Grant Number: 1R21MH077487-01

Project Title: HIV Neuropathogenesis in a Cohort of Long-Term Surviving Young Adults in Romania

PI Information:

Name	Email	Title
ACHIM, CRISTIAN L.	cachim@ucsd.edu	ASSOCIATE PROFESSOR

Abstract: DESCRIPTION (provided by applicant): Chronic neuropsychologic impairment (NPI) is a major complication in HIV infected long-term survivors on antiviral therapy (HAART). The pathogenesis is still unknown but likely candidates are: neurotoxic viral proteins; pharmacologic side effects; behavioral risk factors (e.g. drug abuse); chronic inflammation accompanied by neuroglial activation; the patient genetic background potentially modulating the metabolic and endocrinologic response to infection; age; gender; and also specific opportunistic pathologies. We have now identified a unique patient cohort at the Victor Babes Hospital (VBH) in Bucharest that may help in deciphering some of the specific NP risk factors associated with long term HIV infection. These patients are uniquely qualified for a longitudinal study: they form a highly homogenous cohort (average 18 y. o.) with similar viral strain infection (clade F), HAART regimen (approx. 7 years), and genetic background. We will assemble a cohort of 75 subjects (25 HIV+ with NPI, 25 HIV+ without NPI, and 25 HIV-) that will be studied for 2 years through regular neuromedical and NP exams and clinical laboratory evaluations of serologic and cerebrospinal fluid (CSF) markers of disease. To measure NPI we will use a test battery developed at the HIV Neurobehavioral Research Center (HNRC) at UC San Diego. Specific Aim #1: Demonstrate the cross-cultural applicability in Romania of a comprehensive neuropsychological (NP) test battery that has been extensively validated for detecting and characterizing neurobehavioral effects of HIV-1 infection in the U.S. Specific Aim #2: Identify comorbid factors in the Romanian young adults with HIV and compare them to the degree of NPI. Specific Aim #3: Characterize the neurotoxic potential of the Romanian clade F HIV and its susceptibility to antiviral treatments. This project will demonstrate feasibility and will help develop an infrastructure to perform neurobehavioral an-d virological studies in Romania, where no systematic studies of the neurocognitive manifestations of HIV-1 have been performed. The Romanian cohort could provide a unique insight in the future of HIV- associated NPI in long term-survivors on HAART.

Thesaurus Terms:
AIDS /HIV neuropathy, adolescence (12-20), human immunodeficiency virus 1, long term survivor, neuropathology, young adult human (21-34) Europe, HAART (highly active antiretroviral therapy), biomarker, data collection methodology /evaluation, disease /disorder proneness /risk, longitudinal human study, medical complication, neurotoxicology, virus genetics clinical research, human subject, neuropsychological test

Institution: UNIVERSITY OF CALIFORNIA SAN DIEGO
9500 GILMAN DR, DEPT 0934
LA JOLLA, CA 920930934

Fiscal Year: 2007
Department: PSYCHIATRY
Project Start: 01-JAN-2007
Project End: 31-DEC-2008
ICD: NATIONAL INSTITUTE OF MENTAL HEALTH
IRG: ZRG1

Grant Number: 1R21TW006745-01

Project Title: Preventing FAS/ARND in Russian Children

PI Information: Name	Email	Title
BONNER, BARBARA L.	barbara-bonner@ouhsc.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): This project proposes to establish a new consortium between St. Petersburg State University (SPSU) and the University of Oklahoma Health Sciences Center (OUHSC) to obtain preliminary data critical to developing effective prevention programs in the area of alcohol related brain disorders in Russia. Fetal Alcohol Syndrome (FAS) and Alcohol Related Neurodevelopmental Disorders (ARND) are major problems in Russia due to the high levels of alcohol consumption by women. Children exposed to alcohol in utero can suffer a wide array of neurodevelopmental disorders, from subtle changes in intelligence and behavior to profound mental retardation. These children can also experience varying levels of growth retardation and can be born with defects in major organ systems or malformations of the skeleton system, such as defects of the heart, kidneys, bones, and/or auditory system. Yet, FAS/ARND is theoretically 100% preventable. The focus of this study is to collect preliminary data needed to design a Russian prevention intervention, which will be tested in later studies. The information to be collected will include: (1) the health beliefs about alcohol use during pregnancy, collected from women and their partners; (2) the level of knowledge about the effects of alcohol use during pregnancy among health care providers, and related health care provider practices or actions taken, collected from health professionals, pregnant women, and their partners; and (3) receptivity to public health approaches for prevention of alcohol use during pregnancy. Data will be obtained in two locations in Russia, St. Petersburg and Nizny Novgorod. This data will provide important information to better understand the social factors (e.g., partner drinking), health beliefs (e.g., information and cultural standards) and other factors (e.g., alcoholism) related to women's use of alcohol, or failure to discontinue use, during pregnancy; and the current and potential impact health care professionals might have on these behaviors. In addition to this preliminary research, the consortium will be essential in fostering Russian-American collaboration and capacity building. Capacity building activities will include the establishment of an IRB at the Faculty of Psychology at the SPSU, educational training on human subjects considerations, ethical issues in research, statistical approaches and field methodologies critical to epidemiological and prevention-based research.

Thesaurus Terms:

Commonwealth of Independent States, alcoholism /alcohol abuse prevention, children, developmental disease /disorder, developmental neurobiology, fetal alcohol syndrome, health behavior, health science research potential alcoholic beverage consumption, alcoholism /alcohol abuse, alcoholism /alcohol abuse education, culture, education evaluation /planning, embryo /fetus drug adverse effect, female, health care personnel, international cooperation, sex partner, social conformity, substance abuse related behavior

behavioral /social science research tag, clinical research, human pregnant subject, human subject

Institution: UNIVERSITY OF OKLAHOMA HLTH SCIENCES CTR
HEALTH SCIENCES CENTER
OKLAHOMA CITY, OK 731171213

Department: PEDIATRICS

Project Start: 28-SEP-2003- 28 FEB 2005

ICD: FOGARTY INTERNATIONAL CENTER

Grant Number: 1R21AG028182-01A1

Project Title: Risk Factors brain atrophy, mild cognitive impairment and dementia in Shanghai

PI Information: **Name** **Email** **Title**

BORENSTEIN, AMY aborents@hsc.usf.edu

Abstract: DESCRIPTION (provided by applicant): This is a research development/planning grant application to initiate collaborative studies with investigators in Shanghai, China to study the incidence of and risk factors for brain atrophy, mild cognitive impairment and dementia (under PAR-05-100, "Brain Disorders in the Developing World: Research Across the Lifespan"). China faces a difficult demographic transition over the next 25 years, with 300 million elderly expected by 2030. The one-child policy initiated in 1979 will! result in the "4-2-1" family structure, with each young person taking care of two parents and four grandparents at home, where care for dementia is traditionally received in Asian countries. Recent studies show that rates for dementia are more similar to Western rates than previously believed and that Alzheimer's disease is the most common type of dementia. We propose to develop a large community-based study in Shanghai to investigate the risk and preventive factors that facilitate or inhibit the expression of dementia for submission in our R01, which will result from this R21 work. A better understanding of these factors could lead to interventions that delay the age of onset of cognitive impairment and dementia, resulting in primary prevention of these disorders in China. The proposed research has a high probability of success in China, where the foreign PI, Dr. Zhen Hong has expertise in population-based studies. China offers many advantages for a study of this type, including significant heterogeneity in the exposures of interest, such as educational attainment and diet. In addition, the Chinese population is known to suffer from a high stroke rate, and vascular risk factors interact importantly with Alzheimer neuropathology to produce dementing syndromes; thus the prevention of vascular disease may have important implications for the prevention of dementia. The specific aims of this planning grant are to: (1) further develop and solidify collaborations with the team in Shanghai and define the scope of the research that will be the focus of an R01 application; (2) assess the Shanghai team's resources and needs in order to successfully conduct community-based research; (3) implement cross-training between the U.S. and Chinese groups in the areas of epidemiology and risk factor assessment, clinical diagnosis, neuropsychological testing and MR imaging for the spectrum of dementia disorders; and (4) conduct pilot studies to generate preliminary data necessary for an R01 application.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: UNIVERSITY OF SOUTH FLORIDA
3650 Spectrum Blvd., Ste 160
TAMPA, FL 33612
Fiscal Year: 2007
Department: EPIDEMIOLOGY AND BIOSTATISTICS
Project Start: 15-MAY-2007
Project End: 28-FEB-2009
ICD: NATIONAL INSTITUTE ON AGING
IRG: ZRG1

Grant Number: 5R21NS055353-02

Project Title: Epidemiology and Burden of Neurocysticercosis in Bukina Faso

PI Information: Name	Email	Title
CARABIN, HELENE	helene-carabin@ouhsc.edu	ASSOCIATE PROFESSOR

Abstract:
This abstract is not available.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: UNIVERSITY OF OKLAHOMA HLTH SCIENCES CTR
HEALTH SCIENCES CENTER
OKLAHOMA CITY, OK 731171213

Fiscal Year: 2007

Department: BIOSTATISTICS AND EPIDEMIOLOGY

Project Start: 08-JUN-2006

Project End: 31-MAR-2008

ICD: NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

IRG: ZRG1

Grant Number: 5R01HD053055-02

Project Title: Brain Research to Ameliorate Impaired Neurodevelopment-Home-based Intervention

PI Information:	Name	Email	Title
	CARLO, WALDEMAR A.	ogcaapps@provost.uab.edu	EDWIN M. DIXON PROFESSOR OF PEDIATRICS

Abstract: DESCRIPTION (provided by applicant): Birth asphyxia is a leading cause of neonatal mortality and morbidity in developing countries. Survivors of birth asphyxia have high rates of mental retardation, cerebral palsy, and other neurodevelopmental disorders. Controlled trials and meta-analyses conclude that early intervention programs prevent or minimize cognitive impairment in many high-risk infants. These programs are legislatively mandated in the United States and are the standard of care in developed nations. However, early intervention programs are rarely available in developing countries and thus, to most at-risk infants worldwide. Preliminary evidence from a small randomized controlled trial conducted in a developing country suggests that a program of home-based early intervention improves neurodevelopmental outcome (Mental Developmental Index) in survivors of birth asphyxia but conclusive evidence is not available. Pilot data obtained as part of a planing grant funded by an R21 documented the high prevelence of sequelae for birth asphyxia and feasibility of an early intervention program. The current application aims to identify infants at risk for neurodevelopmental disorders and to evaluate an innovative early intervention program in developing countries utilizing established multidisciplinary collaborations between researchers in the US, Zambia, India, and Pakistan who currently work as part of the NICHD Global Network for Women's and Children's Research on an early phase of the FIRST BREATH multicenter cluster randomized trial on resuscitation. A randomized controlled trial of early intervention will be performed in infants with birth asphyxia identified by abnormal neurological exam during the first week after birth and in normal a comparison group. A home-based, parent-provided, early intervention will be tested in two delivery modes: resource-intensive and resource-limited. If proven effective in developing countries, a home-based early intervention program has the potential of improving cognitive capacity in many at-risk infants worldwide at a cost lower than more expensive special education services. The long term goal of this proposal is to broaden research collaborations and to build sustainable capacity for research to prevent or reduce neurodevelopmental sequelae resulting from birth asphyxia and other important causes of neurodevelopmental impairment in children.

Thesaurus Terms:
developmental neurobiology, disease /disorder proneness /risk, early /brief intervention /therapy, growth /development, home health care, respiratory distress syndrome of newborn clinical trial, human therapy evaluation, longitudinal human study Africa, India, behavior test, clinical research, infant human (0-1 year), international cooperation, southeast Asia

Institution: UNIVERSITY OF ALABAMA AT BIRMINGHAM
1530 3rd Avenue South
BIRMINGHAM, AL 35294

Fiscal Year: 2007

Department: PEDIATRICS

Project Start: 29-SEP-2006

Project End: 31-JUL-2011

ICD: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

IRG: ZRG1

Grant Number: 5R21TW006724-03

Project Title: Pediatric Traumatic Brain Injury in Latin America

PI Information: Name	Email	Title
CHESNUT, RANDALL M.	chesnutr@u.washington.edu	DIRECTOR, NEUROTRAMA

Abstract: DESCRIPTION (provided by applicant): Children who survive severe brain trauma live with profound cognitive impairments that alter their developmental course and define their future possibilities. A formal collaboration exists between brain trauma physicians and researchers in the United States and Latin America. The long-term goal of this working group is to create a structure for professionals and institutions involved in brain trauma that generates research, and facilitates education, certification, and the dissemination of information and resources across Latin America. The structure will be the Latin American Brain Injury Consortium (LABIC). This planning grant will take the first step in establishing LABIC. The Guidelines for the Acute Medical Management of Traumatic Brain Injury in Infants, Children, and Adolescents (Adelson, Bratton, Carney et al., in press) will be implemented in six trauma hospitals in Argentina. Specific aims of the project are: 1. To survey resources and treatment practices for, and outcomes from pediatric TBI in six hospitals in Argentina, in order to assess the need for both guidelines, as well as for a structure for communication and dissemination of information. 2. To develop resources, including education and technology that will expand the capacity of the existing collaboration to implement and evaluate the guidelines. 3. To generate preliminary data about the effect of dissemination strategy on physician understanding and practice, and patient outcomes, by conducting a pilot randomized trial of three strategies for disseminating the pediatric TBI guidelines: provision of the Guidelines publication; provision of the Guidelines publication with a written instructional supplement; provision of the Guidelines publication with instruction, monitoring, and assessment using a simple set of telemedicine tools. 4. To demonstrate the feasibility of conducting research and collecting data in Argentina, and to identify the most reliable data points and methods for data collection. 5. To use our findings to solicit support for the expansion of the project to the rest of Latin America.

Thesaurus Terms:
Hispanic American, brain injury, cognition disorder, international cooperation, patient /disease registry, pediatrics, trauma adolescence (12-20), developmental disease /disorder, information dissemination, medical education, outcomes research, science education, telemedicine
clinical research, human subject

Institution: UNIVERSITY OF WASHINGTON
Office of Sponsored Programs
SEATTLE, WA 98105

Fiscal Year: 2005

Department: NEUROLOGICAL SURGERY

Project Start: 01-NOV-2003

Project End: 31-OCT-2005

ICD: FOGARTY INTERNATIONAL CENTER

IRG: ZNS1

Grant Number: 1R01NS058302-01

Project Title: Traumatic Brain Injury in Latin America: Lifespan Analysis

PI Information: Name	Email	Title
CHESNUT, RANDALL M.	chesnutr@u.washington.edu	DIRECTOR, NEUROTRAMA

Abstract: DESCRIPTION (provided by applicant): The objective of this application is to establish a network of Centers of Excellence within the Latin American Brain Injury Consortium (LABIC) that will, in collaboration with U.S. partners, conduct research and training programs about traumatic brain injury (TBI). Our specific aims are: #1: In a randomized controlled trial in 3 trauma centers in Bolivia, test the effect on outcomes of management of severe TBI guided by information from ICP monitors vs. a standard empiric protocol. #2: In a prospective, observational study in 7 trauma centers in Latin America, test the association between resource availability/medical management and outcomes for patients with severe TBI. #3: Establish a network of research centers with investigators trained and skilled in the design, conduct, and funding of research programs to address TBI and other brain disorders in Latin America. We hypothesize that: #1. Patients with severe TBI whose acute care treatment is managed using ICP monitors will have significantly lower mortality and better neuropsychological and functional recovery at 6 months post-trauma than those whose treatment is managed with the standard protocol. #2. The incorporation of ICP monitoring into the care of patients with severe TBI will minimize secondary complications and decrease length of stay in ICU. #3. The association between treatment and outcomes for patients with severe TBI identified in the randomized trial of ICP monitoring will generalize to the population in the prospective, observational, study. #4. Variations in resource availability and medical management will be significantly associated with mortality and functional recovery for patients with severe TBI, after controlling for patient and injury characteristics. In fulfilling the aims of this project, important research questions will be answered about TBI in an environment of limited resources, aspects of which will generalize to other developing countries as well as to the developed world. Sustainable capacity to conduct research about TBI in Latin America will be established. Within the structure of LABIC, a cadre of professionals will be trained in clinical research who will be equipped to carry out studies that answer questions which are relevant and important to Latin America. These studies will establish a literature base from which Latin American investigators can generate their own guidelines for the treatment of TBI.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: UNIVERSITY OF WASHINGTON
Office of Sponsored Programs
SEATTLE, WA 98105

Fiscal Year: 2007

Department: NEUROLOGICAL SURGERY

Project Start: 15-JUL-2007

Project End: 01-APR-2012

ICD: NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

IRG: ZRG1

Grant Number: 1R21TW006762-01

Project Title: Research in AD: Training, Infrastructure and Pilot Study

PI Information:	Name	Email	Title
	CLARK, CHRISTOPHER MICHAEL.	chris.clark@uphs.upenn.edu	ASSOCIATE PROFESSOR OF NEUROLOGY

Abstract: DESCRIPTION (provided by applicant): This joint proposal in response to TW-03-007, Brain Disorders in the Developing World: Research Across the Lifespan, describes a 2 year needs assessment, research infrastructure development, clinical education and research training plan that seeks to establish a sustainable research collaboration between the Instituto Nacional de Ciencias Medicas y Nutricion in Mexico City and the University of Pennsylvania's Alzheimer's Disease Center in Philadelphia, Pennsylvania. The long-term goal of this proposal is to establish the structural framework and personal connections necessary to carry out collaborative research studies that will address issues of relevance to both Mexico and the United States. Specifically, the proposal will link the faculty and staff of the University of Pennsylvania's Alzheimer's Disease Center, including its Clinica Latina Para Trastornos de la Memoria, with the Geriatric department faculty and staff of the Instituto Nacional de Ciencias Medicas y Nutricion through a series of educational and research programs designed to accomplish the joint goals of both groups. A main focus of this proposal is the implementation of standardized methods of clinical assessment, data handling, and data transfer in order to create the critical infrastructure necessary for successful collaborative research. The clinical assessment protocol will be designed to be compatible with the existing and evolving National Institute on Aging funded National Alzheimer Coordinating Center Minimum Data Set in order to both maximize the ability for comparative analysis and to facilitate future collaborations between the Instituto Nacional de Ciencias Medicas y Nutricion and the 29 Alzheimer's Disease Centers in the United States. A second key goal of this proposal is the development and implementation of joint clinical education programs and clinical research training programs that will focus on issues of brain aging and dementia. And finally, with consideration of the information that comes from the needs assessment component, data from an initial survey of the prevalence of dementia in Mexico City will be used to design and carryout of a pilot clinical research project that will lay the groundwork for a larger study to be proposed in response to a subsequent National Institutes of Health request for applications.

