DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

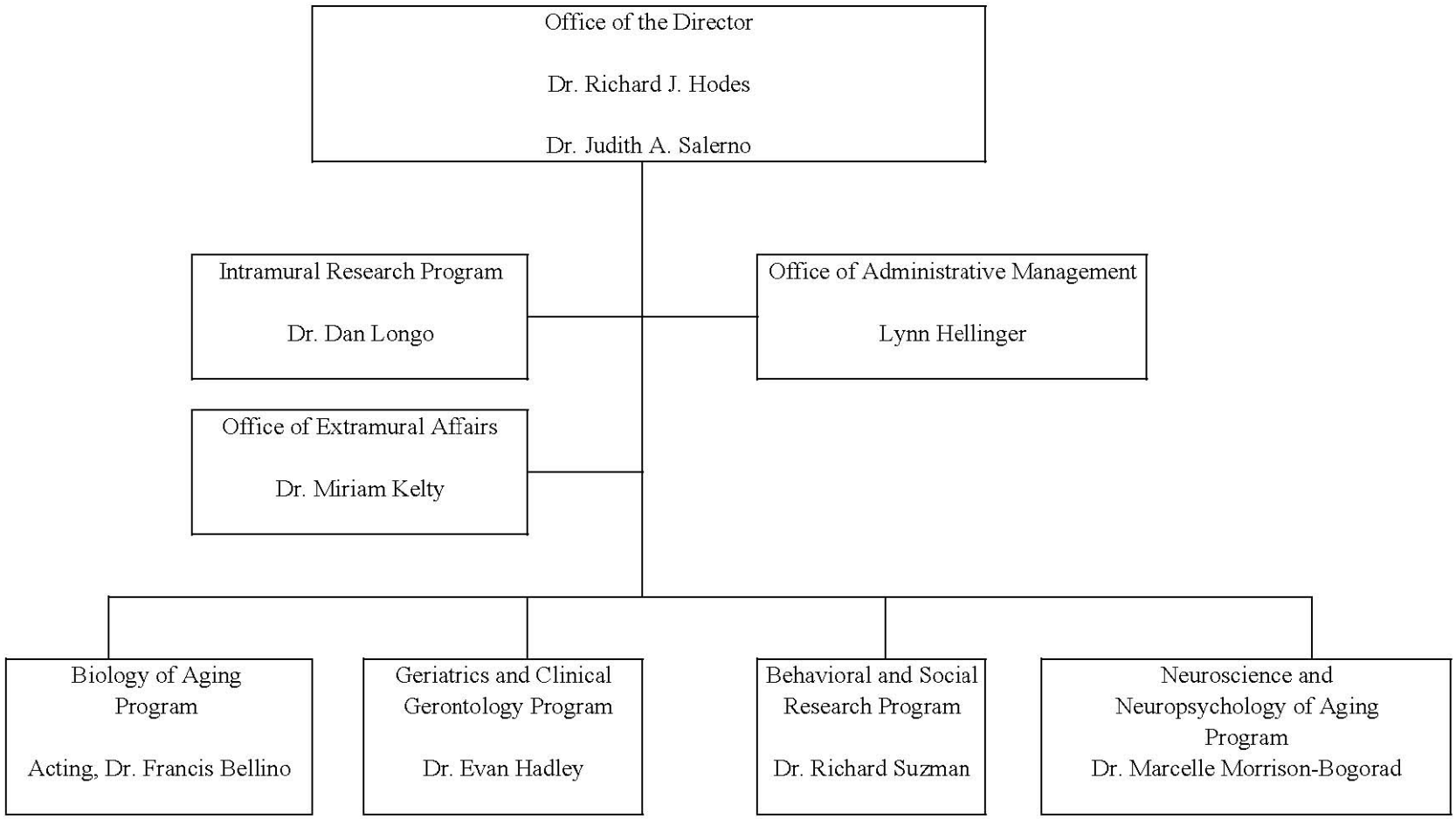
National Institute on Aging

FY 2007 Budget — Page No.

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Organizational Structure



NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

For carrying out Section 301 and title IV of the Public Health Service Act with respect to aging, [$1,057,203,000] *$1,039,828,000*.

[Department of Health and Human Services Appropriations Act, 2006]

National Institutes of Health
National Institute on Aging

Amounts Available for Obligation 1/

Source of Funding	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Appropriation	$1,060,666,000	$1,057,203,000	$1,039,828,000
Enacted Rescissions	(8,676,000)	(10,572,000)	0
Subtotal, Adjusted Appropriation	1,051,990,000	1,046,631,000	1,039,828,000
Real transfer under NIH Director's one-percent transfer authority for Roadmap	(6,651,000)	(9,414,000)	
Comparative transfer from OD for NIH Roadmap	6,651,000	9,414,000	
Subtotal, adjusted budget authority	1,051,990,000	1,046,631,000	1,039,828,000
Unobligated balance lapsing	0	0	0
Total obligations	1,051,990,000	1,046,631,000	1,039,828,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2005 - $1,923,000 FY 2006 - $2,500,000 FY 2007 - $2,500,000
Excludes $1,192,000 in FY 2006 and $21,260,000 in FY 2007 for royalties.

Justification
National Institute on Aging

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended.

Budget Authority:

FY 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
379	$1,051,990,000	374	$1,046,631,000	376	$1,039,828,000	+2	$6,803,000

This document provides justification for the FY 2007 activities of the National Institute on Aging (NIA), including HIV/AIDS-related activities. A detailed description of the NIH-wide FY2007 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR).

INTRODUCTION

There are currently 35 million Americans over the age of 65 – more than at any other time in history. Of these, more than four million are over 85, and some 65,000 have attained their hundredth birthday. In the coming years, the ranks of American elders are expected to swell; the number of individuals age 65 and older likely will double over the next 25 years, reaching 70.3 million and comprising a larger proportion of the entire population, rising from 13 percent today to 20 percent in 2030.[1] Of particular interest is the explosive growth that is anticipated among those most at risk for disease and disability, people age 85 and older, whose numbers are expected to grow from 4.3 million in 2000 to at least 19.4 million in 2050.

The aging of the population presents a number of social and economic challenges as increasing numbers of Americans reach retirement age. It also has important implications for our nation's health. For example, more than half of all Americans over age 65 show evidence of osteoarthritis in at least one joint.[2] Over half of Americans older than 50 have osteoporosis or low bone mass.[3] Cardiovascular disease, cancer, and diabetes remain common among older Americans, and as many as 4.5 million Americans suffer from Alzheimer's disease (AD).[4]

We now know that aging itself is not the cause of disease, disability, and frailty. Rather, disease and disabling processes influenced by age-related changes in the body and by unhealthy choices and sedentary lifestyles are the most important factors in compromising the quality of life for older people. This fundamental shift in thinking was reinforced most recently with insights from the National Long Term Care Survey (NLTCS). According to this study, the rate of disability among older Americans dramatically declined from the 1980s through the mid 1990s, even among people age 85 and older. These findings, along with evidence from a number of clinical trials and other studies, suggest more strongly than ever that disease and disability can be delayed or even prevented through specific interventions.

[1] Federal Interagency Forum on Aging Related Statistics. *Older Americans 2000: Key Indicators of Well-Being.* 2000.
[2] See "Handout on Health: Osteoarthritis," National Institute of Arthritis and Musculoskeletal and Skin Diseases, July 2002.
[3] See America's Bone Health: The State of Osteoporosis and Low Bone Mass in Our Nation. National Osteoporosis Foundation, February 2002.
[4] Hebert LE et al.: Alzheimer disease in the U.S. population: Prevalence estimates using the 2000 Census. Arch. Neurol. 60: 1119-22, 2003.

At the same time, however, this downward trend in disability among the elderly is in real danger of reversal. Data from the National Health Interview Survey have shown that, over the same period, the disability rate actually rose significantly for people ages 18-59, with the two most important causes of disability being musculoskeletal problems, particularly back problems, and mental illness. Findings also indicated that combined disability cases from musculoskeletal problems and diabetes, both of which can be associated with obesity, were increasing more rapidly by the mid-1990s than those from other problems, and that the growing prevalence of obesity is the dominant factor in the rise in disability among individuals ages 50-59.[5] In fact, some demographers are forecasting a complete leveling-off of the disability decline in the coming decade.[6] In addition to the increased suffering at the individual level that such a shift would portend, the socioeconomic implications would be enormous.

The mission of the National Institute on Aging (NIA) is to improve the health and well being of older Americans through an extensive program of high-quality research. The NIA portfolio emphasizes research aimed at increasing the healthspan, or years of healthy, active life expectancy. With guidance from the National Advisory Council on Aging, the NIA conducts and supports research on the biochemical, genetic, and physiological mechanisms of aging in humans and animal models; the structure and function of the aging nervous system; social and behavioral aspects of aging processes and the place of older people in society; and the pathophysiology, diagnosis, treatment, and prevention of age-related diseases, degenerative conditions, and disabilities. In all of its efforts, the Institute pays special attention to reducing health disparities among different groups of Americans. NIA-supported researchers can be found across the Nation, and the Institute also conducts a thriving program of training opportunities for researchers wishing to become involved in aging research.

NIA AND THE NIH ROADMAP

Through a series of broadly-based but integrated initiatives, the ultimate goal of the NIH Roadmap for Medical Research is to accelerate medical discovery and improve people's health. A number of Roadmap initiatives are particularly relevant to aging research:

- The “Molecular Libraries and Imaging” component of the Roadmap will offer biomedical researchers access to small molecules that can be used as chemical probes, providing new ways to explore the functions of genes, cells, and biochemical pathways in healthy aging and disease.
- The “Interdisciplinary Research” initiative will help NIA meet the complex challenges of aging research by encouraging and facilitating the interaction of various disciplines.
- The Roadmap initiative to “Re-Engineer the Clinical Research Enterprise” is studying means to facilitate community-based participation in clinical studies, including clinical trials. Many of the chronic illnesses to which so many older Americans are prone are predominantly cared for in community settings, as opposed to large academic or tertiary-care centers; by bringing clinical trials and other studies into the community, this initiative could have a significant impact on NIA’s clinical research.

[5] Lakdawalla DN, Bhattacharya J, Goldman DP. Are the Young Becoming More Disabled? Health Affairs 23(1): 168-76, 2004.

[6] Goldman DP et al. Consequences of Health Trends and Medical Innovations for the Future Elderly. Health Affairs online special issue “Health and Spending of the Future Elderly.” R5-R17, 2005.

ALZHEIMER'S DISEASE AND THE NEUROSCIENCE OF AGING

Alzheimer's disease (AD) is the most common cause of dementia among people age 65 and older, and is a major public health issue for the United States because of its enormous impact on individuals, families, the health care system, and society as a whole. Scientists now estimate that as many as 4.5 million Americans currently suffer with the disease, and this number is expected to increase almost three-fold by 2050.[7]

People with AD gradually suffer memory loss and a decline in thinking abilities, as well as major personality changes. These losses in cognitive function are accompanied by pathologic changes in the brain, including the buildup of insoluble protein deposits called amyloid plaques and the development of neurofibrillary tangles, which are abnormal collections of twisted protein threads found inside nerve cells. Such changes result in death of brain cells and breakdown of the connections between them. AD advances gradually but inexorably, from early, mild forgetfulness to a severe loss of mental function called dementia. Eventually, people with AD become dependent on others for every aspect of their care. A diagnosis of AD is also associated with a sharply reduced lifespan; for example, the overall median survival for 70-year-olds in the United States is 15.7 years for women and 12.4 years for men, but a recent study found that this drops to 8.0 years and 4.4 years, respectively, for women and men with AD.[8]

Diagnosis of Alzheimer's Disease

Research suggests that the earliest AD pathology begins to develop in the brain long before clinical symptoms yield a diagnosis, and the ability to make an accurate early diagnosis of AD would be highly beneficial. For patients and their families, a definitive early diagnosis provides the opportunity to plan and pursue options for treatment and care, while the patient can take an active role in decision-making. For clinicians, accurate early diagnosis facilitates the selection of appropriate treatments, particularly as new interventions are developed. For researchers, earlier and more accurate diagnosis facilitates clinical studies of new therapies and preventive measures by allowing early and more targeted intervention, before cognitive loss becomes significant.

Nanoparticle-based detection of a possible biomarker for Alzheimer's Disease. Scientists are searching for reliable, valid, and easily attainable biological markers in the blood or cerebrospinal fluid (CSF) that, along with genetic, clinical, and neuropsychological assessments, could identify cases very early in the course of disease. However, in the early stages of disease, concentrations of potential markers may be so low that they cannot be identified accurately using conventional assays. Recently, a new method termed the bio-barcode assay, which uses coated gold nanoparticles as bioprobes, was used to measure the concentration of amyloid-derived diffusible ligands (ADDLs), a potential AD marker, in the cerebrospinal fluid of 30 individuals. ADDL concentrations in the CSF for the subjects diagnosed with AD were consistently higher than the levels taken from non-demented age-matched controls. These results suggest both that elevated levels of ADDLs in the CSF correlate with the presence of the disease and that the bio-barcode assay can be used to measure ADDL concentration in CSF. Although the ultimate significance of this particular marker is not yet known, bio-barcode assays show potential as a

[7] Hebert, op.cit.

[8] Larson EB, Shadlen MF, Wang L, McCormick WC, Bowen JD, Teri L, and Kukull WA: Survival after initial diagnosis of Alzheimer disease. Ann Intern Med 140: 501-509, 2004.

reliable detection method for diagnosing diseases such as AD that is both faster and less expensive than current imaging techniques.

