usually show age-appropriate brain responses within six to nine months after their cochlear implant is turned on. Children who are implanted between the ages of four- to seven-years old show varying amounts of plasticity. In children who are implanted after eight-years old, the scientists found an extremely reduced level of plasticity in response to sound stimulation. Overall, these results suggest that the best time to implant a deaf child is by three-and-a-half years old. These findings are consistent with recent research demonstrating that implanting a child early maximizes the probability of a successful outcome in the child's speech and language development. The time line for brain plasticity that is being defined should help parents and clinicians make informed decisions about the best time to surgically insert a cochlear implant in a deaf child.

In addition, two new exciting advancements in cochlear implants are currently undergoing investigation by NIDCD-supported scientists: binaural implants and a short electrode implant allowing for the combination of electric and acoustic hearing. Binaural (both ears) implants provide a potential avenue for better speech perception in noise, while the short electrode is being designed to be used in experienced, yet unsuccessful, adult hearing aid users with severe-to-profound hearing impairment. Scientists are currently collecting data and the preliminary results are promising. As technology continues to provide advances in cochlear implant design, additional people will benefit from these remarkable devices.

With over 30 years of NIH research investment, the cochlear implant has evolved from an experimental device to a miniature hearing prosthesis that is commercially available to assist those who are profoundly deaf or severely hearing impaired. NIH-supported research has been instrumental in showing the appropriateness of cochlear implants in infants with profound hearing impairment, the age when children could safely be implanted and the importance of early intervention for language development.

SCIENCE ADVANCES

New Gene Discovered as a Cause of Hereditary Deafness

Within the last seven years, over 70 different genes for hearing loss that is not associated with other inherited characteristics (nonsyndromic hereditary hearing impairment) have been mapped and over 25 identified by positional cloning. In addition, several genes essential for normal auditory development and/or function have been identified using mouse models. Recently, scientists have discovered a new gene of unknown function, TMC1, in which mutations cause deafness. TMC1 was discovered through genetic mapping studies of large families with hereditary hearing loss. Different types of mutations can cause two different types of hereditary hearing loss: profound congenital deafness which is inherited in a recessive fashion, and delayed onset, progressive hearing loss which is inherited in a dominant pattern.

NIDCD intramural scientists have identified a mutation in the mouse Tmc1 gene which causes similar types of dominant and recessive hearing loss found in large human family studies. Mouse models permit studies of inner ear structure that are not possible in humans. In mice, mutations in the Tmc1 gene causes defects in the function of the specialized sensory cells of the inner ear, known as hair cells. Hair cells detect and convert the physical stimulus of sound into electrical impulses sent to the brain via the hearing nerve.

This research contributes to new models for studying specific forms of human deafness. Since studies of the inner ear structures are not easy to conduct in humans, using mouse models allow scientists to determine the cellular and functional consequences of mutations in genes that cause hearing impairment.

Discovery of a Novel Deafness Gene

Mutations in the mucolipin gene, Mucolipin1, causes the human disorder mucolipidosis type IV, a neurodegenerative disease. Changes in mucolipin genes may also be associated with other disorders. NIDCD intramural scientists recently identified the gene that causes deafness in the

mouse mutant, *varitint-waddler*, which displays early onset hearing loss and skin pigmentation abnormalities. The gene is Mucolipin3 and belongs to the family of mucolipin genes that play important roles in the transmission of sensory perceptions such as smell, taste, temperature and mechanical stimuli. Given the biological significance of mucolipins and the strong genetic connections between human and mice inherited deafness, it seems likely that Mucolipin3 may be also involved in human hereditary and/or sporadic sensory disorders.

Rapid Renewal of Auditory Sensory Stereocilia Aid Recovery to Hearing Loss

Stereocilia, or hair cell bundles, are fine projections in the inner ear that vibrate when stimulated by sound. The movement of the stereocilia activates a molecular pathway that generates an electrical signal from the auditory nerve to the brain, which is interpreted to be sound. Stereocilia are located in the surface of the inner ear and are supported by a rigid and dense core of filaments. Until recently, this core was thought of as a stable structure whose sole function was to serve as rigid supports for changes in the mechanical constitution of the hair cells.

NIDCD intramural scientists have discovered that there is a continuous renewal of the stereocilia core every 48 hours. This process occurs in the mature bundles during recovery from temporary noise-induced hearing loss and suggests that the stereocilia core structure plays an unforeseen role in this recovery process.

Recognition of this dynamic aspect of stereocilia is essential to the understanding of the development and maintenance of normal sensory function and sheds new light on the unique properties of hair bundles. Such a renewal mechanism could also provide more information on the molecular basis of genetic, environmental, and age-related inner ear disorders that involve malformation or disruption of stereocilia.

A Sound Transduction Motor Protein Facilitates the Speed of Sound

The sensory hair cells in the inner ear of mammals function as the mechanical transmitters of sound. Stereocilia are formed by cone-shaped bundles of sensory hair cells. The movement of the stereocilia initiates the complex pathways of molecular signals that stimulate the auditory nerve which carries information to the brain, eventually becoming the sensory perception of sound. One important component in this pathway is Myosin-1C, a major motor protein involved in the movement of the stereocilia. It is hypothesized that motor proteins serve as the link between the stereocilia's membrane and cell core thereby initiating cell depolarization following sound vibration.

NIDCD-supported scientists are in the process of deciphering how Myosin-1C works. Specifically, they used a chemical-genetic approach to inhibit Myocin-1C motor protein activity in mice by introducing a custom designed amino acid that alters the protein's function. The designer amino acid rendered the protein susceptible to a controllable inhibitor, thus allowing regulation of the protein's motor function. Myosin-1C with a custom amino acid shows diminished function in the presence of inhibitor, but functions normally in the absence of

inhibitors. Naturally occurring Myosin-1C functions normally with and without inhibitor.

These results demonstrate the importance of Myosin-1C in transmitting sound to the brain, allows observation of protein function in a controllable native environment and permits assessment of protein function in a biological process. The findings are invaluable to furthering the development of targeted therapeutic treatments for individuals with hearing impairment and provides alternatives and variations to gene therapy methods. Future treatment strategies will rely on the results of further research on signaling pathways and effector components as means to decipher the molecular properties of mechanoelectrical sound transduction.

Signaling Pathway Regulates Pillar Cell Development in the Inner Ear

In mammals, sound is perceived in the organ of Corti of the cochlea. It is an area of the inner ear that contains sensory hair cells. One of the most striking aspects of the organ of Corti is the arrangement of both sensory hair cells and other cell types in a very regular cell pattern. In particular, the hair cells are arranged in a single row of inner hair cells and three or four rows of outer hair cells. Moreover, the row of inner hair cells are separated from the rows of outer hair cells by a space referred to as the tunnel of Corti. The boundaries of the tunnel of Corti are formed by two rows of specialized pillar cells. Recent studies have shown that normal development of pillar cells and the tunnel of Corti are required for normal hearing to occur. However, despite the importance of the pillar cells in the auditory process, the molecular pathways that are required for their development have not been determined.

NIDCD intramural scientists have demonstrated that the fibroblast growth factor (FGF) signaling pathway plays a key role in regulating pillar cell development. FGFs are secreted molecules that influence several different developmental events by binding to specific FGF receptors on cell surfaces. The scientists determined that a specific FGF receptor, FGFr3, is turned on in cells that develop into pillar cells. In addition, the developing inner hair cells located next to the pillar cells turn on a specific fibroblast growth factor, FGF8. Therefore, both FGF and its receptor are expressed in a pattern that is consistent with a role in pillar cell development.

To begin to examine the role of the FGF signaling pathway, the activation of FGFr3 receptor was blocked using a specific FGFr antagonist. Inhibition of FGFr3 led to an inhibition of pillar cell development. However, if FGFr3 and pillar cell development were partially inhibited for only a brief period of time, then pillar cell development resumed, suggesting that continuous FGF signaling is required for normal pillar cell development. To determine the effects of increased activation of FGFr3, a strong activator of this receptor, FGF2, was added to the developing cochlea. Addition of FGF2 led to an increase in the number of cells that develop into pillar cells. This effect is dependent on the amount of FGF2 added and on the timing of its addition. As the organ of Corti matures, the effects of FGF2 are reduced.

