DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

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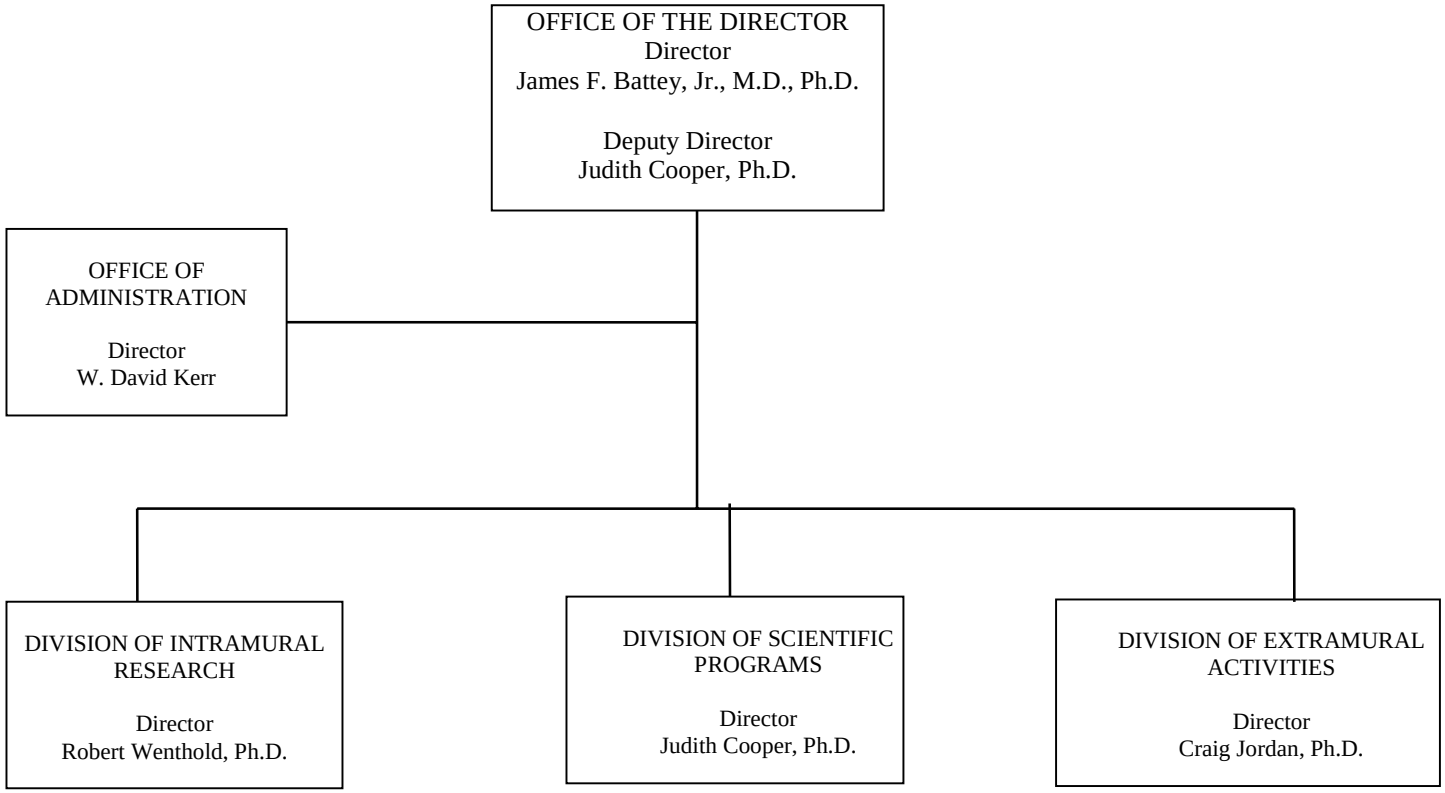

NATIONAL INSTITUTES OF HEALTH

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, [$397,507,000] *$397,432,000* .

[Department of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Consolidated Appropriations Act for Fiscal Year 2005]

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

Amounts Available for Obligation 1/

Source of Funding	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Appropriation	$384,477,000	$397,507,000	$397,432,000
Enacted Rescissions	(2,424,000)	(3,247,000)	0
Subtotal, Adjusted Appropriation	382,053,000	394,260,000	397,432,000
Real transfer under NIH Director's one-percent transfer authority to other ICs	(1,257,000)	0	0
Comparative transfer to NIBIB for Radiology Program	(21,000)	0	0
Comparative transfer to Buildings and Facilities	(86,000)	0	0
Comparative transfer to/from other NIH ICs for NIH Roadmap	1,257,000	0	0
Subtotal, adjusted budget authority	381,946,000	394,260,000	397,432,000
Unobligated balance lapsing	(58,000)	0	0
Total obligations	381,888,000	394,260,000	397,432,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2004 - $1,910,000; FY 2005 -$1,820,000; FY 2006 - $1,900,000
Excludes $94,000 in FY 2005 and $72,000 in FY 2006 for royalties.

Justification

National Institute on Deafness and Other Communication Disorders

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

Budget Authority:

FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
154	$381,946,000	142	$394,260,000	142	$397,432,000	0	$3,172,000

This document provides justification for the Fiscal Year 2006 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 2006 HIV/AIDS activities can be found in the NIH section entitled Office of AIDS Research (OAR).

INTRODUCTION

Disorders of hearing, balance, smell, taste, voice, speech, and language exact a significant economic, social, and personal cost for many individuals. 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.

NIDCD grantee Linda B. Buck, Ph.D., has been awarded the 2004 Nobel Prize in Physiology or Medicine. Dr. Buck shares the award with Dr. Richard Axel for their discoveries that clarify how the olfactory system works. Before 1991, the sense of smell was one of the most enigmatic of our senses. The basic principles of how we recognize and remember about 10,000 different odors were not clearly understood, in part because the molecules that detect different odors were not clearly established. In 1991, Axel and Buck described a very large family of about 1,000 genes that give rise to an equivalent number of olfactory G protein-coupled receptors. These receptors are located on the olfactory receptor cells, which occupy a small area in the upper part of the nasal epithelium.

Axel and Buck's pivotal discovery that receptor proteins must somehow recognize and bind odorant molecules, thereby stimulating the cell to send signals to the brain, provided the tools

needed to answer several basic questions about olfaction: 1) How does the system respond to the thousands of molecules of different shapes and sizes known as odorants?, 2) Does it use a restricted number of non-specific receptors or a large number of relatively specific receptors?, and 3) How does the brain make use of these responses to discriminate between odors? Dr. Buck has received more than $3 million in research grant support over a period of more than 10 years from the NIDCD. Because of this research, we have a better idea of how we smell the roses when we take the time to stop and smell them. Moreover, like all of our senses, our sense of smell plays an important part in our lives. The sense of smell often serves as a first warning signal, alerting us to the smoke of a fire or the odor of a natural gas leak and dangerous fumes. Perhaps more important is that a change in our sense of smell is sometimes a signal of serious health problems. Obesity, diabetes, hypertension, malnutrition, Parkinson's disease, Alzheimer's disease, and multiple sclerosis are all accompanied or signaled by problems like smell disorders.

Story of Discovery: If They Can't Smell Us, They Can't Bite Us

For most people, small biting insects are merely irritating. However, they can also be deadly. The bite of the female *Anopheles gambiae* mosquito spreads malaria, which kills more than a million people each year worldwide. Malaria is also a major cause of death for children in developing nations.

Although there is currently no vaccine in widespread use to prevent malaria infection, research has led to several effective methods to control the disease. Some of these include bed netting, insecticides, and drugs that act on the active and inactive mosquito-transmitted parasites that cause disease once an individual is already infected. Unfortunately, the malaria causing parasites found in areas of the world where infection is widespread are becoming resistant to many currently available drugs. Thus, researchers are desperately searching for new ways to prevent and/or treat malaria.

NIDCD-supported research is developing an innovative approach to stop the spread of malaria. The idea is based upon the discovery that female *Anopheles* mosquitoes, which prefer to feed upon human beings, have a receptor to a specific compound found in human sweat. This receptor enables the mosquito to smell human sweat and target its victims. If scientists can somehow block or inactivate this receptor, the mosquitoes would no longer be able to smell human sweat, and thus would not seek to bite us. If successful, this innovative approach may help break the cycle of malaria transmission.

The Road to Discovery. But how were scientists able to identify the human sweat receptor in malaria-spreading mosquitoes? What led them to believe that such a receptor even existed? The road leading to this groundbreaking discovery begins at least 15 years ago, in NIDCD-supported labs studying the sense of smell in another insect, the common fruit fly *Drosophila melanogaster*.

Drosophila melanogaster is an ideal model for studying the sense of smell, or olfaction. *Drosophila* olfactory systems are simple, yet they function similarly to those of other organisms. The genome of *Drosophila* has been sequenced, providing fertile starting material for identifying olfactory genes. Scientists can measure the response to an odor in a living fly, either by observing its behavior or by recording electrical currents from one or more of its smell-detecting neurons. Finally, *Drosophila*'s role as a classical organism of choice for genetic manipulations has led to development of powerful tools to study individual gene function. All of these characteristics make *Drosophila* a useful tool for identifying genes important for olfaction.

In 1989, NIH-supported scientists identified a *Drosophila* mutant with a specific defect in its ability to detect the odor of benzaldehyde. The flies responded normally to other odors, suggesting that there may be olfactory pathways dedicated to detecting specific odors or related families of odors. Subsequent studies by the same scientists identified and described a molecular pathway inside odor-detecting cells [the inositol 1, 4, 5-triphosphate (IP_3) pathway] that helps transmit a chemical message indicating that an odor has been detected. Because IP_3 pathways usually interact with cell surface receptor proteins, the NIDCD-supported scientists began to search for such receptors in the *Drosophila* olfactory system. In 1999, they published a report describing how they had developed

and used a novel search algorithm on the *Drosophila* genomic sequence database to find potential olfactory receptor proteins. Their search yielded a large multigene family of receptors located in exactly the right place to serve as odor receptors: embedded in the membranes of olfactory receptor neurons.

