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**U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES**

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

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NOTICES

EXTRAMURAL RESEARCHERS' FINANCIAL CONFLICTS OF INTEREST MEETING

P.T. 34; K.W. 1014006

National Institutes of Health
Alcohol, Drug Abuse, and Mental Health Administration

The National Institutes of Health (NIH) and the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) are in the process of developing appropriate further guidance concerning financial conflicts of interest for investigators receiving Government funds. An open meeting will be held on June 27 and 28, 1989, in Masur Auditorium of the Warren G. Magnuson Clinical Center at NIH to provide opportunity for comments from all parties. All interested parties are encouraged to attend this meeting or to submit written comments. You may submit these comments to:

Dr. Katherine L. Bick
Deputy Director for Extramural Research
National Institutes of Health
Shannon Building, Room 144
Bethesda, Maryland 20892

As discussed in the January 20 issue of the NIH Guide for Grants and Contracts (Vol. 18, No. 2), there are growing expressions of concerns about circumstances that might affect investigators' objectivity, or where researchers might unduly influence, or might be perceived to influence, NIH/ADAMHA-funded R&D projects in directions favorable to personal financial interests of themselves, their spouses, children, close professional associates, or organizations where they have appointments or other relationships.

A variety of topics on real, or perceived, conflicts of interest will be discussed at the June 27-28 meeting, such as whether investigators and consultants participating in NIH/ADAMHA-funded studies should hold financial interests in organizations or entities that produce drugs, devices, or other interventions that are evaluated under those awards. Following this meeting, NIH/ADAMHA intend to develop appropriate guidance for such relationships. Guidelines would seek to clarify pertinent types of research situations and personal financial interests, in accord with the PHS Grants Policy Statement, January 1, 1987, revision, concerning Standards of Conduct for Employees for awardee organizations, and to define appropriate distributions of governance between NIH/ADAMHA and awardee organizations. Points to consider in such guidance include requirements for disclosure, approval, and/or restrictions in certain situations as well as possible exceptions to restrictions to permit investigators with unusual skills and expertise to conduct studies which might otherwise be proscribed. (These guidelines should not concern financial benefits resulting from logical steps in product research/development/testing under NIH awards, e.g., Small Business Innovation Research.) The proposed meeting is designed to elicit comment from concerned and interested individuals and institutions prior to development of general guidelines; we invite broad attendance.

Further information concerning this meeting, including planned discussion topics, will be published in the NIH Guide for Grants and Contracts in May.

DATED ANNOUNCEMENTS (RFPs AND RFAs)

PHASE II-B RANDOMIZED CONTROLLED STUDY OF TISSUE PLASMINOGEN
ACTIVATOR FOR ACUTE STROKE - Coordinating Center

RFP AVAILABLE: NIH-NINDS-89-04

P.T. 34; K.T. 0715200, 0755015, 0755018

National Institute of Neurological Disorders and Stroke

The National Institute of Neurological Disorders and Stroke (NINDS) is seeking proposals with the intent of awarding one contract to provide a coordinating center for a Phase II-B randomized controlled clinical study of tissue plasminogen activator for the treatment of acute ischemic stroke. Expertise in the coordination of a multicenter clinical study of a pharmacological treatment and in the management of clinical data collection and analysis is required. RFP-NIH-NINDS-89-03 has been issued separately to solicit

participating clinical centers, with the anticipation of making six to eight clinical center contracts award.

This is an announcement of an anticipated RFP. RFP-NIH-NINDS-89-04 will be issued on or about April 21, 1989, with a closing date for receipt to proposals set for June 21, 1989.

All responsible sources may submit a proposal, which shall be considered by this Agency. To receive a copy of the RFP, you must supply this office with two self-addressed mailing labels. The RFP will be available upon written request to:

Contracting Officer
Ref.: RFP-NIH-NINDS-89-04
Contracts Management Branch, NINDS
National Institutes of Health
Federal Building, Room 901
7550 Wisconsin Avenue
Bethesda, Maryland 20892

RESEARCH ON PATHOGENESIS OF LYME BORRELIOSIS (LYME DISEASE)

RFA AVAILABLE: 89-AI-14

P.T. 34; K.W. 0715125, 0715010, 0715026, 0710070, 0755020, 0765033

National Institute of Allergy and Infectious Diseases
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Date: June 1, 1989
Application Receipt Date: August 1, 1989