These results demonstrate that the FGF signaling pathway plays a key role in regulating the development of pillar cells. The results also provide valuable insights into the mechanisms that ensure the development of a normal organ of Corti. It is likely that pillar cells grow directly

adjacent to the inner hair cells because the hair cells serve as the source of FGF. Since broad activation of FGFr3 can lead to an increase in the number of pillar cells, pillar cells may be regulated by a limited amount of FGF within the inner ear. Since the source of FGF is the inner hair cells, pillar cells will always develop adjacent to them. Future experiments will examine the specific role of inner hair cells in pillar cell development as well as exploring other mechanisms that may exist to ensure that only a single tunnel of Corti develops.

Hearing Loss Due to Thyroid Hormone Resistance

Resistance to thyroid hormone (RTH) is a hereditary disorder that causes tissues and organs to respond to the hormone ineffectively. The thyroid is a gland in the neck that produces a hormone which regulates heart rate, metabolism, growth, mental function, energy and mood. Some forms of RTH are caused by a mutation in the THRB gene which encodes one subunit of a receptor for thyroid hormone, Trß. Individuals with RTH may also have a hearing impairment. Although thyroid hormone is known to be required for normal development of the inner ear, the mechanism by which THRB mutations cause hearing loss has been unknown.

NIDCD intramural scientists are studying a mouse model for RTH that was developed by scientists at the National Cancer Institute. The results of the study indicate that RTH causes hearing loss by making the sensory tissue of the inner ear (cochlea) and the sensory hair cells develop abnormally. It was previously known that mice lacking all Trß receptors have hearing loss, although their hearing loss is not due to abnormal structural development of the cochlea. In contrast, the mutant Trß protein in RTH is not only defective but disrupts the functions of other genes that are required for cochlea development. One of these genes, Tra, is likely to be another receptor subunit for thyroid hormone. Further research could lead to new diagnostic strategies for individuals with hearing impairment and may also provide scientists with further information about the structure of the ear.

Bacterial Biofilms Make Ear Infections Tough to Overcome

Infection or inflamation of the middle ear (otitis media) occurs at least once in 75% of children by their third birthday. Approximately half of these children will have an average of three or more ear infections during their first three years of life. Otitis media (OM) is the most common reason for a child to receive antibiotics and to undergo general anesthetic. In the United States, this represents an annual medical cost and lost wages of approximately $5 billion.[1]

While the socioeconomic impact of the disease is clear, the factors that promote bacterial colonization of the middle ear remain unclear. NIDCD-supported scientists are studying the specific molecular mechanisms that allow bacteria in conjunction with viruses to cause OM.

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[1]National Institutes of Health: Table - Cost of illness and NIH support for selected diseases and conditions. Disease-Specific Estimates of Direct and Indirect Costs of Illness and NIH Support, 1997.

While the three primary bacterial causes of OM have been identified, *Haemophiles influenzae, Streptococcus pneumoniae* and *Moraxella catarrhalis*, how these organisms interact with the middle ear environment to induce OM symptoms is unclear. Recent findings highlight certain physical and environmental features of microscopic organisms that are able to form a protective colony – or mucosa biofilm – that enables bacteria to be more resistant to antibiotics than free-living bacteria of the same species. These mucosal biofilms exist as large congregations of organisms growing on the mucosal surface of the middle ear and are believed to be the contributing factor to chronic OM. Organisms that are part of a biofilm display altered physical, biochemical and physiological characteristics such as reduced cell growth and altered gene expression. The reduced growth rate makes organisms resistant to antimicrobial drugs, and the physical structure of the biofilm provides a shield against the body's immune system, thus providing an incredibly resilient environment for the invading microbes. In addition, longtime exposure to biofilms may result in bone damage. Identifying the process that lead to OM is critical for developing preventative treatment such as vaccines and other strategies designed to block the chronic infectious process.

Gene expression studies using state-of-the-art microarrays will be critical in providing information necessary to understand the OM disease process. This information may lead to new molecular approaches for prevention and treatment of OM.

You Can Teach an Old Owl New Tricks: Plasticity in the Adult Brain

Someone calls your name and you turn to look to see who it is -- a process so automatic it seems simple. But is it? Our ability to localize the source of sound relies on complex computations in the brain which translates auditory localization cues into representations in space. Sound localization cues result from the interaction between the ears, eyes, brain and the incoming sound. Although many animals can localize sound soon after birth, the exact relationships between differences in sound intensity or time of sound arrival between the two ears and locations in space are shaped and modified by experience.

The sound localization pathway has become a model system for studying mechanisms by which the nervous system learns from experience. The barn owl, a nocturnal predator with keen vision and hearing and a highly evolved capacity for sound localization, has been studied extensively. NIDCD-supported scientists have demonstrated that a part of the brain (optic tectum) is the source of a visually-based instructive signal that calibrates auditory information as a map of visual space. When barn owls are raised wearing special prism spectacles that displaces their field of vision, another part of the brain, the external nucleus of the inferior colliculus (ICX), adapts by also shifting the auditory space map according to the optical displacement caused by the prisms. Topographic visual activity in the optic tectum could serve as the template that instructs changes in the auditory space map.

Additional experiments were conducted to investigate the mechanisms of adaptability (plasticity) in the owl's midbrain. Plasticity in the central nervous system that involves learning is generally

more restricted in adults than in young animals and the sound localization pathway has been shown to be far more limited in its ability to adjust to abnormal experience in adult versus juvenile barn owls. In experiments using adult and juvenile owls wearing prism spectacles, it was shown that juveniles learn new associations between auditory cues, such as the time difference it takes sound to reach each ear (interaural time difference or ITD), and locations in visual space; and the young owls acquire new neurophysiological maps of ITD in the optic tectum. Adults owls do neither. However, when the prismatic shift is experienced in small amounts over time, ITD maps in adults owls do adapt. In addition, once the adult brain learned to adapt to the shifts through incremental training, new ITD maps were reacquired when the adult owls were given the spectacle at a later time. These results demonstrate a substantially greater capacity for plasticity in adult brains than was previously recognized, and a strategy for using this capacity that could be applied in other areas of the adult central nervous system.

Understanding how the auditory and visual systems exerts its influence on sound localization pathway reveals some of the mechanisms by which the nervous system adapts to changes in sensory input. In addition, studies on the plasticity of the brain may lead to new methods for teaching normal and learning disabled children as well as develop therapeutic strategies for restoring function to individuals who suffered brain injury or disease.

Discovery of Genetic Hearing Disorder Mistaken for Otosclerosis

Until recently, physicians would have readily diagnosed a hearing-impaired individual with otosclerosis if they observed an immobile or fixed bone, the stapes, in the ear. In individuals with otosclerosis, their stapes bone, which is located in the middle ear, becomes immobile and loses its ability to vibrate, which is how sound energy is transmitted from the outer and middle ear to the inner ear. However, recent studies have uncovered a new cause for the immobile conditions of stapes that mimic the symptoms of otosclerosis. Researchers have discovered a gene mutation which also causes the stapes to malfunction. This mutation causes a form of congenital hearing loss and is called autosomal dominant stapes ankylosis. Unlike otosclerosis, where the hearing loss progresses as a person ages, individuals with stapes ankylosis have the hearing loss at birth. Individuals with stapes ankylosis may also be farsighted, have unusually broader thumbs and big toes, a sloping forehead, a cleft chin and/or other minor skeletal abnormalities. NIDCD-supported scientists have determined that this rare syndrome results from mutations in the gene that codes for noggin, a protein essential for normal bone and joint development. Differentiating otosclerosis from stapes ankylosis is important for selecting the optimal treatment option. While otosclerosis can usually be treated with surgery, it is less effective for individuals with stapes ankylosis, and hearing aids may actually be the best option. The research shows the importance of genetic testing to ensure appropriate treatment for individuals with stapes ankylosis.

Antibiotic Treatment Controls the Vertigo of Ménière's Disease

Ménière's disease is a distressing and often disabling disorder of inner ear function, characterized by spontaneous attacks of vertigo, fluctuating hearing loss, tinnitus and fullness in the ear. While there is currently no cure for the disease, its symptoms are often controlled by restricting the intake of salt and reducing the body's retention of fluid through dietary changes or medication. When vertigo cannot be controlled by diet or medication, surgery is another alternative. Selective severing of a vestibular nerve from the affected ear usually controls vertigo while preserving hearing, but carries surgical risk. An alternative to surgery is injecting multiple doses of the antibiotic, gentamycin, through the eardrum, into the middle ear space (intratympanic injection) to deliver the drug to the inner ear. This treatment has gained popularity for controlling vertigo of Ménière's disease, however, its likely to cause significant sensorineural hearing loss. Recently, it was determined that a single injection of gentamycin through the eardrum is effective in controlling vertigo in most individuals, without the risk of hearing loss associated with higher doses of aminoglycosides and surgical treatment.

