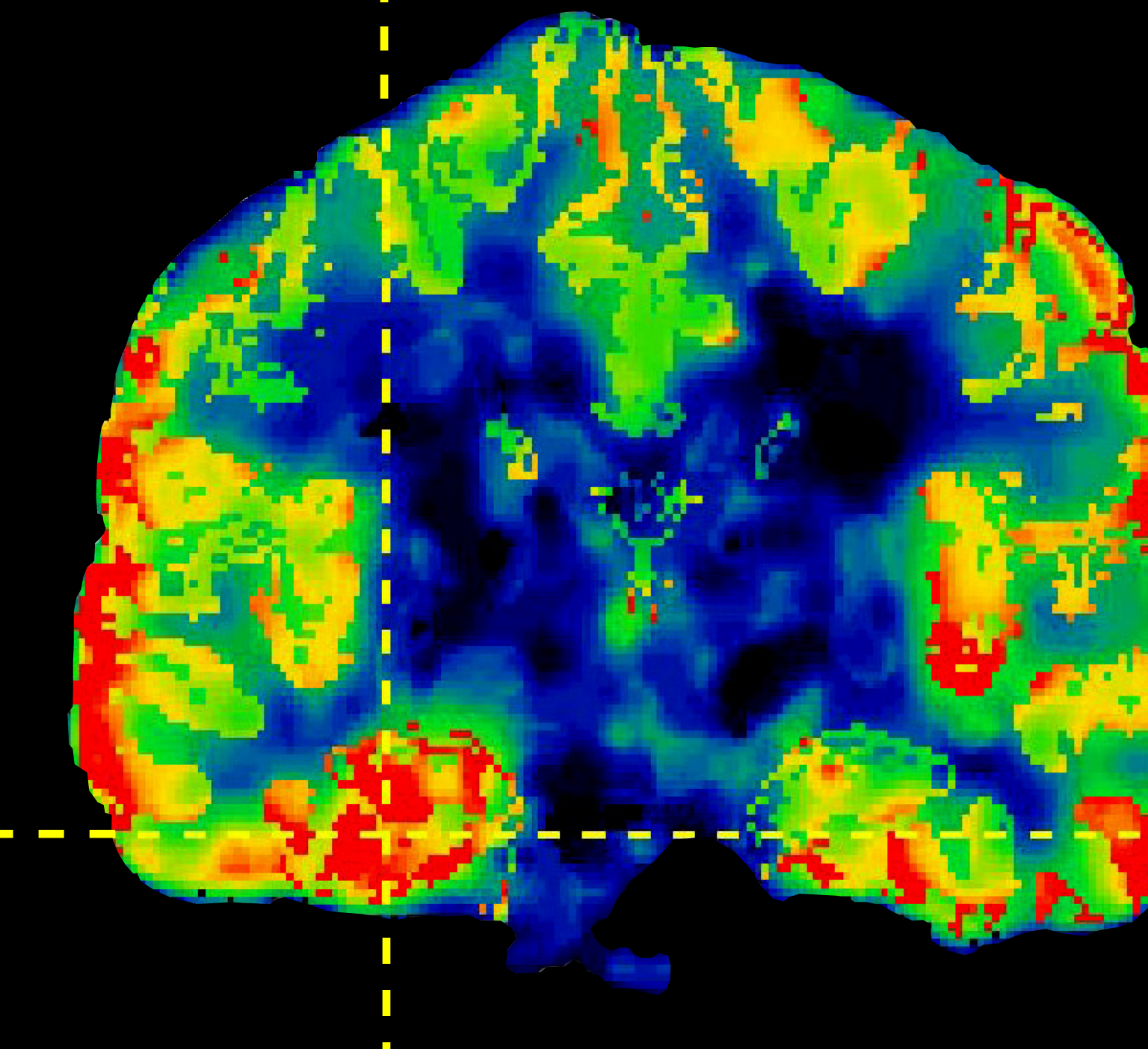
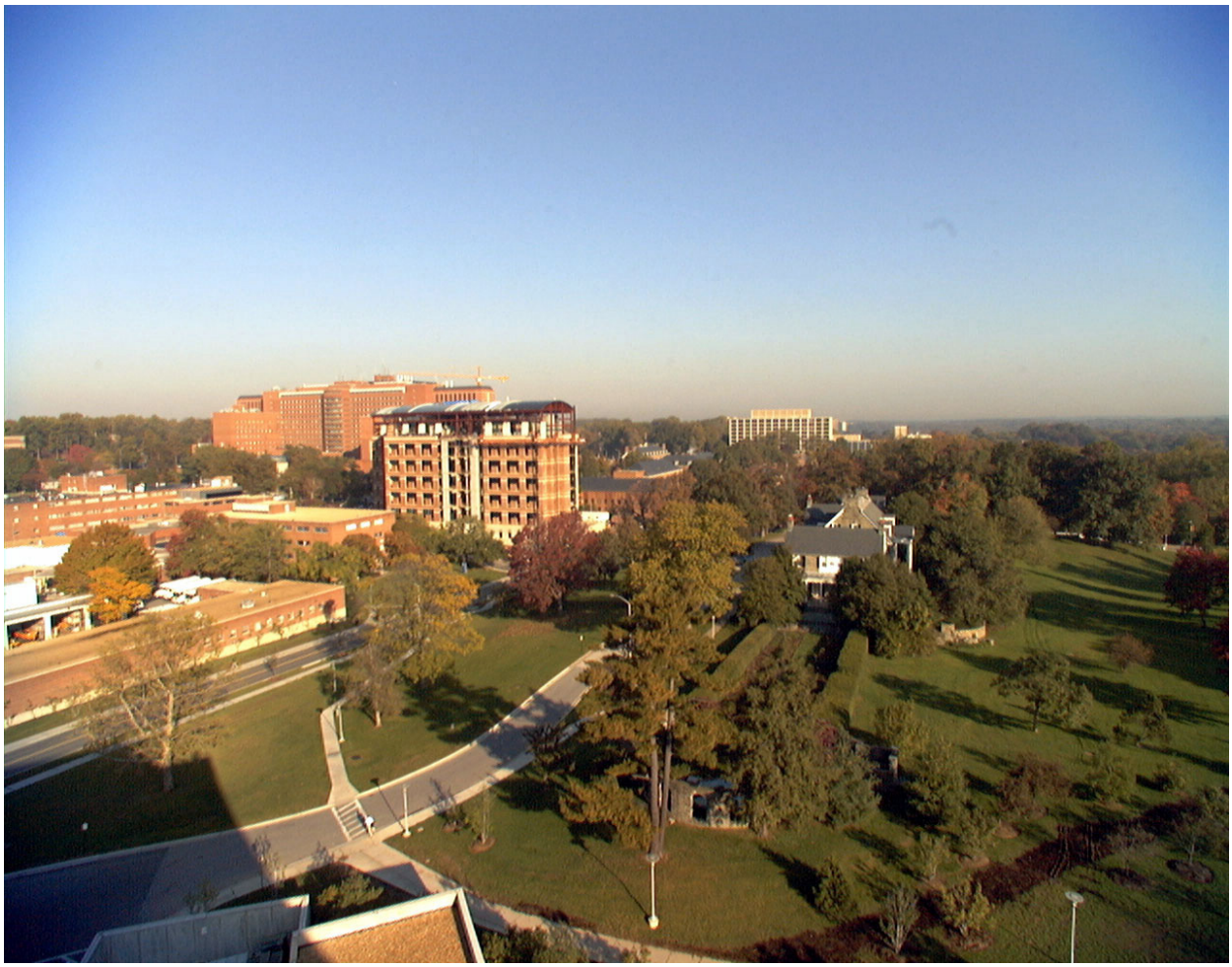
The Clinical Research Program in NINDS