Preventing Alzheimer's Disease

Scientists continue to seek to identify risk and preventative factors for AD in order to delay the onset of the disease or prevent it altogether.

Raloxifene reduces the risk of developing mild cognitive impairment in a clinical trial. Studies of hormonal influences on cognitive aging in women have reported conflicting results, with a number of epidemiologic studies suggesting a decreased risk for AD among users of hormone therapy and more recent clinical trials, notably the Women's Health Initiative Memory Study (WHIMS), showing that post-menopausal women on certain regimens were actually at higher risk for cognitive decline. In a recent study - the Multiple Outcomes of Raloxifene Evaluation (MORE) trial - the selective estrogen receptor modulator (SERM) raloxifene (Evista®), frequently prescribed for the prevention and treatment of osteoporosis, appeared to reduce the risk of cognitive impairment in postmenopausal women. SERMs are compounds that mimic estrogen's actions in some tissues, but block the action of the body's naturally occurring estrogen in others. Raloxifene, like estrogen, promotes bone growth; however, it has anti-estrogenic actions on the breast and uterus that reduce possible cancer-causing stimulation of these tissues post-menopause. Over 5000 MORE participants were assigned to either raloxifene or placebo, and their cognitive function was assessed over the three years of the study. The researchers found that women taking 120 mg/day had a 33 percent lower risk of developing mild cognitive impairment (MCI), frequently a precursor condition to AD, than the other participants. Although extremely preliminary, these results suggest that treatment with raloxifene may offer women cognitive benefits, with fewer health risks than traditional hormone therapy.

DHA protects a mouse model against AD brain pathology. Docosahexaneoic acid (DHA), an omega-3 fatty acid, is involved in multiple functions in the brain, including many related to nerve cell communication. In two recent studies, investigators used AD transgenic mice that were genetically altered to display AD pathology to explore the effects of DHA on the brain. In both of these studies, the investigators fed groups of 17-19 month old mice one of three diets for an average of 100 days – either a control diet (0.09% DHA), a low DHA diet (0%), or a high DHA diet (0.6%). In the first study, the researchers found that the low DHA diet was associated with deleterious effects on brain biochemistry and ultrastructure, as well as cognitive impairment; however, these adverse effects were prevented in the animals receiving the high DHA diet, suggesting that DHA had a protective effect. In the second study, investigators found that the diet high in DHA appeared protective against beta-amyloid production, accumulation, and toxicity, all of which are associated with processes in the human AD brain. In conjunction with previous epidemiological studies suggesting a beneficial effect of DHA consumption on risk of AD, both of these studies indicate a possible role for DHA for the prevention and treatment of age-associated cognitive impairment and AD.

Lifestyle and AD prevention. Studies in mice, dogs, and – increasingly – humans are demonstrating that diet and exercise may have significant benefits on not only physical but also cognitive health. Lifestyle choices that could favorably impact health, particularly cognitive health, are appealing in their potential for accessibility and modest cost. Because such

interventions may be particularly effective at earlier stages of disease development, they could, if validated and widely adopted, have substantial importance for preventing dementia.

Diet: Several previous studies, both epidemiological and laboratory, have suggested that fruits and vegetables that are high in antioxidants may confer protection against cognitive decline with age. In a recent study, data on fruit and vegetable consumption among 13,388 older women over a 10-16 year period were related to subsequent cognitive performance. Researchers found that women consuming the most green leafy vegetables experienced slower decline than women consuming the least amount. Consumption of fruits was not associated with cognition or cognitive decline. The investigators controlled for a wide array of possible confounding factors including education, use of vitamin supplements, physical activity, alcohol intake, and smoking. Findings from this study strengthen the notion that a diet rich in green leafy vegetables potentially may serve to slow cognitive decline.

Exercise: Two recent studies in older adults have demonstrated that engaging in physical activity is associated with better cognitive function, less cognitive decline, and a reduced risk for dementia. In one study, investigators prospectively examined the association between walking and future risk of dementia in older men. Men who walked the least, less than ¼ mile per day, experienced an almost 2-fold increased risk of dementia compared with those who walked the most, more than 2 miles per day. In the second study, researchers examined the association between participation in leisure-time physical activities and cognitive performance and decline in older women. Higher levels of long-term physical activity were strongly associated with better cognitive performance and an approximately 20 percent reduced risk of cognitive decline. This benefit was not restricted to only those engaging in vigorous physical activity. Walking the equivalent of at least 1 ½ hours per week at a 21-30 minutes/mile pace also was associated with better cognitive performance.

Treating Alzheimer's Disease and Cognitive Impairment

To date, the Food and Drug Administration (FDA) has approved four medications for the treatment of mild to moderate AD symptoms and one for the treatment of moderate to severe AD. These drugs improve some patients' ability to carry out activities of daily living, help with behavioral symptoms such as delusions and agitation, and can also help maintain thinking, memory, and speaking skills for a period of time. However, none of these drugs can stop or reverse the disease process, and they appear to help only some patients and only for a period of months to a few years. Finding a truly effective intervention will depend on research progressing on a number of fronts, both in model systems and in humans.

Delay of progression from mild cognitive impairment to Alzheimer's disease (AD) in a clinical trial. Amnestic Mild Cognitive Impairment (MCI), characterized by memory problems not severe enough to be classified as dementia, is considered to be a transitional state that occurs between the cognitive changes of normal aging and very early-stage AD. Previous studies have shown that approximately eight in 10 people who meet criteria for MCI progress to AD within six years of diagnosis and that people with the apolipoprotein E-ε4 (APOE-ε4) gene, the only known genetic risk factor for late-onset AD, progress to AD more rapidly.

The first NIH secondary AD prevention trial, comparing the effects of vitamin E and donepezil (Aricept®) in preventing AD in people diagnosed with amnestic MCI, recently concluded at 69

sites across the U.S. The investigators found that individuals who took donepezil were at reduced risk of progressing to a diagnosis of AD during the first year of the trial, but by the end of the three-year study there was no benefit from the drug. Vitamin E was found to have no effect on AD risk when compared with placebo. As part of the trial, the researchers examined the effect of donepezil and vitamin E on delaying diagnosis of AD among a subset of people with APOE-ε4. While the overall rate of progression to AD was greater in this group, use of donepezil in the APOE-ε4 subset was beneficial for up to three years in reducing the risk of an AD diagnosis.

These findings are the first to suggest than any agent can delay the clinical diagnosis of AD in people with MCI. However, because too little is known about the effects of taking donepezil so early in the disease course on subsequent progression, the results, although promising, do not support a recommendation for the generalized use of donepezil to forestall the diagnosis of AD in people with MCI. Further studies of donepezil and other therapies are needed to assess potential benefit for patients at risk of developing AD.

Do statins protect against AD? Millions of older Americans take medications known as statins to lower cholesterol levels and prevent heart disease and stroke. Some years ago it was reported that the prevalence of AD was significantly lower in individuals who used statins for the treatment of coronary artery disease. This finding prompted researchers and public health officials to investigate whether statins might be useful in treating or preventing AD. Considerable scientific support for this idea has come from studies with animal models. In addition, the first randomized controlled clinical trial designed to test the usefulness of a statin (atorvastatin, Lipitor®) for the treatment of mild to moderate AD showed a cognitive benefit for the statin-treated individuals compared to the placebo group. By contrast, three randomized controlled trials of statins failed to find a protective effect when cognitive decline was considered as a secondary endpoint, and in the past year, findings from three prospective observational studies suggested that statins do not reduce the risk of subsequently developing AD.

Randomized controlled clinical trials remain the gold standard for determining the effectiveness of statins in treating or preventing AD. Currently two large, multi-center, randomized, placebo-controlled clinical trials are underway to assess the efficacy of two different statins for the treatment of mild to moderate AD. One is the NIA-funded CLASP trial using simvastatin (Zocor®), and the other is the industry-funded LEADe trial using atorvastatin. The results of these trials will provide more definitive answers regarding the usefulness of these compounds in the prevention treatment of AD.

Aβ immunotherapy: A therapeutic strategy for Alzheimer's disease. AD pathology is characterized by the accumulation of amyloid plaques and neurofibrillary tangles in the brain. Immunization against amyloid beta (Aβ), or Aβ immunotherapy, is a promising therapeutic approach. Several recent studies have taken advantage of the availability of mouse models that are engineered to exhibit both plaques and tangles in the brain to explore the pathological processes that may be alleviated, and perhaps even reversed, by Aβ immunotherapy.

Recently, researchers injected anti-Aβ antibodies into the hippocampus of transgenic mice that develop both Aβ deposits and neurofibrillary tangles and found that this treatment led to a rapid reduction of extracellular Aβ deposits as well as a reduction of Aβ inside neurons. Surprisingly, this treatment also reversed the early signs neurofibrillary tangle development. When the anti

Aβ antibodies were removed the Aβ pathology re-emerged, followed by the reappearance of tangles. Clearance of Aβ within neurons correlated with reversal of the early signs of cognitive dysfunction. Independent studies from other laboratories have observed similar effects of anti-Aβ antibodies on lesions seen in mouse and rat models of AD. Together, these findings suggest that Aβ immunotherapy may be an effective therapeutic strategy for AD.

Partial rescue of memory function in a mouse model of tauopathy. AD's characteristic neurofibrillary tangles (NFT) consist largely of an abnormal form of a protein called tau. Scientists created a transgenic mouse model whose production of mutant tau could be "switched off" at will. They then allowed the mice to produce tau for a period of time before "switching off" production. They found that that after production of new tau was suppressed, the tau that was already in the brain continued to form NFTs. However, other types of brain damage associated with abnormal tau expression – notably neuron loss – did not occur. Despite continued development of NFTs, spatial memory in these mice was partially restored, suggesting that the processes that lead to memory loss differ from those that cause NFTs in this animal model, and that NFTs do not in and of themselves invariably cause neuron death; these findings also suggest that recovery of memory, even in the presence of pathology, may be possible in the early stages of tauopathies, including AD.

Initiatives in Alzheimer's Disease

In October 2004, the NIA, in conjunction with several other Federal agencies, private companies, and organizations, launched the **Alzheimer's Disease Neuroimaging Initiative** (ADNI) to test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and clinical and neuropsychological assessment can be combined to measure with greater sensitivity the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD). The study could help researchers and clinicians develop new treatments and monitor their effectiveness as well as lessen the time and cost of clinical trials. The project is the most comprehensive effort to date to find neuroimaging and other biomarkers for the cognitive changes associated with MCI and AD. The study, which is taking place at approximately 50 sites across the U.S. and Canada, began recruitment in April 2005; approximately 800 individuals ages 55 to 90 will participate over the five years of the study.

The goal of the **AD Genetics Initiative** is to develop the resources necessary for identifying the remaining late-onset AD risk factor genes, associated environmental factors, and the interactions of genes and the environment. A key component of this initiative is the recruitment of 1000 families with two or more siblings living with AD. To date, an unprecedented alliance of AD Centers, researchers, and outreach personnel, aided by the Alzheimer's Association, has recruited around 800 such families.

The NIH recently released two **Program Announcements aimed at the discovery, development, and preclinical testing** in cellular, tissue, and animal models of novel compounds for the prevention and treatment of the cognitive impairment and behavioral symptoms associated with Alzheimer's disease. The ultimate goal of these PAs is submission of investigational new drug applications to the Food and Drug Administration so that more clinical trials testing promising therapies may be started. The preclinical testing conducted in this program must be followed by human clinical trials to determine if these compounds truly do

have therapeutic benefit; while any direct benefit to patients from the agents tested here may be several years away, the potential long-term public health benefits are enormous.

Advances in Other Areas of Neuroscience

Sleep well to control your appetite. There has been an increasing trend towards shorter sleep times over the last century, with a concurrent trend in the prevalence of obesity in the U.S. Several recent studies have demonstrated a link between sleep and biophysical processes related to appetite and weight control. In one study, young, healthy adults who were restricted to four hours of sleep per night over six days had decreased levels of leptin (a hormone that decreases appetite) and increased levels of ghrelin (a hormone that stimulates appetite) as compared to a fully-rested condition, despite the fact that levels of activity and caloric intake were not altered by sleep restriction. Similar findings were found in a population-based longitudinal study of over 1,000 participants between 45 and 75 years of age: In those who slept less than eight hours per night, body mass index increased as sleep time decreased. As in the first study, short sleep was associated with reduced leptin and elevated ghrelin levels in the blood.
Finally, a study using mice with a mutation that disrupts their circadian rhythms and produces fragmented sleep found a link between sleep disturbances and metabolic syndrome, a cluster of conditions shown to increase risk of heart attack, stroke, and diabetes, suggesting that the brain system controlling the sleep-wake cycle might play a role in regulating appetite and metabolism. Taken together, these findings suggest that getting sufficient sleep may play an important role in weight maintenance.

Parkinson's Disease Genetics: A Decade of Discovery

More than half a million Americans currently live with Parkinson's disease (PD), which is characterized by muscular stiffness, tremor, and difficulty with balance and movement. Typically, the disease progresses until the patient is no longer capable of caring for him- or herself. There is no cure for Parkinson's disease; treatments are largely symptomatic and palliative. PD's symptoms are caused by the death of neurons in the substantia nigra of the brain, an area heavily implicated in muscle control; pathologically, the disease is characterized by the appearance of protein deposits called Lewy bodies in the dead or dying neurons. Whether Lewy bodies are involved in the death of neurons or part of some protective or repair process remains unknown.