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and the National Institute of Allergy and Infectious Diseases (NIAID) announce the availability of an RFA for funding Research on Pathogenesis in Lyme Borreliosis (Lyme disease). This RFA (available upon request) invites applications for funding of research that will increase our understanding of interactions between *Borrelia burgdorferi* and the human host. Increased knowledge in this area will result in substantial improvements in diagnosis and chemotherapy and provide the basis for the development of an effective vaccine. Research projects involving use of tissue culture, animal models, human subjects, molecular techniques and other experimental approaches may be focused upon one or more of the following:

- o Identification and characterization of bacterial factors that act as virulence and colonization factors.
- o Identification and characterization of antigenic and immunogenic determinants presented to the host. The role of antigenic variation in pathogenicity. The mechanism of antigenic variation.
- o The nature of the immune response to *B. burgdorferi*? The relationships between the cell-mediated and humoral responses to *B. burgdorferi*. Characterization of host reactions; protective versus non-protective, specific (to *B. burgdorferi*) versus non-specific. Classes of immunoglobulins produced in response to infection.
- o Characterization of the course of infection after *B. burgdorferi* enters the human host. Identification of organ systems and tissues that are infected and/or inflamed. Characterization of specific tissue tropisms.
- o Characterization of inflammatory responses in relation to the various clinical manifestations associated with Lyme borreliosis. The roles of cytokines in inflammatory responses in this disease.
- o Histopathologic studies of early and late manifestations of the disease.
- o The role of host immunogenetic determinants in susceptibility to the disease and its various manifestations.
- o Development of animal and/or tissue culture models that can be used to obtain insights or answers to the above questions.

- o Development of an improved culture medium that will allow maintenance of *B. burgdorferi* in a virulent form with greater maximum population density.
- o Development of a genetic transfer system in *B. burgdorferi*.
- o Comparison of pathogenesis of Lyme borreliosis with that of other spirochetal diseases such as syphilis and relapsing fever.

Applicants may include several of the above areas in their research proposals. Applicants are encouraged to consider other avenues of investigation that would be appropriate to the goals of this RFA as well.

Awards will be made as individual research project (R01) grants. Domestic universities, medical colleges, hospitals, laboratories and other public or private research institutions, including State and local government units, are eligible to apply for funding. Awards under this announcement to foreign institutions will be made only for research of unusually high merit, need and promise, and in accordance with Public Health Service policy governing such awards.

This is a one-time solicitation for proposals. Ten to 15 awards may be funded on the basis of merit and availability of funds.

The full RFA may be obtained from:

Robert L. Quackenbush, Ph.D.
 Vector-Borne Bacterial Diseases Program Officer
 Microbiology and Infectious Diseases Program, NIAID
 Westwood Building, Room 736
 Bethesda, Maryland 20892
 Telephone: (301) 496-7728

or

Steven J. Hausman, Ph.D.
 Deputy Director, Extramural Program
 National Institute of Arthritis and Musculoskeletal and Skin Diseases
 Westwood Building, Room 403
 Bethesda, Maryland 20892
 Telephone: (301) 496-7495

ONGOING PROGRAM ANNOUNCEMENTS

ALCOHOLISM TREATMENT: MATCHING CLIENTS TO TREATMENTS

P.T. 34; K.W. 0404003, 0785035, 0755018

National Institute on Alcohol Abuse and Alcoholism

PURPOSE

Current research indicates that alcohol dependence and problem drinking are not unitary phenomena or unidimensional syndromes. Instead, there appear to be different types of alcohol-dependent individuals. Individual characteristics other than kind of alcohol problem also seem to affect treatment outcomes. It is becoming evident that both treatment outcomes and costs can be positively affected by the careful matching of patients by their characteristics with the type of treatment provided. This announcement seeks research grant applications to investigate differences among alcoholism treatment regimens in terms of efficacy and cost effectiveness for different types of patients.

RESEARCH OBJECTIVES

The announcement seeks research projects that: (1) study the effects of the careful matching of patient variables with treatment and setting variables; (2) develop prediction techniques to identify treatments most suitable for patients at various points in the development of their alcohol dependency or recovery; and/or (3) assess the relative costs of different types of treatment and settings for different client types.

