

**Report of the Working Group of the NIH
Advisory Committee to the Director on
Research Opportunities in the Basic
Behavioral and Social Sciences**

December 2, 2004

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Basic behavioral and social science research is of critical importance to the mission of the NIH. Although this work does not directly address disease outcomes per se, behavioral and social processes play a critical role in understanding the links of molecular, genetic, and neural processes with health and disease. Basic behavioral and social science research provides knowledge, methodology, and measures that are essential for prediction, prevention, understanding individual variation, and controlling illness, for minimizing the collateral impact of disease, and for promoting health. Because of its centrality to the NIH mission, it is crucial that basic behavioral and social science research be supported and nurtured. In Winter of 2004, a Working Group of the Advisory Committee to the Director (ACD) was established to examine basic behavioral and social sciences research across the NIH (Attachment A). The committee was composed of 14 members representing a wide range of the disciplines and scientific areas in the behavioral and social science (Attachment B). The Working Group was chaired by Dr. Linda Waite of the University of Chicago and an ACD member and charged with reviewing the existing portfolio of basic behavioral and social sciences research, identifying areas of opportunity, examining barriers to the submission and review of applications in this area, and making recommendations for improving NIH's program in basic behavioral and social sciences research (Attachment C).

Background

Over the past several years, representatives of the behavioral and social sciences and Congress have expressed concern about two issues: 1) the need for greater funding for basic behavioral and social sciences research throughout the NIH in general and at the National Institute of General Medical Sciences (NIGMS) in particular and 2) the lack of a trans-NIH strategy for training in the behavioral and social sciences again with a specific concern about NIGMS support. (Attachment D). Recent changes in priorities at NIMH have lead the Institute to curtail funding for research in basic behavioral and social sciences, causing a particular sense of urgency in the research community. Following recent intensified interest by Congress and in conjunction with NIH leadership, a plan was developed to deal with the concerns raised, which included a review by eminent scientists familiar with the NIH and the relevant research. The Office of Behavioral and Social Sciences Research (OBSSR) was given responsibility for coordinating these activities, with substantial input from NIH leadership.

Importance of Basic Behavioral and Social Science for the Mission of the NIH

Robust, stable, and intriguing findings drawn from a wide range of empirical investigations show that social and behavioral factors are associated with essentially every aspect of health and illness, spanning etiology, course, prognosis, prevention, treatment, interface with health care systems, rehabilitation, and quality of life throughout the entire disease process. Moreover, in a wide range of psychiatric, neurological, and physical illnesses, disturbances and disruptions of normal behavioral and social functioning create the greatest burden for patients and families and

create the greatest economic costs. Of course, the most basic behavioral and social science research does not examine diseases or interventions directly, but rather aims to measure, understand, and control processes in ways that will later enable them to be applied to disease and treatment in meaningful ways. As with all types of basic scientific inquiry, be it in genetics, biology, or the behavioral and social sciences, the direct link between a theoretical construct and health is a result of incremental discoveries that accumulate over time. The location of this basic research at NIH fosters the integration of findings from basic behavioral and social science research with biology, chemistry, and genetics and translation into clinical practice. It also focuses this basic research on health.

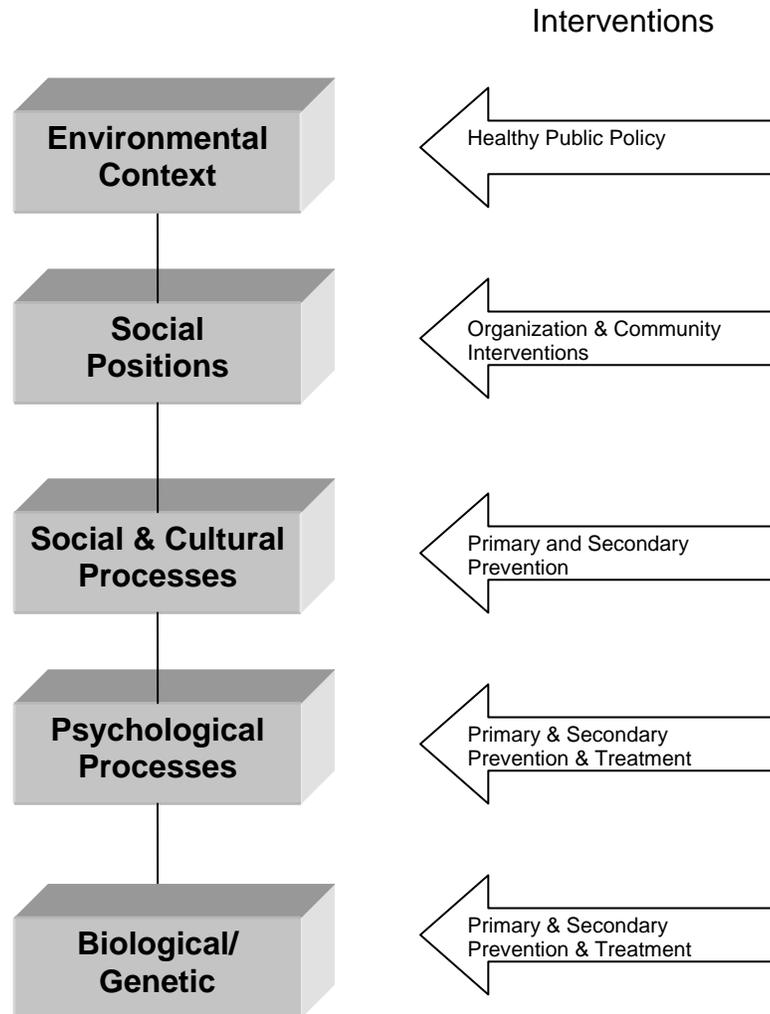
Following are some examples of how basic behavioral and social science findings have shaped understandings about health and illness:

- Experimental research on learning and conditioning with animals and humans introduced behavioral views into models of psychopathology and laid the foundation for most empirically-validated behavioral treatments for the treatment of fears, phobias, depression and other disorders. Many of these behavioral treatments can be used synergistically with or as alternatives to pharmacological treatments.
- General principles of learning and behavior show how harmful behavior can be changed. These observations have led to behavioral change strategies commonly used in prevention programs such as smoking cessation.
- Investigations on social networks and social relationships form the basis for programs that enable families and groups to better assist individuals recovering from an illness.
- Treatments, such as systematic desensitization and exposure therapy, can be traced directly to research on learning in animals.
- Basic research on emotion and affect has provided a more differentiated and nuanced view of the ways that emotional functioning is altered in diseases such as schizophrenia, autism, and a range of neurological disorders.
- Studies of color, motion and pattern perception clarify the role of signals in the retina and visual cortex. This understanding is essential in devising experiments to measure the limits and extent of cortical plasticity following recovery from stroke.
- Basic work on stereotypes, stereotyping and cognitive processing have led to insights about how the medical care system provides unequal treatment to racial minorities even when there is little evidence of external racial bias,
- Research shows that attitudes resulting from strongly persuasive messages are less stable than attitudes based on experience, holding implications for the long-term effectiveness of therapeutic approaches.

It is evident that impressive scientific gains have been made over the past decade in understanding the function of neural circuitry in the brain, neurotransmitters, and genes. Moreover, methodological advances (e.g., in functional magnetic resonance imaging) allow far more precise measurement of biological and genetic factors that contribute to processes of disease and health. However, it is important to note that the application of these scientific advances to the amelioration of disease will most certainly require a much better understanding of the ways that genes, neural circuits, and neurotransmitters impact behavioral and social processes. For this promise to be fulfilled, new methods, theories, and understanding of social and behavioral functions will need to be developed that will be appropriate for linking with the

actions of particular groups of genes and particular neural circuits. At a much more macro level, it is equally clear that environmental contexts and psychological, social, and cultural processes facilitate or constrain vulnerability to disease, risk-taking behaviors, health promotion, proper health care, and re-entry into community living. Figure 1 illustrates the different levels of basic research across environmental context, social position, social and psychological processes, and biological and cellular processes. Figure 1 also shows how basic research in behavioral and social sciences can foster interventions at different levels.

Figure 1. Levels of Causation for Health



Adapted from McKinlay, J. B., & Marceau, L. D. (2000). Public health matters. *American Journal of Public Health*, 90, 25-33, p. 29.

Current Basic Research Portfolio

The Working Group reviewed the current NIH research portfolio in the area of basic behavioral and social sciences research. Institutes and Centers (ICs) provided the Working Group with funding levels and narrative descriptions of the programs within the individual ICs (Attachment E). It is clear that there are a number of strong and vibrant programs that contribute to basic scientific knowledge in this area and support research that forms the foundation for our understanding of the disease etiology and health promotion. It is also clear that many other NIH institutes do not support much, if any, basic behavioral and social science research. The ICs with notable strength in basic behavioral and social science research include the National Institute on Aging, the National Institute on Child Health and Human Development, the National Institute on Drug Abuse, the National Cancer Institute, the National Institute on Alcoholism and Alcohol Abuse, the National Heart, Blood and Lung Institute, and the National Institute of Mental Health. The Working Group applauds these ICs for their past support of basic behavioral and social science research relevant to the NIH mission and encourages them to continue and expand this support. However, it is important to note that all of these institutes that have been supporting basic behavioral and social science research are either linked to a particular developmental period (NIA and NICHD) or a particular set of diseases. There is a clear need for a home for basic behavioral and social science research that is critical for the NIH mission but does not fit into the framework of a particular developmental period or disease.

Opportunities for Funding in Basic Behavioral and Social Sciences at the NIH

While the existing programs have provided important support for basic behavioral and social sciences research, there are many untapped opportunities. Although a comprehensive review is beyond the scope of this Working Group, we identified examples of opportunities that are ultimately likely to make important contributions to understanding and improving health outcomes. These opportunities also demand studies of the biological mechanisms involved.

Macro-Social Behavior

- Social integration and social capital
 - Changes in technology and mobility can undermine neighborhood social networks which, in turn, affect individual capacity for resilience, effectiveness, and connectedness, with implications for health behaviors and health outcomes, all of which need investigation.
 - High levels of immigration have recently altered U.S. race and ethnic relations, changing health outcomes at the level of individual lives, communities, and the Nation. Understanding these dynamics will protect the health of all Americans, old and new, as well as visitors.
- Work-related stresses
 - More demanding jobs and new economic forms challenge the idea of a fixed workplace and its relation to the community, which then impacts work-related stresses, family cohesion, and health; these changes need further study.

- As women have entered the labor force in advanced industrial societies, conflict between work and family has increased, with effects on social stress, human functioning, and health, in ways not fully known.

Social and Interpersonal Behavior

- Stigma and discrimination
 - Prejudice and discrimination create stressors for both perceiver and target; for example, both hate crimes and everyday ethnic incivility pose physical and mental risks via direct stress for targets, indirect stress for other members of target groups, and stress for perpetrators. We need to understand the social processes and biological mechanisms involved.
 - Stigmatization and consequent avoidance of and exclusion from optimal healthcare delivery leads to disparities in health care, perhaps accounting for some health disparities across racial and ethnic groups. This situation needs further study.
- Well-being
 - Well-being depends on motives beyond self-interest, including secure belonging, socially shared understanding, efficacy, self-affirmation, and trust. Studying these motivations can promote healthy behavior, which accounts for enormous differences in individual health outcomes.
 - Self-regulation of emotion, cognition, and behavior depends on a range of genetic, developmental, personality, and social factors, with clear implications for a variety of health behaviors. What factors affect self-regulation? Under what conditions is it impeded or facilitated?
 - Social phenomena affect health and functioning via physiological pathways that might include stress and recovery processes, immune function, endocrine function, and inflammation. We are just beginning to understand the processes involved.
 - Interpersonal processes, memory and executive functions, and emotion systems overlap and combine, suggesting that interdisciplinary teams can address the complex stimuli, complex decisions, and complex environments typical of health behavior.

Perception, Learning, Emotion, and Cognition

- Exercise and cognition
 - Regular moderate exercise improves cognition and prevents onset of Type 2 diabetes, which is a risk factor for dementia. The behavioral and biological mechanisms need to be investigated.
 - People's representations and regulation of habits such as exercise routines and driving may help explain who, when, and how such routines are adopted and endure.
- Fear, anxiety and vigilance
 - Amygdala, hippocampus, and prefrontal cortex operate in long-lasting learning and extinction, with neuronal mechanisms potentially being uncovered at the molecular and cellular levels.
 - Broad mechanisms of arousal, vigilance, and readiness for action follow from basic neural studies of fear, with implications for behavior in emergencies (e.g., accidents

and heart attacks) and in expected but aversive events (e.g., unpleasant medical procedures).

- Emotion, health, and disease
 - The role of stress and emotion in a host of disease states and in the progression of disease-related processes such as immunity and healing has been established.
 - Problems with the regulation of specific emotions have been linked to specific disease processes, such as the role that anger and hostility play in coronary artery disease and hypertension.
 - More precise and differentiated measures of emotional functioning have provided more accurate measures of emotional dysfunction in a range of psychiatric diseases (e.g., schizophrenia, autism) and neurological diseases (e.g., Alzheimer's disease, frontotemporal lobar degeneration) that may provide early warning signs, identify important subtypes, and help monitor improvement with treatment.
- Memory and the life course
 - Short assessment techniques allow physicians to screen for dementia during medical visits. Development of reliable, predictive, easy-to-administer measurement is vital.
 - Older people better remember positive information than negative, pointing to ways to improve the effectiveness of public health messages and holding implications for the assessment and treatment of trauma.
 - Studies combining molecular and cellular techniques with behavioral assessment in animal models are uncovering fundamental mechanisms for memory as well as for disruption of memory in mild cognitive impairment and dementia; these findings are complemented by non-invasive imaging to assess brain regions involved in memory and to follow degenerative processes in the living human brain.
- Perception and behavior
 - Better understanding is needed of the representation of the sensory world in the brain and how that representation leads to behavior.
 - Behavioral studies of perception help develop visual and motor prostheses, improve instrumentation for both normal and impaired individuals, and create training for people losing perceptual capabilities (e.g., age-related macular degeneration) Basic research on perception lays the groundwork.
 - Research on spatial orientation leads to innovations that help people of varying abilities and disabilities navigate space. Novel technologies such as virtual environments promise new insights.
 - It is profoundly important to understand how the brain acquires and retains information. Recent developments in theory and measurement provide opportunities for advances in understanding neural plasticity and regeneration.

Early Development

- Infant temperament
 - Observation and neuro-imaging of young children delineate early individual differences in sensory and emotional processing, with influences over-time on

- development, socialization, and mental and physical health. These differentials need to be explored
- In studies of primate foraging, maternal anxiety and care influence offspring emotionality, with long-term changes in brain regions such as hippocampus. Studies of the relationship between early parenting and brain development hold promise for better understanding of the impact of the social environment on brain development.
- Intergenerational transmission of behavior
 - Behavioral transmission to offspring mediates transgenerational effects on emotionality, which include methylation of DNA, indicating long-term effects on gene expression. We have much to learn about these processes.
 - Cycles of child abuse (abusees becoming the abusers) decreases in individuals possessing alleles of the monoamine oxidase A gene. Why is this the case?
 - Infant pattern recognition
 - Infants rely heavily on detecting correlations between events (pattern detection) to process information, acquire language, and guide behavior. Children at genetic risk for autism and learning disorders apparently fail to understand the salience of such correlations and are unable to attach meaning to patterns. Research on normal perception will be instrumental in early detection and possibly interventions in these serious mental disorders.

Gene-Environment Interactions

- Biology of resilience
 - Genetics and neurobiology of resilience can show vulnerabilities associated with certain genetic traits, early life experiences, and later health habits such as exercise thus, it is important to understand the links among them.
- Precursors of obesity
 - Brain activation patterns to food presentation differ in lean individuals versus obese and recovered obese individuals, which strongly suggest genetic and early life programming during a window of development.
- Biosocial stress markers
 - Vulnerability to depression after a major stressful life event increased in subjects having the short form of the serotonin transporter gene. More understanding is needed to aid diagnosis of vulnerabilities and the mechanism of depression.
 - Chronic stress remodels the brain: it increases amygdala neuron branching, suppresses neurogenesis and branching of dendrites in the hippocampus, and suppresses branching of dendrites in the prefrontal cortex. Results from rodent models resemble structural changes in the human brain in depressive illness. To understand the effects of stress on long-term cognitive and affective reactions, we need to understand the neurological effects.

- **Technology, Measurement and Methodology**
 - Development of technology and methods for collecting biophysical data (biomarkers) in the population setting vastly expands the possibility of deciphering multi-level pathways linking biology, behavior, environment and society.
 - While recent advances in knowledge about the genome have spurred interest in gene-environment interactions, progress will be made only with further investment in research to develop measures to better characterize the relevant social and physical environments.

Cutting Across More Than Two Levels

Some of the most pressing questions about health and illness now facing us involve processes at the level of the population or social group, the individual, organ systems, and the cell. Major advances in understanding these questions will require the skills and collaboration of scientists across a range of disciplines. This will require the integrated training of scientists in biological, behavioral and social sciences. Below we discuss several examples of these overarching challenges and the opportunities for addressing them.

Health disparities continue to be a priority for the NIH. The focus has expanded to include racial/ethnic, socioeconomic and rural/urban disparities in health outcomes. Epidemiological, sociological and demographic studies have revealed linear gradients of morbidity and mortality across socioeconomic status (SES), as reflected in educational attainment or income, which cannot be explained by such factors as smoking or access to health care. The linearity means that these health disparities reach the middle of the SES range, and are not confined to those people with the lowest SES. Moreover, evidence shows that regions of the United States and other nations that show greater gradients of income distribution also show greater effects on such endpoints as mental health and mortality. Racial and ethnic differences also impact health. Clearly, the processes that produce health disparities involve stratification in societies, differential treatment of individuals and social groups, day-to-day interactions among individuals, and affective and physiological responses. New biological and behavioral assessment tools are now available to examine how these gradients “get under the skin” and affect measures of health and quality of life across the life course.

Obesity, diabetes and mood and affective disorders are a growing concern at the NIH. These disorders show disparities across SES and reflect the multiple social, behavioral and biological influences across the lifecourse that must be better understood in order to develop effective treatments. In terms of behavioral treatments, one example is regular, moderate exercise, which has been shown to reduce the incidence of Type II diabetes and to improve executive function and attention, and to have antidepressant effects along with promoting neurogenesis and enhancing neurotrophin levels in the brain. In addition to the physical activity per se, the exercise intervention is also likely to promote social integration and to have other psychological benefits to the participants.

Events early in life play an important role in predisposition to disorders such as obesity, diabetes and mood and affective disorders, but the relevant mechanisms are not well understood

and need intensive inter-disciplinary investigation. Furthermore, data show that early life interventions both in the home and in "head start"- type programs can help to improve both parenting skills as well as the socialization of the children and their readiness to learn. These types of interventions deserve much more emphasis and intensive study, along with implementation of programs such as the "Experience Corps" in Baltimore which brings older adults into schools to assist in the classrooms and school programs. In addition to improving behavior and learning among the children, these programs also benefit the health of the older adult teacher-assistants in similar ways to the benefits of regular exercise. They also improve mood by providing a purpose for living. The social, behavioral and biological aspects of these programs need to be better understood and require collaboration among biological, behavioral and social scientists.

Recommendations

Support for basic behavioral and social science research is critical for advancing the NIH mission. Recent advances in molecular, genetic, and neural areas will create an even greater demand for advances in basic behavioral and social science research if these advances are going to be successfully translated to improving the nation's health and reducing the burden of illness. Although some basic behavioral and social science research is likely to continue to find a home in the ICs where it is seen as meshing with existing programs and priorities, other research-- while extremely germane to the NIH mission-- is unlikely to find a funding source under the current structure. Moreover, as the recent policy and priority shifts within ICs make clear, the current support structure for basic behavioral and social science at NIH is fragile, pointing to the need for a secure and stable home for this important research.

By providing a secure and stable home for basic behavioral and social science research at NIH, the translation of this important research to health and disease applications will be greatly facilitated. We anticipate that this will dramatically enhance the integration of basic and applied research in the behavioral and social sciences at the NIH.

In order to achieve these goals, the Working Group makes two general recommendations, each elaborated in greater detail below:

Recommendation 1: A secure and stable home should be established at NIH that can serve to foster basic behavioral and social sciences research that is not closely linked to the missions of the categorical Institutes and Centers. This will require both staff with appropriate expertise in the behavioral and social sciences and budget sufficient for the task.

Recommendation 2: The basic behavioral and social science research programs that are currently functioning well within ICs should continue in their present form. Efforts should be made to encourage basic behavioral and social science researchers whose research is applicable to specific diseases, conditions, or developmental periods to seek support from the relevant ICs.

The goals of providing a secure and stable home for basic behavioral and social science research at NIH and ensuring NIH-wide support of training in the basic behavioral and social sciences can be achieved most effectively through a two-pronged strategy, the Working Group believes. This strategy centers on OBSSR and an existing non-categorical Institute.

OBSSR

OBSSR would be given increased planning and budget authority for basic research in the behavioral and social sciences at NIH that fits within existing ICs. OBSSR would help develop priorities for basic behavioral and social science research, in conjunction with ICs, and with the advice of the research community. OBSSR would maintain a continuing review of the grants portfolios of ICs in basic behavioral and social science research. It would work with the staff at various ICs to develop research initiatives consistent with the research priorities and would allocate funds to ICs for these initiatives. These research initiatives would then be communicated to the research community by staff and public announcements in a top-down approach to encouraging basic behavioral and social science research.

Because this recommendation would necessitate an increase in the staffing and funding for OBSSR, the Working Group recommends that NIH seek appropriations from Congress for this purpose.

The Office of AIDS Research provides an organizational model for this kind of structure. OAR has responsibility for a sizeable budget but, funds no grants directly. Rather it works with staff of ICs to develop funding priorities, which are then built into future budget requests.

The Working Group feels that this part of the recommended solution has a number of important advantages. OBSSR would start this effort from a strong base of scientific expertise in basic behavioral and social science research. OBSSR is well positioned to review and evaluate the basic behavioral and social science research portfolios of ICs, providing a trans-NIH perspective and program. The Office has close working relations with staff in ICs on which to build this new program. The Office currently works with ICs to develop research initiatives, allowing for an extension and expansion of the current efforts to basic research.

However, the proposed solution leaves investigators who would like to propose research projects in basic behavioral and social science for NIH funding with no obvious Institute to which to submit proposals. OBSSR funds no investigator-initiated grants directly and does not have organizational structures in place to administer a sizeable program of investigator-initiated research in basic behavioral and social sciences. The Working Group recommends that such a research program be established in an existing Institute with the administrative and organizational structures to support such research.

Investigator-Initiated Research in Basic Behavioral and Social Science

Basic behavioral and social science research that is not linked to a disease or a developmental period has no source of funding within the current structure of NIH. The Working Group

recommends that a home within an existing non-categorical Institute be established for basic behavioral and social science research that does not fit within the current IC structure. This would allow the direct funding of basic behavioral and social science research by an institute, building on a great deal of generic experience in developing, managing and funding research. This model has worked well for basic biological research, which is currently supported within NIGMS, and might provide an organizational model for this recommendation. NIGMS, NIA and NICHD are examples of existing non-categorical ICs that could provide a stable and supportive home for basic behavioral and social sciences research.

A non-categorical institute, well-established, and devoted to basic science, with considerable resources would have much to recommend it. Moreover, such an institute also has the structures in place that could support a new section on basic behavioral and social science-- separate grants management, grants oversight programs, links to peer review. Such an institute requires staff familiar with basic behavioral and social sciences research and an organizational structure for dealing with such research. In building this capability at an existing institute, the advice and assistance of OBSSR and the other NIH institutes that have historically funded basic behavioral and social research would be invaluable.

The Working Group recommends that any needed appropriations for the additional staffing and program development that would be needed at to establish such a program be sought from Congress.

REVIEW: The Working Group was also given responsibility for considering issues regarding the review of basic behavioral and social sciences research. The interdisciplinarity of a large portion of the basic research opportunities presents unique challenges for review of the applications, including the development of a pool of reviewers with integrated training in biological, behavioral and social sciences. Also, the changing assessment of where the cutting edge research is occurring in the basic area requires constant evaluation to ensure that the review remains appropriate to the task of finding the most innovative and scientifically meritorious applications. The Working Group recommends that the organization charged with overseeing the research and training in basic behavioral and social sciences research work closely with the Center for Scientific Review to assess the existing review of basic behavioral and social sciences research and ensure that as the area continues to develop the review remains appropriate to the changing array of applications.

Attachment A

Basic Research

OMB Definition: Basic research is defined as systematic study directed toward fuller knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific applications toward processes or products in mind.

Basic research in the behavioral and social sciences is designed to further our understanding of behavioral and social functioning. As is the case for basic research in the biomedical sciences, basic behavioral and social sciences research does not address disease outcomes per se, but is designed to elucidate behavioral and social phenomena. Consequently, basic research may provide essential knowledge necessary for better prediction, prevention, and control of illnesses.

Basic behavioral and social research is divided into three categories: (A) research on behavioral and social processes; (B) biopsychosocial research; and (C) research on the development of behavioral or social procedures for measurement, analysis, and classification.

A. Research on behavioral and social processes involves the study of human or animal functioning at the level of the individual, small group, institution, organization, community or population. At the individual level, this research may involve the study of behavioral factors such as cognition, memory, language, perception, personality, emotion, motivation, and others. At higher levels of aggregation, it includes the study of social variables such as the structure and dynamics of small groups (e.g. couples, families, work groups, etc.); institutions and organizations (e.g. schools, firms, religious organizations, etc.); communities (defined by geography or common interest); and larger demographic, political, economic, and cultural systems. Research on behavioral and social processes also includes the study of the interactions within and between these levels of aggregation, such as the influence of sociocultural factors on cognitive processes or emotional responses. Finally, this research also includes the study of environmental factors such as climate, noise, environmental hazards, and residential environments and their effects on behavioral and social functioning and vice versa.

B. Biopsychosocial research (also known as biobehavioral or biosocial research) involves the study of the interactions of biological factors with behavioral or social variables and how they affect each other (i.e., the study of bidirectional multilevel relationships). Examples of research topics include: behavioral genetics, behavioral and cognitive neurosciences, psychoneuroimmunology, psychopharmacology, and behavioral cardiology.

C. Research on the development of procedures for measurement, analysis, and classification involves the development and refinement of procedures for measuring and analyzing behavior, psychological functioning, or the social environment. This research is designed to develop research tools that could be used in other areas of behavioral and social sciences or in biomedical research.

Examples of research topics in the area include: statistical modeling techniques; memory assessment; behavioral observation procedures; psychometric analysis of self-report instruments; qualitative and ethnographic methods; neuropsychological assessment; psychophysiological methods; pain assessment; and instruments for determining dietary intake; and assessment of medical adherence.

Attachment B

Working Group of the NIH Advisory Committee to the Director on Research Opportunities in the Basic Behavioral and Social Sciences

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Attachment C

Charge to the Working Group on Research Opportunities in the Basic Behavioral and Social Sciences

As part of the examination of basic behavioral and social sciences across the NIH, the NIH Director is establishing this working group of the Advisory Committee to the Director (ACD), NIH. This Working Group is chaired by a member of the ACD and consists of outside experts charged to:

- 1) Address issues related to NIH's support for research in the behavioral and social sciences that is fundamental to the prevention, treatment, and cure of illnesses but is not directed at a specific disease or condition. Specifically to:
 - review the existing portfolio of basic behavioral and social sciences research across the NIH;
 - identify areas of opportunity in basic behavioral and social sciences, consistent with NIH's mission, that NIH should consider supporting; and
 - examine the barriers to the submission and peer review of grant applications in the basic behavioral and social sciences.
- 2) Make recommendations for improving the basic behavioral and social science program of the NIH.
- 3) Complete the review and development of recommendations in the Fall of 2004.
- 4) Provide recommendations to the Advisory Committee to the Director, NIH, for deliberation and final recommendations to the Director, NIH.

Attachment D: Congressional Action on Behavioral Research at the National Institute of General Medical Sciences (NIGMS)

Purpose	Year	Law/Bill No.	Directive from Report	NIH Action to be Taken
Establishment	1962	P.L. 87-838 Sec. 442	“Establishment of Institute of General Medical Sciences. Sec. 442. The Surgeon General is authorized, with approval of the Secretary, to establish in the Public Health Service an institute for the conduct and support of research and research training in the general or basic medical sciences and related natural or behavioral sciences which have significance for two or more other institutes, or are outside the general area of responsibility for any other institute, established under or by this Act.”	
Current Codified Mission Statement	1985	42 U.S.C. §285k	“The general purpose of the National Institute of General Medical Sciences is the conduct and support of research, training, and, as appropriate, health information dissemination, and other programs with respect to general or basic medical sciences and related natural or behavioral sciences which have significance for two or more other national research institutes or are outside the general area of responsibility of any other national research institute.” (July 1, 1944, ch. 373, title IV, Sec. 461, as added Pub. L. 99-158, Sec. 2, Nov. 20, 1985, 99 Stat. 857.)	
Appropriations	FY 1999	Senate Report 105-300 ¹	“Behavioral science research and training.-The Committee encourages NIGMS to support basic research training as part of its mandate to support basic research training in all areas of health-related research.”	NA

¹ Unless otherwise noted, if no House Report language appears in a fiscal year, this means the accompanying House Appropriations report did not contain basic behavioral language.