NIDCD-supported scientists are currently investigating the effect of single-dose intratympanic gentamycin treatment on vestibular function in individuals with Ménière's disease in one ear. Clinical testing demonstrates that a single gentamycin injection into the affected ear markedly reduces the vestibular response when compared with pretreatment levels. Notably, the reduction of this response is not as severe as that seen after surgical treatment. Experimental studies suggest that gentamycin reduces vestibular responsiveness, and hence, vertigo, by causing a toxic effect on the vestibular hair cells, the sensory receptors that detect head motion stimuli and orientation. However, spontaneous activity is preserved in vestibular neurons after gentamycin administration, suggesting that vestibular hair cells are only partially damaged. While these hair cells can no longer respond to some sensory stimuli, they can still release neurotransmitters to the nerves.

This research demonstrates that a single injection of gentamycin through the eardrum is effective at diminishing vestibular response and in controlling vertigo in individuals with Ménière's disease. Follow-up studies of these individuals demonstrate continued recovery of vestibular function over time following gentamycin treatment. Since there is no known cure for Ménière's disease, this finding provides a new treatment strategy that alleviates the disabling vertigo associated with the disease without significant impact to hearing or other risks of surgery.

Odorant Receptors Help Mosquitoes Smell Their Prey

The ability to sense and discriminate chemical clues is important for the behavior of insects. For instance, the sense of smell (olfaction) plays an important role for blood-feeding female mosquitoes in finding a host. Mosquito-borne disease is a serious world health concern and the mosquito is known to transmit a variety of deadly diseases, including malaria, West Nile virus, dengue and yellow fever. Host preference, especially to humans, in the female mosquito is a critical component of disease transmission. A molecular analysis of the mosquito olfactory system may provide opportunities for reducing disease transmission by this insect.

NIDCD-supported scientists are characterizing the genes that play a role in the function of the *Anopheles gambiae* olfactory system and have identified odorant receptor-encoding genes selectively expressed in the olfactory organs of this malaria-transmitting mosquito. The scientists cloned four odorant receptor genes (AgOr1-4) from the mosquito and checked for similarity to the olfactory receptor genes of the fruit fly, *D. melanogaster*. An analysis of the mosquito genes demonstrated no similarities between AgOr3 and AgOr4 and the fly chemosensory receptor genes, suggesting a unique class of mosquito receptors are associated with olfactory-driven behaviors of this insect. Blood-feeding and host preference selection involve only the female mosquito, so the scientists studied the expression of the AgOr genes in the female mosquito's primary olfactory organ – its antennae. AgOr1 alone is expressed in female olfactory tissue, while AgOr3-4 are found in both male and female olfactory tissues. In addition, it was observed that AgOr1 is turned off in the olfactory tissue of the female mosquito 12 hours after a blood meal, which is consistent with decreased host-seeking behavior.

These findings suggest that AgOr1 may detect an olfactory signal that is active in female mosquitoes before but not after a blood meal. Developing selective antagonists to AgOr1 may help to control the transmission of malaria and other mosquito-borne diseases, and may also represent a novel disease prevention approach that is based on an understanding of olfactory receptor genes. In addition, these findings may ultimately be useful in developing new repellants and attractants that are more effective, economical and ecologically friendly.

Loss of Sex Discrimination and Male-Male Aggression

Animals have evolved specific communication strategies to help them identify and attract a mate. Pheromones are a discrete class of chemical cues that signal the sex and the social status of a species and promote coordinated motor programs and physiological changes essential for breeding and aggression among animals of the same species. The highly reproducible and species-specific response to pheromones offers a valuable experimental system for studying the neural basis of genetically pre-programmed behaviors.

NIDCD-supported scientists are studying signal processing in receptor cells of the vomeronasal system in mice. The vomeronasal system (VNO) is an independent component of the olfactory (smell) system and responds to species-specific pheromones that elicit a variety of basic social and reproductive behaviors. The VNO signal transduction involves transient receptor ion channels and pathways that involve a protein called TRP2. The scientists removed genes of the TRP2 ion channel, which eliminated physiological activation of vomeronasal neurons by urine pheromones. This resulted in the failure of the mice to display typical pheromone-evoked aggression towards male intruders and inappropriate courtship behavior. The mice without the TRP failed to discriminate between male and female mice.

The results of this study demonstrate that the loss of a single ion channel type has widespread reproductive and other behavioral consequences, and that a major function of the VNO is to ensure the gender specificity of male mouse behavior by providing the brain with sensory cues that are essential for sex discrimination.

Discovery of an Amino Acid Taste Receptor

Taste is responsible not only for attraction and repulsion to various foods but is also responsible for providing important information about the chemical environment. The basic taste qualities are sweet, sour, salty, bitter and umami (the taste of monosodium glutamate or the taste associated with protein-rich foods). A major challenge in taste research is identifying the various types of taste receptors on the tongue that respond to different structurally diverse compounds. Recently, scientists have identified a taste receptor dedicated to tasting amino acids, the building blocks of proteins that are involved in the biological processes in the body.

It has been known that sweet-, bitter- and umami-tasting substances activate G-protein-coupled receptors in the tongue. NIDCD-supported scientists discovered that two subunits in the T1R family, T1R1 and T1R3, can combine to form a broadly tuned L-amino-acid receptor, T1R1+3, that responds to most of the 20 standard amino acids. The receptor is not sensitive to natural or artificial (i.e., non-amino acid) sweeteners. The T1R1+3 receptor is also responsive to monosodium glutamate, the basic ingredient in umami taste. In contrast, the T1R2+3 receptor is a sweet receptor that does not respond to L-amino acids. These results indicate that the subunit partner to T1R3 (either T1R2 or T1R1) determines whether a receptor will be a sweet or amino acid receptor.

Identification of an amino acid taste receptor provides a new tool to help scientists decode the molecular basis for detecting different taste qualities in mammals.

Do Stutterers Have Different Brains?

People who stutter are often subjected to emotional pain and social stigma due to their dysfluency. An individual who stutters may be more self-conscious about how to produce the sounds of speech, leading many to believe that anxiety or emotional problems are the causes for stuttering. There is no single known cause of persistent developmental stuttering (PDS). Recently, scientists began studying brain activity patterns in the cortical speech-language areas of the brain of individuals who stutter.

NIDCD-supported scientists performed brain imaging studies on two groups of adults; those with or without PDS. The scientists performed quantitative and qualitative measurements of brain imaging scans on these two groups. Results of the analysis showed that differences in the speech-language areas of the brain are more common in adults with PDS, although no one anatomic feature accounted for the group differences. The major anatomic finding was that the size and symmetry of the planum temporale (PT) differed significantly between the two groups. Both right and left PT size were significantly larger in the adults with PDS. The PT is important for higher order processing of language information. These findings may be functionally relevant in view of the effects of delayed auditory feedback on dysfluency and fluency of speech in individuals who stutter and those that do not. Delayed auditory feedback is a means of changing the speech of a speaker so he or she hears it with a delay. This method can sometimes make a dysfluent speaker more fluent. The motor control theory of speech production suggests

that there are two main feedback loops, an outer "linguistic" loop and an inner "phonatory" loop. Thus stuttering can be modeled as a momentary instability in these systems when the timing between these two loops is interrupted.

The results about the PT size and other findings, such as variations of infolding patterns of the brain, demonstrate that atypical size or shape of the speech-language area may put individuals at risk for stuttering. The research suggests that these abnormalities permit normal development of language, but can cause abnormalities in speech.

Children with Speech-Sound Disorders are at Risk for Later Academic Impairments

Children with speech-sound disorders often have difficulties in other areas of language as well. These disorders are characterized by the inability to use speech sounds that are normal for the individual's age and dialect. Speech-sound disorders involve language difficulty affecting an individual's ability to learn and organize speech sounds into a system of sound patterns. Previous studies have demonstrated that speech, language and reading difficulties are common in families of children with speech-sound disorders. Poor awareness of speech skills and a weakness in vocal sound classification in verbal memory may put children of preschool age with speech-sound disorders at risk for later spelling difficulties. Previous studies of children with early speech- sound disorders have not examined spelling outcomes in relation to the type of early speech and/or language disorder.