MECHANISM OF SUPPORT

Support may be requested for a period of up to 5 years (renewable for subsequent periods). Annual awards will be made subject to continued

availability of funds and progress achieved. Grant funds may be used for expenses clearly related and necessary to carry out research projects, including both direct costs which can be specifically identified with the project and allowable indirect costs of the institution. Funds may not be used to establish; add a component to; or operate a treatment, rehabilitation, or prevention service program. Support for research-related treatment, rehabilitation, or prevention services and programs may be requested only for those particular costs and for that period of time required by the research. These costs must be justified in terms of research objectives, methods, and designs which promise to yield important generalizable knowledge and/or to make a significant contribution to theoretical concepts.

ELIGIBILITY

Applications may be made by public or private nonprofit or for-profit organizations such as universities, colleges, hospitals, laboratories, units of State or local governments, and eligible agencies of the Federal government. Women and minority investigators are encouraged to apply.

APPLICATION PROCEDURES

Application kits containing the necessary forms and instructions (PHS 398) may be obtained from:

The National Clearinghouse for Alcohol and Drug Information
Box 2345
Rockville, Maryland 20852
Telephone: (301) 468-2600

Send or deliver the completed application and four signed photocopies to:

Division of Research Grants
Westwood Building, Room 240
National Institutes of Health
Bethesda, Maryland 20892**

Application receipt deadlines are February 1st, June 1st, and October 1st.

INQUIRIES

For further information, contact:

Jacqueline Wallen, Ph.D.
Project Officer, Treatment Research Branch
Division of Clinical and Prevention Research
National Institute on Alcohol Abuse and Alcoholism
Parklawn Building, Room 16C-03
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-0796

GENE THERAPIES FOR AIDS

P.T. 34; K.W. 0745032, 0715008, 0755025, 0755060, 1002008, 1002045, 0755020

National Institute of Allergy and Infectious Diseases

BACKGROUND INFORMATION

The National Institute of Allergy and Infectious Diseases (NIAID) is playing a central role in the investigation of Acquired Immunodeficiency Syndrome (AIDS). Research efforts directed toward the pathogenesis, prevention and treatment of the disease and its sequelae have intensified. The NIAID has undertaken a lead role in organizing scientists into National Cooperative Drug Discovery Groups for the Treatment of AIDS (NCDDG/AIDS). NCDDG/AIDS are comprised of scientists from academic, non-profit, and commercial organizations that interact as a unit, with NIAID support, to conduct preclinical research aimed at the discovery of agents which can be used in the treatment of AIDS. Samples of the research areas currently being investigated by NCDDG scientists include molecular biology of HIV and SIV; development of unique cell culture assays, biochemical screens and small animal models; discovery of new lead compounds and biologics; rational drug design; X-ray crystallography of proteins and drugs; characterization and isolation of natural products; development of delivery systems for new drugs; and development of viral vectors for delivery of anti-viral genes, and antisense nucleic acids. Since the inception of the NCDDG/AIDS in 1986, three potential therapies have been discovered and developed. One anti-HIV compound,

recombinant soluble CD4 (Biogen, Inc.) has already entered clinical trial and two nucleosides, [azidouridine (CS-87) and dideoxydidehydrothymidine (d4T) are expected to enter clinical trial in 1989. Other potential therapeutics identified through the comprehensive efforts of the NCDDG are in earlier states of preclinical development.

The NIAID, through the Developmental Therapeutics Branch of the AIDS Program, will soon launch an NCDDG/OI program to encourage collaborative efforts to discover new therapies targeted to the opportunistic infections associated with AIDS. NIAID also facilitates the acquisition of information on any drug that shows potential in the treatment of HIV infection, fills gaps in the drug development process, provides ancillary information on the rationale of the drug in animal retroviral models, and assists in the transition of promising therapies into clinical trials in NIAID's AIDS Clinical Trial Group program.

The NIAID now wishes to expand the areas of investigator-initiated research currently being funded. This Program Announcement solicits applications from investigators who wish to play an active role in defining the direction of such research. While no funds are specifically set aside for funding grants submitted in response to this Program Announcement, the NIAID regards additional high quality research in this area of high priority.

OBJECTIVES AND SCOPE

The objectives of this Program Announcement are to stimulate research on: (i) development of viral vectors encoding anti-HIV peptides or antisense RNA, and (ii) evaluation of the potential of these vectors to block HIV expression using in vitro systems and small animal models.