Thesaurus Terms:
Alzheimer's disease, Mexico, biomedical facility, health science research analysis /evaluation, health science research support, training
data collection, data collection methodology /evaluation, dementia, public health
clinical research, human data

Institution: UNIVERSITY OF PENNSYLVANIA
3451 Walnut Street
PHILADELPHIA, PA 19104

Fiscal Year: 2004
Department: NEUROLOGY
Project Start: 01-MAR-2004
Project End: 28-FEB-2006
ICD: FOGARTY INTERNATIONAL CENTER
IRG: ZNS1

Grant Number: 1R21TW006706-01

Project Title: Nerve Stimulation to Improve Hand Weakness in Stroke

PI Information: **Name** **Email** **Title**

CONFORTO, ADRIANA B. abconf@usp.br

Abstract: DESCRIPTION (provided by applicant): This proposal intends to develop a novel therapy to increase muscle strength and decrease hand motor disability in chronic stroke patients. There is no universally accepted treatment for long-term motor disability from stroke. Hand motor function significantly impacts independence of stroke patients. Somatosensory input influences activity in the motor cortex and is required for adequate motor performance and motor learning. We have shown that somatosensory stimulation in the form of electrical nerve stimulation, a straightforward and well-tolerated intervention, results in improvement in hand muscle strength when applied to the weak hand of chronic stroke patients, even in the absence of training. Patients with moderate to severe hand disability cannot train well. We will compare the effects of electrical nerve stimulation and motor training to motor training alone, in patients with moderate to severe hand disability, to whom there is no effective alternative treatment available. We expect to generate preliminary data regarding the hypothesis that the stimulation will enhance the effects of training. We will evaluate patient compliance to the research protocol, and will also collect pilot data regarding biological and social/environmental factors that can influence the response to rehabilitative interventions in a Brazilian population. The influence of age, neurophysiological measurements of corticomotor function, family support and social status will be evaluated. It is important to determine which factors underlie response to treatment because, if such knowledge were available, it would be possible to adapt therapies and guide health policies to target these factors. This proposal will provide training in neurophysiological and neurorehabilitation research. We will build research capacity and develop collaboration for future studies regarding: effectiveness of electrical stimulation and training in improving hand strength and decreasing motor disability in chronic stroke patients; prognostic factors for response to rehabilitation therapy. The research will be conducted in a reference university hospital, with full support from the Neurology Department, and will contribute to institutional excellence. This research intends to develop a novel rehabilitative strategy for a condition for which there is no universally accepted treatment, targeting real-life outcomes in a developing country. If successful, these goals may have a major impact in the way chronic stroke patients are treated. The results will be highly valuable to populations in which disability from stroke represents a challenge to health care.

Thesaurus Terms:
South American, hand, neuromuscular stimulator, psychomotor function, rehabilitation, stroke, therapy design /development age difference, family structure /dynamics, functional ability, muscle strength, social status, socioenvironment, therapy compliance Brazil, clinical research, human subject, medical rehabilitation related tag, patient oriented research

Institution: UNIVERSITY OF SAO PAULO
CAIXA POSTAL 11.273-9
SAO PAULO,

Fiscal Year: 2004

Department:

Project Start: 29-SEP-2004

Project End: 28-SEP-2008

ICD: FOGARTY INTERNATIONAL CENTER

IRG: ZNS1

Grant Number: 1R01DA023697-01A1

Project Title: Health & Psychosocial Need: Children with Developmental Disorder in a Time of HIV

PI Information: **Name** **Email** **Title**

DAVIDSON, LESLIE L. lld1@columbia.edu

Abstract: DESCRIPTION (provided by applicant): With the long term goal of intervening to promote better physical and psychosocial functioning of children in South Africa, this study will determine how the ability of children with neurodevelopmental disorders to function cognitively and socially is influenced by both health-related (HIV, anemia, other infection), contextual (socio-economic and environmental, access to care and therapeutic intervention) and psychosocial factors (caregiver characteristics including mental health and substance use, family functioning). Approximately 2000 5 and 6 year old children from a HIV prevalent area will be screened for disability and then assessed before school entry. They will be reassessed 24 months later after school entry. The study will offer HIV testing to children and caregivers and referral for treatment for all conditions identified. Many of these children live with parents who are ill or have parents who have died from AIDS. Additional challenges such as poverty, inadequate access to health care and to education are common; many other risks to child health and well-being, including inadequate nutrition, infection and trauma as well as caregiver depression and substance use affect many children. As a result, many children do not function at optimal levels, and are at risk for developmental disabilities. The study will investigate first cross sectionally and then longitudinally the relationships among neurodevelopmental disorders and the above mentioned risk factors including as outcomes, child cognitive and psychosocial functioning and in the longitudinal aim, school functioning .The study will address both cross sectional and longitudinal relationships, assessing the impact of referral, treatment and access to programs over time. Community ethnographic studies will be linked to the findings of the epidemiologic study to identify culturally appropriate interventions. We will identify factors open to intervention which are known to affect child risk and resilience and work with community leaders in a participatory approach to develop an effective community based intervention. In addition, training in research methods and enhancing research capacity will be one of the key aims of this research. This will involve training public health students, ethnography students, pediatric registrars, allied health professionals and community health workers in both field and classroom teaching and training. This will be managed in collaboration with the UKZN Fogarty Program, the Valley Trust, the Rehabilitation Unit and the Medical School at UKZN with assistance from the Columbia investigators

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: COLUMBIA UNIVERSITY HEALTH SCIENCES
Columbia University Medical Center
NEW YORK, NY 100323702

Fiscal Year: 2007

Department: EPIDEMIOLOGY

Project Start: 01-SEP-2007

Project End: 31-MAY-2012

ICD: NATIONAL INSTITUTE ON DRUG ABUSE

IRG: ZRG1

Grant Number: 3R21TW006786-01S1

Project Title: Prevalence of Post-Stroke Dementia in Mexico

PI Information: **Name** **Email** **Title**

DIAZ, CLAUDIA O. claudido@att.net.mx

Abstract:

This abstract is not available.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: NATIONAL INST OF NEUROLOGY NEUROSURGERY AND NEUROSURGERY
MEXICO,

Fiscal Year: 2007

Department:

Project Start: 29-SEP-2004

Project End: 28-SEP-2007

ICD: FOGARTY INTERNATIONAL CENTER

IRG: ZNS1

Grant Number: 1R21NS058294-01

Project Title: Epidemiology and Etiology of Acute Flaccid Paralysis in Guatemala

PI Information: **Name** **Email** **Title**

DUEGER, ERICA LYNN. edueger@jhsph.edu

Abstract: DESCRIPTION (provided by applicant): Ongoing hospital-based surveillance of acute infectious neurological disease in Guatemala has uncovered a high incidence of acute flaccid paralysis (AFP) in both children and adults. Anecdotal sporadic reports of clusters of AFP with unusual clinical presentation and unknown etiology have also been noted in other Latin American countries. The rapid onset, clinical progression and severity of outcome of the cases in Guatemala suggest they are distinct from the recognized variants of Guillain-Barr syndrome (the most common cause of AFP), but crucial data necessary for elucidating the epidemiology and etiology of AFP in Guatemala are lacking. The long-term goal of our research is to identify intervention points for populations at risk for AFP and to evaluate control strategies for AFP in Latin America by: a) initiating investigations into the underlying etiologies and clinical subtypes of AFP syndrome in adults and children in Guatemala, and b) fostering collaborations for future multisite investigations of AFP across Latin America. Specifically, we will perform a case-control study using AFP patients and hospital controls presenting to Ministry of Health hospitals in Guatemala City to: 1) characterize the clinical, laboratory, and electrodiagnostic features of cases of AFP syndrome in adults and children; 2) compare the epidemiological characteristics, including potential risk factors and socioeconomic variables, between AFP cases and hospital controls, and 3) compare serologic and fecal (culture, PCR, ELISA) evidence of infection with specific suspect etiological agents in AFP cases and controls. We will also develop a collaborative AFP network of public health researchers and clinicians throughout Latin America to forge long-term working relationships aimed at future multisite investigations of AFP epidemiology and prevention in Latin America. Monthly teleconferences and an e-mail forum will promote dissemination and discussion of information regarding patterns and characteristics of AFP cases throughout the region. If preliminary results of the proposed study indicate that specific infectious agents represent significant public health concerns, the feasibility of transferring technology for in-country diagnostic testing for these agents will be examined. The information gathered and relationships forged during the proposed project will support development of a large-scale multisite investigation of potential clinical and public health interventions for AFP in Latin America.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: JOHNS HOPKINS UNIVERSITY
W400 Wyman Park Building
BALTIMORE, MD 212182680

Fiscal Year: 2007
Department: INTERNATIONAL HEALTH
Project Start: 30-SEP-2007
Project End: 31-AUG-2009
ICD: NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
IRG: ZRG1

Grant Number: 1R21MH071212-01

Project Title: Neurocognitive Consequences of HIV/AIDS in South India

PI Information:

Name	Email	Title
FLANIGAN, TIMOTHY P.	tflanigan@lifespan.org	PROFESSOR OF MEDICINE

Abstract: DESCRIPTION (provided by applicant): The human immunodeficiency virus (HIV) epidemic is progressing at an alarming rate in developing and low- to middle-income countries. Treatment of HIV with highly active antiretroviral therapy (HAART) is frequently delayed or unavailable to many infected individuals, and consequently the prevalence of HIV-associated diseases is much higher in these countries compared to high-income countries. In southern India, many patients experience severe immunosuppression and development of neurocognitive and neuroimaging abnormalities. Preliminary studies focused on the evolution of these abnormalities reveal strong relationships between low CD4 cell count and cognitive difficulties, and associations between the volume of specific brain structures and cognitive dysfunction among patients with significant immune system suppression. However, studies have not examined the impact of severely compromised immune systems on the development of neurocognitive and neuroimaging abnormalities among non-demented patients. The purpose of this proposal is to establish a collaborative research partnership between clinical researchers at YRG Care in Chennai, India and researchers at the Brown University Center For AIDS Research to examine brain dysfunction associated with HIV. We propose to: 1) establish the investigative collaboration and conduct needs assessments, 2) develop and implement training modules focused on the assessment of cognitive function, structural neuroimaging abnormalities, and the integration of cognitive, neuroimaging, and laboratory values of disease activity, 3) collect pilot data for a subsequent R01 submission to comprehensively examine the evolution of brain dysfunction in patients with HIV. The pilot study will involve collection of cognitive, structural MRI and laboratory values of disease activity in HIV patients with significant immune system compromise. Cross-sectional and longitudinal analyses will examine the impact of HIV on cognitive and brain morphometric indices. The study will take advantage of the infrastructure currently available at the YRG Care in Chennai, India, and the clinical and research infrastructure established at the Brown CFAR. The developmental grant will yield significant advances in the understanding of brain disorders associated with HIV.

Thesaurus Terms:
HIV infection, cognition disorder, nervous system infection, neuropathology, neuropsychology
cooperative study, epidemiology, helper T lymphocyte, opportunistic infection
Asian, India, clinical research, human subject, leukocyte count, morphometry, neuroimaging, neuropsychological test, patient oriented research

Institution: MIRIAM HOSPITAL
PROVIDENCE, RI 029062853
Fiscal Year: 2003
Department:
Project Start: 29-SEP-2003
Project End: 31-AUG-2005
ICD: NATIONAL INSTITUTE OF MENTAL HEALTH
IRG: ZNS1

Grant Number: 5R21TW007803-02

Project Title: Development of an Intervention for Palauan Youth at Genetic Risk for Psychosis

PI Information: Name	Email	Title
FLORSHEIM, PAUL W.	paul.florsheim@psych.utah.edu	ASSOCIATE PROFESSOR

Abstract: DESCRIPTION (provided by applicant): Researchers have proposed that both genetic and environmental factors can contribute to the development of psychosis during adolescence and young adulthood. Individuals identified as being at high genetic risk for schizophrenia may not develop the disorder if they possess skills for coping with initial symptoms and reducing associated stressors. Understanding how to facilitate resilience and support protective factors among adolescents at risk for schizophrenia has implications for many individuals and communities because schizophrenia occurs across societies. Developing preventive-intervention models for schizophrenia is particularly important for regions of the world where the genetic risk for schizophrenia is particularly high and the medical resources for managing the illness are scarce. For example, the Republic of Palau is an isolated island nation with a population at heightened risk for schizophrenia and other psychotic disorders (Myles- Worsley et al., 1999). This population provides an excellent opportunity for testing preventive-intervention models because (a) the genetic risk status of individuals has been previously identified and (b) the government of Palau is eager to develop nonstigmatizing strategies to address the problem. The goals of the proposed project are to build capacity among Palauan health care providers to conduct intervention research and to pilot an existing preventive-intervention program for the first time among Palauan adolescents at-risk for psychotic disorders. The first year of the project would involve research training workshops, a clinical training workshop, and a workshop in culturally sensitive protocol development. The second year would involve pilot testing a Palauan-adapted preventive-intervention program on a small sample of high-risk youth (n=30). The training component of the grant is designed for Palauan health care providers and will utilize datasets previously collected from Palauan adolescents at-risk for psychotic disorders (Myles-Worsley et al., 1999). This project represents an international collaboration between psychologists and physicians with a wide range of expertise (e.g. preventive-intervention, adolescent treatment, public health, research education, schizophrenia and psychosis). The long-term goal of the project is to build research capacity in a developing nation and to test strategies for conducting a large scale preventive-intervention study targeting adolescents at heightened risk for psychosis, living in isolated regions of the world.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: UNIVERSITY OF UTAH
75 South 2000 East
SALT LAKE CITY, UT 84112

Fiscal Year: 2007
Department: PSYCHOLOGY
Project Start: 01-MAY-2006
Project End: 30-APR-2008
ICD: FOGARTY INTERNATIONAL CENTER
IRG: ZRG1

Grant Number: 1R21NS048840-01

Project Title: Assessment of Stroke Risk and Outcome in Chagas Disease

PI Information:

Name	Email	Title
FURIE, KAREN L.	kfurie@partners.org	ASSOCIATE PROFESSOR

Abstract: DESCRIPTION (provided by applicant): Stroke is an enormous international public health concern, particularly in the developing world where there are limited resources available to provide for an aging population. One of the main contributors to stroke incidence in Brazil is the highly prevalent Chagas disease, a parasitic infection affecting 14% of the population and a major cause of heart failure in Latin America. Chagas disease conveys stroke risk through two established mechanisms, structural cardiac disease and chronic inflammation. Although inflammation is associated with an increased risk of ischemic stroke and poorer outcome, its role has been largely linked to atherogenesis. Chronic inflammation can result in endothelial dysfunction and stimulate the hemostatic system, increasing systemic fibrin production and platelet activation. Adults, young and old, who develop a secondary cardiomyopathy from Chagas, are therefore at higher risk of cardioembolism. Stroke patients usually survive, but can be left with significant disability affecting their health status, productivity, and quality of life. These factors impact caregivers as well. Thus, the social and economic consequences of stroke are vast. The short term goals of this planning grant are to develop a multidisciplinary collaborative infrastructure of investigators and resources in the United States and Brazil to promote clinical stroke research, to provide training for emerging Brazilian clinical stroke researchers, and to determine the resources necessary to support this clinical research effort in future endeavors. As part of this development phase, we will collect pilot data to address two specific aims: (1) to elucidate which of the potential inflammatory and hemostatic markers of stroke risk are associated with chagasic cardiomyopathy, and (2) to determine the mechanism and outcome of stroke in patients with Chagas disease. The long-term goal of this project is to establish non-invasive methods of stroke risk stratification and prediction of stroke outcome in patients with Chagas disease. This work will also facilitate the development of novel anti-trypanosomal, anti-inflammatory, and antithrombotic strategies for stroke prevention and management in Brazil.