Clinical Training Opportunities
National Institute of Neurological Disorders and Stroke (NINDS)
National Institutes of Health (NIH)

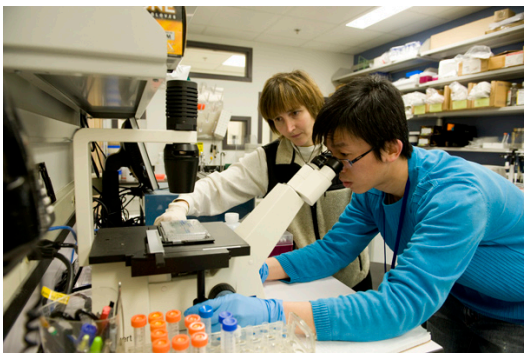
The NINDS intramural clinical program on the NIH campus in Bethesda Maryland offers a unique training and research environment for clinicians interested in becoming physician-scientists. The campus has over 10,000 scientists who work in Basic Science Laboratories and Clinical Branches of the nineteen NIH institutes and centers. The campus houses the Clinical Center, a 240-bed hospital dedicated solely to research. The Bethesda campus is conveniently located just outside Washington D.C., with museums, galleries and cultural activities all just a few stops away on the Washington subway Metro line.

NINDS Clinical Fellowship Programs

Traditionally, the clinical research groups in NIH are organized within Branches, Sections and Units. All provide opportunities to participate in basic and clinical research focusing on disease mechanisms and treatment of a variety of neurological disorders. Clinics associated with each group provide in-depth training in a subspecialty area – movement disorders, neuroimmunology, neurogenetics, stroke, neurorehabilitation, epilepsy, or clinical neurophysiology. The training opportunities in research methods within each group range from molecular biology, biochemistry, cell biology, immunology, genetics, pharmacology, neurophysiology, imaging or clinical trials. The length of training and relative balance of clinical responsibilities and research time of each Branch or Section's clinical fellowship can be viewed on the NINDS website: http://intra.ninds.nih.gov/training/clinicalfellowships.asp.

Applications for clinical fellowships should be made directly to the Branch, Section or Unit Chiefs, as listed in the following paragraphs and on the website noted above.

Neuroimmunology



The Neuroimmunology Branch (NIB) conducts both basic immunological and clinical research into immunologically mediated diseases of the nervous system with particular focus on multiple sclerosis (MS) and HTLV-1 associated neurologic disease. This is a 2-year fellowship with possible extension for up to 5 years, depending on research interests. The fellowship is uniquely suited for individuals who want to pursue a career of physician-scientist and offers opportunity to develop all necessary skills for this career path. All clinical fellows spend about 20% of their time in clinical care activities. The remaining time can be spent either in clinical research or in the laboratory with one of the senior scientists in the Branch. The following areas of research are currently active in the NIB:

- Characterization of the cellular immune response to antigens possibly related to the cause of diseases such as MS
- Characterization of the mechanisms maintaining immune tolerance and their dysfunction in patients with MS
- Studies of virological mechanisms contributing to immunologically mediated diseases of the nervous system
- Development of new therapies in MS and their testing in Phase I/II clinical trials

- Examination of the value of MRI, especially newer imaging techniques, in assessing the natural history and effect of new therapies in MS
- Exploration of immunological and molecular biology techniques; e.g., cDNA microarrays and quantitative PCR, to develop biomarkers for MS

Contacts: Dr. Henry F. McFarland, Chief, NIB,
301-496-1801 (mcfarlandh@ninds.nih.gov)

Dr. Bibiana Bielekova, Investigator, NIB,
301-402-4488 (bielekovab@ninds.nih.gov)

Dr. Steve Jacobson, Senior Investigator, NIB,
301-496-0519 (jacobsons@ninds.nih.gov)

Neurogenetics

The Neurogenetics Branch (NGB) investigates the causes of hereditary neurological diseases with the goal of developing effective treatments for these disorders. Particular areas of research interest include the poly-glutamine expansion diseases (Huntington's disease, Kennedy's disease, and spinocerebellar ataxia), spinal muscular atrophy, muscular dystrophy, hereditary motor neuron disease, and Friedreich's ataxia. The disease mechanisms are studied in cell culture and animal models. Therapeutic trials are currently underway for Kennedy's disease and under consideration for other disorders. A genetic outreach program is in place to identify and characterize patients and families with hereditary neurological diseases.

Contact: Dr. Kenneth H. Fischbeck, Chief, NGB,
301-435-9318 (kf@ninds.nih.gov)

The Cellular Neurology Unit (CNU) investigates the causes underlying hereditary neurological diseases, with a particular focus on the hereditary spastic paraplegias. Disease mechanisms are studied in cell culture and animal models, with an emphasis on detailed cell biological studies in both neuronal and non-neuronal cell types. Current disease-related cellular processes under investigation include mitochondrial and ER dynamics and shaping, autophagy, and endocytosis. In conjunction with these studies, clinical genetic studies are performed to characterize additional families with both new and previously known inherited neurological disorders.

Contact: Dr. Craig Blackstone, Chief, CNU,
301-451-9680 (blackstc@ninds.nih.gov)

Movement Disorders

The Human Motor Control Section (HMCS) offers a Movement Disorders Fellowship. The general mission of the Section is to understand the physiology of normal human voluntary movement and the pathophysiology of different movement disorders. The main techniques employed are: electroencephalography (EEG) and magnetoencephalography (MEG), neuroimaging with positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), transcranial magnetic stimulation (TMS), reflex studies, and biomechanics. The research focuses on problems such as how the brain makes and learns skilled movements. The principal diseases studied are Parkinson disease, dystonia, cerebellar ataxia, psychogenic movement disorders, myoclonus, tremor, tic and startle disorders.

Contact: Dr. Mark Hallett, Chief, HMCS,
301-496-9526 (hallettm@ninds.nih.gov)

Stroke

The Clinical Investigations Section of the Stroke Branch (SB) studies of the intracellular signaling and gene expression that regulate tolerance to ischemia are conducted in primary cultures, preclinical animal models, genetically modified mice, and hibernating ground squirrels. Inflammatory and immune mechanisms for stroke initiation and progression are also studied. When potential targets for stroke prevention or treatment are identified in preclinical models, the findings are translated into proof of principle clinical trials.