From Flies to Mosquitoes. Because olfaction plays a major role in insect behavior, genes important for detecting odors are often conserved across insect species. Thus, the Drosophila lab collaborated with another group of NIDCD-supported researchers to search for odorant receptors in the mosquito that transmits malaria, *Anopheles gambiae*. In 2001, the collaborative group reported that they had identified four genes in *Anopheles* that were expressed only in its olfactory system, suggesting that they code for mosquito olfactory receptors. They also noted another tantalizing detail: one of the putative receptor genes, $AgOr_1$, was expressed only in the female olfactory system, and its expression was down-regulated after the mosquito had fed on human blood.

The scientists began to suspect that $AgOr_1$ was the key. But how does this receptor lead the mosquito to target and bite human beings? Although their studies over the next three years uncovered important information about the molecular genetics of mosquito olfaction, the scientists were initially unable to link the $AgOr_1$ to any of the odors known to attract *Anopheles*.

Mystery Solved at Last. Their breakthrough discovery was finally reported via a brief communication published in the January 15, 2004 edition of the journal Nature. The group determined that female *Anopheles* $AgOr_1$ responds to a component in human sweat. At last, the mystery was solved! Mosquitoes detect the odor of human sweat and home in to feed. Researchers are now working to determine how to exploit this knowledge to help human beings: how can we interfere with the *Anopheles*' ability to detect human sweat and thus prevent it from biting us?

NIDCD's long-term investments in olfactory research first begun in *Drosophila* and now being studied in *Anopheles* mosquitoes are the foundation supporting the current new attempts to halt the spread of malaria. Preventing the bite that transmits malaria will eliminate the danger of drug-resistant infections by preventing infection in the first place. This story of discovery is another example of how basic scientific research in insects can have direct, practical and lifesaving applications for human beings.

SCIENCE ADVANCES

New Candidate Otitis Media Vaccine

Background: Otitis media (OM), an infection or inflammation of the middle ear, is the most common reason for a sick infant to visit a doctor. OM begins when a viral or bacterial infection spreads from the throat to the middle ear. In recent years, NIDCD intramural scientists developed a detoxified Nontypeable *Haemophilus influenzae* (NTHi) vaccine against NTHi using lipooligosaccharide (LOS), a sugar-based component found on the surface of bacteria. In addition to NTHi, NIDCD intramural scientists have also been working on a candidate vaccine for another bacterium that causes OM, *Moraxella catarrhalis (M. catarrhalis*).

Advances: Studies have identified three types of *M. catarrhalis* LOS (A, B, and C) in individuals with otitis media or other respiratory tract infections. Pre-clinical testing in animal models showed that vaccines against type A LOS were safe and effective, eliciting a significant immune response that inhibited bacterial growth. During the past year, NIDCD intramural scientists have developed new vaccines against type B *M. catarrhalis*. The current preclinical tests with the newly developed type B vaccines were also shown to be safe and nontoxic *in vitro* as well as in animal models.

Implications: These type B studies along with the previous type A studies are significant advances towards clinical trials to test these candidate vaccines for safety and efficacy in

humans. It is estimated that the two types of vaccines will be able to prevent over 90% of the cases of OM caused by *M. catarrhalis*. The long term goal is to develop a vaccine that reduces the incidence of OM in children caused by all three major bacterial pathogens: *streptococcus pneumoniae*, NTHi, and *M. catarrhalis*.

Gene Therapy to Prevent Hearing Loss

Background: Hearing impairment is frequently caused by the loss of hair cells in the cochlea of the inner ear. Hair cells, named for the hairlike projections on the top surface of the cell, play a vital role in detecting sound. When sound waves enter the cochlea, they produce corresponding waves in the fluid beneath the hair cells. The wave motion drives the hair cells into an overlying membrane. The "hairs" on the tips of the cells bend, setting off a signaling cascade within the cells. These signals are ultimately carried to the brain by the auditory nerve and interpreted as sound. Many factors can cause individuals to lose hair cells, including normal aging, excessive noise exposure, infections, and treatment with certain antibiotics. After hair cells die, the nerve cells that take the sound message to the brain (spiral ganglion neurons) may also die. Scientists are searching for ways to regenerate or prevent the death of hair cells and spinal ganglion neurons.

Advances: Two groups of NIDCD-funded scientists have now used a viral expression strategy (gene therapy) to prevent death of hair cells and spiral ganglion cells in animals. The first group used a virus to deliver protective antioxidants to hair cells in the cochlea. The treatment was able to prevent antibiotics from destroying hair cells. The second group expressed a protein, called brain derived neurotrophic factor (BDNF), in spiral ganglion cells. This strategy was able to inhibit the death of spiral ganglion neurons after the death of their corresponding hair cells.

Implications: If this observation can be repeated in humans, scientists may be able to prevent or delay hair cell and spiral ganglion cell degeneration resulting in preservation of hearing.

Signals Controlling Hair Cell Development

Background: Normal hearing depends upon the precise development of the organ of Corti, a sound-detecting structure within the inner ear that includes both sensory hair cells and non-sensory supporting cells. Scientists are trying to determine the molecular process that directs the formation of these different cell types. Developing sensory hair cells express the *Math1* gene and *Math1* is required for them to develop; however, its specific molecular role is unknown.

Advances: Through analysis of animals with a mutation in *Math1* and by overexpression of *Math1* in developing ears, NIDCD intramural scientists demonstrated that *Math1* causes developing hair cells to produce signals that coordinate the formation of both hair cells and supporting cells. In particular, developing hair cells send out inhibitory signals that regulate the number of other cells that can develop as hair cells. At the same time, developing hair cells produce inductive signals that recruit nearby cells to develop as supporting cells.

Implications: These results provide valuable insights into the molecular signaling pathways that lead to the overall development and organization of the organ of Corti. Understanding how

molecules direct the formation of sensory hair cells may help scientists develop ways to treat problems resulting from errors in hair cell formation.

Molecular Details of Sound Detection

Background: In humans, sound is detected by the sensory hair cells located within the cochlea of the inner ear. Hair cells have bundles of finger-like protrusions. A cluster of these precisely organized protrusions on a single hair cell is called a stereocilia bundle. The stereocilia bend, setting off a series of chemical and electrical signals within the cells. These signals are ultimately carried to the brain by the auditory nerve and interpreted as sound. Although scientists understand the basic principles of sound detection, the molecular details underlying hair cell function are much less well known.

Advances: NIDCD-funded scientists have described two new molecules expressed in the tips of hair cell stereocilia. One group identified a cell surface adhesion molecule (Cadherin 23, or *CDH23*) that may participate in opening and closing an ion channel to transmit the message that a sound has been detected. Mutations in the gene that makes *CDH23* cause hearing loss and deafness in mice and humans. The protein produced by the gene is the expected size of the tip link protein that joins adjacent hair cells together at their tips. Preliminary results from a second group of researchers suggest that another protein, Myosin-X (*Myo10*) is also located in hair cell projections. Their experiments demonstrate that *Myo10* is responsible for moving proteins into growing axons of nerve cells. These proteins are important for helping nerve cells connect with other nerve cells. Thus, mutations in *Myo10* could disrupt the cellular connections within the stereocilia that are vital to hearing.

Implications: These studies provide insight into how hair cells detect sound on a molecular level. As scientists gain a clearer understanding of molecules important for hearing, they can design improved therapies to treat hearing loss caused by molecular defects in the ear.

Staircase to Hearing: The Role of Myosin 15a in the Stereocilia

Background: As they develop, stereocilia organize into bundles of precisely specified rows of increasing heights forming a characteristic staircase pattern. The movement of the stereocilia initiates the complex molecular signals that stimulate the auditory nerve. The auditory nerve carries information to the brain, eventually becoming the perception of sound. Hearing loss, balance defects, or both occurs if the stereocilia do not develop properly into the staircase bundle. Several years ago, scientists showed that mutations in the *MYO15A* gene, which encodes the protein myosin XVa, are responsible for profound, congenital deafness in humans and mice. The type of myosin found in stereocilia performs work within cells such as moving molecules or vesicles to specific locations.

Advances: Recently, NIDCD intramural scientists, in collaboration with scientists at the University of Michigan, have shown that myosin XVa is essential for the development of the normal length and elongation into the staircase-shaped bundle of stereocilia. Myosin XVa is localized at the tops of hair cell stereocilia in the inner ear of normal hearing mice, and the

amount of this motor protein appears to be directly correlated with the length of a stereocilium. Mice with mutations in Myosin XV have hair cell stereocilia bundles that are abnormally short.

Implications: Scientists have shown that mutations of myosin XVa in humans and mice cause a form of profound congenital deafness. They believe that in individuals with dysfunctional myosin XVa, the loss of hearing is due to a failure of hair cell stereocilia to elongate into their characteristic staircase-shaped bundles. Insight into the biology of the sensory hair cells in the inner ear will foster the design of different therapies and preventative strategies for hearing loss.

Molecular Treadmill Keeps Stereocilia Healthy

Background: Stereocilia, in their staircase pattern, are key cellular organelles located in the inner ear that are responsible for hearing and balance. Although stereocilia are exquisitely sensitive to mechanical vibration and easily damaged by over-stimulation, they must maintain themselves to properly function for an entire lifetime to prevent hearing loss.

Advances: In the past year, NIDCD intramural scientists have made significant advances towards elucidating the mechanisms that underlie the formation, regulation, renewal, and lifespan of stereocilia. The length of stereocilia is highly dependent on the bundles of protein filaments constituting their core foundation. Scientists have now discovered that the entire core, consisting of the protein actin, continuously self-renews and the renewal process is based on a molecular treadmill that operates at rates that are precisely matched to the length of each individual stereocilium. Other studies revealed that the myosin XV protein is necessary for filament elongation and the proper regulation of stereocilia length. Myosin XVa was observed at the tips of the stereocilia. Mutations in the myosin 15a gene result in profound deafness in humans and mice. Another actin-related protein called espin also plays a role in regulating stereocilia length and mutations in the espin gene also results in deafness.