Thesaurus Terms:
cardiovascular disorder epidemiology, cardiovascular disorder risk, myocardial ischemia /hypoxia, myocardium disorder, quality of life, stroke, trypanosomiasis acute phase protein, biomarker, embolism, endothelin, fibrinogen, functional ability, health disparity, hemostatic, inflammation, international cooperation, medically underserved population, socioeconomics, thromboxane, training, von Willebrand factor Brazil, behavioral /social science research tag, clinical research, human subject

Institution: MASSACHUSETTS GENERAL HOSPITAL
55 FRUIT ST
BOSTON, MA 02114

Fiscal Year: 2003

Department:

Project Start: 30-SEP-2003

Project End: 30-JUN-2005

ICD: NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

IRG: ZNS1

Grant Number: 5R21ES013108-02

Project Title: Gene-Enviroment Interaction in Cognition

PI Information:	Name	Email	Title
	GILLIAM, T. CONRAD.	tcg1@columbia.edu	BORNE PROFESSOR OF GENETICS AND DEVELOPM

Abstract: DESCRIPTION (provided by applicant): We propose a collaborative effort between Columbia University (CU) and University of Zulia (LUZ), Maracaibo-Venezuela, to investigate the effects of life conditions and environmental exposures together with genetic factors upon the expression of specific cognitive abilities. We aim to strengthen the capacity of Venezuelan scientists to design and execute research centered on cognitive impairment from birth to advanced age, with emphasis in disorders common in the State of Zulia; including Alzheimer's disease, Huntington's disease and Vascular Dementia. We propose the following specific aims for this exploratory project: 1. To assess the social impact of dementias in the State of Zulia. We will conduct a qualitative ethnographic study among family and caregivers of demented patients, as well as among primary care health professionals, identifying beliefs about cognitive impairment, dementia, knowledge, impact of disease on family life, self esteem, family identity, social reactions, access to health care and quality of care by professionals. 2. To assess current resources and needs and develop and initiate a plan to address these needs to promote the successful conduct of the proposed research and capacity building. 3. To show feasibility and generate preliminary data to justify submission of collaborative research via an R01 grant mechanism and to identify specific research questions that show the greatest promise for advancement. We will test whether a catecoI-O-methyltransferase (COMT) gene variant affects working memory and executive function in Venezuelan families segregating subcortical white matter hyperintensities. Variance accounted for by the gene variant and life conditions and environmental exposures will be examined. 4. To identify training and other capacity-building opportunities in the context of brain health promotion throughout life. At the end of the planning period, we hope to have initiated preliminary studies and to have organized, planned, prepared and assembled an application for a more comprehensive R01 grant involving collaboration between CU and LUZ investigators incorporating both research and capacity building.

Thesaurus Terms:
behavioral genetics, dementia, gene environment interaction, socioenvironment biomarker, catechol methyltransferase, cooperative study, coping, environmental exposure, international cooperation, mental health service, short term memory, social adjustment South American, behavioral /social science research tag, clinical research, human subject

Institution: COLUMBIA UNIVERSITY HEALTH SCIENCES
Columbia University Medical Center
NEW YORK, NY 100323702

Fiscal Year: 2004

Department: GENOME CENTER

Project Start: 30-SEP-2003

Project End: 31-JUL-2005

ICD: NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

IRG: ZNS1

Grant Number: 5R21DA018085-02

Project Title: HIV-1 Cognitive-Motor Disorders: Definition in Argentina

PI Information:

Name	Email	Title
GOODKIN, KARL	kgoodkin@med.miami.edu	PROFESSOR & DIRECTOR

Abstract: DESCRIPTION (provided by applicant): Primary Spanish speaking subjects have been neglected in the research conducted to date on the prevalence of HIV-l-associated cognitive-motor disorder. Argentina is a moderate-resource country that has been highly impacted by the AIDS epidemic. Fundacion Huesped (FH) is the largest clinic for the primary care of HIV-1 infected individuals in Argentina and is highly influential in care delivery policies there. While FH has integrated mental health side-by-side with general medical care since its inception, there is no routine screening of cognitive-motor disorders (minor cognitive-motor disorder and HIV-1 associated dementia). This project will provide a training program to FH staff on the diagnosis and treatment of HIV-1 associated cognitive-motor disorders during the first six months. The educational impact of the program will then be evaluated. Upon confirmation of training by a knowledge-based examination, the second phase of the project will commence During this phase a total of 150 consecutive HIV-1 infected patients seen at the FH will be screened for cognitive-motor disorders. The rate of diagnostic agreement between the University of Miami staff and the Argentinean team will be determined over the first 50 patients. Discrepancies will be reviewed and presented around achieving diagnostic consensus. The final phase of the project will be the review of the last 100 patients seen and any discrepancies amongst these cases. Treatment plan recommendations will also be incorporated into the educational plan and review of cases, although criteria justifying agreement on treatment plan are not as highly developed. Results will be used to validate the HIV University of Miami Annotated Neuropsychological test battery in Spanish (the HUMANS battery) in a homogeneous Spanish-speaking culture (that of Argentina). Current NIMH-funded study hypotheses on aging and HIV-1 infection in Miami will also be preliminarily investigated in the Argentinean cohort to be accrued with the aim of developing a subsequent R01 grant application.

Thesaurus Terms:
AIDS /HIV diagnosis, AIDS dementia complex, HIV infection, South America, neuromuscular disorder diagnosis AIDS therapy, age difference, diagnosis quality /standard, education evaluation /planning, international cooperation, medical education, psychomotor disorder, training clinical research, human subject, neuropsychological test, patient oriented research

Institution: UNIVERSITY OF MIAMI-MEDICAL SCHOOL
1507 Levante Avenue
CORAL GABLES, FL 33124

Fiscal Year: 2004
Department: PSYCHIATRY AND BEHAVIORAL SCIS
Project Start: 30-SEP-2003
Project End: 30-JUN-2006
ICD: NATIONAL INSTITUTE ON DRUG ABUSE
IRG: ZNS1

Grant Number: 1R21TW006665-01

Project Title: Gene Therapy in the Senile Brain and Hypophysis

PI Information:

Name	Email	Title
GOYA, RODOLFO G.	rgoya@netverk.com	

Abstract: DESCRIPTION (provided by applicant): The increase of the elderly population in the urban areas of Argentina is comparable to that of many North American and European cities. Consequently, the incidence of age-related neurological pathologies is becoming a problem of significant medical and economic impact for the country. In this context, the overall goal of the present proposal is to establish a long-term collaboration between the American and Argentine applicants, who share an interest in the potential of gene therapy for the treatment of neurodegenerative diseases. Three specific objectives are proposed: 1) To assess the performance of self-regulating adeno associated viral (AAV) vectors in the brain of old rats. These vectors harbor a reporter gene encoding humanized green fluorescent protein (hGFP) under the control of the tet-off or tet-on promoter system which can be turned off or on, respectively by administration of tetracycline (Tet) or certain Tet derivatives. The above vectors will be stereotaxically injected in the paraventricular, periventricular and arcuate nuclei, all of which contain dopaminergic (DA) neurons of known vulnerability to aging. 2) To assess the therapeutic efficacy of a self-regulating tet-off AAV vector harboring the gene for human glial cell line-derived neurotrophic factor (hGDNF), a potent neuroprotective molecule. The vector will be stereotaxically injected in the arcuate nucleus of 24-month old rats and 6 months later, its ability to prevent the normal age-related loss of hypothalamic tuberoinfundibular DA (TIDA) neurons will be assessed by quantitative immuno-histochemistry for DA neurons and ELISA for hGDNF. Serum PRL levels (an index of TIDA neuron function) will be monitored in the animals throughout the experiment. 3) To construct two self-regulating adenoviral vectors (RAd) harboring suicide genes under the control of the tet-off system. One of the RAds will harbor a hybrid suicide gene coding for a fusion protein between hGFP and HSV1 thymidine kinase (HSV1-TK), which retains fluorescence and HSV1-TK suicide activity. The other RAd will harbor the separate genes for HSV1-TK and hGFP under the control of a bi-directional Tet-off regulatory element. These two vectors, which are expected to be safer than non-regulatable counterparts, will be employed to treat experimental rat prolactinomas. Further to the above specific objectives, contacts with basic and clinical neuroscientists are planned in the US and Argentina in order to assemble a follow up research program focused on senile brain disorders.

Thesaurus Terms:
gene delivery system, gene therapy, hypothalamus, neoplasm /cancer chemotherapy, nervous system disorder therapy, neural degeneration, nonhuman therapy evaluation, pituitary gland, pituitary neoplasm, technology /technique development aging, cell death, dopamine, gene expression, international cooperation, neuron, neuroprotectant, neurotrophic factor, prolactin, reporter gene, transfection /expression vector Adenoviridae, South America, animal old age, female, immunocytochemistry, laboratory rat, stereotaxic technique

Institution: NATIONAL UNIVERSITY OF LA PLATA
ST # 60 & 120, CC455
LA PLATA, 1900

Fiscal Year: 2004
Department:
Project Start: 01-MAR-2004
Project End: 28-FEB-2006
ICD: FOGARTY INTERNATIONAL CENTER
IRG: ZNS1

Grant Number: 1R21TW006764-01

Project Title: Epidemiological Survey of Learning Disabilities in Zambia

PI Information:

Name	Email	Title
GRIGORENKO, ELENA L.	elena.grigorenko@yale.edu	ASSOCIATE PROFESSOR

Abstract: DESCRIPTION (provided by applicant): The proposed study has the following objectives: (1) To establish and solidify a network of Zambian and international researchers qualified to design and carry out a comprehensive study of prevalence and etiology of non-specific and specific learning disabilities in Zambia. Specifically, the current proposal capitalizes on already-established collaborative relationships between various members of the team on this proposal and further extends the existing team to ensure that areas of expertise required for the conductance of the future large-scale epidemiological study of learning disabilities are represented on the emerging international group of researchers. (2) To demonstrate feasibility of conducting such a comprehensive epidemiological study of learning disabilities in Zambia. Specifically, we propose a set of 5 small-scale studies: (a) an assessment development and validation study; (b) a pilot epidemiological study of non-specific and specific learning disabilities among children attending schools in Eastern Province; (c) a pilot study of non-specific and specific learning disabilities among out-of-school children living in Eastern Province; (d) a pilot study of nonspecific and specific learning disabilities among street children-orphans of HIV/AIDS epidemic; (e) a pilot study of etiology of non-specific and specific learning disabilities in Eastern Province. (3) To design a large-scale study designed to assess the magnitude and the nature of basic and applied issues related to non-specific and specific learning disabilities in Zambian school-aged children. (4) To integrate the tasks of capacity building, research training, and research conductance on the issues of non-specific and specific learning disabilities within one project aimed at estimating the prevalence and gaining an insight into epidemiology and the etiology of learning disabilities in Zambia.

Thesaurus Terms:
Africa, developmental disease /disorder, educationally disadvantaged, epidemiology, learning disorder, training child foster care /adoption, disease /disorder prevention /control, disease /disorder proneness /risk, health disparity, human population study, learning African, clinical research, human subject

Institution: YALE UNIVERSITY
47 COLLEGE STREET, STE 203
NEW HAVEN, CT 065208047

Fiscal Year: 2003
Department: YALE CHILD STUDY CENTER
Project Start: 28-SEP-2003
Project End: 28-FEB-2005
ICD: FOGARTY INTERNATIONAL CENTER
IRG: ZNS1

Grant Number: 1R21TW006713-01

Project Title: APOE Genotype in Brazilian Children with Early Diarrhea

PI Information:	Name	Email	Title
	GUERRANT, RICHARD L.	rlg9a@virginia.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): Having defined the magnitude, major new etiologies, key novel mechanisms and short-term and long-term impact of persistent and recurring diarrheal illnesses on cognitive development in a model collaboration and cohort of children born into active prospective surveillance in poor urban areas (shanty-towns) in Northeast Brazil, we now have a unique opportunity to better assign causal relationships by establishing the importance of genetic markers in defining risk, plan prevention strategies for future interventions, and build sustainable human genetic research together with environmental assessment. This proposal directly addresses potentially remediable mechanisms of long-term cognitive impairment, which we have calculated more than doubles the DALY impact of early childhood diarrheal illnesses worldwide. We postulate, based on our previous cognitive outcome data, that the greatest long-term impact will occur in children with persistent and recurring diarrheal illnesses carrying APOE4 alleles, a well-known genetic marker related to poor recovery following brain injury and sporadic, late-onset Alzheimer disease. Since APOE4 is associated with impaired recovery from brain injury, but not with cognitive function in healthy children, an association of APOE4 with impaired cognitive development that we see with heavy diarrhea burdens in favela (shanty-town) children will strongly suggest that these children endure a form of "brain injury" with their heavy diarrheal illness burdens in their most formative first two years of life. Hence, our longstanding collaboration and prospective field cohort surveillance will enable the use of new approaches and genetic technologies to define APOE allele distribution with impaired cognitive development, thus assessing the potential impact of early childhood diarrheal illnesses as a cause of "brain injury" at the critical formative first 2 years of life. This project will also open new opportunities to train both US and international scientists in highly relevant bench and field investigation, holding promise for demonstrating a key intervention targeted at the most vulnerable subset of children in greatest need.

Thesaurus Terms:
Brazil, apolipoprotein E, cognition disorder, developmental disease /disorder, diarrhea, early experience, epidemiology, gene expression, training biomarker, brain injury, disease /disorder prevention /control, disease /disorder proneness /risk, genotype, health disparity, human population study, infant human (0-1 year), neuropsychology, urban poverty area clinical research, human subject

Institution: UNIVERSITY OF VIRGINIA CHARLOTTESVILLE
BOX 400195
CHARLOTTESVILLE, VA 229044195

Fiscal Year: 2003
Department: INTERNAL MEDICINE
Project Start: 28-SEP-2003
Project End: 28-FEB-2005
ICD: FOGARTY INTERNATIONAL CENTER
IRG: ZNS1

Grant Number: 5R01HD053131-02

Project Title: APOE and the Effects of Malnutrition on Cognitive and Intestinal Development

PI Information:	Name	Email	Title
	GUERRANT, RICHARD L.	rlg9a@virginia.edu	PROFESSOR

Abstract:
This abstract is not available.

Thesaurus Terms:
apolipoprotein E, cognition disorder, diarrhea, growth /development, intestine disorder, malnutrition
allele, biological signal transduction, disease /disorder model, executive function, physical fitness, semantics
behavior test, genetically modified animal, histology, immunocytochemistry, laboratory mouse

Institution: UNIVERSITY OF VIRGINIA CHARLOTTESVILLE
BOX 400195
CHARLOTTESVILLE, VA 229044195

Fiscal Year: 2007
Department: INTERNAL MEDICINE
Project Start: 22-SEP-2006
Project End: 31-JUL-2011
ICD: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
IRG: ZRG1

Grant Number: 1R21TW006729-01

Project Title: Zinc Nutrition and Brain Development in Southern Ethiopia

PI Information: Name	Email	Title
HAMBIDGE, K MICHAEL.	michael.hambidge@uchsc.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): The objectives of this proposal are: [1] to develop the necessary resources, including human resources at or/and associated with Debub University, Southern Ethiopia, supported by collaborations with and between the University of Colorado Health Sciences Center and Oklahoma State University, to initiate and sustain a durable research program linking nutrition [micronutrients] and maternal-child brain development and function; [2] to complete pilot studies that will provide an essential cornerstone for the development of a major R01 grant proposal that will be designed to test the following hypotheses: Provision of an optimal quantity of bioavailable zinc during the second and third trimesters of pregnancy and to offspring through the first 2 years will be associated with improved maternal cognitive and behavioral; greater head circumference of neonate [adjusted for gestational age] and improved attention/habituation/intellectual and motor development throughout the first 2 years of life and beyond. These objectives will be achieved by: fully developing a research team in Awassa and associated institutions; an initial planning, consortium-building, needs assessment meeting in Awassa; supporting the development of an IRB with FWA at Debub University; training and cross-training [nutrition and brain function research] in Awassa, Colorado and Oklahoma; pilot testing of tools for studies of brain function in Awassa; pilot nutrition studies including: dietary, biomarker and anthropometrics assessment; assessment of zinc nutritional status, zinc absorption and zinc requirements for this particular population; a second planning meeting to review progress and plan details of R01 proposal; and, finally, the development of the R01 proposal based on the experience and knowledge acquired with this preparatory/pilot R21-supported research.

Thesaurus Terms:
Africa, cognition disorder, developmental disease /disorder, developmental neurobiology, dietary trace element, epidemiology, metal metabolism, nutrition, training, zinc biomarker, brain, developmental nutrition, disease /disorder prevention /control, disease /disorder proneness /risk, health disparity, human population study, nutrient requirement, urban poverty area African, clinical research, human subject, nutrition related tag

Institution: UNIVERSITY OF COLORADO DENVER/HSC AURORA
GRANTS AND CONTRACTS, MAIL STOP F428
AURORA, CO 800450508

Fiscal Year: 2003

Department: PEDIATRICS

Project Start: 28-SEP-2003

Project End: 28-FEB-2005

ICD: FOGARTY INTERNATIONAL CENTER

IRG: ZNS1

Grant Number: 1R01MH080601-01A1

Project Title: HIV, Malaria and Neurobehavioral Development in Early Childhood

PI Information: **Name** **Email** **Title**

HOLDING, PENNY A. cxk21@case.edu

Abstract: DESCRIPTION (provided by applicant): The proposed study will assess the effects of in utero exposure to HIV and of malarial co-infection on children's neurobehavioral development across the first two years of life. The importance of this research is that there is a growing population of children who are exposed to maternal HIV in utero in the presence of other co-infections. However, we have limited knowledge of the consequences of that exposure for the early development of the children born to these women. The central hypothesis of this study is maternal HIV increases risks for birth of children with low birth weight (LBW). These risks are especially high in women who are co-infected with malaria and are mediated by pre-term birth, intrauterine growth retardation (IUGR) and placenta! abnormalities, including chorioamnionitis. LBW and placenta! abnormalities, in turn, lead to developmental delays and to a slowed rate of development across the first two years of life, even when controlling for vertical transmission of HIV. The study will also examine measures of the family environment as moderators of adverse developmental consequences of maternal HIV. Unique features of the study include the use of child assessments that have been standardized on the target population, examination of the independent and conjoint effects of maternal HIV and malaria co-infection, recruitment of local controls with social and economic backgrounds similar to those of the infected women, and the measurement of the pre-natal environment as a risk factor using placental histology. Women will be recruited early in their second semester from the antenatal clinics at two district hospitals in Coast Province, Kenya. They will be seen at regular intervals until delivery and they and their children then followed until the children are 24 months of age. The proposed project will be conducted by a multidisciplinary team from: Case Western Reserve University, Kenya Medical Research Institute, The Kenyan Ministry of Health, International Centre for Reproductive Health, and the African Mental Health Foundation/University of Nairobi. The project also provides the framework for a program of training in pediatric HIV research that will build the technical and research capacity of the collaborating Kenyan institutions.