Appropriations	FY 2000	<p>House Report 106-370</p> <p>Senate Report 106-166</p>	<p>“Behavioral Research and Training.-There is a range of basic behavioral research and training that the institute could support, such as the fundamentals [sic] relationships between the brain and behavior, basic cognitive processes such as motivation, learning, and information processing, and the connections between mental processes and health. The Committee encourages NIGMS to support basic behavioral research and training and to consult with the behavioral science research community and other Institutes to identify priority research and training areas.”</p> <p>“Behavioral Sciences Research and Training.- The Committee is concerned that NIGMS does not support behavioral science research training. As the only national institute specifically mandated to support research not targeted to specific diseases or disorders, there is a range of basic behavioral research and training that NIGMS could be supporting. The Committee urges NIGMS, in consultation with the Office of Behavioral and Social Sciences, to develop a plan for pursuing the most promising research topics in this area.”</p>	<p>HHS-FY 2001 Appropriations justifications:</p> <p>“A number of NIH institutes support basic behavioral research and research training. Primary among these are the National Institute of Neurological Disorders and Stroke, and the National Institute of Mental Health. Supporting explorations of the relationships between the brain and behavior, studies of basic cognitive processes, and examinations of how mental processes contribute to development and health is central to the missions of these institutes and they devote considerable resources to research and research training in basic behavioral areas. NIGMS support for training is linked to the areas of science supported by the Institute, and the behavioral fields mentioned above are not part of the Institute’s research mission. Training in these areas should be supported by institutes with sizable behavioral research programs. A major new research or research training effort in basic behavioral sciences by NIGMS would be duplicative and inappropriate. A few of the institutions supported through NIGMS’ Systems and Integrative Biology training grant program offer participants opportunities to pursue training in the basic behavioral sciences. In addition, individuals supported under the Institute’s Medical Scientist Training Program (which leads to the M.D.-Ph.D. degree) may pursue research training in behavioral sciences if their institution offers that option. In both cases, the grantee institution chooses to offer this option as part of the multidisciplinary training mandated for all of NIGMS’ training programs.</p> <p>The Office of Behavioral and Social Sciences Research is convening a working group of institute representatives to examine how the NIH might best pursue future research training efforts in the behavioral sciences. NIGMS will participate on that working group, which expects to begin its work early in 2000.”</p>
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Appropriations	FY 2001	Senate Report 106-293	<p>“Behavioral Science Research and Training.- The Committee is concerned that NIGMS does not support behavioral science research training. As the only Institute mandated to support research not targeted to specific diseases or disorders, there is a range of basic behavioral research and training that NIGMS could be supporting. The Committee urges NIGMS, in consultation with the Office of Behavioral and Social Sciences, to develop a plan for pursuing the most promising research topics in this area.”</p>	NA
Appropriations	FY 2002	Senate Report 107-84	<p>“Behavioral Science Research and Training.- The Committee is concerned that NIGMS does not support behavioral science research training. As the only Institute mandated to support research not targeted to specific diseases or disorders, there is a range of basic behavioral research and training that NIGMS could be supporting. The Committee urges NIGMS, in consultation with the Office of Behavioral and Social Sciences, to develop a plan for pursuing the most promising research topics in this area.”</p>	<p>HHS FY 2003 Appropriations Justifications-NIGMS: “The Institute’s research training programs mirror the areas of science that fall within the mission of the National Institute of General Medical Sciences (NIGMS). Except for a few fields of inquiry, behavioral studies largely fall outside of the Institute’s research mission, and are instead deemed to be within the missions of other institutes at the National Institutes of Health. The National Institute of Mental health (NIMH), as well as a number of others with missions focused on diseases, support both basic behavioral research and behavioral research in humans, since many disease states have behavioral dimensions. As is customary at the NIH, behavioral research training programs are mounted by those institutes with sizable behavioral research programs. A major new research or research training effort based in behavioral sciences by NIGMS would be duplicative and inappropriate. A few of the institutions supported through NIGMS’ Systems and Integrative Biology (SIB) training grant program offer participants opportunities to pursue training in the basic behavioral sciences. NIGMS intends to highlight this option of including behavioral science departments in SIB training programs when it reannounces [sic] its training programs in the coming months. In addition, individuals supported under the Institute’s Medical Scientist Training Program (which leads to the M.D. - Ph.D. degree) may pursue research training in behavioral sciences if their institution chooses to offer this option as part of the</p>

				<p>multidisciplinary training mandated for all of NIGMS' training programs. NIGMS's individual fellowship support extends to fellows working on the molecular and genetic basis of behavior. In the past, some fellows have studied movement, sensation, and perception.</p> <p>With regard to research, NIGMS supports studies, primarily in model systems, to examine the genetic and biochemical mechanisms underlying behavior. This includes research on the mechanisms underlying specific behaviors related to circadian rhythms, learning and memory, sensation and perception, pain and its management, and analgesia and anesthesia.</p> <p>NIGMS is exploring new areas of opportunity. Together with the Office of Behavioral and Social Sciences Research (OBSSR), NIGMS will soon host a workshop to explore whether it is an opportune time to study how allostatic load (that is, the cumulative "wear and tear" on the body's adaptive responses to stress) influences an individual's reaction to traumatic or surgical injury. Also in a joint effort with OBSSR, NIGMS is exploring the feasibility of supporting Ph.D. biomedical students who wish to receive a Masters degree in the behavioral sciences enhancing their ability to conduct research in that field or in relevant interdisciplinary fields."</p>
Appropriations	FY 2003	Senate Report 107-216 ²	"Behavioral sciences research and training.-As the NIH Institute most concerned with basic research, the NIGMS has provided leadership in basic research on physiological and biological structures and functions that may play roles in numerous health conditions. The Committee encourages the NIGMS to develop collaborations with other Institutes, such as the NCI and NIMH, and the Office of Behavioral and Social Sciences Research to fund basic research to integrate physiological knowledge of pre-disease pathways with behavioral studies."	<p>HHS FY 2004 Appropriations Justifications:</p> <p>"The following section represents FY 2003 Congressional requirements for reports and significant items derived from Senate Report 107-216. These actions discussed below are contingent on inclusion of similar language and funding in the final FY 2003 appropriation and related reports. Additional items may be transmitted at a later date as a result of the final Conference report."</p>

² For FY 2003, the House did not mark up a bill and so there was no House report.

				<p>“The NIGMS primarily supports fundamental areas of biomedical science of a structural or functional nature, which provide the foundation for disease-targeted studies by the other components of the NIH. NIGMS supports a limited number of studies in the area of behavioral research using animal models. Such work is relevant to the study of more complex behaviors in higher organisms supported by other institutes at the NIH.</p> <p>Research training in the behavioral sciences is supported through NIGMS’ Medical Scientist Training Program, Systems and Integrative Biology training program, and programs of the Minority Opportunities in Research Division. All of these programs solicit applications for research training support in a broad range of disciplines, explicitly including the behavioral and social sciences.</p> <p>The NIH Office of Behavioral and Social Sciences Research (OBSSR) has proposed to the Director, NIH that an examination of how NIH might best pursue future research and research training efforts in the basic behavioral and social sciences be conducted. The OBSSR proposal envisioned that a working group of institute representatives will be convened in 2003. NIGMS would participate on that group.”</p>
Appropriations	FY 2004	Senate Report 108-81	<p>“Behavioral Research.-The Committee believes that NIGMS has a scientific mandate to support basic behavioral research because of the clear relevance of fundamental behavioral factors to a variety of diseases and health conditions. The Committee encourages the NIGMS to incorporate basic behavioral research as part of its portfolio, especially in the areas of cognition, behavioral neuroscience, behavioral genetics, psychophysiology, methodology and evaluation, and experimental psychology.”</p>	NA

			<p><i>“Pre-Disease Pathways-</i> The Committee encourages the NIGMS to collaborate with other Institutes, including NCI and NIMH, and the Office of Behavioral and Social Sciences Research to fund research to integrate physiological knowledge of pre-disease pathways with behavioral studies.”</p>	
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**Inventory of Basic Behavioral and Social
Sciences Research at the NIH**

December 2, 2004

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Inventory of Basic Behavioral and Social Sciences Research at the NIH

Basic behavioral and social science research is of critical importance to the mission of the National Institutes of Health (NIH). Although this work does not directly address disease outcomes per se, behavioral and social processes play a critical role in understanding the links of molecular, genetic, and neural processes with health and disease. Basic behavioral and social science research provides knowledge, methodology, and measures that are essential for prediction, prevention, understanding individual variation, and controlling illness, for minimizing the collateral impact of disease, and for promoting health.

The NIH has undertaken a review of the basic behavioral and social sciences program across the Institutes and Centers. As is the case for basic research in the biomedical sciences, basic behavioral and social sciences research does not address disease outcomes per se, but is designed to provide essential knowledge necessary for better prediction, prevention, and control of illnesses. All Institutes and Centers (ICs) were asked to review their portfolios and provide the actual expenditures for basic behavioral and social sciences research in Fiscal Year 2003. The results are presented in the table below. In addition, ICs were asked to provide a description of their current programs in basic behavioral and social sciences research, plans for future initiatives and a discussion of opportunities in basic research that are not currently being address. Each Institute and Center also provided a brief list of grants that they identified as examples of the basic behavioral and social sciences research supported by their organizations. This document contains the individual reports from the NIH Institutes and Center who report having a basic behavioral and social sciences research portfolio. The National Institute of Allergy and Infectious Disease and the National Center for Research Resources reported no basic behavioral and social sciences research and, therefore, do not have program descriptions.

NATIONAL INSTITUTES OF HEALTH					
<u>Behavioral Research and Social Science Research</u>					
(Dollars in millions)					
	All	Basic			
Participating IC	FY2003 Actual	FY2003 Actual	% Basic	FY2003 Total IC Budget	% of Total IC Budget Basic BSSR
NCI	\$291.9	\$50.6	17.3	\$4,592.3	1.1
NHLBI	119.5	48.1	40.3	2,793.7	1.7
NIDCR	22.3	3.5	15.6	371.6	0.9
NIDDK	96.9	26.5	27.3	1,722.7	1.5
NINDS	92.4	48.8	52.8	1,456.5	3.4
NIAID	37.0	0.0	0.0	3,606.8	0.0
NIGMS	12.7	12.7	100.0	1,847.0	0.7
NICHHD	288.0	114.4	39.7	1,205.9	9.5
NEI	56.8	53.0	93.3	633.1	8.4
NIEHS	14.4	12.1	84.0	614.2	2.0
NIA	267.7	210.6	78.7	993.6	21.2
NIAMS	22.1	5.5	24.9	486.1	1.1
NIDCD	72.3	26.2	36.0	370.4	7.1
NIMH	440.7	108.0	24.5	1,341.0	8.1
NIDA	410.7	125.0	30.4	961.7	13.0
NIAAA	196.8	64.6	32.8	416.0	15.5
NINR	105.9	9.0	8.5	130.6	6.9
NHGRI	14.7	3.3	22.5	465.0	0.7
NIBIB	1.0	0.4	39.8	278.3	0.1
NCRR	62.2	0.0	0.0	1,138.8	0.0
NCCAM	14.5	0.7	4.8	113.4	0.6
NCMHD	1.9			185.7	
FIC	7.9	1.8	22.5	63.5	2.8
NLM	2.0	1.6	80.0	300.1	0.5
OD	31.8	9.7	30.5	266.2	3.6
NIH*	2,684.0	936.1	34.9	26,354.2	
*May not add due to rounding.					
Total NIH budget number does not include B&F and Superfund					

Fogarty International Center (FIC)

Basic Behavioral and Social Sciences Research

The Fogarty International Center supports basic behavioral and social science research within several of its programs. As previously reported to you by our budget office, Fogarty supported nearly \$8 million in BSS research and training activities in developing countries in 2003, of which we estimate approximately \$1.8 million to be basic BSS research. Thus, the majority of Fogarty's BSS portfolio is applied work, primarily relating to observational and intervention studies.

Only one of the current FIC programs is largely basic behavioral and social science research. The R21 "Brain Disorders in the Developing World" research program is heavily weighted towards basic research on behavior and particularly cognitive development and function. The "Brain Disorders in the Developing World" program grew out of the recognition of the enormous global burden of disease posed by mental illness and a variety of other conditions affecting brain function and associated behavior.

**Basic Behavioral Research Grants supported by
John E. Fogarty International Center (FIC)**

Grant Number	Grant Title	PI	Institution
R21 TW006713	APOE Genotype in Brazilian Children with Early Diarrhea	Guerrant, Richard	University of Virginia
R21 TW006794	Cognitive and Neurologic Sequelae in Cerebral Malaria	John, Chandy	Case Western Reserve University
R21 TW006804	Cerebral Malaria Neurological Disorders in India	Stiles, Jonathan	Morehouse School of Medicine
K01 TW006084-01A1	The Mediating Influence of Care Quality on Health	Barber, Sarah	UC-Berkeley
R03 TW001191	Neuroanatomic Basis of Cognitive ERP Deficit in Schizophrenia	Javitt, Daniel	Nathan Kline Institute for Psychiatric Research
R03 TW005886	Preperceptual and Perceptual Organization of Sound	Sussman, Elyse	Albert Einstein College of Medicine, Yeshiva University
R03 TW005888	Mexico: APOE, Depression, and Cognition in Late Life	Gallo, Joseph	University of Pennsylvania
R03 TW006014	Genetic and Caregiving Effects on Disordered Attachment	Lyons-Ruth, Karlen	Cambridge Health Alliance
R01 TW006374	Stigma and Mental Illness in Cross-National Perspective	Pescosolido, Bernice	Indiana University

**National Cancer Institute (NCI)
Basic Behavioral and Social Sciences Research**

Budget Overview

The overall NCI budget for Behavioral and Social Sciences Research was \$291.9M in Fiscal Year 2003. The basic behavioral research portfolio totals slightly over \$50M. Mr. Jim Dickens in the NCI Budget Office has confirmed these figures.

Basic Behavioral and Social Sciences Research – Historical Note

Six years ago, NCI had a relatively small portfolio of behavioral research projects, largely focused on intervention studies on smoking, fruit and vegetable consumption, and mammography utilization. At that time, a large proportion of the budget was allocated to contracts with state health departments to support the American Stop Smoking Intervention Study (ASSIST) project, which provided the foundation for CDC's national tobacco control program.

With the establishment of the Behavioral Research Program in the Division of Cancer Control and Population Sciences, NCI undertook a major effort to evaluate, strengthen, and expand both the breadth of the research program and the expertise of the scientists who lead it. In addition to the traditionally supported areas of research, NCI expanded support of interdisciplinary sciences in areas such as risk communication, decision-making, sociocultural research, consumer health informatics, policy analysis, neuroscience, psychometrics, and behavioral genetics.

Today, NCI is home to nationally and internationally recognized senior leaders in behavioral science who are guiding scientific progress that is built on the foundations of transdisciplinary science networks; systems approaches that emphasize the discovery, development, and effective delivery of science; and the growth of communication sciences and practices that make the networks and systems function most effectively. Examples of current initiatives in basic behavioral and social sciences across NCI follow.

Description of Current Program

Methodologic Research on Dietary Assessment

In a large collaborative study, investigators are assessing energy expenditure (using the doubly labeled water technique) and protein intake (via urinary nitrogen excretion) to estimate the error (generally under-reporting) in a food frequency questionnaire and multiple 24-hour recalls. Previous studies, even those "adjusting" for measurement error, took into account biases in the food frequency questionnaire but did not fully consider biases associated with the "reference" instrument (24-hour recall), especially the potential correlation of biases in the two instruments. The information on measurement error from this study will be used in interpreting and adjusting data from the NCI-American Association of Retired Persons Diet Study and other epidemiologic investigations.

Genes and Tobacco Use

NCI scientists are conducting a cancer case control study that will examine tobacco exposure markers, genes hypothesized to play a role in smoking, as well as behavioral measures (depression, anxiety, nicotine dependency) in the 2000 population controls. They also will examine genes that may play a role in both nicotine dependency and lung cancer (i.e. CYP2A6) in both cases and controls. Alcohol-related genes may also be examined. In another research initiative, NCI scientists have performed genotyping on some candidate genes in 1000 current and 1000 former smokers to study candidate genes hypothesized to play a role in smoking persistence. Other behavioral phenotypes can also be examined, i.e. alcohol and obesity.

Genetic Risk of Cancer and Behavior

NCI has established a trans-protocol program of psychosocial and behavioral research studies targeting the members of families at increased genetic risk of cancer. Such studies are critical to the mission of improving the quality of life and the clinical management of high-risk individuals. Specific behavioral research projects will be conducted as supplements to on-going clinical research protocols. The following are examples of questions that are being addressed within clinical studies:

- ❑ What are the consequences of “prophylactic” removal of at-risk target organs, including the extent to which such procedures actually reduce the risk of cancer, the relationship between the procedure and the risk of other medical conditions (including psychological co-morbidities), the impact of the procedure on quality of life, etc?
- ❑ How do individuals at increased genetic risk of cancer weigh the pros and cons of the various management options available, and make a decision as to which path to take?
- ❑ How does membership in a high-risk family affect the interpersonal dynamics between family members and family functioning as a whole, both positively and negatively?
- ❑ How do family members comprehend and cognitively process the terms used in research questionnaires and other data collection instruments?
- ❑ What factors influence decision-making and behavior with regard to cancer surveillance, risk reduction and general health care practices?
- ❑ To what extent does anxiety, depression, and cancer worry constitute clinically significant issues in this context? What community resources are required/available to support affected individuals and their relatives?
- ❑ What coping strategies do family members employ to deal with the multitude of stresses that are related to their high-risk status?

Basic Biobehavioral Research on Cancer-Related Behaviors

This initiative funds research on the links between biology, behavior, and environment as they pertain to cancer-related risk behaviors. NCI funded eight grants under the first issuance and six additional grants under the reissuance in Fiscal Year 2000. An example is provided.

Biobehavioral Immune Interactions in Ovarian Cancer, Susan Lutgendorf, University of Iowa, examines the relationship of stress, depression, social support, and coping in women presenting for surgical diagnosis of ovarian cancer. This work may provide evidence of an inflammatory pathway by which biobehavioral factors may contribute to ovarian cancer.

Biological Mechanisms of Psychosocial Effects on Disease

The overarching goal of the Biological Mechanisms of Psychosocial Effects on Disease initiative is to elucidate the dynamic bidirectional relationships between cancer and human host environments. The intent is to encourage new research that explores how psychosocial characteristics and behaviors of the host influence cancer initiation, progression, and resilience through biological mechanisms (e.g., angiogenesis, DNA damage and repair, apoptosis). New transdisciplinary research—that bridges the divide between basic cancer biology and applied cancer biobehavioral sciences—is needed to fully explore the dynamic interrelationships among cancer cells, surrounding cells, the tumor, and host environments.

Centers for Population Health and Health Disparities

The National Institute of Environmental Health Sciences, National Institute on Aging, NCI, and Office of Behavioral and Social Sciences Research recently awarded eight Centers for Population Health and Health Disparities. The centers support transdisciplinary, multilevel, integrated research to elucidate the complex interactions of the social and physical environment, mediating behavioral factors, and biologic pathways that determine health and disease in populations, leading to an understanding and reduction of health disparities. This leading-edge initiative responds to the recommendations of several recent reports from the National Academy of Sciences and employs NIH's most advanced and innovative population science to address the problem of health disparities. Using a community-based participatory research approach, these centers will engage and include community stakeholders in the planning and implementation of health research. Communities include the elderly, African Americans, poor Whites, and Hispanics. Studies will focus on obesity, cardiovascular disease, breast cancer, prostate cancer, cervical cancer, mental health, gene-environment interactions, psychosocial stress, neighborhood environments, and built environments.

Centers of Excellence in Cancer Communications Research

In Fiscal Year 2003, NCI awarded four Centers of Excellence in Cancer Communications Research to speed advances in cancer communications knowledge. Interdisciplinary teams of researchers develop, implement, and evaluate strategies to improve access to cancer information and the effectiveness and dissemination of efficacious interventions. The centers provide essential infrastructure to facilitate rapid advances in knowledge about cancer communications. Projects include the role of cultural factors in response to colorectal cancer risk reduction messages, decision aids concerning tamoxifen use among women at high risk for breast cancer, and a comparison of the effectiveness of three different approaches to cultural appropriateness on affective, cognitive, and behavioral responses to a series of colorectal cancer risk reduction messages.

Long-Term Cancer Survivors Research Initiative

The population of long-term cancer survivors continues to grow: 63 percent of adult and 78 percent of pediatric cancer survivors survive beyond five years. The Long-Term Cancer Survivors Initiative, first funded in 1998, focused on questions related to the physiological and psychosocial experiences of cancer survivors five or more years post diagnosis, and interventions to promote positive outcomes. An additional round of funding is planned for Fiscal Year 2004. Over 125 applications were received. This request for applications is one of the cornerstone initiatives of NCI's scientific priority in Cancer Survivorship. It directly responds to the recent

Institute of Medicine reports on cancer survivorship, as well as the priorities of the President's Cancer Panel.

Transdisciplinary Tobacco Use Research Centers

Seven Transdisciplinary Tobacco Use Research Centers (TTURCs) were established in 1999 with 5 years of funding by NCI, the National Institute on Drug Abuse (NIDA), and the Robert Wood Johnson Foundation. NCI, NIDA, and the National Institute on Alcohol Abuse and Alcoholism have joined together to fund the reissuance of the TTURCs in Fiscal Year 2004. These novel centers are designed to bridge disciplinary barriers, establish new conceptual frameworks and methods to understand and treat tobacco use, speed the transfer of innovative approaches to communities nationwide, and create a core of new tobacco control researchers. The centers establish critical links across diverse scientific disciplines. They are not only unique for their transdisciplinary science; they have established multiple cross-center collaborations that are unusual in either public or private research ventures. The centers are creating innovative research techniques and technologies that are providing new perspectives on tobacco use and addiction, and are pioneering interventions to decrease tobacco use.

Special Populations Networks

This initiative links cancer researchers and community-based programs to learn more about the causes of cancer disparities in minority communities and to develop and test ways to address and eliminate those causes. NCI research grants are issued to researchers for public health projects that may focus on many communities nationwide or, perhaps, more focused projects in a single county, tribal nation, or specific population subgroup.

These grants include a wide, quite exhaustive list of ethnic minority/underserved groups. Additionally, NCI supports peer-reviewed pilot research grants, many of which are examining behavioral and social sciences research issues. A brief list of examples is provided.

- ❑ Colorectal Cancer Screening Barriers in Appalachia
- ❑ Latinas' Perception of Genetic Testing for BR/OV Cancer
- ❑ Examining Adolescent Cigarette Use in Hawaii
- ❑ Language Barriers to Colonoscopy Screening

Physical Activity Behavior Change Theories

Given the importance of physical activity in the etiology, treatment, and prevention of many chronic diseases, it is important to understand how physical activity behavior can be increased. The purpose of this initiative is to increase the knowledge base necessary to develop effective physical activity interventions in children, adolescents, adults, and older adults. Specifically, this RFA seeks to elucidate the psychosocial, environmental, and physiological factors involved in the mechanisms of physical activity behavior change to better understand the factors involved in the causal pathways that lead to physical activity behavior change. NCI's contributing partners include the National Institute of Diabetes and Digestive and Kidney Diseases, the Office of Behavioral and Social Sciences, NIH Office of Disease Prevention, and NIH Office of Research on Women's Health. This partnership initiative was funded in Fiscal Year 2004.

Future Planned Initiatives

Decision Making Related to Cancer Control

NCI is planning an initiative on decision making related to cancer control. The purpose of this effort is to better understand human decision-making processes so that individuals can make more informed choices regarding their health care. To accomplish this, it is necessary to draw upon research in both the basic and applied arenas, which have historically functioned as separate research domains. This initiative is focused at the level of the individual patient or health care provider, which may involve the patient-provider dyad, the patient-caregiver dyad, the patient-partner dyad, or the patient-family system. In 2003, NCI cosponsored with the Federation of Behavioral, Psychological, and Cognitive Sciences, a one-day meeting devoted to decision research. Proceedings will be published in a journal special issue and will be available on the Web.

Ancillary Studies of Energy Balance and Cancer in Humans

This soon to be released Program Announcement will invite investigator-initiated research applications on energy balance in ancillary studies to NIH-funded research. Epidemiologic and intervention research within human populations can provide essential self-report and objective measures about diet, anthropometry, and physical activity important in unraveling the role of energy balance in cancer risk and prognosis. These measures, including data on psychosocial, cognitive, or basic-biobehavioral factors, can be linked with biologic specimens such as blood, urine, exfoliated cells, and other tissues to study underlying metabolic and genetic etiologic mechanisms in relation to energy balance and cancer. The approach is also to encourage collaboration among scientists working in the areas of nutrition, physical activity, genetics, and other disciplines to utilize existing NIH-funded studies to study the impact of diet, physical activity, and weight on the genetic, epigenetic, genomic, proteomic, and metabolic influences of cancer biology and prevention.

Centers for Transdisciplinary Research on Energetics and Cancer

The Centers for Transdisciplinary Research in Energetics and Cancer (TREC) will involve scientists from multiple disciplines and encompass projects spanning the biology and genetics of energy balance to behavioral, sociocultural, and environmental influences on nutrition, physical activity, weight, energy balance, and energetics. The TREC centers will foster collaboration among transdisciplinary teams of scientists with the goal of accelerating progress toward reducing cancer incidence, morbidity, and mortality associated with obesity, low levels of physical activity, and poor diet. They also will provide training opportunities for new and established scientists who can carry out integrative research on energetics, energy balance, and its consequences. Funding is anticipated for Fiscal Year 2005.

Opportunities Not Currently Addressed

Research on Behavioral and Social Processes

- ❑ Improve accuracy for predicting individual risk by exploring genetics, behavior, and environment. Studies are needed to more fully understand the etiology of behaviors that increase risk for cancer and how these behaviors affect biological factors.
- ❑ Define and understand variables that contribute to cancer health disparities, this includes defining subpopulations and examining poverty/low resources, culture, social injustice, and racialism.
- ❑ Increase knowledge about cancer information needs, beliefs, decision-making processes, and behaviors, and the relationships among these factors among different publics including general populations, the underserved, patients and their caregivers, high-risk groups and health providers.

Biopsychosocial Research

- ❑ Expand studies of smoking and energy balance into multifactorial analyses combining these and other risk factors to more thoroughly understand the complex interactions of these risk factors with multiple genetic factors and environmental exposures over the life course.
- ❑ Increase research efforts to understand the biological, physical, psychological, and social mechanisms, and their interactions, that affect a cancer patient's response to disease, treatment, and recovery.

Research on the Development of Procedures for Measurement, Analysis, and Classification

- ❑ Expand the development and use of tools to assess the health-related quality of life and quality of care of post-treatment cancer survivors and their family members, as well as NCI's capacity to track outcomes for these populations.
- ❑ Develop improved measurement of body mass and composition, physical activity and fitness, and diet and bioactive food components through self-report measures and advances in technology for objective reference measures.

Basic Behavioral Research Grants supported by National Cancer Institute (NCI)			
Grant Number	Grant Title	PI	Institution
2R01CA26582-21	Pain and Symptoms of Cancer: Assessment and Treatment	Cleeland, Charles	University of Texas Md Anderson Can Ctr
5R01CA82346-5	Interactive Decision Aid for Brca 1/2 Mutation Carriers	Schwartz, Marc D	Georgetown University
5R01CA82378-4	Measurement of Adaptive Style in Children with Cancer	Phipps, Sean	St. Jude Children's Research Hospital
5R01CA92704-8	Psychological Intervention for Women with Breast Cancer	Andersen, Barbara L	Ohio State University
5R01CA60616-7	Psychosocial Impact of Pediatric Bone Marrow Transplant	Phipps, Sean	St. Jude Children's Research Hospital
5R01CA63562-9	Biobehavioral Lung Cancer Prevention Program	Lerman, Caryn E	University of Pennsylvania
5R01CA78801-5	Exercise Effects--Mental and Physical Health in Breast Cancer	Perna, Frank M	Boston University Medical Campus
1R01CA104825-1	Biobehavioral-Cytokine Interactions in Ovarian Cancer	Lutgendorf, Susan K	University of Iowa
5R01CA85229-3	Psychostimulants for Fatigue in Ambulatory Men with Prostate Cancer	Roth, Andrew J	Sloan-Kettering Institute for Cancer Res
5R01CA90966-2	Biobehavioral Effects of Emotional Expression in Cancer	Cohen, Lorenzo	University of Texas Md Anderson Can Ctr
5R01CA85819-4	Utility of Momentary Versus Recalled Self Reports	Stone, Arthur A	State University New York Stony Brook
5R01CA86826-3	Behavioral Aspects of Familial Risk for Prostate Cancer	Kash, Kathryn M.	Beth Israel Medical Ctr (New York)
5R01CA96581-2	Impact of Mortality Concerns on Cancer Risk Behavior	Arndt, Jamie	University of Missouri Columbia
5R01CA84036-4	Screening for Ovarian Cancer-- Psychobehavioral Outcomes	Andrykowski, Michael A.	University of Kentucky
5R01CA85464-3	Goal Interference as a Clinical Outcome Measure	Peterman, Amy	Evanston Northwestern Healthcare
5R01CA87595-2	Identify & Reduce Cognitive Biases of Decision Aids	Ubel, Peter A.	University of Michigan at Ann Arbor
1R03CA94773-1	Breast Cancer Patient & FDR Dyads: Interaction & Impacts	Bayer, Laura A.	Washington University

Please note that the highlighted examples are included in the larger NCI portfolio on basic behavioral and social sciences research. These do not appear on the smaller portfolio list that represents only basic behavioral research.

National Center for Complementary and Alternative Medicine (NCCAM) Basic Behavioral Science Research

Description of the Current Program

Many individuals use complementary and alternative medicine (CAM) therapies to promote health, and to treat and prevent disease. The mission of the National Center for Complementary and Alternative Medicine (NCCAM) is to conduct both basic and clinical research on these approaches to investigate their safety and efficacy. Included among the domains studied by NCCAM are mind-body interventions. These interventions focus on interactions between the mind, brain and body and the powerful ways in which psychological, behavioral, social and spiritual factors can directly affect health.

Mind-body research focuses on elucidating the basic mechanisms by which the mind and brain interact with the body to affect health, as well as the mechanisms by which illness can affect the brain and psychological functioning. In addition, mind-body medicine investigates the effects of interventions such as relaxation, meditation, yoga, biofeedback, tai chi, qi-gong, visual imagery, hypnosis, group support, spirituality and prayer on health outcomes, and role of other factors in these processes, such as coping and resilience. The study of basic mechanisms by which these interventions exert their effects is an integral aspect of this research. Thus, because much of this work by necessity must be done as mechanistic studies in humans, basic behavioral science supported by NCCAM is embedded in clinical research funded projects. Some examples of research topics that NCCAM currently supports in this area are given below.