Implications: Assembly of actin proteins by myosin XVa and espin may dynamically form the functional shape of stereocilia. Stereocilia undergo continuous self-renewal, the renewal follows a treadmill mechanism. This process together with myosins may also determine the shape of the stereocilia. This new dynamic view of stereocilia renewal is essential to understanding the development, repair and maintenance of normal sensory function and may provide a new basis to understanding the mechanisms of genetic and age-related hearing and balance disorders. Damage to these stereocilia may be one of the mechanisms responsible for noise-induced hearing loss.

Genetic Similarity and Variability among Ashkenazi Jews and Usher Syndrome Type III

Background: Usher syndrome is a genetic disorder that causes deafness and progressive blindness. Usher syndrome accounts for approximately 5% of all cases of deafness, and over one-half of cases of combined deafness and blindness in children. In one type of Usher syndrome (type III), the hearing loss begins after birth and steadily progresses over time. Usher syndrome type III was previously considered very rare, comprising less than 10% of all individuals with Usher syndrome, except in the Finnish population.

Advances: NIDCD intramural scientists have now shown that Usher syndrome type III is present in the Ashkenazi Jewish community, accounting for approximately 40% of all cases of Usher syndrome in this population. Furthermore, all of the Ashkenazi Jewish cases studied were caused by an identical mutation of the *USH3* gene, which greatly simplifies molecular diagnosis and carrier screening for this disorder. This study showed that there is great variability in the onset and progression of the loss of vision and hearing associated with this specific mutation raising the possibility that interventions may be developed to prevent or retard these degenerative processes.

Implications: This study demonstrated that Ashkenazi Jewish children with progressive hearing loss should undergo ophthalmologic evaluation, and children with a specific kind of blindness, called retinitis pigmentosa, should have routine audiologic testing to screen for Usher syndrome, type III. In combination with genetic testing for this specific mutation, these evaluations will facilitate the early diagnosis of type III Usher syndrome as well as planning for the difficult communication and rehabilitation challenges presented by these dual deficits.

Connecting the Two Sides of the Brain: How do Nerve Cells Cross the Midline?

Background: Nerve cells sprout long fibers called axons, which grow out to contact target cells that are sometimes a relatively long distance away. As nerve cells exit the retina of the eye via the optic nerve, some axons originating on one side of the brain must cross the midline to find their correct targets in specific vision regions on the other side. Cells along the pathway produce molecules that help guide the axons as they grow towards their targets. Gene expression determines where and when cells produce these molecular guidance cues. Because of their fundamental role in brain development, scientists are actively working to identify important axonal guidance genes.

Advances: Individuals with horizontal gaze palsy with progressive scoliosis (HGPPS) are unable to move their eyes to either side. Scientists supported by NIDCD examined the brains of individuals with HGPPS and determined that axons from motor and sensory nerves do not cross the midline properly. In addition, these individuals demonstrate poor development of a nerve center that controls sideways eye movements. The scientists related HGPPS to mutations in a gene called *ROBO3*, which codes for a critical axon guidance molecule. The human *ROBO3* gene is similar to members of a gene complex called "*roundabout*" that guide axons in fruit flies, zebrafish, and mice.

Implications: Scientists may now use this information to screen individuals with HGPPS and their families to determine if they carry the defective gene. This study also provides information on how *ROBO3* functions during brain development, and thus may help scientists develop treatments for HGPPS.

Maternally Inherited Genetic Mutation May Be a Target for Antibiotic-Induced Deafness

Background: Sensorineural hearing loss can be caused by genetic mutations, infections, acoustic trauma, environmental factors, interactions between genes and the environment, or ototoxic (harmful to the inner ear) drugs. Ototoxic drugs, such as a special class of antibiotics called

aminoglycosides, can damage the hearing and balance sensory hair cells located in the inner ear. Some individuals seem especially prone to aminoglycoside-induced deafness. Studies have shown that this aminoglycoside hypersensitivity is often inherited from the mother, suggesting that the mother's genes in the mitochondria (the powerhouse of the cell) may be involved. The mitochondrial DNA mutation, A1555G, is also known to cause deafness not associated with any other problem (nonsyndromic). This mitochondrial mutation is the main target for aminoglycoside antibiotics toxicity.

Advances: NIDCD-supported scientists performed extensive clinical and genetic analyses from a large family group with aminoglycoside-induced and nonsyndromic hearing loss. They have identified a new mitochondrial DNA mutation called C1494T that is thought to be linked to the other mutation, A1555G.

Implications: These data suggest that the new C1494T mutation is another mechanism that renders certain people more susceptible to aminoglycoside ototoxicity and nonsyndromic deafness. If this mechanism can be clearly understood, then treatment and preventative strategies could be developed for individuals prone to aminoglycoside ototoxicity.

A Novel Valve Mechanism for Controlling Fluid Balance in the Inner Ear

Background: The inner ear uses a combination of mechanical and chemical methods to detect sound and spatial orientation (balance.) In order for mechanical and chemical signaling to function properly, the inner ear must maintain tight regulation of the fluids, pressures, and ions in its various compartments. Scientists know that disruption of this tight regulation leads to functional problems, but exactly how the regulation is maintained and how it leads to problems is still unknown. Individuals with Ménière's disease suffer from dizziness and loss of balance. Although scientists believe the disease is due to disrupted regulation of inner ear fluids, ions, and/or pressure, they have not yet established a direct link.

Advances: NIDCD-supported scientists recently described a possible mechanism for fluid regulation in the inner ear. A small tube called the endolymphatic duct connects a balloon-like structure called the endolymphatic sac (ES) to the sensory compartment of the inner ear. The scientists alternately injected or withdrew fluid from the cochlea and measured the resulting changes in ion concentration within the ES. Fluid injection into the sensory compartment of the inner ear caused little change in the ES ion concentration, while fluid removal reduced ES ion concentrations. This suggests that ions (and fluid) pass into the ES and the rest of the inner ear, but that movement is somehow regulated. Anatomical study of the ES revealed a membrane-lined space that may act as a one-way mechanical valve, permitting fluid to flow into the ES when pressure is increased in the inner ear.

Implications: This study helps scientists understand the role that the ES plays in regulation of ions, pressure and fluid within the inner ear. Such information may lead to possible treatments for individuals with Ménière's disease and other disorders thought to be due to problems with inner ear pressure, fluid, and/or ion regulation.

Zebrafish Help Identify Genes Important for Hearing and Balance

Background: Even though the Human Genome Project unlocked our genetic code, it did not explain how genes and proteins interact to achieve final function. One way for scientists to test gene function is to "knock out" a specific gene in an animal and note the impact on that animal. Zebrafish (*Danio rerio*) are vertebrates with numerous characteristics that make them ideal organisms for genetic analysis: rapid life cycle, external fertilization, and transparent embryos that permit scientists to observe their development in real time under a microscope. Scientists can induce mutations in zebrafish by exposing them to mutagenic chemicals. Mutant fish are then identified by observation of abnormal development, function, or behavior and then analyzed to determine which genes are affected.

Advances: NIDCD-funded scientists have recently identified several zebrafish with genetic defects that result in loss of hearing and balance. The gene *nompC* (no mechano receptor potential) codes for a channel in hair cells that enables the cells to conduct the electrical currents needed to detect sound or sense their orientation in the water (balance.) Zebrafish that lack *nompC* are deaf and unable to maintain their balance. The gene *Gemini* codes for a calcium channel that enables the hair cells to relay the message that a sound or change in orientation has been detected. Zebrafish that lack *Gemini* are also deaf and unable to maintain balance. The gene *Ovl* plays a critical role in survival of sensory cells, including those that detect balance and sound, those that detect odors, and those that detect light. Zebrafish that lack *Ovl* generate but then lose sensory neurons in the auditory, vestibular, olfactory, and visual systems. The gene *Sputnik* links the tips of sensory hair cells that detect sound and orientation, enabling them to open electrical channels on neighboring hair cells when deflected. Zebrafish that lack *Sputnik* cannot open channels on neighboring hair cells, and are thus unable to hear or sense balance.

Implications: Normal hearing and balance require the proper development and function of the organs that detect sound and sense orientation. Identifying the genes controlling this process is crucial to understanding how hearing and balance develop. Because some of the genes important for hearing and balance in zebrafish have been discovered using powerful genetic screens, scientists may now search for similar genes in humans. This could lead to genetic tests for human hearing and balance disorders whose underlying causes were previously unknown.

Regulation of Olfactory Receptor Gene Expression

Background: There are about 10 million olfactory receptor (OR) neurons in the nasal epithelium of a mouse. Remarkably, each neuron expresses only one OR gene selected from a family of about 1,000 different OR genes. The molecular mechanism for gene selection is unknown, but has been postulated to involve DNA re-arrangement.

*Advance*s: NIDCD-supported scientists cloned an apparently normal mouse by nuclear transplantation using the nucleus taken from a differentiated OR neuron, which had chosen a single OR gene for expression. The olfactory neuron nucleus was exchanged for the nucleus normally found in a mouse oocyte (egg), and the oocyte developed into a cloned mouse. The cloned mouse expressed a full complement of many types of OR genes, even though the adult OR neuron nucleus used for transplantation expressed only one OR gene.

Implications: The receptor choice by an olfactory neuron does not involve irreversible changes in DNA. If the DNA changes were indeed irreversible, one would expect that the cloned mouse would only express the single OR of the neuron donating the nucleus.

The Importance of Being Tasty

Background: The sense of taste is an important factor in food choice and eating. Taste perception is responsible not only for our preference for eating certain foods, but also for providing important information about our chemical environment, such as avoiding bitter poisonous substances. The sense of taste is responsible for detecting and responding to sweet, bitter, sour, salty, and umami (amino acid) stimuli.