Contact: Dr. John M. Hallenbeck, Chief, SB,
301-496-6231 (hallenbj@ninds.nih.gov)

The Stroke Diagnostics and Therapeutics Section (SDTS) offers a cerebrovascular fellowship. This fellowship provides clinical and research training in acute stroke patient management at the NIH Stroke Program. The program is oriented towards emergency management of cerebrovascular disease with emphasis in neuroimaging, thrombolysis, and other novel therapeutic and diagnostic approaches. The program runs two acute stroke care and research centers in the Washington, D.C., metropolitan area with state-of-the-art dedicated MRI facilities (1.5 T and 3.0 T). The fellows will be provided the opportunity to develop expertise in the management of acute stroke patients, and in applying modern neuroimaging techniques to stroke management.

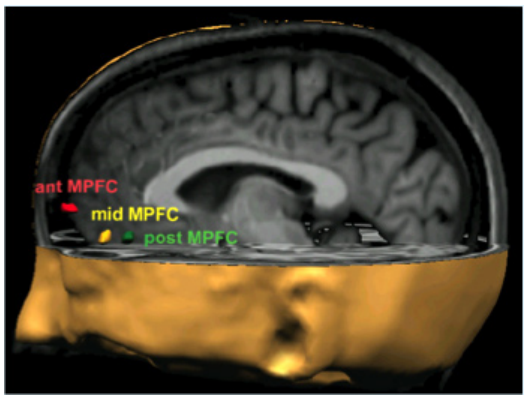
Contact: Dr. Steven J. Warach, Chief, SDTS,
301-435-9321 (warachs@ninds.nih.gov)

Neurorehabilitation

The goal of the Human Cortical Physiology and Stroke Neurorehabilitation Section (HCPS) is to understand the mechanisms underlying plastic changes in the human central nervous system and develop novel therapeutic approaches for recovery of function based on these advances. A multimodality approach is applied to the understanding of mechanisms of plasticity including transcranial magnetic stimulation, PET scanning, fMRI, and EEG. Research protocols are focused on the evaluation of patients with stroke, amputations, and blindness, and to the study of plasticity in healthy volunteers. On the basis of these mechanisms, we are starting to design and test interventions to improve motor disability after human diseases; for example, stroke.

Contact: Dr. Leonardo G. Cohen, Chief, HCPS,
301-496-9782 (cohenl@ninds.nih.gov)

Cognitive Neuroscience



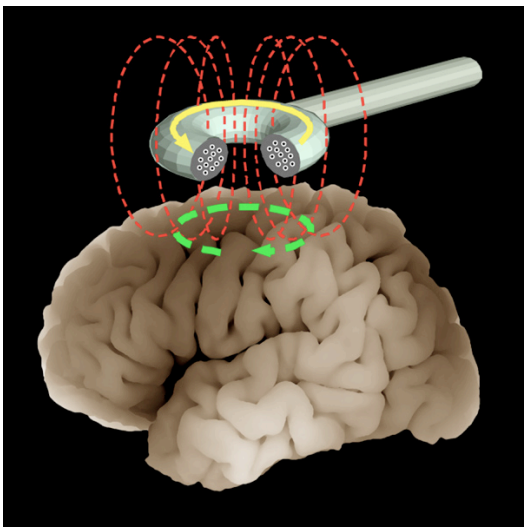
The Cognitive Neuroscience Section (CNS) conducts research on planning, reasoning, social cognition, other "executive functions" and their breakdown in patients with lesions to the prefrontal cortex and related cortical and subcortical structures, and functional neuroplasticity during learning and recovery of function after brain injury. The operating framework to study these processes and their disorders is based on cognitive science theory although we combine this approach with state-of-the-art clinical neuroscience techniques such as positron emission tomography, functional MRI, single-pulse and repetitive transcranial magnetic stimulation, and direct current stimulation. This Section is currently studying patients with frontotemporal dementias, stroke, penetrating and closed head injury, hemispherectomy and corticobasal syndrome.

Contact: Dr. Jordan H. Grafman, Chief, CNS,
301-496-0220 (grafmanj@ninds.nih.gov)

The Brain Stimulation Unit (BSU) focuses on the systems underlying the control of action and emotion in healthy humans and patients with disorders of executive function. Using noninvasive stimulation and functional imaging techniques, the Unit conducts neurophysiological studies on the human reward system and develops new ways of enhancing cognitive functions in patients and healthy subjects. Techniques available include transcranial magnetic stimulation, DC brain polarization, near infrared spectroscopy, functional MRI, and PET. The Unit provides clinical support to, and collaborates with, the Cognitive Neuroscience Section. This arrangement provides extensive expertise and resources

in cognitive science, well-characterized patient groups for study, and the opportunity for qualified clinical fellows to gain unique experience in behavioral neurology, particularly with frontotemporal dementia and related conditions. There is a range of opportunities for non-clinicians as well.