The potential of gene therapy in the treatment of human genetic diseases is under intense study. Several viral vectors, including retroviruses, adenoviruses, herpes simplex virus and helper-dependent viruses have been established and tested in vitro. Recombinant retroviruses have also been delivered in vivo via the hemopoietic system (mice, dogs, monkeys, ferrets) or via implants of retrovirus-transformed fibroblasts, hepatocytes or endothelial cells. Similar vectors are now being considered for gene therapy in humans. Indeed, the infusion of mature lymphocytes transformed ex vivo with a retrovirus vector carrying a reporter (neomycin) gene in cancer patients is underway. DNA vectors with a broad host range and a large insert capacity, such as autonomously replicating herpes simplex amplicons, may also prove suitable for gene therapy. Variants with specific cell tropism are also available, expanding the potential of targeting genes to specific cell populations.

Additional studies are needed to improve existing systems and to design novel transfer modalities applicable to the future treatment of HIV-infected individuals. For example, it may be possible to achieve targeted delivery to HIV-infected cell populations using novel ligands embedded in the vector's membrane which are compatible with the cell's surface receptors or markers (CD4+gp120). Similarly, specific expression within target cells (T4, monocyte/macrophage, others) may be feasible using cell type specific promoters or promoters inducible only in a desired cell population. The potential risk that may be associated with the in vivo use of these vectors should be assessed. For example, integration of provirus DNA may result in insertional mutagenesis, perturbation of cellular gene expression or activation of cellular oncogenes. These possibilities should be analyzed in in vitro systems.

Evaluations of various vectors in small animal studies would yield important information on the applicability of these strategies to in vivo delivery. Several animal models amenable to these studies are being developed [transgenic mice or rabbits harboring HIV genetic elements, immunodeficient mice reconstituted with human immune cells]. Investigators are encouraged to collaborate with laboratories having these resources. A potentially important and unique approach to targeted delivery of anti-HIV agents could result. Results from this research could have broad implications for the treatment of a variety of infectious, immunological and metabolic diseases.

In summary, NIAID wishes to stimulate research in the following:

- o Development of viral vectors encoding anti-HIV peptides or antisense RNAs,
- o Targeting viral vectors to HIV-infected cells using novel ligands,
- o Targeting expression in HIV-infected cells using inducible or cell-type specific promoters, and

- o Evaluation of the in vivo applicability of such vectors using small animal retroviral models.

The approaches outlined above are not intended to be comprehensive or required. Any investigation on the use of vectors for the in vitro or in vivo (small animal models) transfer of a gene expressing antisense RNA or any other gene with potential anti-HIV activity are encouraged under this Program Announcement.

METHOD OF APPLICATION

Use the standard research Grant Application Form PHS 398 (Rev. 9/86). For purpose of identification and processing, the words "Gene Therapies for AIDS" should be typed in item 2 on the face page of the application. The receipt dates are May 1 and September 1, 1989, and January 1, 1990. In order to comply with the expedited review for AIDS applications, mail the complete application and twenty-four (24) exact copies to:

DRG AIDS Coordinator
Westwood Building Room 240
National Institute of Health
Bethesda, Maryland 20892**

REVIEW PROCEDURES AND CRITERIA

Support for this program will be through the traditional research grant. Applications will be reviewed by the appropriate Study Sections designated by the Division of Research Grants. A second review will be made by an appropriate National Advisory Council. Review criteria will be the same as those for traditional research grant applications.

INQUIRIES

Inquiries of a scientific nature may be addressed to:

Nava Sarver, Ph.D.
Senior Scientist
Targeted Drug Development Section
Developmental Therapeutics Branch
AIDS Program, NIAID, NIH
6003 Executive Boulevard
Rockville, Maryland 20892
Telephone: (301) 496-8197

BASIC AND CLINICAL RESEARCH ON NORMAL AND IMPAIRED ORAL-MOTOR FUNCTION

P.T. 34; K.W. 0715148, 0715050, 0715055, 1002034, 0785045

National Institute of Dental Research
National Institute on Deafness and Other Communicative Disorders

Application Receipt Dates: June 1, October 1, February 1

The Craniofacial Anomalies, Pain Control and Behavioral Research Branch of the National Institute of Dental Research (NIDR) invites research grant applications to study neurobiological and physiological processes controlling coordinated oral movements (such as mastication) and to expand knowledge concerning relationships between oral-motor function and dental procedures or abnormal oral conditions. In addition, the Division of Communication and Neurosensory Diseases of the National Institute on Deafness and Other Communicative Disorders (NIDCD) invites research grant applications to study processes involved in normal and disordered speech production and/or swallowing.