Advances: To examine taste signal detection and information processing, NIDCD-supported scientists focused on the isolation and characterization of sweet and umami (amino acid sensing) taste receptors. These receptors provide powerful molecular tools that outline how the taste system is organized and help define the logic of taste coding. Using mice, scientists have demonstrated that sweet and umami taste are strictly dependent on T1R receptor family. Receptors formed from T1R2 and T1R3 proteins together detect sweet substances, while receptors from T1R1 and T1R3 proteins together detect amino acids such as umami.

Implications: Since amino acids (the building blocks of proteins) and sweet substances evoke food intake, these studies demonstrate that the taste substances initiating ingestion and the intake of essential calories share a common receptor type. This can have future implications as scientists seek ways to help find solutions for restoring a person's lost sense of taste, as well as understanding eating behavior.

Gene Therapy May Be Effective in Treating Laryngeal Paralysis

Background: Individuals with laryngeal paralysis typically have disabling symptoms such as loss of voice, difficulty swallowing and airway obstruction. Healthy laryngeal function is necessary for voice production and safe swallowing and is dependent on adequate vocal fold closure. A number of common conditions interfere with a person's ability to adequately close the vocal folds, such as laryngeal paralysis, aging and chronic neurodegenerative diseases (e.g., Parkinson's disease).

Advances: NIDCD-supported scientists have designed a rat laryngeal paralysis model to study novel gene transfer strategies using a muscle specific expression system to enhance local delivery of growth factors. Recent advances in gene therapy have demonstrated that local delivery of growth factors by injection has promoted nerve regeneration and reversed muscle atrophy associated with paralysis. The scientists injected human insulin-like growth factor (hIGF)-1 gene formulation in the paralyzed laryngeal muscle of rats to determine the potential for nerve repair. Positive effects on both muscle and nerve (increased mass) were demonstrated one month following a single injection of this hIGF-I gene formulation. Based on these preliminary findings, it is hypothesized that the ability of hIGF-1 to increase the muscle and nerve mass will be beneficial during the process of nerve regeneration and muscle reennervation.

Implications: The results from animal models are promising and are laying the necessary foundation for future research efforts to restore voice and/or safe swallowing in humans. This study will have direct relevance towards creating a more practical treatment strategy for human disorders, including treatment of laryngeal paralysis and other peripheral nerve injuries.

Functional Magnetic Resonance Imaging Before and After Aphasia Therapy

Background: For more than 150 years, scientists have known that the brain's left hemisphere controls language. Language impairment results if the critical regions of the left hemisphere are compromised by a stroke or other injury to the brain. One of these impairments is called aphasia, which causes a person to have difficulty expressing, understanding, reading or writing language. For nearly as long as scientists have known what parts of the brain control language, they have debated whether the undamaged portions of the left or right hemisphere control recovery from aphasia. The ability to answer this question is critical to advancing the science of aphasia rehabilitation and improving the lives, relationships, and productivity of the one million of Americans who have this disorder[1].

Advances: NIDCD-supported scientists have demonstrated that activity in structures of the brain's right hemisphere parallels performance in word generation before and after language rehabilitation. Functional magnetic resonance imaging (fMRI) was used to measure brain activity during word generation in individuals with stroke before and after they had language therapies to engage the right side of the brain in language production. During fMRI scans, individuals heard a category (e.g., birds) and, in response, spoke aloud one member of the category (e.g., eagle). Brain activity was measured in the speech motor and hearing portions of the right side of the brain. The delay between presenting the category word (bird) and speaking the member word (eagle) was strongly linked with the delay in activity between these right hemisphere hearing and movement portions of the brain. By the end of treatment, the individuals delay in activity between the hearing and motor parts of the right hemisphere reduced to times similar to normal individuals.

Implications: This study supports the concept that right hemisphere organization can play a role in recovery of language production during rehabilitation. The implication is that treatments designed to activate right hemisphere organization in aphasia rehabilitation hold promise for reducing communication disorders, such as aphasia, in individuals after stroke.

Elucidating the Molecular Mechanisms of Stuttering

Background: Stuttering is a speech disorder characterized by involuntary syllable repetitions, syllable prolongations, and interruptions in the smooth flow of speech, known as blocks. Well-described since Biblical times, this disorder can impose severe limits on normal communication and can have profound effects on the lives of the affected individuals. Previous studies have shown that genetic factors play a role in the etiology of stuttering. Scientists are working to identify the underlying genes and to find out how the products of these genes function, both normally and abnormally in individuals who stutter.

[1] The National Aphasia Association, Aphasia Fact Sheet, www.aphasia.org.

Advances: Recently, NIDCD intramural scientists completed and published a genetic linkage study of stuttering. A linkage study uses genetic markers to map the location of a gene or genes that cause a particular trait based on inheritance in families. The scientists studied 68 families from across North America who had at least two relatives who stuttered; some families contained as many as five or six affected individuals. Chromosome 18 showed linkage with stuttering in families studied. Most of the evidence for this gene on chromosome 18 comes from one family, which was the largest family of all those studied. This raised the question of whether defects on this chromosome are causative for stuttering in just this large family, or whether this gene locus is associated with stuttering in many different families. To help answer this question, the scientists repeated their computerized statistical analysis omitting data contributed from the largest family. The results again showed chromosome 18 as the suspected site. The results suggest that mutations in one or more genes on chromosome 18 can cause stuttering in at least one large family, and possibly in the more general population as well.

Implications: Independent analysis using a larger study sample will be needed to confirm the results obtained from this linkage study. However, the results from this study show that the prospect of identifying at least some specific cause of stuttering is indeed realistic.

Specific Regions of Chromosome 3 Linked to Speech Sound Disorder and Dyslexia

Background: Speech-sound disorders (SSDs) are the largest group of communication disorders observed in children requiring special educational services. SSDs are a very complex behavioral disorder with multiple deficits with characteristics that overlap with developmental dyslexia (reading disability). SSDs are highly prevalent in preschool-age children. Children with SSD have varying degrees of delayed speech development, and more than half of these children will encounter academic difficulties in language, reading, and spelling. In most cases, the cause of the SSDs is unknown. Previous studies have suggested that genetic factors may be one possible cause for SSDs, as seen in dyslexia and specific language impairment (SLI). For example, recent genetic studies have identified several likely regions in the genome for dyslexia, including one on chromosome 3.

Advances: Since many individuals with SSDs also have dyslexia, NIDCD-supported scientists examined chromosome 3 for links to SSDs. They analyzed speech, phonology, and reading test scores to examine chromosome 3 in 77 families with a child with SSDs. The test scores showed strong evidence of linkage to chromosome 3 and suggest that a specific region on chromosome 3 may influence both SSDs and dyslexia.

Implications: Identifying the gene(s) that causes SSDs would result in improved diagnosis and early identification of those at risk, allowing for behavioral and educational intervention at a young age. Finding such genes would also give scientists keys insights on how communication occurs in the brain and how speech arose as a mode of communication. In addition, common genetic bases for early SSDs and later reading disorders may be identified.

Locating the Gene for Language and Reading Disorders

Background: Children who fail to develop language normally, given adequate education, and in the absence of factors such as neurological disorders or hearing impairment, are diagnosed as having specific language impairment (SLI). SLI occurs in approximately 7% of children entering grade school and is associated with later difficulties in learning to read.

Advances: Research has consistently demonstrated that SLI occurs in families, suggesting that genetic factors may play an important role in causing this disorder. To prove this theory, scientists are scanning the human genome for the location of the suspected gene that may cause SLI, by studying families where multiple members have language/reading disorders. Previous research on Canadian families showed evidence of a link between a region on chromosome 13 and susceptibility to SLI. To verify and refine the initial findings, scientists performed a second study, but this time in American families, and confirmed the location of a gene for SLI susceptibility on chromosome 13.

Implications: This same region of chromosome 13 has been implicated in autism, a developmental disorder that affects behavior in children. It is known that some children with autism show language deficits that are similar in form to those seen in children with SLI. This research has been expanded to include collaborations with scientists studying autism and has resulted in a new autism research project, which focuses on language genetics.

NIH Roadmap

Translational Research in Human Communication Disorders

A critical component of the NIH Roadmap theme "Re-engineering the Clinical Research Enterprise" is that to improve human health, scientific discoveries must be translated into practical applications. As part of its mission, NIDCD continues to seek ways to facilitate the translation of basic biomedical or behavioral research discoveries in the field of deafness and other communication disorders into new clinical and research tools, prostheses and assistive devices, behavioral therapies or interventions and medications. Emphasis of NIH Roadmap initiatives on translational research will advance NIDCD's mission by encouraging collaborative partnerships between scientists who study basic biological and behavioral processes and those who study the etiology, diagnosis, treatment and prevention of deafness and other communication disorders and the delivery of those services to those with these disorders.

New Initiatives in Human Communication Research

- Speech Processor Optimization for Cochlear Implants
  Approximately 60,000 people worldwide have received cochlear implants (CI)[2]. There is widespread variability in success in understanding speech among individuals with CIs. This variability is due to many factors, including age, degree of hearing loss, and CI equipment differences. The goal of this RFA is to support the development of innovation

[2] NIDCD Fact Sheet, Cochlear Implants, http://www.nidcd.nih.gov/health/hearing/coch.asp.

and enhancements for CI to improve the ability to hear and understand speech across users.

- The Role of Neuroimaging in Aphasia Rehabilitation
  In adults, the term "aphasia" is typically defined as the language problems (comprehension and/or expression) resulting from stroke. It is estimated that in the US approximately 80,000 individuals become aphasic each year and that one million persons currently have aphasia[1]. A number of studies have shown that the language deficits of aphasia often are amenable to treatment, at both onset and many years beyond. Various treatments are available, but robust data affirming their efficacy are limited. This RFA seeks research that examines the potential of neuroimaging technology in the rehabilitation of individuals with aphasia.