Physical Effects of Expectations – Science of the “Placebo Effect”

NCCAM sponsored a large Trans-NIH conference on the “Placebo Effect” that subsequently led to multi-institute Requests for Applications (RFAs) that resulted in funding of basic behavioral research grants that focus on identifying the mechanisms underlying this phenomenon. This line of research is important because knowledge of the mechanisms underlying the effects of expectation, as one mechanism for the placebo effect, on the experience of pain, opens the possibility of designing scientifically-based methods to harness these effects and by doing so, optimize medical and psychological interventions. It is well known that the expectation of analgesia during administration of an inactive placebo activates endogenous opioid neurotransmitter systems, in turn regulating sensory and affective qualities of pain. NCCAM is funding research that is elucidating the neuronal and neurochemical networks by which expectancy-associated sensory, emotional and cognitive appraisals are translated into neurobiological effects. This research seeks to examine the effects of a placebo intervention with expectation of analgesia on/mu-opioid neurotransmission, directly in human subjects with positron emission tomography (PET) and other molecular imaging techniques.

In a related project supported by NCCAM, Functional Magnetic Resonance Imaging (fMRI) is enabling the characterization of brain mechanisms involved in placebo analgesia in a clinical population which experiences visceral pain as part of their clinical syndrome. This project capitalizes on previous work with Irritable Bowel Syndrome (IBS) patients, who are known to show a powerful and reliable placebo response to specific expectancy response sets. This study

is obtaining brain images of IBS subjects and examining whether placebo responses selectively activate specific brain regions, and comparing those responses to peripherally applied analgesia to differentiate brain and central nervous system related mechanisms from those in the periphery.

For basic research on the “placebo effect” to be translated into clinical practice, another level of basic behavioral and social research is needed. NCCAM is funding a study that is investigating the relationship of biological pathways to individual differences in behavioral and psychological factors that relate to belief, conditioning, expectancy and meaning. Finally, another study is investigating the effect of patient-provider interaction on placebo effect. Understanding how patient-provider interaction can promote wellness through placebo effect may directly contribute to health outcomes.

Meditation, Hypnosis and Guided Imagery

NCCAM currently supports investigations into the effects of meditation and relaxation-based interventions on a wide range of clinical conditions, from eating disorders to cardiovascular disease. Of particular relevance here, NCCAM is also supporting research on the basic mechanism by which these treatments work. For example, NCCAM is funding research using Functional Magnetic Resonance Imaging (fMRI) to define the neural mechanisms underlying the meditative state, differentiate this state from three control states, and determine how meditation modulates autonomic function. Such knowledge could be useful for identifying new medical applications for this intervention, including those aimed at promoting health and preventing disease.

The mechanisms underlying the effects of mind-body interventions can also be studied in patient populations. Research has suggested that women with breast cancer experience considerable stress with concurrent impairment of cell-mediated immunity. The mechanisms underlying the many reported correlations between stress and various measures of immune function remain to be elucidated. While breast cancer patients who enroll in stress management interventions report improved quality of life, there is interest in exploring the physiological effects of various interventions. If it could be shown that stress management both reduced self-reported stress and improved immune outcomes, this could provide evidence that stress reduction could improve health outcomes to which immune function is critical. Thus, as part of NCCAM’s basic behavioral science portfolio, NCCAM is funding research to evaluate the impact of hypnosis and guided imagery on biological markers of stress and immune function, specifically diurnal cortisol secretion, NK cell activity, white blood cell response to breast cancer-specific antigens and delayed type hypersensitivity.

Tai Chi and Yoga

The specific pathways by which certain illnesses result in disability are not always fully understood. Clinical research can shed light on these pathways by comparing interventions that have different physiological effects. For example, NCCAM is funding research investigating whether Tai Chi, which focuses on motor control, will result in greater improvements in dynamic gait and stability in Parkinson’s patients than exercise focused on fitness and caloric expenditure. Should the Tai Chi result in greater improvement than the comparison group; it would shed light

on the extent to which the primary disability in Parkinson's disease stems from motor dysfunction and the extent to which it may be amenable to treatment. In another study, NCCAM is studying the effects of Yoga on attention in two cohorts, a healthy aging cohort and patients with multiple sclerosis. In addition to investigating clinical outcomes such as cognitive abilities, investigators are evaluating the mechanisms by which yoga may have effects.

Pain

One of the primary reasons that patients seek CAM therapies is the treatment of pain. NCCAM funds considerable research in the area of pain, including basic research on animal models for chronic pain. Among these studies are basic behavioral science investigations that compare different animal models for pain, evaluating both behavioral and biochemical parameters. As with the other studies in NCCAM's basic behavioral portfolio, many of these studies investigate a range of CAM interventions, including botanicals and other natural products, such as soy and tart cherry, which are thought to have analgesic effects, while also exploring basic biochemical and behavioral mechanisms.

Future Planned Initiatives

NCCAM will continue to support basic and clinical research in mind-body medicine. Basic research on mechanisms will be a cornerstone of these investigations because it provides critical information about the design of interventions as well as variables that are useful in evaluating intervention effects. The opportunities for future research in mind-body include the following:

- Identification of the common and specific features of widely used mind-body medicine practices
- Investigations of the neurological, endocrine, autonomic, immunological, behavioral, and psychological mechanisms of effective mind-body interventions
- Basic studies to develop reliable and valid methods for assessing states of relaxation and meditation, spirituality, and emotion.
- Research to explore the value of CAM therapies to enhance resilience, coping and wellness
- Investigations to identify the pathways by which negative and positive mood states impact health outcomes, including studies of resistance to infection, resiliency, expectancy, and coping.
- Studies of basic mechanisms by which CAM mind/body behavioral interventions may complement and enhance conventional medical therapies, to accelerate the healing process.
- Understanding the physiology and biochemistry of expectancy (as part of the placebo effect)

**Basic Behavioral Research Grants supported by the
National Center for Complementary and Alternative Medicine (NCCAM)**

Grant Number	Grant Title	PI	Institution
R01 AT00606	Relaxation-Related CAM Therapies for Chronic Back Pain	Daniel C. Cherkin, Ph.D.	Center for Health Studies
P01AT002024	Mindfulness-Based Stress Reduction, Stress Arousal, and Immune Response in Early HIV	Susan Folkman, Ph.D.	UCSF
<i>R01AT001414</i>	Enhancing the Placebo Effect in Irritable Bowel Syndrome	Ted Kaptchuk, OMD	Harvard Medical School
R01AT002490	Neuroendocrine Mechanisms in Yoga Treatment of Insomnia	Sat Bir Khalsa, Ph.D.	Brigham and Women's Hospital
R24AT002681	Mind/Brain/Body Interactions in Stress-related Disorders	Emeran Mayer, MD	UCLA
U19AT002656	Complementary and Alternative Medicine: Expectancy and Outcome	Barry S. Oken, MD	Oregon Health and Science University
R01AT002454	Tai Chi Mind-Body Therapy for Chronic Heart Failure	Russell Phillips, MD	Israel Deaconess Medical Center

**National Center on Minority Health and Health Disparities (NCMHD)
Basic Behavioral and Social Sciences Research**

Description of Current Program

As part of its mission, NCMHD encourages and supports basic behavioral and social science research that reduces, and ultimately eliminates health disparities in this country. In support of this endeavor, NCMHD has a variety of research projects in its portfolio.

The majority of these projects are funded through NCMHD's two Loan Repayment Programs. These programs seek to recruit and retain health professionals at the doctorate level to conduct health disparities and/or clinical research at a qualified institution for 2 or more years. In exchange for this research service, the programs repay a portion of the participant's outstanding educational loan debt.

NCMHD Loan Repayment Programs

Basic behavioral and social science projects currently funded by NCMHD include themes that range from the socioeconomic, psychological and/or behavioral impact of a disease to cultural competence and communication between physicians and patients. In reducing, and ultimately eliminating health disparities, it must be acknowledged that multiple intrinsic and extrinsic factors act in concert to cause disease, and therefore, emphasis must be placed on the elucidation of these factors and the biological pathways as they contribute to health disparity outcomes. Logically, the identification of these factors necessitates culturally competent health professionals. Health professionals must learn how to relate to and communicate with the target audience in order to affect behavior modification. The lack of cultural competence in and of itself represents an obstacle to effectively interacting with society's diverse populations, and contributes to the prevalence of health disparities in this country.

NCMHD IC Collaborations

NCMHD also seeks other opportunities through NIH IC collaborations to include basic behavioral and social science research projects in its portfolio. One of these co-funded projects is the *Community Characteristics and Physical Activity Among Adolescent Girls*, is co-funded with the Nation Heart, Lung and Blood Institute (Grant No.: 5R01HL071244, PI: Deborah Cohen, Institute: Rand Corporation). The focus of the research is on the influence of environmental factors on physical activity. The study will be conducted in urban, suburban and rural areas across the country.

Another project in which NCMHD is involved is the *Emotional Distress and Risky Behaviors in Asian Youth* that is co-funded with the National Institute of Nursing Research (Grant No.: 5K01NR008334, PI: Mayumi A. Willgerodt, Institute: University of Washington). The project seeks to fill a significant gap in nursing research by conducting a cross-cultural examination of family and peer variables associated with emotional distress and risky behaviors in Asian American adolescents. The final result of this study is to develop a community-based, family focused, culturally appropriate prevention programs that will address these behaviors.

Future Planned Initiatives

Future NCMHD initiatives to address basic behavioral and social science research and increase NCMHD's current portfolio will continually be developed within NCMHD's statutorily mandated programs. These programs include the Loan Repayment Program for Health Disparities Research, the Research Endowment Program and the Centers of Excellence Program (Project EXPORT). NCMHD will continue to encourage the grantees address these areas within their specific activities.

Additional opportunities to engage in and support basic behavioral and social science research will be channeled through NCMHD's Office of Community-Based Research. The purpose of the Office of Community-Based Research includes the development and implementation of community-based research programs for the National Institutes of Health with a focus on disease prevention, implementation of health messages in relevant racial and ethnic minority and medically underserved communities, and elucidating barriers to effective health care.

Basic Behavioral Research Grants Supported by National Center on Minority Health and Health Disparities (NCMHD)			
Grant Number	Grant Title	PI	Institution
	SocioDemographic Determinants of Health Insurance Coverage Among Young Adults	Callahan, Stephen	Vanderbilt University
	Examining Social Determinants of Ethnic Disparities in Health	Bennett, Gary	Harvard University
	Monitoring of Socioeconomic Trends in Mortality and Disease Incidence	Chen, Jarvis	Harvard University
	The Effect of Race, Neighborhood and Social Networks on Transition into Injection Drug Use and Association with HIV and HCV	Fuller, Crystal	Columbia University
	Hablemos Juntos – Improving Patient-Provider Communication for Latinos	Jacobson, Holly	University of North Texas
	Racial and Ethnic Approaches to Community Health	Stephens, Torrance	Emory University
	The Social Dynamics of Racial/Ethnic Disparities in Health Encounter Communication	Pope, Charlene	University of Rochester
	Study of Socio-Environmental Factors and the Biophysiologic Mechanisms Involved in Lung Cancer Formation	Gibbons, Michael	Johns Hopkins University
	Health Disparities Among Infants and Children: The Role of Social Stratification, Social Class Relations, and Socioeconomic Status	Finch, Brian	Rand Corporation

National Eye Institute (NEI)
Basic Behavioral and Social Sciences Research

Description of Current Program

The National Eye Institute (NEI) supports a range of projects that have both direct and indirect bearing on behavioral research. A significant portion of the NEI grant portfolio supports neuroscience research aimed at understanding visual perception and related behavioral actions including studies related to attention and behavioral responses to particular visual inputs. The NEI also supports an expanding research portfolio dealing with the consequences of low vision and blindness rehabilitation. A comprehensive description of these activities, including the goals and objectives of future research, is contained in the most recent NEI strategic plan: **National Plan for Eye and Vision Research** which can be accessed at www.nei.nih.gov/strategicplanning.

Progress has been made in clarifying behavioral processes related to visual perception. Our understanding of how the brain processes visual information, how neural activity is related to visual perception, and how visual processing interacts with other brain systems underlying cognition and guides behavior. Studies of visual processing have identified neuronal activity that is correlated with the decision to execute a particular behavior in response to a particular visual stimulus, rather than simply correlated with either the stimulus or the action alone. These studies have led to promising theories and have identified neuronal substrates in which visual information is mapped to behavioral action. Studies of the function, circuitry, and organization of higher order visual processing centers in the brain have shown the effect of attention and top-down cognitive influences on visual processing.

In low vision and blindness rehabilitation research, psychometric measures for characterizing disability and assessing quality of life issues have improved. This has helped researchers recognize the importance of psychosocial factors in vision loss, and the new measures have been applied to rehabilitation research for evaluating the outcomes of intervention programs. Technologies for low vision enhancement and wayfinding have continued to improve, allowing for advances in mobility research on ways people with normal vision and visual impairment get around using visual, auditory, and haptic cues from the environment.

Cognitive and other behavioral factors based on perception of the environment also play an important navigational role in walking and driving. There has been progress in raising awareness of visual impairment and rehabilitation. Education and outreach programs in schools, community centers, and elsewhere are teaching ways to prevent vision loss and manage visual impairment. Well-written and targeted educational materials, many on the Web, are helping convey the message that progress is being made to understand and overcome vision loss and develop technologies for managing visual impairment. Research is underway to determine behavioral aspects to accessing rehabilitation services. The NEI has begun developing outreach and communication strategies for the American Indian and Alaska Native population. The NEHEP conducted an environmental scan of the vision-related programs and services provided to American Indians and Alaska Natives and identified gaps in eye health information, program services, and materials targeted to these groups.

**Basic Behavioral Research Grants supported by
National Eye Institute (NEI)**

Grant Number	Grant Title	PI	Institution
R01EY001139-27	Behavioral Measures of Binocular Vision	Harwerth, Ronald S.	University of Houston
R01EY001189-31	Eye Movement Control-Role of Brain Stem Neurons	Sparks, David Lee	Baylor College of Medicine
R01EY002857-23	Object Recognition & Navigation—Normal & Low Vision	Legge, Gordon E.	University of Minnesota Twin Cities
R01EY005603-19	Cortical Processing of Visual Motion	Newsome, William T.	Stanford University
R01EY011347-33	Cortical Mechanisms In Perception and Behavior	Gross, Charles G.	Princeton University

**National Heart, Lung, and Blood Institute (NHLBI)
Basic Behavioral and Social Sciences Research**

Description of Current Program

The National Heart, Lung, and Blood Institute (NHLBI) supports a wide variety of research on the prevention, etiology, genetics, and treatment of heart, blood vessel, lung, blood, and sleep diseases and disorders. Numerous behavioral and social factors (e.g., tobacco use, diet, adaptation to social circumstances, episodic stress, sedentariness, and obesity) contribute to the pathophysiology of these disorders and therefore influence their incidence, prevalence, prevention, and treatment. The Institute supports many large-scale observational studies that investigate associations between behavioral and social factors and disease. These can lead to a better understanding of complex interactions and suggest avenues for prevention and improved treatment. Disease prevention programs target all of the proven, and many of the suspected, behavioral risk factors. Clinical trials involving behavioral interventions have been conducted in many areas, and continue to be planned.

Although the majority of the Institute's behavioral and social sciences research budget is dedicated to applied and clinical research, basic or fundamental behavioral and social sciences research is also represented in the NHLBI's portfolio. The definition of basic research as "systematic study directed toward fuller knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific application toward processes or products in mind" was used as a guiding principle in the examples selected for this report. Nonetheless, in some instances clinical or applied research with a basic behavioral research component is also described.

The purpose of this report is to describe 1) basic behavioral and social sciences research currently supported by the NHLBI; 2) initiatives under consideration by the Institute; and 3) research needs not currently addressed. Also included is a list of selected grants that illustrate basic behavioral and social sciences research supported by the NHLBI.

Aggression. Recent NHLBI genetics research has focused on aggression, a prominent feature of many clinical conditions (such as antisocial personality disorder) that is also associated with increased cardiovascular risk, a common cause of criminal incarceration, and a frequent concomitant of alcohol and other substance abuse. Research suggests that in addition to being influenced by environmental determinants, aggressive temperament is also influenced by genetic factors. For example, reduced central nervous system (CNS) serotonergic activity is associated with human aggression, as seen in clinical, forensic, and non-patient samples. Life history of aggression and anger-related personality traits, as well as CNS serotonergic responsivity, are associated with polymorphisms of two genes regulating elements of the serotonergic system: tryptophan hydroxylase and monoamine oxidase A. Research supported by the NHLBI is evaluating additional polymorphisms associated with the serotonergic system to assess their relationship to specific anger-related traits, temperament, and hostility.

Stress and other emotions. Stress is not a unitary phenomenon, and each organism responds to stress in a unique manner that reflects its particular experience, life history, and genetic code.

One of the most important factors in developing resilience to stress is thought to be the influence of early environmental events that shape an organism's biology and behavior. Early environmental events can be studied through pre- and post-natal manipulations in animal models by using maternal separation and cross-fostering to determine their effects on behavioral, cardiovascular, and neural response systems. A study funded by the NHLBI may provide important new data regarding the influence of early life events on biobehavioral processes that regulate the stress response in adults. A working group to identify further research needs on stress is described below under the heading “Future Planned Initiatives”.

Several studies have shown that major depression and associated symptoms, such as hopelessness, are an important independent risk factor for development of ischemic heart disease (IHD) and for death after a myocardial infarction. Depression also has been found to be associated with thrombosis and hemostasis in studies independent of those demonstrating its association with cardiovascular disease. This finding led to the study of mechanisms through which mood states, particularly depression, influence platelet function. It is thought that patients with major depression have increased levels of the functional platelet GPIIb/IIIa receptor. The GPIIb/IIIa receptor binds to fibrinogen and other ligands and mediates the final common pathway by which platelet aggregation and adhesion occur. The Institute supports research in patients with major depression to determine the specific molecular pathways—and their relative contributions—that convert platelet GPIIb/IIIa receptor from a low-affinity to a high-affinity conformation.

Sleep. The National Center on Sleep Disorders Research maintains an extensive portfolio of fundamental research on behavioral, social, and neurobehavioral aspects of sleep. The NHLBI sleep and neurobiology program includes clinical research on how sleep disturbance due to lifestyle or sleep disorder impairs daytime function, diminishes quality of life, reduces school/workplace performance, and increases the risk of depression and motor vehicle accidents. Funded research includes studies to elucidate the psychoneuroimmunological mediators of stress related to sleep deprivation, the genetic bases for abnormalities in sleep or wakefulness, and the basic neurobiological mechanisms that link sleep disorders to cardiovascular disease risk. A link to a recently completed strategic plan, which includes the status of basic research, is provided below under the heading “Research Needs”.

Asthma. The NHLBI’s basic behavioral research program in asthma includes a small but important group of studies investigating the role of psychosocial factors in functioning of the airways and in precipitating asthma. The studies provide data that are crucial for informing basic behavioral science about the most promising pathways and specific mechanisms that link stress and asthma. A further objective of research in asthma is to develop valid instruments for measuring behavioral factors in asthma management. Two studies are validating self-report instruments of adherence compared to electronic monitoring devices—one in children, the other in adults. Another study is seeking to determine the age at which children can report their asthma status reliably. Findings from these studies will be an important contribution to methods and measures used in the behavioral sciences.

Behavioral risk factors: body mass, exercise, tobacco use. In addition to several studies of the genetics of metabolism and obesity, NHLBI-supported investigators are studying the

relationships between weight loss, obesity, and gastric bypass derangement. The causes of obesity in the face of equivalent-calorie diets are not understood completely. Scientists are investigating why some animals fed a moderately high-fat diet become obesity-prone, and others do not. The Institute also supports studies of the basic physiology of exercise and on the effect of nicotine on the cardiovascular and pulmonary systems.

Development of technologies. The NHLBI supports a significant number of projects developing new or improved methods of measuring behavioral, social, and related variables. New technologies are essential for basic studies of lifestyle risk factors and social processes. Projects include methods for dietary assessment in children and adults, statistical causal analysis systems for processing complex data from research designs involving encouragement rather than explicit interventions, and statistical systems for analyzing complex longitudinal data in the behavioral sciences.

Future Planned Initiatives

•*Stress research.* Because of the key role of stress in the physiology of mammalian species, the NHLBI convened a Working Group on the Cardiovascular Consequences of Chronic Stress on June 14-15, 2004. The Working Group identified research needed to elucidate the basic mechanisms underlying pathological cardiovascular events mediated/caused by stress. Working group recommendations for basic behavioral research include studies of neuroplastic modifications induced in nervous system pathways by long-term stress, research on vascular responses to stress, development of appropriate imaging tools, and studies on social stress influences on energy metabolism, eating behavior, and obesity. The Executive Summary of the Working Group Report is available at http://www.nhlbi.nih.gov/meetings/workshops/heart_stress.htm , and a full report is being prepared for publication.

Technology and methods. Two initiatives are under development for the Small Business Innovation Research and Small Business Technology Transfer programs to encourage Bioengineering Approaches for Prevention and Treatment of Overweight and Obesity. Their purpose is to develop technologies for assessing energy balance and measuring individual energy usage.

Research Needs

Lifestyle change and adherence to medical regimens. Improvement in healthy lifestyles could substantially reduce not only the current worldwide epidemic of overweight and obesity, but also addictive behaviors such as substance abuse and alcoholism, and unhealthy health habits such as sedentariness and tobacco use. Furthermore, lack of adherence to medical regimens reduces the effectiveness of known treatments for chronic conditions such as hypertension and cardiovascular diseases. Finally, non-adherence exacerbates illnesses caused by known pathogens (e.g., TB, HIV, other sexually transmitted agents) due to the development of treatment resistant strains. Progress in this area will require further basic behavioral research in such areas as motivation, emotion, translation of sensory input into perceptually meaningful signals, the

effects of sensory input on decision making, risk perception, and the development of risk perception in childhood. More research is also needed on the effects of early life influences or critical periods in the development of relevant behavioral characteristics, the degree to which they are acquired or genetically determined, and the extent to which they may result from interactions between genetic and acquired influences.

Stress research. Although the biological responses to emotional stress are understood at a basic level, numerous links in the cascade of responses to stress are only hypothesized, rather than proven or understood in detail. The direct steps and detailed links in the cascade, which occur at the level of genes and proteins, transporters, intracellular second messenger systems, and transcription factors, remain to be elucidated. The role of the molecular responses to stress in regulating immune responses and inflammatory processes involved in airway and vascular function are poorly understood. Moreover, neither the plasticity of the molecular response nor the extent to which compensating adaptations are possible have been studied. Finally, although researchers suspect that critical periods exist in early development that alter vulnerability to stress-related illness in adulthood, this hypothesis and the nature of behavioral adaptations involved require further research and testing.

New research tools and instruments are needed to characterize acute and chronic stress and depression and anxiety in the presence of somatic illnesses such as pulmonary, cardiovascular, and blood diseases.

Genetic research. The importance of gene-environment interactions is now widely acknowledged. Nonetheless, the importance of the behavioral environment is not yet fully appreciated. Genetic research will achieve its full potential more rapidly with the development of a general classification of behavioral phenotypes. Although some progress has been made in behavioral phenotyping of isolated mental disorders (e.g., autism, Lesch-Nyhan syndrome) behavioral phenotypes have not been established for many conditions (e.g., stress, resilience) that have implications for somatic illnesses. The Institute supports several studies to identify polymorphisms that regulate nervous and endocrine system responses to stress and affect cardiovascular regulation.

Cognitive function. Cognitive function is a fundamental process that underlies risk assessment and is involved in a myriad of lifestyle choices. A recent study showed that, although dietary salt restriction improved memory and learning in a salt-resistant rat strain, certain cognitive tasks were impaired in a related, but salt-sensitive strain. How various electrolyte sensitivities influence cognitive abilities has not been investigated previously. Research on the role of salt sensitivity on cognitive function may lead to improved understanding of the basic mechanisms underlying cognitive processes.

Sleep research. Basic behavioral and social science research needs in sleep include elucidating the physiological and behavioral adaptations to chronic sleep restriction; understanding the neurobehavioral effects of chronic partial sleep loss at various circadian phases; identifying factors that account for individual differences in sleep need and in differential vulnerability to cognitive deficits in response to sleep deprivation; and developing new methods for quantifying the structure of sleep, both in sleep laboratories and natural environments. The NHLBI National

Center on Sleep Disorders Research recently published a strategic plan describing numerous basic behavioral and neuroscience research needs in sleep research. The report is available at <http://www.nhlbi.nih.gov/health/prof/sleep/>
http://www.nhlbi.nih.gov/health/prof/sleep/res_plan/index.htm.

**Basic Behavioral Research Grants supported by
National Heart, Lung, and Blood Institute (NHLBI)**

Grant Number	Grant Title	PI	Institution
5R01 HL065137-04	Neurogenetics, Serotonin, and Human Aggression	Manuck, Stephen,	University of Pittsburgh
2P01 HL036587-15A1	Genetics of Biobehavioral Risk Factors for CVD	Williams, Redford,	Duke University
1R15 HL073894-01	Early Experiences and Adult Responses to Stress	Sanders, Brian,	Drake University
5R01 HL065523-03	Depression, Epinephrine, Serotonin, and Platelet Function	Musselman, Dominique,	Emory University
1R01 HL079457-01	Analyzing Complex Longitudinal Data in Behavioral Sciences	Hogan, Joseph	Brown University
5R01 HL065719-03	Stress and Immunity in Pediatric Asthma	Nassau, Jack	Rhode Island Hospital
1R01 HL077453-01	Adaptation of Circadian Responses to Light Treatment	Czeisler, Charles	Brigham and Women's Hospital
5R01 HL062567-03	Causal Analysis of Encouragement Design Studies	Zhou, Xiao-Hua	Indiana University, Purdue
P01 HL069999-03	Stress-Related Mechanisms of Hypertension Risk	Treiber, Frank	Medical College of Georgia
5R01 HL073081-02	Memory Errors in Children's Dietary Recalls	Baxter, Suzanne	University of South Carolina, Columbia

**National Human Genome Research Institute (NHGRI)
Behavioral and Social Sciences Research**

The National Human Genome Research Institute (NHGRI) led the National Institutes of Health's (NIH) contribution to the International Human Genome Project (HGP), which had as its primary goal the sequencing of the human genome. This project was successfully completed in April 2003. Now, the NHGRI's mission has expanded to encompass a broad range of studies aimed at understanding the structure and function of the human genome and its role in health and disease.

After completing a more than year-long planning effort, the NHGRI created a vision document to guide the institute into a new era of genomic research. The vision, formulated into three major themes: genomics to biology, genomics to health, and genomics to society, includes six crosscutting elements (resources, technology development, computational biology, training, ethical, legal and social implications, and education) relevant to all three themes. As part of making this vision a reality, the NHGRI supports a broad array of behavioral and social science research performed by extramural researchers and also conducts such research in its own intramural program.

Description of Current Program

Ethical, Legal, and Social Implications Research Program

The NHGRI's Ethical, Legal and Social Implications (ELSI) Program was established in 1990 as an integral part of the Human Genome Project to foster basic and applied research, and support education and outreach. The ELSI program funds and manages studies related to the ethical, legal, and social implications of genetic and genomic research, and supports workshops, research consortia, and policy conferences related to these topics. Through the ELSI program the NHGRI funds a number of research grants in behavioral and social sciences research.

The NHGRI co-funds with the National Heart, Lung, and Blood Institute a large, five-year, multi-center clinical trial designed to examine issues surrounding phenotypic and genotypic screening for iron overload and hereditary hemochromatosis. The study examines attitudes about, acceptance of, and impact of screening in a diverse population (about 50% of the participants will come from minority communities).

The ELSI Research Program currently funds a number of projects on the ethical, legal, and social implications for both individuals and diverse population groups of genetic variation research. Human genetic variation research, especially as it relates to risk factors for common, complex disorders, is leading to increased knowledge regarding variation among individuals and how this variation may contribute to the health status of individuals. It is also leading to more knowledge about variation within and among different racial and ethnic groups (to the extent that such groups can reasonably be identified) and how this variation may contribute to the aggregate health status of those groups. The NHGRI's initiative to develop a haplotype map of the human genome will make it possible to conduct human genetic variation research (in particular, disease gene association studies) more quickly and efficiently than ever before, resulting in even more

rapid proliferation of this new information. Information regarding variation within and among groups, in particular, will increasingly be generated, because the map will facilitate association studies in selected populations in which certain diseases are more or less prevalent. While the ultimate goal of studies aimed at relating human genetic variation to disease risk is the improvement of human health, concerns have been raised that the findings of some genetic variation research may be misunderstood. Concerns also have been raised that such findings, if interpreted incorrectly and misused, will exacerbate, rather than ameliorate, already-existing health disparities among racial, ethnic, and socio-economic groups.

The ELSI Research Program also funds projects that examine issues surrounding genetic testing in Alzheimer disease and in obesity. These multifaceted grants include assessments of knowledge and attitudes toward genetic testing, interest in and demand for testing, and the impact of testing on individuals and their families, and the development of effective strategies for educating people and health care providers about the benefits, risks, and limitations of genetic testing. Also funded are a number of projects to examine how individuals from diverse racial, ethnic, and socio-economic groups view and are affected by genetic information and technologies, such as those utilized in newborn screening and prenatal screening and diagnosis.

Other ELSI funded projects include research on important policy issues regarding genetic and genomic information, such as issues surrounding DNA profiling and the use of DNA forensics in the criminal justice system, DNA patent practices and policies at academic institutions, concerns and expectations of persons with disabilities, and behaviors and experiences with genetic discrimination among physicians.

Social and Behavioral Research Branch

In December 2003, NHGRI launched a new branch - the Social and Behavioral Research Branch (SBRB) within the NHGRI's Division of Intramural Research. The SBRB has the overarching and broad objective to investigate social and behavioral factors that facilitate translation of genomic discoveries for health promotion, disease prevention and health care improvements. This research encompasses four conceptual domains: identifying "best practices" in genetic counseling; developing and evaluating behavioral interventions; evaluating community involvement strategies in genomic research and dissemination; and understanding social, ethical, and policy implications of genomic research.

The increasing availability of genetic technologies capable of identifying the presence of gene mutations that predispose individuals to increased risk for a variety of diseases has increased the need for original research across a broad area of behavioral and social science topics. Presentation of options for genetic testing, conveying risk implications, and related counseling presents challenges for individuals, families, health care providers, communities and the larger society. Current research within the SBRB includes: decision monitoring for adolescent participants in gene transfer research; genetic and environmental risk assessment for cancer; preferences of families for recruitment approaches to genetics research; coping strategies of families that include individuals with a chromosome abnormality (e.g., individuals with Friedreich Ataxia, hereditary nonpolyposis colorectal cancer, or Marfan syndrome); and

exploring adult adoptees' perceptions regarding the value of personal and familial genetic health information.