We don't yet fully understand the causes of PD, which are likely to be multifactorial and complex. Until recently, scientists believed that PD developed as a result of exposure to a virus, a neurotoxin, or some other environmental agent. However, recent studies, most led or supported by the NIH, have demonstrated that in a small but significant number of cases, PD may be caused by mutations in one or more genes.

The studies described here have involved familial, or inherited, forms of the disease. Familial PD is rare – scientists currently estimate that around 15 percent of PD is directly inherited. However, the discovery of genes for familial PD has assumed critical importance. Because the same genes and proteins that are altered or missing in inherited cases may also be affected in sporadic (non-inherited) cases by environmental factors, studying the genes responsible for the inherited cases can help researchers understand sporadic cases of the disease. Identifying gene defects can also help researchers understand PD's underlying pathology, develop better animal models, identify new drug targets, and improve diagnosis. The discovery of PD genes has opened a window on the inner workings of the disease, providing valuable insights that may eventually contribute to a cure.

The notion that PD may, in some cases, have a genetic basis is not new. There are articles on possible genetic contributions to PD dating back 100 years, and the notion that a small proportion of cases of PD are primarily genetic goes back several decades. However, it was only with the advent of new techniques for rapid genetic analysis in the late twentieth century that scientists had the tools to really effectively seek PD genes. In 1990, investigators identified a large Italian-American family whose members suffered from what appeared to be an inherited form of PD. This family drew the attention of investigators at a major NIH workshop on PD in 1995;

workshop participants concluded that sufficient family data existed for application of modern methods to enable the identification of genes fairly quickly. As a direct result of this workshop, the investigators began to collaborate with NIH scientists on DNA analysis of family members, and in 1997, the genetic culprit – a mutation on the alpha synuclein gene – was identified.

The revelation that some PD could, indeed, be an inherited disease galvanized two separate lines of research: The search for additional PD genes, and investigation into the nature of the alpha-synuclein protein itself. Researchers quickly found that alpha synuclein is a core component of Lewy bodies in both familial and sporadic PD, a discovery that led to the refinement of alpha-synuclein immunostaining techniques as an improved tool for the study of PD pathology. Then, in 2003, NIH investigators made a major discovery regarding the alpha synuclein gene: In a study of an affected family, too many copies of the normal gene caused PD and related neurological conditions. Because the pathology of typical Parkinson's disease was similar to the pathology in this family, the finding was relevant to both inherited and sporadic PD.

Meanwhile, in 2002, Japanese researchers studying a different PD family discovered a linkage of PD to a gene locus somewhere on chromosome 12. NIH researchers recently identified the gene underlying chromosome-12 linked PD, and showed that two mutations in this gene, LRRK2, can cause familial PD. The LRRK2 gene codes for a protein called dardarin, about which little is known. In addition, the group identified a third LRRK2 mutation, called G2019S, as a cause of PD in families from the U.S. and Canada. Following this discovery, the same group of researchers worked with other groups from North America and England to show that this single mutation causes disease in approximately five percent of PD in cases with a positive family history. Interestingly, they also determined that this mutation causes disease in one percent of PD in which there is no obvious family history. In other populations, such as the Portuguese, it accounts for 9 percent of clinic-based patients. As such, this is the most common genetic cause of PD identified to date.

Alpha-synuclein and LRRK2 are only two of the genes that have been identified since 1997; other genes have offered further insight into the mechanisms of disease. For example, like alpha-synuclein, the parkin and UCH-L1 genes are implicated in the removal of protein deposits in the PD brain, and DJ-1 and Pink-1 appear to play a role in protecting the mitochondria – the cells' energy centers -- from oxidative stress, which has long been hypothesized to be important in PD's pathogenesis. These latter two genes are helping us to understand environmental/toxicant pathways that had been known prior to gene discovery.

In addition to the information we're gaining about PD through discovery of related genes, these discoveries may have relevance to other neurological disorders and conditions. For example, the mechanism of disease in the alpha synuclein triplication study is similar to that seen in people with Down syndrome, where patients have three copies of the gene for the amyloid precursor protein, the precursor to beta-amyloid, which accumulates, leading to a form of Alzheimer's disease. This suggests that the same kind of disease mechanisms may be at work in a variety of diseases characterized by protein accumulation in and around cells in the brain.

The search for Parkinson's disease genes has accelerated tremendously in the past decade and has led to important insights about the condition. In the future, elucidating the genetic bases of PD may enable us to identify molecules and pathways that are targets for therapeutic and preventive interventions, to the potential benefit of thousands of Americans who have PD or are at risk.

Low calorie diet protects against Parkinson's disease symptoms in monkeys. The causes of Parkinson's disease are unknown, but increasing evidence suggests that diet and lifestyle may affect the risk of this disease. Recently, NIH researchers found that monkeys who had been maintained on a diet with 30 percent fewer calories than normal controls had significantly higher levels of locomotor activity and less nerve cell damage than control animals when subjected to a neurotoxin to produce PD-like symptoms. Additional findings indicated that the beneficial effects of the low calorie diet may be the result of increased production of two different nerve cell growth factors by brain cells.

Notch protein critical for learning and memory. During brain development, stem cells divide and then form nerve cells, which connect with each other to establish functional nerve cell

circuits. Previous studies had shown that a protein called Notch, which resides on the surface of neural stem cells, controls the formation of nerve cells from the stem cells. Researchers recently created transgenic mice that develop and reproduce normally, but have reduced levels of Notch. These mice exhibited impaired communication at synapses between neurons that are critical for learning and memory in the hippocampus. When a protein that activated Notch was applied to the hippocampus, communication at the synapses was enhanced. These findings suggest an important role for Notch in learning and memory processes and indicate that Notch may be a target for interventions to improve learning and memory.

Discovery of a new population of stem cells in the brain. Stem cells show great promise in treating neurological diseases such as AD and PD. NIH researchers have identified a new population of stem cells, astrocyte precursor cells (APC), in the brain and spinal cord. APCs are derived from a glial-restricted precursor cells (a known type of stem cell); this differentiation is a normal aspect of development, and GRP cell differentiation is biased towards the APC lineage after injury. This bias is due to changes in the brain environment that are characteristic of many neural injuries. Identifying a novel progenitor population and demonstrating its role in development significantly advances our understanding of the capability of the nervous system to replace lost or damaged glial cells. This finding may also have important therapeutic implications.

Gene therapy and exercise as promising therapy for ALS. Amyotrophic lateral sclerosis (ALS) is a progressive and debilitating neurodegenerative disease in which specific neurons in the spinal cord, the motor neurons, degenerate, leading to muscle paralysis and death. In a recent study, investigators successfully used a gene therapy-based approach using a viral vector to treat a mouse model of ALS. In this study, the vector was modified to include a gene that encodes a small interfering RNA (siRNA) – e.g., a molecule designed to interfere with the activity of a specific gene. This particular siRNA was designed to shut down production of the mutant SOD1 protein, which is implicated in the disease. The treatment led to a decrease in the mutant SOD1 protein in the motor neurons, and to an improvement in motor function in the ALS mice. In a separate study, investigators treated ALS mice with a viral vector carrying a gene for insulin-like growth factor 1 (IGF-1), an established neuroprotective agent. Some mice were also allowed to exercise in running wheels. Exercise or treatment alone had therapeutic benefits, including enhanced motor neuron survival, improved motor function, and prolonged life-span. However, exercise in combination with IGF-1 gene delivery provided the greatest benefit on mouse survival and function. The beneficial effect of exercise was dependent on the duration of exercise. These two studies add to the growing body of evidence implicating gene therapy as a very promising therapeutic approach for neurodegenerative diseases, and suggest that future clinical trials should consider incorporating a physical activity regimen in order to get maximal therapeutic benefits in treating neurodegenerative diseases.

REDUCING DISEASE AND DISABILITY

Some 79 percent of people age 70 and older have at least one of seven potentially disabling chronic conditions (arthritis, hypertension, heart disease, diabetes, respiratory diseases, stroke, and cancer).[9] The burden of such chronic conditions is felt not only by individuals, but also by families, employers, and the health care system.

[9] National Center for Health Statistics. *Health, United States, 1999 with Health and Aging Chartbook.* Figure 11, pg. 41. Hyattsville, MD: 1999.

The role of circulating osteoblast "precursor" cells in bone health. Normal bone growth during childhood and maintenance of bone health at subsequent stages of life is in part related to the availability of bone "precursor" cells, which can divide and mature into osteoblasts (cells that make bone) or osteoclasts (cells that break bone down) and therefore serve as a reservoir of cells that can be used to promote bone growth and preserve bone health. Osteoblast precursor cells reside primarily in the bone marrow. A small population has been previously identified in the blood, but the role of these cells in bone health has been unclear.

In a recent study, investigators obtained blood samples from adolescent boys (13-15 years old), adult males (28-49 years old), and three males with fracture. They found functional osteoblast precursor cells in the circulation in significantly greater numbers than had been previously identified. Moreover, levels of osteoblast precursor cells were elevated in men with fractures, suggesting a role for these cells in fracture repair. These findings suggest a more significant circulatory component to the bone formation process than has been previously recognized, and may have relevance to the development of new therapeutic strategies for bone health, as well as to enhancement of fracture healing in humans with impaired fracture repair mechanisms.

Paclitaxel-coated stent reduces restenosis following balloon angioplasty. Restenosis, the gradual narrowing of the arteries that occurs as a consequence of vascular healing that follows angioplasty, is aggravated by the implanting of stents (tiny metal scaffolds placed inside the artery at the injury site to hold the vessel open). Restenosis usually occurs within six months of angioplasty and results from the migration of cells from the middle of the arterial wall into the inner layer of the artery, where they multiply and block normal blood flow. Recognizing that cell division is crucial to the development of restenosis, NIH scientists tested the anticancer drug paclitaxel (Taxol®), which arrests cell division, as a means of preventing the tissue growth that leads to vessel narrowing. They found that stents coated with paclitaxel can significantly delay restenosis, at lower doses and with less toxicity than the higher anticancer doses of the drug. The investigators obtained a patent for these paclitaxel-coated stents, and a cooperative research and development agreement was established with private industry partners.

Today, paclitaxel is one of only two drugs that, when applied to stents, have been shown to safely reduce the incidence of restenosis in humans. FDA approval of paclitaxel-coated stents was granted in March 2004, and currently over 70 percent of the drug-eluting stents used worldwide are paclitaxel-coated. Approximately 1.8 million patients worldwide have received paclitaxel-coated stents to date.

Exendin-4 as a treatment for type 2 diabetes. NIH investigators searching for potential treatments for type 2 diabetes conducted a study of the compound exendin-4. This compound is an analog of the gut hormone GLP-1, which is naturally released after eating and which can lower blood sugar in people with diabetes when given in sufficient doses. Study participants received injections of the drug twice daily for a month. The investigators found that: 1) exendin-4 is well tolerated, 2) it retains efficacy for at least one month, 3) there were no unexpected side effects, and 4) it is at least as effective in lowering blood glucose as current treatments for type 2 diabetes. In April 2004, the Food and Drug Administration approved exenatide (Byetta™), a synthetic derivation of exendin-4, for the treatment of type 2 diabetes.

ACE gene variations, exercise, and physical decline. Clinical trials of exercise to improve strength and enhance aerobic conditioning have shown benefit in improving physical function in

older adults. However, individual responses to exercise programs vary, and the differences in response appear to have a strong genetic component. Research in younger persons has suggested that differences in response to exercise may be related to naturally-occurring differences in a gene for angiotensin-converting enzyme (ACE), a protein that is important in regulating blood pressure. To determine whether these gene variations are related to differences in response to exercise and the development of functional limitations, researchers interviewed 3075 adults, ages 70 through 79 years, about their usual activity during the week before the interview. Genetic studies were performed to categorize each participant as having one of three variations in the ACE gene. Participants were interviewed regularly over a four-year period to determine whether mobility limitations had developed, and rates of developing mobility limitations were compared among exercise groups and genotypes. The investigators discovered that, among older individuals who exercised, people with one of the three variations were more likely to develop mobility limitations than those with other variations. They also found that, regardless of their gene variations, individuals who exercised were less likely to develop mobility limitations than those who did not. This information may ultimately contribute to the design individually-tailored exercise programs to maximize the mobility and independence of older persons

Decreased sensitivity in the brain to estrogen may help explain menopausal changes. The menstrual cycle is maintained through precisely-calibrated interaction between the brain and the ovaries. After the final menstrual cycle, there is a marked decline in estrogen (E) levels. Leading up to this event, changes in menstrual cycle regularity and hormonal patterns occur, as does an increase in symptoms such as hot flashes and night sweats. In one recent study, investigators observed different patterns of hormone fluctuations among perimenopausal women. In one group of women, E levels increased in the early part of the cycle, as is normal among premenopausal women, and this was followed by a surge of luteinizing hormone (LH) – the usual and expected response. In the second, the E levels increased as usual, but LH levels did not. In the third group, E levels did not increase as the cycle progressed and there was no LH surge, but LH levels were higher for most of the cycle. The women in the third group had significantly more hot flashes and night sweats than those in the other two groups. These findings 1) suggest that a specific hormonal pattern linked to increased hot flashes reflects alterations in the sensitivity of the brain to estrogen and 2) provide new clues about hormone influences on hot flashes and night sweats as women approach menopause.