- Congenital Cytomegalovirus (CMV) and Hearing Loss in Infants and Children
  Many children suffer from hearing loss that develops during the first few years of life. The public health impact of congenital CMV infection is largely due to its ability to damage the central nervous system, including the auditory system. The limited number of population-based studies of the etiology of hearing loss in infants suggested that congenital CMV infection is a leading cause of sensorineural hearing loss in children. The results of this initiative will provide critical information on whether infants should, in addition to newborn hearing screening, be screened at birth for the presence of CMV.

Innovation in Management and Administration

NIDCD Mentors Directory

The NIDCD is using innovative ways to develop and enhance the environment for deaf or hard-of-hearing students interested in research careers in human communication. In response to an action plan that was developed after the October 2002 NIDCD Meeting on Biomedical and Behavioral Research Careers for Deaf Individuals, the NIDCD launched a directory of NIDCD-funded scientists who are committed to mentoring deaf or hard-of-hearing students, postdoctoral fellows, and junior scientists interested in research careers within the seven mission areas of the NIDCD: hearing, balance, smell, taste, voice, speech, and language. Because deaf and hard-of-hearing individuals depend on visual tools for communication, the NIDCD posted the Mentors Directory on their website. By searching the NIDCD Mentors Directory online, individuals interested in being mentored in these areas can identify and then contact prospective mentors who appear compatible with their research interests, career stage and location. To date, approximately 115 scientists from the NIDCD extramural grantee and intramural communities have registered on the Directory to serve as mentors.

The NIH Neuroscience Blueprint

Overview -- The Blueprint is a framework to enhance cooperation among fourteen NIH Institutes and Centers that support research on the nervous system. Over the past decade, driven by the science, the NIH neuroscience Institutes and Centers have increasingly joined forces through initiatives and working groups focused on specific disorders. The Blueprint builds on

this foundation, making collaboration a day-to-day part of how the NIH does business in neuroscience. By pooling resources and expertise, the Blueprint can take advantage of economies of scale, confront challenges too large for any single Institute, and develop research tools and infrastructure that will serve the entire neuroscience community.

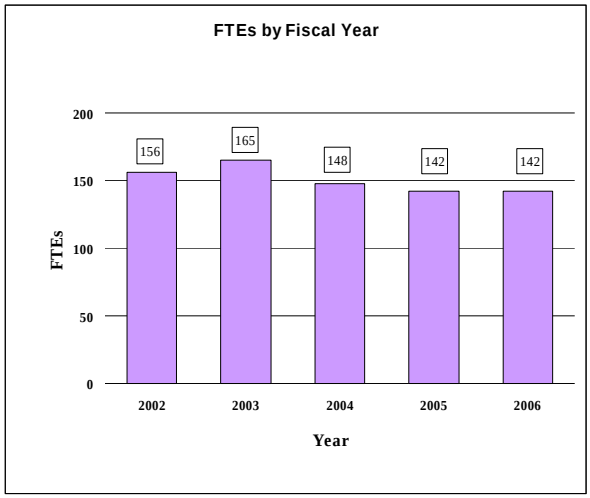
FY2005 -- For fiscal year 2005, the Blueprint participants are developing an initial set of initiatives focused on tools, resources, and training that can have a quick and substantial impact because each builds on existing programs. These initiatives, with the participation of all Blueprint Institutes, include an inventory of neuroscience tools funded by the NIH and other government agencies, enhancement of training in the neurobiology of disease for basic neuroscientists, and expansion of ongoing gene expression database efforts.

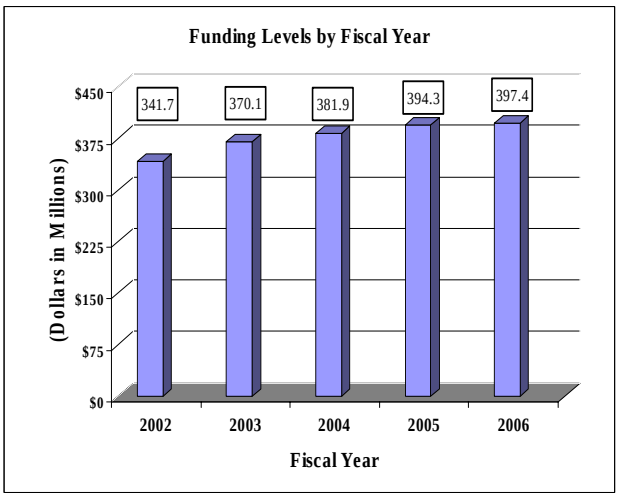
FY2006 -- Advances in the neurosciences and the emergence of powerful new technologies offer many opportunities for Blueprint activities that will enhance the effectiveness and efficiency of neuroscience research. Blueprint initiatives for fiscal year 2006 will include systematic development of genetically engineered mouse strains of critical importance to research on nervous system and its diseases and training in critical cross cutting areas such as neuroimaging and computational biology.

Budget Policy

The Fiscal Year 2006 budget request for the NIDCD is $397,432,000, an increase of $3,172,000 and 0.8 percent over the FY 2005 Final Conference Level. Also included in the FY 2006 request, is NIDCD's support for the trans-NIH Roadmap initiatives, estimated at 0.89% of the FY 2006 budget request. This Roadmap funding is distributed through the mechanisms of support, consistent with the anticipated funding for the Roadmap initiatives. A full description of this trans-NIH program may be found in the NIH Overview.

A five-year history of FTEs and Funding Levels for NIDCD is shown in the graphs below.





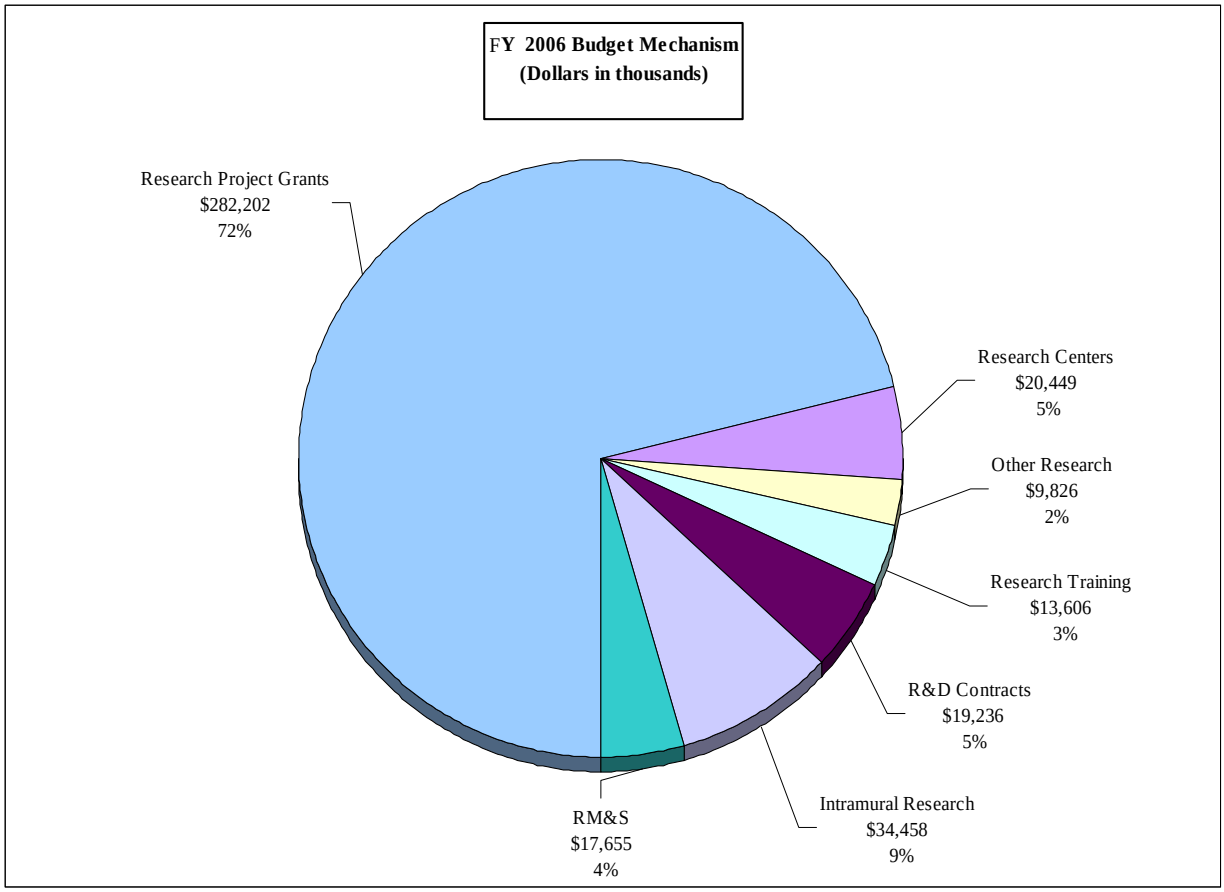
NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while pursuing new research opportunities. The average cost of competing RPGs will be held at the FY 2005 level. There will be no inflationary increases for direct, recurring costs in Noncompeting continuation RPGs.