With the formation of the new SBRB, research priorities will broaden and deepen. A research priority is to increase the evidence base for methods underlying “best practices” in genetic counseling for individuals and families that can result in informed decisions, and encourage, when appropriate, taking preventive actions. Identification of genetic susceptibility markers for common diseases heralds the coming of personalized medicine. Therefore, a new area of research to which SBRB researchers will give priority is evaluating the potential of communication of genetic susceptibility information to promote lifestyle risk factor reduction, such as smoking cessation. National surveys indicate that the health care work force is not ready or adequately trained to convey susceptibility results for complex disorders or provide related support services. Thus, a third priority for SBRB researchers is to develop and evaluate genetic counseling approaches that can be disseminated to primary care and public health contexts. Evaluating community interests in research and dissemination of genomics to promote health also will be a research priority for SBRB. In this domain, the branch plans to conduct research to understand community perceptions and preferences related to genomic discoveries and research. In turn, the knowledge gained will be used to develop and evaluate outreach and community participation approaches. Lastly, SBRB will give priority to research in bioethics and social policy, in particular to research relating to the ethical and policy implications of integrating genetics into clinical practice and of involving of human subjects in genomics research

Future Planned Initiatives

In August 2003, the ELSI Research Program issued a Request for Applications inviting the development of Centers of Excellence in ELSI Research (CEERs). CEERs will bring together investigators from multiple disciplines to work in innovative ways to address important new, or particularly persistent, ethical, legal, and social issues related to advances in genetics and genomics.

The CEER program is designed to support the development of research centers that will identify and investigate ELSI research questions best approached through intensive and extended collaboration among investigators from multiple disciplines, using diverse methodologies. The investigators in a CEER are encouraged to consider new ways to explore these questions, design innovative and efficient research projects, propose and disseminate health or social policy options based on Center research and, when feasible, facilitate policy development pertinent to a specific issue. Center applicants were particularly encouraged to identify cutting-edge research topics and approaches that have the possibility of leading to high-payoff solutions to important ELSI problems.

Basic Behavioral Research Grants supported by National Human Genome Research Institute (NHGRI)			
Grant Number	Grant Title	PI	Institution
1 R01 HG002830-01	Learning about Research in North Carolina	Corbie-Smith	University of North Carolina, Chapel Hill
1 R01 HG002689-01	Distrust, Race/Ethnicity, and Predictive Genetic Testing	Armstrong, Katrina	University of Pennsylvania
1 R03 HG002499-02	Values, Attitudes and Beliefs in Obesity Genetic Testing	Segal, Mary	University of Pennsylvania
5 R01 HG002191-03	Race and Public Communication about Human Variation	Condit, Celeste	University of Georgia
1 R01 HG002431-02	Views of Privacy of Genetic Information	Klitzman, Robert	New York State Psychiatric Institute
1 R01 HG002686-01	Parent Communication of BRCA 1/2 Test Results to Child	Tercyak, Kenneth	Georgetown University
1 R01 HG002213-04	Risk Evaluation and Education for Alzheimer's Disease	Green, Robert	Boston University Medical Campus
1 R01 HG002170-02	Enhancing Patient Prenatal Education – A Feasibility Study	Sorenson, James	University of North Carolina, Chapel Hill
1 R01 HG003228-01	Use of Genetics in Neurologists' Clinical Practices	Browner, Carole	University of California, Los Angeles
1 R01 HG002085-04	Expanded Newborn Screening for Metabolic Disorders	Waisbren, Susan	Children's Hospital

**National Institute on Aging (NIA)
Basic Behavioral and Social Sciences Research**

The research pursued by the NIA covers a wide range of issues and concerns aimed at improving the quality of life for older people and their families. Research is focused in four general areas – the biology of aging, reducing disease and disability, Alzheimer’s disease and cognitive changes, and the behavioral and social aspects of aging. In addition to NIA’s Intramural Research Program (IRP), four extramural programs in NIA administer research that corresponds to these areas: the Biology of Aging Program (BAP), Geriatrics and Clinical Gerontology (GCG) Program, Neuroscience and Neuropsychology (NNA), and the Behavioral and Social Research (BSR) Program. The majority of activity in basic behavioral and social sciences research is conducted through the BSR and NNA extramural programs and through the IRP.

Description of Current Program

The National Institute on Aging (NIA) supports basic social and behavioral research and research training on the processes of aging at both the individual and societal level - focusing on how people change over the adult life course, on the interrelationships between older people and social institutions, and on the societal impact of the changing age-composition of the population. Emphasis in this arena is placed upon the dynamic interplay between the aging of individuals and their changing biomedical, social and physical environments and on multi-level interactions among psychological, physiological, social and cultural levels.

The NIA also supports a broad spectrum of research and training aimed at a better understanding of age-related normal and pathological changes in the structure and function of the nervous system and how such changes affect behavior, as well as research relevant to those geriatric problems arising from psychiatric and neurological disorders associated with aging, particularly Alzheimer’s disease. Because changes in brain functions are related to many age-related decrements in function that require institutional care, this research can have a profound influence on the quality of life of older individuals, as well as significant implications for public policies involving the nature and quality of healthcare services.

The NIA recognizes the importance of integrating genetics and genomics with the behavioral and social sciences, and places an emphasis on developing such research relevant to the NIA mission. In all of these aspects of basic social and behavioral research, NIA is committed to addressing racial and ethnic issues and health disparities, not only with respect to appropriate scientific questions, but also with respect to the training of investigators.

Areas of Research Emphasis:

- **Demography and Epidemiology** - Embraces such topics as medical and bio-demography; changes in the age-structure of populations, as well as studies on the prevalence and incidence of disease and disability, and age trajectories of health; life expectancy and active life expectancy; forecasting functioning, disability, morbidity, and mortality; migration and geographic concentrations of older people; rural-urban comparisons; distributions of health services and the long-term care system; race, ethnic, and socioeconomic variations; and genetic epidemiology and population genetics.

- **Health and Retirement Economics** - Concentrates on the economics of aging, including but not limited to, economic and health antecedents and consequences of work and retirement; pensions and savings; health insurance and health care expenditures; Medicaid, Medicare, and Social Security; interrelationships between health and economic status, including issues related to wealth, poverty, productivity, human capital development, and economic development; the economic costs of disability; cost-effectiveness of interventions; impact of taxation policies on older people; and cross-national comparisons.
- **Health and Social Institutions** - Encourages research on the impact of a wide range of formal health care and related services, with particular emphasis on long-term care systems and settings and on the health and well-being of older persons. In addition, research examines how social institutions (e.g., work, family, religion, community, living arrangements) influence health outcomes in the later years and the ways in which people influence, and are influenced by, the network of cultural and social institutions surrounding them.
- **Behavioral Medicine and Interventions** - Stimulates research on health behavior (prevention, lifestyle, disability postponement) and illness behavior (care, care seeking, and coping) that emphasizes the impact of the social and psychological environment and their related processes upon the health of older persons, including research on diverse populations. The NIA portfolio also contains physiological and clinical research related to the interaction of individuals with social and psychological processes such as stress.
- **Cognitive Aging** - Supports research on changes in cognitive functioning over the life course. Studies are encouraged that examine the influence of contexts (behavioral, social, cultural, and technological) on cognitive functioning and life performance of aging persons; investigate the effects of age-related changes in cognition on activities of daily living, social relationships, and health status; and develop strategies for improving everyday functioning through cognitive interventions. Major research topics include: higher-order cognitive processes (e.g., problem-solving, decision-making), social cognition, memory strategies, perceptual skills, and reading and speech comprehension. Research is also welcomed that explores the role of individual difference factors in cognitive functioning, e.g., motivation, self-efficacy, beliefs about aging, emotions, and sensory limitations.
- **Psychological Development and Integrative Science** - Promotes research that applies an integrative approach to the study of health, behavior, stress and coping, and well-being over the life course. Studies are encouraged that 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.
- **Neuropsychology and Neurobiology of Aging** - Promotes research on the mechanisms underlying how attention, learning, memory, spatial orientation, language, affect, reasoning, decision-making, and judgment may change with age and experience, especially research on the interactions between the brain and behavior; mechanisms involved in neuronal plasticity in response to environmental influences and age; and cellular and molecular mechanisms involved with permanent changes in neuronal function as a result of external stimuli. Also of

interest, are studies involving age-related mechanisms underlying sleep-wakefulness cycles and behavioral sequelae in the aged, since abnormal sleep in the older person often reflects concurrent disease states associated with alterations of circadian rhythmicity and can have profound impact on behavior, cognition, other morbidities, and mortality. Research is supported from different disciplines including those of basic molecular and cellular neurobiology, experimental and physiological psychology, cognitive science, clinical neuropsychology, systems neuroscience, behavioral neurobiology, psychiatry, and neurology to expand understanding of the mechanisms and processes underlying cognitive, affective, and perceptual behavior over the adult life-course.

- **Dementias of Aging** – Supports basic, clinical, and epidemiological studies of the etiology, diagnosis, and treatment of Alzheimer's disease (AD) and other dementias and treatable brain disorders of older people. Of particular relevance are population studies that include the development of diagnostic screening instruments and behavioral markers for cognitive decline and AD for use in heterogeneous and culturally varied populations, including studies of neuropsychological batteries; clinical trials of pharmacologic agents and studies of behavioral and environmental interventions, individually and in combinations to prevent age-related cognitive decline, mild cognitive impairment or development and progression of AD; and studies to preserve function and reduce excess disability, including research on wandering, insomnia, pacing, agitation, and feeding and dressing difficulties.

Future Planned Initiatives

- **Biodemography and Behavioral Genetics.** The NIA will foster the development of biodemography by commissioning papers from experts on promising directions, such as extensions of theory to include multiple genes and multiple phenotypes and collaborative work on aging by physiologists, geneticists and demographers.

The 2003 NIA “Environmental Workshop for Genetically Informative Studies on Aging” identified social environments as a main theme, and proposed new work on the role of genes in shaping social environments and how social environments may affect genetic expression. Papers from this symposium will be published in 2005.

The NIA has asked the National Academy of Sciences (NAS) to hold a follow-up meeting to an earlier NIA-sponsored NAS workshop on the potential costs and benefits of collecting biological indicators in household surveys, which resulted in the publication “Cells and Surveys: Should Biological Measures Be Included in Social Science Research?” The NAS would review the enormous advances in the types of biological measures that are being collected in social science surveys and the statistical techniques that are being used to analyze them. Among other topics, the planned workshop would address new statistical methods to incorporate biological measures into social science research; ethical issues associated with collection and storage; the types of biological measures that social scientists should collect; and future research directions.

- **Disability Decline and Related Interventions.** The NIA is supporting a series of workshops organized by the National Bureau of Economic Research to take stock of current

research on pathways to disability, alternative measures of disability, and explanations for changing disability and societal implications of the trend. One of the workshops has identified promising “small interventions with big results” in decision-making. The NAS Committee on Population has also been asked to convene a workshop to develop a research agenda for interventions that could maintain or accelerate the trend for disability decline. International collaborative studies partially sponsored by NIA, notably the English Longitudinal Study of Aging and the Surveys of Health and Retirement in Europe, should help us understand the U.S. disability decline in a comparative context.

The NIA also plans to review the empirical base for the design of interventions that integrate biological, behavioral and social factors to preserve physical and cognitive function, in order to encourage this area of research toward interventions to accelerate disability decline among older people.

- **Cognitive Training.** There is interest in cognitive training or interventions as protection against cognitive decline. In March 2003, researchers met to discuss their varied perspectives on what might be included in the next generation of intervention and training studies. This highly successful NIA symposium proposed many ideas for new approaches to cognitive interventions that involved lifestyle changes and cognitive engagement activities; revised papers from the symposium will be published as a special issue of a journal. NIA staff will also continue to work with the investigators involved in the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) trials on promising intervention research.
- **Decision making.** The Health and Retirement Survey (HRS) is increasingly interested in cognitive change with age as an important moderator for measures of mental health, insurance coverage, financial status, family support systems, labor market status, and retirement planning. The HRS is collaborating with cognitive psychologists to improve the psychometric properties of the cognitive measures in the HRS currently. Several of the Roybal Centers are exploring innovations such the relation of emotional regulation to health-related choices and the use of Internet panels to study economic decisions of older people.
- **Sleep.** It has been estimated that insomnia affects about a third of the older population in this country. This inability to have restful sleep at night results in excessive daytime sleepiness, attention and memory problems, depressed mood, falls, and lowered quality of life. The NIA worked with the National Sleep Foundation (NSF) to develop their first Leadership Congress on Sleep, Health and Aging, held in 2003. A report of the meeting will be published in JAMA, and a report on the final recommendations from this meeting is in preparation. The NIA will be a co-sponsor of a major conference on “Frontiers of Knowledge in Sleep and Sleep Disorders: Opportunities for Improving Health and Quality of Life” in 2004. A State-of-the-Science Conference on Insomnia is being planned, with NIMH as the lead, for FY 2005.
- **Stress and Disease.** A growing body of evidence has implicated family care-giving as a risk factor for health. Significantly higher levels of proinflammatory cytokines have been found in men and women chronically stressed by care giving for a spouse with dementia than those

- of similar individuals who did not have care giving responsibilities. Compared to non-caregivers, men and women who provide care to a spouse with a dementia report more infectious illness episodes, they have poorer immune responses to influenza virus and pneumococcal pneumonia vaccines, their wounds heal more slowly, and they are at greater risk for developing hypertension and coronary heart disease. To explore the current state of knowledge on the role of inflammation on aging and in the development of many chronic diseases of aging, identify gaps in understanding, and determine opportunities for future research, the NIA has planned a multidisciplinary “Workshop on Inflammation, Inflammatory Mediators, and Aging” in 2004.
- **Executive Function/Dysfunction and Aging.** Behaviors such as organization, sequencing, monitoring decisions, inhibition of irrelevant information, and management of multiple tasks have been collectively termed executive function. In recognition of the importance of executive function to maintaining independence and functional capacity, two workshops were held in 2003 – one supported by NIA and another that was a trans-NIH workshop. In order to develop an integrated plan to implement recommendations from these workshops, a Steering Committee on executive function and aging will be formed in 2004 as a forum to address ways to stimulate research in this area.
- **Cognitive and Emotional Health Project:** Known as the “Healthy Brain Project,” this trans-NIH initiative involving NIA, NIMH and NINDS is an effort to assess the state of longitudinal and epidemiological research on demographic, social and biologic determinants of cognitive and emotional health in aging adults and the pathways by which cognitive and emotional health may reciprocally influence each other. A number of activities have been undertaken to accelerate the pace of scientific advances in these fields, including creation of an NIH website (<http://trans.nih.gov/cehp>). During 2004, a blue ribbon committee (Critical Evaluation Study Committee) will review and critically analyze the extant literature on factors for maintaining cognitive and emotional health in the adult; the committee’s analyses are expected to be presented in a final report in January 2005.
- **Cognitive Reserve:** It has been repeatedly noted that there is no clear direct relationship between the degree of brain pathology and the clinical manifestations in a variety of central nervous system insults, such as stroke and AD. The concept of a reserve - the degree of cognitive flexibility or brain plasticity that is inherent in an individual, or acquired as a result of experiences, or both - is now being invoked to address these effects. The NIA held an exploratory workshop, “Brain/Cognitive Reserve and Aging,” in 2003 that provided a forum to hear recent research results on theories and advancements about cognitive reserve and the aging brain. Widespread interest in the concept indicated to NIA that this was an important area of research that would have impact on how we consider the function and the plasticity of the aging brain, and NIA will be considering ways to stimulate research in this developing area.

Opportunities Not Currently Addressed

The NIA is interested in exploring additional research on intrinsic and extrinsic factors for maintaining cognitive and emotional health into older age and for delaying the onset of diseases

such as AD, for both minority and white elderly; pre- and post-caregiving behavior and roles; interventions that target the coping strategies and behavior of both caregiver and recipient simultaneously; and the most effective behavioral interventions for health promoting activities (e.g., physical activity; diet) and the means to translate those interventions into clinical practice and practical lifestyle changes.

Basic Behavioral Research Grants supported by National Institute on Aging (NIA)			
Grant Number	Grant Title	PI	Institution
R37 AG005739	Improvement of Visual Processing in Older Adults;	Ball, Karlene K.	University of Alabama at Birmingham
P30 AG012846	Michigan Center on the Demography of Aging	Bound, John	University of Michigan at Ann Arbor
P01 AG018911	Social Isolation, Loneliness, Health & the Aging Process	Cacioppo, John T.	University of Chicago
P01 AG022500	The Biodemography of Life Span	Carey, James R	University of California/ Davis
R01 AG023347	Biological Risk Underlying Education Health Differences	Crimmins, Eileen M.	University of Southern California
R37 AG019905	Pathogenesis of Physical Disability in Aging Women	Fried, Linda P.	Johns Hopkins University
R03 AG021796	The Affective Profiles of Typical Experiences	Kahneman, Daniel	Princeton University
R01 AG007137	Dynamic Growth & Change in Adult Intellectual Abilities	McArdle, John J.	University of Virginia Charlottesville
P01 AG020166	Integrative Pathways to Health and Illness	Ryff, Carol D.	University of Wisconsin/ Madison
R01 AG017056	Biological Explanation of SES Differences in Health	Seeman, Teresa	University of California/ Los Angeles
P01 AG008761	Oldest-old Mortality – Demographic Models and Analysis	Vaupel, James W.	Duke University
N01 AG09740	Health and Retirement Study	Willis, Robert J.	University of Michigan
P01 AG005842	Economics of Aging	Wise, David A.	National Bureau of Economic Research
R01 AG016206	Cognitive Test Performance of African American Elders J.	Manly, Jennifer	Columbia University
R37 AG017609	Neurobiological Consequences Of Hypertension And Age	Moss, Mark B.	Boston University
R01 AG016714	Behavioral and Imaging Approaches to Implicit Memory in Aging	Stern, Yaakov	Columbia University

**National Institute on Alcohol Abuse and Alcoholism (NIAAA)
Basic Behavioral and Social Sciences Research**

Current Programs

Alcohol Consumption, Reward, Sensitization, Tolerance, Dependence, Relapse

Alcohol dependence, commonly called alcoholism, is characterized by an abnormal desire to procure and drink alcohol, and by drinking excessive quantities once alcohol is obtained. NIAAA supports research in humans and in animal models that seeks to understand the behavioral manifestations of alcoholism, including excessive alcohol seeking, excessive alcohol drinking, and craving, and to identify the environmental and biological determinants that contribute to the development of alcoholism. This research attempts to describe how conditions of alcohol availability exacerbate the motivation to drink, and drive the development of alcohol dependence; how tolerance, sensitization, dependence, and withdrawal mediate excessive alcohol drinking; and how repeated exposure alters neurological processes, thereby increasing susceptibility for relapse to drinking and engendering the consumption of higher alcohol doses once relapse occurs.

An important component of NIAAA's behavioral research program is to understand the learning and conditioning processes that lead people to seek out environments in which alcohol drinking occurs, and how these environments elicit alcohol craving and trigger relapse to drinking. In addition, NIAAA supports research studies of brain peptide systems that are associated with eating and eating disorders. These systems may also influence alcohol drinking, and the abnormal functioning of these systems may be a factor in the development of alcohol dependence.

NIAAA supports research of human and animal investigations to determine the neural mechanisms underlying the causes and consequences of drinking. One strategy of this research is to alter specific neuronal processes at the molecular level, and subsequently examine the effects of these molecular manipulations on the expression of alcohol-related behaviors. Molecular manipulations may include disruptions of neurotransmitter receptor function, of enzymes that regulate synaptic and neuronal activities, and of the molecular interactions between proteins within neurons. A second approach employs both naturally-occurring and artificially-induced genetic variations in animal models to identify genes and pathways relevant to alcohol consumption, sensitization, excessive drinking, tolerance, dependence and withdrawal. Both classical breeding techniques and newer molecular genetics and genomics approaches are used to generate animal models to study these behaviors. These studies have been instrumental in defining those brain processes and neural circuitry which underlie voluntary alcohol consumption, tolerance to alcohol's effects, and deficits in motor activity and in learning and memory associated with alcohol intoxication.

Chronic alcohol ingestion can result in several behavioral neuroadaptations towards alcohol, including the development of tolerance, sensitization, and dependence. Abstinence can lead to withdrawal effects and relapse to drinking. Research on the biochemistry, anatomy, and physiology of these neuroadaptive processes is beginning to clarify the nervous system's

response to chronic alcohol consumption. NIAAA supports an integrative program that combines the development of animal behavioral models with molecular, cellular, and systems level measures of brain function to enhance the understanding of the behavioral response to alcohol. The Integrative Neuroscience Initiative on Alcoholism (INIA) was created to support and facilitate multidisciplinary, collaborative research across scientific disciplines and research institutions. The INIA WEST consortium is lead by George Koob of the Scripps Research Institute (AA13517 *Integrative Neuroscience Initiative on Alcoholism*) and is a collaborative project among Baylor College of Medicine, Indiana U/Purdue U., Oregon Health & Science University, the Scripps Research Institute, SRI International, U. of Colorado Health Sciences Center, and U. Texas at Austin. The theme of the INIA WEST consortium is “*The Neurobiological Basis of Excessive Drinking*”. The goal of that consortium is to understand the neurobiological basis for the “loss of control” of alcohol intake, and to identify the neuroadaptive changes occurring in a region of the brain, the amygdala, that makes up part of the brain’s reward circuitry. The consortium uses a common set of resources in the pursuit of scientific goals and provides opportunities for cross-disciplinary collaborations between alcohol researchers and investigators from other research areas.

Stress effects

Stress is a major environmental contributor to alcohol drinking, craving, and relapse. The variety of stressful events and the variation among individuals in their ability to cope with stress, make understanding mechanisms of stress-induced drinking challenging. NIAAA supported research evaluates stressful conditions giving rise to alcohol drinking and associated hormonal and neuronal responses. Laboratory models developed by stress researchers are incorporated in animal studies using models of alcohol drinking and relapse. These projects identify characteristics of stressors that induce individuals to drink heavily, precipitate relapse, or increase ongoing drinking as well as the characteristics of individuals that make them susceptible. They also examine associated changes in the Hypothalamus-Pituitary-Adrenal Axis, identify neural circuits associated with stress-induced drinking, and delineate enduring changes resulting from chronic alcohol exposure and chronic stress exposure.

INIA EAST, another collaborative consortium, comprises the Medical University at South Carolina, University of Memphis, University of Tennessee Health Sciences Center, University of Tennessee – Battelle, LLC-Oak Ridge National Laboratory, Vanderbilt University, and Wake Forest University Health Sciences) and is led by Kathleen Grant of Wake Forest University. The theme of INIA EAST (AA13641, INIA) is “*Stress-Anxiety of Alcohol Abuse.*” The consortium seeks to understand how stress contributes to excessive alcohol consumption and to identify the genes, neurochemical pathways, neural circuits and behavioral responses involved in alcohol-stress interactions.

Aggression and Impulsivity

Basic research on alcohol-heightened aggression and impulsivity explores relationships between alcohol drinking and violence. For example, does alcohol drinking cause people to become violent, do violent environments cause people to drink heavily, or both? NIAAA supports laboratory models that allow studying environmental, personality, cognitive, and biological risk

factors for alcohol-heightened aggression in animal and human subjects. Studies measuring human aggression in the laboratory allow scientists to examine hormonal and neurochemical underpinnings of alcohol-heightened aggression, as well as the influence of cognitive strategies, and psychiatric and sociological influences.

Adolescence/Underage Drinking

The NIAAA supports basic behavioral and biopsychosocial research in the following areas: 1) neurobiological mechanisms and risk factors for alcoholism during late childhood through adolescence; 2) the relative contribution and/or interaction of genetic, environmental, and social factors (e.g., stress, peer influences) with neurobiological mechanisms in the development of adolescent alcohol abuse; 3) evaluation of the immediate and long-term consequences of heavy drinking during adolescence on cognitive/brain functioning; and 4) the contribution of early alcohol exposure to excessive drinking and abnormal cognitive and social functioning during subsequent developmental stages.

Cognition and Brain Damage

Brain damage is a common outcome of chronic heavy drinking. Even mild-to-moderate drinking can adversely affect cognitive functioning, and 50-75% of detoxified alcoholics manifest some degree of cognitive impairment. Susceptibility to alcohol-induced brain damage depends on many factors such as age, gender, and nutritional status.

Using neuroimaging, neurophysiological and cognitive techniques, researchers are assessing:

- a) The nature and extent of alcohol's effects on the brain and cognition.
- b) The effects of alcohol on the emotional/motivational system.
- c) The interaction of age, gender and alcohol consumption on cognitive and brain function.
- d) Reversibility of deficits with prolonged abstinence.

Understanding the contribution of cognitive impairment to relapse and the potential of recovery of brain and cognitive function to successful treatment outcome are important goals.

The NIAAA funds numerous studies on Fetal Alcohol Spectrum Disorders (FASD). The FASD studies include both animal model studies and human studies; many of these involve neuroimaging and behavioral measures and thus seek structure-function relationships in FASD. For example, in a study by Clair Coles, Emory U. (AA014373 *Prenatal alcohol exposure: Adult Neurocognition*), the relationship between brain structure and neuropsychological deficits in adult, prenatally ethanol exposed subjects, is investigated by using structural and functional MRI and diffusion tensor imaging.

Behavioral Genetics Studies

The development of alcoholism is influenced by underlying biological susceptibility factors, by environmental factors, by complex interactions among genes, and between genes and environment. The Behavioral Genetics Program includes an eight-site (SUNY Downstate Medical Center, U. Connecticut, Indiana U., Iowa U., VA Medical Research Foundation and U.

California at San Diego, Washington U., Southwestern Foundation for Biomedical Research at San Antonio Texas, Rutgers U.) national consortium entitled The Collaborative Study on the Genetics of Alcoholism (COGA). Henri Begleiter, SUNY Downstate Medical Center has been the leader on the COGA project (AA08401) that has been supported by the NIAAA for nearly 15 years as a co-operative agreement. The overarching goal of the COGA project is to identify and characterize genes that affect the susceptibility to develop alcohol dependence and related behavioral and biological phenotypes and to measure associated environmental features, with emphasis on the cascade of events that leads to the onset of the disorder. COGA will also initiate a prospective study of adolescents and young adults from high risk and control families for clinical, behavioral, biological and genetic studies and test the hypothesis that behavioral impulsivity may be a major subcomponent of an underlying biological variation that influences susceptibility to alcoholism and various behaviorally related phenotypes.

Many NIAAA behavioral genetics studies involve the relationship between genetics and alcohol consuming behavior. In the broader view, these studies seek to define how the genetic makeup of an individual influences reward seeking behavior. In this case a specific application relevant to the NIAAA mission of alcohol consumption is the behavioral concern. Recently funded studies have identified chromosomal regions containing genes that influence alcohol related behaviors. Specific genes within those regions are being subsequently tested to identify relevant relationship with alcohol-related behaviors and critical pathways involved in alcohol abuse and dependence. Genetic aspects of multiple complex behaviors are being studied in NIAAA funded projects. For example, some investigators in the INIA East consortium are focused on identifying the genetic variables that determine stress reactivity. Since stress facilitates relapse to alcohol dependency, it is hypothesized that genetic contributions that increase stress reactivity increase the risk for relapse.

Miscellaneous New Developments

Recent data indicate that alcohol dependence may occur much earlier in life than previously realized. Therefore, studying alcohol use, abuse and dependence is a primary focus of the NIAAA. The COGA project is about to begin a new series of studies on adolescents and young adults. In order to provide a more reliable measure of alcohol abuse and dependence the COGA team is testing, validating, and developing/improving an instrument for better diagnosis in adolescence and young adults.

Alcohol dependence is a complex disease; indeed, research shows evidence that, as with other chronic conditions, there may be subtypes of alcoholism; thus it remains difficult to study alcoholism genetically, physiologically, biochemically, or with reference to relevant environmental factors without valid sub-classifications. Investigators in the COGA project use physiological endophenotypes to assist them in developing novel alcohol relevant phenotypes for study that may subdivide the population into individuals with similar risk factors.

New multivariate models are being developed within the COGA project and other NIAAA sponsored projects to test hypotheses about outcomes resulting from the interactions of risk, individual factors, and environment.

Medications development studies include rodent and primate studies examining a variety of small molecules and their effect on various aspects of alcohol consumption. New behavioral animal models are being developed and tested for potential as screening methods for medications.

Future Planned Initiatives

- Acute alcohol consumption affects many biological processes, and chronic alcohol leads to multiple neuroadaptive responses. Continued research is needed to study the effects of acute and chronic alcohol consumption at the molecular level, further characterize known molecular targets and identify new targets, and determine the contributions of these molecular entities towards the behavioral responses to alcohol drinking.
- Systems biology and neurocomputational approaches should be used to describe or model the interactions between biological processes within the brain and nervous system, and to predict the effect of alcohol consumption on neuronal function, thereby facilitating and enhancing the study of alcohol abuse and addiction research.
- Support is planned for mechanistic studies (at the basic animal behavioral model level) for combined alcohol and nicotine abuse.

Unique Opportunities

- New imaging technologies (fMRI; DTI; and multimodal imaging fMRI, MEG) offer opportunities to study extent of alcohol-induced brain damage as well as progression of recovery.
- INIA will develop animal imaging technologies that enable controlled experimental studies of the effects of chronic alcohol exposure on brain structure and function.

Opportunities Not Currently Addressed

- Study of the effects of patterns of chronic heavy drinking during adolescence, including binge drinking, on normal brain, cognitive, and behavioral development.
- Study of how possible alterations in normal brain and behavioral development as a result of early exposure contribute to the maintenance and continuation of drinking.
- Individual differences in neurobiological risk and behavioral/temperamental risk markers including:
 - 1) The extent to which behavioral, physiological, and neural measures of emotion identify children and adolescents at risk for alcohol abuse.
 - 2) The degree to which individual differences in emotional reactivity to stress or trauma during development produce differential vulnerabilities to alcohol abuse and dependence,

and conversely, does alcohol intake during adolescence produce differences in emotional reactivity.

- 3) The use of neuroimaging technology to identify neural risk markers during development.