Thesaurus Terms:

HIV infection, child psychology, developmental neurobiology, malaria, nervous system infection, pregnancy infection, secondary infection Plasmodium falciparum, embryo /fetus hypoxia, longitudinal human study, low birth weight infant human, placenta, vertical transmission, women's health Africa, behavioral /social science research tag, clinical research, human pregnant subject

Institution: CASE WESTERN RESERVE UNIVERSITY
10900 EUCLID AVE
CLEVELAND, OH 44106

Fiscal Year: 2007
Department: NONE
Project Start: 28-AUG-2007
Project End: 30-APR-2012
ICD: NATIONAL INSTITUTE OF MENTAL HEALTH
IRG: ZRG1

Grant Number: 1R21TW006805-01

Project Title: Developing a Measure of Brain Insults In Kenyan Children

PI Information: **Name** **Email** **Title**

HOLDING, PENNY A. cxk21@case.edu

Abstract: DESCRIPTION (provided by applicant): A major limitation in the investigation of brain disorders in Sub-Saharan Africa is the absence of appropriate and standardized assessment tools and procedures. Within the time frame of this project, a developmental checklist written to monitor and evaluate the psychomotor development of infants and young children (The Kilifi Developmental Checklist) will be evaluated. Its statistical and psychometric properties will be investigated in preparation for production as a published test. Its sensitivity will be investigated in relation to both biological and social variables. These variables will be measured by the administration of assessments of infant information processing, event related potentials, and a Kenyan adaptation of the HOME inventory. The local scientists and early childhood practitioners who will be recruited to carry out this project will receive training and supervision from an international team of psychologists and neuroscientists. Future research initiatives will be able to build upon the foundation of skill and expertise that this training and experience will provide. The longer-term objective is to provide scientists in East Africa with a rigorously developed methodology for the investigation of the sequelae of brain disorders of pre-natal and peri-natal origin.

Thesaurus Terms:
brain disorder diagnosis, child (0-11), diagnosis design /evaluation, diagnosis quality /standard, neural information processing, neuropsychological test, psychometrics, psychomotor disorder Africa, cooperative study, evoked potential, gender difference, human population study, language development, psychomotor function, socioeconomics behavioral /social science research tag, clinical research, electroencephalography, field study, human subject, questionnaire, statistics /biometry

Institution: KENYA MEDICAL RESEARCH INSTITUTE (KEMRI)
MBAGATHI RD
NAIROBI, 00200

Fiscal Year: 2003

Department:

Project Start: 28-SEP-2003

Project End: 28-FEB-2005

ICD: FOGARTY INTERNATIONAL CENTER

IRG: ZNS1

Grant Number: 1R21NS048839-01

Project Title: Developing Approaches to Reducing Stigma of Epilepsy

PI Information: **Name** **Email** **Title**

JACOBY, ANN ajacoby@liverpool.ac.uk

Abstract: DESCRIPTION (provided by applicant): Epilepsy is the world's most common brain disorder, affecting some 50 million people worldwide. There is general agreement that stigma and exclusion are common features of epilepsy in both the developed and developing countries and a major contributor to the burden associated with the condition. Reducing the stigma of epilepsy is therefore key to reducing its impact and so improving quality of life. In order for effective health policy initiatives to be implemented to reduce the stigma of epilepsy, a number of issues first need to be addressed. These include addressing cultural variations in the meaning attached to having epilepsy and hence the way in which stigma is played out; and defining appropriate outcomes and methods for assessing them. This project will address these issues and so inform development of culturally appropriate approaches to reducing stigma and discrimination. The project will involve ethnographic studies to explore prevailing beliefs and attitudes to epilepsy in two developing countries, China and Vietnam. It will define theoretical models of stigma and its link to disease burden. It will develop validated and culturally specific measures of outcome for use in future intervention studies. Through its implementation, the project will enhance social science research capacity in these two countries and facilitate development of strong collaborations for future related research activities.

Thesaurus Terms:
attitude, epilepsy, prejudice, psychosocial separation, racial /ethnic difference belief, community, family, health care personnel, health care policy, health science research support, quality of life, training China, behavioral /social science research tag, clinical research, human subject, interview, southeast Asia

Institution: UNIVERSITY OF LIVERPOOL
The Foundation Building
LIVERPOOL, L69 3BX

Fiscal Year: 2003
Department:
Project Start: 30-SEP-2003
Project End: 31-AUG-2005
ICD: NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
IRG: ZNS1

Grant Number: 7R21TW006794-03

Project Title: Cognitive and Neurologic Sequelae in Cerebral Malaria

PI Information: **Name** **Email** **Title**

JOHN, CHANDY C. ccj@umn.edu ASSOCIATE PROFESSOR

Abstract: DESCRIPTION (provided by applicant): The long-term goal of this project is to relate specific immune responses to infectious diseases to subsequent neurological and neuropsychological deficits. The objectives of the present proposal are to establish the infrastructure and trained personnel to conduct such studies and to generate preliminary data on the relationship between serum IL-10 and TNF-alpha levels and neurological and neuropsychological deficits in children with cerebral malaria (CM). Malaria is the leading cause of death in children under 5 years of age in Uganda. CM is known to be a leading cause of malaria-related mortality in Uganda, but morbidity from CM, particularly the effect of CM on cognitive function, has not been well-characterized. We propose to assess the general incidence of CM in Uganda through retrospective chart review and a prospective study categorizing malaria-related disease (e.g. CM, severe malarial anemia) in all individuals admitted with malaria at Mulago Hospital, Kampala and Kabale Hospital, Kabale. We then propose to study the relationships between CM, immune responses to this condition and neurological and neuropsychological sequelae in a multi-disciplinary collaboration of physicians, developmental specialists and scientists from Case Western Reserve University (CWRU), Indiana Wesleyan University and Makerere University, Uganda. The long-standing collaboration between CWRU and Makerere University in the areas of tuberculosis and HIV research and the well-equipped immunology laboratory shared by these institutions will facilitate the performance of this project. The project will have a training component with both group education and individual training modules and an infrastructure component with support for testing equipment, supplies and simple renovation of spaces for clinical assessment and data management. The training modules will include a core curriculum for all study personnel and trainees with courses in clinical areas (malaria pathogenesis; care of the acutely ill child; neurological examination), neuropsychological (assessment of child cognition and development), immunology (host defense and infection, principles of laboratory immunology) and ethics in scientific research. In addition to the core curriculum, individual study personnel and trainees will receive hands-on training in the above areas as appropriate to their role in the study. In the second year of the study, courses in study design and scientific writing will be given for senior personnel. Infrastructure improvement will focus on dedicated clinical and office space and computing facilities for a Center for Cerebral Malaria Research that will support the proposed research. Trained personnel will undertake a pilot study in which serum IL-10 and TNF-alpha levels are compared in children with and without CM and then compared to neuropsychological and neurological parameters in children with CM at the time of discharge, and 1, 3, and 12 months later. This preliminary data will be the foundation for future studies investigating a broader range of antecedent immune factors in CM and neurological and cognitive function.

Thesaurus Terms:
Africa, cognition disorder, epidemiology, malaria, nervous system infection, neuropsychology, training
brain injury, curriculum, disease /disorder prevention /control, disease /disorder proneness /risk, health disparity, human population study, interleukin 10, tumor necrosis factor alpha African, clinical research, enzyme linked immunosorbent assay, human subject

2007 Follow up:

Michael Boivin: Co-Investigator

International Neurologic and Psychiatric Epidemiology Program (INPEP), College of Osteopathic Medicine, Michigan State University, 324 West Fee Hall, East Lansing, MI 48824: Michael.Boivin@hc.msu.edu

Title: Long-term cognitive impairment in children with cerebral malaria

Abstract: **Background:** Cerebral malaria (CM) affects more than 785,000 African children every year. We previously documented an increased frequency of cognitive impairment in children with CM 6 months after their initial malaria episode. The present study was conducted to determine the long-term effects of CM on the cognitive function of these children. The present study is also exploring the immunopathogenic mechanisms of CM in brain injury. Cytokine production within the central nervous system (CNS) has been implicated in the pathogenesis of murine cerebral malaria.

We hypothesized that CNS cytokine levels are elevated in human cerebral malaria and involved in subsequent neurologic and cognitive impairment.

Methods: Children 5-12 years of age presenting to Mulago Hospital, Kampala, Uganda with CM (n=44) or uncomplicated malaria (UM, n=54), along with healthy, asymptomatic community children (CC, n=89), were enrolled in a prospective cohort study of cognition. Cognitive testing was performed at enrollment, 6 months, and 2 years later. Primary outcome was presence of a deficit in one or more of three cognitive areas tested. In part two of our study, cerebrospinal fluid (CSF) and serum levels of 12 cytokines or chemokines important in P. falciparum infection or other central nervous system infections were measured in 76 CM Ugandan children during illness, and 8 control children. These measures were related to cognitive performance at 6 month follow-up.

Findings: At 6-month follow-up, 21.4% of CM children had cognitive impairment in either attention, working memory, or tactile-based learning. Only 5.7% of the CC children had cognitive impairment (P=.01). At 2 year follow-up testing, 26.3% of children with CM and 12.5% with UM had cognitive deficits in one or more areas, as compared to 7.6% of CC (P=0.006 and 0.37 for children with CM and UM, respectively). Deficits in children with CM were primarily in the area of attention (CM, 18.4% vs. CC, 2.5%, P=0.005). After adjustment for age, gender, nutrition, home environment and school level, children with CM had a 3.67-fold increased risk of a cognitive deficit as compared to CC (95% confidence interval, 1.11, 12.07, P=0.03). Cognitive impairment at 2- year follow-up was associated with hyporeflexia on admission (P=0.03) and neurologic deficits 3 months after discharge (P=0.05).As compared to control children, children with CM had higher CSF levels of specific pro-inflammatory (interleukin (IL)-6, CXCL-8/IL-8, granulocyte-colony stimulating factor (G-CSF), all P<0.001, tumor necrosis factor-$_{alpha}$ (TNF-$_{al}$, P=0.02) and anti-inflammatory (IL-1ra, P<0.001) cytokines. There was no correlation between CSF and serum cytokine levels for any cytokine except G-CSF, and CSF levels of CXCL8/IL-8 were greater than serum concentrations. Elevated TNF-$_{a}$ levels on admission were associated with an increased risk of neurologic deficits 3 months after the episode (odds ratio 1.55, 95% confidence interval, 1.10, 2.18, P=0.01) and correlated negatively with age-adjusted scores for attention (Spearman's rho, -0.34, P=0.04) and working memory (Spearman's rho, -0.32, P=0.06) 6 months after the CM episode.

Conclusions: CM is associated with long-term cognitive impairments in one out of four child survivors. Our immunology findings provide the first human evidence of CNS production of cytokines and chemokines in survivors of CM. Elevated CSF TNF-$_{a}$ levels at the time of the CM episode are associated with subsequent neurologic and cognitive impairment.Future studies should further investigate the immunopathogenic mechanisms involved in CM brain injury, so as to develop interventions aimed at prevention and rehabilitation.

Institution: UNIVERSITY OF MINNESOTA TWIN CITIES
450 MCNAMARA ALUMNI CENTER
MINNEAPOLIS, MN 554552070
Fiscal Year: 2004
Department: PEDIATRICS
Project Start: 01-JUL-2005- 28 Feb2008
ICD: FOGARTY INTERNATIONAL CENTER

Grant Number: 1R21MH080611-01

Project Title: NeuroAIDS in Cameroon: Molecular determinants

PI Information:	Name	Email	Title
	KANMOGNE, GEORGETTE	gkanmogne@unmc.edu	

Abstract: DESCRIPTION (provided by applicant): HIV-related neurocognitive disorders (HNCD) are common in infected patients, ranging from neurocognitive deficits to dementia. These complications have been well documented, both in the pre- and post-antiretroviral therapy (ART) periods. However, the vast majority of these studies were done in developed countries and involved patients infected with the predominant B subtype of HIV-1. Twenty six of the 40.3 million people currently living with HIV/AIDS are in sub-Saharan Africa and 83% of AIDS patients from this region do not have access to ART. Current published studies on neuroAIDS in Africa are mostly case reports and there is a need for structured, well-controlled studies that assess the incidence and prevalence of HNCD among infected people in Africa. A recent study in Uganda suggests that infection with HIV-1 subtype D compared to other clades increases the likelihood of rapid death from AIDS. The HIV epidemic in Cameroon is unique and is characterized by a very broad genetic diversity; infection with multiple HIV strains has been documented in Cameroon. The effect of this genetic diversity on the susceptibility and development of neuroAIDS is not known. Furthermore, whether other HIV genotypes differ in incidence, prevalence, or rate of progression of neuroAIDS or in systemic HIV manifestations is unclear. We hypothesize that HIV genotype can influence the patient's susceptibility to neuroAIDS and disease progression. The principal investigator has initiated a collaboration with the University of Yaound to characterize the epidemiology of neuroAIDS in Cameroon and its molecular determinants The objective of this pilot study is to adapt, normalize and implement in Cameroon neuromedical and neurobehavioral test procedures, demonstrate the feasibility of collecting and transferring samples to UNMC for molecular testing: Aim 1: Train Cameroon investigators in neuromedical and neurobehavioral testing, Aim 2: Pilot test in Cameroon of a subset of a National Institute of Mental Health AIDS workgroup-recommended neuropsychological test battery; and neuromedical evaluation of HIV+ patients; Aim 3: Establish the feasibility of transferring samples from Cameroon to the University of Nebraska Medical Center and set up molecular studies by sequencing the HIV envelope in a small group of samples from HIV+ patients with and without HNCD. This phase of the study will determine the feasibility of identifying and recruiting participants, implementing NP test instruments in Cameroon and getting samples. It will provide normative data for neurocognitive testing among Cameroon population and lay the ground work for our future R01 which objective will be to perform a more definitive study of the epidemiology and molecular determinants of neuroAIDS in Cameroon. PROJECT RELEVANCE Neurological complications are common among HIV-infected individuals and there is a need to study theses complications in sub-Saharan Africa, the region worst affected by the HIV/AIDS pandemic. This proposal investigates whether infections with HIV isolates that have a particular genetic characteristic makes patients more susceptible to neurocognitive disorders. It will provide knowledge on the epidemiology of neuroAIDS in Cameroon and build the capacity for future neuroAIDS research and therapeutic testing in Cameroon.

Thesaurus Terms:
AIDS dementia complex, Africa, genetic susceptibility, genotype, nervous system disorder epidemiology, virus genetics
African, academic achievement, cerebrospinal fluid, genetic strain, virus characteristic
clinical research, human subject, neuropsychological test

Institution: UNIVERSITY OF NEBRASKA MEDICAL CENTER
OMAHA, NE 681987835

Fiscal Year: 2007

Project Start: 18-MAY-2007- 30-Apr-2009

ICD: NATIONAL INSTITUTE OF MENTAL HEALTH

Grant Number: 1R21TW006761-01

Project Title: Cognitive-Brain Phenotyping of Atypical Chinese Children

PI Information:

Name	Email	Title
KARMILOFF-SMITH, ANNETTE	a.karmiloff@ich.ucl.ac.uk	

Abstract: DESCRIPTION (provided by applicant): The present proposal describes a series of planning activities to develop an international collaborative program of research on cognitive and brain phenotypes of mentally retarded Chinese children with genetic disorders. Specifically, an international team of medical, psychological, genetic, and computational researchers from P.R. China, the United Kingdom, the United States, and Canada will collaborate to study Chinese children with Fragile-X syndrome (FXS), Williams syndrome (WS), and Down syndrome (DS). The specific aims of the present research planning proposal are:(1) To assess the existing research infrastructure at the Chinese institution (Zhejiang University) for conducting the proposed research activities, (2) To enhance the research capacities of our Chinese research team through workshops and short-term training; (3) To conduct pilot studies that (a) test the feasibility of a computer-assisted 3D photography-based system for identifying a large population of mentally retarded children whose facial dysmorphology may suggest FXS, WS or DS and verify such identifications by genetic tests, (b) translate, adapt, and pilot-test procedures developed by the researchers in UK, US, and Canada to assess children with genetic disorders in terms of their abilities in the areas of language, executive function, and faces and visual-spatial information processing, and compare the Chinese children's cognitive profiles with the existing profiles of affected Western children; (c) use event-related potential techniques to examine the neuro-physiological correlates of a small group of the Chinese children with WS, FXS, and DS when they process language and face-spatial information, and compare the results with those obtained with the existing samples of affected Western children. Based on the outcome of 1,2, and 3, the international interdisciplinary team will develop a R01 research proposal that will systematically examine cognitive and brain functions or dysfunctions of Chinese children with Williams, Fragile-X, and Down syndromes from infancy to middle childhood. Our long-term goal is to chart the developmental trajectories of cognitive and brain development in children with genetic disorders, to understand the interaction between genetic abnormality and neuro-cognitive development in different socio-cultural contexts, and to provide information for the creation of syndrome-specific and, if necessary, culture-specific intervention programs.