The NIDR and NIDCD seek to accelerate research progress in this area by inviting meritorious applications dealing either with fundamental processes underlying the control of coordinated oral movements, or with clinically relevant aspects of oral-motor function.

BACKGROUND

Considerable scientific progress has been made over the past decade toward delineating neurobiological processes controlling limb movements and locomotion, respiratory movements, and eye movements. In contrast, relatively little attention has been directed toward understanding neurobiological and physiological processes involved in coordinated oral movement, except as they directly affect speech production. Yet oral motor behaviors-- including those

involved in mastication, drinking, and suckling-- have important biological significance and remain among the most fundamental behaviors required for survival. Movements of the jaw and the surrounding musculature are integrally involved, in animals and in humans, in tasks as diverse as manipulating objects, attack and defense, communicating through facial expressions, and producing vocalizations.

Oral-motor function is of particular interest to dentistry because oral behaviors affect oral conditions or dental treatments. For example, proper motor control of the jaw and tongue is required for successful use of dental prostheses. Habitual, persistent movements of the jaw and tongue can produce morphological malformations requiring orthodontic treatment. Impaired chewing can limit food intake and nutrition, and can also prompt interventions to improve masticatory efficiency, such as functional appliances, orthodontic treatment, or orthognathic surgery. Chronic hyperactivity (jaw clenching) in masseter muscles appears to be an important causal factor in development of temporomandibular joint (TMJ) pain--a sometimes disabling condition which may afflict as many as one in every ten adults. Bruxism (i.e., tooth-grinding) and dyskinesias involving the jaw and tongue (seen in tardive dyskinesia, senility, stroke, and comas for example) all involve oral-motor behaviors and remain poorly understood. Through an enhanced understanding of how the oral-motor system operates, more effective prevention and management of many of these clinical conditions should become possible.

RESEARCH GOALS

Fundamental studies are needed to delineate fully the neural pathways and processes underlying oral-motor behaviors. Recent research indicates that four major brain stem motor pools (trigeminal, facial, vagal, and hypoglossal) are involved in oral-motor behaviors. Two distinct neural networks governing rhythmic jaw movements (chewing) and some of the movements involved in drinking (lapping-like movements) have also recently been demonstrated in animals. However, knowledge of the structures and processes involved in initiation, control and coordination of oral movements remains very incomplete. Suitable topics for fundamental research include, but are not limited to: studies of the anatomical and physiological significance of connections between nuclei in the neural networks involved in oral-motor control; studies of the neuroanatomical and physiological characteristics of outputs from these neural networks to motoneurons; studies of the processes and structures involved in input from other parts of the central nervous system to the neural networks controlling oral-motor behaviors; and studies of the neurochemical process (i.e., neurotransmitters and neuromodulators) involved in activation and operation of these neural networks.

Basic studies on muscle physiology and adaptation as related to oral-motor function also fall within the scope of this announcement. Examples include, but are not limited to, basic studies on histochemical and physiological properties of masticatory muscles, studies of muscle adaptation following use of devices modifying oral motor function, and studies identifying physiological processes influencing oral-motor function changes associated with interventions such as orthognathic surgery or orthodontic treatment.

Though some sound methodologies have been developed to assess oral-motor function both in the laboratory and natural environments, procedures for evaluating oral-motor function require additional development and standardization. Assessments may include, though are not limited to, measurement of factors such as chewing efficiency, muscular fatigue, biting force, limitations of mandibular movements. Also needed are studies clarifying how adaptation to morphologic change occurs within the oral-motor system when, for example, teeth are removed, dentures are inserted, or orthodontic treatment produces tooth movement. Of additional interest are improved approaches for tracking and monitoring complex movement patterns, evaluating associations between growth and development and oral-motor function, and for developing adequate mathematical models of repetitive oral-motor behaviors and complex movement patterns.

Other clinical research topics may include, though are not limited to: relationships between oral-motor function and oral pathologies (e.g., TMJ pain, severe tooth wear or mobility) or relationships between oral-motor function and dental treatment failures (e.g., broken or abraded restorations, orthodontic relapses, failure to adapt to dental prostheses). In addition, studies of pathological conditions involving disturbances of oral-motor function (e.g., tardive dyskinesia, coma, stroke, or bruxism) are encouraged, particularly as they relate to expanding understanding of mechanisms underlying motor control.