Contact: Dr. Eric M. Wassermann, Chief, BSU,
301-496-0151 (wassermanne@ninds.nih.gov)



Surgical Neurology

The Surgical Neurology Branch (SNB) offers one- or two-year combined basic science, translational and clinical fellowships. Fellows participate in clinical studies of conditions involving neurosurgical intervention, including brain tumors, pituitary tumors, syringomyelia, von-Hippel-Lindau disease, Neurofibromatosis Type-1/2, epilepsy, and neurodegenerative disorders. Current areas of interest include:

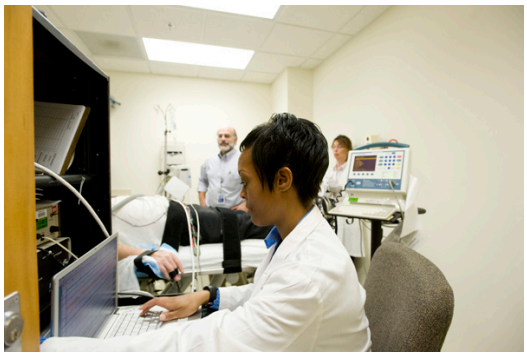
- Investigation of a new delivery technique to perfuse targeted regions of the brain
- Laboratory studies using regional therapies in models of epilepsy and Parkinson disease
- Genetics of familial Chiari I malformation
- Pathophysiology of syringomyelia
- Biology of primary brain tumors, including gliomas, pituitary tumors and tumors associated with von-Hippel-Lindau disease
- Molecular and cell biology of apoptosis
- The basis of steroid therapy for cerebral edema produced by tumors
- Potential therapeutic uses of nitric oxide for cerebral vasospasm.

Contacts: Dr. Russell R. Lonser, Chair, SNB,
301-594-8113 (lonserr@ninds.nih.gov);

Dr. John Heiss, Head, Clinical Unit, SNB,
301-594-8112 (heissj@ninds.nih.gov)

Neurocardiology

The Clinical Neurocardiology Section (CNCS) conducts mainly patient-oriented research in neurocardiologic disorders, with emphasis on catecholamine systems. Current and planned research of the Section focuses on biomarkers to identify presymptomatic or early Parkinson disease (PD) and related disorders, and tracking the status of catecholaminergic innervation in the brain and periphery in those disorders; on mechanisms of loss of catecholaminergic neurons; and on new treatments based on results about biomarkers and mechanisms. Research



methodologies include clinical autonomic function testing, cardiac sympathetic neuroimaging by 6-[18F]fluorodopamine positron emission tomography (PET), high resolution brain 6-[18F]fluorodopa PET, and neurochemical assays to assess central and peripheral catecholaminergic functions. The CNCS offers a fellowship in clinical neurocardiology and autonomic disorders.

Contact: Dr. David S. Goldstein, Chief, CNCS,
301-496-2103 (goldsteind@ninds.nih.gov)

Epilepsy

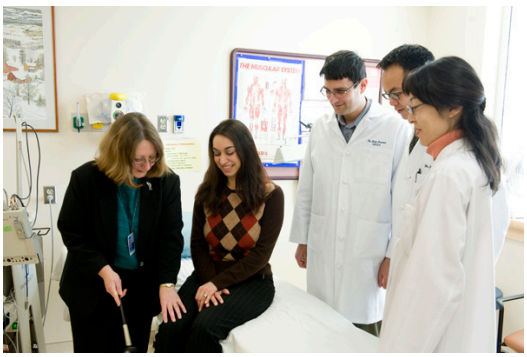
The Clinical Epilepsy Section (CES) carries out clinical research on epilepsy including: functional mapping with PET, fMRI, and MEG; PET receptor imaging; clinical pharmacology of antiepileptic drugs; clinical trials of new treatments such as surgical approaches and transcranial magnetic stimulation; and studies of families with epilepsy. This Section offers a two-year fellowship. The first year is devoted to Clinical Epilepsy and the second year to Clinical Neurophysiology in collaboration with the EEG Section. We have close relationships with Children's National Medical Center. Fellows usually engage in a research project for both years. Opportunities are available to combine animal with human imaging studies.

Contact: Dr. William H. Theodore, Chief, CES,
301-496-1505 (theodorw@ninds.nih.gov)

Clinical Neurophysiology

EEG

The Electroencephalography Section (EEG) provides the clinical service of electroencephalography, evoked potentials, intraoperative and invasive monitoring, and polysomnographic recording for NIH. Magnetoencephalography (MEG) is an optional activity. The program of training and research in Clinical Neurophysiology provides eligibility for the ABPN board examination in Clinical Neurophysiology and the ABEM board examinations.