Basic Behavioral Research Grants supported by National Institute of Alcohol Abuse and Alcoholism (NIAAA)			
Grant Number	Grant Title	PI	Institution
5R01 AA012882-03	Hypothalamic Peptides in the Control of Alcohol Intake	Hoebel, Bartley G.	Princeton University
5R01 AA013341-04	Neuronal Signaling in Alcohol Preference	Pandey, Subhash G.	University of Illinois , Chicago
5R01 AA012478-05	Long Term Effects of Ethanol Exposure During Adolescence	Swartzwelder, H. Scott	Duke University
5R01 AA013983-02	Behavioral Neurobiology of Aggression	Miczek, Klaus A.	Tufts University, Boston
4R37 AA012525-06	Adolescent Alcohol Adaptation: Tolerance and Stress	Spear, Linda P.	Binghamton University
5R01 AA012895-03	Cognitive Mechanisms of Alcohol Abuse	Fillmore, Mark T.	University of Kentucky
5R01 AA-012164-05	Probing Affective and Cognitive Effects on Alcohol	Lang, Alan R.	Florida State University
5R37 AA007112-18	Affective and Cognitive Changes in Alcoholism	Berman, Marlene O.	Boston University Medical Campus
5R21 AA013454-03	5HT1B Receptor in Antisocial Alcoholics	Moss, Howard B.	University of Pennsylvania
5R01 AA13860-02	Drug Treatment of Ethanol Seeking in Rat and Monkey	Czachowski, Cristine L.	Brown University
5R01 AA014373-02	Prenatal alcohol exposure: Adult Neurocognition	Coles, Clair	Emory University
5U01 AA13517-04	Integrative Neuroscience Initiative on Alcoholism	Koob, George	Scripps Research Institute
5U01 AA13641-04	Stress-Anxiety of Alcohol Abuse	Grant, Kathleen	Wake Forest University
2U10 AA08401-16	Collaborative Study on the Genetics of Alcoholism (COGA)	Begleiter, Henri	SUNY Downstate Medical Center

**National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
Basic Behavioral and Social Sciences Research**

The NIAMS is committed to supporting promising research in behavioral and social sciences related to arthritis, musculoskeletal and skin diseases. The Institute has increased its emphasis in this area both within the Institute and in our collaborations with other NIH components. In the fall of 2000, the NIAMS created a new extramural program to foster the development of basic and clinical behavioral research, and hired a behavioral scientist to lead this program. The current program supports a wide array of research that examines behavioral, psychological, and social factors and their interaction with physiological processes in the prevention, etiology, course, management, and outcomes of disease.

Description of Current Program

We have further developed our portfolio in the behavioral and social sciences by highlighting projects directly related to basic research in this discipline. Basic research areas currently funded include cognitive and social mechanisms, pain, and stress, especially in rheumatic diseases and fibromyalgia. One study in fibromyalgia patients is the first to examine the effects of experimental stress on pain perception and functional activity in brain structures that process pain, independently of the influence of affective disorders. The results of this study will advance our knowledge regarding the effects of stress on abnormal pain sensitivity and the biologic processes that underlie this sensitivity in persons with fibromyalgia.

The Institute continues to explore areas of need in behavioral and social science research. In September 2002 the NIAMS sponsored a meeting to assess the NIAMS program in fibromyalgia. The process was designed to enhance communication and promote collaboration among investigators, invigorating research efforts aimed at understanding, treating, and preventing this disorder. The Institute is evaluating how to best implement behavior and social science related recommendations from this meeting. Partly in response to this meeting and to address a growing need within the research community, in FY 2002 the NIAMS solicited applications for interdisciplinary biopsychosocial rheumatic, musculoskeletal, and skin disease conference grants and paid one in FY 2003 that is related to basic behavioral and social sciences research. In addition, career awards in biopsychosocial rheumatic, musculoskeletal, and skin disease research were solicited in FY 2003. A number of awards were made in FY 2004 to facilitate the development of researchers able to integrate biomedical and behavioral approaches. The NIAMS may re-issue these solicitations in the future. Research on sleep processes and their interaction with chronic diseases mechanisms and symptoms is another area of future research the NIAMS has interest in exploring.

Opportunities Not Currently Addressed

Important opportunities in basic behavioral and social science research not currently addressed in the NIAMS research portfolio include psychoneuroimmunological research in our autoimmune diseases; psychoneuroendocrinological research; psychosocial processes influencing health disparities; decision making, coping with chronic disease, and health-related behaviors;

biopsychosocial mechanisms of fatigue; and family and social processes relevant to chronic disease in children.

Basic Behavioral Research Grants supported by National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)			
Grant Number	Grant Title	PI	Institution
5-R01-AR-43136-09	Fibromyalgia: Central Factors in its Etiopathogenesis	Bradley, Laurence A.	University of Alabama
5-R01-AR-46122-05	Neuroendocrine Alterations in Fibromyalgia and Ibs	Chang, Lin	UCLA
5-R03-AR-47619-02	Cognitive Function & Executive Control in Fibromyalgia	Glass, Jennifer M.	University of Michigan
5-R01-AR-46056-04	Pain, Supraspinal Serotonin and Neurotrophic Factors	Hackshaw, Kevin V.	Ohio State University Research Foundation
1-R01-AR-47410-01-A2	Glutamate in Peripheral Afferents During Inflammation	Miller, Kenneth E.	Oklahoma State University Ctr. Health Sci.
5-R01-AR-46303-05	Sex Hormones, Stress, and Pain in Fibromyalgia	Okifuji, Akiko	University of Utah
5-R01-AR-49125-02	Brain Connections	Petri, Michelle A.	Johns Hopkins University
5-R21-AR-48403-02	Sleep Fragmentation Effects on Murine Cii-Induced Ar	Postlethwaite, Arnold E.	University of Tennessee
5-R21-AR-49163-02	Brain Cell Death in Mrl Mice: Targets and Mechanisms	Sakic, Boris	McMaster University
5-R01-AR-49999-02	Patient-Provider Interaction & Response to Acupuncture	Suarez-Almazor, Maria E.	Baylor College of Medicine
5-R01-AR-47652-03	Stress Induces Skin Mast Cell Activation & Vasodilation	Theoharides, Theoharis C.	Tufts University School of Medicine
1-U13-AR-50279-01	Fibromyalgia Workshop: The Next Advances	Nelson, David V.	Oregon Health and Sciences University

National Institute of Biomedical Imaging and Bioengineering (NIBIB)
Basic Behavioral and Social Sciences Research

The National Institute of Biomedical Imaging and Bioengineering (NIBIB) upholds the mission to improve human health by leading the development and accelerating the application of biomedical technologies. The Institute is committed to integrating the physical and engineering sciences with the life sciences to advance basic research and medical care. Furthermore, the Institute supports the development of several technologies whose applications extend into the behavioral and social sciences.

Description of Current Program

At present, the NIBIB supports four research projects with relevance to the behavioral and social sciences, and two of these projects can be considered basic or fundamental research. Both projects focus on improving imaging modalities to more accurately study brain function. In both cases, the imaging techniques are employed to elucidate the regions of the brain associated with specific behavioral traits. The NIBIB is also supporting advanced sensor and informatics technologies that could facilitate behavioral and social sciences research. It is hoped that the development of enhanced research tools will empower basic and fundamental research, so that a greater understanding of human behavior can be achieved.

The NIBIB has not planned any future initiatives directly focused on the behavioral and social sciences. However, the Institute will continue to support technology development for tools that may be used to facilitate basic and fundamental research in the behavioral and social sciences.

Basic Behavioral Research Grants supported by National Institute of Biomedical Imaging and Bioengineering (NIBIB)			
Grant Number	Grant Title	PI	Institution
5R01EB000461-04	Integrated Functional Imaging of the Human Brain	Gore, John C.	Vanderbilt University
5R01EB000360-09	Serotonin Receptor Ligands for Spect Imaging	Kang, Hank F.	University of Pennsylvania

**National Institute of Child Health and Human Development (NICHD)
Basic Behavioral and Social Sciences Research**

The National Institute of Child Health and Human Development (NICHD) mission is to ensure that babies are born healthy and continue to develop normally, through childhood, to reach their full physical, cognitive, and emotional potential. Therefore, NICHD-sponsored research begins before conception and continues through the developmental stages of infancy, childhood, and adolescence, where the foundations of adult health and well-being are established. As implied by its mission, the NICHD supports research that encompasses a broad array of studies that explore the interaction of genetic, biological, behavioral, cognitive, and sociodemographic processes that influence human reproduction, as well as the transformation of a single cell into a healthy, socially well-adjusted, and productive individual. Central to this mission, the NICHD portfolio encompasses behavioral and social sciences research that spans cognitive and social development, learning, literacy, fertility, pregnancy, mortality, HIV and AIDS, and population movement.

Description of Current Program

Basic behavioral and social sciences research is an integral part of the NICHD mission. In addition, the Institute supports training and career development to increase the number of highly qualified researchers conducting basic behavioral and social science research. A significant portion of the Institute's research in this area is supported by the Child Development and Behavior Branch, located in the NICHD Center for Research on Mothers and Children, and the Demographic and Behavioral Sciences Branch, located in the NICHD Center for Population Research.

Child Development and Behavior Branch

NICHD-supported research in child development and behavior includes psychological, psychobiological, and educational development from conception to maturity. Studies include examining the relationships among genetics, growth, the environment, and life experiences. In addition, researchers are examining how these processes and factors affect cognitive, neural, social, emotional, reading, mathematic, and language development, as well as the neurological processes underlying learning disabilities. Scientific findings from studies of normal development, and how and why these processes go awry can help researchers develop clinical research efforts to improve prevention strategies appropriate at different ages and developmental stages.

Developmental Psychobiology and Cognitive Neuroscience. The NICHD supports basic research on the normally developing brain. Researchers are examining how genetic and environmental factors affect the brain's ability to regulate the development of behavior, and how behavior can, in turn, affect brain development. The studies target individual and gender differences at different developmental stages, and identify biological, hormonal, and behavioral indices that can be used to predict sensory, motor, cognitive, and socio-emotional outcomes.

Early Learning and School Readiness. The Institute also supports basic research examining the experiences children need from birth to age eight to help prepare them to learn, read, and succeed

in school. Studies are designed to identify cause-effect relationships between children's early experiences and their social competence and emotional well-being. Researchers are also examining how parents and other adults and peers, childhood education methods, and curricula affect and prepare children from diverse backgrounds for kindergarten and primary school.

Human Learning and Learning Disabilities. NICHD-supported researchers are examining how young children develop reading and written language skills, and how these skills continue to develop throughout the lifespan. Research includes examining the interactions of environmental, experiential, instructional, cognitive, linguistic, genetic, ethnic, and neurobiological factors over time and at different stages of reading and language skill development. Studies also examine normal and abnormal language development among bilingual/multilingual children, adolescents, and adults. Another area includes research on how language and literacy skills are acquired in adolescence and adulthood to identify adolescents at risk for school failure and to enhance adult literacy. Finally, in a parallel manner, the Institute supports basic studies on problem solving and scientific reasoning for mathematics and science cognition.

Cognitive, Social, and Affective Development. The Institute supports basic research to better understand how children and adolescents develop cognitively, socially, and emotionally within different family, cultural, social, and environmental contexts. Studies also examine interpersonal processes such as forming and maintaining relationships, and developing morals, social competence, and social behavior. In addition, researchers are examining child development in high-risk settings such as in violent, abusive or neglectful environments, or in families experiencing poverty, unemployment, or parental depression or divorce.

Demographic and Behavioral Sciences Branch

In addition to research on child development and behavior, the NICHD's congressionally mandated mission includes support of studies examining the processes that underlie human population growth and dynamics. In addition, researchers are examining the influence of the processes on individual, family, and community well-being. Research in this area includes studies on the demographic processes of fertility, mortality, and migration, and on the interrelationships of these areas within larger social, economic, and cultural processes. The social and behavioral sciences are well positioned to shed light on how social and economic disparities arise and persist, and to work with biomedical sciences to understand how these disparities affect health.

Preventing Unintended Pregnancy and HIV Transmission. The NICHD supports basic behavioral research to better understand how to prevent unintended pregnancy and sexually transmitted infections such as HIV/AIDS. Studies target not only adolescent populations, but also addresses risk and prevention across the reproductive years. The research stresses a population-based, multi-level understanding of risk and prevention, focusing on social, economic, interpersonal, and policy influences in addition to characteristics at the individual level. In addition to providing basic data needed to guide research, the NICHD collaborates with the National Center for Health Statistics in conducting the National Survey of Family Growth (NSFG) every six years. The NSFG is a nationally representative survey of reproductive health and behavior among U.S. men and women of reproductive age.

Family and Fertility. The Institute supports research that combines two research areas, fertility and family, to examine the interrelationships among creating partnerships, having children, and raising them. This combined approach is shedding new demographic light on what constitutes and what events mark the formation of a family. Research in this area also includes examining male fertility and fatherhood, and families formed outside of marriage – through remarriage or through cohabiting relationships.

Policy, the Family, and Human Development. The NICHD supports research on family and community environments as well as changing policies that shape human development. Furthermore, the Institute supports research on understanding the mechanisms in these environments that affect child and adolescent development. Research in this scientific area contributes to understanding the healthy development of the next generation of citizens, workers, and parents. For instance, the NICHD supports intergenerational research examining the ways in which families allocate resources between generations to adapt to changing circumstances, including changing public policies, and how this allocation affects the well-being of children and families.

In addition, the Institute contributes to a benchmark series of key indicators of child well-being, published annually in *America's Children: Key National Indicators of Well-Being*. Produced under the auspices of the Federal Interagency Forum on Child and Family Statistics, the series disseminates demographic information on the economic, educational, developmental, health, and family status of children that is essential for monitoring the future of the nation's population and for informing policy.

Similarly, the NICHD Family and Child Well-Being Research Network facilitates multi-disciplinary research on family and child well-being and makes research findings in these areas accessible to the public-policy process. For instance, the Network created the Developing a Daddy Survey (DADS) project, which successfully established a common conceptual framework and overlapping measures of fathering in several population-based studies. Furthermore, researchers developed a compendium of fatherhood measures that will soon be available via the World Wide Web and CD-ROM.

Health and Mortality. The NICHD's program in health and mortality encompasses three broad and interrelated goals: 1) examining the relationship between demographic processes and health; 2) examining health from a population perspective; and 3) supporting the integration of social science, behavioral, and biomedical approaches to understanding health. This includes understanding how these forces influence mortality from the prenatal period up through middle age.

Population Distribution and Movement. The NICHD supports research on immigration, internal migration, and the relationship between population dynamics and the physical environment. Movement and distribution of populations within and across national boundaries affect population growth rates, the diversity of local and national populations, and the pressure of population on local environments, and ultimately the well-being of individuals, families, and communities.

Future Planned Initiatives

Research Base to Assess Early Childhood Learning and School Readiness. Supporting the basic research needed to provide parents, educators, and communities with the tools they need to improve the educational attainment of all children is a high priority for the NICHD. Significant academic, public, and political attention is focused on the educational achievement of all children, beginning with preschoolers, with certain federal funds tied to school systems' performance. To evaluate performance, however, preschool programs need scientifically-based tests to measure accurately how well they prepare young children for later school success. In particular, tests are needed to measure program performance with non-English speaking, ethnically diverse, and educationally at-risk preschoolers. For the most part, such tests do not exist, leaving preschool programs unable to measure their performance to improve the programs or to help qualify for federal funding. To address this gap, the NICHD is planning to develop, refine, validate, and scale-up tests to assess how well preschool programs help young children – especially those at risk of school failure – to achieve “school readiness,” cognitively, socially, and behaviorally.

Developing Study Designs to Evaluate the Health Benefits of Workplace Policies and Practices. The NICHD plans to support the development of study designs to evaluate the health benefits of workplace policies and practices. This effort is the first step in a long-term, coordinated research program to identify, develop, and test effective workplace policies and practices that promote health and well-being for individuals, families, communities, and workplaces.

Science and Ecology of Early Development. Launched in 1997, the Science and Ecology of Early Development (SEED) project was designed to assess the effects of poverty on child development. The NICHD, along with its SEED partners, will re-issue a Program Announcement to continue to foster the development of a science base concerning how living in low-income families affects the immediate and long-term well-being of children. The initiative encourages research on the social, economic, cultural, and community-level factors associated with poverty that affect developmental processes and outcomes for children.

Infrastructure for Data Sharing and Archiving. The population research community creates and shares large-scale population-based datasets. As the complexity of datasets increase, the resources needed to protect the privacy of human subjects while providing continued access to data have also increased. To address this issue, the NICHD will support the development of an infrastructure for a data sharing and archiving program. The effort will enable the population research community to use large-scale, complex datasets for secondary research analysis while protecting the privacy of human subjects.

Opportunities Not Currently Addressed

The initiatives described above should begin addressing current research gaps. The expanded research in early learning, the new program in mathematics and science, and the initiative to build infrastructure for data sharing represent the first steps in filling important gaps in research and research infrastructure.

Basic Behavioral Research Grants supported by National Institute of Child Health and Human Development (NICHD)			
Grant Number	Grant Title	PI	Institution
R01HD033437	Neurobiology of Cognitive Functioning in Infancy	Sullivan, Regina	University of Oklahoma, Norman
R01HD038949	Ethnic, Familial Influences on School Performance	Chao, Ruth	University of California, Riverside
P01HD001994	Visual Word Identification: Phonology and Morphology	Turvey, Michael	Haskins Laboratories, Inc.
R01HD039501	Bilingual Early Language and Literacy Support	Innocenti, Mark	Utah State University
R01HD032336	Gender Socialization in Middle Childhood and Adolescence	McHale, Susan	Pennsylvania State University
R01HD036916	Fragile Families and Child Well-Being	McLanahan, Sara	Princeton University
R01HD044761	Nonmarital Childbearing: Social Policy and Union Formation	Manlove, Jennifer	Child Trends, Inc.
R03HD040328	Consequences of Residential Mobility During Childhood	Pettit, Becky	University of Washington
R03HD043084	Demographic Models of Multiracial Population Growth	Goldstein, Joshua	Princeton University
R01HD025482	Demographic Responses to a Changing Environment	Rindfuss, Ronald	University of North Carolina, Chapel Hill

**National Institute on Deafness and Other Communication Disorders (NIDCD)
Basic Behavioral and Social Sciences Research**

Description of Current Program

The mission of the National Institute on Deafness and Other Communication Disorders (NIDCD) is to conduct and support research and research training in the normal and disordered processes of hearing, balance, smell, taste, voice, speech and language. Accordingly, the NIDCD devotes considerable resources to research relevant to the behavioral and social sciences as defined by the Office of Behavioral and Social Sciences Research (OBSSR) at the National Institutes of Health (NIH). In particular, the NIDCD conducts and supports research that is related to disease prevention and health promotion and that addresses the special biomedical and behavioral needs of individuals who have communication impairments or disorders.

Behavioral and social sciences research supported by the NIDCD includes basic and clinical studies in each of the mission areas of the Institute. Studies evaluate normal and disordered communication processes across the lifespan, clinical and applied behavioral medicine, language development and speech acquisition, cognition and perception, and normal and disordered sensory-motor function. Examples of research are included below.

- The effect on speech and language skills of deaf children who have a cochlear implant are being examined in six U.S. implant centers. The benefits obtained from the cochlear implant are related to the child's dependence on spoken language for communication and the amount of auditory, speech and language training the child receives after implantation. The study will evaluate the predictive value of variables as they relate to outcomes of oral language acquisition, speech recognition skills, selective attention and problem-solving skills, behavioral and social development, parent-child interactions, and quality-of-life measures in children. The results of this study will contribute to the understanding of the factors predicting implant-associated language use, communication competence in early childhood, psychosocial development, and the perceived value of early cochlear implantation in the light of associated costs. Conclusions will enable a refined approach to implant candidacy when considering rehabilitative strategies designed to optimize the development of children with severe-to-profound sensorineural hearing loss (SNHL).
- Functional imaging techniques are being used to characterize brain activation patterns in normal subjects and individuals with neurological disorders affecting human communication. Brain activation patterns characterized using positron emission tomography (PET), functional magnetic resonance imaging (fMRI) or other brain mapping techniques may be used to characterize physical presentation and other neurological consequences of human disorders. Several methods were taken including PET studies of conversation in subjects fluent in English and American Sign Language (ASL) that revealed common activations in a widespread array of regions and suggested a novel model for lateralization of brain activity during narration. Furthermore, additional studies in a bilingual individual with childhood brain damage showed evidence of increased right hemisphere activity compared to normal controls during spontaneous

speech in both English and ASL, suggesting the possibility that plasticity, unmasking of neural pathways, and/or other adaptation of language function in the right hemisphere might occur.

- Neural mechanisms govern the decision to ingest or reject the contents of the oral cavity, but currently, little is known about this process. Using different analyses, including behavioral analysis, NIDCD-supported scientists are looking at different parts of the brain and how they factor in processing taste and activity relevant to ingestion. The results may show why excess ingestion of carbohydrates, fats, and sodium is highly correlated and may be causally related to obesity, diabetes and hypertension.
- NIDCD-supported scientists are looking for deeper insight into the mental processes responsible for the uniquely human capacity for spoken language comprehension. This basic research should have important implications for understanding both normal and disordered communication systems that depend on the spoken word.
- One of the key goals of the Ethical, Legal and Social issues (ELSI) program is to identify, analyze and address the ethical and social implications arising as a result of advances due to the Human Genome Project. Scientists are trying to understand the attitudes and concerns of deaf adults and hearing parents of deaf children towards several issues related to genetic testing and technological advances in management of the deaf. Through a variety of instruments, scientists will assess the impact of genetic testing and counseling before and after parents are identified with or without genes for deafness.

Auditory/Perceptual Processing by Infants with Hearing Loss: Issues in Assessment and Management

This RFA continues NIDCD activities in research on the Early Identification of Hearing Impairment. There is now a cohort of infants who have been identified with hearing impairment at a few weeks of age. Questions regarding intervention and management are numerous and clinical decision-making is difficult. Clinicians are faced with decisions regarding the type and effectiveness of various early intervention/management strategies at ages much younger than previously encountered. Measurement tools and techniques that are sufficiently sensitive or developed for measuring/evaluating progress or benefit of various habilitative strategies in these infants do not exist, there is no empirical database to guide these decisions, and the time window in which the decision-making must occur is extremely short. This initiative focuses on auditory/perceptual processing by infants with hearing loss. Research in this initiative is multidisciplinary, and focuses on the auditory system, speech and language, cognition, memory and learning.

The Role of Neuroimaging in Aphasia Rehabilitation

Approximately 800,000 individuals in the United States become aphasic each year and about one million persons in the U.S. currently have aphasia. A number of studies have shown that the language deficits of aphasia are amenable to treatment, both at onset, and many years beyond. A number of treatments are available, but robust data affirming their efficacy are limited. In recent

years, the development of neuroimaging techniques has enabled researchers to more clearly document the site and extent of the lesion. Recently, researchers have begun to explore the possibility of using neuroimaging findings to predict long-term outcome as well as response to intervention. Much research is urgently needed in order to fully capitalize on the potential of neuroimaging in the rehabilitation of individuals with aphasia. For example, the temporal stability of imaging results must be determined; the linguistic/cognitive task difficulty must be further examined; approaches to the pooling of patient data (lesion location, language abilities and disabilities) must be developed; techniques are needed to document physiological changes in response to particular interventions; and the feasibility of using neuroimaging to predict functional outcomes or the likelihood of retention skills post-treatment will be examined.

Identification and Classification of Childhood Speech-Sound Acquisition Disorders of Unknown Origin

Speech-sound acquisition disorders are common childhood communication disorders, with estimates ranging from 3% to as high as 10% in preschool and school aged children. Research studies have linked delayed and/or disordered speech in children to decreased overall communication skills with consequences reported in psychosocial, educational and vocational development and success. Historically, speech-sound acquisition disorders of unknown origin were classified as “functional.” More recently, these disorders have been termed “developmental phonologic disorders”, or “phonological/articulatory disorders” terms that highlight the links to other domains of language. The NIDCD conducts and supports biomedical and behavioral research and research training in normal and disordered processes of speech production and perception. Multi-disciplinary teams are charged in investigating the identification, assessment and treatment of childhood speech-sound acquisition disorders of unknown origin.

Workshop on Speech Production and Cleft Palate

The NIDCD is sponsoring a workshop on the universal characterization of speech production in speakers with cleft palate. The workshop entitled “Towards universal characterization of speech production in speakers with cleft palate” will be held Spring 2004. Participants will consist of small group of 10-15 clinicians and scientists that will review the background and rationale of developing a universal speech reporting system. Presentations will cover topics such as evaluation procedures, parameters of the system, guidelines in the description of speech, speech sampling, use of scales and scoring, data management and mapping. The goal of the workshop is to work towards adoption of a universal system for cleft palate speakers and to identify next steps.

Basic Behavioral Research Grants supported by National Institute on Deafness and Other Communication Disorders (NIDCD)			
Grant Number	Grant Title	PI	Institution
R01 DC004797	Child Development after Cochlear Implantation	Niparko, John	Johns Hopkins University
R01 DC004336	Engineering the Vocal Fold Extracellular Matrix	Gray, Steven D.	University of Utah
R01 DC001758	Four-Dimensional Tongue Behavior in Speech	Stone, Maureen L.	University of Maryland Baltimore Professional School
R01 DC003904	Behavioral Analysis of OMPS in Odor Processing	Youngentob, Steven L.	Upstate Medical University
R01 DC000240	Neural Systems of Ingestive Behavior	Norgren, Ralph	Pennsylvania State University
R01 DC004153	Plasticity in the Vestibuloocular Reflexes & Perception	Seidman, Scott H.	University of Rochester
R01 DC002658	Spoken Word Recognition	Luce, Paul A.	State University of New York at Buffalo
R01 DC005831	Societal Impact of Advances in Genetic Deafness	Pandya, Arti	Virginia Commonwealth University
R01 DC003180	Neural Basis of Communication Sound Perception	Wang, Xiazqin	Johns Hopkins University
Z01 DC00031	PET and FMRI Activation Studies	Braun, Allen	NIDCD, DIR, Voice Speech and Language Branch

**National Institute on Dental and Craniofacial Research (NIDCR)
Basic Behavioral and Social Sciences Research**

Description of Current Program

NIDCR's Behavioral and Social Science Research program is the focal point for the support of basic and applied behavioral and social science research relevant to the prevention, treatment, and outcomes of oral diseases or treatments.

Basic science areas currently supported within NIDCR's Basic Behavioral and Social Science Research portfolio include the following:

- Research to clarify biobehavioral relationships among oral tissue changes or fluctuations in oral disease status, environmental and/or behavioral conditions.
- Mind-body research that focuses on processes through which experimentally induced or naturally occurring stressors influence conditions or diseases affecting oral tissues (e.g., oral mucosal wound healing, immunity to oral infections)..
- Research on linkages between cognitive, emotional, or behavioral processes and the perception of acute pain during clinical dental procedures.
- Studies examining linkages between behavioral processes and the onset, exacerbation, or treatment of persistent, recurrent, or chronic pain manifesting in the craniofacial region (e.g., temporomandibular muscle and joint disorders or TMJDs).
- Studies developing improved approaches for measuring the sociopsychological impacts of oral diseases or oral treatments (e.g., oral health related quality of life) in both adults and children.

The current NIDCR portfolio particularly emphasizes those aspects of basic behavioral science focused on measurement/methodology development and biobehavioral processes, rather than underlying behavioral or social processes per se.

The relative accessibility of the oral cavity and oral fluids (e.g., salivary measures of drug or tobacco use, salivary cortisol measures) has benefited basic biobehavioral research broadly, and not only research conducted with NIDCR support. Efforts to expand the use of oral biomarkers in basic biobehavioral research and to improve the reliability and validity of their use by behavioral researchers may be particularly worthy of additional discussion or consideration by the committee.

Future Planned Initiatives

Three announcements NIDCR issued in FY 04 include potential opportunities for basic research on biobehavioral processes or measurements. This reflects NIDCR's recognition that improved

measurement of risk factors, outcomes, and the processes influencing health care will make key contributions to improving clinical oral health research overall.

- PA DE 04-022 Epidemiological and Behavioral Research in Oral Health;
- PA DE 04-031 Oral Health of Special Needs and Older Populations;
- RFA DE 04-009 Exploratory and Developmental Grants in Clinical Research

Specifically, each of the announcements includes a call for research to develop improved outcome measures for assessing impacts of oral diseases or dental treatments across various population groups.

As applications responsive to these announcements are reviewed and funded, NIDCR anticipates a continuing expansion of the NIDCR research portfolio focusing on improving measures and methods for assessing outcomes directly relevant to patients and health care consumers (e.g., quality of life measures) as well as the more traditional clinical outcome measures. This is particularly important because a number of dental interventions (orthodontic treatments, orthognathic surgery, surgeries for cleft lip/palate or other craniofacial conditions, esthetic dentistry) are justified in large part based on their presumed social and personal benefits.

NIDCR has also participated with OBSSR and other ICs in initiatives in efforts to stimulate the development of sensitive behavioral outcome measures and methods, as well as biobehavioral research

- PA OD 02-072: Methodology and Measurement in the Behavioral and Social Sciences;
- RFA RM-04-011 Dynamic Assessment of Patient-Reported Chronic Disease Outcomes;
- RFA-RM-04-013 Supplements for Methodological Innovations in the Behavioral and Social Sciences
- PA-03-152 Biobehavioral Pain Research.

Several additional NIDCR RFAs scheduled be funded in FY05 contain significant opportunities for the inclusion of basic behavioral science research, as related to either measurement or biobehavioral processes.

- RFA DE-05-007 Prospective Studies on Craniofacial Pain and Dysfunction
- RFA DE 05-006 General Dental Practice-Based Research Network

NIDCR initiatives currently under development, including an initiative to encourage research on the prevention and reduction of oral complications of cancer therapies, will invite basic behavioral research efforts supporting the overall aims of the project (e.g., research on key sociocultural and behavioral processes influencing providers' and patients' adoption of effective regimens for the prevention of such complications).

In general, NIDCR plans to seek out opportunities to incorporate basic behavioral and social science research topics and approaches within broader research initiatives tackling oral diseases

and their treatments. In addition, NIDCR seeks to accelerate the translation of results from basic studies on oral health-relevant measures or biobehavioral processes into clinical intervention/clinical trials research.

Opportunities Not Currently Addressed

Practice-based measurement issues.