MECHANISM OF SUPPORT

Support for this program can be provided through research grants, including regular project grants (R01), small grants (R03), FIRST awards (R29) and Small Business Innovation Research grants (R43/44). Policies that govern research grant programs of the National Institutes of Health will prevail.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this announcement will be reviewed in accordance with the usual NIH peer review procedures for research grants (Study Section). Review criteria include the significance and originality of the research goals and approaches; feasibility of the research and adequacy of the experimental design; training, experience, research competence, and dedication of the investigator(s); adequacy of available facilities; provisions for the protection of human subjects and the humane care of animals; and appropriateness of the requested budget relative to the work proposed.

Funding decisions will be based on the Study Section's and an appropriate National Advisory Council's recommendations regarding scientific merit and program relevance, and the availability of appropriated funds.

Questions concerning this announcement may be addressed to Dr. Patricia S. Bryant at the address given below. Applications for research grants should be submitted on form PHS-398, and the special instructions for small grants and FIRST awards should be followed when applicable. Application forms and special instructions are available in the business or grants office at most academic or research institutions, or from the Division of Research Grants, National Institutes of Health. Applications will be accepted in accordance with the customary dates for new applications on an indefinite basis at the appropriate deadlines for the support mechanisms selected. For R01's and R29's these are: June 1, October 1, February 1.

Small Business Innovation Research grant applications should be submitted on form PHS-6246-1. Receipt deadlines for Small Business Innovation Research applications are: April 15, August 15, and December 15.

The phrase "ORAL-MOTOR FUNCTION RESEARCH" should be typed on line 2 of the face page of the application. The original and six copies should be sent or delivered to:

Grants Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, Maryland 20892-4500**

Applicants are encouraged to contact NIDR staff prior to applying. Contact:

Patricia S. Bryant, Ph.D.
Health Scientist Administrator
Craniofacial Anomalies, Pain Control
and Behavioral Research Branch
National Institute of Dental Research
Westwood Building, Room 506
Bethesda, Maryland 20892-4500
Telephone: (301) 496-7807

Applicants interested in oral motor function as related to speech production or swallowing should, prior to applying, contact Dr. Judith A. Cooper at the address/telephone number indicated below. (NIDR is responsible for speech projects to cleft lip/palate or other craniofacial anomalies; applicants interested in speech projects in this area should contact Dr. Patricia Bryant.)

Judith A. Cooper, Ph.D.
Health Scientist Administrator
Division of Communication and Neurosensory Disorders
National Institute of Deafness and Other Communicative Diseases
Federal Building, Room 1C06
7550 Wisconsin Avenue
Bethesda, Maryland 20892
Telephone: (301) 496-5061

This program is described in the Catalog of Federal Assistance No. 13.122. Awards will be made under authorization of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended), the Small Business Innovation Development Act, Public Law 97-219 and the Health Research

Extension Act of 1985, Section 453 and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

SENSE OF CONTROL OVER THE LIFE COURSE

P.T. 34; K.W. 0404000, 0715095, 0414005, 0745035

National Institute on Aging
National Institute of Child Health and Human Development

INTRODUCTION

The National Institute on Aging (NIA) and the National Institute on Child Health and Human Development (NICHD) invite the submission of grant applications for research projects designed to specify the nature, antecedents, and consequences of sense of control over the life course. "Sense of control" refers to people's interrelated beliefs and expectancies about (a) their ability to perform behaviors leading to desired outcomes and about (b) the responsiveness of the environment to their behaviors.

Emphasis is placed upon investigations of the environmental, cultural, social, behavioral, and biomedical ANTECEDENTS of the emergence, maintenance, and alteration of sense of control from early childhood to the later years of life. Additional emphasis is directed at specifying the processes by which sense of control produces CONSEQUENCES, e.g., by affecting health, ability to cope with stress, adaptation to institutional settings, or in such domains of everyday functioning as school or work performance. Attention is also focused on developing independent, yet convergent, age-appropriate MEASUREMENT instruments for use with children, parents, and with adults in the middle and later years. INTERVENTION research aimed at enhancing health and effective functioning is encouraged.

BACKGROUND

Research has demonstrated that sense of control is an important contributor to a wide variety of behaviors (e.g., susceptibility to social influence, intellectual achievement, coping with stress) and to mental and physical well-being. Yet, little is known about the cultural, social, environmental, behavioral, and biomedical processes involved in shaping sense of control throughout development and aging, or mediating the effects of sense of control on behaviors and well-being in different domains of functioning.