In a recent NIDCD-supported study, the spelling errors of 52 children with history of speech-sound disorders were analyzed to predict the association between weaknesses in spoken language skill in early childhood and school-age spelling abilities. Children four- to six-years old in 87 families were recruited to study the correlation between early speech-sound disorders with spelling impairments. Based on their preschool language skills, the children were assigned to one of two study groups if they were diagnosed with a speech-sound disorder or speech-sound disorder with additional language impairment. Follow-up measures were administered in the areas of speech-sound, spelling, reading, language and the collective influence of the family. The findings of this study support previous research indicating that children with early speech-sound disorders are at risk for later spelling difficulties. Spelling difficulties may come from speech-sound processing deficits that persist even after the speech-sound disorder is resolved later in life. Evidence from studying these families raises the possibility of a common genetic cause for speech/language and written language disorders. In this study, the number of family members with speech, language, reading and spelling disorders exceeded expected frequency for these disorders in the general population. Although the genetic cause for these disorders is not known, specific signs of the disorder suggest a male gender bias since brothers were also more likely to have the disorder than sisters.

The findings of this study reveal that preschool children with speech-sound disorders are at risk for later spelling impairments even after productive speech disorders have resolved. Preschool children with both speech-sound and language disorders are likely to have more severe spelling problems than preschoolers with only speech-sound disorders. Careful follow-up of children

with both disorders are needed even after the speech-sound disorder has resolved. In addition, a family history of spelling difficulties may identify children at risk for developing written language disorders.

A Critical Period for American Sign Language Processing

Signed languages such as American Sign Language (ASL) are natural languages similar to spoken languages, and thus enable scientists the opportunity to examine the effects of language structure and the manner by which the brain processes and organizes language. It has long been known that the left side of the brain is involved with learning spoken language. However, scientists have learned that users of ASL utilize the right hemisphere (RH) as well as the left hemisphere (LH) of the brain.

NIDCD-supported scientists are examining the effect that age of language acquisition has on the parts of the brain involved in language processing. Scientists are studying bilingual individuals that know two languages that differ in both their structure and their modality: an audible-oral language, (English), and the a visual-manual language (American Sign Language). The unique demands of processing ASL may use certain parts of the right side of the brain not known for processing spoken languages. However, the ability for the right side of the brain to learn ASL may change with age, suggesting that a "critical" or "sensitive" period in development exists when ASL is learned early in life and brain regions can be activated for processing signed language.

The scientists used functional magnetic resonance imaging (fMRI) to compare brain activation of two groups of individuals who were fluent in spoken English and ASL. Although all subjects were native learners of spoken English, one group learned ASL in early childhood from deaf parents whose primary language was ASL, and the other group learned ASL in early adulthood (after puberty). The scientists observed that certain regions within the right side of the brain were activated by ASL even after puberty, however, the magnitude of these activation were less than in early learners of sign language. Early signers showed strong activations in one region of the right hemisphere, the angular gyrus (AG), but this region did not show significant activation in the late signers. It seems that there is a critical period during development that incorporates the AG for processing ASL.

The results reveal that exposure to a language that makes extensive use of hand, arm and facial movements can lead to a specialized type of language processing by the AG but only if that language is learned early in life. This region of the brain may possess some biological bias toward the processing of human motion, shape and location information, which enables it to be specialized for processing a spatial language such as ASL. The AG appears less susceptible to change after puberty, and thus, for signed language as well as other natural languages, the nature and timing of language input have significant effects on the identity and configuration of the language systems of the brain.

A Possible Gene for Childhood Language Disorders

Children who fail to develop language normally (in the absence of factors such as neurological disorders, hearing impairments, or lack of adequate opportunity) have specific language impairment (SLI). Although some children with SLI will successfully learn to compensate when they become adults, many do not. SLI has a prevalence of approximately 7% in children entering school and is associated with later difficulties in learning to read. Research studies have consistently demonstrated that SLI clusters in families, suggesting that genetic factors may be an important cause of SLI.

NIDCD-supported scientists are scanning the genome for the location of the gene suspected of causing SLI, by studying families where multiple members have with language/reading disorders. The study showed significant evidence of a link between a region of chromosome 13 and susceptibility to SLI. Further analysis also suggests two additional gene locations on chromosomes 2 and 17 that may play a role in SLI. In addition, mutations in the same region in chromosome 13 is implicated in autism, and some children with autism show language deficits that are very similar to SLI.

New Initiatives in Human Communication Research

Auditory/Perceptual Processing by Infants with Hearing Loss

As many as 33 children are born each day in the U.S. with a significant hearing impairment. As more newborns are screened for hearing loss, a cohort of infants are being identified very early in life. Clinicians are faced with decisions regarding the type and effectiveness of various early intervention and management strategies for children much younger than previously encountered. Measurement tools and techniques that are sufficiently sensitive or developed for measuring or evaluating progress or benefit of various habilitative strategies in these infants do not exist. In addition, there is no empirical database to guide these decisions, and the time frame in which the decision making must occur is extremely short. The NIDCD is supporting an initiative on auditory/perceptual processing by infants with hearing loss with the long-term goal of determining the appropriate and optimal habilitative strategies for developing communication skills.

Cellular Repair Studies of the Auditory and Vestibular Systems

Regenerative and reparative methodologies have potential for enhancing the function and subsequent quality of life for individuals with a hearing or balance disorder. Current reparative technology involving the use of stem cell biology to restore lost function with the replacement of damaged or diseased cells holds great promise. NIDCD is sponsoring an initiative that will explore putative progenitor cell source, developmental progenitor cell lineages, auditory and vestibular transplantation methods, and molecular signaling events that lead to fully functional and integrated cells and the restoration of hearing and balance.

New Approaches for Analysis, Treatment and Prevention of Otitis Media

Otitis media (middle ear infection) in children is a major health problem in the U.S. The widespread use of oral antibiotics to treat otitis media has resulted in an alarming increase in antibiotic-resistant bacterial strains, which cause otitis media as well as other potentially fatal diseases including pneumonia, meningitis and septicemia. NIDCD seeks to capitalize on state-of-the-art molecular, genetic and genomic technologies by sponsoring an initiative to develop alternative strategies and new approaches for the analysis, prevention and treatment of otitis media.

Innovation in Management and Administration

NIDCD research administrators are using innovative ways to stimulate and foster research on human communication. The Institute constantly consults with the scientific community to develop a priority setting process that ensures the current state-of-the science and current health needs are addressed. To address these needs, the NIDCD continues to develop administrative procedures that enable the efforts of researchers interested in communication sciences and its disorders.

Updating the NIDCD Strategic Research Plan

In January and February of 1999, the NIDCD convened a group of 18 experts to help formulate a Strategic Plan for the Institute for Fiscal Years 2000-2002. This Strategic Planning Group, comprised of scientists and other members of the public, was asked to identify areas of research that either presented an extraordinary opportunity or compelling need that fell within the purview of the Institute's mission. They reviewed all the research supported by the NIDCD as well as other NIH-wide scientific initiatives. In addition, presentations from public organizations interested in research supported by NIDCD were given so that the public's perspective could help to shape the Strategic Plan. The final draft of the plan was discussed in detail at a subsequent meeting of the National Deafness and Other Communication Disorders Advisory Council. To keep current with the state-of-the-science and with advances in the field, the NIDCD Advisory Council reviewed and updated the scientific version of the Strategic Plan at its January 18, 2002, meeting. The scientific version later became the basis for a plain language version. Each version highlighted the extraordinary research opportunities and compelling needs of individuals who have communication disorders.

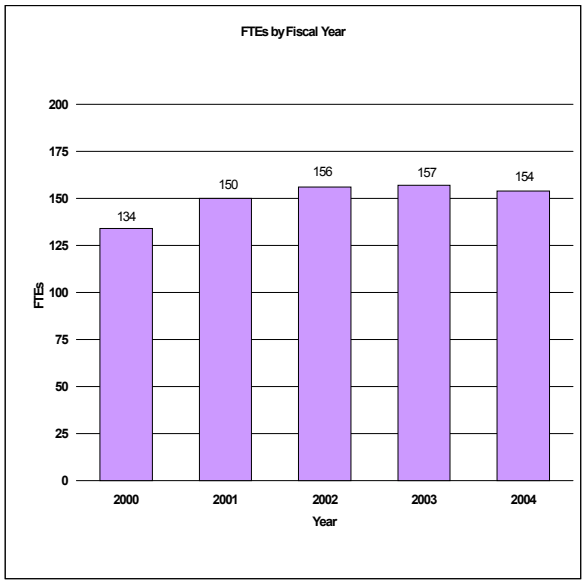
Redesigning the NIDCD Website

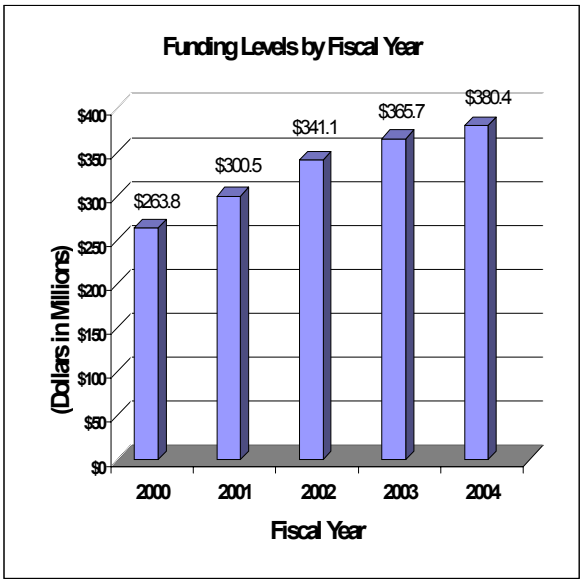
The NIDCD Website is the primary tool for the Institute to provide accurate and up-to-date information about NIDCD's research findings to a variety of audiences. The website is undergoing a major revision based on recommendations of a Needs Assessment study conducted in FY 2001. The key recommendations from that study for improving the usability of the site included: using lay language; designing predictable screen templates; developing a primary navigation structure; and creating task flows that match user needs. The new site will provide an