Thesaurus Terms:
Chinese, Downs syndrome, Williams syndrome, brain disorder, cognition disorder, fragile X syndrome, middle childhood (6-11), phenotype computer human interaction, culture, functional ability, geographic difference, health science research analysis /evaluation, international cooperation, language, neural information processing, training clinical research, genetic screening, human subject, three dimensional imaging /topography

Institution: UNIVERSITY COLLEGE LONDON
GOWER STREET
LONDON, WC1E 6BT

Fiscal Year: 2003
Department:
Project Start: 28-SEP-2003
Project End: 28-FEB-2005
ICD: FOGARTY INTERNATIONAL CENTER
IRG: ZNS1

Grant Number: 1R01AG029802-01

Project Title: Development of RNAi as Treatment for Neurodegeneration

PI Information:	Name	Email	Title
	KOSIK, KENNETH S.	kosik@lifesci.ucsb.edu	HARRIMAN PROFESSOR OF NEUROSCIENCE RESEA

Abstract: DESCRIPTION (provided by applicant): Alzheimer's disease, already a serious global disease afflicting large segments of the population, is about to burgeon into an even larger problem as the baby-boomer bubble approaches retirement age. The disease remains incurable; however validated therapeutic targets are known. RNA interference (RNAi) technology poses a potential therapeutic option which requires further investigation. Targeting the mRNA rather than the protein offers major advantages in the ease of designing a highly specific inhibitory agent and rapidly advancing approaches to RNAi delivery suggest that the method can be developed into a therapy. Our hypothesis is that RNAi will prove to be an effective and selective strategy to slow, and perhaps even reverse, the pathogenic processes in inherited and sporadic AD. This proposal follows the completion of an R21 award of the same title. The announcement for this award was an RFA from the Fogarty Institute for proposals related to Brain Disorders in the Developing World and a major goal of the program was to build research capacity at the foreign site. The successful completion of the R21 aims is described in the preliminary data. The collaborative effort poses two questions concerning the cause and possible treatment of neurofibrillary pathology in AD. One question is whether suppression of Cdk5, an increasingly accepted disease target, can modify neurofibrillary pathology in an animal model. Cdk5 is an enzyme that phosphorylates tau protein and in so doing is thought to contribute to the conversion of the protein into an insoluble aggregate known as the neurofibrillary tangle. Cdk5 will be targeted by RNAi delivered in a viral vector. The second question is whether BACE1 inhibition by RNAi delivery can retard or prevent the development of neurofibrillary pathology in an animal with both plaques and tangles. The studies proposed here are intended to continue building research capacity at the foreign site which is now in a position to launch these studies. In addition to the established collaboration between the Kosik laboratory and the foreign site, two consultants will contribute to capacity building. They are Bev Davidson who will advise on the establishment of a viral core and Frank LaFerla who will contribute the triple transgenic mice to the vivarium at the foreign site.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: UNIVERSITY OF CALIFORNIA SANTA BARBARA
3227 Cheadle Hall
SANTA BARBARA, CA 93106

Fiscal Year: 2007

Department: NEUROSCIENCE RESEARCH INSTITUTE

Project Start: 15-SEP-2007

Project End: 30-JUN-2012

ICD: NATIONAL INSTITUTE ON AGING

IRG: ZRG1

Grant Number: 1R01AG029802-01

Project Title: Development of RNAi as Treatment for Neurodegeneration

PI Information:	Name	Email	Title
	KOSIK, KENNETH S.	kosik@lifesci.ucsb.edu	HARRIMAN PROFESSOR OF NEUROSCIENCE RESEA

Abstract: DESCRIPTION (provided by applicant): Alzheimer's disease, already a serious global disease afflicting large segments of the population, is about to burgeon into an even larger problem as the baby-boomer bubble approaches retirement age. The disease remains incurable; however validated therapeutic targets are known. RNA interference (RNAi) technology poses a potential therapeutic option which requires further investigation. Targeting the mRNA rather than the protein offers major advantages in the ease of designing a highly specific inhibitory agent and rapidly advancing approaches to RNAi delivery suggest that the method can be developed into a therapy. Our hypothesis is that RNAi will prove to be an effective and selective strategy to slow, and perhaps even reverse, the pathogenic processes in inherited and sporadic AD. This proposal follows the completion of an R21 award of the same title. The announcement for this award was an RFA from the Fogarty Institute for proposals related to Brain Disorders in the Developing World and a major goal of the program was to build research capacity at the foreign site. The successful completion of the R21 aims is described in the preliminary data. The collaborative effort poses two questions concerning the cause and possible treatment of neurofibrillary pathology in AD. One question is whether suppression of Cdk5, an increasingly accepted disease target, can modify neurofibrillary pathology in an animal model. Cdk5 is an enzyme that phosphorylates tau protein and in so doing is thought to contribute to the conversion of the protein into an insoluble aggregate known as the neurofibrillary tangle. Cdk5 will be targeted by RNAi delivered in a viral vector. The second question is whether BACE1 inhibition by RNAi delivery can retard or prevent the development of neurofibrillary pathology in an animal with both plaques and tangles. The studies proposed here are intended to continue building research capacity at the foreign site which is now in a position to launch these studies. In addition to the established collaboration between the Kosik laboratory and the foreign site, two consultants will contribute to capacity building. They are Bev Davidson who will advise on the establishment of a viral core and Frank LaFerla who will contribute the triple transgenic mice to the vivarium at the foreign site.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: UNIVERSITY OF CALIFORNIA SANTA BARBARA
3227 Cheadle Hall
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Fiscal Year: 2007

Department: NEUROSCIENCE RESEARCH INSTITUTE

Project Start: 15-SEP-2007

Project End: 30-JUN-2012

ICD: NATIONAL INSTITUTE ON AGING

IRG: ZRG1

Grant Number: 3R21NS055639-01S1

Project Title: CNS Involvement in the HIV Population in Ethiopia: A Post-mortem Forensic Study

PI Information: **Name** **Email** **Title**

LANGFORD, TERESA DIANNE. dianne.langford@temple.edu

Abstract:
This abstract is not available.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: UNIVERSITY OF CALIFORNIA SAN DIEGO
9500 GILMAN DR, DEPT 0934
LA JOLLA, CA 920930934

Fiscal Year: 2007

Department: PATHOLOGY

Project Start: 06-SEP-2006

Project End: 31-MAY-2008

ICD: NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

IRG: ZRG1

Grant Number: 1R21TW006678-01

Project Title: Promoting Child Development: Yale-Ankara Collaboration

PI Information:

Name	Email	Title
LEVENTHAL, JOHN M.	john.leventhal@yale.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): In the proposed project, Ankara University (AU) will partner with Yale University (YU) to develop a research infrastructure and strengthen the capacity for conducting research focused on the recognition, prevention, and treatment of developmental problems and disabilities in infants and young children and their families in Turkey. The proposal builds upon: (1) the preliminary studies by the AU investigators focused on the gaps in the Turkish health care system concerning children's developmental needs, (2) the collaboration of the Turkish investigators with the Turkish Ministry of Health and the WHO, and (3) the earlier collaboration between the Principal Investigator at AU and investigators at YU. The capacity building activities will take place both at AU and YU. At AU, a research center will be established in the Developmental-Behavioral Pediatrics Unit, and a pediatric fellow, research psychologist, and research assistant will be funded. Two Yale investigators will visit AU per year and will give structured workshops and contribute to the ongoing research activtities. Two investigators per year from AU will visit YU where they will work with a mentor/collaborator and benefit from the educational experiences in the 3 participating Yale Departments -- Pediatrics, Child Study Center, and Epidemiology and Public Health. The pilot research projects, which will be developed collaboratively between AU and YU, will focus on understanding the developmental needs of young children - - both normal and those with developmental disabilities - - and the kinds of services available to these children in Turkey. The first study examines the knowledge, skills, and attitudes of health care professionals in Turkey regarding early childhood development, developmental problems, and services available. The second study examines the needs of families related to promoting the development of infants and young children with developmental problems and disabilities. The third study investigates the needs of families related to the promotion of the development of normal infants and young children. These proposed projects will help establish the research center, and the results of these studies will be used to develop larger, full scale research studies and interventions to improve the health care system's response to the developmental needs of young children.

Thesaurus Terms:
Middle East, developmental disease /disorder, health care service availability, health care service planning, health science research support, infant human (0-1 year), international cooperation, pediatrics, preschool child (1-5) child health care personnel, child physical development, child psychology, child with disability, family, interdisciplinary collaboration, patient care personnel attitude behavioral /social science research tag, clinical research, health services research tag, human subject

Institution: YALE UNIVERSITY
47 COLLEGE STREET, STE 203
NEW HAVEN, CT 065208047

Fiscal Year: 2003
Department: PEDIATRICS
Project Start: 28-SEP-2003
Project End: 28-FEB-2005
ICD: FOGARTY INTERNATIONAL CENTER
IRG: ZNS1

Grant Number: 1R21DA018095-01

Project Title: Neurodevelopmental Outcome in Russian Orphanage

PI Information: Name	Email	Title
MILLER, LAURIE C.	lmiller1@tufts-nemc.org	ASSOCIATE PROFESSOR

Abstract: DESCRIPTION (provided by applicant): Russian orphanage children frequently have multiple risk factors at birth, including prenatal drug and alcohol exposure, prematurity, intrauterine growth retardation, congenital microcephaly, and lack of prenatal care. After entry into institutional care, the children often exhibit progressive physical and neurodevelopmental problems. These multiple risk factors place these children at high risk for permanent neurodevelopmental disabilities. However, few interventions are offered to children exhibiting these difficulties. We propose a project to promote and develop the research capacity of our Russian colleagues and stimulate their efforts to improve the neurocognitive outcomes of the children in their care. This work will explore the still incompletely understood contributions of the environment in promoting optimal brain development in young children. We will develop a center for training and research in the identification, prevention, and remediation of developmental disabilities among young orphanage children in the Murmansk Region of Russia (where we have done volunteer work for several years). This center will develop the capacity for evidence-based research to prevent and reduce developmental disabilities among these children, train personnel to develop and examine models for rehabilitation effectiveness, and establish a foundation for future clinical trials of interventions to prevent and remediate these disabilities. Collaborations with professionals in more urban areas of Russia (St. Petersburg) and the U.S. will utilize the Internet and specially prepared web sites. Our multi-disciplinary team members have expertise in the care and rehabilitation of institutionalized children, neurodevelopmental training, and clinical research. Our proposed project includes didactic conferences, practical training in basic research methods and study design, and several pilot projects designed to develop the research capacities of our Russian colleagues and provide the basis for a future R01 application.

Thesaurus Terms:
developmental disease /disorder, developmental neurobiology, infant human (0-1 year), nervous system disorder, preschool child (1-5), rehabilitation child care, embryo /fetus toxicology, extended care facility, institutional care facility, international cooperation, outcomes research, training Commonwealth of Independent States, clinical research, human subject, medical rehabilitation related tag

Institution: NEW ENGLAND MEDICAL CENTER HOSPITALS
750 WASHINGTON ST
BOSTON, MA 021111533

Fiscal Year: 2003

Department:

Project Start: 30-SEP-2003

Project End: 30-JUN-2005

ICD: NATIONAL INSTITUTE ON DRUG ABUSE

IRG: ZNS1

Grant Number: 5R21TW007554-02

Project Title: Community management of mental retardation in Pakistan: An exploratory study

PI Information: **Name** **Email** **Title**

MIRZA, ILYAS iqmirza@gmail.com

Abstract: DESCRIPTION (provided by applicant): Mental retardation is associated with enormous personal, social, and economic costs as a result of early onset and lifetime disability. The stigma associated with these disorders is also a barrier to help seeking. Pakistan, a low income country, has the highest level of reported mental retardation among the low-middle- income countries. The prevalence estimates for Pakistan vary from 19.1/1000 for serious retardation to 65/1000 for mild retardation. There is an urgent need to develop expertise that would provide effective and contextually appropriate management and rehabilitation of these disorders. Such expertise would need to be disseminated at the community health-worker level and utilize the existing strengths and resources of families and communities in Pakistan. The broad long-term aim of this application is to develop and to implement a system of psychological and educational intervention for carers of mental retardation in Pakistan. To achieve this, we intend to develop and demonstrate evidence based practice, that is rooted in the local context, and systematically disseminate these to the community-based primary health care providers in Pakistan. This would be achieved by adaptation of an existing psycho-educational approach, grounded in cognitive-behavior theory and delivered to carers in the community by local health workers, to improve infant health outcomes. This approach has been successfully piloted in Pakistan and is currently being evaluated through a large cluster randomized trial funded by the Wellcome Trust, UK. Preliminary data indicates that this approach is culturally appropriate and acceptable to both health workers and the community at large. Any adaptation of an intervention to another context or condition needs to be informed by rigorous qualitative information and this is the intention of our preliminary proposal. The aim of this preliminary proposal is 1. To explore the attitudes and beliefs of carers of those with mental retardation with regard to its causation, and management, 2. Their experience, including positive practices, of caring using focus groups and a semi-structured interview, 3. Delineate pathways to care for those with mental retardation, and 4. Using qualitative methodology explore the beliefs about treatment of mental retardation of health care providers along this pathway. At an institutional level, we intend to develop and enhance the profile of an existing 25-year-old center for special education and training in Lahore, Pakistan to an international center for collaborative research in mental retardation and service development. Thus it will enhance research and development capacity between Pakistan and UK for future related research activities.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: HUMAN DEVELOPMENT RESEARCH FOUNDATION
SECTOR F-7/3
ISLAMABAD, 44000

Fiscal Year: 2007

Department:

Project Start: 01-MAY-2006

Project End: 30-APR-2008

ICD: FOGARTY INTERNATIONAL CENTER

IRG: ZRG1

Grant Number: 1R21DA018093-01

Project Title: Developmental Disabilities in a Time of AIDS

PI Information: **Name** **Email** **Title**

MIRIAM, ADHIKARI adhikari@ukzn.ac.za

Abstract: DESCRIPTION (provided by applicant): The main aims of this planning grant will be to constitute and strengthen a partnership between a multi-disciplinary research group from the biological, social, rehabilitation and population sciences, primarily based in South Africa and the United States, and to prepare, in the next 2 years, for a research program on developmental disabilities in children 2-6 years of age against the backdrop of a rampant HIV epidemic. Key preparatory activities will include the review of screening and assessment tools developed for 2-phase international childhood disability surveys and their adaptation for South African populations; the development of population screening methods for HIV infection in young children; the development and pilot testing of HIV counseling, consent and testing procedures within the context of multi-disciplinary professional assessments; and the development of a new tool for functional assessments of disability by mid-level rehabilitation workers. These methods and procedures and the proposed field and data operations will be field tested in a 2-phase childhood disability pilot study in a limited sample of 2000 children in the target age group. This pilot study will provide an approximation of the proportion of children likely to screening positive for disability, the proportion of these children likely to be confirmed on professional assessment and the HIV zero-prevalence rate in the general population of children in the 2-6 year age range. These studies will effectively prepare for the more rigorous design and more effective implementation of a 2-phase disability survey in South African children with the statistical power to provide precise and valid measures of the prevalence, types and causes of disability and the relative contribution of HIV infection to this disease burden. The task of preparing for and implementing this pilot study, with the active support and guidance of the US and consultant group, will serve as the key research training exercise in this planning grant and will develop the epidemiological insights and specific skills to undertake a future research program on 'Developmental Disabilities in the Time of HIV'.

Thesaurus Terms:
HIV infection, developmental disease /disorder, epidemiology, health survey, mass screening, preschool child (1-5) international cooperation, middle childhood (6-11) Africa, clinical research, human subject, questionnaire

Institution: UNIVERSITY OF KWAZULU-NATAL
UNIVERSITY ROAD
DURBAN, 3630

Fiscal Year: 2003
Department:
Project Start: 30-SEP-2003
Project End: 30-JUN-2005
ICD: NATIONAL INSTITUTE ON DRUG ABUSE
IRG: ZNS1

Grant Number: 1R21HD053057-01A1

Project Title: Neuro-developmental Disabilities Among Children in India: An INCLEN Study

PI Information: **Name** **Email** **Title**

NAIR, MKC inclen@inclen.org

Abstract: DESCRIPTION (provided by applicant): INCLEN will estimate the prevalence and risk factors of neuro-developmental disabilities (NDD) among children in India. Due to lack of health and educational services in India, NDD are unrecognized and unmanaged, especially conditions like autistic spectrum disorders, thus contributing to the socioeconomic, psychological and educational deprivation of affected children. Goals of the proposed research include: (1) strengthening research capacity in India through collaboration with US expert scientists; and (2) development of policies, programs and services to children with NDD. Scientific evidence is essential for framing policies and programs on NDD issues within India. The major activities of this study include: development and validation of clinical and field tools for the identification and diagnosis of NDD by Indian and US experts and the development of research capacity strengthening skills to perform multi-centre collaborative studies. The proposed study is a cross-sectional survey with a population of children aged 2-9 years in urban and rural settings drawn from five different geographical zones of India. The sample size of 45,000 children has been calculated on the expectation of 4% prevalence of NDD. A cluster sampling method using population proportionate to size technique will be used. The primary screening will be conducted by a team of medical and social scientists specially trained to use the validated screening tool after taking informed consent. All those detected by the screening test as well as a sample of those who screen negative for NDD will be subjected to clinical validations by pediatricians using criteria developed by national and International experts. Strict quality assurance will be maintained at all stages of the study. The National Trust, Ministry of Social Justice and Empowerment, Government of India has expressed keen interest to utilize the results of the study for policy planning in India. According to scant data available, there is an assumption that developmental disabilities are much more prevalent in developing countries. Establishing baseline data will enhance efforts to prevent and achieve early interventions for this overlooked population. The experience gained in this study will be used to develop a R01 in order to generate similar data in other low and middle-income countries through. INCLEN is dedicated to improving the health of disadvantaged populations by promoting equitable healthcare based on the best evidence.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: INTERNTL CLINICAL EPIDEMIOLOGY NETWORK
SUITE 411
PHILADELPHIA, PA 19104

Fiscal Year: 2007
Department:
Project Start: 30-SEP-2007
Project End: 31-AUG-2009
ICD: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
IRG: ZRG1

Grant Number: 5R21MH071213-02

Project Title: Cellular Tropism & Reservoir in Brain with HIV-Clade C

PI Information:

Name	Email	Title
NATH, AVINDRA	anath1@jhmi.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): Studies from populations infected with HIV-clade B virus suggest that patients often develop a dementing illness with important socioeconomic consequences. However, the most common HIV infection worldwide is with HIV-clade C and very little information is available with regards to its neurological manifestations. An important difference between the two clades is that HIV-clade C is nearly exclusively chemokine receptor CCR5 tropic. Since CCR5 expressing cells are present in the central nervous system predominantly in microglia and to a lesser degree in astrocytes, neurons and endothelial cells, it is important to determine the cellular tropism of this virus in brain of HIV-clade C infected patients. Populations infected with HIV-clade C have a high incidence of opportunistic infections and this is often the presenting manifestation of HIV infection. Another important question that remains unanswered is that do HIV infected cells invade the brain during the course of a CNS opportunistic infection? Since the types of cells that make up the inflammatory infiltrates may be different for the various opportunistic infections, it is also important to determine which patients may be at a greater risk for developing HIV encephalitis following treatment of the opportunistic infections. A major obstacle to studying the neuropathological consequences of HIV-clade C infection has been the lack of neurological, neuroradiological or neuropathological services available in areas and populations infected with this virus. The National Institute of Mental Health and Neurosciences in Bangalore, India is unique because all the above services are available at this institute and it has an established brain bank. A unique feature if this brain bank is it has short autopsy times, of 2-8 hours in most cases. Hence, we propose to augment the existing facilities, establish assays for detection and quantification of HIV in brain tissue by immunohistopathology, in situ hybridization, RT-PCR and quantitation of proviral DNA to address the above questions. We believe this will serve as a nidus for the development of several projects to address the neuropathogenesis of HIV infection and develop a rational design for therapeutic approaches and vaccine development.

