DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

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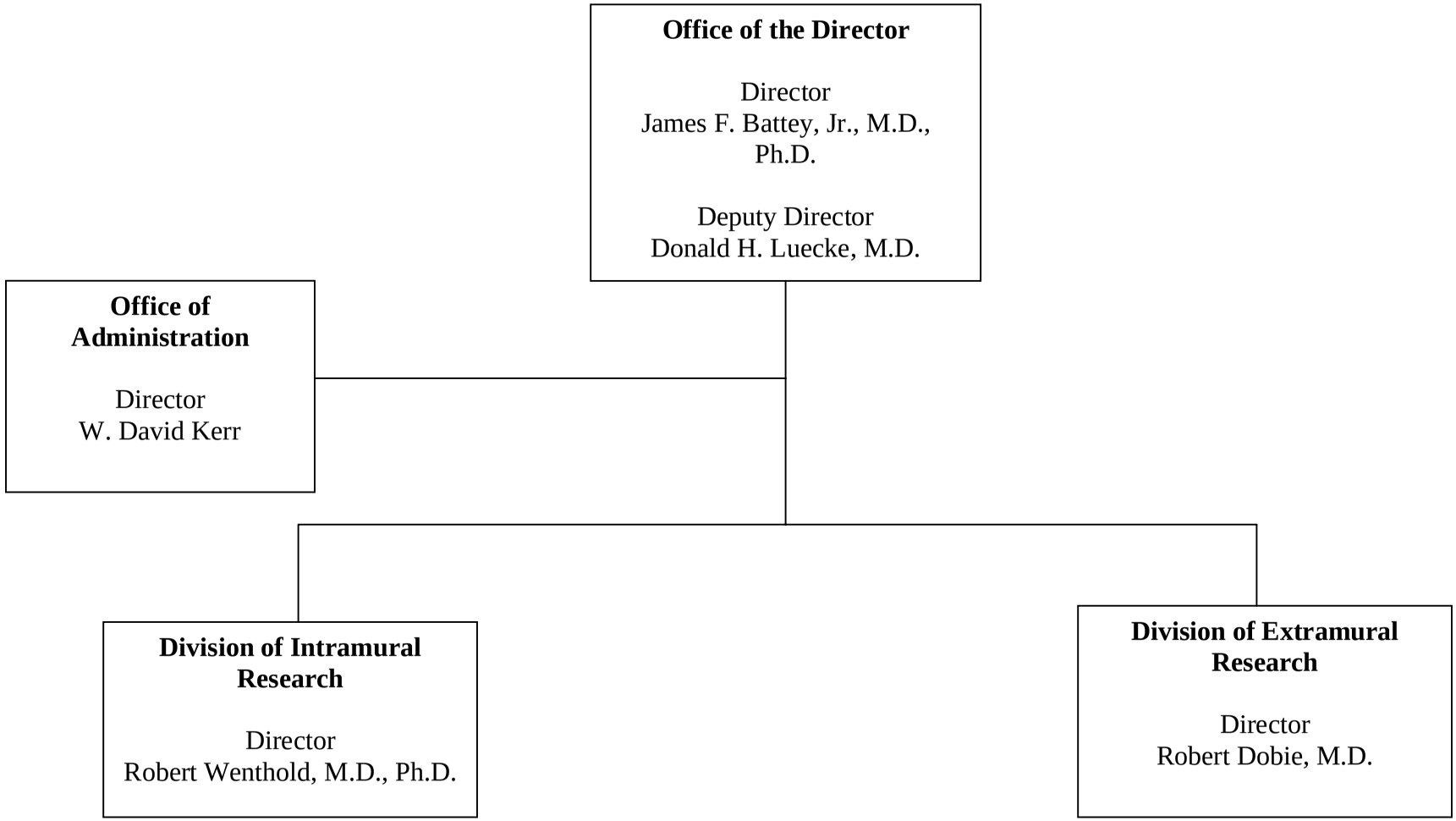

NATIONAL INSTITUTES OF HEALTH

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, [$300,581,000] *$336,757,000*.

[Departments of Labor, Health and Human Services, Education, and Related Agencies Appropriation Act, 2001, as enacted by the Consolidated Appropriations Act, 2001 (P.L. 106-554)]

Amounts Available for Obligation 1/

Source of Funding	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate
Appropriation	$265,185,000	$300,581,000	$336,757,000
Enacted Rescission	(1,414,000)	(100,000)	---
Subtotal, Adjusted Appropriation	263,771,000	300,481,000	336,757,000
Real transfer to:			
Other NIH Institutes through the NIH Director's one-percent transfer authority	(222,000)	---	---
Other HHS Agencies through Secretary's one-percent transfer authority	(55,000)	---	---
HHS for the Office of Human Research Protection		(63,000)	---
Comparative transfer from:			
Office of the Director for the Academic Research Enhancement Award program	680,000	708,000	
Comparative transfer to:			
Other NIH Institutes as a result of a change in assessment formula for Central Services funding	(110,000)	---	
Subtotal, adjusted budget authority	264,064,000	301,126,000	336,757,000
Unobligated balance lapsing	(46,000)	---	---
Total obligations	264,018,000	301,126,000	336,757,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2000 - $984,705 FY 2001 - $4,000,000 FY 2002 - $4,000,000
Excludes $54,107 in FY 2000 and $65,059 in FY 2001 for royalties.

Justification

National Institute on Deafness and Other Communication Disorders

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Authorizing Legislation - Sections 301, 464 and 487 of the Public Health Service Act, as amended. Reauthorizing legislation will be submitted.
Budget Authority:

FY 2000 Actual		FY 2001 Estimate		FY 2002 Estimate		Increase or Decrease	
FTE	BA	FTE	BA	FTE	BA	FTE	BA
134	$264,064,000	150	$301,126,000	156	$336,757,000	+6	+$35,631,000

This document provides justification of the Fiscal Year 2002 activities of the National Institute on Deafness and Other Communication Disorders, including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2002 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

INTRODUCTION

The United States recently celebrated the 10th Anniversary of the signing of the Americans with Disabilities Act, a law enacted in 1990 to promote integration, equal opportunity, and inclusion of millions of Americans afflicted with a disability. Even with this legislation, individuals affected by a communication disability may still find it difficult to enter the labor force and live a productive life because of the daily challenges they face from their disorder. It is often impossible for them to perform the simple acts of speaking, listening, or otherwise making their wants and needs understood. 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 approximately 46 million 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, the advent of exciting new research tools, and new highly trained scientists, 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: The Speed of Sound -- Rapid Motor Protein of Inner Ear Identified

Millions of Americans, especially middle-aged and older individuals, suffer from mild to moderate hearing loss. It is likely that a defect in the most sensitive elements in the inner ear, the hair cells, causes this type of hearing deficit. The hair cells of the inner ear are sensory receptor cells that give humans and other mammals the remarkable ability to hear. The two distinct types of hair cells, outer and inner, have different functions in the auditory process. As sound travels to the ears, down the ear canal, through the bones of the middle ear and into the inner ear, the outer hair cells amplify the mechanical vibrations produced by the sound. The amplification of sound by the outer hair cells occurs through a process known as electromotility. When the cell responds to sound, molecules pass through the cell's membrane causing electrical changes in the cell allowing it to rapidly change its length and stiffness. In response to the sound-evoked electrical changes, the slender cylindrical outer hair cell will alter its length by as much as five percent. The length changes amplify the vibrations, which are sensed by the inner hair cells that send auditory information to the brain. When outer hair cells are lost or destroyed, hearing becomes insensitive, closely spaced frequencies can no longer be discriminated, and the immense range of sound intensities can no longer be differentiated.

Scientists have hypothesized that a highly specialized motor protein that packs the cell's membrane drives outer hair cell motility. As soon as the outer hair cell electromotility process was discovered approximately 15 years ago, scientists began a search to identify the motor molecules that are involved. The difficulty, as with most research involving the ear, is working with the delicate organs of the inner ear, encased in some of the hardest bones in the body, and the small number of sensory hair cells. With support from the NIDCD, scientists have recently isolated the protein responsible for outer hair cell electromotility. In order to search for the gene that codes for the motor protein, the scientists arduously isolated approximately 1,000 outer hair cells and a similar number of inner hair cells from gerbils. The scientists determined that these sensory cells share most active genes, but that certain genes are expressed only in either the outer or inner hair cells. Since only outer hair cells are involved in electromotility, the genes that code for the motor protein should be expressed in outer hair cells alone. Several unique clones were identified and one of these, *Prestin*, later proved to be the gene coding for the motor protein. The name *Prestin* (from the musical term presto, indicating a rapid tempo) was selected to emphasize one of the most interesting features of this protein in the cellular motor process, its speed in changing the length of outer hair cells. Outer hair cells can elongate and contract at rates close to 100,000 times a second!

To prove that *Prestin* is the correct gene, scientists expressed prestin in cells that normally do not express the protein and showed that prestin-producing cells exhibited electromotility. This result functionally identified prestin as the long-sought-after motor protein of the outer hair cells of the inner ear.

With the discovery of this important gene, scientists are asking many new questions about how the *Prestin* gene impacts hearing: are there naturally occurring mutations of *Prestin* that are responsible for certain types of hearing impairment in humans? If so, will it be possible to use gene therapy to restore *Prestin* function in hearing-impaired individuals who have a defect in the gene? What are the consequences in the auditory system of mice that do not express the prestin protein? Do mice that express too much of it exhibit hearing abnormalities? Future research on *Prestin* should lead to significant advances in the understanding of the auditory system, and may lead to the development of new therapeutic measures for hearing impairment.

