

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Neurological Disorders and Stroke

Headache Research



Francis S. Collins, M.D., PhD.
Director, NIH

Introduction

In its report on the Fiscal Year 2010 appropriation for the Department of Health and Human Services, the Committee on Appropriations stated:

“The Committee urges NINDS to: (1) solicit grant applications for fundamental and translational research on headache disorders with Requests for Applications, and (2) recruit new investigators with career training and transition awards. The Committee encourages NINDS to establish a screening program for therapies for headache disorders comparable in scope to the Anticonvulsant Screening Program. The Committee commends NINDS for recently initiating a process towards defining Headache Disorders Research Benchmarks and requests a report to the Committees on Appropriations of the House of Representatives and the Senate on the progress of this program by December 1, 2009.” (House Report No. 111-220, p. 117)

The following report has been prepared by the National Institutes of Health (NIH) of the Department of Health and Human Services in response to this request.

Background

Headache disorders are among the most common disorders of the nervous system. While epidemiology of headache disorders is not well documented, the World Health Organization (WHO) estimates that in developed countries, Tension Type Headache (thought to have musculoskeletal involvement) affects two-thirds of adult males and over 80% of females. WHO further estimates that 3000 migraine attacks occur each day for every million people, and that chronic daily headache occurs in one in every 20 adults each day.¹

Headache may occur as a primary disorder or secondary to a number of other conditions. Chronic headache and the long-term effects of coping with them (including stress, medication, behavioral and lifestyle changes) may predispose headache sufferers to other illnesses, including depression. Headache may impact an individual’s employment, social activity, and family life.

The National Institutes of Neurological Disorders and Stroke (NINDS) funds research to address the underlying causes and mechanisms contributing to headache disorders and to develop treatments for these debilitating disorders.

¹ World Health Organization, Fact Sheet No 277, March 2004.

Recent Funding Opportunity Announcements Relevant to Headache Research

In the past few years, the NIH has issued Funding Opportunity Announcements (FOAs) to encourage research in headache disorders. In January 2007, the NINDS issued a FOA on “Migraine: Neural Mechanisms and Risk Factors for Progression.” This announcement solicited grant applications on research to address the susceptibility, risk factors, mechanisms, and preventive measures relevant to the progressive nature of migraines. Grants funded through this announcement include projects: to understand the genetic and hormonal basis for susceptibility to migraine; to study abnormalities in the structure of the arteries supplying blood to the brain and in cerebral blood flow in migraine patients using advanced imaging techniques; to understand the role of inflammation in chronic daily headache and how this contributes to the progression from episodic to chronic headache; and to assess the risk of permanent brain dysfunction, including cognitive impairment, from recurrent migraine attacks.

In addition, in early 2007, the NINDS, along with the National Institute on Deafness and Other Communication Disorders (NIDCD), the National Institute of Dental and Craniofacial Research (NIDCR), and the National Institute of Environmental Health Sciences (NIEHS) issued a FOA on the “Neurobiology of Migraine.” This announcement solicits grant applications on innovative research to expand our current knowledge of neurobiological mechanisms underlying migraine. Recent NINDS studies funded through this FOA include a project to study migraine triggers, specifically the role of ovarian hormones, and a whole genome association study in a large cohort of women to identify genes and genetic variants involved in migraine.

A new initiative of the NIH Blueprint - a collaborative framework through which 16 NIH institutes, centers, and offices support neuroscience-related research - is focused on facilitating partnerships between pain scientists and non-pain neuroscientists to understand the underlying neural changes responsible for the transition from acute to chronic pain. The funding opportunity announcement for this program was recently issued in September 2009, and grant applications are currently being accepted. Headache researchers are strongly encouraged to apply for funding through this program.