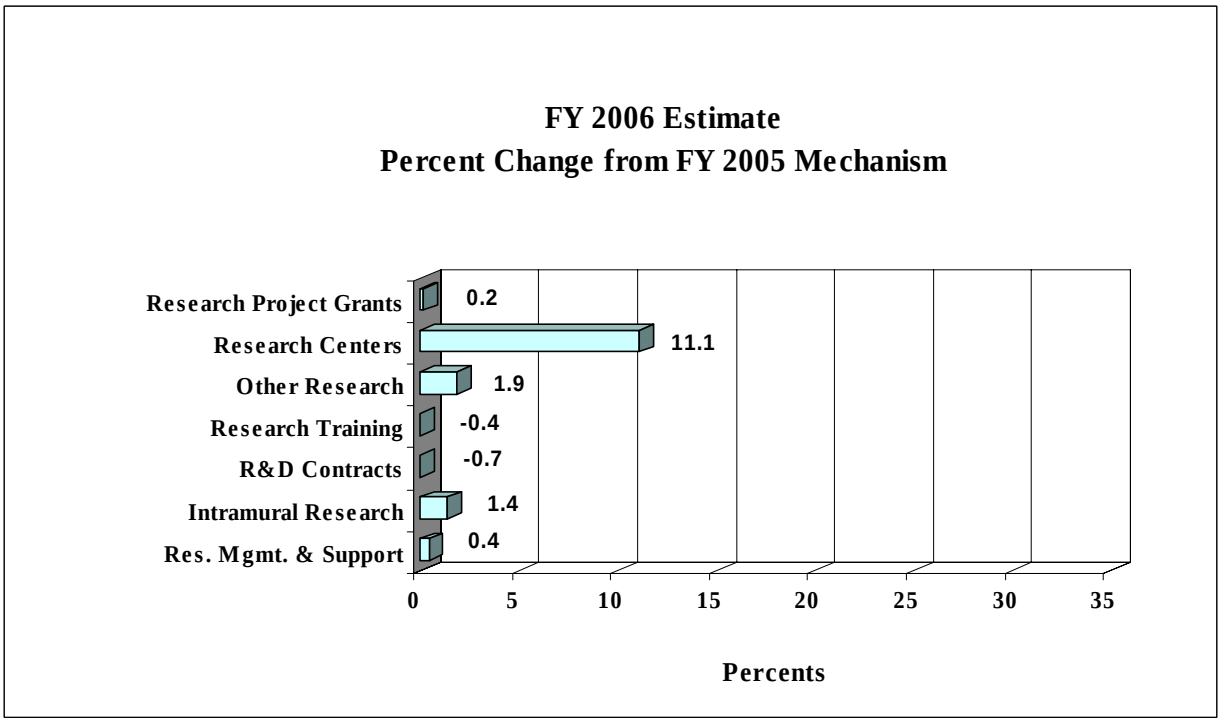
Advancement in medical research is dependent on attracting the best and the brightest to pursue careers in biomedical research. In the Fiscal Year 2006 request, stipend levels for post-doctoral recipients supported through the Ruth L. Kirschstein National Research Service Awards will increase by 4.0% for those with 1-2 years of experience, with all other stipends remaining at the FY 2005 levels. NIH will also provide an increase of $500 per post-doctoral fellow, for increased health insurance costs. This increase in stipends and health benefits is financed within the FY 2006 request by reducing the number of Full-Time Training Positions by one. NIDCD will support 348 pre- and postdoctoral trainees in full-time training positions.

The Fiscal Year 2006 request includes funding for 24 research centers, 66 other research grants, including 46 clinical career awards, and 47 R&D contracts. Intramural Research increases by 1.4 %, and Research Management and Support increases by 0.4%.

NIDCD is participating in the NIH Neuroscience Blueprint. The FY 2006 request includes $2,000,000 for a variety of Neuroscience Blueprint initiatives, including neuroscience cores, training initiatives, and the Neuromouse project.

The mechanism distribution by dollars and percent change is displayed below.


FY 2006 Budget Mechanism
(Dollars in thousands)
Research Project Grants
$282,202
72%
Research Centers
$20,449
5%
Other Research
$9,826
2%
Research Training
$13,606
3%
R&D Contracts
$19,236
5%
Intramural Research
$34,458
9%
RM&S
$17,655
4%


FY 2006 Estimate
Percent Change from FY 2005 Mechanism
Research Project Grants
Research Centers
Other Research
Research Training
R&D Contracts
Intramural Research
Res. Mgmt. & Support
0.2
11.1
1.9
-0.4
-0.7
1.4
0.4
0
5
10
15
20
25
30
35
Percents

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

Budget Mechanism - Total

MECHANISM	FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	659	$197,289,000	691	$213,173,000	642	$205,510,000
Administrative supplements	(27)	1,502,000	(27)	1,556,000	(27)	1,500,000
Competing:						
Renewal	70	26,494,000	59	23,298,000	67	26,626,000
New	163	39,020,000	139	34,314,000	159	39,216,000
Supplements	0	0	0	0	0	0
Subtotal, competing	233	65,514,000	198	57,612,000	226	65,842,000
Subtotal, RPGs	892	264,305,000	889	272,341,000	868	272,852,000
SBIR/STTR	44	9,107,000	46	9,300,000	46	9,350,000
Subtotal, RPGs	936	273,412,000	935	281,641,000	914	282,202,000
Research Centers:						
Specialized/comprehensive	22	17,335,000	21	18,154,000	23	20,100,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	160,000	0	250,000	1	349,000
Comparative medicine	0	100,000	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	22	17,595,000	21	18,404,000	24	20,449,000
Other Research:						
Research careers	42	7,302,000	45	7,951,000	46	8,109,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	0	0	0	0	0	0
Biomedical research support	0	7,000	0	9,000	0	11,000
Minority biomedical research support	0	0	0	0	0	0
Other	19	1,706,000	20	1,684,000	20	1,706,000
Subtotal, Other Research	61	9,015,000	65	9,644,000	66	9,826,000
Total Research Grants	1,019	300,022,000	1,021	309,689,000	1,004	312,477,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	148	5,726,000	143	5,700,000	142	5,700,000
Institutional awards	203	7,792,000	205	7,956,000	206	7,906,000
Total, Training	351	13,518,000	348	13,656,000	348	13,606,000
Research & development contracts	47	19,657,000	47	19,363,000	47	19,236,000
(SBIR/STTR)	(0)	(18,000)	(0)	(0)	(0)	(0)
	FTEs		FTEs		FTEs	
Intramural research	83	32,640,000	81	33,976,000	81	34,458,000
Research management and support	65	16,109,000	61	17,576,000	61	17,655,000
Total, NIDCD	148	381,946,000	142	394,260,000	142	397,432,000
(RoadMap Support)		(1,312,000)		(2,458,000)		(3,554,000)
(Clinical Trials)		(3,201,000)		(3,300,000)		(3,315,000)

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

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2004 Actual FTEs	FY 2004 Actual Amount	FY 2005 Appropriation FTEs	FY 2005 Appropriation Amount	FY 2006 Estimate FTEs	FY 2006 Estimate Amount	Change FTEs	Change Amount
Extramural Research:								
Deafness and Other Communication Disorders		$333,197		$342,708		$345,319		$2,611
Subtotal, Extramural research		333,197		342,708		345,319		2,611
Intramural research	83	32,640	81	33,976	81	34,458	0	482
Res. management & support	65	16,109	61	17,576	61	17,655	0	79
Total	148	381,946	142	394,260	142	397,432	0	3,172

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

Summary of Changes

FY 2005 Appropriation				$394,260,000
FY 2006 Estimate				397,432,000
Net change				3,172,000
	FY 2005 Appropriation		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$10,652,000		$128,000
b. Annualization of January 2005 pay increase		10,652,000		100,000
c. January 2006 pay increase		10,652,000		185,000
d. One less day of pay		10,652,000		(25,000)
e. Payment for centrally furnished services		5,507,000		28,000
f. Increased cost of laboratory supplies, materials, and other expenses		17,817,000		336,000
Subtotal				752,000
2. Research Management and Support:				
a. Within grade increase		6,885,000		105,000
b. Annualization of January 2005 pay increase		6,885,000		65,000
c. January 2006 pay increase		6,885,000		120,000
d. One less day of pay		6,885,000		(26,000)
e. Payment for centrally furnished services		2,579,000		13,000
f. Increased cost of laboratory supplies, materials, and other expenses		8,112,000		146,000
Subtotal				423,000
Subtotal, Built-in				1,175,000

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

Summary of Changes--continued

CHANGES	2005 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	691	$214,729,000	(49)	($7,719,000)
b. Competing	198	57,612,000	28	8,230,000
c. SBIR/STTR	46	9,300,000	0	50,000
Total	935	281,641,000	(21)	561,000
2. Research centers	21	18,404,000	3	2,045,000
3. Other research	65	9,644,000	1	182,000
4. Research training	348	13,656,000	0	(50,000)
5. Research and development contracts	47	19,363,000	47	(127,000)
Subtotal, extramural				2,611,000
	FTEs		FTEs	
6. Intramural research	81	33,976,000	0	(270,000)
7. Research management and support	61	17,576,000	0	(344,000)
Subtotal, program		394,260,000		1,997,000
Total changes	142		0	3,172,000

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

Budget Authority by Object

	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	142	142	0
Full-time equivalent of overtime & holiday hours	0	0	0
Average ES salary	$146,368	$149,295	$2,927
Average GM/GS grade	12.2	12.2	0.0
Average GM/GS salary	$80,363	$82,211	$1,848
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$114,885	$117,182	$2,297
Average salary of ungraded positions	99,937	101,936	1,999

OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	$7,425,000	$7,707,000	$282,000
11.3 Other than Full-Time Permanent	4,455,000	4,625,000	170,000
11.5 Other Personnel Compensation	209,000	217,000	8,000
11.7 Military Personnel	116,000	120,000	4,000
11.8 Special Personnel Services Payments	2,250,000	2,320,000	70,000
Total, Personnel Compensation	14,455,000	14,989,000	534,000
12.0 Personnel Benefits	3,001,000	3,116,000	115,000
12.1 Military Personnel Benefits	55,000	57,000	2,000
13.0 Benefits for Former Personnel	26,000	27,000	1,000
Subtotal, Pay Costs	**17,537,000**	**18,189,000**	**652,000**
21.0 Travel & Transportation of Persons	553,000	548,000	(5,000)
22.0 Transportation of Things	43,000	43,000	0
23.1 Rental Payments to GSA	0	0	0
23.2 Rental Payments to Others	1,162,000	1,151,000	(11,000)
23.3 Communications, Utilities & Miscellaneous Charges	1,028,000	1,018,000	(10,000)
24.0 Printing & Reproduction	213,000	211,000	(2,000)
25.1 Consulting Services	258,000	256,000	(2,000)
25.2 Other Services	1,155,000	1,144,000	(11,000)
25.3 Purchase of Goods & Services from Government Accounts	29,824,000	29,739,000	(85,000)
25.4 Operation & Maintenance of Facilities	2,097,000	2,078,000	(19,000)
25.5 Research & Development Contracts	9,209,000	9,209,000	0
25.6 Medical Care	1,577,000	1,562,000	(15,000)
25.7 Operation & Maintenance of Equipment	1,884,000	1,867,000	(17,000)
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	**46,004,000**	**45,855,000**	**(149,000)**
26.0 Supplies & Materials	3,595,000	3,561,000	(34,000)
31.0 Equipment	780,000	773,000	(7,000)
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	323,345,000	326,083,000	2,738,000
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	**376,723,000**	**379,243,000**	**2,520,000**
Total Budget Authority by Object	**394,260,000**	**397,432,000**	**3,172,000**