Science Advances

Expanding Efforts to Identify Hearing Impairment in Newborns

In many states, efforts are underway to screen all newborn infants for hearing impairment before discharge from the hospital. This screening will identify many more infants with hearing impairment at an early age when appropriate intervention can be started that will optimize their long-term speech and language skills. Scientists supported by the NIDCD have examined the importance of age at enrollment in intervention programs and subsequent language outcomes for a group of deaf and hard-of-hearing children. Significantly better language scores were associated with early enrollment. Children enrolled before 11 months of age had stronger vocabulary and verbal reasoning skills at 5 years of age than did children enrolled at a later time. High levels of family involvement correlated with positive language outcomes, and conversely, limited family involvement was associated with significant language delays at age 5, especially when intervention began later in childhood. These results provide further evidence that children will benefit when early identification of hearing loss is combined with an early intervention strategy that actively involves family participation.

The NIDCD has supported a five-year, multi-center study on neonatal hearing impairment and scientists continue to publish new findings in this area. For example, data from the study demonstrated that the three methods commonly used in neonatal hearing screening work equally well, and that successful programs with accurate referral rates can be designed and implemented using any of the three methodologies. The study also showed that monitoring an infant's behavior to an auditory stimulus (behavioral audiometry) can be done reliably for children at 8 to 12 months of age. In addition to advances in screening methodologies, the appropriate training of qualified personnel to conduct hearing screening is important to contributing to reliable test results.

The NIDCD continues to collaborate with federal agencies and the scientific community to facilitate research on early identification of hearing impairment. Leadership of the NIDCD, Centers for Disease Control and Prevention (CDC), and the Health Resources and Services Administration (HRSA) met in May 2000 to provide updates on current issues, discuss future activities and enhance and coordinate the federal effort on activities related to the early identification of hearing impairment. In September 2000, the NIDCD convened the third meeting of the Working Group on Early Identification of Hearing Impairment to assist the Institute in identifying additional research opportunities in the field. Recommendations from previous working group meetings have resulted in additional research related to newborn hearing screening, such as optimizing the fitting of hearing aids in infants, monitoring auditory development in children receiving amplification at an early age, evaluating speech therapy in toddlers, and studying the effects of very early cochlear implantation on language development. As research on neonatal hearing screening advances, new questions will emerge. In addition, it is critical that adequate numbers of research-oriented clinicians be trained to meet this need.

Cochlear Implants Are Cost Effective

The cochlear implant is the only sensory neural prosthesis in widespread clinical use. This device converts sound into electrical impulses on an array of electrodes surgically inserted into the inner ear, bypassing the outer hair cells and stimulating the auditory nerve directly. Over 20,000 Americans with profound hearing impairment have received cochlear implants with approximately one-half of the recipients being children. One of the expected benefits of cochlear implantation in children is improved acquisition of spoken language. Recent data indicate that the improvements in speech perception and speech production shown in children with cochlear implants have also resulted in better language and reading performance. In addition, a recent analysis was conducted to determine the cost effectiveness of cochlear implants in children. Various outcome measures were used and information was collected from parents of profoundly deaf children who had, or had not, received an implant. The study showed that cochlear implants improve the children's quality of life, and result in a net saving to society. The cost benefit is in the form of fewer demands on special education and greater wage-earning opportunities for implant recipients.

New areas of investigation in cochlear implant technology are being supported. Two recent examples include: binaural implants and a short electrode implant. Binaural implants, or implants in both ears, may facilitate better speech perception in noisy environments. The short electrode is being designed for use in adults with severe-to-profound hearing impairment who experience little benefit from hearing aids. As technology continues to provide advances in cochlear implant design, additional populations of individuals will benefit from these remarkable devices.

Otitis Media is Linked to a Strong Genetic Component

Otitis media (OM), or middle ear infection, is the most common reason why a sick child visits a physician, and is the most common reason that children receive antibiotics or undergo surgery. Previous anatomical, physiological, and epidemiological studies have raised the question of whether the likelihood of having multiple bouts of this common disease has a hereditary component. NIDCD-supported scientists began studying twins and triplets to determine the extent to which this common disease might be due to genetic factors. Twin and triplet studies are a powerful method of determining the relative contribution of genetics to a disease because the potentially confounding effect of environmental factors is significantly reduced with this type of study design. The results of the study, which utilized 175 sets of newborn twins and triplets, clearly indicate that there is a strong genetic component to the rate of occurrence of otitis media in children.

The implications of these findings are numerous for both immediate and future improvements in treatment of OM. Primary care physicians can follow siblings and offspring of affected children

as potentially high-risk cases. These children could be monitored more closely for early detection and treatment of disease, reducing the risk of hearing loss. In addition, identification of the genetic factors mediating this effect could eventually result in genetic diagnostic tests to identify individuals with enhanced risk. Finally, studies of the molecular basis for the increased risk and frequency of otitis media could lead to new approaches for intervention and treatment of this disease.

Eliminating Health Disparities in Hearing Disorders

Visits by children to physicians for acute otitis media (OM) costs several billion dollars annually in the United States.[1] In addition to the discomfort and risk of more serious infection, such as meningitis, OM is also associated with disabilities such as hearing deficits, reading disorders, and language delays. OM is reported to occur at a disproportionately high rate among Native American children. A number of articles have been written about OM and Native Americans, some suggesting that there are anatomical differences between the eustachian tube of Native Americans and other Americans. It has also been reported that there are differences in the rate of OM among the various Native American tribes.

As noted earlier, there is a complex genetic basis for susceptibility to OM. Native Americans were not included in this study, leaving open the possibility that allelic variants of one or more genes may confer susceptibility to OM in Native Americans. The NIDCD plans to examine the hypothesis that allelic variants in one or more genes may underlie the increased susceptibility of Native Americans for OM.

Although Native Americans have a high prevalence of chronic OM, prospective studies among Native American infants and young children are sparse. An NIDCD-supported project is studying the epidemiology of OM and hearing loss among Native Americans from birth to age two, and is seeking to define the relative importance of known and new risk factors in this population. A community program assessment of services has been conducted regarding the benefits of breast feeding in reducing infections in infants, tobacco control, and nutrition for prenatal infants and mothers. The findings from this assessment indicate that intervention programs should focus on tobacco control, a significant risk factor for OM in this population, and there appears to be a gap in services addressing infant exposure to parental smoking. The NIDCD plans to initiate intervention and outreach efforts to reduce the burden of OM in Native Americans caused by risk factors identified in the study.

Rapid Progress in the Mapping and Cloning of Genes Responsible for Hereditary Hearing Impairment

NIDCD-supported scientists continue to make impressive scientific progress in mapping and

cloning genes responsible for hereditary hearing impairment. Over the past few years, the chromosomal location of over 60 genes whose mutation results in hereditary hearing impairment

have been identified. In the past three years, nearly 20 genes have been identified whose mutations cause hereditary hearing impairment.

This highly successful effort has several fundamental implications for the treatment of individuals with genetically based hearing impairment. The identification of the gene, or DNA sequence, that mediates hearing loss enables the scientist or clinician to rapidly identify individuals carrying the defective gene even if the hearing loss has a delayed onset and is not yet evident. Furthermore, as each mutation in a specific deafness gene is correlated with the specific physiological characteristics of the hearing loss, the opportunity arises for improved medical treatment and monitoring based on the clinical profile shown to be associated with a specific gene mutation.

In addition, the identification and isolation of genes responsible for hereditary hearing impairment immediately provides a powerful tool to determine how the mutation results in deafness by targeted mutation or deletion of the identified gene in an animal model. The animal model can provide information on which structures of the ear are affected, as well as the molecular and physiological defects that result in hearing impairment, and provide a system to test potential new therapies. This information is extremely valuable in identifying possible ways to prevent or treat the onset of deafness.

Common Changes to the GJB2 Gene and Hereditary Deafness

Mutations in the *GJB2* gene on human chromosome 13 are the cause of approximately one-third of all cases of recessive deafness in the United States. The *GJB2* gene encodes for a gap junction protein that is important for communication between adjacent cells in the inner ear. In addition to mutant forms of *GJB2*, there are variants, or polymorphisms, of *GJB2* that are common in the population. It is critical for scientists to discriminate between benign polymorphic variants and mutations in GJB2 resulting in hereditary hearing impairment. One of the more common polymorphisms, called M34T, is known to significantly decrease the intercellular communication activity of *GJB2* when expressed in model systems in vitro, and M34T has been thought to cause deafness. Scientists at the NIDCD have found a family with hereditary deafness in which the M34T variant is not associated with deafness. This finding suggests that M34T, as well as some other polymorphisms, is not always a deafness-causing variant of *GJB2* even though the variation affects molecular function. The result of this research has important implications for understanding the function of the *GJB2* gene in relation to the inner ear. It also provides physicians information necessary for counseling individuals with *GJB2* polymorphisms such as M34T.

Gene Cloned for Syndrome That Causes Deafness and Blindness

Usher syndrome type 1 is an inherited sensory defect involving profound deafness, balance disorders and eventual progression to blindness. It is the most common genetic cause of a syndrome leading to blindness and deafness in Americans. Studies of affected families in the U.S. and abroad indicate that there are at least six distinct genes whose mutations result in this devastating inherited disease. NIDCD-supported scientists are collaborating with researchers from France, Germany, Lebanon, and Japan to identify the defective gene responsible for one form of this disorder, USHER1C. They identified the defective *USHER1C* gene in unrelated families with this syndrome in the U.S., Lebanon, and Europe.

The gene encodes a protein called harmonin (from the Greek word harmonia, meaning "assembling") that is expressed in the sensory cells of the inner ear. The protein made by *USHER1C* is structurally similar to a group of well-studied proteins known to be involved in assembling multi-protein complexes, which mediate critical cellular functions in a number of organs including the ear. Identification and study of harmonin in mice revealed that the protein is distributed in the semicircular canals and cochlea of the inner ear.