As practice-based research expands, measurement issues in provider behaviors and more effective, sensitive means to document changes in provider behaviors are critically needed. Many approaches currently used (e.g., chart audits, prescriptions written and/or filled per automated records) are relatively insensitive to the most important processes involved in the behavioral changes involved in translation of new research findings into health care.

Basic science initiatives pertinent to community-based, or practice-based, research would be of particular interest to NIDCR because of its commitment to expanding practice-based clinical trials and translational research, reflected both in research grants recently funded and current grant solicitations (RFA:General Dental Practice Based Research Network).

Developing stronger methodologies for measuring key characteristics of provider and patient behaviors and health care delivery in “real world” settings is a key program objective seen as helping contribute to the scientific quality and potential impact of clinical research utilizing dental practice based networks.

**Basic Behavioral Research Grants supported by
National Institute of Dental and Craniofacial Research (NIDCR)**

Grant Number	Grant Title	PI	Institution
R01 DE13208-04	Sex vs. Gender in Pain Perception	Robinson, Michael	University of Florida
R01 DE12470	Menstrual Cycle Effects on TMD Pain and Other Symptoms	LeResche, Linda	University of Washington
R01 DE13813	Neurobehavioral Correlates of Craniosynostosis	Speltz, Matthew	Children's Hospital/Regional Med Cntr – Seattle, Wa
R01 DE12754	Puberty and Gender Differences in Pain Responsivity	Zeltzer, Lonnie	UCLA
R01 DE12792	Psychosocial, Genetic, Biologic Factors in Wound Healing	Marucha, Phillip	University of Illinois
R01 DE13956	Dental Fear and Anticipation of Pain: Imaging the Brain	Bradley, Margaret	University of Florida
R01 DE13546	Quality of Life among Youth with Craniofacial Conditions	Patrick, Donald	University of Washington
U01 DE13331	Research Diagnostic Criteria – Reliability and Validity	Schiffman, Eric	University of Minnesota
R01 DE13732	Child Oral Health Quality of Life Questionnaire	Broder, Hillary	University of Med/Dent NJ

**National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
Basic Behavioral and Social Sciences Research**

Description of Current Program

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) supports 120 research projects in the area of basic behavioral and social sciences. The majority of these projects are funded through the R01 mechanism, and totaled \$26.5 million for fiscal year 2003. The goal of NIDDK-supported basic behavioral and social research is to provide essential knowledge necessary for better prediction, prevention, and control of illnesses. The basic behavioral and social research portfolio is divided into three categories: (A) research on behavioral and social processes; (B) biopsychosocial research; and (C) research on the development of procedures for measurement, analysis, and classification.

A. Research on Behavioral and Social Processes

This category contains projects studying feeding behavior, motivation, memory, and environmental factors that influence behavioral functioning. There is a compelling need to identify the behavioral mechanisms and dietary attributes which foster over consumption (hyperphagia) of high-fat foods. Examples of NIDDK research in this area include investigations of:

- independent and interactive contributions to oral sensations (palatability), caloric density, and the unique post-ingestive effects of dietary fat to the control of intake.
- psychobiological factors that influence the preference for and consumption of carbohydrate-rich and fat-rich foods.
- mechanisms that regulate feeding behavior in individuals eating a high-fat diet, specifically by characterizing signals generated from the gastrointestinal tract that govern food intake.

In addition, post-absorptive fuel metabolism in the liver may play a role in feeding behavior by producing a neural stimulus (or stimuli) that is transduced to the central nervous system to control food intake. One study is assessing whether and how altered hepatic energy metabolism is a contributing cause of hyperphagia. In another study, variables that affect the regulation of food intake and growth in the infant are being investigated during the first year of life, specifically, how early maternal-infant feeding interactions involving infant hunger and satiety cues may influence food intake.

Excess body weight has been associated with an increased risk of several medical conditions, including type 2 diabetes, cardiovascular disease, and certain cancers. Behavioral treatments have demonstrated successful short-term weight loss, though long-term results are quite poor. A number of NIDDK studies are attempting to identify motivational factors that may improve long-term weight loss or prevent excess weight gain, including:

- whether dissatisfaction with weight loss upon completion of a weight loss program is associated with weight regain. In an effort to improve satisfaction with weight loss, investigators will emphasize physical appearance changes or health changes or both during the standard behavioral weight loss treatment.

- an assessment of which one of three treatment formats (group meeting, correspondence course, no-treatment control) over 36 months improves prevention of weight gain. Subjects in the group meeting and correspondence course formats will participate in 24-month behavior weight control (motivational) programs. Two additional studies will examine whether motivational factors can influence children to increase physical activity and prevent excess weight gain. Since current weight loss programs remain relatively ineffective, such approaches to primary prevention may prove efficacious.

Environmental factors that promote increased caloric intake and decreased energy expenditure are believed to underlie much of the present trend towards excess weight gain. Investigators are exploring environmental factors related to the development of excess weight gain. The identification of environmental variables associated with excess weight gain has important implications for health policy and targeted prevention efforts.

As children progress through school, information acquisition becomes increasingly visual at the same time that adolescents with diabetes begin to experience difficulties mentally-processing images. Visual memory and learning are virtually unstudied in youth with diabetes, even though difficulties with verbally-based acquisition skills have been documented. Impediments to knowledge retention or learning have a negative impact on the implementation of diabetes treatment regimens and can affect metabolic control, compromising both further cognitive functioning and long-term health status. An NIDDK study is investigating the functional impact of memory and learning skills on daily self-care behaviors of children.

B. Biopsychosocial Research

This category contains research projects studying behavioral neuroscience and behavioral genetics. Understanding normal and dysfunctional body weight regulation requires knowledge of the factors that initiate, maintain, and terminate an individual meal. Each of these aspects of meal consumption is influenced by oral and post-oral factors, whose separate and integrative contributions to satiety are not fully understood. Following ingestion and the initiation of digestion, nutrients trigger a variety of post-ingestive signals from upper gastrointestinal and vascular sites that terminate feeding, produce satiety, and reduce the appetitive nature of food. Feeding behavior is controlled in part by post-absorptive fuel metabolism. The liver monitors fuel metabolism and generates signals that the brain uses to control feeding behavior. NIDDK researchers are studying which liver cell types are the source of hepatic signals that control feeding behavior, and which neurons are involved in the transmission and processing of hepatic metabolic hunger signals.

Scientists are also trying to elucidate the central nervous system (CNS) mechanisms that underlie the increase in body adipose tissue mass that is associated with consuming a high fat diet. CNS anabolic effectors are those which, when activated, elicit increased food intake and decreased energy expenditure, resulting in increased stored energy in the form of adipose tissue mass. CNS catabolic effector pathways do just the opposite—they decrease food intake and increase energy expenditure resulting in decreased adipose tissue mass. Hormones responsive to the level of adiposity inhibit anabolic pathways while activating catabolic pathways; the balance between these pathways ultimately governs the animal's feeding behavior. Investigations are underway to determine whether maintenance on a high-fat diet:

- alters the activity and/or signaling sensitivity to the adiposity signals, insulin and leptin.
- decreases catabolic activity and/or signaling in the paraventricular nucleus, site of most of these leptin/insulin-responsive pathways.
- reduces the ability of insulin and leptin to cross the blood-brain barrier such that the brain receives an inaccurate (reduced) signal regarding body fat content.
- lowers the sensitivity of the brain to insulin and leptin.

NIH-supported investigators are investigating the mode of action of insulin and leptin in the CNS by:

- assessing whether the actions of insulin and leptin in the hypothalamus potentiate brainstem response to meal satiety signals, such as cholecystokinin (CCK).
- identifying the subset of hypothalamic arcuate nucleus neurons that respond to insulin and leptin.
- examining whether a gender difference exists in the central control of energy homeostasis, with insulin controlling the male system and leptin controlling the female system.

The hypothalamic melanocortin system plays a key role in the regulation of food intake. Genetic mutations that cause absent or aberrant expression of these hormones result in an obese phenotype. Both the mechanism of melanocortin action and how signals engage targets in the systems related to food intake remain unclear. Recent data, however, indicate that melanocortin may transduce its signal via the mitogen-activated protein kinase (MAPK) signal transduction pathway. NIDDK-supported studies currently investigating these areas include:

- characterization of the afferent neuronal and humoral signals that communicate information about caloric intake into the melanocortin system.
- assessment of the functional importance of melanocortin receptors on neuronal activity in the lateral hypothalamic area and the hypothalamic paraventricular nucleus (PVN).
- identification of CNS neurons expressing melanocortin receptors.
- determination if neurons expressing melanocortin receptors innervate key CNS autonomic control sites.
- examination of MAPK activation by melanocortin.
- identification of the subset of neurons activated by MAPK.
- examination of melanocortin-induced changes in neuron gene expression.
- assessment of whether melanocortin and opioid peptides affect feeding behavior in a coordinated manner.

Neuropeptide Y (NPY) is present in high concentrations in the mammalian brain and elicits a powerful feeding response. NIDDK-sponsored investigators will seek additional information regarding feeding behavior by determining whether NPY, rather than acting to increase food intake, is actually the central mediator of food anticipatory responses. NPY activation of Y1 and Y5 cell receptors in the PVN leads indirectly to activation of the cyclic AMP-response element binding protein (CREB) transcription factor with subsequent regulation of CREB-dependent genes. These biochemical events translate into a hunger signal. PYY₃₋₃₆, a peripheral homologue of NPY, activates hypothalamic Y2 receptors to turn off the hunger stimuli. Scientists are investigating whether the changes in circulating hormones that regulate feeding

behavior alter hypothalamic CREB activity in these NPY stimulated pathways, and whether PYY₃₋₃₆ blunts the activity of CREB to elicit a satiety signal. A second NIDDK study is examining whether body weight management during adulthood is directly determined by NPY-regulated hypothalamic feeding circuits established during a “critical period” during postnatal development.

Glucagon-like-peptide-1-(7-36) amide (GLP-1) is an intestinal hormone that has important effects on insulin secretion and glucose metabolism. GLP-1 is also produced in the CNS in a discrete group of neurons in the caudal brainstem. A single receptor specific for GLP-1 is expressed by neurons in certain regions of the brain, including the hypothalamus and caudal brainstem. Recent data indicate that signaling through the GLP-1 receptor may regulate feeding behavior. NIDDK scientists are evaluating the role of the CNS GLP-1 system in mediating satiety.

Ghrelin, produced by the stomach and hypothalamic neurons, appears to regulate food intake by acting on hypothalamic pathways. An NIDDK-supported study is examining ghrelin’s effect on food intake in mice strains with altered metabolic functions.

Corticotropin releasing factor (CRF) is the principal neuroregulator of the hypothalamic-pituitary-adrenal (HPA) axis, which acts within the brain to integrate endocrine, autonomic, and behavioral responses to stress. Many human disorders, including anorexia nervosa, obesity, drug addiction, and depression are associated with perturbations of the HPA axis. Two studies are examining whether mice bearing targeted disruptions for the CRF receptors CRF-1 and CRF-2 genes have altered HPA function.

The hypothalamic peptide, melanin concentrating hormone (MCH), is important in the regulation of energy balance. Mice bearing targeted disruptions in the MCH gene have a lean phenotype, with a 25 percent reduction in total body weight and 50 percent reduction in total body fat. These MCH knock-out mice also have reduced levels of leptin and a 15 percent reduction in food intake. NIDDK scientists are examining the cause of the lean phenotype in detail. An additional study is assessing the impact of a high-fat diet to modulate weight gain in MCH knock-out mice.

Amylin peptide is concurrently produced and secreted with insulin by the pancreas in response to a meal. Systemic administration of amylin to rats strongly reduces food intake. In contrast, amylin receptor blockade has been reported to increase food intake. An NIDDK study is testing whether amylin acts as a hormonal signal to the brain to reduce food intake in rat and amylin-null mutant mouse models.

C. Research on the Development of Procedures for Measurement, Analysis, and Classification

This category contains research projects that support instrument development. Current NIDDK support of a Small Business Innovation Research Phase II study may allow production and testing of a technically refined dietary self-management software suite. The final product will be examined for its effectiveness to improve dietary self-management and user satisfaction.

Energy metabolism plays an important role in body weight control and overall nutrition. Changes in energy expenditure can alter energy balance. Advances in technology and

biomedical engineering can facilitate the accurate measurements of autonomic nervous system activity, energy metabolism, and physical activity. NIDDK-supported scientists will utilize a unique combination of a whole-room indirect calorimetry chamber, a force platform floor, and an electronic activity sensing system to quantify the amount of energy expenditure and physical activity that occurs in a 24-hour period. In addition, multiple portable movement detectors and a novel force measurement insole device were developed to accurately determine the type, intensity, duration, and frequency of the physical activities performed during 7 days of free living.

Future Planned Initiatives

NIDDK has several initiatives to encourage research focused on basic behavior and social sciences.

2004 Initiatives

- *Mechanisms of Physical Activity Behavior Change (Obesity)*

This initiative will support studies that identify 1) the psychosocial, environmental, and physiological factors involved in changing physical activity behavior; and 2) the physiological factors that may influence adoption of an active lifestyle.

- *Partnerships between Basic and Clinical Researchers in Obesity*

This initiative will encourage research that will increase our understanding of the different biological mechanisms controlling energy balance.

- *Translational Research for the Prevention and Control of Diabetes*

This initiative will support studies that improve strategies to promote the adoption of healthy lifestyles which will reduce obesity and diabetes.

2005 Initiatives

- *Partnerships between Basic and Clinical Researchers in Obesity*

- *Long-Term Weight Maintenance – Basic and Clinical Studies*

- *Site Specific Approaches for Prevention or Treatment of Pediatric Obesity*

- *Modifiable Determinants of Excessive Weight Gain and Obesity Among Children*

- *Neurobiological Basis of Obesity (Obesity Task Force)*

Opportunities Not Currently Addressed

While we feel our current portfolio is addressing highest priority opportunities, through continual portfolio monitoring and meetings with investigator groups and other advocacy organizations, we are always open to new initiatives to address new opportunities.

**Basic Behavioral Research Grants supported by
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)**

Grant Number	Grant Title	PI	Institution
P01DK056116-04S1	Peripheral and Central Interactions in Energy Balance	Flier, Jeffrey S.	Beth Israel Deaconess Medical Center
P01DK026741-24	Biology of Neuroendocrine Peptides	Vale, Wylie W. Jr.	Salk Institute for Biological Studies
P01DK055819 -05	Hypothalamic Control of Feeding and Metabolism	Cone, Roger D.	Oregon Health and Science University
R01DK057561-03	Hypothalamic Regulation of Energy Homeostasis	Wardlaw, Sharon L.	Columbia University Health Sciences
R01DK060711-02	Ghrelin in Hypothalamic Regulation of Energy Balance	Horvath, Tamas L.	Yale University
R01DK062202-02	Mechanism of Neuronal Regulation by Leptin and Insulin	Cowley, Michael J.	Oregon Health and Science University
R01DK053301-06	Leptin Action and Central Melanocortin Systems	Elmquist, Joel K.	Beth Israel Deaconess Medical Center
R01DK053109-09A2	Metabolic Control of Feeding Behavior	Friedman, Mark I.	Monell Chemical Senses Center
R01DK062348-02	CNS Action of Appetite Suppressant Aminosterol	Ahima, Rexford S.	University of Pennsylvania
R01DK065171-01	Central Serotonergic Pathways Regulating Energy Balance	Heisler, Lora K.	Beth Israel Deaconess Medical Center

**National Institute on Drug Abuse (NIDA)
Basic Behavioral and Social Sciences Research**

Description of Current Program

Given the complex nature of drug abuse and addiction, behavioral and social services research continue to be integral components of NIDA's research portfolio, with approximately \$400 million spent in these areas in FY2003. Approximately \$125 million of this total is spent on basic behavioral research. NIDA is interested in increasing the impact of behavioral science research on public health, especially by using our knowledge in this area to steer children and young adults away from drug use.

Adolescents, young adults, and those who suffer from mental illnesses are some of the most vulnerable groups to develop problems with drug abuse and addiction. Moreover, women who abuse drugs do so at the highest rates during their childbearing years, risking harm to not only themselves, but to future generations as well. Basic research can provide new ideas and strategies to reduce and prevent drug use in these populations and can inform us how to appropriately treat individuals who are already abusing drugs to prevent their escalation to addiction and its myriad health and mental health complications, including HIV.

Basic behavioral research has played an important role in increasing our understanding of the mechanisms and processes that underlie addiction. NIDA supports both human and animal experimental research within a broad context of behavioral and cognitive factors related to drug addiction. NIDA researchers look at variables such as individual differences (e.g. "sensation-seeking," drug history, prior learning experiences, or prenatal drug exposure); environmental factors (e.g. learning and conditioning, parenting), genetic predispositions (in humans and in animal models), as well as motivational factors that may contribute to drug craving or relapse. For example, some of our current grantees are finding out about the different pathways to addiction and how exposure to cues can activate certain areas of the brain that can lead to relapse. Other basic behavioral grants are using animal models to look at social stress and models of aggression in animals to provide us with information about the role that stress plays in drug abuse and relapse. NIDA also supports studies that look at the effects of drugs on memory and learning, perceptions, as well as supporting studies that determine the abuse liability of different drugs. NIDA supports research that will lead to a better understanding of risk-taking behavior in general, such as research on self-control or impulsivity. Studies on social factors, such as peers, schools and family as they influence the development of drug abuse are also supported.

NIDA also supports a robust basic behavioral portfolio that is systematically examining the developmental consequences of drugs of abuse on children born to mothers who abuse drugs. For example, we have an ongoing longitudinal study of a population that was prenatally exposed to the effects of cigarettes and marijuana, which has been followed since birth in 1978. We have looked separately at the effects of marijuana and cigarettes and have learned much about the cognitive outcomes from each, especially the effect on executive function of the subjects, now 20-23. We are also learning more about the impact of prenatal cocaine exposure on arousal and attention regulatory functions. Another grantee studying prenatal cocaine exposure is looking at inhibitory control and emotional regulation. This cohort has been studied at regular intervals

since birth to 8^{1/2} years. The grantee is especially interested in examining the effects of cocaine exposure on peer relationships, psychological adjustment, and initiation of high-risk behaviors like substance use, delinquency and unsafe sex. This portion of NIDA's portfolio is informing us about the behavioral and social functioning of some specific populations.

NIDA-supported researchers are using state-of-the art imaging tools like positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) to understand the linkage between changes in behavior with changes in neuronal function. Using computational models of cellular reward and information transmission, researchers have developed an innovative behavioral task anatomically targeted to the mesoaccumbal/limbic system. A large body of evidence has implicated these circuits in cocaine dependence, yet elucidation of the relationship between the function of these regions and the addiction syndrome has been hampered by the lack of knowledge about the role of these structures in human cognition. It is anticipated that this basic behavioral research will lead to important new insights into the cognitive neuroscience of human addiction. Neuroimaging tools will also provide us with more insight into the degree to which use of +/- 3 4-methylenedioxymethamphetamine (MDMA or "ecstasy") and cannabis during late adolescence affect brain functioning. Researchers will look at cognitive performance and will compare the results from imaging studies in those who use MDMA and cannabis to their previous findings in adolescents with alcohol disorders. A secondary aim of this project is to refine assessment methods by developing procedures for establishing days of sobriety in youth and validating measures of intoxication and post-intoxication effects to help ascertain the pharmacology of drugs taken by teens.

We know that adolescence is the age at which drug use and other risky behaviors usually begin. Thus, NIDA will be concentrating its research efforts to understand why this is one of the riskiest periods for drug experimentation and abuse in the lifespan of the individual. This will include an investigation of the brain structural, functional and neurochemical characteristics and the associated behavioral changes that occur during childhood and adolescence. Once we begin to more thoroughly understand the unique cognitive and emotional processes characteristic of adolescence such as judgment, decision-making, learning and conditioned responses, sensitivity to reinforcers, group dynamics and risk-taking behaviors among others, we will be better poised to design interventions to reduce drug experimentation and addiction. The role that both genetics and the environment play in both vulnerability and resilience of adolescents to addiction is also a priority in NIDA's research portfolio. For example, a better comprehension of which genes may put an individual at risk for drug abuse and addiction and to understand the neurobiological processes underlying those genetic risks and how this translates into behavior will serve to guide interventions to counteract them. Particularly, an understanding of how environment can facilitate or protect a subject with genetic vulnerability to drug abuse will allow us to use that knowledge to create behavioral interventions to either protect him/her from environmental risks or to strengthen environmental protective effects. Equally important is discerning what the impact of licit and illicit drug use is on the brain during this growth period in adolescence. NIDA also plans to encourage research that does not just look at the individual person, but at the interactions that occur in groups. Specifically, we are concerned with how peers and social networks impact on the choices made by adolescents and young adults.

Because drug abuse is not a disorder that typically occurs in isolation but is one that can impact

the onset and course of other diseases and problems, including AIDS and mental disorders, NIDA is committed to addressing co-morbidity. Co-morbidity between drug abuse and mental illness is common. Recent epidemiologic studies show that between 30 and 60 percent of drug abusers have concurrent mental health diagnoses including personality disorders, major depression, schizophrenia, and bipolar disorder. Similarly those afflicted with mental illness are at a higher risk for drug abuse and addiction. These co-morbidities affect the clinical outcome and the effectiveness of therapeutic interventions. For example in adolescent substance abusers concomitant depression or attention-deficit/hyperactivity disorder (ADHD) is associated with early dropout and poor outcomes in drug abuse treatment interventions. Research to investigate the mechanisms underlying this co-morbidity is likely to be informative not only for the understanding of addiction but also mental illness.

Given that the proportion of AIDS cases resulting from drug abuse has steadily increased over the course of the past two decades with those most heavily affected including racial and ethnic minorities, women, adolescents, and gay and bisexual men, NIDA will maintain a strong HIV/AIDS research portfolio to find effective ways to reduce the risk of infection in vulnerable populations. Of concern continues to be the dissemination through intravenous drug use but also the deleterious effects that drug intoxication has on the judgment of the individual and on his/her decision to engage in risky sexual behavior. Behavioral research will continue to play a major role in preventing the role that drugs of abuse have on the spread of this and other diseases. We have grantees studying the relationships among socioeconomic factors, egocentric risk factors and individual risk factors to reduce the risk of HIV infection among women. Grantees are also studying cohorts of injecting drug users to determine ways to reduce the spread of HIV/AIDS and other infectious diseases, including hepatitis. By better understanding macro-level risk factors such as neighborhood social disadvantage and heroin purity compared to individual risk factors, researchers will be better poised to curtail the spread of diseases. An ongoing cooperative basic behavioral research study is examining how highly prevalent HIV infection spreads from high risk iv drug users into the non drug using communities in which they live. Also given that there is no effective hepatitis C virus (HCV) vaccine, we are using basic behavioral research to establish a cohort of current IDUs with newly acquired HCV infection to examine the natural history of early HCV infection. We are currently supporting studies to examine the feasibility of interferon therapy for newly acquired HCV infection among IDUs. The untreated group within the cohort will also be studied to examine the natural history of early HCV infection.

NIDA also supports research directed toward improving the precision and efficiency of epidemiological (survey) studies; developing assessment protocols for use in general populations; developing new sampling, surveillance, culturally appropriate data collection methods; and refining statistical tools to analyze survey data.

In addition to the research highlighted here, NIDA prioritizes the training of future researchers. NIDA is committed to cultivating researchers who can develop innovative basic and clinical research that help us understand normal and pathological behavior and apply it to the burden of disease.

These are very exciting times for the behavioral sciences; the increasing knowledge from

neurobiology and genetics coupled with technological advances such as brain imaging have opened the possibility to investigate the neurobiological processes underlying healthy human behavior and its disruption by drugs of abuse and addiction. The challenge ahead of us is to integrate the findings from these diverse disciplines to start to build the landscape that will allow us to understand the interaction between the brain and behavior such that we can use this knowledge to prevent drug abuse and to treat addiction.

Future Planned Initiatives

- NIDA has put forth a “Brain, Behavior, and Health” Initiative that it anticipates supporting with other NIH Institutes. The Initiative will allow us to integrate, at multiple levels, the information necessary to understand brain function and human behavior to improve the public’s health. To begin the launch of this initiative, NIDA has developed a matrix that outlines five major areas of study, including: genes, proteins, cells, circuits and pathways, and behavior. In the behavioral area some of the major questions to be addressed include (1) What are the neurobiological determinants of behavior? (2) What are the interactions between brain, behavior and environment? (3) What are the fundamental components of complex behaviors?
- NIDA plans to encourage more research to allow us to better understand some of the proximal factors, particularly the cognitive and emotional factors, that go into actual decisions to take drugs. New technologies will be utilized (hand held computers etc) to capture real time data from study participants.

Opportunities Not Currently Addressed

- There remains a need to develop valid cognitive and behavioral measures that can be used to further map brain function and ultimately neurobiological development and disease.
- Models are needed that can better simulate the full array of human states, behaviors, and experiences associated with drug addiction, such as the often uncontrollable compulsion to take drugs that we now define as the essence of addiction. We are also interested in having models that can help us better understand the cyclical nature or bingeing phenomenon that we see clinically for many drugs.
- Models are needed that focus on group interactions and how decisions are made in those circumstances in order to increase our understanding of how peer influences affect drug taking and other risky behaviors. This information can help us more effectively design prevention interventions targeting youth within these settings.

Basic Behavioral Research Grants supported by National Institute on Drug Abuse (NIDA)			
Grant Number	Grant Title	PI	Institution
5 R01 DA14523-03	Women's Risk Networks: Resources, Infection and Change	Miller, Maureen	Columbia University
R01 DA04874	Prenatal Cannabis and Cigarette Exposure	Fried, Peter	Carleton University
K02 DA00222	Arousal Regulatory Functions in Cocaine-Exposed Children	Mayes, Linda	Yale University
2 R01 DA12568-05	Incidence of HIV Infection in a Cohort of IV Drug Users	Strathdee, Steffanie	Johns Hopkins University
1 R01 DA15999-01	Longitudinal Cohort of Newly Acquired HCV Infection	Kaldor, John M.	The University of New South Wales
1 K05 DA00473-01	Neuroplastic Adaptations Engendered by Drugs of Abuse	Robinson, Terry	University of Michigan
5 R01 DA02632-24	Psychomotor Stimulants and Aggression	Miczek, Klaus	Tufts University
5 R01 DA11716-05	Cognitive Aspects of Addiction- Related Behavior	Kantak, Kathleen	Boston University
2 R01 DA08467-06A1	Novel Methods to Explore Mechanisms of Cocaine Abuse	Weiss, Friedbert	The Scripps Research Institute
1 R01 DA018019-02	<i>Behavioral and Environmental Phenotypes for Tobacco Use</i>	Swan, Gary	SRI International
R01DA14813	Neurocognitive Prerequisites for Preventing Drug Abuse	Fishbein, Diana H.	Research Triangle Institute

**National Institute of Environmental Sciences (NIEHS)
Basic Behavioral and Social Sciences Research**

Description of Current Program

Division of Intramural Research

The National Institute of Environmental Health Sciences is dedicated to reducing the burden of diseases and dysfunctions associated with the environment. This mission is accomplished by conducting basic and applied research into the effects of environmental exposures on biological systems and human health, on the identification of susceptible human subpopulations, and on the interaction between the environment, genetics, and age. Through a multidisciplinary biomedical research program, disease prevention and intervention efforts, and communication and education programs, the Institute strives to make a significant contribution to human health.

The studies conducted by the Division of Intramural Research (DIR) are often long term and high risk in nature and involve unique components, such as the NIEHS contribution to the National Toxicology Program, epidemiological studies of environmentally associated diseases, and intervention and prevention studies to reduce the effects of exposures to hazardous environments. The DIR addresses the environmental component of many different diseases. Environmental agents do not show disease boundaries, and the identification of the environmental causes and mechanisms of one disease can lead to new insights into other diseases.

NIEHS Intramural research related to behavioral and social science includes efforts on the actions of stress response hormones, pesticides, lead, and other environmental exposures that may play a key role in various neurological and behavior-related diseases. For example, intramural scientists studying the effects of glucocorticoids have found that the actions and signaling pathways of these stress response hormones are important to the NIEHS mission. Chronic elevation of glucocorticoids due to prolonged environmental stress and/or chronic therapeutic intervention with glucocorticoids has numerous detrimental actions on human health. Glucocorticoids regulate numerous aspects of physiology including glucose homeostasis, protein metabolism, skeletal growth, connective tissue metabolism, respiratory function, immune surveillance and components of human behavior.

Other NIEHS Intramural research involves studying neurodegenerative diseases such as Amyotrophic Lateral Sclerosis (ALS) and Parkinson's Disease as related to environmental exposures. A current major study is working to elucidate non-cancer health effects among farmers, licensed pesticide applicators, and their families and is one of the largest cohorts of farmers studied to date. Five-year follow up studies will explore the relationship to pesticides and diseases such as Parkinson's Disease, macular degeneration, lupus, and childhood diabetes.

Additionally, NIEHS DIR programs are active in the National Children's Health Initiative (NCHI). The NCHI is representative of the public's concern for the health of children. Under this framework, there are a number of issues that have been raised with regard to the potential for adverse effects to arise from childhood exposure to chemicals in the environment. These concerns are not only for the acute effects that could occur in the child but also the long term or latent effects that may be due either to subtle changes in the nervous system that could lead to a

deficit in cognitive and communication functioning as well as the generation of a susceptible population to events that occur later in life. The individual studies within DIR are focused toward providing potential new test methods to detect alterations in the developing nervous system, to identify the level of exposure that may be considered adverse, and in providing additional information regarding interpretation of currently available data for regulatory agencies.

Current NIEHS Intramural studies will provide valuable tools in addressing questions as they relate to human neurodegenerative diseases and other behaviorally-related diseases. At the completion of these studies we should have a better understanding of the interaction between environmental exposures and the development and progression of nervous system pathophysiology. These studies may allow us to identify critical windows for therapeutic intervention and identify methods to prevent their causes.

Environmental Health Sciences Centers (EHSC)

The intent of the Environmental Health Centers is to stimulate a multidisciplinary approach to a joint research program so as to increase and strengthen productivity and to generate new ideas or approaches via collaborative efforts. This helps to integrate and promote research in existing projects and establish an administrative framework that is conducive to the conduct of interdisciplinary research in environmental health sciences. By providing a Center structure and core resources, this support enhances the productivity of traditional research grants and fosters interaction among a group of established investigators carrying out high quality research related to effects of environmental factors on human health. These Centers thus provides an added dimension to a research effort such that the net accomplishment is greater than that possible by the support of individual projects alone.