Contact: Dr. Susumu Sato, Chief, EEG,
301-496-5121 (satos@ninds.nih.gov)

EMG

The Electromyography Section (EMG) offers a one-year fellowship that can be combined with a second year as a clinical research fellow in the Human Spinal Physiology Unit. The EMG fellowship is an ACGME-certified training program in Clinical Neurophysiology with a formal

curriculum of study. The fellow has rotations in EEG and EMG at NIH, Children's National Medical Center, and Walter Reed Medical Center. Fellows who complete this year are eligible for the ABPN board examination in Clinical Neurophysiology and the ABEM board examinations.

Contacts: Dr. Tanya Lehky, training program co-director,
301-496-7428 (lehkyt@ninds.nih.gov);

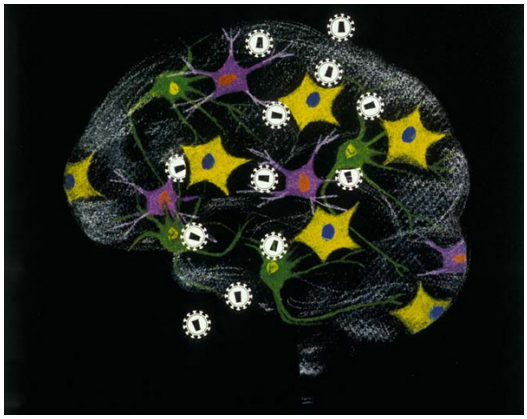
Dr. Mary Kay Floeter, Chief, EMG,
301-496-7428 (floeterm@ninds.nih.gov)

The clinical research fellowship in the Human Spinal Physiology Research Unit (HSPU) carries out patient-oriented research within the EMG section. Current clinical protocols focus on the physiology and imaging of motor neuron disorders and spasticity. This fellowship is particularly suitable for fellows who have already had Clinical Neurophysiology training and wish to gain research experience. The training plan is customized for each fellow, but generally includes coursework in clinical research or statistics, participation in protocols, and instruction in protocol design.

Contact: Dr. Mary Kay Floeter, Chief, EMG,
301-496-7428 (floeterm@ninds.nih.gov)

NINDS Basic-Clinical Translational Research Fellowships

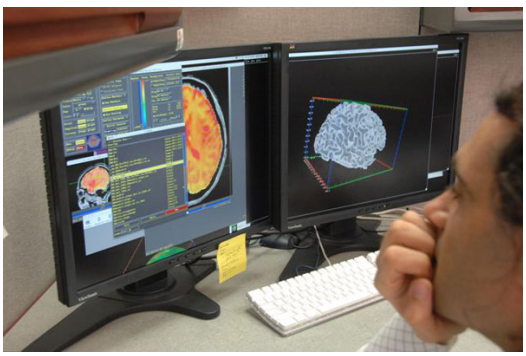
This combined fellowship, new in 2009, is an individualized fellowship program aimed at M.D.s or M.D./Ph.D.s interested in basic research applicable to neurological diseases or in emerging fields of specialization. The program is intended for clinicians with basic laboratory experience who wish to gain further training in laboratory-based research while improving clinical skills or for clinicians interested in emerging disciplines in neurological clinical research, such as neurological imaging. Clinicians who have completed a clinical fellowship year are encouraged to apply. The successful candidate will spend the majority of time in basic research with a primary mentor, but will spend one day each week in clinical activities, such as working in a specialty clinic with a clinical supervisor and attending rounds and clinical conferences. Interested applicants should identify a primary mentor from the NINDS faculty list and send a 1-2 page outline of their suggested fellowship focus and career goals, along with a curriculum vita, addressed to the proposed mentor and the NINDS Clinical Director at NINDSclinicalfellowships@ninds.nih.gov. Applications will be evaluated for programmatic and scientific appropriateness by the Scientific and Clinical Directors.