Coronary calcium is a predictor of heart disease in asymptomatic individuals. While calcium is critical to many cellular functions of the body and to bone health, the presence of calcium deposits in blood vessels indicates the development of coronary heart disease (CHD), one of the leading causes of death in the United States for both men and women. Measurement of the extent of calcification in the arteries (known as coronary artery calcium, CAC) may be used clinically to determine the likelihood of subsequent heart attack or stroke in individuals. Findings from a recent observational study suggest that measuring CAC via electron-beam tomography, a noninvasive imaging technique, may also be of value in predicting CHD-related events in individuals who do not demonstrate any signs of heart disease. The ability to detect the earliest stages of CHD in asymptomatic individuals could facilitate the development of more effective prevention strategies and thereby lessen the public health burden of CHD and related deaths.

Initiatives: Reducing Disease and Disability

Although several studies suggest that physical exercise may prevent physical disability in older persons, we lack definitive evidence. The **Lifestyle Interventions and Independence for Elders (LIFE) study** has been designed to conclusively determine whether physical exercise is effective for preventing major mobility disability or death. Currently in its pilot phase, this clinical trial involves comparison of a physical exercise program of moderate intensity with a health education intervention among 400 sedentary persons ages 70-85 years who are at risk of disability.

Based on results of this pilot study, a full-scale, phase III clinical trial, which may involve up to 4,000 participants, is planned for FY 2007. Despite the existence of suggestive data, to date no clinical trials have been completed to definitively establish the effectiveness of an exercise regimen in preventing disability. The public health implications of findings from such studies, when completed, will be tremendous.

Testosterone trials in older men -- Many older men have levels have circulating levels of testosterone well below the range found in healthy young men. Many older men also have conditions that may be related to low testosterone levels – loss of muscle mass, sexual and cognitive dysfunction, and others. Though epidemiologic data and some small intervention studies indicate that testosterone treatment for men with low testosterone levels might indeed alleviate some of these conditions, there are no conclusive clinical trials data on this issue, nor are the adverse effects of this therapy in these populations well understood.

In 2002, the Institute of Medicine (IOM) of the National Academies released a report entitled *Testosterone and Aging – Clinical Research Directions*. In the report, a committee of experts made a number of recommendations, including an initial focus on conducting short-term efficacy trials of testosterone therapy in men ages 65 and over with testosterone levels below those of young adult men, and with conditions or symptoms for which evidence indicates that testosterone treatment may be effective. In response to the IOM recommendations, in September 2005 NIH-supported investigators initiated planning activities, including biostatistical and other data analyses needed for trial design and protocol development. This planning project will be followed by submission (conditional on NIH acceptance) and peer review of a proposal for a full-scale project, which is currently slated to begin mid-2007.

Testosterone supplements remain widely available over the counter, despite the fact that we lack a full understanding of their safety and efficacy. As with hormone therapy in women – epidemiologic evidence suggesting an array of benefits was later refuted by clinical trials demonstrating, in some cases, serious health risks – a full understanding of the risks and benefits of testosterone therapy would have significant public health impact.

BIOLOGY OF AGING

Aging is accompanied by gradual changes in most body systems. Research on the biology of aging focuses on understanding the cellular and molecular processes underlying these changes as well as those accompanying the onset of age-related diseases. As scientists learn more about these processes, studies can be designed to understand when and how pathological changes begin, providing important clues toward developing interventions to prevent or treat disease.

As with other areas of scientific inquiry, interdisciplinary investigation is increasingly identified as a cornerstone of discovery in the biology of aging. For example, NIA supports the Longevity Consortium, a system for rapid generation, review, and funding of new projects to identify and understand longevity genes. This consortium brings together epidemiologists, geneticists, population biologists, statisticians, and others with an interest in the genetic and molecular basis for longevity, and draws on the study populations of fifteen of the largest human aging studies.

Discovery of a new Fanconi anemia gene. Fanconi anemia (FA) is a genetic disease characterized by congenital defects, bone marrow failure, and cancer susceptibility. A group of FA proteins function as a complex machine that is thought to participate in DNA repair; however, the interactions between FA proteins and DNA are poorly understood. NIH researchers have identified a new gene, FANCM, which is mutated in one subgroup of FA patients. FANCM appears to act as an engine that moves the FA DNA repair complex along damaged DNA, and may provide a target for therapies that enhance the FA DNA damage response in patients.

Stem cells and tissue repair. Myocardial infarction or "heart attack" occurs when blockage of one or more of the arteries supplying blood to the heart causes *ischemia*, or loss of blood flow to the heart tissue. The resulting loss of oxygen delivered to those tissues, or *hypoxia*, causes cell death. According to data from the NIH, 1.1 million Americans have heart attacks each year, and in 460,000 the heart attack proves fatal. Recent studies have shown that the body's naturally-occurring stem cells, found within the damaged organ itself and/or drawn from elsewhere (e.g., the bone marrow), may play a key role in recovery from ischemia. Injecting a source of stem cells into the body, either through the circulation or at the site of injury, is known as "cell therapy" and is a rapidly expanding area of research with great clinical promise.

Several recent studies have provided new insight into the mechanisms of tissue repair. In the first study, investigators isolated stem cells from rats' hearts, then induced heart attacks in the rats. The stem cells were then reinjected into the blood stream. The investigators found that the cells were incorporated primarily in the damaged region of the heart, and had developed into myocytes, endothelial cells, and vascular smooth muscle cells, all of which are essential for heart function. Importantly, the cell therapy led to the formation of new capillaries in the damaged region of the heart, and heart function was better preserved as compared to control animals. In closely related studies using dogs and mice, researchers demonstrated that two specific growth factors – hepatocyte growth factor and insulin-like growth factor-1 – could stimulate migration and development of cardiac stem cells in the damaged region of the heart, with beneficial results similar to those described above.

These studies provide new information about the role of stem and progenitor cells in tissue repair. Although further research is needed, these findings suggest that clinical treatment to reduce damage after a heart attack may be possible by growth factor-stimulated recruitment of endogenous cardiac stem cells.

Progenitor cells and potential replacement or support populations defined in adult skeletal muscle. For several decades, the major population of cells responsible for adult muscle maintenance and repair has been thought to be the satellite cells. However, recent evidence indicates that there are several populations of cells in muscle that may be able to form muscle fibers, in addition to the satellite cell. In a recent study, investigators used a variety of means to

compare the role of distinctly characterized satellite cells and other muscle and bone-marrow-derived cell populations in muscle formation. They found that the satellite cell is the only cell resident in the muscle that is fully capable of forming functional muscle fibers; however, results also show that bone marrow-derived cells in the muscle may also be induced to form muscle without fusion with muscle fibers. These cells, while associating with the muscle fiber, appear to be functionally distinct, and may provide important support functions for muscle fibers or progenitors, while the satellite cells provide the major muscle regenerative capacity.

***Klotho* overexpression extends life span in mice.** Previously, investigators noted that a defect in *Klotho* gene expression in mice accelerates the degeneration of multiple age-sensitive traits. In recent studies, several independent lines of transgenic mice that overexpress *Klotho* outlived wild-type controls by 20-30 percent. Through these studies, the investigators determined that Klotho peptide appears to function as a peptide hormone that modulates the insulin/IGF-I signaling pathway and thereby regulates mammalian aging and longevity through effects on cellular metabolism and energy production. This finding opens up the possibility that klotho protein may be useful in the treatment of age-related disorders.

Bone marrow stem cells may cause some age-related changes in tissue function. Most studies of tissue aging look within the tissue or to external (hormonal) factors to identify molecular and cellular mechanisms that compromise tissue function with advancing age. However, evidence is accumulating that in some tissues, bone marrow-derived progenitor cells external to the tissue may be involved in age-related functional decline. In one recent study of a mouse model of renal glomerulosclerosis, at type of kidney disease, older mice with the condition that received bone marrow transplants from younger mice had reduced kidney damage, suggesting that progenitor cells from the bone marrow played a key role in determining the extent of damage and repair. In a different study, investigators found evidence for germline stem cells (GSC) that continuously populate adult ovarian follicles, in direct conflict with the current dogma that follicle formation terminates around the time of birth. These GSCs appear to originate in the bone marrow and can be found in peripheral blood, which carries these cells to the ovary. These studies have implications for both understanding the biology of age-related tissue dysfunction and for therapeutic interventions to ameliorate declining function.

Consequences of cellular senescence in living tissue. Cellular senescence, or the cessation of cell division, has been widely studied in the test tube; however, its relevance to human aging is not well understood. Cellular senescence is achieved in a variety of human tissues by two primary mechanisms: Shortening of telomeres (unique structures at the ends of chromosomes) and expression of cell cycle inhibitors, including those coded in the INK4/ARF locus. NIA-supported researchers have recently made several important findings related to cellular senescence in living tissue:

- Gene expression from the INK4/ARF locus increases in several tissues of mice as a function of age. The increase is retarded by caloric restriction and correlates with age-related tissue dysfunction, suggesting that INK4/ARF expression can be used as a biomarker of aging *in vivo*.
- Telomere shortening may be accelerated by chronic emotional stress.
- Senescent non-malignant fibroblasts can increase the cancer susceptibility of nearby cells, in addition to leading to a decrease in tissue function.

- In several mouse models of premature aging, age-related pathology only becomes apparent in animals that also display shortened telomeres, suggesting that telomere shortening is necessary for the phenotypes of premature aging to be revealed.

In summary, recent research indicates that far from being purely a laboratory-generated phenomenon, cellular senescence is involved in both normal and pathologic processes in living tissue. In fact, cellular senescence may play a significant role in the development of age-related disabilities and pathologies.

BEHAVIORAL AND SOCIAL RESEARCH

Behavioral and lifestyle factors have a profound impact on health throughout the life span. For example, older adults can help to prevent disease and disability and improve their quality of life through healthy behaviors such as proper nutrition and exercise, use of preventive health care, and avoidance of smoking and alcohol abuse. NIA research on behavioral and social factors in aging encompasses a number of areas, including economic implications of aging at both the personal and societal levels, the effects of behavior and attitude on health, and the demographics of aging.

Separate neural systems value immediate and delayed rewards. When given a choice in the "here-and-now," people frequently choose courses of action that lead to immediate rewards, while making very different choices when considering future actions. For example, it is well-established that people often express great eagerness to quit smoking, initiate an exercise program, or begin to contribute to a retirement savings plan…tomorrow. In a recent study, investigators used functional magnetic resonance imaging (fMRI) to measure the brain activity of participants as they chose between an *immediate* monetary reward and a *later* monetary reward. They found that when the participant considered the immediate reward, the brain's limbic system, which is implicated in "emotional" brain processes, was activated, while the more cognitively-oriented lateral prefrontal cortex was activated when the participants considered the longer-term reward. These results converge with those of a series of recent imaging studies that have examined interactions between prefrontal cortex and limbic mechanisms in a variety of behavioral contexts, ranging from economic and moral decision making to more visceral responses such as pain.

Collectively, these studies suggest that human behavior is often governed by a competition between lower level, automatic processes, which may reflect evolutionary adaptations to particular environments, and the more recently evolved, uniquely human capacity for abstract general reasoning and future planning. Increasing our understanding of the dichotomy between the brain's innate response to short- and longer-term rewards is an important first step in developing interventions to discourage tempting but potentially harmful short-term choices while promoting healthier long-term behaviors.

Clinical Practice Guidelines and quality of care for older patients with multiple comorbid diseases. In recent years, Clinical Practice Guidelines (CPGs), which are based on clinical evidence and the consensus of experts, have been developed to guide physicians regarding the management of common medical problems, thus to standardize care and improve its quality for many chronic conditions. However, most CPGs focus on a single disease, and approximately half of persons 65 years and older have three or more concurrent medical conditions. To explore

the applicability of current CPGs to the care of older individuals with several co-occurring diseases, researchers identified the most common chronic medical problems among older persons and then assessed whether the corresponding CPGs addressed issues relevant to older patients with combinations of co-occurring diseases, such as goals of treatment, burden to patients and caregivers, patient preferences, and quality of life. Researchers discovered that most CPGs did not modify or discuss the application of their recommendations for older patients with multiple comorbidities; did not comment on short- or long-term goals of treatment or the burden of care associated with treatment; did not give guidance about incorporating patient preferences into the treatment plan; and in general did not "fit together" well for patients with multiple medical problems. Overall, this study demonstrated that, for older patients with co-occurring medical problems, adherence to CPGs for individual diseases may be counterproductive and even potentially harmful. Additional research is needed to explore methods for adapting existing CPGs or developing new guidelines that optimize care for older individuals.

HEALTH DISPARITIES

The health status of racial and ethnic minority groups in the U.S. has improved steadily over the last century. Despite such progress, disturbing disparities in health persist between majority and minority populations. Demographic projections predict a substantial change in the racial and ethnic makeup of the older population, heightening the need to examine and reduce differences in health and life expectancy

Hospital quality and racial differences in heart attack treatment and outcomes. Black patients who have suffered a heart attack or are at risk are less likely than white patients to receive invasive procedures such as percutaneous coronary interventions (PCI) and coronary artery bypass grafts (CABG), and much evidence suggests that they are less likely than whites on average to receive low-intensity treatments such as aspirin and beta-blocker prescriptions. A key unresolved question is the extent to which the racial disparities are due to physicians and hospitals providing poorer quality care for their black patients than for whites, or whether black patients are more likely than whites to be treated in facilities providing lower quality care for all their patients.