Centers for Children's Environmental Health and Disease Prevention Research (CEHC)

The goal of this program is to promote translation of basic research findings into applied intervention and prevention methods. Designed around a central scientific theme, the Children's Centers conduct multidisciplinary basic and applied research in combination with community-based prevention research projects to support studies on the causes and mechanisms of children's disorders having an environmental etiology, to identify relevant environmental exposures, to intervene to reduce hazardous exposures and their adverse health effects, and to eventually decrease the prevalence, morbidity and mortality of environmentally-related childhood diseases.

Environmental Justice (EJ)

The primary objective of this program is to establish methods for linking members of a community who are directly affected by adverse environmental conditions, with researchers and health care providers. Since the distinctive needs of individual communities and their inhabitants are rarely considered in identifying environmental health problems and devising appropriate medical intervention tactics, this program is designed to develop new modes of communication and to ensure that the community actively participates with researchers and health care providers in developing responses and setting priorities for intervention strategies. Projects are committed to enhancing minority participation in research studies and to facilitating communication among environmental health researchers, community health care providers and community members.

Community Based Participatory Research (CBPR)

This initiative aims to implement culturally relevant prevention/intervention activities in economically disadvantaged and/or underserved populations adversely impacted by an environmental contaminant. It is intended not only to foster refinement of scientifically valid intervention methods but also to strengthen the participation of affected communities in this effort. Community-based prevention/intervention research thus seeks to expand our knowledge and understanding of the potential causes and remedies of environmentally related disorders, while at the same time enhancing the capacity of communities to participate in the processes that shape research approaches and intervention strategies. Research projects are conducted in a manner that reinforces collaboration between community members and research institutions. Relevant results are disseminated to the community in clear, useful terms. These studies are designed to be culturally appropriate, i.e., due consideration is given to the social, economic, and cultural conditions that influence health status.

Health Disparities Program (HD)

The goal of this program is to improve the knowledge and behavior of disadvantaged or underserved community members regarding prevention, detection, and treatment of environmentally related diseases and health conditions, and thereby reduce incidence and mortality rates of such diseases and conditions. Through this program NIEHS is advancing the science to elucidate underlying causes and mechanisms responsible for disparities in health. An extension of this program led to the establishment of the Centers for Population Health and Health Disparities (see below).

Ethical Legal and Social Implications of Environmental Health Research (ELSI)

An essential component in preventing and minimizing adverse health effects is public involvement in research programs. However, researchers and public health professionals are increasingly faced with problems such as recruitment and retention of participants, consent and confidentiality issues. These problems are further exacerbated by the public's lack of knowledge of research studies and scientists' lack of understanding of challenges facing the community. With a view to addressing these challenges, the NIEHS, in partnership with the National Human Genome Research Institute (NHGRI), developed the Partnerships to Address Ethical Challenges in Environmental Health program. The projects in this program develop methods of education to address social, ethical, and legal concerns of the public in research endeavors related to gene-environment interactions, environmental health hazards, and disease susceptibility.

Centers for Population Health and Health Disparities (CPHHD)

The purpose of Centers for Population Health and Health Disparities is to support interdisciplinary research leading to an understanding and reduction of health disparities in domestic populations. The projects in this program are multi-level, integrated research projects that elucidate the complex interactions of the social and physical environment, mediating behavioral factors, and biologic pathways which determine health and disease. These Centers create an environment conducive to interdisciplinary and reciprocally beneficial collaborations among biomedical scientists, social scientists and affected communities with the common goal of improving population health and reducing health disparities. This is a trans-NIH program

sponsored jointly by the National Institute of Environmental Health Sciences (NIEHS), the National Cancer Institute (NCI), the National Institute on Aging (NIA), and the Office of Behavioral and Social Science Research (OBSSR).

Projects in Neurobehavioral Toxicology

The NIEHS supports a wide variety of research in the field of neurobehavioral toxicology from animal to human-based studies. A majority of the studies have looked at the neurotoxic effects of heavy metals and the mechanisms by which they affect the developing brain (the period of greatest vulnerability to most neurotoxicants.) For example, lead studies the Institute has supported have influenced public policy in lowering the acceptable level of lead contamination tolerated in children and adults through the epidemiology studies, whole animal studies and in vitro studies all supporting the neurocognitive effects of lead on the hippocampal area of the brain which is involved in learning and memory. Other NIEHS-supported work examining the neurotoxicity of organic mercury has also contributed to public health policy in the form of contaminated fish advisories especially to women of child-bearing age, again because of results from epidemiological and basic studies. Other areas of concern supported by the Institute are agricultural chemicals and industrial chemicals that have neuroendocrine disrupter properties.

Planned Initiatives

The NIEHS launched a three year initiative, The Fetal Basis of Adult Disease: Role of the Environment in 2002. This initiative is designed to investigate the contribution of prenatal environmental exposures to disease outcomes that are observed much later in life. The first two years of this initiative have focused on adult-onset disorders. Grants awarded from this initiative have included studies of behavioral and cognitive impairments (e.g., age-related memory loss). The final year of this initiative will expand the areas of emphasis to include neurobehavioral and other disorders that occur during adolescence.

The Environmental Justice: Partnerships for Communication will be re-issued in 2004 for funding seven-nine projects in 2005. This initiative is in partnership with the National Institute for Occupational Safety and Health.

A new five year initiative on Obesity and the Built Environment is being issued by NIEHS in partnership with the National Institute of Child Health and Human Development and the Office of Behavioral and Social Sciences. This request for application will support projects that will delineate the significance and impact of the built environment on individual and population health by understanding the roles played by planning, housing structure, transportation issues, and the availability of public and green spaces as determinants of physical activity, nutrition, and access to healthy foods. Of particular interest is in studies conducted in vulnerable populations (such as, children, aging, low SES communities). The outcome of this program is to improve public health and impact policy by developing models that would promote environmentally healthful lifestyles.

Several institutes and centers at NIH are collaborating on a program announcement on community-based participatory research entitled Community Participation in Health Promotion and Disparities Research. The goal of this program announcement with a special review is to

support research on health promotion, disease prevention, and health disparities that is jointly conducted by communities and researchers. The promise of community participation in all aspects of the research process is that better informed hypothesis will be tested, more effective interventions will be developed and the translation of the research results will be easier. This PAR will use NIH research project grant (R01) and exploratory/developmental grant (R21) award mechanisms.

Future Planned Initiatives

A number of future activities are being considered that could enhance existing NIEHS programs in behavioral and social science research.

Aging and Environmental Health

The first activity under consideration is the development of an NIEHS Program in Aging and Environmental Health. The rationale for this program derives, in part, from marked behavioral and lifestyle changes (e.g., in income, nutrition, mobility, use of prescription medication) among the elderly that produce unique patterns of exposure or are themselves risk factors for disease and dysfunction.

The NIEHS currently funds a wide variety of research projects that address some aspects of aging, including efforts within the Comparative Mouse Genomics Center Consortium and in the neurodegenerative and cardiovascular disease portfolios. These current efforts are disparate, however, and could benefit from being part of a cohesive NIEHS Aging Program. This Program could provide a framework for integrating the efforts of our current grantees and for attracting new investigators that could capitalize on new findings emerging in the field of aging.

As a first step, we are considering convening a workshop in FY05 to bring together aging researchers and environmental health scientists to identify promising areas of research and to recommend approaches for fostering meaningful research collaborations between researchers in the fields of aging and environmental health science.

Improved animal models of gene-environment interactions in behavioral neurotoxicology

A second area under development concerns improvements in behavioral methods to examine gene-environment relationships in animal models. Behavioral toxicology has been instrumental in identifying and characterizing the effects of neurotoxicants on the function of both animals and humans. In the past, most of behavioral toxicology research has been descriptive with little basis in understanding mechanisms. The state of the science today requires an emphasis on determining the relationships among behaviors, brain chemistry and metabolism, and gene expression to link cause and effect. The availability of a variety of technological and methodological advances to aid in the development of appropriate animal models and systems will do much to move the field of behavioral toxicology forward. In order to facilitate this research expansion and development, the NIEHS is sponsoring a workshop in April 2004 the goal of which is to bring together experts in behavioral genetics and behavioral neurotoxicology to inform each other of the potential use new methods, technologies and tools could have on the field of behavioral neurotoxicology and to establish a more mechanistic basis for the role of toxic exposure in behavior and cognitive deficits. This workshop will be the beginning of the

development of a program that will encourage the use of powerful genetic and technological approaches and sophisticated behavioral/cognitive assessments to determine the influence of environmental neurotoxicants in the gene-exposure effect-behavioral interrelationship.

Translational research to link basic science and human studies

Finally, the NIEHS is considering a variety of novel ways to foster the translation of basic science knowledge into the clinical arena. One concept under consideration would support the extension of an existing basic science project to human populations. For example, targeted funds could be provided to a researcher who is developing an animal model of an environmentally-induced behavioral disorder for the purpose of forming meaningful research collaborations with a clinical investigator who studies that behavioral disorder.

**Basic Behavioral Research Grants supported by
National Institute of Environmental Health Sciences (NIEHS)**

Grant Number	Grant Title	PI	Institution
R01 ES011352	Reducing Pesticide Exposures to Farmworkers Children	Eskenazi, Brenda	University of California, Berkeley
R25 ES011077	Asthma and Lead Prevention in Chicago Public Housing	Knight, John Q.	Safer Pest Control Project
R01 ES010904-02	MOHAWK Culture, Behavior, Toxicant Exposure and Health	Schell, Lawrence M.	State University of New York, Albany
R25 ES012085-02	Ethical Challenges in Lead Poisoning Prevention Research	Farfel, Mark R.	Johns Hopkins University
R01 ES012397-02	Increasing Non-Motorized Travel to School	Ward, Dianne S.	University of North Carolina, Chapel Hill
P01 ES11269	Environmental Factors in the Etiology of Autism	Pessah, Isaac	University of California, Davis
P50 ES012382-01	Center for Interdisciplinary Health Disparities Research	Gehlert, Susan	University of Chicago
P30 ES12072	New Mexico Environmental Health Sciences Center	Burchiel, Scott W.	University of New Mexico, Albuquerque

**National Institute of General Medical Sciences (NIGMS)
Basic Behavioral and Social Sciences Research**

The NIGMS Mission

The authorizing legislation for the National Institute of General Medical Sciences (NIGMS) states that “the general purpose of the National Institute of General Medical Sciences is the conduct and support of research, training, and as appropriate, health information dissemination and other programs with respect to general and basic medical sciences and related basic and behavioral sciences which have significance to two or more national research institutes or are outside the general area of responsibility of any other national research institute.” NIGMS addresses this mission almost exclusively through extramural investigator-initiated research and training programs. The projects supported by the NIGMS are in the most basic and fundamental areas of biomedical science and provide the foundation for subsequent disease-targeted studies supported by the other components of the NIH. Much of NIGMS-supported research involves the use of a wide range of organisms to study genetic mechanisms, metabolic pathways, and neurocircuitry that, through evolutionary conservation, are relevant for understanding human biology and mechanisms of human disease studied by other NIH institutes and centers. Many of the deepest and most powerful insights into human biology, from fundamental principles of biochemistry and genetics through organizing and operating principles in complex physiological networks, have come from studies of model organisms. Powerful tools including, but not exclusive to, those related to the sequencing of the human and other genomes are opening up new horizons for the study of complex biological systems including those related to behavior.

Description of Current Program

NIGMS supports behavioral research in all three categories of basic behavioral and social science research defined by the NIH’s Office of Behavioral and Social Sciences Research: biopsychosocial research; basic research on behavioral and social processes; and methodological research. NIGMS also provides funding for research training in the behavioral and social sciences through institutional research training grants and individual fellowships. Most of these training opportunities are provided under the Medical Scientist Training Program, Systems and Integrative Biology training grants, and programs administered by NIGMS’s Minority Opportunities in Research Division.

Basic Biopsychosocial Research

NIGMS supports biopsychosocial research—including behavioral neuroscience, behavioral genetics, and psychophysiologic research—to examine the genetic and biochemical mechanisms underlying behavioral phenotypes. This research is aimed at providing a better understanding of the underpinnings of a variety of areas of behavioral functioning including circadian rhythms, learning and memory, reproductive behavior, sensation and perception, aggression, pain and its management, the effect of anesthetics on memory and cognition, behavioral effects of drugs and steroid hormones, and addiction to psychoactive drugs or drugs of abuse.

Some major areas of research supported by NIGMS, and specific examples from studies currently in progress, are provided in the sections that follow:

- **Brain function and its relationship to behavior**

Mutant studies of aggression in *Drosophila*: Aggression is a nearly universal feature of the behavior of social animals but little is known of the neural mechanisms that underlie the behavior. NIGMS-supported research uses model organisms to study the genetic basis of this complex pattern of behavior. The long-term goals of the present studies are to identify genes and molecules, subtypes of neurons, and neuronal pathways important in aggression.

Genetic analysis of reproductive behavior in worms: Behaviors leading to sexual reproduction are essential for the survival of most animal species, yet little is presently known about how the nervous system generates appropriate motivational states and appetitive and consummatory sexual behaviors. NIGMS supports research on the genetic basis of sexual motivation and behavior in model systems such as the nematode.

Molecular neurobiology of sleep/wake cycles and other behavioral rhythms: Daily oscillations of behavior are prominent—and gene products and the ways they form clockworks are analogous—across a broad array of species. Brain-behavior studies of chronobiology in model systems may provide insights into the nature of certain rhythm-related disorders of humans, some of which are associated with genetic variations in the experimental systems.

Transcription factor regulation in learning and memory: Regulation of gene expression is considered essential for the establishment of long-lasting cellular changes that underlie the formation of long-term memory. NIGMS is supporting research on the role of transcriptional gene regulation in acquisition and long-term retention of memory. A basic understanding of how memories are formed will enable the design of appropriate and effective treatment and prevention strategies for the various neurologic and neuropsychiatric conditions that display alterations in memory processing, such as Alzheimer's disease and stroke.

- **Psychoneuroimmunology**

NIGMS supports research to identify and characterize the systems of hormones and neurotransmitters that mediate stress responses. Examples can be found in NIGMS's program of basic research in Anesthesia and Integrated Systems; among the many areas are stress reduction and the improvement of clinical outcomes among patients undergoing surgery.

- **Psychopharmacology**

Mechanisms of methamphetamine neurotoxicity: Current research includes studies on the oxidative processes that are triggered by methamphetamines which may damage serotonergic and dopaminergic pathways in brains of animal models to cause neurotoxicity .

Psychostimulant Response Pathways: A model system is being used to study the pathways regulating responses to free base "crack" cocaine. Conservation has been shown with vertebrate

animal models both in the types of cocaine induced behaviors and in the biochemical and signaling pathways underlying these behaviors. The research also shows sensitization to repeated cocaine exposures, a process that is likely to represent a component of the addictive process in humans.

- **The neurobiology of pain and its management**

Non-pharmacological interventions to control pain: In addition to studying pharmacological agents, NIGMS supports research on behavioral treatments for pain. Current research focuses on the treatment of pain in hospitalized burn patients using novel combinations of virtual reality and psychological interventions (hypnosis), as well as offering a comprehensive longitudinal follow-up study on the psychological outcome of burn patients. This paragraph should be combined with the following one. Both deal with pain and are artificially separated.

- **Behavioral interventions to improve clinical outcomes of burn and trauma victims**

NIGMS's program in trauma and burn supports research on the full array of treatments, including behavioral interventions. NIGMS is supporting more research to better understand the mechanisms by which the vagus nerve, which can be controlled by neurological and behavioral means, exerts its anti-inflammatory action. Other ongoing work examines the role that physical exercise plays in the clinical outcomes of severely burned children.

- **Genetics, Networks, and Behavior**

Complex systems research: Behavior is governed by a complex network of genetic factors, environmental circumstances, and individual experience. Understanding how these complex systems operate is important for human health from the psychological, sociological, and pharmacological perspectives. Previous studies of behavior have focused on the roles of specific genes and their interactions with other genes and with the environment. However, the same gene, in different environments, may interact differently with other components of the network. For example, specific genes may be expressed differently in different strains of flies or mice. NIGMS supports research not only to develop analytical tools for studying the genetics of behavior and to identify the genetic components of behavior, but also to begin building a comprehensive framework for understanding complex and phenotypically plastic traits resulting from interactions between genotype and environment. (Is the following example supported in PPBC? It doesn't appear to match anything in GDB.) For example, previous work has shown that social status affects behavior and regulates reproductive state, growth rate, and stress reactivity at the molecular, neuroanatomical, and endocrine levels. Systems research is being supported to determine how tissue-specific gene expression profiles differ between dominant and subordinate males, to uncover how these profiles change during changes in social status, and to understand the functional networks involved in these behavioral changes.

Pharmacogenetics: Related research is supported through a major NIGMS initiative in pharmacogenetics; the study of how genes affect the way people respond to medicines (part of an individual's physical "environment"). Investigators supported through this program are conducting biobehavioral studies to examine how responses to several treatments for depression

are affected by genetic variation and to identify the specific genes responsible for differences in clinical outcomes.

- **The role of behavior in the evolution of infectious diseases**

A predictive science of infectious disease depends on our ability to anticipate with some confidence the behavior of host/parasite systems. The ability of an infectious organism to spread depends on not only characteristics of the infectious agent but also on population dynamics, the behavior of the animal host, the environment (including the social environment), and the effects of human interventions. NIGMS supports multidisciplinary research to examine this array of influences on the evolution and transmission of infectious diseases, to anticipate the conditions under which new infectious diseases will emerge and old ones will re-emerge, and to design protocols to treat and prevent the spread of infection. In FY 2004, NIGMS launched a new initiative in this area, the Models of Infectious Disease Agent Study (MIDAS). One of the main objectives of MIDAS is to develop tools to conduct surveillance and predict the spread of infectious diseases using models that incorporate social networks, the effectiveness and consequences of human intervention strategies, the distribution of stockpiles and inventories of treatments, scheduling of response activities, and allocation and use of manpower and other resources.

Research on Behavioral and Social Processes

- **Health disparities**

Through its Minority Opportunities in Research Division, NIGMS supports research on health disparities and sociocultural studies of health-risk behavior patterns and interventions. Examples of currently funded research include:

- Offspring of outpatients with dysthymic disorder: outcomes and mediators of risk: an analysis of the impact on children's behavior when the parents suffer from major depressive disorder.
- Development of sexual health intervention for African-American young women: research to determine the role of peer influences on sexual knowledge and behavior among African-American women ages 18-25 using quantitative and qualitative methods, in order to develop and utilize a culturally relevant, social network HIV sexual health intervention.
- Adaptation of minority first generation college students: research to identify factors that predict positive academic outcomes for ethnic minority college students who are the first members of their family to attend college. The most important among these factors has been found to be social support from family and friends.
- Individualism, collectivism and attitudes toward seeking mental health treatment: research to ascertain how cultural norms of individualism and collectivism shape attitudes toward seeking professional mental health help.
- Effects of identity/career development on mental health: a study that focuses on the protective effect of identity and career development on the mental health of adolescents, and particularly examines ethnic variability in this relationship.

- Physiologic stress/blood pressure in Filipino immigrants: research on nonprofessional workers in the hotel industry in Hawaii, on the effects of immigration, job strain, and cultural consonance on stress and blood pressure.

- **The ethical, legal and social implications of genetic research**

NIGMS is one of several NIH institutes to participate in a program to solicit research projects that anticipate, analyze and address the ethical, legal, and social implications of the discovery and use of new information and technologies resulting from human genetic and genomic research. Among the areas of particular interest are studies that examine: issues in the ethical, legal and social factors that influence the translation of genetic information to improved human health; the use of genetic and genomic information and technologies in non-health care settings; the impact of genetics and genomics on concepts of race, ethnicity, kinship and individual and group identity; the implications, for both individuals and society, of uncovering genetic and genomic contributions to not only disease, but also ‘normal’ human traits and behaviors; and how different individuals, cultures and religious traditions view the ethical boundaries for the uses of genetics and genomics.

- **Science education research and program evaluation**

An important part of NIGMS’s mission is to ensure that future research workforce needs are met. The recruitment and retention of minorities currently underrepresented in the biomedical and behavioral sciences is essential to meeting this goal and NIGMS supports several minority research training programs. To assist both NIGMS and its grantees to optimize the training of biomedical and behavioral researchers, NIGMS has initiated a program of behavioral and social science research to study science education and research training programs.

Methods and Tools Development

Methods for regulating gene expression to study behavior: NIGMS supports research to regulate transgene activity in both time and space. This research is of particular interest for the molecular genetic analysis of behavior. Experiments are being conducted in model systems to test the ability of this approach to regulate the expression of genes important for learning and memory.

Institutional Research Training Programs

NIGMS solicits applications for research training support in a broad range of disciplines, including the behavioral and social sciences, through several of its existing training programs.

The Medical Scientist Training Program (MSTP): The research interests of MSTP alumni, who hold both an M.D. and a Ph.D. degree, are diverse. Former students of MSTP programs have established successful research careers in behavioral neuroscience, the genetic basis of cognitive dysfunction and mood regulation, and psychiatric epidemiology.

Systems and Integrative Biology (SIB): The current SIB grants fall into three broad areas of research training: neurobiology, physiology, and biomedical engineering. Support is provided

for training in behavioral and cognitive neuroscience using multidisciplinary approaches to study the nervous system and the link between neural development, activity, and behavior. Included is research in sensory processing, sensory and cellular transduction, neuroethology, the biological basis of substance abuse and addiction, the neurobiology of stress, the neuropharmacology of social behavior, and the mechanisms of neurological and behavioral disorders.

Neuroscience Training: NIGMS also participates in an NIH-wide neuroscience training program to encourage broad, early-stage training in the neurosciences. An example of one of the grants supported through this program, one cofunded by NIGMS, provides students in Stanford University School of Medicine's neurosciences program with an integrated education that involves the study of all levels of nervous system function from molecules to behavior.

Biostatistics: In FY 2004, NIGMS will initiate an interdisciplinary research training program in biostatistics. Statistical methods are used in broad range of scientific disciplines, several with ties to the behavioral sciences, including epidemiology, behavioral genetics, psychology, neuroscience, the social sciences, public health, and health services research.

Individual Fellowships

In addition to institutional training grants, NIGMS also administers individual fellowships and the Pharmacology Research Apprenticeship Program to provide support for fellows working in many of the same biobehavioral areas in which NIGMS provides research funding. Fellowships to increase diversity are also available in many areas of the behavioral and social sciences.

Examples of research currently supported through fellowships include:

- A study of the impact of social networks: a study of the impact of health and nutrition on the social networks of women living in poverty.
- Racial stress coping scale: a study of the health effects of exposure to racism, hostility, modes of anger expression, and styles of coping. These characteristics are examined for their relationship to stress-induced increases in blood pressure, cardiac output, and total peripheral resistance.
- Can future controversies over genetics be prevented?: a political science study to examine how the actions taken and decisions made by researchers, policy makers and others, resulted in a variety of recent controversies over new technologies and techniques dependent on our knowledge of genetics.

Future Planned Initiatives

Tremendous opportunities are present with regard to both research and training related to basic behavioral sciences. The successes of the reductionist approach to biological systems have laid the groundwork for more integrative approaches to biomedical research. These approaches naturally include many aspects of basic behavioral research as tools are now available for studying the influences of basic biological components such as genes and biochemical pathways on behavior as well as the influences of behavior on these components. These interactions can now sometimes be addressed even up to the level of social networks. NIGMS is receiving and is

actively seeking proposals related to the behavior at the genetic, biochemical, and cellular level of resolution. Furthermore, NIGMS is actively participating in an initiative among the Institutes and Centers with interests in the neurosciences referred to as the Neuroscience Blueprint. Among the goals of this initiative is identifying and highlighting research opportunities as they relate to behavior as one of the ultimate outputs of the nervous system.

For several decades, NIGMS has taken an interdisciplinary approach to training with training grants spanning formerly distinct fields and extant academic units by design to stimulate interdisciplinary training and research. This approach has already been used to expand training in Systems and Integrative Biology and Neuroscience into areas of behavioral and social science. Continued expansion of the reach of these programs into the behavioral sciences both within the framework of existing programs, as well as interdisciplinary training initiatives that are components of the NIH Roadmap for Medical Research will further enhance the training goals of NIGMS.

Basic Behavioral Research Grants Supported by National Institute of General Medical Sciences (NIGMS)			
Grant Number	Grant Title	PI	Institution
1U01GM070694-01	Population Mobility Models of Urban Disease Outbreak	Eubank, Stephen	University of Calif-Los Alamos Nat. Lab
3U01GM070708-01S1	Computational Models of Infectious Disease Threats	Burke, Donald	Johns Hopkins University
1U01GM070698-01	Pilot Projects for Models of Infectious Disease Agent Study	Wagener, Diane	Research Triangle Institute
1U01GM070749-01	Containing Bioterrorist and Emerging Infectious Diseases	Longini, Ira	Emory University
3R01GM054339-08S1	Molecular and Cellular Studies of Circadian Rhythms	Young, Michael	Rockefeller University
5R01GM063929-03	Regulated Gene Expression and Drosophila Behavior	Davis, Ronald	Baylor College of Medicine
5R01GM064566-03	Tachykinin Regulation of Anxiety and Stress Responses	Heath, Mark	Columbia University Health Sciences
5R01GM066778-02	Molecular Neurobiology of Behavioral Rhythms	Hall, Jeffrey	Brandeis University
5R01GM066897-02	Genetic Analysis of Nematode Behavior	Emmons, Scott	Yeshiva University
1R01GM067645-01	Mutant Studies of Aggression in Drosophila	Kravitz, Edward	Harvard Medical School
2S06GM008194-240056	Dietary Restriction, Aging, Learning, and LTP	Barea-Rodriguez, Edwin	University of Texas, San Antonio
5S06GM008102-320076	Transcription factor/regulation in Learning and Memory	Pena-de Ortiz, Sandra	University of Puerto Rico, Rio Piedras
1R01GM068946-01	Mathematic Descriptions-Multifactorial Gene Expression	Rodriguez-Zas, Sandra	University of Illinois, Urbana-Champaign

**National Institute of Mental Health (NIMH):
Basic Behavioral and Social Sciences Research**

Description of Current Program

The basic behavioral science portfolio of the NIMH is distributed among four of the five extramural divisions: Division of Neuroscience and Basic Behavioral Science (DNBBS), Division of Adult Translational Research and Treatment Development (DATR), Division of Pediatric Translational Research and Treatment Development (DPTR), and Division of AIDS and Health and Behavior Research (DAHBR). Within DNBBS, the Behavioral Science and Integrative Neuroscience Research Branch focuses on basic research on cognitive, affective, social, motivational, and regulatory systems in humans, non-human primates, and other animals. The three translational divisions (DATR, DPTR, DAHBR) focus on basic research more directly relevant to mental disorders as well as research related to risk for psychopathology and risky health behaviors. In general, the entire basic behavioral science portfolio falls within three fundamental domains: Basic Behavioral Processes; Behavioral and Integrative Neuroscience; and, Risk for Psychopathology.

In an era of increasing mental health burden and slowing fiscal growth, NIMH is looking to optimize its impact on public health. To help set clear priorities to achieve this goal, the NIMH sought the advice of its National Advisory Mental Health Council (NAMHC), which in turn established a workgroup to conduct a thorough review of the current basic brain and behavior portfolio and to make recommendations for predicting which areas are most likely to yield discoveries that ultimately will benefit people with mental disorders

The workgroup report, *Setting Priorities for the Basic Sciences of Brain and Behavior* (<http://www.nimh.nih.gov/council/brainBehavioralScience.cfm>) provides recommendations about ways to sharpen the focus and impact of the basic science portfolio to better serve the mission of the institute. The over-arching principles that guided the report provide a frame of reference for advancing basic behavioral science in mental health. These principles include: (1) basic brain and behavioral research should be undertaken in the service of the public health mission of NIMH; (2) basic research that integrates or translates across levels of analysis – from genetic, to molecular, to cellular, to systems, to complex overt behaviors and situations – should be given high priority; (3) research and training that is interdisciplinary should be more heavily emphasized in the basic portfolio; and, (4) the time is right to invest more in developing the tools that will allow intensive study of how complex interpersonal, social, and cultural environments affect behavior at the integrative systems level. Based on these principles, the report outlines specific tools and areas of research particularly ripe for increased investment, areas ready for refocus, and areas better served by other Institutes.

Taking into account these recommendations, as well as recommendations from a previous NAMHC report on *Translating Behavioral Science into Action* (<http://www.nimh.nih.gov/council/archivereports.cfm>) and input from various other stakeholders, NIMH is re-setting priorities for its research portfolio. Three key factors are being used to evaluate new applications submitted for funding: relevance to the mission, traction for making rapid progress, and innovation. Given that some areas of basic behavioral science are far

removed from rapid application to etiology, diagnosis, or interventions, how can these criteria be applied? We are placing higher priority on those basic research studies that (a) link behavior, brain, and experience and/or (b) are informed by and, in turn, informs our understanding of etiology, our need for diagnostics, and our quest for new interventions to prevent or treat mental and behavioral disorders.

I. Basic Behavioral Processes

The NIMH basic behavioral science portfolio supports research on basic affective, biobehavioral, cognitive, personality, and social processes.

A. Affect and Biobehavioral Regulation

This thematic category supports research on the basic processes, development, and regulation of positive and negative emotion, mood, and motivational systems and behaviors, and the interactions of these with nervous, endocrine and gene systems, cognition, biological rhythms, and social variables.

- 1) **Individual differences in affect** - Aims to describe the origins of affective style.
- 2) **Affective structure** – Focuses on questions about how to conceptualize affect.
- 3) **Emotion perception & expression** – Focuses on the function of emotion, i.e., provide information to others through distinctive facial and vocal expressions.
- 4) **Affect regulation** – Focuses on the suppression of affect and on the ways that affect regulation is acquired and changes across the life span.
- 5) **Genetic & caregiver effects on affect** - Uses behavior genetics and behavioral methodologies to delineate the factors that shape emotionality and temperament across the life span.
- 6) **Social processes in affect** – Focuses on the role the social environment plays in affect development and regulation.
- 7) **Stress response & adaptation** – Attempts to uncover the mechanisms that mediate the effects of psychological and behavioral stress on mental and physical health.
- 8) **Reproductive behaviors** - Focuses on behaviors related to mating, sex, gestation, parenting, puberty, and parent/infant interactions and associated physiological and hormonal processes that have an impact on the affective or motivational functioning of individuals or family groups.
- 9) **Biological rhythms** – Concerns behaviors regulated in part by biological rhythms, especially pulsatile, circadian, and seasonal profiles.