Neurovirology Research

Viral infections of the nervous system initiate a cascade of cellular and molecular events resulting in acute, chronic or persistent injury. The Laboratory of Molecular Medicine and Neuroscience (LMMN) and the Viral Immunology Section, NIB, have basic and translational research programs which investigate pathogenesis of viral infections in the nervous system tracking the cellular events from time of initial infection through the course of neurological manifestation and disease progression. Principal Investigators focus on agents that are neurotropic and neurovirulent through lytic infection and/or immune mediated cytotoxicity including the human polyomavirus, JCV, the etiologic agent of progressive multifocal leukoencephalopathy, HIV-1 associated encephalopathy, Human Herpes Virus 6 associated with autoimmune diseases, HTLV-1 and myelopathy and LCMV, lymphocytic choriomeningitis virus and immune mediated brain damage. These programs employ state-of-the-art technology to dissect the mechanisms of viral-induced neurological diseases including:

- Multiple color laser flow cytometry for identification of cell phenotypes involved in viral inflammation and entrance to the brain
- Two-photon live cell imaging of immune cells in the brain using rodent models of viral associated inflammation
- Immunological assays for defining the functions of T regulatory cells in immune-mediated pathogenesis
- Quantitative polymerase chain amplification, qPCR, for detection of viral genome sequences in clinical tissues using CLIA certified/validated assays
- Cell culture models of human brain-derived stem cells directed to neuronal or glial lineage pathways that define viral tropism
- DNA binding proteins for viral promoters to select cell susceptibility factors



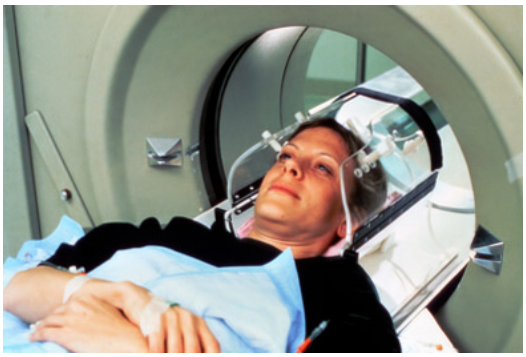
Active participation in bench experiments as well as clinical studies define these research programs as translational in focus with disease as an end point of study derived from basic science questions.

Contacts: Dr. Eugene O. Major, Chief, LMMN,
301-496-1635 (majorg@ninds.nih.gov);

Dr. Dorian McGavern, Investigator, LMMN,
(mcgavernd@mail.nih.gov);

Dr. Steve Jacobson, Chief, Viral Immunology Section, NIB,
301-467-0519, (jacobsonS@ninds.nih.gov)

Neurological Imaging



The intramural program has a strong imaging program from basic molecular imaging to human studies. Active studies include *in-vivo* imaging in animals using PET, optical imaging, and MRI imaging to study ion fluxes, metabolism, and gene expression. Technical developments in MRI to extend spatial resolution and understand the relation of functional MRI to neuronal architecture are being applied to clinical studies of the structural anatomy, tissue metabolism, tissue perfusion, and blood oxygenation level dependent contrast in both normal and diseased human brains. For clinicians interested in applications of imaging to research in neurological disorders, this fellowship offers an opportunity for combining training in advanced imaging techniques with a clinical focus. Though the fellow would have a primary mentor from among the neuroimaging faculty in the Laboratory of Functional and Molecular Imaging (LFMI), he would be expected to collaborate closely with a clinical investigator in a specific disease area.

Contacts: Dr. Alan Koretsky, Chief, LFMI,
301-402-9659 (koretskya@ninds.nih.gov);

Dr. Jeff Duyn, Investigator, LFMI,
301-594-7305 (jhd@helix.nih.gov);

Dr. Afonso Silva, Investigator, LFMI,
301-402-9703 (as378c@nih.gov)

Benefits and Eligibility

There are numerous opportunities for formal instruction at the NIH. Clinical fellows are encouraged to take formal coursework in the Principles and Practice of Clinical Research and Principles of Clinical Pharmacology, as well as workshops in grant writing, statistics, and career development skills. NINDS hosts weekly seminars in basic and clinical neuroscience. The nineteen institutes of the NIH present dozens of seminars every week on a wide variety of medical and scientific topics. Trans-institute interest groups provide a forum for interacting with top scientists and clinicians in areas outside of Neurology.

Clinical Fellows entering at the PGY5 level are paid a salary of about $66,000 and can receive a salary supplement for taking in-house call ($15-25,000, depending on number of fellows participating). Salary increases are determined annually by Federal guidelines. Fellows receive Federal employee health insurance and benefits.
In addition to Branch-funded fellowship slots, there are competitive

funding mechanisms available for intramural post-doctoral clinical fellowships. A competitive award to make the transition to an independent academic position following a NINDS fellowship is available. An intramural loan repayment program is available for clinical fellows to repay educational debts, http://www.lrp.nih.gov/about/intramural.

To be eligible for Clinical Fellowships, physicians must have completed an accredited residency training program and hold an unrestricted U.S. license (or be in the process of applying for a license that will be issued within one year of the starting date). Residents in accredited Neurosurgery residency programs may be eligible for fellowships on a case-by-case basis prior to completion of residency training.