In a recent study, researchers analyzed the records of over 1.13 million adults who were treated for acute myocardial infarction (AMI) at over 4,200 non-federal hospitals from 1997 to 2001. They found that patients of all races were at higher risk of mortality in hospitals with a disproportionate share of African-American heart attack patients. Patients treated at largely minority-serving hospitals were not sicker and did not have more severe heart attacks than patients at other hospitals. The differences in outcomes also were not explained by patients' income, the hospitals' AMI patient volume, region of the country, or urban status.

In related work, investigators reviewed data on Medicare patients treated for AMI in 1994 and 1995 to assess the extent to which differences in the actual hospitals where blacks and whites were treated explain the differences observed in the frequency of specific treatments and in subsequent mortality. They used statistical techniques that allowed them to study whether black and white patients treated *at the same hospital* received different care and had different outcomes, rather than (as in previous studies) whether patients treated at hospitals with similar measurable characteristics had similar outcomes. They found that the overall black-white gap in lower-intensity medical procedures such as prescription of beta-blockers and ACE inhibitors was

entirely explained by differences in hospitals attended; however, blacks received fewer surgical treatments requiring complex referrals and follow-up, such as catheterization, PCI, and CABG, than whites attending the same hospitals. Both of these studies suggest that black-white differentials in medical procedures known to be effective would be greatly reduced by hospital-level interventions to improve quality of care.

INNOVATIONS IN COMMUNICATIONS

NIHSeniorHealth.gov. The NIHSeniorHealth website continues to be a major initiative that enables the growing number of "wired seniors" to find credible aging-related health information in an online format that is compatible with their cognitive and visual needs, as evidenced by NIH-supported research. Conceived by NIA and jointly developed with the National Library of Medicine, the website now includes 23 health topics developed by eleven NIH Institutes. Each month, 140,000 unique visitors browse over a half a million pages. NIHSeniorHealth serves as a model for web designers seeking to make sites accessible to older adults. To increase the number of older adults online, NIA has developed and is evaluating a senior-friendly computer training curriculum for those who train older individuals to use computers.

Special Populations Outreach. The NIA is expanding its efforts to develop and disseminate information to an increasingly diverse older population. For example, the NIA has a broad outreach program to Hispanic health and community centers, libraries, churches, hospitals, and doctors to promote NIA's extensive and increasing Spanish-language publication portfolio. Available materials include booklets and facts sheets on exercise, home safety, caregiving, and AD, as well as 25 Spanish *Age Pages* and *Conversando con su medico*, a cultural adaptation of *Talking with Your Doctor*.

Facilitating Clinical Trials Recruitment. The NIA works with the Alzheimer's Disease Centers to support the Institute's ongoing AD clinical trials program. Communications staff provide expertise in establishing communications plans, identifying audiences, crafting messages, developing materials, and coaching study coordinators in the use of media resources. For example, NIA developed and distributed an award-winning recruitment tool kit for the AD Genetics Study and currently is working with the AD Neuroimaging Initiative to conduct focus groups with the target audience and develop a comprehensive recruitment strategy.

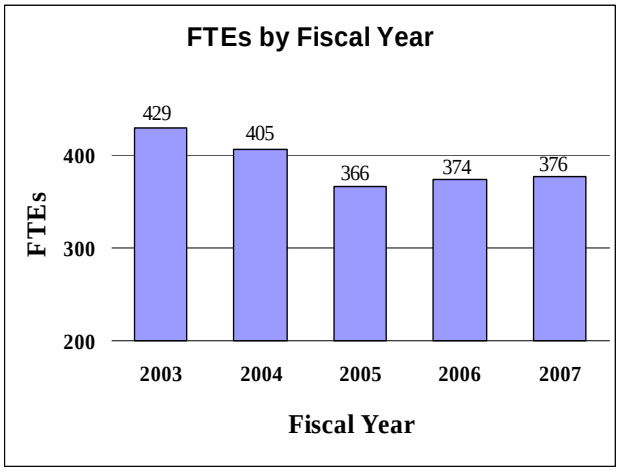
CONCLUSION: Meeting New Challenges through Aging Research

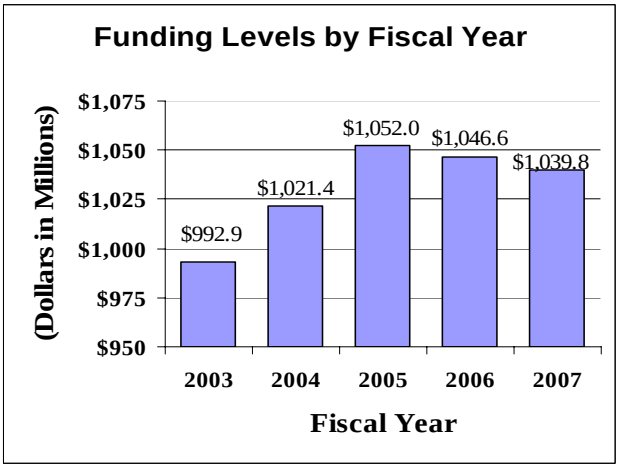
As our population rapidly grows older, it is ever more urgent that we find effective ways to address the often devastating diseases and conditions associated with advanced age. Since the NIA's founding in 1974, groundwork has been laid for today's important advances in understanding basic aging, preventing disease and disability, including AD, and defining special social and behavioral issues for older individuals, their families and caregivers, and clinicians. The latest studies provide additional basic understandings as well as improved interventions to treat, and even prevent, some of the more devastating and disabling aspects of aging. With such research continued and intensified, we can move forward in meeting the promise of a healthy old age by improving the health and well being of older people in America.

BUDGET POLICY

The Fiscal Year 2007 budget request for the NIA is $1,039,828,000, a decrease of $6,803,000 and -0.6 percent from the FY 2006 appropriation. Included in the FY 2007 request is NIA's support for the trans-NIH Roadmap initiatives, estimated at 1.2 percent of the FY 2007 budget request. 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 NIA are shown in the graphs below. Note that as the result of several administrative restructurings in recent years, FTE data is non-comparable.





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. We estimate that the average cost of competing RPGs will be approximately $342,000 in FY 2007. While no inflationary increases are provided for direct recurring costs in noncompeting RPGs, where the NIA has committed to a programmatic increase for an award, such increases will be provided.

NIH must nurture a vibrant, creative research workforce, including sufficient numbers of new investigators with new ideas and new skills. In the FY 2007 budget request for NIA, $630,000 will be used to support 7 awards for the new K/R "Pathway to Independence" program.

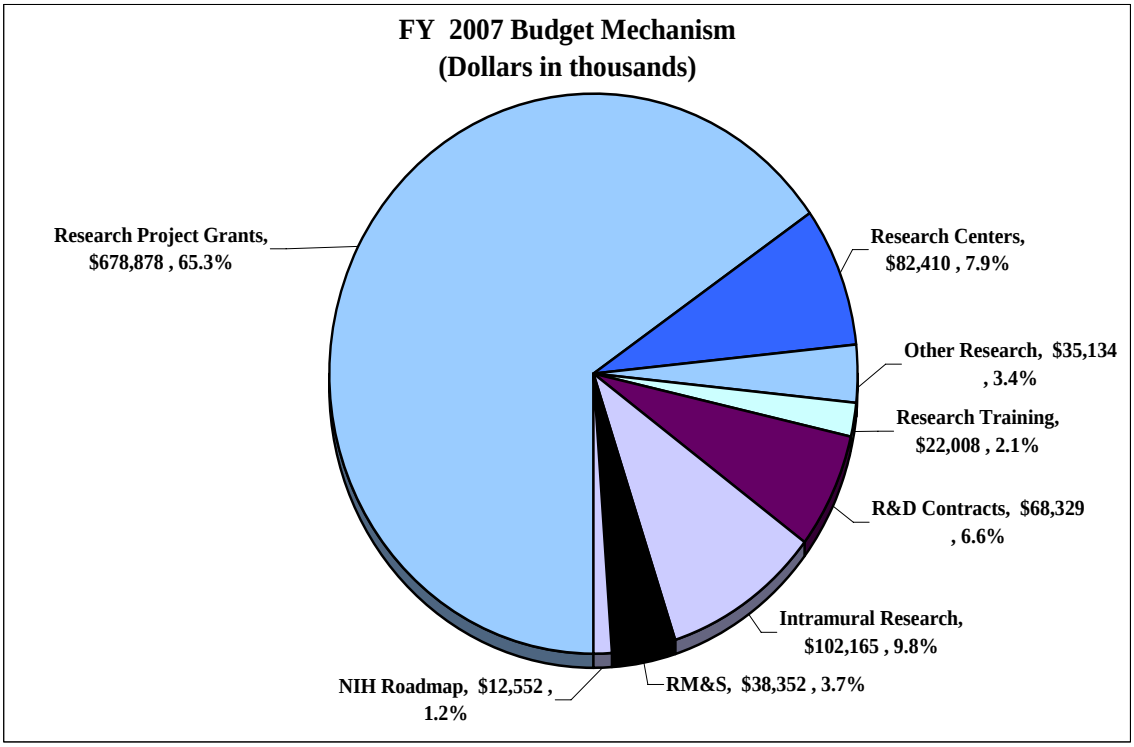
NIA will also support the Genes, Environment, and Health Initiative (GEHI) to: 1) accelerate discovery of the major genetic factors associated with diseases that have a substantial public health impact; and 2) accelerate the development of innovative technologies and tools to measure dietary intake, physical activity, and environmental exposures, and to determine an individual's biological response to those influences. The FY 2007 request includes $1,794,000 to support this project.

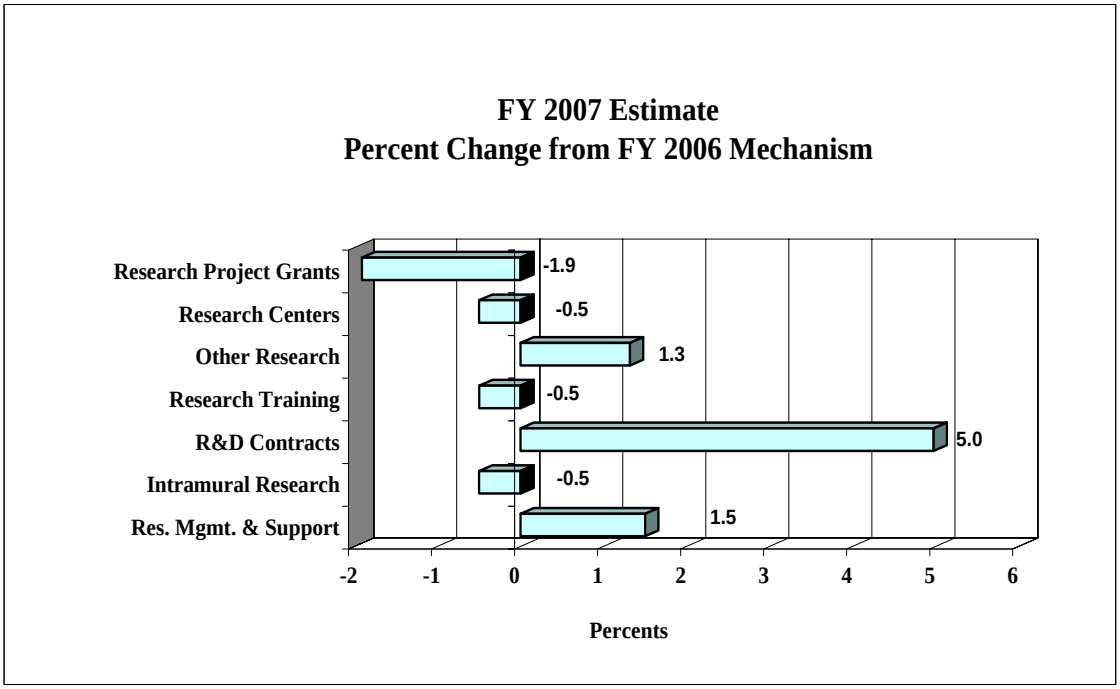
In the FY 2007 request, stipend levels for trainees supported through the Ruth L. Kirschstein National Research Service Awards will remain at the FY 2006 levels.

The FY 2007 request includes funding for 77 research centers, 247 other research grants, including 215 career awards, and 132 R&D contracts. Intramural Research decreases by -0.5

percent and Research Management and Support increases by 1.5 percent.