- 10) **Thermoregulatory & feeding behaviors** - Investigates how healthy thermoregulatory and feeding behaviors are integral to both the development and maintenance of good physical and emotional health.

B. Cognitive Science

This thematic category encompasses empirical and theoretical research on the fundamental principles and mechanisms of cognition.

- 1) **Perception and representation of objects and space** - Emphasis is on central, rather than peripheral, levels of processing. Elucidates the processes by which large amounts of rapidly changing information from multiple sources is extracted, integrated, interpreted, and acted upon.
- 2) **Visual-spatial attention** - Examines attention to and inhibition of perceptual information, automatic and strategic control of attention, visual search, and the roles of attention in perception and memory.
- 3) **Temporal, sequential, and numerical processing** - Addresses issues of perception and memory of time intervals, learning and representation of sequences and quantities, and the sequential and hierarchical organization of behavior.
- 4) **Classical and instrumental conditioning** - Investigates mechanisms of conditioning and extinction, the relation of conditioning with other cognitive processes, conditioning of biologically significant behaviors and within naturalistic environments, and the conditioning bases of behavioral treatments.
- 5) **Memory organization and processes** – Includes encoding, storage, and retrieval processes; short-term, working, and long-term memory; memory consolidation; organization of information in memory; and types and systems of long-term memory.
- 6) **Classification and conceptual knowledge** – Includes understanding of causality, expert knowledge, cross-cultural differences in knowledge structure, and the relations of conceptual processes with perception, learning, and language.
- 7) **Understanding of affect and mentality** - Examines how people conceive of affect, self, other minds, consciousness, and of the determinants of one's own and others' behavior.
- 8) **Reasoning, decision-making, and choice** - Examines the mechanisms and strategies employed in various forms of reasoning; problem solving; temporal, reward, and contextual influences on decision-making; the conditioning bases of choice behavior; and judgments and choice in social contexts.
- 9) **Human communication and language** - Investigates language comprehension, production, and development at the discourse, semantic, syntactic, and lexical

levels; language processes within social interaction; and gestural, facial, and other forms of non-linguistic communication.

- 10) **Animal communication** - Investigates non-human analogues of human communication and language abilities.
- 11) **Executive function** - Examines the planning, control, coordination, and monitoring of cognition and complex behaviors; allocation of time and effort; and error detection and correction.
- 12) **Influences of affect and stress on cognition** - Addresses the effects of mood, emotion, and physical and psychological stress on memory, decision-making, and executive function.
- 13) **Interdisciplinary Behavioral Science Center** - Organized into eight major projects at sites in the US and UK, the Center is building explicit models of visual perception, conceptual knowledge, language processing and acquisition, executive function, and learning and development to help understand normal and disordered human cognition.

C. Personality and Social Cognition

This thematic category comprises basic research on personality processes, goals and motivational orientations, social cognition, and interpersonal processes.

- 1) **Personality variation** – Examines origins, development, maintenance, and change of consistent individual differences and relation to mental health. Includes trait structure and organization of the personality system, genetic influences, and biological correlates.
- 2) **Self-concept** - Concerns processes by which self-concepts are formed, maintained, and changed; includes regulation of self-esteem and self-image; setting goals and standards.
- 3) **Behavioral regulation** - Focuses on the psychological and psychophysiological attributes and mechanisms that contribute to adaptive regulation of mental processes and behavior. Contributors to self-regulation include motivations, goals, cognitive strategies, socialization influences, interpersonal relationships, and the neurophysiological components of these factors.
- 4) **Social information processing** - Includes examination of both explicit and implicit social-cognitive processes (e.g., attitudes, biases, attributions), as well as neural pathways.
- 5) **Social motivations and goals** – These are powerful regulators of behavior and often operate outside of awareness, thus making them difficult to change: e.g. the distinction between approach and avoidance motivations.

- 6) **Mechanisms of stereotyping and prejudice** - Identifies the cognitive and social processes underlying stereotyping.
- 7) **Interpersonal relationships and social support** - Examines interpersonal interaction within the context of significant relationships; includes support exchanges, self-esteem regulation and emotion regulation within relationships, attachment (child and adult),

II. Behavioral and Integrative Neuroscience

The research in this portfolio is targeted at understanding the normative operation of brain structures and functions that are directly or indirectly relevant to mental disorders.

Understanding normative function is necessary to comprehend the pathophysiology and/or etiology of these disorders. Each of the disorders can be understood in terms of alterations in one or more of these scientific cluster areas.

A. Fundamental Systems Neuroscience

- 1) **Learning & Plasticity** - Includes a wide range of research into the neural mechanisms of learning and plasticity with a primary focus on associative learning procedures such as fear conditioning. Brain plasticity has significance for the malleability of neural and behavioral systems such as those reflected in the branch's birdsong portfolio.
- 2) **Attention** - Involves human studies employing ERP and fMRI technology. The emphasis here is on understanding the role of different brain areas in selectively attending to different sensory cues in the environment.
- 3) **Perception** - Emphasis is on complex aspects of perception in higher order cortical structures, including object representation, face processing, visual imagery, and categorization of objects.
- 4) **Neuroanatomy** - Understanding the neural circuitry of behavior first requires knowledge of the basic structure and connectivity of relevant brain regions.
- 5) **Theoretical** - Uses specialized systems in specific species as well as neural network and computational models.

B. Integrative Systems Neuroscience

- 1) **Memory** - Focuses on the role of hippocampal and prefrontal cortex circuitry in supporting various categories of memory function, including declarative and procedural memory, spatial memory, and working memory. Animal work using electrophysiological techniques and human work including brain imaging studies is supported.

- 2) **Social/Sex/Affiliative Behavior** - Engages a wide range of different animal models, taking advantage of some species-specific findings that have developed, such as in the vole. Use of non-human primates, as well as fish, rat, lizard, hamster, and bird models, take advantage of unique characteristics to gain an understanding of general principles related to the role of specific circuitry and/or neuroendocrine systems.
- 3) **Sleep** - Studies involve understanding REM sleep generation mechanisms, as well as an interest in the relationship to arousal mechanisms and interactions with the circadian system
- 4) **Motivation** – Focuses primarily on the relationship to appetitive and goal-directed behavior.
- 5) **Circadian Rhythms** – Includes studies of the electrophysiology, neurochemistry, hormonal regulation and anatomical connectivity of the suprachiasmatic nucleus and associated structures.
- 6) **Stress** - Examines the function of the HPA axis, particularly its neural regulation and its relation to stress, and effects on the hypothalamus and innervation by serotonin and arginine-vasopressin systems, as well as modulation of the HPA axis by other circuitry. Other aspects include extinction mechanisms, and the neural regulation of fearfulness and anxiety. An important new direction links sex differences, hormones, learning, and neurogenesis.
- 7) **Motor/Navigation/Spatial** – Investigates the role of the hippocampus and neocortex (including parietal areas) in spatial cognition; also includes studies related to navigation: how the overall spatial map and head direction systems combine to allow animals choices and patterns of decisions as they move through their environment.

III. Risk for Psychopathology

Many of the basic processes described under the basic behavioral science portfolio and behavioral & integrative neuroscience portfolio are also examined within the context of risk for psychopathology and risky behaviors related to HIV/AIDS. Some examples of this research include studies that address the social and environmental context in which decisions are made regarding HIV risk-taking behavior. Also included in this category is research on family processes that may contribute to the development of psychopathology, as well as individual factors such as affect regulation, which may indicate a predisposition toward psychopathology or targets for rehabilitation of functioning.

Basic Behavioral Research Grants Supported by National Institute of Mental Health (NIMH)			
Grant Number	Grant Title	PI	Institution
5R01MH061995-03	Oxytocin, Postnatal Experience & Adult Maternal Behavior	Pedersen, Cort A.	University of North Carolina, Chapel Hill
2R01MH058147-06	Emotion Regulation and its Consequences	Gross, James J.	Stanford University
5R01MH046516-14	Synaptic Transmission in Fear Conditioning Circuits	LeDoux, Joseph E.	New York University
5R01MH012717-34	Information Processing, Search, and Retrieval	Shiffrin, Richard	Indiana University, Bloomington
5R01MH049227-12	Mapping Personality Trait Structure	Goldberg, Lewis R.	Oregon Research Institute
5R01MH066034-02	Selective Attention and Control Mechanisms in the Brain	Hopfinger, Joseph B.	University of North Carolina, Chapel Hill
5R01MH049414-11	Personality and Health from Childhood to Adulthood	Caspi, Avshalom	University of Wisconsin, Madison
1R01MH065851- 01A2	Cognitive Models of HIV Decision Making in Young Adults	Patel, Vimla L.	New York State Psychiatric Institute
5R01MH062601-03	Psychobiological Studies of Stress in Young Children	Gunnar, Megan R.	University of Minnesota
5R10MH055714-08	ERP and FMRI Studies of Visual Attention	Mangun, George R.	University of California, Davis

**National Institute of Neurological Disorders and Stroke (NINDS)
Basic Behavioral and Social Science Research**

Description of Current Program

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to reduce the burden of neurological disorders by conducting and supporting research on the normal and diseased nervous system. To this end, NINDS supports a broad portfolio of basic and clinical behavioral research. This includes basic studies of the neural bases of cognition and behavior, and clinical studies of the adverse effects of neurological disease on cognitive and behavioral functioning, along with the development of behavioral interventions designed to ameliorate the symptoms of some neurological disorders.

A major portion of the NINDS behavioral research portfolio consists of cognitive and behavioral neuroscience research aimed at understanding the neural bases of a variety of cognitive and behavioral processes. These include studies of sensation and perception (e.g., visual, auditory, somatosensory), attention, motor behavior and movement, learning and memory, language abilities (both reading and writing), and higher cognitive processes. For example, one project aims to determine the neural substrates of decision-making at the neuroanatomical and neurochemical level, and to apply this knowledge to understand the component processes of decision-making in the human brain, in both health and disease. Another project focuses on the cellular neuroplasticity underlying learning and memory, and the synaptic changes in the mammalian hippocampus. Other NINDS-funded studies focus on regulation of the sleep-wakefulness cycle, food intake, body weight, the neural basis of pain perception and response to pain, and neuroendocrine control of reproductive behaviors. For example, one funded project studies the physiological processes mediating deficits in female reproductive behaviors that are seen in nutritional infertility.

These studies are being done on a variety of levels, from the molecular and cellular to the physiological and systems level. For example, the molecular and cellular bases of learning and memory are being studied in several animal model systems. One study aims to understand the mechanisms underlying sensitization, a simple form of non-associative learning, in the marine mollusk *Aplysia californica*. At the physiological and systems level, the neural bases of perception and attention are being studied in animal models by measuring changes in brain electrical activity as the animal performs behavioral tasks that require it to shift its attention from one task to another.

The development of powerful new imaging technologies such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) is giving researchers the extraordinary ability to study the neural bases of a variety of cognitive processes in humans in real time. For example, NINDS-funded researchers are using these techniques to study normal language development and how this development is altered in children with reading disabilities such as dyslexia. Other researchers are using these techniques to study differences in brain activity between normal individuals and brain lesion patients in order to gain a better understanding of the neural bases of language, face recognition, and decision-making ability, among other processes.

In addition to studying the neural basis of cognitive functions in the healthy brain, NINDS also supports research on the adverse effects of neurological disease on cognitive and behavioral functioning in disorders such as stroke, Parkinson's disease, and traumatic brain injury. In May 2002, NINDS and three other NIH institutes issued a program announcement with set-aside funds (PAS) for "Basic and Translational Research on the Cognitive Sequelae of Parkinson's Disease" to understand the underlying neurobiological mechanisms associated the deficits in executive function, memory, learning, and other cognitive processes in patients with Parkinson's disease.

An exciting new initiative called "Cognitive and Emotional Health: The Healthy Brain Project," will provide a foundation for translation of basic research into clinical practice. The NINDS, NIA, and NIMH have joined efforts on this trans-NIH initiative, the overall goal of which is to assess the state of longitudinal and epidemiological research on demographic, social, and biologic determinants of cognitive and emotional health in aging adults and the pathways by which cognitive and emotional health may reciprocally influence each other. More information on this initiative can be found at: <http://trans.nih.gov/CEHP/>.

NINDS intramural researchers are also conducting a wide range of research to understand the functions of the human brain including cognitive neuroplasticity, social cognition, memory, amnesia, and learning. They use a range of techniques including behavioral measures and imaging technologies to support their research on the neurobiology of higher cognitive functions and other complex behaviors.

Future Planned Initiatives

In June 2003, NINDS, together with other NIH Institutes, sponsored a workshop on "Executive Function: Current Knowledge and Future Research Opportunities," to bring together leaders in the field to discuss current research findings in executive function, assess the state of knowledge regarding executive function in the healthy and injured/diseased states, and set a research agenda for future studies of executive function. As a follow-up to this meeting, NINDS released a Request for Information (NOT-NS-04-012; April 6, 2004) to explore the market interest and capabilities relating to the development of valid, reliable and domain specific tasks of Executive Function for measurement and adequate intervention of executive dysfunction in neurological disorders. The development of domain specific tasks of executive function would be of considerable value to many of NINDS's current and future research programs in neurological disorders where dysfunction in cognitive processes are integral components of functional outcomes and quality of life for affected parties. Information from this notice may aid in the design of a possible future solicitation.

On September 23-24, 2004, the NINDS held a meeting entitled "Cognitive Rehabilitation Interventions: Moving from Bench to Bedside." The goal of this workshop was to promote the use of evidence-based interventions in the evaluation, treatment, and assistance of patients with disorders of the brain affecting higher thought processes. The workshop brought together multidisciplinary teams of scientists including neurologists, cognitive neuroscientists, psychologists, occupational therapists, pharmacologists, functional imaging experts and

computational modelers in order to accelerate progress in the field of cognitive rehabilitation. Three teams were formed prior to the workshop to address the following areas: (1) Brain Tumor: Cognitive Deterioration / Rehabilitation of Memory and Attention Mechanisms; (2) Stroke: Unilateral Neglect / Rehabilitation of Spatial Attentional Disorder; and (3) Traumatic Brain Injury: Executive Function / Rehabilitation of Regulatory Cognitive Processes. Each team developed a white paper, which summarized the state of the science and made recommendations to address these three areas in the future. The NINDS will be working to follow-up on the discussions and recommendations from this meeting, with the immediate goal of stimulating research into more effective interventions, and with the longer range goal of determining how to better translate cognitive neuroscience findings into the clinic.

Opportunities Not Currently Addressed

The NINDS is interested in pursuing areas of research to help expand our understanding of the neural basis of cognitive, behavioral, and perceptive processes in the healthy and diseased state. Through workshops, conferences, initiatives, and solicitations, NINDS works to encourage research in areas where important scientific opportunities exist. Areas of interest that may be explored in the future include the mechanisms by which partial and total sleep deprivation seriously impair cognitive function; cognitive aspects of pain disorders; the neurologic underpinnings and consequences of obesity; high-throughput tools for brain and behavior; and the cognitive and behavioral effects of a number of neurological disorders.

**Basic Behavioral Research Grants supported by
National Institute of Neurological Disorders and Stroke (NINDS)**

Grant Number	Grant Title	PI	Institution
2R01NS035467	Seasonal Plasticity in Steroid-Sensitive Neural Circuits	Ball, Gregory F.	Johns Hopkins University
5R01NS033574	Ontogeny of Structure & Function at Hippocampal Synapses	Harris, Kristen M.	Medical College of Georgia
5R01NS035360	Cortical Control of Movement	Keller, Asaf	University of Maryland, Baltimore
5P50NS022343	Center for the Neural Basis of Language and Learning	Trauner, Doris A.	University of California, San Diego
2R01NS019895	Analysis of the Neural Control of Behavior	Byrne, John H.	University of Texas Health Sciences Center - Houston
1R21NS045074	Mapping the Anatomy of Decision Making	Fellows, Lesley K.	University of Pennsylvania
2R01NS023684	Neural Substrates for Reproductive Behavior	Kelley, Darcy B.	Columbia University
1R01NS043480	ADHD In Girls: Neuroimaging and Executive Behavior	Denckla, Martha B.	Kennedy Krieger Research Institute
2R01NS010873	Hormones, Brain Function, and Behavior	Wade, George N.	University of Massachusetts, Amherst
1F32NS046184	Pre-Existing Affect and Pain Recall: Mediating Factors	Gedney, Jeffrey J.	University of Florida

**National Institute of Nursing Research (NINR)
Basic Behavioral and Social Sciences Research**

The National Institute of Nursing Research (NINR) supports clinical and basic research to establish a scientific basis for the care of individuals across the life span. Nursing science integrates both biological and behavioral processes in the study of health and disease. Thus, NINR has historically had a major focus in biobehavioral research, emphasizing the whole person. Consequently, the majority of our portfolio is relevant to behavioral research. These research programs examine all levels of biobehavioral functioning, from the individual cell and biological markers to the individuals, groups and communities as relevant for health and health care problems encountered by patients, families, and caregivers. This includes a focus on the special needs of at-risk and under-served populations, with emphasis on health disparities.

Description of Current Program

1. Current Program Activities (2004 Priorities)

The NINR program activities highlighted below have targeted areas relevant to basic behavioral and social sciences research.

Chronic Illness Self-Management and Quality of Life – NINR is expanding initiatives in self-management and quality of life for individuals with chronic illness. Specific target areas for expansion include the following: Influence of age, gender, cultural/ethnic factors, and impact of technological advances.

End-of-Life: Bridging Life and Death – NINR has demonstrated leadership on end-of-life research at NIH since 1997, convening workshops and spearheading several RFAs and PAs. Recent workshops on EOL issues in patients with genetic illnesses, EOL in elderly persons and ethical issues of EOL and an upcoming State of the Science Conference will help provide the basis for continued growth of EOL research. Targeted areas: gender and minority issues in end-of-life care; international end-of-life studies; and ethical issues of EOL care and research.

Enhancing Health Promotion Among Minority Men - The difference in life expectancy of African American men and European American men in the US is greater than the difference in life expectancy between women and men in the US. Launch of this initiative will solicit studies of lifestyle factors that may be amenable to early intervention. Target areas include factors that influence health promoting behaviors of minority men; identification of creative approaches for involving families, social networks and/or communities in enhancing health promotion.

Decreasing Low Birth Weight and Premature Birth Among Minority Populations - Low birth weight and premature birth rates show continued and worsening disparities; e.g., African Americans, Native American and Alaskan natives have a approximately 50% higher infant mortality rates than white women. A major targeted area of research includes a better understanding of the biological and psychosocial mechanisms that contribute to adverse pregnancy outcomes in minority families.

Nursing Research Training and Centers – NINR is working to increase the pool of investigators to conduct biobehavioral research and facilitate early entry in to doctoral training and career development programs. In addition, NINR is expanding its Research Centers program to foster development of research-intensive environments and interdisciplinary opportunities and to increase the number of research projects aimed at eliminating health disparities.

2. NINR sponsors, and co-sponsors with other institutes and centers, initiatives focused on populations across the lifespan, including children and adolescents, young and middle-aged adults, as well as older and old adults. Specific science areas include the following: Chronic Illness; Health Promotion and Risk Reduction in Adults and Children; Cardiopulmonary Health; Neurofunction and Sensory Conditions; Immune Responses and Oncology; Reproductive Health; Genetics; and, End of Life and palliative care. Again, although NINR’s research in the aforementioned areas covers the broader spectrum of behavioral and social science research, there are significant and growing numbers of investigations in the area of basic behavioral and social science research.

The following are selected examples of relevant initiatives that are sponsored or co-sponsored by NINR in 2003/2004

PA-04-153: Health Disparities among Minority and Underserved Women

PA-04-121: Understanding Mechanisms of Health Risk Change in Children and Adolescents

PA-04-092: Long-term Weight Maintenance:Basic and Clinical Studies

PA-99-045: Low Birth Weight in Minority Populations

PA-02-165: Race/ethnic Disparities in the Incidence of Diabetes Complications

PA-03-170: Health Promotion Among Racial and Ethnic Minority Males

PA-00-001: Aging Women and Breast Cancer.

PA-02-165: Race/Ethnic Disparities in the Incidence of Diabetic Complications.

PA-02-102: The Role Of Gene-Environmental Interactions Underlying The Health Disparity Of Premature Birth.

PA-99-021: Biobehavioral Pain Research

PA-04-085: Research on Autism and Autism Spectrum Disorders

3. NINR’s Centers Program is building infrastructure as well as a cadre of scientists devoted to developing the breadth and depth of knowledge in a broad range of basic behavioral and social science areas. A brief description as well as selected examples of exploratory and core center programs are provided below.

P20 Exploratory Research Center

Purposes: Important mechanism for building & maintaining intellectual and physical resources

- Provides funding for institutions that are developing research programs
- Fosters interdisciplinary research
- Provides mechanism to support infrastructure development and centralization of research resources

Selected Examples of Current P20 Centers:

- University of Florida – Biobehavioral Research

- Duke University — Trajectories of Aging & Care in Nsg Science
- Emory University – Symptoms, Symptom Interactions, & Health Outcomes
- Montana State University – Chronic Health Conditions in Rural Dwellers – Injury Mechanisms & Related Responses
- University of Illinois – Cardiovascular and Respiratory Health

P30 Core Research Centers

Purposes: Important mechanism for building & maintaining intellectual and physical resources

- Fosters interdisciplinary research
- Provides mechanism to support delivery of research results to clinical practice community
- Provides funding for institutions at various developmental stages of nursing research capability

Selected Examples of Current P30 Core Research Centers:

- University of California, Los Angeles--Vulnerable Populations Research
- University of North Carolina-CH – Chronic Illness in Vulnerable People
- University of Pittsburgh – Chronic Disorders
- University of Washington, Seattle – Women’s Health Research
- Indiana University, Austin—Quality of Life in Chronic Illness

4. Recent NINR Work Groups have been convened to explore the potential for advancing the science in various basic behavioral and social science areas of research as well as the broader spectrum of biobehavioral research. Selected previous and future work group meetings are summarized.

Moving the Research Agenda Forward For Children With Cancer

The National Institute of Nursing Research (NINR) and the Office of the Director/Office of Rare Diseases (ORD) at the National Institutes of Health (NIH) convened the workshop "**Moving the Research Agenda Forward For Children With Cancer**" on August 5-6, 2003 in Bethesda, Maryland. This workshop brought together 13 experts from diverse fields such as nursing science, pediatric oncology, psychology, medical anthropology, and communication sciences among others. These experts discussed issues related to diagnosis, treatment, quality of life, survivorship, relapse and end of life care in order to develop and move the research agenda forward for children with cancer in the 21st century. There was consensus among participants that biobehavioral and sociocultural aspects of the pediatric cancer experience are understudied areas. Despite great advances, cancer is the leading cause of death, from disease, in children outside of the immediate newborn period. Therefore, it is understandable that research has focused more on survival and cure than on the biobehavioral/sociocultural issues faced by pediatric cancer patients. A paradigm shift may be necessary to view the whole life course as a continuum in order to effect further progress in prevention, treatment, palliation, and long-term survival, involving the full range of the child’s experience as a member of a family and society. The *Journal of Pediatric Oncology Nursing* has agreed to publish the proceedings.

Optimizing Pregnancy Outcomes in Minority Populations

The National Institute of Nursing Research (NINR), National Institutes of Health (NIH), convened the workgroup “**Optimizing Pregnancy Outcomes in Minority Populations**” on March 3-4, 2003 in Bethesda, Maryland. This workgroup brought together researchers in the fields of nursing, epidemiology, psychology, and clinical and basic sciences in a collaborative, multi-disciplinary approach to address this issue and formulate future research strategies. Nine white papers on the following topics were presented and discussed: Psychosocial and Biological Influences on Pregnancy in Minority Populations; Stress and Neuroendocrine Mechanisms in Prematurely and LBW Outcomes; Behavioral Influences and Maternal Health During Pregnancy; Defining Risk and Risk Factors; Environmental Exposure and Biological Mechanisms Affecting Pregnancy Outcomes; Identification of Physiological Pathways and Biochemical Markers; Measurement of Psychosocial Constructs; and, Methodological Considerations in Designing Multidisciplinary Biobehavioral Research on Prematurely and LBW. With partial funding from the Office of Rare Disease, these papers, along with an additional paper highlighting research gaps and recommendations for future directions are currently being published as a group in the American Journal of Obstetrics and Gynecology.

Future Planned Initiatives

Increasing Opportunities in Biobehavioral Research

A work group meeting is scheduled for the summer of 2004 with a diverse and multidisciplinary group of researchers with expertise in biobehavioral research and in rare disease. The workgroup meeting will be sponsored by the NIH Office of Rare Diseases. The goal of the meeting is to bring together a group of biological, behavioral, and immunological experts to examine the existing body of knowledge and to develop recommendations on a research agenda for biobehavioral research opportunities. A specific rare disease will be used as a model for discussions about gaps in biobehavioral research.

Opportunities not Currently Addressed

1. NINR strongly supports areas of science related to health disparities. Additional work is needed NINR is committed to advancing the science in this area.
2. NINR also targets obesity prevention and management studies and participates in the NIDDK Look AHEAD clinical trial for weight reduction in type 2 diabetes. More research is needed in this area from a basic behavioral perspective.
3. NINR has significantly increased funding for diabetes research during the past five years. More biobehavioral studies are needed for children and adolescents developing both type 1 and type 2 diabetes and for basic behavioral and social sciences research in other chronic diseases, especially in children, the oldest old, and in rural populations.

**Basic Behavioral Research Grants supported by
National Institute of Nursing Research (NINR)**

Grant Number	Grant Title	PI	Institution
5T32 NR007106-5	Biobehavioral Nursing Research Training Program	Mitchell, Pamela	University of Washington
5P20 NR007791-03	Biobehavioral Research Center (BRC)	Yucha, Carolyn	University of Florida
5R01 NR004141-08	Menopausal Transition: A Biobehavioral Model of Symptoms	Mitchell, Ellen	University of Washington
5R01 NR003695-10	Longitudinal Trajectories of Adolescents Born Preterm	McGrath, Margaret	University of Rhode Island
5R01 NR007666-03	Gene Expression – Environmental Link in Cerebral Ischemia	Briones, Teresita	University of Illinois, Chicago
1R15 NR008489-01	Hypertension – Prevention Beliefs Among African American	Peters, Rosalind	Wayne State University
1R15 NR005054-01A2	Teen Pregnancy Prevention Social Comparison Uses Scales	Tigges, Beth	University of New Mexico
5K01 NR007676-03	Black Caregivers of Older Adults: Trust and Health Care	Bonner, Gloria	University of Illinois, Chicago

National Library of Medicine (NLM) Basic Behavioral and Social Sciences Research

The National Library of Medicine supports basic behavioral and social science research (BSSR) through its extramural grant programs for biomedical informatics. Behavioral and social sciences research is supported both by traditional research grants and resource grants for scholarly works. In 2003, we estimate that approximately \$2,000,000 was awarded to support in BSS research, of which approximately \$1,600,000 was in support of basic research. NLM's BSSR portfolio emphasizes aspects of computational and information sciences as they relate to human behavior, including how information is used to make professional and personal health decisions and in learning.

Research Grants in Biomedical Informatics and Bioinformatics

NLM's research interests in informatics center on health-related information – its representation in computers and its use by humans in thinking, learning and problem solving. Because biomedical research and clinical medicine are information-intensive and increasingly computerized, there are many basic behavioral and social science issues to be explored relating to human-computer interaction. For example, some projects focus on the way humans characterize, gather and synthesize information they need for a purpose. Another research theme is the proper representation of computer-based knowledge, in order to improve understanding (i.e., health literacy) or to improve clinical or personal health decisions. The table below presents examples of funded grants in these areas. An area of need continues to be support for the

NLM Grants for Scholarly Works in Biomedicine and Health

NLM supports the preparation scholarly works of value to US health professionals, public health officials, biomedical researchers, and philosophers and historians of the health sciences. These works include histories, critical reviews and research aids. Perhaps 25% of the grants awarded in this program related to issues of social interaction, social roles and personal behavior in terms of their health effects, or their effects on the health care process. Often, these works also try to bridge the literatures of basic biology and clinical care, to provide a broader contextual analysis. The grants table below lists 3 examples, identified by their G13 grant numbers. These resource grants are not, in the strict sense, basic BSSR, but they support unique research activities related to behavioral and social themes.

Basic Behavioral Research Grants supported by National Library of Medicine (NLM)			
Grant Number	Grant Title	PI	Institution
1 R01 LM008154-01	Using the Internet to Improve Patient's Self-Management of Chronic Illness	MILLER, DEBORAH M	CLEVELAND CLINIC FOUNDATION
1 R01 LM008192-01	Clinical decision-making using a data-driven display	HARRISON, JAMES H	UNIVERSITY OF PITTSBURGH AT PITTSBURGH
1 R03 LM007947-01	Exploring Technical Work Using Cognitive Artifacts	COOK, RICHARD	UNIVERSITY OF CHICAGO
1 R01 LM007894-01A1	Cognition and Error Management for Critical Care	PATEL, VIMLA L	COLUMBIA UNIVERSITY HEALTH SCIENCES
1 R01 LM007709-01A1	Evaluating an Internet-Based Curriculum about Herbs	KEMPER, KATHI J	WAKE FOREST UNIVERSITY HEALTH SCIENCES
1 R03 LM008302-01	Health information we searches by low-literacy adults.	STEINMAN, RICHARD	UNIVERSITY OF PITTSBURGH AT PITTSBURGH
1 R03 LM008240-01	Information Needs in Cardiovascular Intensive Care	MOSS, JACQUELINE A	UNIVERSITY OF ALABAMA AT BIRMINGHAM
5 G13 LM007584-02	Gender Matters and Health: The Role of Choice and Policy	BIRD, CHLOE E	RAND CORPORATION
5 G13 LM007638-02	Youth Violence: Interventions in Emergency Departments	KETTERLINUS, ROBERT D	PHILADELPHIA HEALTH MANAGEMENT CORP
5 G13 LM007666-02	Character and Gender in Psychiatric Ethics	RADDEN, JENNIFER	UNIVERSITY OF MASSACHUSETTS BOSTON