Thesaurus Terms:
HIV infection, brain cell, chemokine receptor, human immunodeficiency virus, nervous system infection, neuropathology, virus infection mechanism opportunistic infection, protein localization, tissue resource /registry Asian, India, histopathology, immunocytochemistry

Institution: JOHNS HOPKINS UNIVERSITY
W400 Wyman Park Building
BALTIMORE, MD 212182680

Fiscal Year: 2004
Department: NEUROLOGY AND NEUROSURGERY
Project Start: 29-SEP-2003
Project End: 31-AUG-2006
ICD: NATIONAL INSTITUTE OF MENTAL HEALTH
IRG: ZNS1

Grant Number: 1R21TW006697-01

Project Title: Epidemiological Research on Autism in China

PI Information:

Name	Email	Title
NEWSCHAFFER, CRAIG J.	cnewscha@drexel.edu	PROFESSOR AND CHAIRMAN

Abstract: DESCRIPTION (provided by applicant): The planning and pilot research activities proposed in this application are intended to build collaborative relationships and research capacity around the conduct of epidemiological research of autism spectrum disorders (ASD) in China. The Center for Autism and Developmental Disabilities Epidemiology (CADDE) at the Johns Hopkins Bloomberg School of Public Health will team with the Institute of Reproductive and Child Health (IRCH) at Peking University. CADDE is currently engaged in a number of large, population-based ASD epidemiology projects in the US and IRCH has a long track record of conducting population-based prenatal, child health, and developmental disabilities research in China, including major projects partnering with US collaborators. ASD is a severe, brain-based developmental disability whose prevalence appears to be on the rise in the developed countries but whose prevalence in China, a nation including 680 million children under age 14, is largely unknown. ASD is a very complex disorder of unknown etiology that appears to involve multiple epistatic genes and potential gene-environment interaction. Launching research efforts in populations where the genetic background and exposure distributions may differ from populations already studied should hasten progress toward revealing important heritable and nonheritable risk factors. Under the planning grant, the US-China team will: 1) develop a feasible approach for implementing an ASD prevalence study in the Weifang area of Shandong Province; 2) develop a strategy for expanding the prevalence study to a population-based etiologic study; and 3) conduct pilot research activities informing this research development. Pilot activities will include translation and adaptation of ASD screening and diagnostic tools as well as implementation of a limited-scale prevalence study in the WeiCheng District of Weifang that uses the newly adapted tools. This will allow for both field-testing of recruitment and data collection processes and evaluation of the adapted screening/diagnostic methods through expert review.

Thesaurus Terms:
China, autism, developmental disease /disorder, disease /disorder etiology, epidemiology, human population study, training data collection methodology /evaluation, human population genetics, medical outreach /case finding, perinatal clinical research, human data, human subject

Institution: JOHNS HOPKINS UNIVERSITY
W400 Wyman Park Building
BALTIMORE, MD 212182680

Fiscal Year: 2003
Department: EPIDEMIOLOGY
Project Start: 28-SEP-2003
Project End: 28-FEB-2005
ICD: FOGARTY INTERNATIONAL CENTER
IRG: ZNS1

Grant Number: 1R21TW007997-01

Project Title: Building Sustainable Research Capacity at Mansoura Egypt

PI Information:

Name	Email	Title
NIMGAONKAR, VISHWAJIT L.	nimga+@pitt.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): The aim of this application is threefold: (1) to build research infrastructure in Mansoura, Egypt through collaboration with Mansoura University Hospital; (2) to conduct a focused research project investigating the hypothesis that there is increased consanguinity among parents of patients with schizophrenia as compared to parents of unaffected controls; and (3) to collect data that will enable a future R01 grant. This project will enable training for three Egyptian psychiatrists in clinical evaluation techniques through workshops and teaching at the University of Pittsburgh and Mansoura University Hospital. One other individual will be trained in basic molecular genetic techniques, and relevant equipment will be purchased in order to initiate genetic molecular research at Mansoura University Hospital. All the trainees will learn data management and data analysis techniques. Trainees will experience hands-on learning through participation in a focused research project investigating the rate of parental consanguinity among Egyptian patients diagnosed with schizophrenia (n=100) compared with a group of controls (n=100) who have a similar distribution of socio-economic status, age and gender as the patients. Preliminary studies have suggested higher rates of parental consanguinity among patients with schizophrenia than among controls, and this study will further investigate this hypothesis. Controls (n=100) and parents of controls (n=200) are already being recruited through a previously funded FIRCA study. Patients with schizophrenia (n=100) and their parents (n=200) will be ascertained by the Egyptian trainees. Schizophrenia is a common, lifelong, disabling illness which receives relatively little attention in developing countries. Research into the epidemiology of schizophrenia in Egypt is sparse and testifies to the neglected state of this field. Ongoing efforts to map susceptibility genes for schizophrenia have suggested complex interactions between several genetic and environmental factors. Most such studies have been conducted among Caucasians. Complementary investigations of other ethnic groups may yield useful insights, especially if unusual patterns of inheritance are observed.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: UNIVERSITY OF PITTSBURGH AT PITTSBURGH
350 THACKERAY HALL
PITTSBURGH, PA 15260

Fiscal Year: 2007

Department: PSYCHIATRY

Project Start: 01-APR-2007

Project End: 31-MAR-2009

ICD: FOGARTY INTERNATIONAL CENTER

IRG: ZRG1

Grant Number: 1R21ES015472-01

Project Title: Neurotoxic effects of solvents on working children

PI Information: **Name** **Email** **Title**

NUWAYHID, IMAN A. nuwayhid@aub.edu.lb

Abstract: DESCRIPTION (provided by applicant): Significant neuroanatomical and neuromaturation changes take place during adolescence and are reflected n the maturation of abstract reasoning, affect, and cognition. Hence, exposure of millions of adolescent working children in developing countries to solvents might affect their cognitive and behavioral development, in a previous original study in Lebanon, we reported that male working children exposed to solvents performed worse on neurobehavioral assessment than non-exposed working children. The study had several imitations. The exposed children were recruited from 4 kinds of workplaces with variable solvent exposure. Exposure was assessed only once (4-hour passive monitoring) and a follow up study was not planned. This R21 application, a collaborative between the American University of Beirut (AUB) and the Oregon Health & Science University (OHSU), aims at building capacity at AUB and replicating the previous work towards ubmitting an R01 follow-up study. OHSU will bring in 30 years of experience in neurobehavioral research and their Behavioral Assessment and Research System (BARS) which was applied in different occupations, anguages, and age groups. A cohort of 100 male children (10-17 years) working in mechanics (exposed mainly to Methyl Ethyl Ketone and Toluene) and 100 male non-exposed working children will be recruited from a poor neighborhood in north Lebanon, in collaboration with the Center for Working Children in that neighborhood. The program has enrolled 68 working children in the past 18 months. The study will adapt BARS to the Lebanese context, pilot test it, train local researchers, and then use it to compare the performance of exposed to non-exposed children. The study will also develop a strategy to assess exposure of children to solvents using a combination of direct observation at work, passive air monitoring, and biological monitoring. The long-term goal is to submit an R01 application in which these children are followed-up for 3 years, whereby their exposure to solvents is carefully assessed, their neurobehavioral performance is retested in addition to a set of neurophysiological tests, and a functional MRI is performed on those with the worst exposure or performance. The R01 will address the controversial issues of long-term solvent neurotoxicity and the use of neurobehavioral testing as an early indicator of adverse neurotoxic effects. The findings will inform policy on child labor and solvent exposure.

Thesaurus Terms:
adolescence (12-20), environmental exposure, middle childhood (6-11), neurotoxin, occupational hazard, solvent air sampling /monitoring, color vision, hazardous substance, ketone, toluene, visual perception
clinical research, human subject, male, neuropsychological test

Institution: AMERICAN UNIVERSITY OF BEIRUT
BLISS STREET
BEIRUT, 11-0236

Fiscal Year: 2007
Department:
Project Start: 15-SEP-2007
Project End: 31-AUG-2009
ICD: NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
IRG: ZRG1

Grant Number: 5R21TW007800-02

Project Title: Genetic analysis of cholinergic function: implications to Alzheimer's disease.

PI Information: **Name** **Email** **Title**

PRADO, MARCO ANTONIO. mprado@icb.ufmg.br

Abstract:

In many degenerative disorders neurons that secrete acetylcholine malfunction. The main objective of this research program is to understand how cholinergic neurons regulate cognitive processing and how cholinergic dysfunction affects behavioral outputs. In order to do that we are establishing the means to become independent in generating genetically modified mice. Our initial approach targets the vesicular acetylcholine transporter (VAChT) gene. The VAChT is a key component for the storage of acetylcholine in synaptic vesicles and controls the amount of acetylcholine that can be secreted by cholinergic neurons. However, acetylcholine is a key neurotransmitter in the peripheral system as well as in the central nervous system. Hence, genetic alterations that suppress acetylcholine release are incompatible with life.

We approached this problem by decreasing the expression of VAChT (VAChT Knock down mice), rather than generating a classical Knockout (KO) mice. Our experiments have shown a key role for cholinergic tone in recognition memory and also how this transporter controls the storage of acetylcholine in vesicles. To further understand how cholinergic tone controls brain function we also generated brain region specific KO mice. These mice had the VAChT gene deleted in the forebrain, are born in the expected mendelian ratio and survive for up to two months. We are currently investigating the phenotypes in these mutant mice and using the same approach to generate novel models of cholinergic dysfunction with more restrictive deletion pattern. Moreover, we are also generating constructs to produce mice with hypercholinergic function. We expect to reveal how cholinergic tone controls learning and memory and develop novel approaches to ameliorate cholinergic dysfunction in neurodegenerative disorders.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: FEDERAL UNIVERSITY OF MINAS GERAIS
BOX 1621, MINAS GERAIS
BELO HORIZONTE,

Fiscal Year: 2007

Department:

Project Start: 15-APR-2006

Project End: 28-FEB-2008

ICD: FOGARTY INTERNATIONAL CENTER

IRG: ZRG1

Grant Number: 5R01AG028188-02

Project Title: Age related Cognitive Loss in Mumbai, India

PI Information: **Name** **Email** **Title**

PUROHIT, DUSHYANT P. dushyant.purohit@mssm.edu

Abstract: DESCRIPTION (provided by applicant): This project is designed to further develop and facilitate collaborative research on age-related cognitive loss at the TN Medical College/Nair Hospital in Mumbai (Bombay) India, working in conjunction with the Mount Sinai Alzheimer's Disease Research Center (ADRC). This collaboration was initiated through support of an R21 Developmental Grant under the Brain Disorders in the Developing World: Research Across the Lifespan initiative. We now propose a more extensive RO1 grant to further develop the capabilities of our Indian colleagues to carry out research clinical evaluations and longitudinal assessments of cognitive function in the elderly as well as the preparation of postmortem brain specimens for neuropathologic diagnosis and brain banking. Epidemiologic studies of elderly Indian populations indicate that prevalence rates for Alzheimer's are dramatically lower than are seen in the developed nations. In this project, we will enroll, clinically assess, diagnose and longitudinally follow a cohort of 150 elderly individuals from Mumbai with mild to moderate cognitive impairment as well as a comparative group of 100 normal elderly controls. In addition, we will develop a facility for performing neuropathologic characterization and diagnostic evaluation of clinically evaluated subjects who come to autopsy during the course of the study. In doing this we will characterize the clinical features, natural history and neuropathologic correlates of cognitive loss among the urban elderly inhabitants of Mumbai. Finally, we will collect brain specimens from 120 elderly subjects from Mumbai who come to autopsy and are free of cognitive impairment (based on a postmortem Clinical Dementia Rating Score or CDR of 0). These brains will be compared with an age-matched series of brains obtained from the Mount Sinai Brain Bank collection (CDR=0) for the extent and distribution of neurofibrillary tangles and beta- amyloid deposits in the form of senile plaques, diffuse plaques and vascular amyloid accumulations. In this way, we will determine if, as our preliminary data suggest, in the course of normal aging the inhabitants of Mumbai show a decreased tendency to develop these cardinal neuropathologic features of Alzheimer's disease. In carrying out this project it is our overall objective to develop a center of expertise in research on age-related cognitive loss in Mumbai. The methodology we propose is patterned on that of the Clinical, Neuropathology, Database, and Education and Information Transfer Cores of the Mount Sinai ADRC, an established, effective and highly productive NIA-funded ADRC.

Thesaurus Terms:

India, cognition disorder, human old age (65+), psychological aspect of aging
Alzheimer's disease, amyloid protein, biomedical facility, longitudinal human study, memory disorder, neuritic plaque, neurofibrillary tangle, neuropathology, postmortem, short term memory, technology /technique development, tissue resource /registry behavioral /social science research tag, clinical research, human subject, neuropsychological test

Institution: MOUNT SINAI SCHOOL OF MEDICINE OF NYU
OF NEW YORK UNIVERSITY
NEW YORK, NY 100296574

Fiscal Year: 2007

Department: PATHOLOGY

Project Start: 01-SEP-2006

Project End: 31-JUL-2011

ICD: NATIONAL INSTITUTE ON AGING

Grant Number: 1R21HD047828-01

Project Title: Psychiatric Disorders /HIV Interface in Women in Congo

PI Information:

Name	Email	Title
RYDER, ROBERT W.	ryder@bu.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): University of North Carolina's School of Public Health (UNC), Johns Hopkins University's School of Medicine (JHU) and the African Studies Center, Department of Social and Cultural Anthropology, Catholic University (CU), Leuven, Belgium propose to strengthen the psychiatric disorders (PD) research capacity of the Center for Teaching and Research in Social Science for sub-Saharan Africa (CERDAS)/Kinshasa School of Public Health (KSPH), University of Kinshasa in Kinshasa, Congo. This multi-step research and capacity building process will occur through expansion/reinforcement of the existing CERDAS/KSPH partnership with UNC, JHU and CU. Our initial efforts will focus on: 1) The interplay between PD and incident and prevalent cases of HIV infection observed in large cohorts of pregnant women and their nuclear families we currently follow in Kinshasa's (population approximately 9 million) largest maternity, Kingasani Maternity (KM) (annual number of deliveries approximately 10,000) located in Ndjili (population approximately 2 million). Ndjili will also be the site for our community-based (CB) PD research. 2) The incidence and consequences of postnatal depression (PND) in this same KM population. Our studies will be CB. PD is often stigmatizing. CEDRAS/CU has conducted field research in Ndjili for 15+ years with traditional healers caring for patients with PD who sock treatment at "hidden" local healing sites operating out of contact with Western-orientated facilities. Our group has solid credible/effective contact with these local healers. Basing our studies at KM/Ndjili will further facilitate our efforts to reach into the target community to "unearth" patients with PD who would otherwise remain unenumerated (important in epi studies), undiagnosed and untreated. We intend to use the existing infrastructure at our highly effective prevention of mother to child HIV transmission intervention program at KM to study PD and PND in our population. In the R24 grant we will first identify essential areas for short-term research and assign KSPH MPH scholar physicians to conduct carefully mentored research. Carefully selected Brain Disorder Fellows (BDF) will receive 12 months mentored training in Leuven Baltimore/Chapel Hill. Returning to Kinshasa, BDF will receive re-entry grants for additional research projects to inform our R01 grant preparation. Periodic meetings in Kinshasa among all collaborators will enable us to collectively prepare a competitive R01 grant.