interface with end users' needs in mind, major content revisions, and improved navigation design. The site will be tested for usability at various stages in the design process by actual users. The anticipated launch date for this new site is November 2002. After the new site is live, the NIDCD will continue to evaluate the new site, including an online survey, to determine if the enhancements increase user satisfaction.

Budget Policy

The Fiscal Year 2004 budget request for the NIDCD is $380,377,000, including AIDS, an increase of $14,643,000 and 4.0 percent over the FY 2003 amended President's Budget Request. A five year history of FTEs and Funding Levels for NIDCD are shown in the graphs below. Note that Fiscal Years 2001 and 2000 FTEs are not comparable for the NIH Human Resources functional consolidation.





NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities. NIDCD's budget request provides an average cost increase of 2.5 percent for Research Project Grants (RPGs).

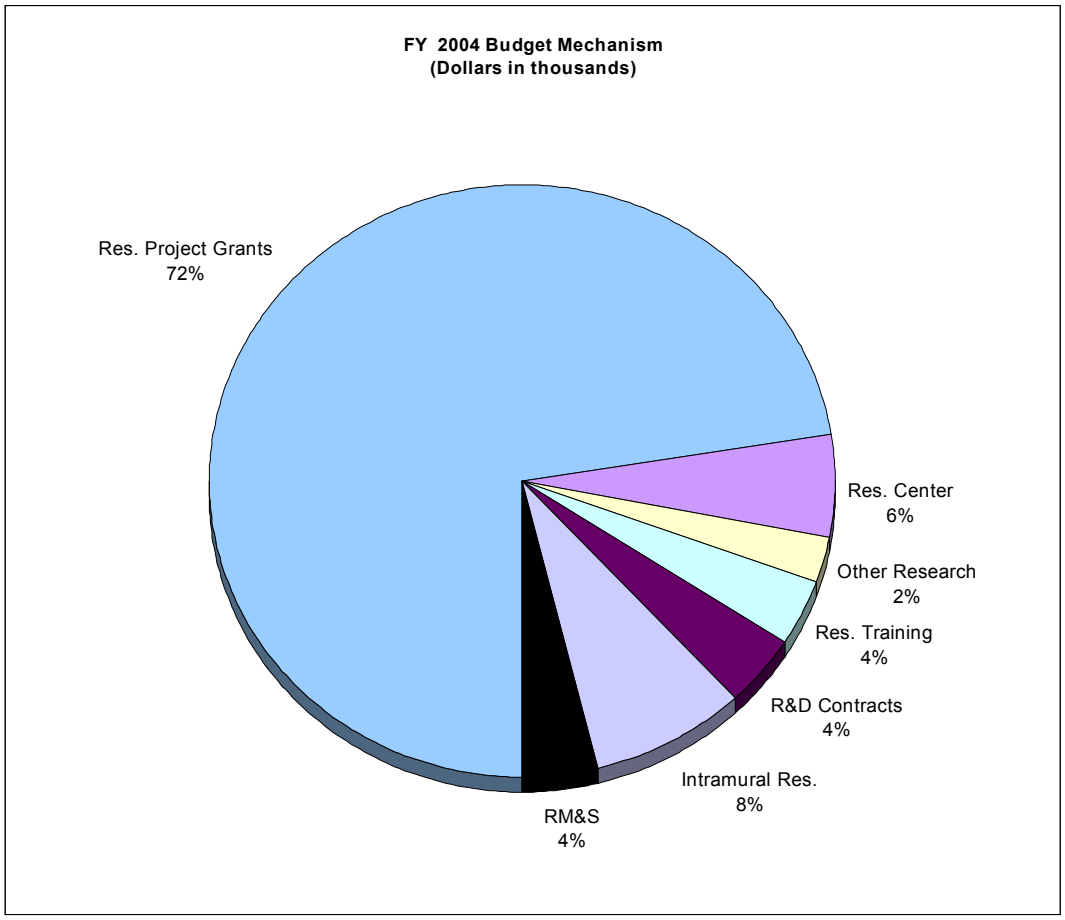
Also in FY 2004, NIDCD will fully fund 8 new RPG grants, including 6 Academic Research Enhancement Awards (AREA), and 2 Shannon awards.

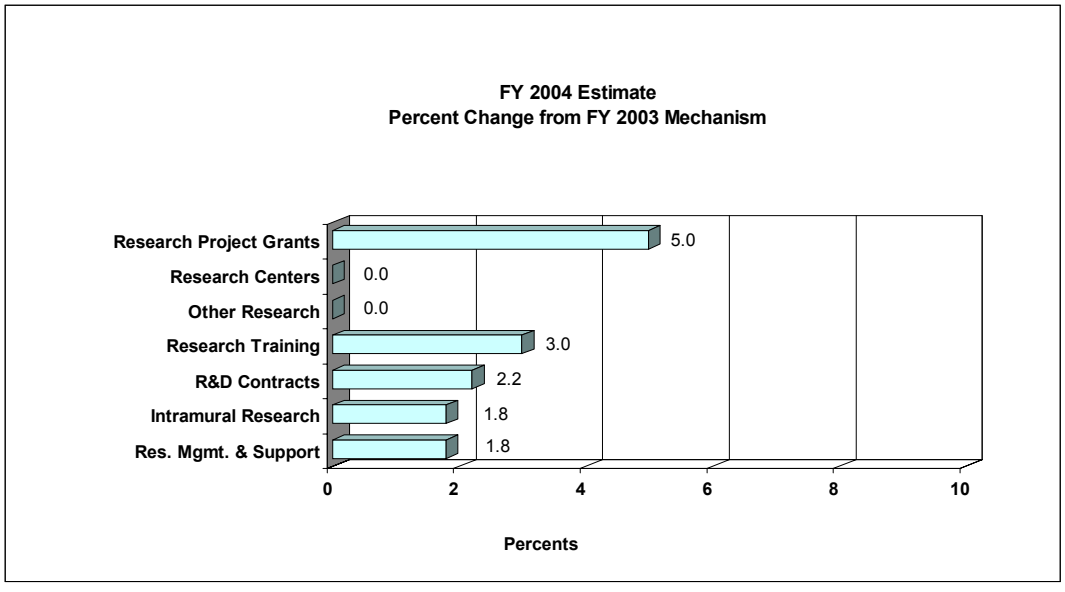
Promises for advancement in medical research are dependent on maintaining the supply of new investigators with new ideas. In the Fiscal Year 2004 request, NIDCD will support 332 pre- and postdoctoral trainees in full-time training positions, the same number as in FY 2003. Stipend levels for NRSA trainees will increase by 4 percent over Fiscal Year 2003 levels for predoctoral fellows, and from 4 to 1 percent, based on years of experience, for postdoctoral fellows.

The Fiscal Year 2004 request includes funding for 26 research centers, 61 other research grants, including 43 clinical career awards, and 37 R&D contracts. Intramural Research and Research Management and Support receive increases of 1.8 percent over FY 2003.

In addition, the budget request provides $310,000 for Best Pharmaceuticals for Children Act studies.