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

Salaries and Expenses

OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease	Percent Change
Personnel Compensation:				
Full-Time Permanent (11.1)	$7,425,000	$7,707,000	$282,000	3.8
Other Than Full-Time Permanent (11.3)	4,455,000	4,625,000	170,000	
Other Personnel Compensation (11.5)	209,000	217,000	8,000	3.8
Military Personnel (11.7)	116,000	120,000	4,000	3.4
Special Personnel Services Payments (11.8)	2,250,000	2,320,000	70,000	3.1
Total Personnel Compensation (11.9)	**14,455,000**	**14,989,000**	**534,000**	**3.7**
Civilian Personnel Benefits (12.1)	3,001,000	3,116,000	115,000	3.8
Military Personnel Benefits (12.2)	55,000	57,000		
Benefits to Former Personnel (13.0)	26,000	27,000	1,000	3.8
Subtotal, Pay Costs	**17,537,000**	**18,189,000**	**652,000**	**3.7**
Travel (21.0)	553,000	548,000	(5,000)	-0.9
Transportation of Things (22.0)	43,000	43,000	0	0.0
Rental Payments to Others (23.2)	1,162,000	1,151,000	(11,000)	-0.9
Communications, Utilities and Miscellaneous Charges (23.3)	1,028,000	1,018,000	(10,000)	-1.0
Printing and Reproduction (24.0)	213,000	211,000	(2,000)	-0.9
Other Contractual Services:				
Advisory and Assistance Services (25.1)	258,000	256,000	(2,000)	-0.8
Other Services (25.2)	1,155,000	1,144,000	(11,000)	-1.0
Purchases from Govt. Accounts (25.3)	12,667,000	12,550,000	(117,000)	-0.9
Operation & Maintenance of Facilities (25.4)	2,097,000	2,078,000	(19,000)	-0.9
Operation & Maintenance of Equipment (25.7)	1,884,000	1,867,000	(17,000)	-0.9
Subsistence & Support of Persons (25.8)	0	0	0	0.0
Subtotal Other Contractual Services	**18,061,000**	**17,895,000**	**(166,000)**	**-0.9**
Supplies and Materials (26.0)	3,593,000	3,559,000	(34,000)	-0.9
Subtotal, Non-Pay Costs	24,653,000	24,425,000	(228,000)	-0.9
Total, Administrative Costs	**42,190,000**	**42,614,000**	**424,000**	**1.0**

NATIONAL INSTITUTES OF HEALTH

National Institute on Deafness and Other Communication Disorders

SIGNIFICANT ITEMS IN SENATE APPROPRIATIONS
COMMITTEE REPORT

FY 2005 Senate Appropriations Committee Report Language (S. Rpt. 108-345)

Item

Clinical Evaluation of Hearing Loss -- The Committee encourages NIDCD to partner with other Institutes at NIH to support the development of functional neuroimaging technology with more precise spatial and temporal resolution, as well as better molecular probes to monitor brain activity (p. 140).

Action taken or to be taken

At the NIH, the NIMH and NINDS are the lead institutes for neuroimaging technology research, including development of devices and systems with improved spatial and temporal resolution, as well as better molecular probes. NIDCD has an active portfolio of research projects involving imaging research as it applies to deafness and communications disorders, and collaborates with other institutes when appropriate.

One example relates to aphasia research. In (May, 2002) NIDCD sponsored a planning workshop to formulate research recommendations on aphasia intervention and use of neuroimaging techniques. The workshop was entitled, "The Role of Neuroimaging in the Study of Aphasia Recovery and Rehabilitation: Research Needs and Opportunities." Other NIH institutes conducting aphasia research were invited to participate. As a result of the workshop, NIDCD issued a Request for Applications (RFA) entitled "Role of Neuroimaging in Aphasia Rehabilitation", which was co-sponsored by NIBIB. NIDCD continues to participate in trans-NIH activities related to aphasia, as well as collaborate with other institutes to foster and advance research in this area.

In another example, NIDCD is participating in a new Program Announcement released on September 29, 2004: Manufacturing Processes of Medical, Dental, and Biological Technologies (PA-04-161). Sponsored by the CDC, FDA, and 19 NIH Institutes and Centers, this PA will stimulate research on technology for the manufacture of novel diagnostic imaging devices for both invasive and non-invasive techniques.

In NIDCD's intramural research program, scientists are using state-of-the-art neuroimaging techniques, including PET, functional MRI, high density EEG, to: characterize cerebral activity in the normal brain and in patients with neurological disorders affecting voice, speech and language; provide tools necessary to translate these relatively nonspecific findings into the domain of neurochemistry though the development of novel ligands (which can serve as

molecular probes to monitor brain activity); explore the use of neuroimaging techniques as adjuncts in genetic studies; and utilize neuroimaging methods in studies of the evolution of language.

Item

Early Detection and Intervention – It is now clear that early treatment of hearing loss is essential for normal language acquisition. However, the Committee notes that there are many children with late onset and progressive hearing loss who are not identified by Universal Neonatal Hearing Screening [UNHS], so parents and clinicians should be made aware of this in NIDCD newsletters and on the NIDCD website. The Committee supports expanded research on the early detection, diagnosis, and intervention of infants with deafness and other communication disorders. This should include exploring the role of intrauterine exposure to cytomegalovirus [CMV] in progressive hearing impairment. It is also critical to recognize that otitis media, or middle ear infection, is among the most frequent reasons for a sick child to visit the doctor within the first few years of life. The use of antibiotics to treat this disorder is resulting in more strains of bacteria that cause otitis media to be resistant to first and second line antibiotics. The Committee encourages NIDCD to explore alternative ways to either treat or prevent otitis media, which exacts an estimated public health burden of about $5,000,000,000 a year in the United States (p. 141).

Action taken or to be taken

In FY 2004, NIDCD obligated nearly $12 million for research on infant assessment and intervention, an active and important area of the institute's research portfolio. Infants who are born deaf or hard-of-hearing have a better chance of learning language if the hearing loss is found immediately after they are born and if they learn a spoken or signed language as early as possible. For this reason, many states are testing infants for hearing loss right immediately after birth.

In an effort to disseminate health information to parents and clinicians on the importance of early identification and treatment, a series of NIDCD publications on early identification and follow-through for hearing loss and deafness in infants were developed. These family-centered publications address issues of possible hearing problems identified in newborn screening, emphasize the importance of follow-up and provide information to the parent about various interventions and services. These publications are disseminated through the NIDCD newsletter, and through gateway audiences such as the American Academy of Pediatrics, the American Speech-Language-Hearing Association, etc., and by exhibits, health fairs, Web presence and direct outreach to physician and nursing publications and organizations. NIDCD also supports extramural research grants focusing on health communication related to early identification of hearing loss.

Congenital cytomegalovirus (CMV) infection occurs in around 0.5 to 1.5% of live births in the U.S. The public health impact of congenital CMV infection is largely due to its ability to damage the central nervous system, including the auditory system. Hearing loss may be present at birth or may develop during the first few years of life and progress in severity over time. In FY 2005, NIDCD plans to award a new contract solicited under the RFP (request for proposals)

entitled "The Natural History of CMV related Hearing Loss and the Feasibility of CMV Screening as Adjunct to Hearing Screening in the Newborn." The goals of this new initiative are to correlate CMV status at birth with the presence of permanent and/or progressive sensorineural hearing loss; to acquire information on the incidence, time course and audiologic outcomes of CMV related hearing loss; and to determine the extent to which CMV screening can improve detection and predictions of either existing or progressive hearing loss if combined with physiological metrics already in use for newborn hearing screening. It is hoped that the results of this contract will provide critical information on whether infants should, in addition to newborn hearing screening, be screened at birth for evidence of intrauterine CMV infection.

Otitis media (middle ear infection) is the most common reason for a young child to be taken to a physician, and is the most frequent reason that doctors prescribe antibiotic therapy for children. Repeated bouts of otitis media can lead to hearing loss, underscoring the need for a vaccine to prevent this costly and destructive disease. NIDCD intramural scientists have developed a candidate vaccine to prevent otitis media caused by common bacterial pathogens, and have completed Phase I testing of this vaccine in clinical trials. Results of this trial suggest that this investigational vaccine may be useful in preventing otitis media in children. NIDCD-supported scientists have also determined that a strong genetic link is associated with the rate of occurrence of otitis media in children. Studies of the genetic mechanisms responsible for the increased risk and frequency of this disease could lead to additional approaches for intervention and treatment.

Item

Hearing Devices – The Committee encourages the NIDCD to expand research that would improve the benefits of cochlear prostheses and improve remediation of less-than-profound hearing loss through hearing aids and/or new prostheses and drug-delivery systems. Building on the successful clinical implementation of the cochlear implant, the Committee encourages NIDCD to explore the feasibility of electrical stimulation applied to the vestibular system to treat balance disorders (p.141).