As first formulated, "perceived locus of control for reinforcements" referred to an individual's expectations about whether rewards and punishments (valued outcomes) were contingent upon his/her behaviors (internal locus of control) or upon powerful other people, fate, or chance (external locus of control). Most research on this topic has been concerned with people's generalized expectations rather than expectations for specific situations or domains of life (e.g., one's own health). Moreover, these generalized expectations have often been treated as a personality trait, implying stability over time and across situations.

Alternative formulations have emerged that specify and elaborate the concept of locus of control. The term sense of control is used here to connote this elaborated conceptualization. First, many researchers argue for multiple dimensions as opposed to a single internal-external dimension. For example, these efforts: (a) disaggregate the internal-external dimension, claiming that an individual may hold both internal control and external control expectations; (b) distinguish among various kinds (e.g., contingent vs. non-contingent) and sources (e.g., fate, random, or powerful others) of external and internal control (e.g., skill, effort); (c) identify separate internal vs. external expectations for positively and negatively valenced outcomes; and (d) separate expectations about one's ability to perform behaviors from expectations about whether outcomes (reinforcements) are contingent upon those behaviors. Second, growing attention is given to situation-specific as opposed to generalized control expectations. For example, scales have been developed to measure sense of control in such behavioral domains as physical health, mental health, academic achievement, and political activities. Third, the elaboration and disaggregation of sense of control are influenced by conceptual and empirical research on related topics, (e.g., learned helplessness, mastery, attributional processes and styles, independence vs. dependence, and mindlessness).

SPECIFIC OBJECTIVES

The NIA and NICHD seek research and research training grant and research career award applications for the study of sense of control in children and parents as well as in middle-aged and older adults. Of special interest is research that moves beyond description to elucidation of the complex processes involved in the antecedents and consequences of sense of control within specific domains of functioning among children, adults, or older people or over the entire life course. The Institutes encourage research on developmental processes, individual differences, and instrument development. This is NOT a one-time invitation for applications, but rather a continuing call for research on this topic. Many researchable issues fall within the scope of this announcement. The following are illustrations of appropriate topics, but applications need not be limited to these:

ANTECEDENTS OF SENSE OF CONTROL OVER THE LIFE COURSE

- o What are the antecedents, causes, origins of sense of control at various ages? How do individuals develop and maintain sense of control in relation to age-related gains and losses in actual competence? What is the relationship between perceived and actual efficacy (in specific behavioral domains)?
- o What are the roles of biological functioning, health, social comparison processes, personal and vicarious experience, cultural beliefs, and age-stereotypes in fostering stability or change?
- o How do attributional processes, styles, and biases influence sense of control (e.g. reactions to success vs. failure)? Do these processes, styles, and biases change with development or aging?
- o Are there different age-related patterns of change in generalized vs. situation-specific sense of control? Under which conditions do particular patterns occur?
- o What are the sources of individual and cohort differences in kinds and levels of sense of control?
- o How do the characteristics of social situations and roles affect sense of control? Can these characteristics be manipulated, through behavioral and social interventions, to bolster sense of control and with what consequences?

CONSEQUENCES OF SENSE OF CONTROL

- o How is sense of control related to specific behavioral or health consequences (e.g., school performance, parenting styles, health maintenance, morbidity)? Do these relationships change with age and under what circumstances?
- o What processes (e.g., immunological responses, compliance to medical regimens) link sense of control to specific biological, behavioral, and social outcomes (e.g., health, intellectual performance, social relationships)?
- o Under which conditions are low vs. high sense of control beneficial or detrimental? What are the consequences of discrepancies between the degree of control actually available in the environment and sense of control?
- o Are there different consequences stemming from sense of control over the occurrence of an event vs. coping with an event after its occurrence?

CONCEPTUAL AND METHODOLOGICAL ISSUES

Generalized vs. Situation-Specific Sense of Control

- o What is the relationship between generalized and situation-specific sense of control? Is generalized sense of control developed from specific situational expectancies? Are some domains more important than others in influencing the development of a generalized sense of control? Are there age-related changes in the relative significance of domains?
- o Under which conditions is generalized sense of control a better or worse predictor of behaviors and outcomes than situation-specific sense of control?

Dimensionality of Sense of Control

- o How are the various dimensions interrelated? Are there developmental sequences or patterns in emergence of dimensions or age-related changes in their relationships?

Methodological Issues

- o Are existing measuring instruments age-appropriate (i.e., reliable and valid) for generalized and situation specific sense of control? Are measures sensitive to age-related changes?
- o What are the comparative advantages and disadvantages of profiles on several dimensions vs. a single summarizing measure?