These findings will allow for genetic-based diagnosis of Usher syndrome before a deaf individual begins to lose sight. Early diagnosis will permit the study of the complete progression of retinal degeneration and provide opportunities for possible treatment before the retinal degeneration begins. The harmonin protein can be used to identify other interacting proteins in the inner ear. Such information could greatly clarify the role of the molecular components that are involved in sound transduction and may clarify the bases for the sensory defects in Usher syndrome and other related genetic auditory disorders.

Mouse Deafness Gene Identified After a Half Century of Research

A great deal about deafness in humans has been learned from the earlier identification of mutations that cause hearing impairment or vestibular disorders in mice. For example, the jerker mouse was first described in 1941. It was deaf and had a distinctive abnormal gait and head movements. Now after 60 years, the gene mutation responsible for causing deafness and balance dysfunction in the jerker mouse has been identified by NIDCD-supported scientists.

Sensory hair cells within the auditory and vestibular systems transfer environmental cues to the nervous system. In this process, stereocilia (finger-like projections) at the surface of hair cells are involved as mechanoelectrical signal transducers to detect sound and motion. Stereocilia are attached to the hair cell by a core actin bundle that gives the stereocilia the necessary organization and rigidity to enable it to move precisely to create an electrical signal upon receiving environmental cues. A cross-linking protein, actin-bundling protein, is responsible for linking stereocilia in parallel rows to maintain crucial interactions with each other.

Scientists have determined that the jerker mouse carries a mutant gene for the actin-bundling protein, espin. Suspecting that disorganized stereocilia seen in the jerker mouse could be due to improper actin bundling, scientists looked for normal espin proteins in the jerker mouse and found none. Further investigation revealed a mutation in the espin gene of the jerker mouse. Finally, the investigators discovered that the espin gene mapped to chromosome 4, the same genetic position where the jerker locus had previously been mapped using classical mouse genetic techniques. This discovery opens the possibility for detailed analysis of the molecular defect of the well-studied jerker mouse. Such studies will provide insight into the basis for hearing loss in this mouse model as well as the precise hair cell interactions required for the successful mechanoelectrical transduction of sound.

An Animal Model for Pendred Syndrome

Pendrin, the gene responsible for causing Pendred syndrome, was recently identified by a scientist in the intramural research program of the National Human Genome Research Institute (NHGRI) at NIH. Individuals with this disorder have sensorineural deafness and goiter (enlargement of the thyroid gland). In a collaboration between NHGRI and NIDCD intramural scientists, genetic analysis has shown that mutations in *Pendrin* occur in deaf individuals without thyroid disease, indicating that the gene is responsible for a much broader spectrum of deafness than only those individuals with Pendred syndrome. To determine the cause of this disorder, the *Pendrin* gene was deleted in mice and analysis of this mouse model was conducted. The mutant mice were found to be deaf and have a variable spectrum of balance problems similar to symptoms of individuals with Pendred syndrome. The scientists observed swelling in parts of the developing inner ear in the mutant mouse embryos. The resulting fluid imbalance within the inner ear subsequently leads to the destruction of the sensory hair cells necessary for hearing. The association between loss of *Pendrin* function and abnormal fluid accumulation in the inner ear is expected since the pendrin protein is known to encode a chloride/iodine transporter. This mutant mouse model provides important clues about inner ear pathology associated with the human syndrome. It will serve as an invaluable tool for understanding the function of *Pendrin* and normal fluid homeostasis in the inner ear.

How Loud is Too Loud? Determining Vulnerability to Noise-Induced Hearing Loss

The search for a safe and reliable pre-exposure index of vulnerability to acoustic injury has been an important research challenge in studying noise-induced hearing loss (NIHL), due to the tremendous differences in pathology observed among individuals exposed to similar noise. By knowing who is at risk for NIHL, focused and effective preventive measures can be developed and targeted to those individuals. An NIDCD-supported scientist has recently developed a procedure in an animal model to screen for risk of NIHL. The procedure is simple and

nontraumatic, and involves measuring a neuronal feedback pathway to the inner ear. The feedback pathway is thought to protect the ear from acoustic injury, and individual differences in the feedback pathway appear to underlie the differences in vulnerability to NIHL. The application of this assay to humans is a logical and very exciting next step.

As a result of a workshop that focused on cutting-edge research in cell and molecular biology and genetics that impact the biology of NIHL, the NIDCD and the National Institute on Aging are cosponsoring an activity targeting research on NIHL, including a) cell injury, cell death, and cell survival, b) susceptibility to NIHL with a focus on environmental and genetic factors, and c) protection and rescue from NIHL from a biological/pharmacological perspective.

New Directional Hearing Aid Provides Better Speech Quality

NIDCD support of a Small Business Innovation Research (SBIR) grant has resulted in a new commercial hearing aid product. The Radiant Beam Array (RBA) was developed as a collaborative effort between the NIDCD, Cardinal Sound Labs, Inc., and Starkey Laboratories. The device is based upon the work originally developed at Stanford University with NIDCD support. The RBA uses six spatially separated microphones with directional signal processing. This technology maximally amplifies sounds that are directly in front of the listener and minimally amplifies sounds from the sides and rear, thus providing a substantial improvement in the signal-to-noise ratio for speech recognition by the user. This results in a greater ability to understand speech in the presence of noise and reverberation. The RBA is worn on the user's chest like a necklace and may be worn under clothing. Output from the RBA is transmitted via a wireless link to any hearing aid that has a telecoil or in conjunction with a Starkey telecoil module. The RBA is suitable for new and previous hearing aid users who have a wide range of moderate-to-profound hearing loss.

Normal Development of the Olfactory System is Dependent on Neuronal Activity

A blocked nasal cavity, damaged olfactory epithelium, or frontal head trauma may cause severe but reversible biochemical and structural changes in the olfactory bulb of the brain, resulting in changes in the ability to smell and perceive odors. A unique characteristic of the olfactory system is its ability to restore function following regeneration of the injured olfactory epithelium and/or nerves in the roof of the nose. Understanding the cellular and molecular mechanisms underlying such neuronal plasticity may contribute to knowledge about factors that regulate the recovery of function in other damaged areas of the central nervous system.

An NIDCD-supported study addresses whether odor-induced neuronal activity is important in establishing the projection patterns of individual olfactory receptor neurons and in restoring

normal olfactory function. In the olfactory system, a single odorant receptor is expressed in each olfactory receptor neuron. Ordinarily, the olfactory receptor neurons that express the same odorant receptor send converging nerve projections to the olfactory bulb. In order to test the hypothesis that such projections are activity-dependent, scientists developed a mouse model where neurons that express a single odorant receptor (P2) cannot be excited by odorant binding. These investigators found that in the olfactory receptor neurons that expressed the P2 odorant receptor, the projections to the olfactory bulb were altered. The normally precise, converging projections were replaced with a widely spread projection. These findings indicate that odorant-induced neural activity shaped and pruned the projections of olfactory receptor neurons, and the lack of such activity results in abnormal projections that presumably affects olfactory function.

Responses of Vomeronasal Neurons to Natural Stimuli

The sense of smell plays a crucial role in the detection and identification of volatile chemical stimuli in the environment and is one of the important means by which mammals communicate with their surroundings. The vomeronasal organ (VNO) of some mammals plays an essential role in the detection of pheromones, chemical cues secreted by animals that influence sexual, reproductive, and other social behaviors. A study conducted by NIDCD-supported scientists provides the first systemic analysis of the response of a large group of VNO neurons to pheromones. The results show that the characteristics of the VNO sensory response appear remarkably different from the odor detection and coding process of the main olfactory system. Pheromone-induced behaviors and endocrine changes clearly involve complex sensory recognition going beyond sex determination. The VNO is also involved in identification of the species, familial status, and even individual identity of animals. A better understanding of these functional characteristics will help determine what role, if any, the VNO plays in human behavior.

Molecular Biology of Taste Signal Transduction

The application of contemporary cellular, molecular, biochemical, anatomical, and electrophysiological methodologies, and the use of animal models have resulted in substantial advances in understanding the basic mechanism of taste. For example, a long history of NIDCD-supported research has shown that taste perception involves four basic taste qualities: sweet, sour, salty, and bitter. In a recent study, a fifth taste has been recognized and its taste receptor identified -- umami -- the taste of monosodium glutamate or the taste associated with protein-rich foods. From this finding, scientists have determined that each taste quality appears to be mediated by a distinct biochemical pathway. Salty (Na^{++} ions) and sour (acidic H^{+} ions) activate specialized voltage dependent/independent ion channels in the membrane of the taste receptor cells in the taste buds in the tongue. In contrast, umami-, sweet-, and bitter-tasting substances activate G-protein-coupled receptors, but until now, none of these receptors has been definitively

identified.

In a series of elegant molecular biological studies, scientists have characterized the diverse structure, function and expression of a large family of mammalian G-protein-coupled receptors, called T2Rs, which are selectively expressed in taste receptor cells of the tongue and palate. T2R receptors were shown to be involved in bitter taste perception in humans and mice. T2R receptors signal through the G-protein, gustducin, which was shown in earlier NIDCD-supported studies to be critical for the responses to bitter-tasting and possibly sweet-tasting compounds.

In other NIDCD-funded laboratories, scientists are exploring the variety of signal transduction mechanisms associated with bitter and sweet taste receptors. Their research suggests that different bitter and/or sweet receptors may activate distinct second messenger cascades, and that different bitter compounds (such as caffeine) may activate different signal transduction circuits, providing a basis for bitter coding. These various genetic and molecular biological studies have made significant contributions to the understanding of the structural and functional properties of taste receptors associated with bitter-taste quality perception. Similar approaches are being developed to explore the uniquely modified G-protein coupled, glutamate receptor that is implicated in umami perception.