Other Training Opportunities

Resident Elective Rotations

Short-term elective rotations lasting from one to three months are available for residents in accredited Neurology or Neurosurgery Residency Programs. The rotation is intended to provide exposure to clinical or translational research and to subspecialty neurological practice in an academic environment. Residents are expected to participate in subspecialty clinics and in journal clubs, rounds, and seminars. The program for each resident will be individualized under the supervision of a faculty mentor and area of research interest in their applications. Applications should be made by e-mail with a letter of interest and curriculum vita to the NINDS Clinical Director at NINDSclinicalfellowships@ninds.nih.gov.

Medical Student Clinical Electives

Short-term 4 or 8 week rotations with one of the NINDS clinical research groups provides the student with an exposure to patient-oriented research and an opportunity to receive advanced clinical training in Neurology. Students are encouraged to identify clinical research interests and facility in their applications. Areas of faculty research can be viewed at the NINDS faculty webpage http://intra.ninds.nih.gov. Applications are submitted to the NIH Clinical Center's Office of Clinical Research Training and Medical Education. Students must be enrolled in an U.S. accredited medical school and have completed their school's required clerkship rotation in Neurology, and have basic skills in history taking and the neurological examination. Eligibility requirements can be found at http://www.cc.nih.gov/training/students/clinical_electives.html.

Year-long Research Programs for Medical Students

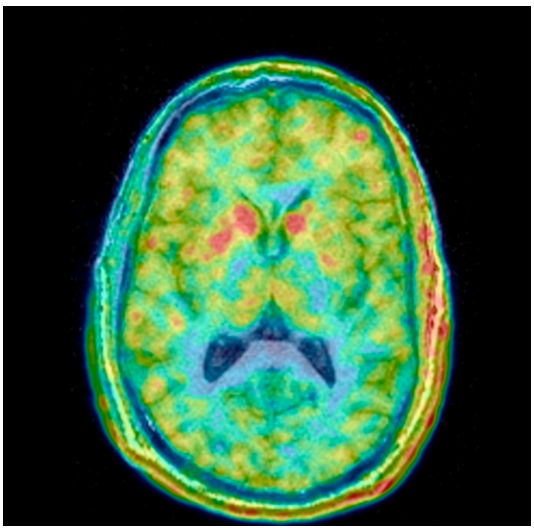
NIH sponsors two programs for medical students who wish to take a year off for research. Both programs are competitive, with applications due in early January for students who begin in July. The Howard Hughes Medical Institute-NIH program is oriented toward basic research, and the Clinical Research Training Program provides training in clinical or disease-oriented research.

Clinical Research Training Program

The Clinical Research Training Program (CRTP) is a 12-month program designed to attract the most creative, research-oriented medical students to the intramural campus of the NIH. Participants, known as Fellows, spend a year engaged in a mentored clinical or translational research project in an area that matches their personal interests and goals.

An individual program is developed for Fellows, who attend clinics, see patients on the wards, and work with a principal investigator in laboratories on selected clinical research projects. Fellows learn about translational research, that first step from the bench to the bedside and back to the bench; attend lectures on clinical research; and participate in an interactive, group learning experience with members of the class and leading NIH physicians and scientists.

Applications are handled through an electronic submission process on an annual cycle. The application deadline is typically in January. Applications can be submitted through the website, http://www.cc.nih.gov/training/crtp/crtp.html. Additional information on eligibility requirements, stipends, and housing can also be found on the website.



Howard Hughes Medical Institute (HHMI)-NIH

The HHMI-NIH Research Scholars Program was established in 1985 to give outstanding students at U.S. medical schools the opportunity to receive research training at the NIH. Research Scholars spend nine months to a year on the NIH campus, conducting basic, translational or applied biomedical research under the direct mentorship of senior NIH research scientists.

The Howard Hughes Medical Institute provides the administration and funding for the program, including the salaries and benefits for the Research Scholars. The NIH provides advisors, mentors, laboratory

space, and equipment and supplies for laboratory work. Most students participate as Research Scholars after their second or third year of medical school. Completion of basic science coursework prior to participation in the program is recommended.

To be eligible, a student must be in good standing at a medical school in the United States or Puerto Rico and must receive permission from the school to participate. Prior research experience may be advantageous but is not required. Students are not eligible if they are enrolled in a combined medical, dental, or veterinary/Ph.D. program (e.g., M.D./Ph.D.) or Ph.D., or Sc.D. program, or if they already have an M.D., D.D.S., D.V.M., or a Ph.D. or and Sc.D. in a laboratory-based science. The application deadline is January 10. Applications and additional information can be viewed on the website http://www.hhmi.org/cloister.

National Institute of Neurological Disorders and Stroke

U.S. Department of Health and Human Services
National Institutes of Health
National Institute of Neurological Disorders and Stroke
Clinical/Research Fellows Program
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