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





NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Budget Mechanism - Total

MECHANISM	FY 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	1,086	$535,182,000	1,057	$507,451,000	1,094	$502,093,000
Administrative supplements	(118)	15,171,000	(116)	13,079,000	(114)	7,150,000
Competing:						
Renewal	98	56,788,000	112	64,590,000	111	63,950,000
New	275	71,749,000	314	81,534,000	310	80,408,000
Supplements	3	466,000	3	464,000	3	464,000
Subtotal, competing	376	129,003,000	429	146,588,000	424	144,822,000
Subtotal, RPGs	1,462	679,356,000	1,486	667,118,000	1,518	654,065,000
SBIR/STTR	81	25,115,000	81	24,988,000	81	24,813,000
Subtotal, RPGs	1,543	704,471,000	1,567	692,106,000	1,599	678,878,000
Research Centers:						
Specialized/comprehensive	77	82,702,000	77	81,792,000	77	81,383,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0
Comparative medicine	0	1,043,000	0	1,032,000	0	1,027,000
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	77	83,745,000	77	82,824,000	77	82,410,000
Other Research:						
Research careers	199	25,791,000	210	27,485,000	215	27,978,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	2	994,000	2	983,000	2	978,000
Biomedical research support	0	0	0	0	0	0
Minority biomedical research support	0	1,338,000	0	1,323,000	0	1,316,000
Other	29	4,140,000	30	4,886,000	30	4,862,000
Subtotal, Other Research	230	32,263,000	242	34,677,000	247	35,134,000
Total Research Grants	1,850	820,479,000	1,886	809,607,000	1,923	796,422,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	52	2,276,000	49	2,251,000	49	2,240,000
Institutional awards	560	20,088,000	540	19,867,000	537	19,768,000
Total, Training	612	22,364,000	589	22,118,000	586	22,008,000
Research & development contracts	147	62,336,000	132	65,090,000	132	68,329,000
(SBIR/STTR)	(0)	(57,000)	(0)	(57,000)	(0)	(57,000)
	FTEs		FTEs		FTEs	
Intramural research	244	102,805,000	250	102,678,000	252	102,165,000
Research management and support	122	37,355,000	124	37,785,000	124	38,352,000
NIH Roadmap for Medical Research	0	6,651,000	0	9,353,000	0	12,552,000
Total, NIA	366	1,051,990,000	374	1,046,631,000	376	1,039,828,000
(Clinical Trials)		(73,164,000)		(72,600,000)		(71,900,000)

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Budget Authority by Activity

(dollars in thousands)

ACTIVITY	FY 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural research		$ 905,179		$896,815		$886,759		($10,056)
Intramural research	244	102,805	250	102,678	252	102,165	2	(513)
Research management & support	122	37,355	124	37,785	124	38,352	0	567
NIH Roadmap for Medical Research		6,651		9,353		12,552		3,199
Total	366	1,051,990	374	1,046,631	376	1,039,828	2	(6,803)

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Summary of Changes

FY 2006 Estimate				$1,046,631,000
FY 2007 Estimated Budget Authority				1,039,828,000
Net change				(6,803,000)
	FY 2006 Appropriation		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$38,932,000		$535,000
b. Annualization of January 2006 pay increase		38,932,000		302,000
c. January 2007 pay increase		38,932,000		651,000
d. Payment for centrally furnished services		12,201,000		183,000
e. Increased cost of laboratory supplies, materials, and other expenses		51,545,000		1,071,000
Subtotal				2,742,000
2. Research Management and Support:				
a. Within grade increase		15,947,000		218,000
b. Annualization of January 2006 pay increase		15,947,000		124,000
c. January 2007 pay increase		15,947,000		267,000
d. Payment for centrally furnished services		5,307,000		80,000
e. Increased cost of laboratory supplies, materials, and other expenses		16,531,000		316,000
Subtotal				1,005,000
Subtotal, Built-in				3,747,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Summary of Changes--continued

CHANGES	2006 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	1,057	$520,530,000	37	($11,287,000)
b. Competing	429	146,588,000	(5)	(1,766,000)
c. SBIR/STTR	81	24,988,000	0	(175,000)
Total	1,567	692,106,000	32	(13,228,000)
2. Research centers	77	82,824,000	0	(414,000)
3. Other research	242	34,677,000	5	457,000
4. Research training	589	22,118,000	(3)	(110,000)
5. Research and development contracts	132	65,090,000	132	3,239,000
Subtotal, extramural				(10,056,000)
	FTEs		FTEs	
6. Intramural research	250	102,678,000	2	(3,255,000)
7. Research management and support	124	37,785,000	0	(438,000)
11. NIH Roadmap for Medical Research	0	9,353,000	0	3,199,000
Subtotal, program		1,046,631,000		(10,550,000)
Total changes	374		2	(6,803,000)

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Budget Authority by Object

	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	374	376	2
Full-time equivalent of overtime & holiday hours	1	1	0
Average ES salary	$158,385	$163,770	$5,385
Average GM/GS grade	11.4	11.4	0.0
Average GM/GS salary	$79,251	$81,946	$2,695
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$93,593	$96,775	$3,182
Average salary of ungraded positions	120,124	124,208	4,084

OBJECT CLASSES	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	$22,201,000	$23,133,000	$932,000
11.3 Other than Full-Time Permanent	11,206,000	11,677,000	471,000
11.5 Other Personnel Compensation	1,088,000	1,134,000	46,000
11.7 Military Personnel	568,000	592,000	24,000
11.8 Special Personnel Services Payments	9,440,000	9,837,000	397,000
Total, Personnel Compensation	44,503,000	46,373,000	1,870,000
12.0 Personnel Benefits	9,887,000	10,304,000	417,000
12.2 Military Personnel Benefits	407,000	424,000	17,000
13.0 Benefits for Former Personnel	80,000	83,000	3,000
Subtotal, Pay Costs	**54,877,000**	**57,184,000**	**2,307,000**
21.0 Travel & Transportation of Persons	1,114,000	1,131,000	17,000
22.0 Transportation of Things	247,000	251,000	4,000
23.1 Rental Payments to GSA	0	0	0
23.2 Rental Payments to Others	6,000	6,000	0
23.3 Communications, Utilities & Miscellaneous Charges	846,000	850,000	4,000
24.0 Printing & Reproduction	463,000	465,000	2,000
25.1 Consulting Services	827,000	831,000	4,000
25.2 Other Services	10,093,000	9,243,000	(850,000)
25.3 Purchase of Goods & Services from Government Accounts	71,711,000	70,040,000	(1,671,000)
25.4 Operation & Maintenance of Facilities	5,971,000	6,001,000	30,000
25.5 Research & Development Contracts	43,482,000	46,721,000	3,239,000
25.6 Medical Care	386,000	388,000	2,000
25.7 Operation & Maintenance of Equipment	2,385,000	2,397,000	12,000
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	**134,855,000**	**135,621,000**	**766,000**
26.0 Supplies & Materials	9,992,000	10,142,000	150,000
31.0 Equipment	3,149,000	3,196,000	47,000
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	831,725,000	818,430,000	(13,295,000)
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	4,000	0	(4,000)
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	**982,401,000**	**970,092,000**	**(12,309,000)**
NIH Roadmap for Medical Research	**9,353,000**	**12,552,000**	**3,199,000**
Total Budget Authority by Object	**1,046,631,000**	**1,039,828,000**	**(6,803,000)**

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Salaries and Expenses

OBJECT CLASSES	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$22,201,000	$23,133,000	$932,000
Other Than Full-Time Permanent (11.3)	11,206,000	11,677,000	471,000
Other Personnel Compensation (11.5)	1,088,000	1,134,000	46,000
Military Personnel (11.7)	568,000	592,000	24,000
Special Personnel Services Payments (11.8)	9,440,000	9,837,000	397,000
Total Personnel Compensation (11.9)	**44,503,000**	**46,373,000**	**1,870,000**
Civilian Personnel Benefits (12.1)	9,887,000	10,304,000	417,000
Military Personnel Benefits (12.2)	407,000	424,000	17,000
Benefits to Former Personnel (13.0)	80,000	83,000	3,000
Subtotal, Pay Costs	**54,877,000**	**57,184,000**	**2,307,000**
Travel (21.0)	1,114,000	1,131,000	17,000
Transportation of Things (22.0)	247,000	251,000	4,000
Rental Payments to Others (23.2)	6,000	6,000	0
Communications, Utilities and Miscellaneous Charges (23.3)	846,000	850,000	4,000
Printing and Reproduction (24.0)	463,000	465,000	2,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	308,000	309,000	1,000
Other Services (25.2)	10,093,000	9,243,000	(850,000)
Purchases from Govt. Accounts (25.3)	40,963,000	38,958,000	(2,005,000)
Operation & Maintenance of Facilities (25.4)	5,971,000	6,001,000	30,000
Operation & Maintenance of Equipment (25.7)	2,385,000	2,397,000	12,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**59,720,000**	**56,908,000**	**(2,812,000)**
Supplies and Materials (26.0)	9,975,000	10,125,000	150,000
Subtotal, Non-Pay Costs	72,371,000	69,736,000	(2,635,000)
Total, Administrative Costs	**127,248,000**	**126,920,000**	**(328,000)**

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

SIGNIFICANT ITEMS IN HOUSE AND SENATE
APPROPRIATIONS COMMITTEE REPORTS

FY 2006 House Appropriations Committee Report Language (H. Rpt. 108-636)

Item

Alzheimer's disease - The most common cause of dementia, Alzheimer's disease has become one of the most serious threats to the Nation's health and economic well-being. Today, an estimated 4.5 million Americans--one in ten persons over age 65 and nearly half of those over 85--suffer from Alzheimer's disease. That toll will rise to 5.1 million by 2010 and 7.7 million by 2030 unless scientists find ways to stop or slow the progression of the disease process. And unless answers are found soon, Alzheimer's disease will wreak havoc not only on family budgets but on public funds as well. Over the next decade, Medicare spending on beneficiaries with Alzheimer's will more than triple, to $189 billion, while Medicaid spending over the same period will rise to $27 billion. In light of these social and economic imperatives, the Committee was troubled to learn that NIA's investment in Alzheimer research declined in fiscal year 2004 from the previous year. Given the enormous human and financial toll this disease is exacting on society, the Committee strongly urges NIH to expand its investment in Alzheimer research toward an overall goal of $1 billion. NIA should continue to assign the highest priority to this effort. (p. 86)

Action taken or to be taken

Alzheimer's disease (AD) research at the National Institute on Aging (NIA) and the National Institutes of Health (NIH) continues to be a high-priority research area. Since its inception in 1974, the NIA has dedicated the majority of its allocated disease research budget to the study of AD and AD-related processes. The FY 2004 AD spending decrease was the result of an unusually high number of grant applications across all NIA programs and a disproportionate increase in the number of meritorious non-AD relevant applications received that year.

Data indicate that the FY 2004 decrease in AD funding was a unique event and does not represent a persistent trend. The NIH and NIA have funded several major initiatives in FY 2005 to stimulate AD research.

In October 2004, the NIA, in conjunction with several other Federal agencies, private companies, and organizations, launched the **Alzheimer's Disease Neuroimaging Initiative** (ADNI) to test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and clinical and neuropsychological assessment can be combined to measure with greater sensitivity the progression of mild cognitive impairment (MCI) and early Alzheimer's disease. Identification of such markers would mean that clinical trials could be carried out faster and less expensively, important to rapid development of new and effective interventions. The project is the most comprehensive effort to date to find neuroimaging and other biomarkers for the cognitive changes associated with MCI and AD. The study, which is

taking place at approximately 50 sites across the U.S. and Canada, began recruitment in April 2005; approximately 800 individuals ages 55 to 90 will participate over the five years of the study at a funding level of $60 million shared by the ADNI partners.

Another important research endeavor, the **AD Genetics Initiative,** is designed to develop the resources necessary for identifying late-onset AD risk factor genes, associated environmental factors, and the interactions of genes and the environment. A key component of this initiative is the recruitment of 1000 families with two or more siblings living with AD. To date, an unprecedented nation-wide alliance of AD Centers, researchers, and outreach personnel, aided by the Alzheimer's Association, has recruited around 800 such families.

The NIH recently released two **Program Announcements aimed at the discovery, development, and preclinical testing of novel compounds** in cellular, tissue, and animal models for the prevention and treatment of the cognitive impairment and behavioral symptoms associated with Alzheimer's disease and with age-related cognitive decline. With $7 million in committed FY 2006 funds, the ultimate goal of these PAs is submission of investigational new drug applications to the Food and Drug Administration to stimulate the development of clinical trials of promising therapies. The preclinical testing conducted in this program must be followed by human clinical trials to determine if these compounds truly do have therapeutic benefit. The potential long-term public health benefits to emerge from these studies may be considerable.

Item

Down syndrome - The Committee commends NIA for its support of studies to examine the cellular, molecular and genetic bases for age-related neuropathological and cognitive abnormalities in people with Down syndrome. The Committee encourages NIA to further examine these abnormalities and to devise new methods for diagnosing and treating them. Given that all people with Down syndrome develop the neuropathological changes of Alzheimer's disease, and that many or most go on to suffer dementia, NIA is encouraged to consider how studies of the Down syndrome population might enhance the ability to understand, diagnose and treat Alzheimer's disease. The Committee encourages NIA to coordinate its research with NICHD, NINDS, NIMH and other institutes. (p. 86)

Action taken or to be taken

Down syndrome (DS) is the most common genetic cause of cognitive disability of humans, affecting 1 per 1,000 live births. A number of NIA investigators work on DS, as many of these individuals develop some AD symptoms relatively early in life and most develop full-blown AD by middle age. Basic science studies focus on the AD-like pathological changes that take place early in life, and how they develop into full-blown AD pathology in middle age.

In collaboration with NICHD and NCCAM, NIA is currently sponsoring a clinical trial of vitamin E in older DS patients with AD. NIA is also funding a second clinical trial to investigate the effects of a combination of lipoic acid and vitamins E and C in a similar patient population. NIA-supported researchers are also conducting a study of the contribution of polymorphisms in genes involved in estrogen biosynthesis and estrogen receptor function to rate of cognitive decline and risk of Alzheimer's disease in women with DS. Prior studies in the general population suggest that the dramatic declines in estrogen levels following menopause

may play an important role in the etiology of AD. Among women with DS, the average age at onset of menopause is 46 and the average age at onset of AD is 50-55. Thus, in women with DS, the short interval between menopause and AD provides a unique opportunity to examine the influence of endogenous estrogen activity on disease risk in a prospective study.