Bitter Taste Is Not Created Equal

Contrary to the theory that bitter substances are perceived to taste the same, NIDCD-supported scientists have recently determined that taste cells are much better at distinguishing among bitter flavors than previously thought and that taste buds can recognize the many unique bitter flavors that land on the tongue. When a taste receptor is activated by a bitter compound or other stimulus, it triggers a rise in calcium concentrations inside the taste cell, which in turn causes the cell to release its neurotransmitter, sending the “bitter” signal to the brain. The scientists injected a fluorescent marker of calcium activity into taste cells taken from a rat's tongue. If the cells could distinguish between bitter flavors, some bitters would cause a rise in calcium, and an accompanying rise in fluorescence, while other cells would not. Five strongly bitter compounds that are commonly used as ingredients in medicines that taste bitter were tested on the marked taste cells. The scientists observed that 65% of the cells fluoresced strongly in response to just one of the bitter compounds. About 25% of the cells responded to two compounds, whereas just 7% reacted to three or more of the bitters. Cell responses to the different bitter substances also varied in amplitude, length, and sensitivity. This research demonstrates that taste perception involves multiple cells and molecular mechanisms and taste cells appear to be specific for different bitter compounds.

Brain Regions in Language Production

For many years, it was thought that brain activity associated with human language function was restricted to the classic language areas in the left side of the brain in a "language organ." More recent studies have shown that other regions in the brain also participate in language function. In order to identify the brain regions that play an essential role in the production of language, NIDCD scientists utilized neuroimaging technology to conduct a unique study on the spontaneous generation of narrative in English and American Sign Language (ASL) in hearing individuals who were native users of both languages. It was expected that different areas of the brain would function during spoken or signed language because ASL has organizational properties similar to spoken language but uses an entirely different mode of expression (gestural/visual versus vocal/auditory). However, similar areas of the brain were active during both spoken language and ASL, and these areas were widespread throughout the brain. The left side of the brain classically associated with oral speech was robustly activated during sign production and activation even extended to regions on the right side of the brain. Anterior and posterior regions of the brain may play distinct roles in early and late stages of language production. This study is a novel model for investigating lateralization of brain activity during language generation.

Language Impairment in Autism

Autism is diagnosed when a child develops abnormal or impaired social interaction, communication difficulties, and a severely restricted repertoire of activity and interests prior to his/her third birthday. One cardinal feature of autism is the delay or absence of spoken language. NIDCD-supported scientists have recently investigated language functioning in a group of 89 children between 4- and 14-years old, who were diagnosed with autism. This study was the first to investigate language profiles on a large sample of children with autism. The children were administered a series of standardized language tests measuring their ability to produce sounds for speech, say words, and put words together with appropriate grammar. The researchers found significant differences in language skills, although articulation skills (or how the sounds of the language are produced) remained normal in all the children. Different subgroups of children with autism were identified on the basis of their performance on the language measures. Some children with autism have normal language skills, while others have language skills significantly below their age expectations. The performance profile across the standardized measures for the language-impaired children with autism was similar to the profile of children with specific language impairment (SLI). These findings suggest that there may be overlapping or shared characteristics among families with SLI and autism. Future studies will need to investigate the neurocognitive mechanisms underlying language processing in children with SLI, autism and perhaps other disorders, in order to advance the understanding of language disorders in children.

Mapping a Gene for Severe Pediatric Gastroesophageal Reflux

Gastroesophageal reflux (GER) affects persons of all ages and is characterized by the back flow of stomach contents into the esophagus. The clinical spectrum of GER can be mild, which results in heartburn, to severe, which can result in death from choking on regurgitated food. Children with severe GER have an increased incidence of acute and chronic infections in the upper respiratory tract, which predisposes them to voice disorders. GER has not previously been considered to be a hereditary disease, although a few reports have suggested that a genetic component may contribute to the incidence of GER. To determine if a genetic basis exists, NIDCD-supported scientists conducted a genome-wide scan of families affected by severe pediatric GER. These studies revealed that severe pediatric GER followed an autosomal dominant pattern of inheritance. This finding eventually led to mapping a gene for GER to chromosome 13q14. Determining the genetic basis for GER is important for understanding the physiological processes that underlie severe pediatric GER. Efforts are currently underway to determine the gene's location on chromosome 13 with greater precision and then to identify the gene itself.

Innovation in Management and Administration

NIDCD program directors are using innovative ways to initiate research training and career development opportunities for individuals interested in research on human communication. There is a national need for additional minority scientists in fields of basic, clinical, and health services research. To address these needs, the NIDCD recently launched two programs that will encourage students, in particular minority individuals, to pursue careers in communication sciences and its disorders.

NIDCD Partnership Program Expands to National Level

In 1994, the NIDCD launched a pilot program, The Partnership Program, with the support of the NIH Office of Research on Minority Health. The program is designed to enhance opportunities for underrepresented minority individuals to participate in fundamental and clinical research in hearing, balance, smell, taste, voice, speech, and language. Four academic centers that serve students, faculty, and staff who are minority individuals underrepresented in biomedical and behavioral research currently participate in the pilot program: Morehouse School of Medicine/Atlanta University Complex, University of Puerto Rico School of Medicine/University of Puerto Rico, University of Alaska System, and Gallaudet University. Through this program, there is opportunity for exchange of personnel between the NIH and the academic centers. This program not only fosters activities for students, but provides career development for faculty, administrators, and NIDCD staff. The long term goal for the program is recruitment and retention of individuals from underrepresented groups to research careers in human communication.

To date, approximately 65 students and faculty members have participated in The Partnership Program. Each participant is paired with a mentor -- a senior researcher at NIH -- and works under the mentor's supervision in the research lab for a period of one month to two years. Another 14 faculty and staff members have come to NIDCD to learn about grants review, management, and administration through workshops as well as short-term placements in the grants offices.

Beginning in 2001, the program will invite applications from underrepresented minorities and persons with disabilities enrolled in undergraduate, graduate, or medical schools across the U.S., as well as minority faculty and grants administrators from universities. This will increase opportunities for individuals beyond the initial partner affiliates.

NIDCD Collaborates with University of Maryland Graduate Program

The Division of Intramural Research (DIR) of the NIDCD and the graduate program in Neuroscience and Cognitive Science (NACS) of the University of Maryland, College Park (UMD), have a shared interest in scientific progress as well as graduate education in the field of human communication. In providing mutual support of these interests, NIDCD research scientists will provide a program of research training and co-mentoring to doctoral (pre-Ph.D.) students at NIDCD's research facilities. NIDCD scientists will serve on thesis committees and attend examination and committee meetings of the students they are mentoring; join in efforts to establish collaborative research with NACS faculty; participate in graduate courses, seminars, and journal clubs at UMD; continue communication with NACS faculty who are involved with co-mentoring these students; and orient students wishing to rotate through NIDCD laboratories as well as to devise short-term training programs.

In turn, the UMD will provide the basic formal educational structure for students within its graduate program. All students need to meet the requirements for courses and degree programs as set up by NACS and UMD. In addition, the NACS staff will provide long-term commitments to the students for continued education as long as the students remain in good standing in the program, encourage graduate students to rotate through, and/or have short-term research opportunities in NIDCD laboratories, and provide adjunct faculty appointments for those NIDCD staff members working with NACS students who assist in teaching at UMD.

New Activities

Cochlear Implants Reveal Plasticity in the Adult Central Auditory System

One of the most significant advances in the field of auditory science in recent decades is the

development of the cochlear implant. Most adults and children with implants show a remarkable ability to understand speech, and cochlear implants are increasingly the primary choice for deaf children and their parents wanting education in a mainstream setting. While cochlear implants have improved the lives of thousands of people, very little is known of the effects of this device on the central auditory system. The improvements seen in children's speech performance after implantation offer strong evidence for the plasticity (adaptability) of the developing nervous system. However, recent studies have also shown that the adult brain has considerable plasticity and can even regenerate new neurons under certain circumstances. Knowing how the brain responds to auditory input from cochlear implants is necessary in understanding how the brain uses the information provided by these devices.

A growing number of neuroimaging laboratories are now conducting research to evaluate the flexible or plastic nature of various kinds of brain function, but few have specifically examined plasticity within the central auditory system. A collaboration among scientists from NIDCD, Johns Hopkins University, and Gallaudet University will examine changes within the auditory system of hearing-impaired individuals following cochlear implantation, as the brain changes over time to meet new demands of auditory and speech perception. Using positron emission tomography (PET) imaging technology, NIDCD scientists will follow the evolution of brain activation patterns from the time of initial activation of the cochlear implant and as the individual's spoken language performance improves over time. Two groups will be evaluated: those who became deaf later in life and acquired spoken language before the onset of deafness, and those who became deaf at a young age and acquired language skills without hearing spoken language. Previous research has shown that individuals who lose hearing early in life and are implanted as adults develop spoken language at a much slower rate than individuals who lose their hearing after normal language development. Differences in brain activity patterns associated with language may help to explain this phenomenon.

Developing a Gene Database for the Inner Ear

Knowing which genes are expressed in a cell is an important step in understanding the molecular processes involved in that cell's function. In the inner ear, the organ of Corti is responsible for detecting sound and transducing the sound into electrical energy which is then transmitted to the brain. The organ of Corti is comprised of a limited number of different cells: sensory cells or hair cells which are directly involved in sound detection and transduction, and supporting cells which play roles in the structural and metabolic support of hair cells. Knowing which genes are expressed by these cells would aid scientists in their study of normal hearing and in their understanding of both genetic and environmental causes of hearing loss.
NIDCD scientists are generating an expressed sequence tag (EST) database to identify genes expressed in the mouse organ of Corti. This is accomplished by first establishing a collection of DNA sequences (a cDNA library) from the organ of Corti and then sequencing thousands of individual clones present in that library. This effort will identify many of the genes expressed in

the organ of Corti. This information will be made available to all scientists in established public databases maintained by the National Library of Medicine. Coupled with NIH's effort to sequence the entire human and mouse genome, scientists will be able to more easily identify genes expressed in the organ of Corti, providing an important resource for the characterization of genes expressed in both the normal and disordered cochlea.