Thesaurus Terms:
Africa, African, HIV infection, comorbidity, female, mental disorder, mental health epidemiology, postpartum depression family, women's health clinical research, human pregnant subject

Institution: UNIVERSITY OF NORTH CAROLINA CHAPEL HILL
Office of Sponsored Programs
CHAPEL HILL, NC 27599

Fiscal Year: 2004
Department: EPIDEMIOLOGY
Project Start: 15-JUL-2004
Project End: 30-JUN-2006
ICD: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
IRG: ZNS1

Grant Number: 5R21TW006804-02

Project Title: Cerebral Malaria Associated Neurological Disorders in India

PI Information:

Name	Email	Title
STILES, JONATHAN K.	jstiles@msm.edu	ASSOCIATE PROFESSOR

Abstract: DESCRIPTION (provided by applicant): Plasmodium falciparum is the most common parasite to infect central nervous system and the leading cause of diffuse encephalopathy in young children. This encephalopathy is associated with 10-14% of mortality with an estimated annual death of 1-2.5 million annual deaths. P. falciparum is the most lethal species among the four human malaria parasites (P. falciparum, P. vivax, P. malariae, P. ovae) and it has been estimated that it infects 300-500 million people per year. About 1% of all cases of falciparum malaria results in cerebral malaria and thus affects central nervous system at least in 3 million people especially young children. In the absence of effective vaccine to protect against malaria coupled with the increasing anti-malaria drug resistance globally, malaria is re-emerging as a major public health threat in the tropics and subtropics. Most of the studies conducted to date to understand the long and short term effects of malaria on brain and brain function have focused largely on malaria-induced gross neurological defects but very little data is available on the impact of this disease on learning cognitive function and neuro-psychology. Previous studies in our laboratory using human post mortem brain and serum samples from West Africa indicated that RANTES and corresponding receptors CCR1, CCR3, and CCR5, play a very important role in brain immunopathogenesis that may result in neurological impairment or dysfunction. We hypothesize that cerebral malaria induces neurological impairment and reduces cognitive function. A corollary to this hypothesis is that this neurological impairment is mediated by immunopathogenesis. We propose a multidisciplinary international partnership involving Morehouse School of Medicine, Centers of Disease Control and the Medical Research Center (ICMR), Jabalpur, India to address the role of immunopathogenesis in malaria-induced neurological impairment following P. falciparum malaria in a population most affected by malaria in the sub-continent of India. The first specific aim will conduct preliminary retrospective and prospective epidemiological investigations to assess the extent of long-term neurological impairment associated with CM caused by P. falciparum in central India where falciparum malaria i s widespread. The second specific aim will conduct preliminary investigations to determine the potential immunopathological factors associated with neurological impairment after recovery from cerebral malaria. This proposal will pursue epidemiology and molecular immunology of cerebral malaria as well as capacity building in India. Data from the proposed research will reveal t he molecular basis of cerebral malaria induced neurological and cognitive impairment.

Thesaurus Terms:
India, central nervous system disorder, cerebral cortex, cognition disorder, encephalography, immunopathology, malaria, medical complication arthropod borne communicable disease, chemokine, cooperative study, cytokine receptor, learning disorder, longitudinal human study, nervous system disorder epidemiology, neuropsychology, receptor expression Plasmodium falciparum, blood chemistry, clinical research, enzyme linked immunosorbent assay, human subject, microarray technology, polymerase chain reaction, proteomics, statistics /biometry

Institution: MOREHOUSE SCHOOL OF MEDICINE
720 Westview Dr SW
ATLANTA, GA 30310

Department: MICROBIOLOGY, BIOCHEMISTRY & IMMUNOLOGY

Project Start: 28-SEP-2003

Project End: 28-FEB-2008

ICD: FOGARTY INTERNATIONAL CENTER

Grant Number: 5R01HD053216-02

Project Title: Pediatric HIV-encephalopathy in DRC: effect of ART & role of compartmentalization

PI Information: **Name** **Email** **Title**

VAN RIE, ANNELIES vanrie@email.unc.edu

Abstract: DESCRIPTION (provided by applicant): In contrast to the US and Europe, the pediatric HIV/AIDS epidemic in sub-Saharan Africa continues to expand. Perinatal HIV infection has a significant impact on brain development, and the achievement and maintenance of developmental milestones. Even though more than 80% of childhood HIV infections occur in Africa, the impact of HIV/AIDS on the health of African children remains poorly documented. No data exists on the impact of antiretroviral treatment on neurodevelopment in resource poor settings. The mechanisms of HIV neuroinvasion and neuropathogenesis over the course of infection remain largely unknown. Neurovirulent substrains may be responsible for the development of HIV-encephalopathy. The evolution of unique HIV lineages in the CNS has been shown to play a role in the development of HIV- associated dementia. No data are available on the potential role of HIV CNS compartmentalization in HIV encephalopathy in young children. We propose to conduct a prospective longitudinal community-based study to determine the first order (HIV exposure and infection) and second order (maternal AIDS and AIDS orphans) effects of the HIV epidemic on the neurodevelopment of young children in the Democratic Republic of Congo. We will also perform a cross- sectional characterization of HIV env compartmentalization in the CNS in HIV-infected infants (prior to initiating ART) to test the hypothesis that unique HIV env lineages are present in CNS versus peripheral compartments, and to provide insight into the pathogenesis of HIV-associated CNS disease in young children. Finally, we will perform a longitudinal characterization of HIV env CNS compartmentalization in children whose CNS manifestations do not reverse following ART. A better understanding of how HIV impacts neurodevelopment and causes encephalopathy in children would ultimately aid in the development of therapeutic strategies to prevent neurological complications experienced by children and adults alike.

Thesaurus Terms:
AIDS dementia complex, AIDS education /prevention, AIDS therapy, HIV infection, human therapy evaluation, nervous system disorder epidemiology, pediatric AIDS, virus infection mechanism
AIDS /HIV diagnosis, early diagnosis, gene expression, health disparity, health science research support, infant human (0-1 year), longitudinal human study, preschool child (1-5), virus genetics, virus load
Africa, clinical research, human subject, patient oriented research

Institution: UNIVERSITY OF NORTH CAROLINA CHAPEL HILL
Office of Sponsored Programs
CHAPEL HILL, NC 27599

Fiscal Year: 2007

Department: EPIDEMIOLOGY

Project Start: 01-AUG-2006

Project End: 31-MAY-2011

ICD: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

IRG: ZRG1

Grant Number: 1R21MH071214-01

Project Title: Neurodevelopment and HIV/AIDS

PI Information: **Name** **Email** **Title**

VAN RIE, ANNELIES vanrie@email.unc.edu

Abstract: DESCRIPTION (provided by applicant): The HIV/AIDS epidemic is one of the greatest humanitarian and health challenges facing the global community. The HIV/AIDS epidemic in sub-Saharan Africa has resulted in an explosion in the numbers of orphaned children and a rapidly expanding pediatric HIV/AIDS epidemic. Studies in the US and Europe have demonstrated that a major consequence of perinatal HIV infection is the significant impact on brain development and, subsequently, on the achievement and maintenance of developmental milestones. It is quite likely that in the coming decades, HIV will be the most frequent cause of neurodevelopmental delay in sub-Saharan Africa. Even though more than 80% of childhood HIV infections occur in Africa, the impact of HIV/AIDS on the health of African children remains poorly documented. The introduction of antiretroviral therapy will not only extend the survival but also profoundly affect the social and physical functioning of children and their families and change pediatric HIV/AIDS from an acute to a chronic disease requiring a comprehensive approach to care from birth through school-going age. The HIV epidemic is not only affecting HIV infected children but is making millions of children vulnerable. The illness of a parent marks the beginning of erosion of the family and trauma in the emotional and material life of a child. As educational opportunities are key components of a "safety net" program for vulnerable children, there is a need for studies to fully explore the neurodevelopmental consequences of being confronted with parents suffering from AIDS. During the two planning grant years, we will perform a cross-sectional study on the neurodevelopment of children confronted with HIV/AIDS, in order to build the capacity to perform a Iongitudinal cohort study on HIV-related neurodevelopment and central nervous system (CNS) disorders in the Democratic Republic of Congo (DRC). Although there is a pressing need for pediatric HIV/AIDS research, there is an equally great need for the training of qualified investigators, especially sub-Saharan Africans, to contribute to and lead research efforts. We propose to develop a North-South (US, Europe, DRC) and South-South (South Africa, DRC) collaborative "Neurodevelopment and HIV/AIDS" research program to investigate the neurodevelopment and CNS disorders of children confronted with HIV/AIDS and to contribute to the long-term goal of building sustainable capacity in neurodevelopmental research at the University of Kinshasa, DRC.

Thesaurus Terms:
child psychology, developmental disease /disorder, developmental neurobiology, epidemiology, pathologic process, pediatric AIDS child physical development, child welfare, child with disability, nervous system disorder epidemiology, parent deprivation Africa, behavioral /social science research tag, clinical research, human subject

Institution: UNIVERSITY OF NORTH CAROLINA CHAPEL HILL
Office of Sponsored Programs
CHAPEL HILL, NC 27599

Department: EPIDEMIOLOGY

Project Start: 29-SEP-2003

Project End: 31-AUG-2005

ICD: NATIONAL INSTITUTE OF MENTAL HEALTH

Grant Number: 1R21DA018086-01

Project Title: Neuro-Cognitive Aspects of Opiate Abuse & Antisocial Behavior

PI Information: **Name** **Email** **Title**

VASSILEVA, JASMIN L. jvassileva@psych.uic.edu

Abstract: DESCRIPTION (provided by applicant): Rates of heroin addiction are increasing worldwide with concomitant legal and health costs, including increased risk of HIV and hepatitis C viral transmission. However, at present it is difficult to impossible to study the consequences of "pure" heroin use since the majority of addicts are polysubstance-dependent. Further, co-morbid conditions, such as Antisocial Personality Disorder (APD) and psychopathy, additionally complicate the clinical picture and daily function of heroin-dependent persons. Study of the effect of drugs of abuse on the brain and the development of addiction are particularly difficult, due to difficulty in isolating drug effects on cognition from dysfunction associated with co-morbid conditions. We propose to develop a program of studies with the long-term goals of investigating neurocognitive aspects of brain function in drug addicts with and without a diagnosis of ASPD / psychopathy. This program will be developed in Bulgaria, a low-middle income country in Southeastern Europe with significantly high prevalence of heroin addiction. Bulgaria's geographical position make it a key country on the "Balkan Drug Route", one of the main routes for international drug traffic from South-West Asia to Western Europe, through which approximately 80% of the heroin currently used in Western Europe passes. Consequently, heroin is easily available in the country, and in fact heroin addiction has become one of the most significant health and legal problems. Patterns of heroin addiction in Bulgaria are unique in that polysubstance dependence is uncommon. Consequently study of Bulgarian addicts provides a unique opportunity to evaluate neurocognitive and psychiatric consequences of relatively "pure" heroin use. In addition, the nature of the Bulgarian legal system facilitates the opportunity to study heroin dependent subjects both with and without APD because all detainees arrested for drug-related charges undergo mandated medical and psychiatric evaluation prior to disposition of their cases. We have partnered with physicians and mental health professionals in Sofia who have access to a large population of pre-trial detainees, a large majority of whom have been detained for drug-related crimes. Research on addiction and its neuro-cognitive consequences is minimal in Bulgaria, despite a significant need to address these concerns. In the proposed project the PI, her colleagues the University of Illinois-Chicago, and at the Clinic of Forensic Psychiatry and Psychology at the State University Hospital of Neurology and Psychiatry in Sofia, Bulgaria, will initiate the development of resources for studies of neuro-cognitive function in heroin addicts with and without APD/psychopathy, and without polysubstance dependence. This preliminary work will culminate in a pilot study of neuro-cognition in heroin addicts with and without ASPD/psychopathy and an R01 application based on these pilot findings and other hypotheses developed in the course of the two years.

Thesaurus Terms:
drug addiction, heroin, neurophysiology, psychometrics, psychopathology antisocial personality, cognition, comorbidity, cooperative study, decision making, health science research support, international cooperation, legal /correctional, neurotoxicology, psychological test, short term memory Europe, behavioral /social science research tag, clinical research, human subject

Institution: UNIVERSITY OF ILLINOIS AT CHICAGO
310 AOB, M/C 672
CHICAGO, IL 60612

Fiscal Year: 2003

Department: PSYCHIATRY

Project Start: 30-SEP-2003

Grant Number: 1R21AA016747-01

Project Title: Fetal Alcohol Spectrum Disorders in the Phase 1 cohort of the Safe Passage Study

PI Information:

Name	Email	Title
VYTHILINGUM, BAVANISHA	bv@sun.ac.za	

Abstract: DESCRIPTION (provided by applicant): In the Western Cape of South Africa, Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Spectrum Disorders (FASD) continue to be a significant public health problem, with rates of FAS of over 70/1000, the highest reported rates in the world. Unfortunately, the diagnosis of FASD is usually only made once a child has begun school or even later, thus a missing a critical developmental window for intervention. The PASS Research Network is a collaborative project that aims to delineate the roles of prenatal alcohol exposure in SIDS and unexplained stillbirth and has completed a pilot study in Cape Town, South Africa. Consequently, this study has collected a vast amount of information on alcohol exposure and neurobehavioral and physiological data in the prenatal and early infancy periods, and represents one of the few prospective collections of this data. We propose to create an infrastructure that allows us to follow the children enrolled in this pilot study through age 2. This would afford us the opportunity to compare vast amount of information collected and relate this information to neurobehavioral and physiological changes that manifest during the toddler years, helping us to determine early markers for FASD. It would also us to assess feasibility for follow up of the much larger cohort that will be enrolled into the PASS study in Phase II. Accordingly, the additional aims of this study include identifying areas at the Cape Town site that would limit feasibility of follow up studies, developing strategies to rectify these limitations, and building local capacity in neurodevelopmental assessment, research skills and data management. Despite numerous efforts at intervention, use of alcohol in pregnant women the Western Cape remains high. By identifying early markers of FASD, this project aims to contribute to earlier diagnosis and thus intervention during critical developmental phases.

Thesaurus Terms:
Africa, alcoholic beverage consumption, early diagnosis, embryo /fetus toxicology, fetal alcohol syndrome, heart rate biomarker, child psychology, developmental disease /disorder, frustration, longitudinal human study, teratogen clinical research, human subject, infant human (0-1 year), neuropsychological test, preschool child (1-5)

Institution: STELLENBOSCH UNIVERSITY TYGERBERG CAMPUS
BOX 19063
TYGERBERG, 7505

Fiscal Year: 2007

Department:

Project Start: 01-SEP-2007

Project End: 31-AUG-2009

ICD: NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

IRG: ZRG1

Grant Number: 1R21ES013109-01

Project Title: Prenatal pesticide exposure in South Africa: CNS Effects

PI Information:

Name	Email	Title
WHITE, ROBERTA F.	rwhite@bu.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): Due to endemic contamination of the environment in areas of South Africa by pesticides used in agriculture and for disease prevention, the neurotoxicity of these substances is of major concern as a health hazard among inhabitants of rural areas. Several classes of pesticides are known to be neurotoxic in adult populations with occupational and environmental exposures to them and some pesticides are well established as endocrine disruptors, affecting sexual maturation during prenatal growth and in children. However, very little is known about the effects of these chemicals on central nervous system (CNS) development in utero and in early childhood. Knowledge concerning the neurodevelopmental effects of these substances is of critical importance because of the fragility of the brain in early development, the known structural and neurochemical effects of pesticides on the brain, and potential neurotoxicity during development secondary to endocrine disruption. Children in South Africa are particularly susceptible to the effects of environmental exposure to pesticides in utero because of maternal exposure to pesticides. This work has important public health implications in South Africa, including documentation of the severity and types of pesticide exposure identified through biological and environmental assessments and the acquisition of new knowledge concerning the neurodevelopmental effects of exposures to these chemicals. Such knowledge will be important for public health policy in South Africa, including development of primary prevention and educational programs designed to reduce exposure and adverse health effects. It was also be applicable to development of public health policy in other parts of the world, including the United States. Longitudinal investigation of the effects of prenatal pesticide exposure on neurodevelopment of children in South Africa is the long-range goal of the work proposed in this application for pilot funding. The procedures described in the proposal will be pursued in order to develop the collaborative mechanisms, pilot methods, and feasibility studies that will facilitate the design and completion of such an investigation. The communities of interest are rural areas in KwaZulu-Natal, where pesticide contamination is widespread. Collaboration between district health personnel, scientists at the University of Cape Town and the University of Natal in South Africa, and investigators at Boston University is key to the project.