The mechanism distributions by dollars and percent change are displayed below:


FY 2004 Budget Mechanism
(Dollars in thousands)
Res. Project Grants
72%
Res. Center
6%
Other Research
2%
Res. Training
4%
R&D Contracts
4%
Intramural Res.
8%
RM&S
4%


FY 2004 Estimate
Percent Change from FY 2003 Mechanism
Research Project Grants
Research Centers
Other Research
Research Training
R&D Contracts
Intramural Research
Res. Mgmt. & Support
5.0
0.0
0.0
3.0
2.2
1.8
1.8
0
2
4
6
8
10
Percents

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Budget Mechanism - Total

MECHANISM	FY 2002 Actual		FY 2003 Amended President's Budget		FY 2004 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	617	$170,325,000	645	$183,411,000	675	$197,635,000
Administrative supplements	(36)	1,544,000	(36)	1,600,000	(36)	1,600,000
Full funded	0	0	0	0	8	1,100,000
Single year	237	63,286,000	250	69,500,000	237	66,550,000
Subtotal, competing	237	63,286,000	250	69,500,000	245	67,650,000
Subtotal, RPGs	854	235,155,000	895	254,511,000	920	266,885,000
SBIR/STTR	39	7,689,000	42	8,243,000	45	9,000,000
Subtotal, RPGs	893	242,844,000	937	262,754,000	965	275,885,000
Research Centers:						
Specialized/comprehensive	25	20,109,000	26	21,500,000	26	21,500,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	25	20,109,000	26	21,500,000	26	21,500,000
Other Research:						
Research careers	42	6,493,000	43	6,648,000	43	6,648,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	0	0	0	0	0	0
Biomedical research support	0	1,195,000	0	0	0	0
Minority biomedical research support	0	0	0	0	0	0
Other	18	2,602,000	18	2,680,000	18	2,680,000
Subtotal, Other Research	60	10,290,000	61	9,328,000	61	9,328,000
Total Research Grants	978	273,243,000	1,024	293,582,000	1,052	306,713,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	127	4,429,000	147	5,298,000	147	5,458,000
Institutional awards	205	8,251,000	185	7,720,000	185	7,950,000
Total, Training	332	12,680,000	332	13,018,000	332	13,408,000
Research & development contracts	31	13,341,000	36	14,019,000	37	14,329,000
(SBIR/STTR)	(0)	(0)	(0)	(0)	(0)	(0)
	FTEs		FTEs		FTEs	
Intramural research	75	28,552,000	75	30,609,000	74	31,160,000
Research management and support	81	13,310,000	82	14,506,000	80	14,767,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, NIDCD	156	341,126,000	157	365,734,000	154	380,377,000
(Clinical Trials)		(3,556,000)		(3,824,000)		(3,993,000)

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Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2002 Actual FTEs	FY 2002 Actual Amount	FY 2003 Amended President's Budget FTEs	FY 2003 Amended President's Budget Amount	FY 2004 Estimate FTEs	FY 2004 Estimate Amount	Change FTEs	Change Amount
Extramural Research:								
Deafness and Other Communication Disorders		$299,264		$320,619		$334,450		$13,831
Subtotal, Extramural research		299,264		320,619		334,450		13,831
Intramural research	75	28,552	75	30,609	74	31,160	(1)	551
Res. management & support	81	13,310	82	14,506	80	14,767	(2)	261
Total	156	341,126	157	365,734	154	380,377	(3)	14,643

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National Institute on Deafness and Other Communication Disorders

Summary of Changes

2003 Amended President's Budget				$365,734,000
2004 Estimated Budget Authority				380,377,000
Net change				14,643,000
	2003 Amended President's Budget Base		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$8,371,000		$106,000
b. Annualization of January 2003 pay increase		8,371,000		66,000
c. January 2004 pay increase		8,371,000		129,000
d. One extra day of pay		8,371,000		33,000
e. Payment for centrally furnished services		5,325,000		107,000
f. Increased cost of laboratory supplies, materials, and other expenses		16,913,000		338,000
Subtotal				779,000
2. Research Management and Support:				
a. Within grade increase		8,019,000		136,000
b. Annualization of January 2003 pay increase		8,019,000		64,000
c. January 2004 pay increase		8,019,000		124,000
d. One extra day of pay		8,019,000		31,000
e. Payment for centrally furnished services		1,653,000		33,000
f. Increased cost of laboratory supplies, materials, and other expenses		4,834,000		101,000
Subtotal				489,000
Subtotal, Built-in				1,268,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Deafness and Other Communication Disorders

Summary of Changes--continued

CHANGES	2003 Amended President's Budget Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	645	$185,011,000	30	$14,224,000
b. Competing	250	69,500,000	(5)	(1,850,000)
c. SBIR/STTR	42	8,243,000	3	757,000
Total	937	262,754,000	28	13,131,000
2. Research centers	26	21,500,000	0	0
3. Other research	61	9,328,000	0	0
4. Research training	332	13,018,000	0	390,000
5. Research and development contracts	36	14,019,000	37	310,000
Subtotal, extramural				13,831,000
	FTEs		FTEs	
6. Intramural research	75	30,609,000	(1)	(228,000)
7. Research management and support	82	14,506,000	(2)	(228,000)
8. Cancer control and prevention	0	0	0	0
9. Construction		0		0
Subtotal, program		365,734,000		13,375,000
Total changes	157		(3)	14,643,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Deafness and Other Communication Disorders

Budget Authority by Object

	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	157	154	(3)
Full-time equivalent of overtime & holiday hours	0	0	0
Average ES salary	$142,500	$142,500	$0
Average GM/GS grade	10.8	10.8	0.0
Average GM/GS salary	$65,878	$67,196	$1,318
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$104,328	$107,555	$3,227
Average salary of ungraded positions	67,411	68,759	1,348
OBJECT CLASSES	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	$7,697,000	$7,880,000	$183,000
11.3 Other than Full-Time Permanent	3,492,000	3,554,000	62,000
11.5 Other Personnel Compensation	404,000	410,000	6,000
11.7 Military Personnel	0	0	0
11.8 Special Personnel Services Payments	1,870,000	1,920,000	50,000
Total, Personnel Compensation	13,463,000	13,764,000	301,000
12.1 Civilian Personnel Benefits	2,925,000	3,012,000	87,000
12.2 Military Personnel Benefits	0	0	0
13.0 Benefits for Former Personnel	2,000	2,000	0
Subtotal, Pay Costs	**16,390,000**	**16,778,000**	**388,000**
21.0 Travel & Transportation of Persons	577,000	580,000	3,000
22.0 Transportation of Things	50,000	52,000	2,000
23.1 Rental Payments to GSA	0	0	0
23.2 Rental Payments to Others	555,000	560,000	5,000
23.3 Communications, Utilities & Miscellaneous Charges	516,000	520,000	4,000
24.0 Printing & Reproduction	161,000	162,000	1,000
25.1 Consulting Services	101,000	102,000	1,000
25.2 Other Services	1,800,000	1,800,000	0
25.3 Purchase of Goods & Services from Government Accounts	22,682,000	23,052,000	370,000
25.4 Operation & Maintenance of Facilities	320,000	325,000	5,000
25.5 Research & Development Contracts	7,282,000	7,595,000	313,000
25.6 Medical Care	287,000	290,000	3,000
25.7 Operation & Maintenance of Equipment	1,206,000	1,220,000	14,000
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	**33,678,000**	**34,384,000**	**706,000**
26.0 Supplies & Materials	4,325,000	4,330,000	5,000
31.0 Equipment	2,882,000	2,890,000	8,000
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	306,600,000	320,121,000	13,521,000
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	0	0	0
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	**349,344,000**	**363,599,000**	**14,255,000**
Total Budget Authority by Object	**365,734,000**	**380,377,000**	**14,643,000**

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National Institute on Deafness and Other Communication Disorders

Salaries and Expenses

OBJECT CLASSES	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$7,697,000	$7,880,000	$183,000
Other Than Full-Time Permanent (11.3)	3,492,000	3,554,000	62,000
Other Personnel Compensation (11.5)	404,000	410,000	6,000
Military Personnel (11.7)	0	0	0
Special Personnel Services Payments (11.8)	1,870,000	1,920,000	50,000
Total Personnel Compensation (11.9)	**13,463,000**	**13,764,000**	**301,000**
Civilian Personnel Benefits (12.1)	2,925,000	3,012,000	87,000
Military Personnel Benefits (12.2)	0	0	
Benefits to Former Personnel (13.0)	2,000	2,000	0
Subtotal, Pay Costs	**16,390,000**	**16,778,000**	**388,000**
Travel (21.0)	577,000	580,000	3,000
Transportation of Things (22.0)	50,000	52,000	2,000
Rental Payments to Others (23.2)	555,000	560,000	5,000
Communications, Utilities and Miscellaneous Charges (23.3)	516,000	520,000	4,000
Printing and Reproduction (24.0)	161,000	162,000	1,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	51,000	52,000	1,000
Other Services (25.2)	1,800,000	1,800,000	0
Purchases from Govt. Accounts (25.3)	9,402,000	9,448,000	46,000
Operation & Maintenance of Facilities (25.4)	320,000	325,000	5,000
Operation & Maintenance of Equipment (25.7)	1,206,000	1,220,000	14,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**12,779,000**	**12,845,000**	**66,000**
Supplies and Materials (26.0)	3,570,000	3,573,000	3,000
Subtotal, Non-Pay Costs	18,208,000	18,292,000	84,000
Total, Administrative Costs	**34,598,000**	**35,070,000**	**472,000**

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

SIGNIFICANT ITEMS IN THE SENATE APPROPRIATIONS COMMITTEE REPORT

The following section represents FY 2003 Congressional requirements for reports and significant items derived from Senate Report 107-216. These actions discussed below are contingent on inclusion of similar language and funding in the final FY 2003 appropriation and related reports. Additional items may be transmitted at a later date as a result of the final Conference report.