Cell Talk: Identifying Interacting Proteins in the Organ of Corti

In recent years, there have been a number of genes identified that are critical for the function of the inner ear. Most of these have been identified using a genetic approach, but a few have been identified using more traditional molecular biological and biochemical approaches. Unlike many other biological systems, the inner ear is small and inaccessible; furthermore, cells of the inner ear cannot be maintained in culture easily. Such limitations impede progress in the biochemical and cell biological characterization of genes associated with deafness as well as those involved in various inner ear functions.

NIDCD scientists are using yeast two-hybrid techniques to identify interacting proteins in the organ of Corti. Complementary DNA libraries, which express parts of most proteins present in the organ of Corti, are screened with a known protein to identify unknown interacting partner proteins. This process identifies both known and novel proteins, some of which may be found only in the inner ear. Identification of interacting proteins has two important applications. First, knowing which protein interacts with another particular protein is very useful in characterizing the function of each protein. Second, the interacting proteins are often novel or expressed only in a particular tissue, such as the organ of Corti. The yeast two-hybrid technique will be of great value in understanding the biochemical interactions critical for inner ear function.

Biological Mechanism of Noise-Induced Hearing Loss

Noise-induced hearing loss (NIHL) continues to be a major public health issue. Ten million Americans have already suffered irreversible damage from noise and 30 million more are exposed to dangerous noise levels each day.[2] The NIDCD will initiate research to address the biological consequence of noise as a primary cause of hearing loss. Identifying mechanisms of cellular injury and survival, understanding genetic factors influencing susceptibility, and identifying pharmacologic approaches for protection and rescue from NIHL are goals of this research.

Sensory Motor Functions Response to Gravity

The NIDCD is collaborating with the National Aeronautics and Space Administration (NASA) to

stimulate research utilizing specific, well-characterized transgenic and mutant animal models to elucidate molecular bases for the normal development and function of sensory-motor mechanisms that detect and respond to gravity. These functions are essential for control of balance and posture, locomotion, other volitional movements and spatial orientation. Using animal models to study sensory function in response to gravity will promote new research on the underlying mechanisms responsible for vestibular disorders.

The Need for Innovative Rehabilitation Interventions

Millions of Americans suffer disabling injuries or diseases each year. In addition, dysfunction can result from age-related changes to the systems of the body. Innovative rehabilitation strategies are lacking for these individuals. The NIDCD is collaborating with the National Institute of Child Health and Human Development and the National Institute on Aging to apply advances in bioengineering, cognitive science, and other neurosciences to the clinical environment by encouraging the development of new techniques and therapies for rehabilitation treatments. Specifically, the NIDCD is planning to support research on the development and improvement of devices, pharmacologic agents, and strategies for habilitation and rehabilitation of individuals with communication disorders resulting from physical and/or cognitive dysfunction. This research could lead to interventions that utilize assistive technology to develop advanced, highly specific sensory and communicative aids for individuals with hearing impairment; interventions that use speech/language therapy and other behavioral techniques for individuals recovering from stroke or traumatic brain injury; and additional interventions that utilize physiotherapy for individuals with balance and mobility dysfunction.

High Impact Research: Feasibility Studies

High impact research involves pilot or feasibility studies in which the technological, methodological, or theoretical approach to a problem lacks a historical precedent or sufficient preliminary or baseline data, but whose successful outcome would have a major impact on a scientific area or field. The NIDCD is planning high impact research activities that have the potential for breakthrough or major contribution in the basic and clinical biomedical sciences of human communication. This activity will promote pilot testing of novel scientific experimental hypotheses, develop new or novel techniques or technologies, and acquire a body of data that is potentially high impact for the scientific enterprise.

Developing Bioengineering Research Partnerships

Bioengineering integrates physical, chemical, or mathematical sciences and engineering principles for the study of biology, medicine, behavior, or health. It advances fundamental

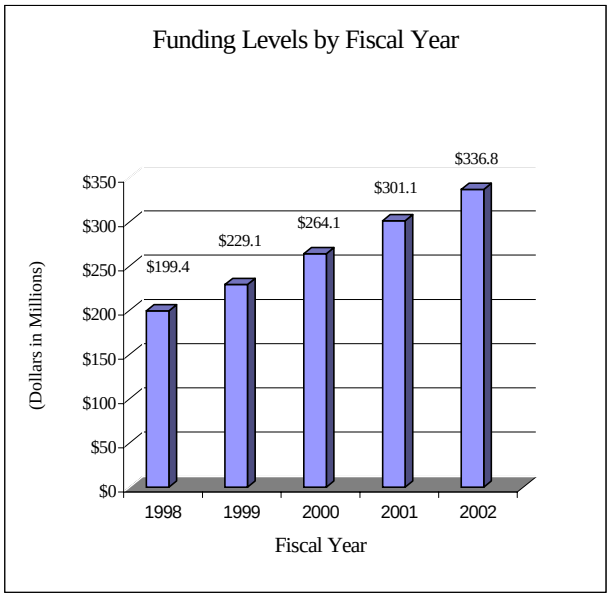
concepts, creates knowledge from the molecular to the organ systems level. Bioengineering fosters the development of innovative materials, processes, implants, devices, and informatics approaches for the prevention, diagnosis, and treatment of disease, for patient rehabilitation, and for improving health. The NIDCD is collaborating with other institutes and centers at NIH on this research activity that incorporates interdisciplinary partnerships to address important biological or medical research problems.

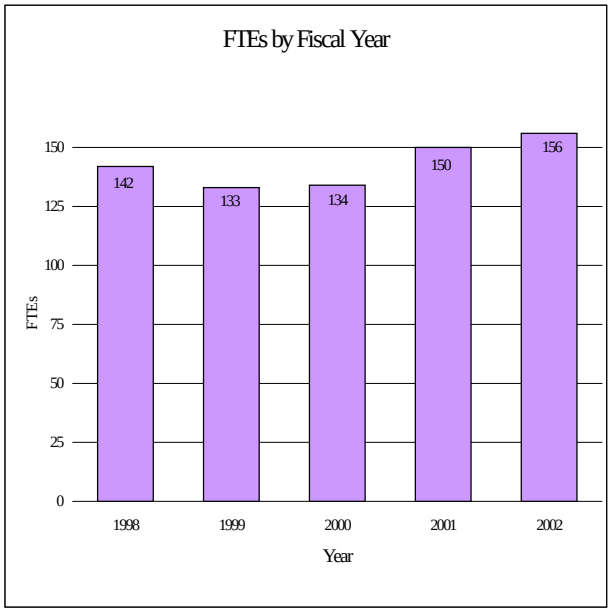
Research Core Centers

The NIDCD has recently begun the Research Core Center Program as a means of promoting cooperative interaction among basic and/or clinical investigators in a manner that will enrich the effectiveness of ongoing research and promote new research directions. The aim of the Core Center is to stimulate multidisciplinary approaches already established in NIH-funded laboratories to solve complex research challenges. NIDCD recognizes the value of the core services as an intellectual hub where cooperative and interactive research will be supported and stimulated.

Budget Policy

The Fiscal Year 2002 budget request for the NIDCD is $336,757,000, including AIDS, an increase of $35,631,000 and 11.8 percent over the FY 2001 level, and $72,693,000 and 27.5 percent over FY 2000. A five year history of FTEs and Funding Levels for NIDCD are shown in the graphs below:





One of NIH's highest priorities 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. The Fiscal Year 2002 request provides average cost increases for competing RPGs equal to the Biomedical Research and Development Price Index (BRDPI), estimated at 4.3 percent. Noncompeting RPGs will receive increases of 3 percent on average for recurring direct costs. In FY 2002, total RPGs funded will be 852 awards, an increase of 64 awards over the FY 2001 Estimate, the highest annual total ever awarded.

Promises for advancement in medical research are dependent on a continuing supply of new investigators with new ideas. In the Fiscal Year 2002 request, NIDCD will support 260 pre- and postdoctoral trainees in full-time training positions. An increase of 10 percent over Fiscal Year 2001 levels is provided for stipends and training-related expenses (e.g., health insurance, research supplies and equipment, and travel to scientific meetings).

The Fiscal Year 2002 request includes funding for 26 research centers, 59 other research grants, including 25 new clinical career awards, and 26 R&D contracts. The R&D contracts mechanism also includes support for 5 contracts for the Extramural Clinical and Pediatric Loan Repayment Programs.

Research Management and Support

Two public health campaigns will move ahead more effectively with adequate RMS funds. The first campaign would increase public awareness and reduce the incidence of preventable forms of hearing loss. Many Americans lack information about the risk of dangerously high levels of noise in home and recreational environments. Hearing loss associated with these environmental causes is clearly preventable, and a public health message from the NIDCD and other partners to increase awareness of exposure to high decibel noises needs to be conveyed.