Persons with DS typically display abnormal structure and function of the synapses, which are the sites of communication between brain cells. A February 2005 meeting sponsored by NINDS with support of the NIA entitled "Down Syndrome: Toward Optimal Synaptic Function and Cognition" brought basic synaptic biologists together with basic and clinical researchers working on DS to discuss the synaptic biology of DS and to identify particular synaptic functions or proteins that might be deficient, therefore may be therapeutic targets.

Item

Parkinson's disease - The Committee commends NIA on its collaboration with Parkinson's researchers at NINDS Udall Centers in helping to discover new Parkinson's susceptibility genes, including dardarin, the most recently discovered Parkinson's gene by an NIA scientist. This research will prove to be invaluable in the development of improved methods of diagnosis, as well as neuroprotective and neurorestorative treatment of Parkinson's disease. The Committee encourages continued collaborations, including additional intramural activities, between NINDS, NIMH, and NIA to enhance understanding of neurodegenerative diseases, particularly Parkinson's. (p. 86)

Action taken or to be taken

NIA's collaborations in this area with other laboratories, both at NIH and elsewhere, have proven extremely fruitful and are expected to continue. For example, NIA intramural scientists, in collaboration with others, have now shown that dardarin mutations directly cause approximately 5 percent of Parkinson's disease cases, making such mutations the most common genetic cause of PD identified to date. Now, these scientists are using dardarin gene mutations to model the disease process, first in cellular and then in animal model systems. Recent results indicate that activity of the protein gene product is required for damaging effects of the protein, at least in cultured cells, potentially suggesting new therapeutic strategies for this disease. NIA scientists are also collaborating with scientists at NINDS to apply HapMap resources to identify other Parkinson's disease risk genes. (The goal of the International HapMap Project is to develop a haplotype map of the human genome, the HapMap, which will describe the common patterns of human DNA sequence variation.)

Item

Age-related bone health - The Committee is aware that age-related bone loss costs $17 billion annually. NIA is urged to address cell senescence and altered cell phenotype in age-related bone diseases, aging's impact on bone response to loading, bone matrix and quality, and bone marrow; and the role of exercise, new anabolics, and stem cells in elderly bone. (p. 87)

Action taken or to be taken

The NIA supports a broad range of research on age-related bone loss, including basic research on bone development and maintenance at the molecular and cellular levels, as well as clinical studies of interventions to forestall age-related bone loss. Ongoing activities are as follows:

- In 2005, the NIA released a Request for Applications (RFA) entitled "The Adipogenic Phenotype in Aging Musculoskeletal Tissues, which calls for research on the effects of aging on the formation of bone vs. fat cells in the bone marrow. The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) will collaboratively fund these awards in FY 2006.
- Several research projects are ongoing under the NIA Program Announcement (PA) "Aging Musculoskeletal and Skin Extracellular Matrix," including a study of collagen function in skeletal aging and a study of age-related changes in the composition and function of joint cartilage. This PA, which is also co-funded by NIAMS, will be re-issued in 2006.
- With the National Cancer Institute, the National Institute on Deafness and Other Communication Disorders, the National Institute on Dental and Craniofacial Research, and the National Institute of Diabetes and Digestive and Kidney Diseases, the NIA supports a PA entitled "Age-Related Changes in Tissue Function: Underlying Biological Mechanisms," which, among other topics, solicits research on changes in adult stem cells and their environment that result in altered tissue and organ function with age.
- The NIA also supports clinical studies on the effects of exercise and of various compounds (e.g., flavonoids, fatty acids, etc.) on bone loss.
- NIA intramural scientists are conducting studies to identify biological indicators of bone quality as assessed by micro-CT in animal models of arthritis and physical inactivity – two conditions that commonly occur among older adult patients. Using this technique, we hope to understand the deleterious effects of arthritis together with physical inactivity on bone quality and how this is influenced by muscle mass and cytokine concentrations.
- State-of-the-art techniques for the evaluation of bone health have been integrated into the Baltimore Longitudinal Study of Aging, including assessment of bone density and age-related changes in the structural integrity of bone. These data will be linked to the systematic evaluation of health behaviors and physiologic and structural evaluations of other body systems, as well as to biological sample banks that can be used to identify indicators of bone health the identification of potential therapeutic targets.

Item

Quality of Life - The Committee encourages studies on quality of life in patients with osteoporosis before and after treatment, and strategies for optimizing treatment of frail nursing home patients at high risk for osteoporotic fracture. The Committee also encourages NIA to expand research on the role of environmental and lifestyle factors associated with osteoporosis and Paget's disease and to work in conjunction with NIAMS on models for Paget's disease. (p. 87)

Action taken or to be taken

The NIA supports a broad range of research on osteoporosis, including basic research on bone development and maintenance at the molecular and cellular levels, as well as clinical studies of interventions, including diet and exercise, to forestall age-related bone loss, osteoporosis and potentially improve quality of life. Ongoing activities are as follows:

- Research relevant to osteoporosis currently being conducted under a Program Announcement entitled "Frailty in Old Age: Pathophysiology and Interventions." The primary goal of this solicitation is to foster research that will enhance our understanding of the complex biology and pathophysiology underlying the geriatric syndrome of frailty. A second goal is to promote the development and testing of interventions targeting pathways believed to play a mechanistic role in the development and progression of frailty.
- A study of trochanteric padding to prevent hip fracture among nursing home patients is ongoing, as are a number of studies on etiology and prevention of falls among older individuals, particularly nursing home patients.
- Several basic research projects are ongoing under the NIA Program Announcement (PA) "Aging Musculoskeletal and Skin Extracellular Matrix," also co-funded by NIAMS, and the PA will be re-issued in 2006. This announcement also called for applications on "How altered matrix composition or structure may predispose tissues to diseases commonly associated with aging, such as Paget's disease or osteoarthritis."
- The NIA supports research on lifestyle factors associated with osteoporosis. For example, a new grant supports studies on effects of intake of certain fatty acids on development of osteoporosis in mice. Another study looks at the effects of aging and vitamin D status on the development of bone-forming cells in the marrow.
- In 2006, with NIAMS, NIA will co-fund a meeting focusing on the etiology, evaluation, and treatment of Paget's disease and fibrous dysplasia of bone.

FY 2006 Senate Appropriations Committee Report Language (S. Rpt. 109-103)

Item

Age-related bone health - The Committee is aware that age-related bone loss costs $17 billion annually. NIA is urged to address cell senescence and altered cell phenotype in age-related bone diseases, aging's impact on bone response to loading, bone matrix and quality, and bone marrow; and the role of exercise, new anabolics, and stem cells in elderly bone. (p. 130)

Action taken or to be taken

Please refer to page NIA- 33 of this document for NIA's response to this significant item.

Item

Alzheimer's disease - The most common cause of dementia, Alzheimer's disease has become one of the most serious threats to the Nation's health and economic well-being. Today, an estimated 4.5 million Americans--one in ten persons over age 65 and nearly half of those over 85--suffer

from Alzheimer's disease. That toll will rise to 5.1 million by 2010 and 7.7 million by 2030 unless scientists find ways to stop or slow the progression of the disease process. And unless answers are found soon, Alzheimer's disease will wreak havoc not only on family budgets but on public funds as well. Over the next decade, Medicare spending on beneficiaries with Alzheimer's will more than triple, to $189 billion, while Medicaid spending over the same period will rise to $27 billion. In light of these social and economic imperatives, the Committee was troubled to learn that NIA's investment in Alzheimer research declined in fiscal year 2004 from the previous year. Given the enormous human and financial toll this disease is exacting on society, the Committee strongly urges NIH to expand its investment in Alzheimer research toward an overall goal of $1 billion. NIA should continue to assign the highest priority to this effort. (p. 130)

Action taken or to be taken

Please refer to page NIA-31 of this document for NIA's response to this significant item.

Item

Bone Marrow Failure Diseases - Every year, between 20,000 and 30,000 Americans are diagnosed with bone marrow failure diseases, which include aplastic anemia, myelodysplastic disorders (MDS), and paroxysmal nocturnal hemoglobinuria (PNH). The highest incidence of these diseases occurs with people age 60 or older, and the number of cases of these diseases will increase each year as the American population continues to age. The Committee urges NIA to collaborate with NHLBI and NCI on research aimed at gaining a better understanding of the causes of these diseases and effective treatments and cures. (p. 30)

Action taken or to be taken:

In 2005, the NIA and the NHLBI released a Request for Applications entitled "Anemia in the Elderly." The goal of this solicitation is to explore the epidemiology, pathophysiology, and clinical aspects (diagnosis, treatment, and prevention) of anemia in older persons; research topics include the extent to which myelodysplasia contributes to "unexplained" anemia in the elderly. Awards under this RFA are anticipated for late 2006. The NIA also supports several basic studies involving age-related changes in hematopoietic stem cells, which – when dysfunctional – are implicated in diseases of the bone marrow. These include studies of changes in DNA repair of hematopoietic stem cells as a function of age, genetic and environmental regulators of stem cell aging, and the role of the stem cells' microenvironment on their function.

Item

Demographic and Economic Research – The Committee commends NIA for supporting the Centers on the Demography of Aging program and expanding its program to include four new centers in 2004 and for supporting the economic and demographic components of the Roybal Centers for Applied Gerontology program. The Committee encourages the Institute to sustain the economic viability of these centers programs in their quest to conduct essential economic and demographic population research as the United States and world age rapidly. The committee encourages NIA to provide the scientific knowledge on population aging issues, especially by fully supporting the Health and Retirement Survey and National Long-Term Care Survey. Data

from these surveys are particularly important for understanding the budgetary impact of population aging and for Congress as it deliberates potential changes to the Social Security, Medicare, and Medicaid Programs. (p.131)

Action taken or to be taken:

The NIA currently supports 13 Centers on the Demography of Aging to support the infrastructure and pilot data necessary for research and program development in demography, economics, and epidemiology. Ongoing activities at the Demography Centers include the award of a contract to the Population Reference Bureau to write a series of research briefs highlighting policy-relevant research ongoing at the Centers; these research briefs will be used to help disseminate research findings to policy makers and to the general public. In addition, in response to a request from the Assistant Secretary for Planning and Evaluation at the Department of Health and Human Services, the NIA is working with the Demography Centers to establish a seminar series for ASPE staff that will draw on the research conducted in the 13 NIA centers.

The ten Edward R. Roybal Centers for Applied Gerontology concentrated in the past year on development of infrastructure for community, industry, and university research and technology partnerships; application and development of new survey techniques and methodology; advances in the forecasting of population health and economic decision making; translation of cognitive theory into cognitive intervention and utility; translation of heath care findings for community populations; application of affective and cognitive theory to medical decision making; development of interactive assessment tools for patient management; and assessment of mobility of older populations.

The Health and Retirement Study (HRS), now in its seventeenth year with seven waves of data, provides a uniquely rich longitudinal data set for the community of scientific and policy researchers who study the health, economics, and demography of aging. Over the past year, HRS data was enhanced through sub-studies such as the ADAMS (Aging, Demographics, and Memory Study) study, which is the first truly national study of dementia prevalence, completing more than 850 in-home assessments. Other innovative sub-studies include mail surveys on diabetes, consumption and time use, and prescription drug coverage. HRS is also adding new content to the study to collect physical measures, enhanced psychosocial measures, cognitive measures to include executive functioning, and biomarker data including blood and DNA.

In addition, HRS is making plans for future developments, to include a new refresher cohort in 2010 of mid-Boomers, born 1954-1959, in-home assessments of cognitive status on selected panel members in the supplemental dementia study, enhanced health content of the survey, and vignettes for calibration of self-reported health and disability.

For nearly twenty-five years, the National Long-term Care Survey (NLTCS) has been the leading source of estimates for disability trends among the elderly population, both institutionalized and living in the community. This longitudinal survey is designed to study changes in the health and functional status of older Americans (aged 65+); it also tracks health expenditures, Medicare service use, and the availability of personal, family, and community resources for caregiving.

Current funding for the NLTCS runs through September 2006. In October 2005, the NIA and the National Academy of Sciences held expert meeting to consider the strengths and weaknesses

of the NLTCS and how such a survey might be redesigned to best address state-of-the-art research questions about disability dynamics. Participants raised a number of issues that are currently under consideration, including the advisability of collecting biomarkers and associated implementation strategies; increasing the frequency of data collection, as the current five-year interval may be too long to effectively track disability changes in the older population; collecting more detailed data on the living arrangements of the disabled; and adding to the screener questions to collect more information about the non-disabled in order to better assess prevalence. The NLTCS Data Monitoring Board recommended that we pursue these issues and options more concretely with another NAS expert meeting. The NLTCS is widely viewed as offering an unparalleled resource for understanding the disability and functioning of the American elderly population, and the NIA remains committed to maintaining a widely-available data resource to analyze disability dynamics throughout the Nation.