Special Populations

- o Are there ethnic, racial, or cultural differences in sense of control over the life course? What are their origins and consequences?
- o Are there gender differences in levels, origins, and consequences of sense of control? Are they related to the greater life expectancy of women over that of men or to women's comparatively higher levels of morbidity?

INTERVENTIONS TO ENHANCE HEALTH AND EFFECTIVE FUNCTIONING

Intervention studies involving older people living in nursing homes or relocating to residential retirement facilities point to changes in sense of control as an important link to morbidity, mortality, depression, cognitive functioning, involvement in activities, and length of stay in nursing homes. Other research suggests that changes in sense of control influence the degree and kind of health-care practices that people of all ages follow. However, little is known about the social, psychological, or biological mechanisms that link sense of control to health and effective functioning. Consequently, the NIA and NICHD encourage intervention (field experimental) research in various settings (e.g., the home, school, community, workplace, nursing homes), that: (a) manipulate behavioral, social, or environmental factors affecting sense of control; (b) measure change in sense of control; and (c) specify the mediators between sense of control and its impact upon health and effective functioning in children, adults, and older people.

INCLUSION OF MINORITIES AND WOMEN

The NIH urges applicants for grants to give added attention (where feasible and appropriate) to the inclusion of minorities and women in the study populations for research into the etiology of diseases, research in behavioral and social sciences, clinical studies of treatment and treatment outcomes, research on the dynamics of health care and its impact on disease, and appropriate interventions for disease prevention and health promotion. If minorities or women are not included in a given study, a clear rationale for their exclusion should be provided. Merely including an arbitrary number of such participants in a study is insufficient to guarantee generalization of results. In attempting to include minority groups or women in a particular study, attention must be paid to research design and sample issues.

METHODOLOGY

While research applications need not be limited to any particular method of data collection or analysis, the use of reliable and valid measures of sense of control and of its antecedents and consequences is essential. Consideration should be given to the relative advantage for given research objectives of cross-sectional vs. longitudinal or cohort designs, or to the use of experimental, quasi-experimental, observational, or survey research designs in a variety of settings (e.g., laboratory, school, community, residence, health-care institutions, workplace). The use of appropriate pre-existing data sets for secondary analyses is encouraged, although the collection of original data may be required in specific instances.

BACKGROUND READINGS - SELECTED EXAMPLES

M. M. Baltes and P. B. Baltes (eds.), *The Psychology of Control and Aging*. Hillsdale, NJ: Lawrence Erlbaum Associates, 1986.

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REVIEW CRITERIA AND APPLICATION PROCEDURES

Research project grant (R01) and FIRST (R29) applications, fellowships (F32, F33), and research career development awards (K04) will be reviewed for scientific and technical merit by an appropriate Initial Review Group of the Division of Research Grants. All other applications will be reviewed by an appropriate Institute review group. Secondary review will be by the corresponding National Advisory Council. Applications compete on the basis of scientific merit with all other applications. The review criteria are the traditional considerations underlying scientific merit. Potential applicants are encouraged to discuss their project with NIA or NICHD staff in advance of formal submission. Requests for additional information should be addressed to:

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Behavioral and Social
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National Institute on Aging
Building 31C, Room. 5C32
Bethesda, Maryland 20892

Sarah L. Friedman, Ph.D.
Human Learning Branch
National Institute of Child
Health and Human Development
Executive Plaza North 633B
Bethesda, Maryland 20892

Applicants should use the regular research project application form (PHS 398, Rev. 9/86) or the fellowship application form (PHS 416-1), which are available at the applicant's institutional Application Control Office or from the Office of Grants Inquiries, Division of Research Grants, NIH (301-496-7441). To expedite the application's routing, please check the box on the application form's face sheet indicating that your proposal is in response to this announcement and print (next to the box) SENSE OF CONTROL OVER THE LIFE COURSE.

The application (with six copies) should be mailed to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, Maryland 20892**

Receipt dates for Research Project Grant, Career Development Award, and FIRST Award applications are February 1, June 1, and October 1 of each year. Those for the National Research Service Awards applications are January 10, May 10, and September 10.

This program is described in the Catalog of Federal Domestic Assistance No. 13.866, Aging Research, and No. 13.865, Research for Mothers and Children. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241 and 41 USC 289) and be subject to PHS Grant Policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.