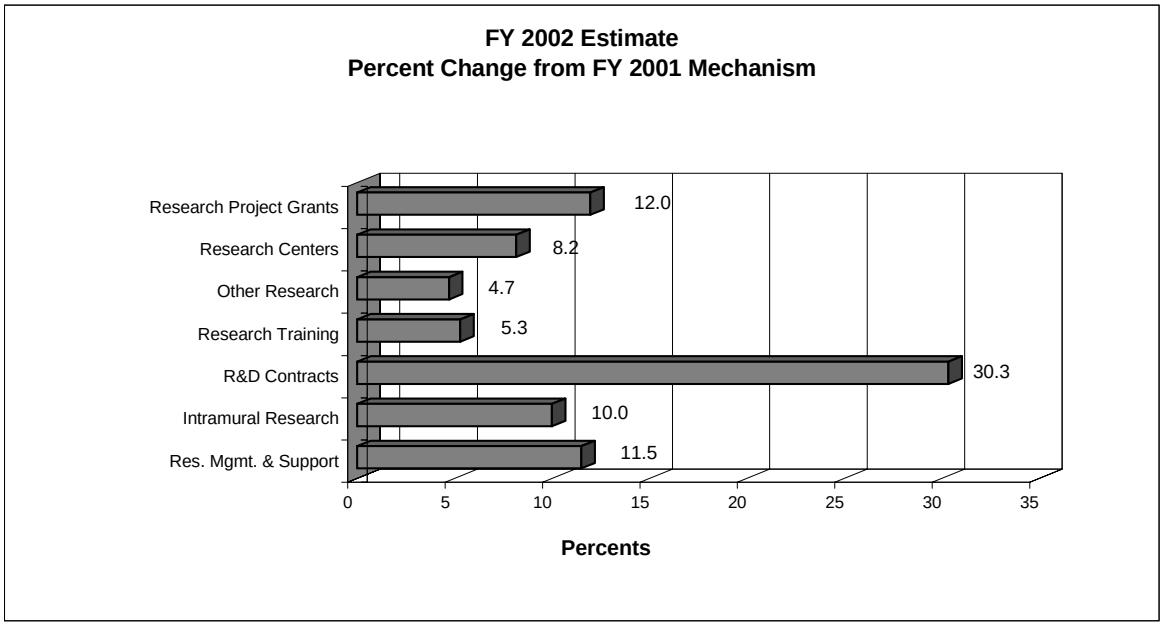
The second health education campaign that NIDCD would develop and implement would be to collaborate with other agencies to educate parents and health care providers about the importance of hearing screening for newborns to detect deafness or hearing impairment. As many as 33 children per day are born with hearing impairment which without appropriate and timely identification and intervention, interferes with the development of communication, impeding academic performance. This campaign would encourage parents and caregivers to "Test your Baby at Birth" followed by a "Commitment to Communication for Life" to ensure the best lifelong outcomes for these children. The increased awareness of the importance of early hearing screening and intervention would result in a greater likelihood that a child who was deaf

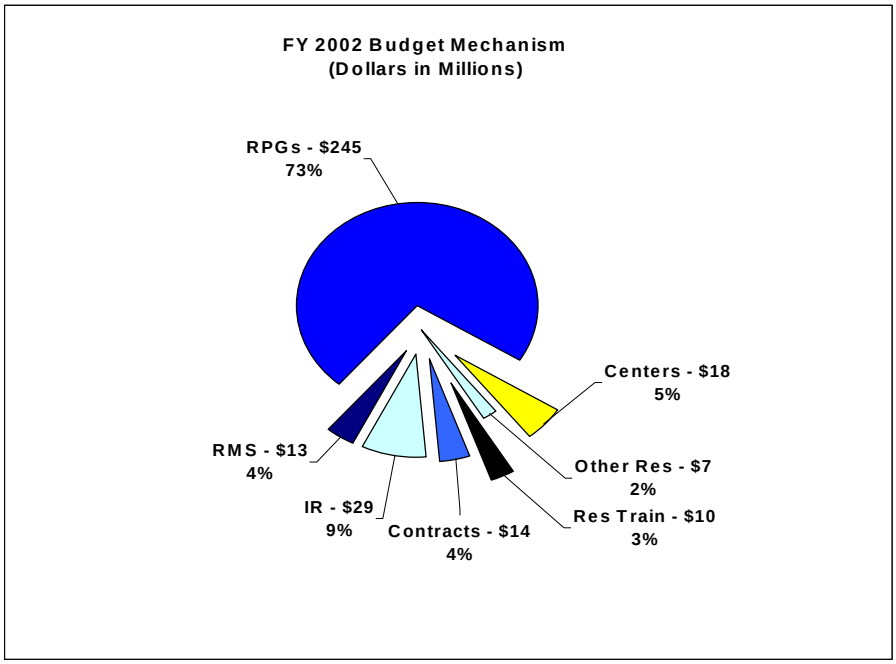
or who had a hearing impairment would enjoy academic, social, and vocational success.

The NIDCD has launched a number of new grant and contract collaborative activities in recent years with special emphasis on human and mouse genetics. Other activities will be started in the next few years as well. Additional Health Science Administrators will be required to effectively administer and monitor them. A new activity to fund training for pre-doctoral scientists is also a focus we have for FY2002. There will also be a need for additional staff to perform accelerated review of individual training grants.

It will be necessary for the NIDCD to upgrade and further develop certain IT programs. Enhancements will be made to our web services, both the public site and the Intranet. Extensive work will be done on these services to meet the Electronic and Information Technology Accessibility Standards. Upgrading and developing IT programs will enhance and streamline operations and will empower employees to work more effectively and promote efficiency in all entities of job performance.

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




FY 2002 Budget Mechanism
(Dollars in Millions)
RPGs - $245
73%
Centers - $18
5%
Other Res - $7
2%
Res Train - $10
3%
Contracts - $14
4%
IR - $29
9%
RMS - $13
4%

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Budget Mechanism

MECHANISM	FY 2000 Actual		FY 2001 Estimate		FY 2002 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	507	$128,102,000	551	$154,831,000	596	$172,450,000
Administrative supplements	(80)	2,817,000	(30)	1,100,000	(30)	1,100,000
Competing:						
Renewal	64	23,561,000	67	24,708,000	73	28,124,000
New	134	29,431,000	138	31,427,000	151	35,771,000
Supplements	0	0	0	0	0	0
Subtotal, competing	198	52,992,000	205	56,135,000	224	63,895,000
Subtotal, RPGs	705	183,911,000	756	212,066,000	820	237,445,000
SBIR/STTR	34	6,103,000	32	6,890,000	32	7,728,000
Subtotal, RPGs	739	190,014,000	788	218,956,000	852	245,173,000
Research Centers:						
Specialized/comprehensive	17	16,446,000	18	16,900,000	26	18,281,000
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 Institution	0	0	0	0	0	0
Subtotal, Centers	17	16,446,000	18	16,900,000	26	18,281,000
Other Research:						
Research careers	44	4,378,000	47	4,843,000	43	5,110,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	0	45,000	0	0	0	0
Biomedical research support	0	0	0	0	0	0
Minority biomedical research support	0	0	0	0	0	0
Other	13	1,189,000	15	1,766,000	16	1,811,000
Subtotal, Other Research	57	5,612,000	62	6,609,000	59	6,921,000
Total Research Grants	813	212,072,000	868	242,465,000	937	270,375,000
Training:	FTTPs		FTTPs		FTTPs	
Individual awards	65	2,115,000	78	2,826,000	115	3,766,000
Institutional awards	208	6,078,000	197	7,032,000	145	6,614,000
Total, Training	273	8,193,000	275	9,858,000	260	10,380,000
Research & development contracts	22	10,730,000	23	10,526,000	31	13,720,000
(SBIR/STTR)	(0)	(0)	(0)	(0)	(0)	(0)
	FTEs		FTEs		FTEs	
Intramural research	59	22,779,000	69	26,470,000	73	29,117,000
Research management and support	75	10,290,000	81	11,807,000	83	13,165,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, NIDCD	134	264,064,000	150	301,126,000	156	336,757,000
(Clinical Trials)		(4,340,000)		(4,804,000)		(5,409,000)

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2000 Actual		FY 2001 Estimate		FY 2002 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural Research:								
Deafness and Other Communication Disorders		$231,233		$262,849		$294,475		$31,626
Subtotal, Extramural research		231,233		262,849		294,475		31,626
Intramural research	59	22,771	69	26,470	73	29,117	4	2,647
Research management and support	75	10,060	81	11,807	83	13,165	2	1,358
Total	134	264,064	150	301,126	156	336,757	6	35,631

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Summary of Changes

2001 Estimated budget authority				$301,126,000
2002 Estimated budget authority				336,757,000
Net change				35,631,000
	2001 Current Estimate Base		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$7,462,000		$96,000
b. Annualization of January 2001 pay increase		7,462,000		71,000
c. January 2002 pay increase		7,462,000		207,000
d. Extra day of pay		7,462,000		29,000
e. Payment for centrally furnished services		4,694,000		469,000
f. Increased cost of laboratory supplies, materials, and other expenses		14,314,000		408,000
Subtotal				1,280,000
2. Research Management and Support:				
a. Within grade increase		6,727,000		116,000
b. Annualization of January 2001 pay increase		6,727,000		65,000
c. January 2002 pay increase		6,727,000		190,000
d. Extra day of pay		6,727,000		27,000
e. Payment for centrally furnished services		1,234,000		123,000
f. Increased cost of laboratory supplies, materials, and other expenses		3,846,000		165,000
Subtotal				686,000
Subtotal, Built-in				1,966,000

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Summary of Changes--continued

CHANGES	2001 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	551	155,931,000	45	17,619,000
b. Competing	205	56,135,000	19	7,760,000
c. SBIR/STTR	32	6,890,000	0	838,000
Total	788	218,956,000	64	26,217,000
2. Centers	18	16,900,000	8	1,381,000
3. Other research	62	6,609,000	(3)	312,000
4. Research training	275	9,858,000	(15)	522,000
5. Research and development contracts	23	10,526,000	8	3,194,000
Subtotal, extramural				31,626,000
	FTEs		FTEs	
6. Intramural research	69	26,470,000	4	1,367,000
7. Research management and support	81	11,807,000	2	672,000
Subtotal, program		301,126,000	2	33,665,000
Total changes	150		2	35,631,000

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders
Budget Authority by Object