Item

Epilepsy - As the population ages, the Committee is concerned about the rapidly growing incidence of epilepsy in senior citizens. Age-related epilepsy caused by stroke, cardiovascular disease, brain tumors, and Alzheimer's disease severely impacts the well-being, independence, and health care needs of these vulnerable patients. The Committee urges the Institute to make research in epilepsy a priority and to coordinate research efforts with the NINDS. (p. 131)

Action taken or to be taken

NIA supports a number of research projects related to epilepsy. For example, the Institute is currently supporting neurobiological studies on glutamate receptors, on excitotoxic neuronal cell death, and on the electrophysiology of neuronal excitability; although not directly focused on epilepsy, these basic studies have the potential to provide insight into the etiology and pathological mechanisms underlying epilepsy. NIA is also supporting a study looking, in part, at the association of certain polymorphisms in the IL-1 cytokine gene with inflammatory processes and neuropathological changes in tissues from patients with Alzheimer's disease, Down syndrome, head injury, and epilepsy. Another study is looking at factors, including age and drug metabolism, involved in phenytoin toxicity in patients prescribed phenytoin for seizure disorders.

With NINDS, in 2005 the NIA released a Program Announcement entitled "Collaborative Awards in Epilepsy Research for Junior Investigators." The purpose of this initiative is to 1) focus attention of junior investigators on research in epilepsy; 2) promote the interaction of basic researchers and clinical scientists; and 3) provide information leading to the prevention and cure of epilepsy. The ultimate goal of this PA is to bring about meaningful advances in understanding the factors that contribute to the development of epilepsy, and to develop interventions and effective treatments that improve the quality of life of people with epilepsy. In addition, representatives from NIA, NIMH and NINDS met with representatives from CURE (Citizens United for Research in Epilepsy) in 2005 to discuss epilepsy-related research supported by NIH and to learn more about CURE's interest in communicating information about epilepsy to scientists and the public.

The NIA will continue to work with NINDS and other ICs via the Interagency Epilepsy Working Group to identify and support relevant research, including workshops such as those proposed from the recent NINDS Epilepsy Benchmarks meeting. Initiatives undertaken through the NIH

Neuroscience Blueprint, a framework to enhance cooperative activities among fifteen NIH Institutes and Centers that support research on the nervous system, may also facilitate progress in epilepsy research.

Item

Health of Older Workers – The Committee acknowledges the NIA's efforts to build a research agenda focused on maximizing older workers' safety, health, productivity, and life satisfaction. NIA is encouraged to collaborate with other agencies, institutes, and centers to further develop this research agenda. In particular, the Committee supports efforts to develop new surveys or piggyback on existing surveys as appropriate to enhance the data available to NIA on aging workers, the designs and parameters of various jobs, and related health information. Research should be conducted to assess the effectiveness, benefits, and costs of worksite health promotion programs and techniques tailored to older workers, and other workplace policies that may influence health and safety. (p. 131/132)

Action taken or to be taken

There has been little study of the cognitive and functional needs of the aging worker in the US, yet cognitive ability and functionality in the work place are significant sources of variance in worker productivity. The NIA has commissioned and received three review papers on work and aging, covering the European concept of "workability," the use of technology in the work force, and definitions of work complexity in the literature. To continue developing research announcements related to the cognitive and functional needs of the older worker, a workshop is planned for 2006 to investigate the factors that contribute to worker functional ability. Participants will provide input on the issues of physiological and cognitive functionality, factors that improve cognitive functioning in the older worker, and the means for developing assessments for functionality.

In addition, the NIA has partnered with the U.S. Census Bureau on the Longitudinal Employer Household Dynamics Project, the mission of which is to combine federal and state administrative data on employers and employees with core Census Bureau censuses and surveys to improve the quality and understanding of survey products, and to conduct or facilitate research on emerging social and economic policy issues. Of particular importance is the development of a data infrastructure of integrated household and firm datasets that relate employers to their employees and vice-versa. This infrastructure facilitates longitudinal research applications in both the household/individual and firm/establishment dimensions, and fills an important gap in the available data on older workers by providing information on the demand side of the labor market.

Item

Osteoporosis - The Committee encourages studies on quality of life in patients with osteoporosis before and after treatment, and strategies for optimizing treatment of frail nursing home patients at high risk for osteoporotic fracture. The Committee also encourages NIA to expand research on the role of environmental and lifestyle factors associated with osteoporosis, Paget's disease, and osteogenesis imperfecta, and to work in conjunction with NIAMS on models for Paget's disease. (p. 132)

Action taken or to be taken

Please refer to page NIA-34 of this document for NIA's response to this significant item.

Item

Parkinson's disease - The Committee commends NIA on its collaboration with Parkinson's researchers at NINDS Udall Centers in helping to discover new Parkinson's susceptibility genes, including dardarin, the most recently discovered Parkinson's gene by an NIA scientist. This research will prove to be invaluable in the development of improved methods of diagnosis, as well as neuroprotective and neurorestorative treatment of Parkinson's disease. The Committee encourages continued collaborations, including additional intramural activities, between NINDS, NIMH, and NIA to enhance understanding of neurodegenerative diseases, particularly Parkinson's. (p. 132)

Action taken or to be taken

Please refer to page NIA-33 of this document for NIA's response to this significant item.

Item

Racial and Ethnic Health Disparities in Later Life - The Committee commends NIA's systematic attempts to build a research agenda to help understand racial and ethnic health disparities in later life. NIA is encouraged to build on its behavioral genetics research program in order to assess genetic and environmental factors in racial and ethnic differences simultaneously, in studies that permit identification of main effects and of interactions. (p132)

Action taken or to be taken:

Advances in genetics, genomics, and statistical methodology have increased our ability to investigate the influence of genes on behavior. Further, it is well recognized that genes may interact with environmental factors to cause variations in genetic expression; efforts to study the interactions of genes and the environment hold much promise for understanding variation in aging. The NIA promotes research that integrates behavioral and social science research with genetics to help elucidate the etiology of complexly determined behaviors that affect how we age, to address gene-environment and gene-behavior interactions, and to gain insight into factors that shape population patterns and rates of aging. For example, the stability and/or change in the contribution of genes and environmental factors to individual differences in risk factors for illness and health behaviors among African Americans over time is still unknown. Using data from the NIA-supported Carolina African American Twin Study of Aging, investigators have begun to describe the origins of variability in health, illness, and health behaviors. The overall goal of this study is to conduct a longitudinal examination of the origins of variability (genetic and environmental factors) in factors that contribute to cardiovascular risk. In another ongoing study, investigators are attempting to identify AD susceptibility genes among Hispanics of Caribbean descent. Hispanics, particularly those from the Caribbean Islands, currently represent 4 percent to 6 percent of population over age 65, but they are the most rapidly increasing ethnic group in this age category in the US. With the increase in numbers of Hispanic elderly, this ethnic group will face many of the diseases associated with advanced age, including AD; in fact,

the investigators have found evidence of a higher prevalence of AD among Hispanics in New York City, and the risk of developing AD in this population also appears to be increased.

Finally, the NIA's ongoing **Healthy Aging in Neighborhoods of Diversity across the Life Span** (HANDLS) study is a community-based, epidemiologically driven research effort designed to focus on evaluating health disparities in socioeconomically diverse African Americans and whites in Baltimore. This unique study assesses physical parameters as well as evaluating genetic, biologic, demographic, psychosocial, and psychophysiological parameters of Black and White participants in higher and lower socioeconomic status over a 20-year period. The full study began in November 2004 within the Reservoir Hill area of Baltimore. Thus far, the study has recruited 989 participants, and recruitment is ongoing.

Item

Social Psychology - NIA is requested to study the feasibility of expanding its portfolio of basic research on social psychology, particularly basic research on stigma and race; well-being; and emotion, heath and disease. (p. 132)

Action taken or to be taken:

NIA supports a long-standing behavioral and social science research program in aging. The extramural research program has a diverse portfolio, including social psychology. The program promotes an integrative approach to the study of health, behavior, stress and coping, and well-being over the life course. Research and training often combine diverse levels of analysis and examine reciprocal interactions among these levels. Examples include the effects of sociocultural, psychological (social, personality), biological, and genetic processes on behavioral and functional aging. Health Disparities research continues as a growing area of study. There are significant differences in adult and old age health and survival across racial and ethnic groups. There are also differences by education, income, wealth, nativity, county, and region. NIA is developing initiatives to study the sources of these differences, the life course processes leading to health disparities, and the potential for interventions to reduce health disparities.

To help set the course for social psychological research on aging, NIA commissioned a study from the National Academy of Sciences' Committee on Aging Frontiers in Social Psychology, Personality, and Adult Developmental Psychology. Preprints of this report, titled, *When I'm 64*, were received in October 2005. Based on their review of health needs and research opportunities, the committee recommended that NIA concentrate support on the areas of motivation and behavior change, social and emotional influences on decision making, social engagement and cognition, and the effects of stereotypes. NIA staff will use the recommendations and supporting detail in setting priorities and developing research portfolios in the coming years.

Item

Thrombosis - The Committee is very pleased with the Institute's plans to further research on anemia and its impact on the elderly, and encourages NIA to continue its collaborative research efforts with other Institutes on the best strategies to diagnose and treat elderly patients with anemia. The Committee believes that NIA collaboration could also be helpful for another area of

age-related hematology research, the study of venous and arterial thrombosis, blood clots that can lead to heart attacks, strokes, or respiratory dysfunction. In light of research findings that age is one of the most important risk factors for thrombosis, the Committee urges NIA and NHLBI to collaborate on a research agenda exploring the underlying causes of thrombosis and its impact on the elderly. (p. 132)

Action taken or to be taken

Advanced age is associated with a dramatic increase in venous and arterial thrombosis. However, the influence of age on disorders of hemostasis is poorly understood, and the biologic mechanisms responsible for this increased risk – and the interactions of these mechanisms – are yet to be fully explored. At present, the NIA is collaboratively working with NHLBI and professional groups to develop a research agenda on thrombosis in the elderly population. The immediate plan is to bring together a working group or think tank in 2006 to identify the needs and research priorities of this area. The recommendations of these experts will help shape the future directions of NIH efforts on thrombosis in the elderly and its complications.

In addition to this planned collaboration, the NIA is supporting several studies of thrombosis and its complications. For example, arterial thrombi often form at the site of a ruptured atherosclerotic plaque. In the VALIDATE Study (Vascular Aging: The Link that Bridges Age to Atherosclerosis), scientists in the NIA Intramural Program are characterizing the composition and structure of atherosclerotic plaques, as well as their longitudinal change over a three-year time period, in an effort to identify risk factors (beyond cholesterol) that underlie the progression and/or rupture of these plaques. Such risk factors, when identified, could serve as future targets for interventions aimed at preventing atherosclerotic plaques from rupturing and, by extension, the formation of arterial thrombi.

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2006 Amount Authorized	FY 2006 Appropriation	2007 Amount Authorized	FY 2007 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$1,024,513,000	Indefinite	$1,017,820,000
National Institute on Aging	Section 41B	42§285b	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	22,118,000		22,008,000
Total, Budget Authority				1,046,631,000		1,039,828,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1998	495,202,000 2/	509,811,000	520,705,000	519,279,000
1999	554,391,000 2/ 3/	565,574,000	596,521,000	596,521,000
Rescission				(395,000)
2000	612,599,000 2/	651,665,000	680,332,000	690,156,000
Rescission				(3,667,000)
2001	721,651,000 2/	790,299,000	794,625,000	786,039,000
Rescission				(285,000)
2002	879,961,000	873,186,000	909,174,000	893,443,000
Rescission				(313,000)
2003	958,155,000	958,155,000	1,000,099,000	1,000,099,000
Rescission				(6,501,000)
2004	994,411,000	994,411,000	1,031,411,000	1,024,598,000
Rescission				(6,557,000)
2005	1,055,666,000	1,055,666,000	1,094,500,000	1,060,666,000
Rescission				(8,676,000)
2006	1,057,203,000	1,057,203,000	1,090,600,000	1,057,203,000
Rescission				(10,572,000)
2007	1,039,828,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research
3/ Reflects a decrease of $1,679,000 for the budget amendment for Bioterrorism

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Office of the Director	23	25	25
Intramural Research Program	244	250	252
Office of Administrative Management	25	25	25
Office of Extramural Affairs	25	24	24
Biology of Aging Program	13	13	13
Geriatrics & Clinical Gerontology Program	11	11	11
Behavioral & Social Research Program	11	11	11
Neuroscience & Neuropsychology of Aging Program	15	15	15
Total	366	374	376
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2003	10.7
2004	10.9
2005	10.9
2006	11.4
2007	11.4

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

Detail of Positions

GRADE	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Total ES Positions	4	4	4
Total - ES Salalry	612,708	631,702	651,287
GM/GS-15	31	31	31
GM/GS-14	28	28	28
GM/GS-13	30	30	30
GS-12	72	72	72
GS-11	39	39	39
GS-10	1	1	1
GS-9	25	25	25
GS-8	18	18	18
GS-7	11	11	11
GS-6	11	11	11
GS-5	3	3	3
GS-4	0	0	0
GS-3	0	0	0
GS-2	0	0	0
GS-1	0	0	0
Subtotal	269	269	269
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	6	6	6
Senior Grade	0	0	0
Full Grade			
Senior Assistant Grade			
Assistant Grade			
Subtotal	6	6	6
Ungraded	92	92	92
Total permanent positions	0	0	0
Total positions, end of year	371	371	371
Total full-time equivalent (FTE) employment,end of year	366	374	376
Average ES salary	$153,177	$158,385	$163,770
Average GM/GS grade	11.4	11.4	11.4
Average GM/GS salary	$76,645	$79,251	$81,946

NATIONAL INSTITUTES OF HEALTH
National Institute on Aging

New Positions Requested

	FY 2007		
	Grade	Number	Annual Salary
Intramural Research	13	2	$85,000
Total Requested		2	