Training Opportunities in Headache Research

The NINDS funds a number of headache researchers who are at the beginning or early stages of their careers. Projects to three new investigators were funded through the “Migraine: Neural Mechanisms and Risk Factors for Progression” and the “Neurobiology of Migraine” FOAs. In addition, the NINDS currently funds a

number of career development awards in headache, including K08s (Mentored Clinical Scientist Research Career Development Award), K23s (Mentored Patient-Oriented Research Career Development Award), and an F30 (NINDS Medical Student Dual Degree – MD/PhD – Program). Research being carried out by these investigators is addressing important questions relevant to the clinical care and treatment of migraine, including: a clinical study of migraine and opioid function, a study to optimize the Emergency Department diagnosis and treatment of migraine, a project looking at the association between migraine and obesity, and a study to examine sex differences in migraine mechanisms.

The topic of training and career development for headache researchers was discussed at some of the initial headache planning meetings convened by the NINDS and is expected to be one of the major topics discussed at a larger planning meeting being organized for Spring 2010. (See “Headache Disorders Planning Activities” below.)

Developing Therapies for Headache Disorders

The NINDS has developed several initiatives to enable investigators pursuing drug discovery and therapy development to find new treatments for a disease. The NINDS Cooperative Program in Translational Research is a milestone-driven program for preclinical therapeutic development projects with the goal of an Investigational New Drug (IND) or Investigational Device Exemption (IDE) application to the Food and Drug Administration (FDA). The program includes funding opportunities for pilot projects to generate tools and proof-of-principle for therapeutics development, full-scale single-component or multi-component research projects directed at developing new therapies, small business awards, and funding for research resources. Researchers conducting translational studies in any areas within the NINDS mission, including headache disorders, are encouraged to apply for funding through the program.

In addition, an FY 2011 NIH Blueprint initiative is focused on drug development for nervous system disease. The FOA, “Drug Discovery for Nervous System Disorders” was issued by five of the Blueprint institutes, including the NINDS, in early October 2009. Proposals utilizing a wide range of therapeutic approaches, including high-throughput screening projects, are accepted through this announcement. Researchers working in the discovery, design, and preclinical testing of innovative therapies for headache disorders are encouraged to apply.

NINDS believes that these programs will be more effective and less limiting in identification and pre-clinical development of compounds for the treatment of

headache disorders than the epilepsy Anticonvulsant Screening Program, which is limited to only initial screening of compounds.

Headache Disorders Planning Activities

The NINDS has been moving ahead with efforts to develop a long-term strategy to support and promote headache research and develop Headache Disorders Research Benchmarks. The NINDS is engaging all stakeholders in the process to identify priorities and opportunities for headache research. To this end, the NINDS has organized small meetings and discussions in preparation for a larger planning meeting to be held in Spring 2010. The NINDS led informal discussions during the NIH co-sponsored 6th Headache Research Summit in October 2008 about how best to approach a large-scale planning effort in headache research. The NINDS held similar discussions with physicians and researchers from the Chronic Migraine Treatment Trial that is part of the NINDS Clinical Research Consortium.

The NINDS also organized a meeting prior to the American Academy of Neurology meeting in April 2009 to discuss the status of the field and to further develop plans for the Spring 2010 meeting. The purpose of this meeting was to begin to identify gaps and opportunities in the current research portfolio, categorize resources needed to promote headache research and therapy development, and start to think about partnerships that will best achieve these goals. Topics discussed included the development of therapeutic targets and training the next generation of researchers and physician-scientists in headache. These will be major themes of the 2010 meeting. These discussions helped lay the groundwork for and will aid in the identification of the appropriate individuals to invite to the Spring 2010 meeting. The April 2009 meeting included headache researchers as well as researchers from other areas whose expertise might help to inform the field. The Spring 2010 meeting is expected to include a similar makeup of participants.

Conclusion

Headache disorders are a debilitating problem worldwide. Through its funding of individual investigators, encouraging further research through FOAs, and supporting headache researchers at the early stages of their careers, the NINDS hopes to make a difference in the understanding and treatment of these disorders. The Headache Planning activities currently underway will help to identify gaps and opportunities in the field and hopefully serve as a catalyst to encourage researchers to pursue studies in this area.