Action taken or to be taken

The NIDCD is supporting and encouraging new research that would improve the benefits of cochlear prostheses as well as provide benefits for those with less-than-profound hearing loss. An exciting advancement in cochlear implants is the possibility of a short electrode which is inserted only partially into the cochlea and is designed to be used in experienced, yet unsuccessful, adult hearing aid users with severe-to-profound hearing impairment focused in the higher frequencies of sound. This new electrode is currently being tested in limited patient groups. Newer studies are also investigating the benefits of binaural cochlear implantation (a cochlear implant in each ear), the use of a cochlear implant in one ear and a hearing aid in the other (bimodal stimulation), and the development of new listening and training paradigms to increase the performance of current cochlear implant users.

In addition to these ongoing activities, we expect to award one or more new grant applications in FY 2005 in response to a current RFA on Speech Processor Optimization for Cochlear Implants; this initiative seeks to stimulate innovation in the design of cochlear implants to provide gains in

patient benefit, especially under conditions that are currently correlated with poor patient performance. NIDCD is also developing new implant designs, which incorporate electrodes able to stimulate very restricted groups of neurons. Part of the current research activities include drug delivery systems as well, which will be needed in the future as we combine the power of new molecular tools with electrical stimulation. As technology continues to advance, additional populations of individuals will have the potential to benefit from these remarkable devices.

Hearing aid users want devices that enable them to better understand speech. Two recent surveys demonstrate this desire for improved understanding of speech in noise [3and 4.]. Of all available technologies, directional microphones have shown the most promise for addressing this problem, as demonstrated by clinical studies of individuals with hearing loss. NIH-supported scientists have been studying the tiny fly *Ormia ochracea*, which has such sensitive directional hearing that it has inspired ideas for a new generation of hearing aids as a model for scientists and engineers to use in developing new miniature directional microphones.

The NIDCD and DVA have completed a collaborative multi-site study, "Long-Term Follow-up of Patients in the NIDCD/VA Hearing Aid Clinical Trial" and the results of that study were presented at the annual meeting of the American Speech-Language-Hearing Association, November 18, 2004. Publications will be submitted soon. The results of this study promise to provide direction to clinicians about why some people continue to use hearing aids successfully after they are initially fit with aids and why others do not. Understanding and predicting these outcomes will provide the basis for better diagnostic and aural rehabilitation programs.

NIDCD sponsored a workshop on Electrical Stimulation of the Vestibular Nerve on June 3 and 4, 2004. Fifteen presentations were given by extramural scientists to identify opportunities for development of neural prostheses able to electrically stimulate the vestibular portion of the eighth nerve. Roundtable discussions were held to discuss needs for further basic research, technology platforms for research and development, safety concerns, and to identify clinical populations that would benefit from initial applications of this technology. NIDCD is currently considering these needs and further actions will be forthcoming.

Item

Language Acquisition – The Committee encourages the NIDCD to explore the biological bases of infant speech perception and language acquisition. This should include studies on the impact of partial or profound hearing loss (p.142).

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

[3] Kochkin S. MarkeTrak V: Why my hearing aids are in the drawer: The consumer's perspective. Hear J 53:34-41, 2000.
[4] Kochkin S. MarkeTrak VI : 10-Year customer satisfaction trends in the US hearing instrument market. Hear Rev 9: 14-25, 2002.

million individuals in the United States have some form of language impairment. Exploration of the biological bases of infant speech perception and language acquisition centers on the developing brain, to further our understanding of the neural basis for language and subsequent disorders. The NIDCD supports research projects investigating the role of each hemisphere of the brain in communication and language, and early specialization of the brain. Brain imaging studies are defining the relationship between brain development and speech and language.

NIDCD-supported scientists are also examining how infants, who can acquire any human language, become native speaker-listeners of the ambient adult language. Studies are examining infants' speech perception comparing American English, Danish, French, Italian and Korean. The neural basis of language-specific perceptual attunement is being studied using fMRI (functional magnetic resonance imaging) technology.

NIDCD also supports studies on the impact of partial or profound hearing loss. For example, in FY 2004 the NIDCD funded several new grants in response to an RFA entitled "Auditory/Perceptual Processing by Infants with Hearing Loss: Issues in Assessment and Management", continuing NIDCD activities in the early identification of hearing impairment. Using a multidisciplinary approach, researchers are addressing difficult questions regarding intervention, management and evidence based clinical decision-making.

Item

Stuttering **–** The Committee received testimony concerning stuttering which affects approximately 3 million people in this country. It was learned that healthy individuals who stutter are often labeled as unintelligent, eccentric, mentally ill and/or emotionally disturbed. NIDCD is encouraged to conduct a workshop in fiscal year 2005 on stuttering, which will examine the current state of the science as well as to identify future research opportunities in the field of stuttering and to report to the Committee on the plans for the workshop at next year's hearings (p.142).

Action taken or to be taken

Stuttering is a communication disorder with notable physical and emotional challenges to the speaker and sometimes listener. Though not life threatening, it can be life altering. NIDCD supports and conducts research on stuttering with the goal of reducing its burden on people who stutter. In the past two years one type of treatment for stuttering has received significant media coverage which in turn motivated the NIDCD to review the field of stuttering.

A two and a half day workshop is being planned for March 21-23, 2005 to review what is known about stuttering. The workshop will be held in Washington, DC. Some advocacy groups have expressed interest in co-sponsoring the workshop and details of co-sponsorship are currently being coordinated. Most panel speakers have been invited and are experts in their respective scientific fields. NIDCD-supported scientists and other recognized clinicians and scientists in the field of stuttering will be invited to participate. The workshop will cover: neural, behavioral, genetic, psycholinguistic, and psychosocial variables as well as treatment. The goal is to review the state of the science and generate research recommendations. The workshop audience size

will be small to allow for fruitful discussion among participants. The NIDCD anticipates issuing an initiative as an outcome of this workshop.

Item

Tinnitus – The Committee encourages the Institute to expand its research into mechanisms underlying peripheral and central tinnitus (p.142).

Action taken or to be taken

The NIDCD plans to issue a Program Announcement early in calendar year 2005 to encourage applications for grants to support research on understanding the causes of tinnitus, as well as better ways to diagnose and treat tinnitus

Item

Translational Research – The Committee encourages NIDCD to support research activities aimed at accelerating the translations of new findings from the laboratory bench to the bedside. With the exciting new insights and findings of our molecular and basic sciences in understanding the mechanisms of cell death and disease processes, it is important to provide support for those activities that will translate these findings into new interventions and technologies to better prevent and treat deafness and other communication disorders (p.142).

Action taken or to be taken

Translational research is a critical component of the NIH Roadmap theme, "Re-engineering the Clinical Research Enterprise". To improve human health, scientific discoveries must be translated into practical applications. As part of its mission, NIDCD facilitates the translation of basic biomedical or behavioral research discoveries in the field of deafness and other communication disorders into new clinical and research tools, prostheses and assistive devices, behavioral therapies or interventions and medications. In April 2004, NIDCD held a workshop on Translational Research in Hearing and Balance to identify barriers to and opportunities in translational research and to consider new NIDCD activities and initiatives in support of translational research. In advance of the workshop, seventeen extramural scientists were provided background information on translational research and held pre-workshop teleconferences in the following four areas: Molecular Diagnostics and Therapeutics, Bridging Basic Science to Clinical Science, Clinical Studies, and Introduction and Emergence into Clinical Practice. The NIDCD is currently acting upon several of the workshop recommendations and is in the process of developing initiatives to encourage collaborative research that will have hasten the translation of basic research findings to have practical impact on the treatment and prevention of deafness and other communication disorders. The NIDCD has placed additional importance in translation by creating a new branch within the Division of Scientific Programs to coordinate extramural translational research for the institute. A recruitment action is presently underway for a senior scientist to head this new branch.

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

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2005 Amount Authorized	FY 2005 Appropriation	2006 Amount Authorized	2006 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$380,604,000	Indefinite	$383,826,000
National Institute on Deafness and Other Communication Disorders	Section 464	42§285b	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	13,656,000	b/	13,606,000
Total, Budget Authority				394,260,000		397,432,000

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/
1997	$179,090,000 2/	$189,243,000	$182,693,000	$188,422,000 3/
1998	192,477,000 2/	198,373,000	198,583,000	(0)
1999	213,184,000 2/ 4/	216,995,000	229,887,000	198,857,000
Rescission	0	0	0	(152,000)
2000	235,297,000 2/	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	334,161,000	349,983,000	342,072,000
Rescission				(397,000)
2003	365,929,000	351,376,000	372,805,000	372,805,000
Rescission				(2,423,000)
2004	380,377,000	380,377,000	384,577,000	384,477,000
Rescission	0	0	0	(2,424,000)
2005	393,507,000	393,507,000	399,000,000	397,507,000
Rescission				(3,247,000)
2006	397,432,000			

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 $77,000.
4/ 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 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Office of the Director	4	4	4
Office of Administration	36	33	33
Division of Extramural Activities	9	9	9
Division of Scientific Programs	16	15	15
Division of Intramural Research	83	81	81
Total	148	142	142
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2002	10.8
2003	11.2
2004	12.2
2005	12.2
2006	12.2

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

Detail of Positions

GRADE	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Total - ES Positions	1	1	1
Total - ES Salary	$143,498	$146,368	$149,295
GM/GS-15	22	20	20
GM/GS-14	8	7	7
GM/GS-13	16	15	15
GS-12	16	15	15
GS-11	13	12	12
GS-10	2	2	2
GS-9	6	6	6
GS-8	4	4	4
GS-7	2	2	2
GS-6	0	0	0
GS-5	1	1	1
GS-4	0	0	0
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	90	84	84
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General			
Director Grade	1	1	1
Senior Grade			
Full Grade			
Senior Assistant Grade			
Assistant Grade			
Subtotal	1	1	1
Ungraded	61	61	61
Total permanent positions	91	85	0
Total positions, end of year	155	150	150
Total full-time equivalent (FTE) employment,end of year	148	142	142
Average ES level	ES-4	ES-4	ES-4
Average ES salary	$143,498	$146,368	$149,295
Average GM/GS grade	12.2	12.2	12.2
Average GM/GS salary	$78,787	$80,363	$82,211