Thesaurus Terms:
Africa, developmental neurobiology, embryo /fetus toxicology, environmental exposure, pesticide biological effect health disparity, hormone inhibitor, longitudinal human study, neurogenesis, neuropsychology, rural area
African, clinical research, human subject

Institution: BOSTON UNIVERSITY MEDICAL CAMPUS
715 ALBANY ST, 560
BOSTON, MA 021182394

Fiscal Year: 2003
Department: ENVIRONMENTAL HEALTH
Project Start: 30-SEP-2003
Project End: 31-JUL-2005
ICD: NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
IRG: ZNS1

Grant Number: 1R21AG028187-01A1

Project Title: Immunization Approaches for Alzheimer's Disease

PI Information: Name	Email	Title
WISNIEWSKI, THOMAS M.	thomas.wisniewski@med.nyu.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): This proposal seeks to develop a collaboration between the PI and Dr. Goni and Dr. Chabalgoity at the University of Uruguay. The Pi's laboratory is developing a novel immunization approach which is non-toxic for the treatment of Alzheimer's disease (AD) related amyloid in model mice, as well as vaccination to treat prion diseases. A major problem with vaccination approaches for these disorders in humans is potential toxicity. Both Dr. Goni and Chabalgoity are Immunologists, with Dr. Chabalgoity having a long experience with the development of various vaccines. The toxicity noted with the AD vaccine in humans has been linked to excessive cell mediated immunity, resulting in encephalitis in a about 6% of patients, whereas the beneficial amyloid clearing effects have been associated with humoral immunity. One way of inducing primarily a humoral, antibody mediated immune response is to induce mucosal immunity. We propose: 1. To develop mucosal active immunization for use in Alzheimer transgenic model mice using Salmonella vaccine strains, with the aim of inducing primarily a humoral immune response which will not be associated with toxicity. These will be used in conjunction with our Aft homologous peptides, which are non fibrillogenic and non-toxic. 2. Behavioral studies will be done and the amyloid burden will be determined in vaccinated and control AD model mice. The presence of any hemorrhages will be assessed. These histological measurements will be correlated with Ali peptide brain levels both in the soluble and insoluble fractions. 3. In the AD model animals the Th-1 versus Th-2 response will be monitored by the profile and magnitude of cytokine production as well as specific antibody titers in the Gl tract and systemically. In order to characterize the kind of humoral immune response generated, monoclonal antibodies will be produced using lymphocytes extracted from the Peyer's patches and spleens of mice with a positive outcome. This proposal will greatly enhance capacity building at the University of Uruguay with the transfer of AD transgenic model expertise and monoclonal antibody production capability. In addition it will produce preliminary data for the development of potentially non-toxic vaccination approaches for the treatment of AD. Lay Summary: AD is the most common cause of dementia. Vaccination is potentially an effective treatment, but is associated with significant toxicity in about 6% of patients. We propose studies to help develop safe, effective vaccines.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: NEW YORK UNIVERSITY SCHOOL OF MEDICINE
550 1ST AVE
NEW YORK, NY 10016

Fiscal Year: 2007

Department: NEUROLOGY

Project Start: 15-APR-2007

Project End: 31-MAR-2009

ICD: NATIONAL INSTITUTE ON AGING

IRG: ZRG1

Grant Number: 1R21MH080612-01

Project Title: Research and Training on HIV/AIDS Neuropathogenesis in Zambia

PI Information:

Name	Email	Title
WOOD, CHARLES	cwood1@unl.edu	UNIVERSITY PROFESSOR

Abstract: DESCRIPTION (provided by applicant): A substantial number of untreated HIV-1 patients ultimately develop HIV-associated neurological diseases, including dementia (HAD). However, in sub-Saharan Africa, where the impact of the AIDS pandemic is most devastating, the total impact of HIV-associated neurological diseases is unknown. This represents a critical gap in scientific knowledge because almost two-thirds of the individuals living with HIV/AIDS reside in sub-Saharan Africa - a number of the countries in the region have infection rates to as high as 30 - 40% of their total population. Our long-term research goal is to understand the neuropathogenesis of HIV infection, the impacts of AIDS-associated neurological diseases and antiretroviral treatment on HAD in the African setting, and to design effective interventions to prevent or impede HAD development. However, the goal of this R21 planning grant application is to determine the impact and extent of HIV-associated neurological diseases in Zambia and to build the necessary in-country capacity for conducting HIV-1 neuropathogenesis research. The need for the proposed work is exacerbated by the fact that HIV-1 prevalence rate in Zambia is one of the highest in sub-Saharan Africa The proposed study represents a new direction for the participating investigators and leverages infrastructure established by the University of Nebraska-Lincoln, the University of Miami, the University of Zambia School of Medicine, and the University Teaching Hospital for research and training regarding HIV-1 and AIDS and their associated malignancies. The project goal will be achieved by completing three specific aims: 1) developing tools needed to evaluate the extent of HIV- associated neurological diseases in Zambia; 2) determining the prevalence and underlying pathology of HIV-associated dementia in subtype C infected individuals in Zambia; and 3) providing short-term training for Zambian neurologists, pathologists, and neurovirologists - both in-country and in the U.S. - to develop the tools and technology needed to address the first two proposed aims and to develop the neuroAIDS research infrastructure. The proposed work will lay the necessary foundation for a Zambian HIV-1 neuropathogenesis program by linking U.S. and Zambian partners, and by providing the necessary training and support to generate crucial preliminary data regarding the extent of HIV-associated neurological diseases in Zambia. The preliminary data collected as part of this effort will serve as the basis for a follow-up R01 application.

Thesaurus Terms:
AIDS dementia complex, AIDS therapy, Africa, antiAIDS agent, disease /disorder etiology, human immunodeficiency virus 1, neuropathology, neuropharmacology, training brain injury, cell type, workshop
clinical research, human subject, neuropsychological test, postmortem, tissue resource /registry

Institution: UNIVERSITY OF NEBRASKA LINCOLN
LINCOLN, NE 685880430
Fiscal Year: 2007
Department: CENTER FOR VIROLOGY
Project Start: 01-AUG-2007
Project End: 31-JUL-2009
ICD: NATIONAL INSTITUTE OF MENTAL HEALTH
IRG: ZRG1

Grant Number: 1R21DA021422-01A1

Project Title: Brain Changes with Cannabis and Methamphetamine

PI Information: Name	Email	Title
YURGELUN-TODD, DEBORAH A.	ytodd@mclean.harvard.edu	ASSOCIATE PROFESSOR

Abstract: DESCRIPTION (provided by applicant): The overall aims of this revised proposal are to build on existing MRI/functional MRI capacity in South Africa and to apply newly implemented structural and functional imaging techniques to examine brain function in adolescents of the Western Cape region of South Africa who are heavy users of methamphetamine alone or in combination with cannabis. Over the past several years we have initiated a research collaboration between the Brain Imaging Center (BIC) at McLean Hospital, Harvard Medical School and the Brain Imaging Group (BIG) at the University of Stellenbosch made possible through a NIDA sponsored supplementary grant award. The proposed R21 is designed to consolidate and extend this collaboration by training collaborative South African partners in MR methodology and the application of MR techniques while simultaneously collecting data on the effects of methamphetamine and cannabis use. Functional magnetic resonance imaging capacity, recently installed in South Africa, will be expanded by a) providing workshops and tutorials on fundamental concepts underlying MR methods; b) describing strategies for optimization of structural and functional imaging protocols in order to maximize image quality and facilitate optimal co- registration of functional to structural data at the individual level; c) reviewing approaches for development and validation of neurocognitive activation paradigms for use with fMRI; d) training of South African investigators in image processing and analysis of morphometric and functional imaging data to develop independent image analysis capacity using SPM and brain voyager software and; e) evaluating hardware and software needs for implementing MR spectroscopy. These fMRI techniques will be applied to test the hypothesis that frontal dysfunction, as measured by reduced BOLD signal in the anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex (DLPFC) will be present in adolescents, aged 13-17, of the Western Cape region of South Africa, who are heavy users of methamphetamine alone (n=10) or in combination with cannabis (n=10), relative to matched non-using controls (n=10). An R01 application will then be prepared based on the data acquired during the R21 period.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: MC LEAN HOSPITAL (BELMONT, MA)
115 MILL STREET
BELMONT, MA 02478

Fiscal Year: 2007

Department:

Project Start: 01-JUL-2007

Project End: 31-MAY-2009

ICD: NATIONAL INSTITUTE ON DRUG ABUSE

IRG: ZRG1

Grant Number: 1R01TW008040-01A1
Project Title: Development Stress, Exercise, and Vulnerability to Neuronal Injury

PI Information:	Name	Email	Title
	ZIGMOND, MICHAEL J.	zigmond@pitt.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): Researchers representing the University of Pittsburgh and two institutions in South Africa, the University of Cape Town and the University of Stellenbosch are seeking funds as part of an overall effort between our institutions to examine a specific hypothesis pertaining to the impact of environment on brain and behavior and also to help create within the academic community in Cape Town a regional center of excellence in neuroscience and in professional skill training. Their hypothesis is that exposure of developing animals to severe stress will have a significant detrimental effect on brain and increase its vulnerability to neuronal death, but that this can be offset through an exercise intervention program. There are five specific aims: four are research aims and one is a set of capacity building objectives. Research objectives: Aim 1 - To examine the impact of a developmental stressor (maternal separation) on several variables related to the vulnerability of the brain, including (a) the hypothalamic-pituitary-adrenal (HPA) axis, (b) mitochondrial function, and (c) alterations in a specific class of proteins (neurotrophic factors) by using a proteomic screen. Aim 2 - In addition, the state of central dopamine neurons will be carefully examined. Aim 3 - To examine the effects of exercise (voluntary running) on these same variables, and then to determine whether the effect of maternal separation can be offset by later exposure to exercise. Aim 4 -To examine the effects of maternal separation on the vulnerability of dopaminergic neurons to oxidative stress using 6- hydroxydopamine as the stressor, then determine whether any increase in vulnerability caused by the maternal separation can be offset by exercise. Aim 5 - Capacity building objectives: To further develop the research capacity of the Universities of Cape Town and Stellenbosch as well as other institutions in the Western Cape through attendance by faculty and trainees at international meetings, participation in specific courses on research methodology, and provision of instruction in other professional skills, such as oral and written communication, applying for research funds, and responsible conduct of research. The research team believes that their research project will provide important insights into epigenetic influences on behavior and brain function more generally, and also serve as a context for promoting the research capacity of two key institutions in southern Africa.

Thesaurus Terms:
There are no thesaurus terms on file for this project.

Institution:	UNIVERSITY OF PITTSBURGH AT PITTSBURGH 350 THACKERAY HALL PITTSBURGH, PA 15260
Fiscal Year:	2007
Department:	NEUROLOGY
Project Start:	01-APR-2007
Project End:	28-FEB-2011
ICD:	FOGARTY INTERNATIONAL CENTER
IRG:	ZRG1

Grant Number: 1R01TW008040-01A1

Project Title: Development Stress, Exercise, and Vulnerability to Neuronal Injury

PI Information:

Name	Email	Title
ZIGMOND, MICHAEL J.	zigmond@pitt.edu	PROFESSOR

Abstract: DESCRIPTION (provided by applicant): Researchers representing the University of Pittsburgh and two institutions in South Africa, the University of Cape Town and the University of Stellenbosch are seeking funds as part of an overall effort between our institutions to examine a specific hypothesis pertaining to the impact of environment on brain and behavior and also to help create within the academic community in Cape Town a regional center of excellence in neuroscience and in professional skill training. Their hypothesis is that exposure of developing animals to severe stress will have a significant detrimental effect on brain and increase its vulnerability to neuronal death, but that this can be offset through an exercise intervention program. There are five specific aims: four are research aims and one is a set of capacity building objectives. Research objectives: Aim 1 - To examine the impact of a developmental stressor (maternal separation) on several variables related to the vulnerability of the brain, including (a) the hypothalamic-pituitary-adrenal (HPA) axis, (b) mitochondrial function, and (c) alterations in a specific class of proteins (neurotrophic factors) by using a proteomic screen. Aim 2 - In addition, the state of central dopamine neurons will be carefully examined. Aim 3 - To examine the effects of exercise (voluntary running) on these same variables, and then to determine whether the effect of maternal separation can be offset by later exposure to exercise. Aim 4 -To examine the effects of maternal separation on the vulnerability of dopaminergic neurons to oxidative stress using 6- hydroxydopamine as the stressor, then determine whether any increase in vulnerability caused by the maternal separation can be offset by exercise. Aim 5 - Capacity building objectives: To further develop the research capacity of the Universities of Cape Town and Stellenbosch as well as other institutions in the Western Cape through attendance by faculty and trainees at international meetings, participation in specific courses on research methodology, and provision of instruction in other professional skills, such as oral and written communication, applying for research funds, and responsible conduct of research. The research team believes that their research project will provide important insights into epigenetic influences on behavior and brain function more generally, and also serve as a context for promoting the research capacity of two key institutions in southern Africa.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: UNIVERSITY OF PITTSBURGH AT PITTSBURGH
350 THACKERAY HALL
PITTSBURGH, PA 15260

Fiscal Year: 2007
Department: NEUROLOGY
Project Start: 01-APR-2007
Project End: 28-FEB-2011
ICD: FOGARTY INTERNATIONAL CENTER
IRG: ZRG1

Grant Number: 5R01NS055627-02

Project Title: Retrovial Infections of the Nervous System in Peru

PI Information:

Name	Email	Title
ZUNT, JOSEPH R.	jzunt@u.washington.edu	ASSOCIATE PROFESSOR

Abstract: DESCRIPTION (provided by applicant): The overarching goals of this RO1 application are to study the clinical epidemiology and pathogenesis of retroviral, opportunistic and tropical infections of the nervous system in Peru, building on research collaborations and investigations initiated during the R21 grant entitled "Central Nervous System Infections in Peru"; and to continue development of neurologist investigators in academic and research institutions in selected cities throughout Peru. The specific aims of this grant are to 1) define the risk determinants and clinical manifestations of HTLV-II, HTLV-I, HIV infections and of coinfections with two or more of these three retroviral pathogens in the four largest cities in Peru; 2) establish a national reference center for clinical research on HTLV infection for conduct of cohort studies of the natural history, clinical manifestations, and pathogenesis of HTLV-I and -II infections in persons referred from blood banks; and 3) examine the influence of these three retroviral infections on the natural history of opportunistic and tropical infections of the CNS in persons with retroviral infection. During our R21 planning grant, we discovered that HTLV-II infection was unexpectedly prevalent in selected populations in Lima (the capital) and two of the largest cities in the Amazon Jungle. In addition, we developed research collaborations with neurologists in Lima (the capital), Iquitos (Jungle), Arequipa (Andes Mountains), and Trujillo (Coast), and determined the most common manifestations of neuroAIDS in Iquitos and Arequipa; and through conferences and in-country training, provided research and human subjects training to over 200 experienced and new clinical investigators - many of them neurologists. Concurrently, UW-led HIV/AIDS-related research funding in Peru has grown to $5,000,000 per year from NIH and from private foundations, providing an outstanding foundation for further development of a CNS retroviral research program. The Collaborative Network for Tropical Neurologic Infectious Diseases established with researchers in nongovernmental and Ministry of Health institutions in Peru, with the U.S. Naval Medical Research Center Detachment (NMRCD) in Peru, and with Universities in Peru and the United States, will support future research on the clinical epidemiology of retroviral infections and their interactions with emerging tropical infections in Peru and eventually the Andean Region. In addition to continuing our investigations, we plan to continue training activities to address the research, education, training, and mentoring needs and opportunities related to CNS infection identified during the R21 planning grant.

Thesaurus Terms:

There are no thesaurus terms on file for this project.

Institution: UNIVERSITY OF WASHINGTON
Office of Sponsored Programs
SEATTLE, WA 98105

Fiscal Year: 2007

Department: NEUROLOGY

Project Start: 10-SEP-2006

Project End: 31-MAY-2011

ICD: NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

IRG: ZRG1

Grant Number: 1R21NS048838-01

Project Title: Central Nervous System Infections in Peru

PI Information:

Name	Email	Title
ZUNT, JOSEPH R.	jzunt@u.washington.edu	ASSOCIATE PROFESSOR

Abstract: DESCRIPTION (provided by applicant): This R21 application proposes further development of research collaborations between the University of Washington and the Instituto de Ciencias Neurologicas (ICN), the only tertiary referral center for neurologic disease in Peru. The primary goal of this grant will be to carry out necessary pilot studies to inform the planning and preparation for an application for funding of research on CNS infections affecting Peruvians, emphasizing: 1) HIV/AIDS and HIV co-infection; and 2) acute viral meningoencephalitis. Current UW-led HIV/AIDS research in Peru is supported by NIH, and from a private foundation, the Wellcome Trust, and provides an excellent foundation for development of a NeuroAIDS research program. Of particular interest will be research on the pathogenesis, clinical epidemiology, and management of AIDS-related co-infections of the CNS, including neurocysticercosis a very common and well studied condition in Peru and multidrug-resistant tuberculosis, which affects 43% of HIV-infected individuals with TB in Lima. Peru also provides a good opportunity for research on tropical meningoencephalitis, capitalizing on a recently established Global Emerging Infections Surveillance (GELS) system coordinated by the U.S. Navy Medical Research Center Detachment (NMRCD) in Peru, which provides the unique opportunity to leverage addition of sentinel surveillance for acute meningoencephalitis. In collaboration with investigators at the University of Texas-Galveston, such a system could support future research on clinical epidemiology of emerging problems in tropical viral meningoencephalitis, such as dengue and West Nile viruses, in Peru. At the beginning of the initial year, with the assistance of our External Advisory Committee, and a team of internationally-recognized co-investigators and Peruvian investigators, we will conduct research workshops to assess research, education, training, and mentoring needs and opportunities related to NeuroAIDS and acute meningoencephalitis at the ICN; followed soon by development of a preliminary research agenda and initiation of relevant pilot studies. The second year will be used to complete and analyze these pilot studies and prepare the R01 application.

Thesaurus Terms:
AIDS /HIV neuropathy, Peru, central nervous system, comorbidity, emerging infectious disease, health science research support, infectious encephalitis, nervous system disorder epidemiology, nervous system infection
AIDS education /prevention, AIDS therapy, Cestoda, Cryptococcus neoformans, Enterovirus, Toxoplasma gondii, West Nile virus, antiAIDS agent, cognition, counseling, dengue virus, health science research potential, human T cell lymphotropic virus type 1, human immunodeficiency virus, international cooperation, neurologic manifestation, opportunistic infection, training, tuberculosis AIDS /HIV test, clinical research, human subject, mass screening, serology /serodiagnosis

Institution: UNIVERSITY OF WASHINGTON
Office of Sponsored Programs
SEATTLE, WA 98105

Fiscal Year: 2003
Department: NEUROLOGY
Project Start: 30-SEP-2003
Project End: 31-AUG-2005
ICD: NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
IRG: ZNS1