Item

Dysphonia - The Committee continues to be pleased with the NIDCD's expanding intramural research program with respect to dysphonia. The Committee encourages the NIDCD to explore possibilities for a more active extramural research effort on dysphonia, and collaboration with other NIH Institutes on this important disorder. (p. 129)

Action taken or to be taken

Individuals who suffer from dysphonia may experience impairment of voice quality, hoarseness, or even difficulty with speaking. To understand the basis of voice disorders, NIDCD supports an active portfolio in the physiological and neurological insights into the etiology of dysphonia with the goal of developing mechanisms for assessing and treating this disorder. Current research projects are focusing on the quantitative description of vocal fold dynamics, the physiology and measurement of vocal fold vibration, and genetic studies of laryngeal paralysis, as well as the basis of normal and disordered laryngeal function and speech. NIDCD is expanding research efforts in voice disorders by co-sponsoring a Program Announcement with the National Institute of Neurological Disorders and Stroke, the National Eye Institute, and the National Institute of Child Health and Human Development for new research on the underlying causes of human dystonia, which includes disorders involving the muscles involved in voice and speech, and potential therapeutic strategies for treatment. To further attract scientist to study the normal and disordered conditions of voice, NIDCD is awarding pre- and post-doctoral training grants for new and developing investigators.

Item

Genetic deafness – The Committee encourages the NIDCD to conduct research into the genetic basic for normal and disordered communication, especially auditory system proteomics, and into interventions that prevent or treat genetic deafness. (p. 129)

Action taken or to be taken

In many children born with hearing impairment, the underlying cause is a mutation in a gene whose function is essential for normal auditory function. A number of these genes have been identified, and several of these genes have been found to have mutations that account for a significant fraction of hereditary hearing impairment. The NIDCD has played and will continue to play a major role in locating a multitude of genes for syndromic and nonsyndromic forms of hearing impairment. At present, over 70 genes causing nonsyndromic hereditary hearing impairment have been mapped to intervals on particular chromosomes, many by collaborative efforts involving NIDCD-supported scientists. These genes encode a remarkable array of proteins with different functions. By understanding the identity and function of these genes and their associated proteins, scientist will be able to determine the cause of hereditary hearing impairment, and provide optimal intervention strategy for these children as soon as possible, thereby maximizing the child's potential for developing language skills. Genetic analysis of families participating in this research will help identify the location of the genetic mutations responsible for hereditary hearing impairment. This genetic information will ultimately aid in the precise and timely diagnosis of infants identified with a hearing impairment, thereby helping parents plan for the educational and habilitation needs of their children at the earliest possible opportunity. In addition, results of this research investment will foster the development of more precise genetic screening methods, novel intervention and prevention strategies, and more effective treatment methods.

Item

Hair cell regeneration – The Committee urges NIDCD to give a high priority to new and important directions for inner ear hair cell regeneration. (p. 130)

Actions taken or to be taken

In humans, excessive loss of auditory sensory cells (inner hair cells) results in deafness and hearing impairment. These sensory cells are established early in development and do not grow back following injury. The NIDCD places high priority on research involving the development and regeneration of auditory sensory cells of the inner ear. Intramural scientist are examining the molecular and cellular processes that regulate hair cell development and growth. Findings from this research will potentially enable further research determining the factors leading to the growth and development of hair cells. In addition, NIDCD intramural scientists have demonstrated that fibroblast growth factor (FGF) signaling pathways plays a key role in regulating hair cell development.

Item

Hearing devices – The Committee encourages the NIDCD to expand research that would

improve the benefits of cochlear prostheses and improve remediation of the less-than-profound hearing loss through hearing aids and/or new prostheses and drug-delivery systems. (p. 130)

Action taken or to be taken

Approximately 28 million Americans have a hearing impairment. The NIDCD supports numerous grants for scientists to conduct studies on hearing aid research and development. These studies include research on the application of new signal processing strategies and ways to improve sound transmission and reduce noise interference, as well as psycho-physical studies of the impact of abnormal hearing function on speech recognition. To improve hearing aid performance, especially in noisy situations, NIDCD has entered into two collaborative ventures. The first was formed between NIDCD and the Department of Veterans Affairs (VA) to expand and intensify hearing aid research and development. In the second collaboration, the National Aeronautics and Space Administration (NASA) and the VA have joined NIDCD in surveying all Federal laboratories for acoustic and electronic technologies that might improve hearing aids. The most promising technologies have been presented to auditory scientists and hearing aid manufacturers with the hope of forming research partnerships that will lead to commercial application of these technologies. Other studies focus on the best ways to select and fit hearing aids in children. Further research will determine the best ways to manipulate speech signals in order to enhance understanding.

The NIDCD has played a significant and important role in sponsoring the development of cochlear implant technology. With over 30 years of NIH research investment, the cochlear implant has evolved from an experimental device to a miniature hearing prosthesis that is commercially available to assist those who are profoundly deaf or severely hearing impaired. Two new exciting advancements in cochlear implants are currently undergoing investigation by NIDCD-supported scientists: binaural implants and a short electrode implant allowing for the combination of electric and acoustic hearing. Binaural (both ears) implants provide a potential avenue for better speech perception in noise, while the short electrode is being designed to be used in experienced, yet unsuccessful, adult hearing aid users with severe-to-profound hearing impairment. As technology continues to provide advances in cochlear implant design, additional people will have the potential to benefit from these remarkable devices.

Item

Language acquisition – The Committee encourages the NIDCD to explore the biological bases and genetics of language, as well as infant speech perception and language acquisition. It also encourages the Institute to develop clinical applications such as genetic screening for all communication disorders. (p. 130)

Action taken or to be taken

Language is the expression of human communication through which knowledge, belief, and behavior can be experienced, explained, and shared. It is estimated that between six and eight million individuals in the United States have some form of language impairment. The NIDCD continues to supports language research to expand the understanding of the role of each hemisphere of the brain in communication and language, of early specialization of the brain, and of the recovery process following brain damage. This research is intended to further understanding of the neural basis of language disorders. NIDCD-supported scientists are examining a variety of issues related to speech and language development. Brain imaging studies are defining the relationship between brain development and speech and language.

Genetic studies are investigating the likelihood that at least some speech and language problems may be inherited or passed down from parents to their children. NIDCD-supported scientist are scanning the genome for the location of a gene that may be associated with Specific Language Impairment (SLI), by studying families with members characterized with language/reading disorders. This study showed significant evidence of a link between chromosome 13 and susceptibility to SLI. NIDCD will continue to support research about SLI to reveal important genetic factors in finding genes for complex language disorders.

Infants are capable of exploiting many cues, including acoustic information to locate word boundaries in fluent speech. NIDCD supports research that focus on infant acquisition of voice expression. At present, the diagnostic significance of infants' expressive tone cannot be determined because the normal course of voice expression development has not been documented. To address this issue, NIDCD-supported scientist are implementing research projects to uncover the developmental course of attention to cues and the learning mechanisms that allow infants to discover what acoustic events in speech signify word boundaries. Other research efforts include identifying predictors of SLI, examining the stability of language delay, and describing the different paths of development taken for vocabulary, grammar, and phonology in infants. This research will provide a model for infant acquisition of multiple acoustic regularities associated with word boundaries. In addition, the findings from this research will provide an estimate of the earliest age or developmental period in which normal and abnormal patterns of voice expression can be distinguished.