	FY 2001 Estimate	FY 2002 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	150	156	6
Full-time equivalent of overtime and holiday hours	0	0	0
Average ES salary	$130,259	$134,949	$4,690
Average GM/GS grade	10.5	10.5	0.0
Average GM/GS salary	$58,316	$60,416	$2,100
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)	$99,274	$102,848	$3,574
Average salary of ungraded positions	$52,797	$54,698	$1,901

	OBJECT CLASSES	FY 2001 Estimate	FY 2002 Estimate	Increase or Decrease
	Personnel Compensation:			
11.1	Full-Time Permanent	$7,092,000	$7,747,000	$655,000
11.3	Other than Full-Time Permanent	2,721,000	2,939,000	218,000
11.5	Other Personnel Compensation	354,000	382,000	28,000
11.8	Special Personnel Services Payments	1,608,000	1,754,000	146,000
11.9	**Total Personnel Compensation**	**11,775,000**	**12,822,000**	**1,047,000**
12.0	Personnel Benefits	2,412,000	2,622,000	210,000
13.0	Benefits for Former Personnel	2,000	2,000	0
	Subtotal, Pay Costs	**14,189,000**	**15,446,000**	**1,257,000**
21.0	Travel & Transportation of Persons	409,000	457,000	48,000
22.0	Transportation of Things	33,000	37,000	4,000
23.1	Rental Payments to GSA	0	0	0
23.2	Rental Payments to Others	625,000	650,000	25,000
23.3	Communications, Utilities & Miscellaneous Charges	530,000	578,000	48,000
24.0	Printing & Reproduction	173,000	189,000	16,000
25.1	Consulting Services	46,000	49,000	3,000
25.2	Other Services	1,627,000	1,801,000	174,000
25.3	Purchase of Goods & Services from Government Accounts	16,424,000	21,636,000	5,212,000
25.4	Operation & Maintenance of Facilities	1,412,000	1,562,000	150,000
25.5	Research & Development Contracts	6,886,000	6,424,000	(462,000)
25.6	Medical Care	394,000	429,000	35,000
25.7	Operation & Maintenance of Equipment	1,025,000	1,171,000	146,000
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**27,814,000**	**33,072,000**	**5,258,000**
26.0	Supplies & Materials	2,721,000	3,023,000	302,000
31.0	Equipment	2,309,000	2,550,000	241,000
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	252,323,000	280,755,000	28,432,000
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	**286,937,000**	**321,311,000**	**34,374,000**
	Total Budget Authority by Object	**301,126,000**	**336,757,000**	**35,631,000**

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Salaries and Expenses

OBJECT CLASSES	FY 2001 Estimate	FY 2002 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$7,092,000	$7,747,000	$655,000
Other Than Full-Time Permanent (11.3)	$2,721,000	$2,939,000	218,000
Other Personnel Compensation (11.5)	$354,000	$382,000	28,000
Special Personnel Services Payments (11.8)	$1,608,000	$1,754,000	146,000
Total Personnel Compensation (11.9)	**11,775,000**	**12,822,000**	**1,047,000**
Civilian Personnel Benefits (12.0)	$2,412,000	$2,622,000	210,000
Benefits to Former Personnel (13.0)	$2,000	$2,000	0
Subtotal, Pay Costs	**14,189,000**	**15,446,000**	**1,257,000**
Travel (21.0)	$409,000	$457,000	48,000
Transportation of Things (22.0)	$33,000	$37,000	4,000
Rental Payments to Others (23.2)	$625,000	$650,000	25,000
Communications, Utilities and Miscellaneous Charges (23.3)	$530,000	$578,000	48,000
Printing and Reproduction (24.0)	$173,000	$189,000	16,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	$46,000	$49,000	3,000
Other Services (25.2)	$1,627,000	$1,801,000	174,000
Purchases from Govt. Accounts (25.3)	$11,851,000	$12,767,000	916,000
Operation & Maintenance of Facilities (25.4)	$1,412,000	$1,562,000	150,000
Operation & Maintenance of Equipment (25.7)	$1,025,000	$1,171,000	146,000
Subsistence & Support of Persons (25.8)	$0	$0	0
Subtotal Other Contractual Services	**15,961,000**	**17,350,000**	**1,389,000**
Supplies and Materials (26.0)	$2,721,000	$3,023,000	302,000
Subtotal, Non-Pay Costs	20,452,000	22,284,000	1,832,000
Total, Administrative Costs	**34,641,000**	**37,730,000**	**3,089,000**

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

SIGNIFICANT ITEMS IN HOUSE, SENATE AND CONFERENCE APPROPRIATIONS COMMITTEE REPORTS

FY 2001 House Appropriations Committee Report Language (H. Rpt. 106-645)

Item

Dysphonia **-** The Committee continues to be pleased with NIDCD's intramural research with respect to dysphonia and encourages NIDCD to enhance its extramural research efforts. (p. 89)

Action taken or to be taken

The NIDCD Extramural Research Program in Voice currently supports projects that focus on spasmodic dysphonia, which may be a form of dystonia. NIDCD-supported projects are providing physiological and neurological insights into the etiology of spasmodic dysphonia and methods for assessment and treatment. Examples include projects that examine methods for quantifying the irregular vocal fold oscillations in spasmodic dysphonia for the objective assessment of vocal hyperfunction as well as the perceptual qualities of the impaired voice.

Item

Hearing Screening Research **-** The Committee urges NIDCD to enhance research on the efficacy of new screening techniques through all available mechanisms, as appropriate, including clinical studies on screening methodologies and studies on the efficacy of intervention and follow-up and related research. (p. 89)

Action taken or to be taken

Scientists supported by the NIDCD have examined the importance of age at enrollment in intervention programs and subsequent language outcomes for a group of deaf and hard-of-hearing children. Significantly better language scores were associated with early enrollment. Children enrolled before 11 months of age had stronger vocabulary and verbal reasoning skills at 5 years-of-age than did children enrolled at a later time. In addition, the NIDCD has supported a five-year multi-center study on neonatal hearing impairment, which suggested that all three methodologies worked well.

NIDCD is supporting research studies for the development of improved techniques for fitting hearing aids to infants and young children. These studies will enhance understanding of auditory learning and acclimatization in relation to the hearing and fitting process. A long-term objective is the investigation of spoken language skills in children with hearing loss who have received early, accurate audiologic assessment and appropriate fitting of amplification. In addition, NIDCD is supporting research studies on language abilities of prelingually deafened children who have received cochlear implants.

An example of NIDCD's continued collaboration with the hearing screening research scientific community is the Third Workshop of the NIDCD Working Group on Early Identification of Hearing Impairment, which was held in September, 2000. The purpose of the workshop was to identify critical research needs in the area of early identification of hearing impairment, and to delineate research priorities. Attendees included representatives from the Centers for Disease Control and Prevention (CDC), the Albert Einstein College of Medicine, as well as other members of the scientific community.

Item

Neurofibromatosis [NF] **-** The Committee encourages NIDCD to enhance its NF research and to coordinate its efforts with other Institutes conducting NF research. (p. 89)

Action taken or to be taken
The NIDCD continues to support studies to determine whether specific mutations in the NF2 gene result in different levels of disease severity. In addition, NIDCD continues to support the development of several new technologies to enhance the successful treatment of NF2 patients, such as development of a Doppler ultrasound cochlear blood flow monitor that will provide benefits in intra-operative monitoring during acoustic neuromasurgery, and as a diagnostic aid for sudden deafness. The NIDCD is also supporting the development of specialized auditory prosthesis for NF2 patients which stimulates the auditory brain stem directly. This device has recently received FDA approval.

Item

Research Collaborations **-** The Committee is aware of the collaborative efforts NIDCD has with the National Space Biomedical Research Institute and encourages the Institute to continue such collaborations. (p. 89)

Action taken or to be taken
The NIDCD continues to participate in a collaborative effort involving transfer of funds from the Division of Life and Biomedical Sciences and Applications Division, NASA. NIDCD support continues for a project on the integration of multi disciplinary sensory data with the major aim of developing a comprehensive model of the olfactory pathway as a paradigm for the basic steps in

sensory processing.

Item

Translating Research to Practice - NIDCD is encouraged to enhance efforts to translate basic science into better human health through all available mechanisms, as appropriate, including patient-oriented clinical research trials. (p. 89)

Action taken or to be taken

NIDCD continues to pursue the challenge of understanding normal and disordered processes of human communication by sponsoring patient-oriented clinical research trials. Clinical trials, as well as other clinical studies, are scientific studies that help doctors find ways to improve health and health care. Many of today's treatments for illness are based on the results of past clinical trials. NIDCD currently has 10 protocols that include 9 with active accrual of new subjects, and 1 follow-up of previously enrolled subjects. Currently ongoing clinical research trial topics include immunotherapy of advanced squamous cell carcinoma of the head and neck, efficacy of methotrexate in the treatment of autoimmune inner ear disease, identification of hereditary auditory processing deficits, stuttering, speech motor control and language processing, the efficacy of chin tuck vs. thickened liquid administration in the prevention of asperation pneumonia, and the safety and immunogenicity of a nontypeable haemophilus influenzae vaccine for otitis media. In addition, NIDCD recently announced two activities: The Clinical Trial Planning Grant, and Investigator-Initiated Clinical Trials, to encourage the conduct of clinical trials related to disorders of hearing, balance, smell, taste, voice, speech and language.

FY 2001 Senate Appropriations Committee Report Language (S. Rpt. 106-293)

Item

Clinical research - The Committee urges NIDCD to pursue the NIH goal and increase its efforts to fund patient-oriented clinical research conducted by physician-scientists. (p. 157)

Action taken or to be taken

Please refer to pages 2 and 3 of this document for NIDCD’s response to this significant item regarding patient-oriented clinical research conducted by physician-scientists.

Item

Dysphonia - The Committee encourages NIDCD to explore possibilities for a more active extramural research effort on dysphonia. (p. 157)

Action taken or to be taken

Please refer to page 1 of this document for NIDCD's response to this significant item regarding dysphonia.

Item

Neurofibromatosis **-** The Committee urges the Institute to consider the progress being made in research into the causes and prevention of neurofibromatosis, and to determine whether such progress offers new research opportunities consistent with the Institute's mission. (p. 157)

Action taken or to be taken

Please refer to page 2 of this document for NIDCD's response to this significant item regarding neurofibromatosis.

Item

Noise-Induced Hearing Loss **-** The Wise Ears campaign has the potential to make significant inroads towards educating Americans of all ages. The Committee has included sufficient funds to expand this promising new activity. (p. 157)

Action taken or to be taken

Ten million Americans have suffered irreversible damage from noise, and thirty million are exposed to dangerous levels of noise each day. WISE EARS! is the national health promotion and education campaign designed to increase awareness in the American public and workers that noise induced hearing loss (NIHL) is preventable and to motivate audiences to take action against NIHL by becoming knowledgeable about the problem and solutions. The NIDCD has led, in collaboration with NIOSH, the development of an 80-organization coalition consisting of national organizations, regional and local organizations, voluntary groups, unions and industry groups, and state and local government agencies. This prevention campaign has made considerable inroads in information dissemination by using several different approaches to expand outreach efforts to the public. The NIDCD has also begun addressing support for research into the causes of acquired deafness and the effects of noise on hearing.

At the national level, a WISE EARS! objective, reducing noise-induced hearing loss among children, adults, and workers, was included as part of the Healthy People 2010 initiative, the nationwide health promotion and disease prevention agenda of the Department of Health and Human Services. The WISE EARS! coalition has been significantly strengthened by the addition of more than 20 new organizations, including such prominent groups as the Girl Scouts of America, National 4-H program, American Association of Occupational Health Nurses, Inc.,

Howard Leight Industries, Hearing Education and Awareness for Rockers, American Association of Retired Persons (AARP), Hearing Aid Music Foundation-Listen Smart, and Florida Atlantic University, all of whom have extensive outreach capability.

The Institute has redoubled efforts to specifically reach diverse audiences by increasing its presence at national conferences such as the National Hispanic Medical Conference, Health Disparities Conference, and the National Urban League; engaging audiences at the local level, for example, with presentations to community leaders at the Great Brook Valley Health Center and high school students in the trades in Worcester, Massachusetts; partnering with the Indian Health Service, as a new coalition member, to reach American Indian populations; and, targeting dissemination to ensure the provision of health information to Latino/Latina communities, elementary and secondary schools, industrial and construction workers as well as trade organizations, farmers and other occupations in rural areas, and vocational and technical high schools. A Parents Page and Kids and Teachers Page, utilizing interactive technology, were launched at the NIDCD web site to increase awareness of the importance of hearing conservation and the problem of noise-induced hearing loss, introduce and reinforce scientific understanding of hearing and the science of sound, and provide opportunities for individuals to influence the awareness and understanding of others.

The NIDCD will be conducting an evaluation on WISE EARS! elements for three particular audiences including industrial workers, Hispanic/Latino/Latina individuals, and American Indian Youth under 17 years old. As part of that evaluation, focus group message testing will be done to ensure the campaign is effectively increasing the understanding and knowledge of NIHL within those populations.

To address the need for research into the biological mechanisms of noise-induced hearing loss, the NIDCD released a Request for Applications (RFA) in May, 2000 on Biological Mechanisms of Noise-Induced Hearing Loss. The goals of this research include identifying mechanisms of cellular injury and survival, understanding genetic factors influencing susceptibility, and identifying pharmacologic approaches for protection and rescue from NIHL. It is anticipated that grants will be awarded in 2001.

FY 2001 Conference Appropriations Committee Report Language (S. Rpt. 106-1033)

Item

Hearing Research **-** The conferees urge NIDCD to continue research on inner ear hair cell regeneration with special emphasis on gene delivery and gene transfer technology with specific relevance to the inner ear and the development of improved hearing aids and cochlear implants using digital processes. The conferees also urge NIDCD to continue to recruit experts from the field of molecular and cellular biology and genetics. (p. 139)

Action taken or to be taken

The NIDCD places high priority on research involving the development and regeneration of auditory sensory cells (hair cells) of the inner ear. The loss of auditory hair cells in humans leads to deafness and hearing impairment. The NIDCD is expanding research in this area by capitalizing on the finding that Notch-mediated lateral inhibition, a molecular mechanism involved in determining cell fate in the mammalian nervous system, regulates the number of progenitor cells that develop as hair cells. In addition, the importance of *Math1*, a mouse gene

that directs precursor cells in the inner ear to become hair cells, has been determined and warrants further research.

Gene therapy targeting the inner ear is being pursued vigorously by a number of NIDCD-supported laboratories. Scientists are testing potential viral vectors, including adenovirus, adeno-associated virus, lentivirus, vaccinia virus, and herpes simplex virus, for their efficiency in transferring therapeutic genes into specific organelles of the inner ear. Significant progress has been made in identifying such vectors as well as those systems capable of accurate and efficient delivery without imparting toxic effects on delicate inner ear structures. Progress has also been made in testing a range of specific proteins (made by transferred genes) for their effects on blocking or reversing inner ear pathology. Gene products under investigation include fibroblast growth factor, brain-derived neurotrophic factors, ion channels, and immune factors such as the interleukin-1 receptor antagonist. In addition, pump or injection systems to deliver therapeutic transgenes are being tested using various inner ear entry procedures such as cochleostomy or perfusion through the round window membrane.

Technical innovation is resulting in the development of improved hearing aids and cochlear implants. NIDCD extramural researchers are developing a wireless communication system which will transmit speech in both audio and text format; as well as developing a novel method to reduce noise and reverberation that could be incorporated into a modern digital hearing aid. Signal processing algorithms and non-line-of-signal digital infrared technology are the applications used in these studies. Cochlear implants have been shown to improve spoken language acquisition in deaf children. Research to develop new electrode systems for cochlear implants is underway.

In order to enhance the recruitment of scientists to Institute programs who are well versed in genetics, and in molecular and cellular biology, NIDCD has made significant enhancements to its research training and career development programs. A new pre-doctoral fellowship program and an enhanced postdoctoral fellowship utilizing an expedited review process forms the foundation for attracting new expertise to these sensory neuroscience areas.

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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.

[2]NIH Consensus Development Conference: Consensus Statement - Noise and Hearing Loss, Vol. 8, No. 1, January 1990.

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2000 Amount Authorized	2001 Estimate	2002 Amount Authorized	2002 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$291,268,000	Indefinite	$326,377,000
National Institute on Deafness and Other Communication Disorders	Section 464	42§285	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	9,858,000	b/	10,380,000
Total, Budget Authority				301,126,000		336,757,000

a/ Funding provided under the Departments of Labor, Health and Human Services, Education, and Related Agencies Appropriations Act, 2001 (P.L. 106-554).

b/ Reauthorizing legislation will be submitted.

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Appropriation History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1993	$157,301,000	$153,466,000	$157,301,000	$154,814,000 2/
1994	153,088,000	162,823,000	162,813,000	162,823,000
1995 3/	167,129,000	166,155,000	167,129,000	166,761,000 4/
Rescission				(101,000)
1996	172,399,000 3/	174,852,000	170,540,000 3/	174,852,000
Rescission				(119,000)
1997	179,090,000 3/	189,243,000	182,693,000	188,422,000 5/
1998	192,477,000 3/	198,373,000	198,583,000	198,857,000
1999	213,184,000 3/6/	216,995,000	229,887,000	229,887,000
Rescission				(152,000)
2000	235,297,000 3/	251,218,000	261,962,000	265,185,000
Rescission				(1,414,000)
2001	276,418,000	301,787,000	303,541,000	300,581,000
Rescission				(100,000)
2002	336,757,000			

1/ Reflects enacted supplements, recissions, and reappropriations.
2/ Excludes the enacted administrative reduction of $1,528,000.
3/ Excludes funds for HIV/AIDS Research Activities consolidation in the NIH Office of AIDS Research.
4/ Excludes enacted administrative reductions of $125,000.
5/ Excludes enacted administrative reductions of $77,000.
6/ Reflects a decrease of $650,000 for the budget amendment for bioterrorism.

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate
Office of the Director	8	8	8
Office of Administration	40	40	40
Division of Intramural Research	59	69	73
Division of Extramural Research	27	33	35
Total, NIDCD	134	150	156
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
1998	10.5
1999	10.5
2000	10.5
2001	10.5
2002	10.5

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

Detail of Positions

GRADE	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate
ES-6	0	0	0
ES-5	0	0	0
ES-4	1	1	1
ES-3	0	0	0
ES-2	1	1	1
ES-1	0	0	0
Subtotal	2	2	2
Total - ES Salary	$251,464	$260,517	$269,869
GM/GS-15	12	12	12
GM/GS-14	14	15	16
GM/GS-13	13	14	14
GS-12	15	16	17
GS-11	10	11	11
GS-10	2	2	2
GS-9	13	14	15
GS-8	12	12	13
GS-7	9	11	10
GS-6	0	1	2
GS-5	4	6	6
GS-4	4	4	4
GS-3	1	1	1
GS-2	2	2	2
GS-1	1	1	1
Subtotal	112	122	126
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
Co-Step	0	0	0
Subtotal	1	1	1
Ungraded	45	52	53
Total permanent positions	101	111	115
Total positions, end of year	160	176	182
Total full-time equivalent (FTE) employment,end of year	134	150	156
Average ES level	ES-3	ES-3	ES-3
Average ES salary	$125,732	$130,259	$134,949
Average GM/GS grade	10.5	10.5	10.5
Average GM/GS salary	$56,289	$58,316	$60,416