Item

Noise-induced hearing loss – The Committee continues to be concerned by the number of Americans who suffer from noise-induced hearing loss. The NIDCD's Wise Ears! Campaign has the potential to make significant inroads towards educating Americans of all ages and the Committee strongly supports its expansion. (p. 130)

Action taken or to be taken

More than 30 million Americans of all ages are exposed to dangerous levels of noise each day. Although noise-induced hearing loss (NIHL) is completely preventable, some 10 million Americans have already suffered irreversible loss of hearing. To help address this problem, WISE EARS!® (http://www.nidcd.nih.gov/health/wise/index.htm), a public education campaign to prevent noise-induced hearing loss, was launched on July 4, 1999. Since that time, NIDCD has developed and expanded its coalition partners to include nearly 90 organizations that represent workers, employers, health and medical professionals, advocates for children and older Americans, teachers, parents, children, unions, industry, agencies of the federal, state and local governments, university audiology programs and clinics, and the general public. NIDCD links its partners through an electronic newsletter that keeps all partners informed of one another's activities and creates opportunities for collaboration.

WISE EARS!® efforts are expanding to reach a larger audience. For example, during the past year, the following new initiatives have been implemented:

- NIDCD introduced new members to the WISE EARS!® Coalition, including an organization that represents manufacturers concerned about limiting noise exposure from such products as snow-blowers, lawnmowers and leaf-blowers.

- WISE EARS!® has been focusing its attention on noise induced hearing loss associated with firearms by instructing hunters and shooters to wear ear protection. WISE EARS!® participated in the 2002 Outdoor Writers Association of America (OWAA) conference to encourage outdoor writers to cover the topic of noise-induced hearing loss, and NIDCD developed a full one page insert on prevention of noise-induced hearing loss which will appear in the 2003 *Hunter Handbook*, an annual publication that is distributed to instructors of hunting and shooting and used for classroom training material.

- Other WISE EARS!® activities extended to all 50 states and included outreach to older Americans; teachers; students; nurses; pediatricians; and health fairs for women, for families, for African-American, American Indian and Hispanic/Latino/Latina and Pacific Islander and Asian-American groups.

- NIDCD developed a CD ROM Tool Kit incorporating all WISE EARS!® materials to allow groups to create their own materials and find sponsorship for their programs.

- NIDCD produced syndicated health tips on saving your hearing in 1,064 newspapers across 32 states with a readership of 92.6 million people as well as distribution to Spanish-language newspapers. After conducting focus groups with workers and with Hispanic/Latino/Latina and African American families, NIDCD

developed a fact sheet in Spanish as a companion to WISE EARS!®.

- Through its science education efforts, NIDCD has developed a new curriculum supplement, written for middle school students and delivered over the Web and in print, "How Your Brain Understands What Your Ear Hears," that has noise-induced hearing loss prevention for young teens as its capstone lesson. The NIDCD is partnering with the National Institute on Occupational Safety and Health (NIOSH) to plan for a national summit this year to increase dissemination of noise-induced hearing loss information to specific audiences over the next five years.

Item

Presbycusis – Presbycusis, the gradual loss of hearing from aging, will become more common as the Nation's population grows older. The Committee encourages research on the central and peripheral mechanisms leading to presbycustic hearing loss and on strategies that would prevent hearing loss in our senior population. (p. 130)

Action taken or to be taken

Hearing loss is one of the most common conditions affecting older adults. About 30-35 percent of adults between the ages of 65 and 75 years have a hearing loss. It is estimated that 40-50 percent of people 75 and older have a hearing loss. In the aging auditory system, NIDCD continues to make research discoveries that demonstrate changes in the regulation of fluid composition and auto regulation of cochlear blood flow which may underlie some of the biologic effects of aging on auditory function. Improved behavioral and electrophysiological techniques for measuring auditory function are providing more accurate assessments of the peripheral and central components of age-related hearing impairment. Moreover, it is likely that mutation of certain genes known to cause profound hereditary hearing impairment also cause presbycusis. A recent NIDCD-supported study has demonstrated that a clear genetic component exists for age-related hearing loss by measuring several different hearing thresholds at specific frequencies that are most commonly affected in presbycusis. NIDCD is supporting further research in order to formulate innovative strategies to minimize or delay hearing loss in presbycusis.

Item

Tinnitus – The Committee encourages the Institute to expand its research into mechanisms underlying peripheral and central tinnitus. (p. 130)

Action taken or to be taken

Tinnitus is a ringing, roaring, buzzing, or clicking sound that occurs inside the head, and is estimated to effect at least 12 million Americans. People with severe cases of tinnitus

may find it difficult to hear, work, or even sleep. The NIDCD supports several biomedical research projects that cover a variety of aspects of the condition, for example: developing a comprehensive database and an understanding of the phenomenon of tinnitus that accompanies sensorineural hearing loss; tinnitus and sound masking devices; the role of calcium imbalance in inducing cochlear tinnitus; and otoacoustic emissions and cochlear function. The NIDCD is also supporting several non-invasive imaging studies with the goal of differentiating the various kinds of tinnitus.

NATIONAL INSTITUTES OF HEALTH
National Institute on Deafness and Other Communication Disorders

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2003 Amount Authorized	2003 Amended President's Budget	2004 Amount Authorized	2004 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$352,716,000	Indefinite	$366,969,000
National Institute on Deafness and Other Communication Disorders	Section 464	42§285b	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	13,018,000	b/	13,408,000
Total, Budget Authority				365,734,000		380,377,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.
b/ Reauthorizing legislation will be submitted.

NATIONAL INSTITUTES OF HEALTH
National Institute on Deafness and Other Communication Disorders

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1995 2/	$167,129,000	$166,155,000	$167,129,000	$166,761,000 3/
Rescission	0	0	0	(101,000)
1996	172,399,000 2/	174,852,000	170,540,000 2/	174,852,000
Rescission	0	0	0	(119,000)
1997	179,090,000 2/	189,243,000	182,693,000	188,422,000 4/
1998	192,477,000 2/	198,373,000	198,583,000	198,857,000
1999	213,184,000 2/ 5/	216,995,000	229,887,000	229,887,000
Rescission	0	0	0	(152,000)
2000	235,297,000 2/	251,218,000	261,962,000	265,185,000
Rescission	0	0	0	(1,414,000)
2001	276,418,000	301,787,000	303,541,000	300,581,000
Rescission	0	0	0	(100,000)
2002	336,757,000	334,161,000	349,983,000	342,072,000
Rescission	0	0	0	(397,000)
2003	365,929,000			
2004	380,377,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.
3/ Excludes enacted administrative reductions of $125,000.
4/ Excludes enacted administrative reductions of $77,000.
5/ Reflects a decrease of $650,000 for the budget amendment for bioterrorism. Excludes enacted administrative reductions of $77,000.

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2002 Actual	FY 2003 Amended Pres. Budget	FY 2004 Estimate
Office of the Director	8	8	8
Office of Administration	38	39	38
Division of Extramural Research	35	35	34
Division of Intramural Research	75	75	74
Total	156	157	154
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2000	10.5
2001	10.5
2002	10.8
2003	10.8
2004	10.8

NATIONAL INSTITUTES OF HEALTH
National Institute on Deafness and Other Communication Disorders

Detail of Positions

GRADE	FY 2002 Actual	FY 2003 Amended Pres. Budget	FY 2004 Estimate
ES-6	0	0	0
ES-5	0	0	0
ES-4	0	1	1
ES-3	1	0	0
ES-2	0	0	0
ES-1	0	0	0
Subtotal	1	1	1
Total - ES Salary	$137,901	$142,500	$142,500
GM/GS-15	21	21	21
GM/GS-14	7	7	7
GM/GS-13	16	16	16
GS-12	17	17	17
GS-11	14	14	14
GS-10	1	1	1
GS-9	17	17	17
GS-8	11	11	11
GS-7	2	2	2
GS-6	1	1	1
GS-5	3	3	3
GS-4	3	3	3
GS-3	5	5	5
GS-2	1	1	1
GS-1	0	0	0
Subtotal	119	119	119
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	1	1	1
Director Grade	0	0	0
Senior Grade	0	0	0
Full Grade	0	0	0
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	1	1	1
Ungraded	56	56	56
Total permanent positions	109	109	109
Total positions, end of year	177	177	177
Total full-time equivalent (FTE) employment, end of year	156	157	154
Average ES level	ES-3	ES-4	ES-4
Average ES salary	$137,901	$142,500	$142,500
Average GM/GS grade	10.8	10.8	10.8
Average GM/GS salary	$63,897	$65,878	$67,196