Highlights from the National Headache Foundation’s 6th Headache Research Summit

On October 29 and 30, 2008, the National Headache Foundation held their 6th Annual Headache Research Summit at the National Institutes of Health in Bethesda, Maryland to present findings from recent translational and clinical research in migraine. See Figure 1. The goals of the summit were to exchange information about advances in migraine research, promote translational research efforts, and support young investigators in their quest for answers to novel hypotheses relative to migraine disorder.

Figure 1. Headache Research Summit Agenda

<table>
<thead>
<tr>
<th>Wednesday, October 29</th>
<th>Thursday, October 30</th>
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<tbody>
<tr>
<td><strong>Location:</strong> Fairmont Hotel, Ballroom 2</td>
<td><strong>Location:</strong> NIH Campus, Building 50</td>
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<tr>
<td><strong>REGISTRATION</strong></td>
<td><strong>REGISTRATION</strong></td>
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<tr>
<td>1:00pm to 5:00pm</td>
<td>7:50am to 8:00am</td>
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<td><strong>RECEPTION</strong></td>
<td><strong>BREAKFAST</strong></td>
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<tr>
<td>6:00pm to 6:30pm</td>
<td>7:50am to 7:50am</td>
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<tr>
<td><strong>DINNER</strong></td>
<td><strong>BREAKFAST</strong></td>
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<tr>
<td>6:30pm to 7:30pm</td>
<td>7:50am to 8:00am</td>
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<tr>
<td><strong>Welcome and Introduction</strong></td>
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<tr>
<td>Seymour Diamond, MD</td>
<td>Seymour Diamond, MD, MBA, FANZ, FAHS</td>
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<tr>
<td>7:35pm to 8:35pm</td>
<td>8:00am to 10:00am</td>
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<tr>
<td><strong>Translational Research and Migraine</strong></td>
<td><strong>Neuroimaging of Headache</strong></td>
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<tr>
<td>Michael A. Moskowitz, MD</td>
<td>K. Michael Welch, MD, CB, FRCP, Chair</td>
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</tbody>
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**White Matter Lesions**
Roma M. Dafer, MD, MPH

**Preclinical Imaging of CSD, Relevance to Migraine**
Andrew Charles, MD

**Imaging Aura with MRI, PET and SPECT Scans**
Pied Michael Curran, MD

**Novel Techniques (e.g., Tensor Imaging)**
Shelia Aurora, MD

**10:00am to 10:15am**
**REFRESHMENT BREAK**

**VIEWING OF POSTERS**

**10:15am to 12:15pm**

**Mechanisms and Neurogenetics of Migraine**
Kathy L. Gardner, MD, Chair

**Familial Hemiplegic Migraine**
Kathy L. Gardner, MD

**Preclinical Physiological Models**
Andrew Foster, PhD

**Models of Sensitization**
Rami Burschak, PhD

**Preclinical Behavior Models**
Andrew H. Atin, MD, PhD

**12:15pm to 1:15pm**
**LUNCH**

**1:15pm to 3:15pm**
**Epidemiology, Risk Factors, Temporal Profile**
Richard B. Lipton, MD, Chair

**Natural Course of Illness**
Richard B. Lipton, MD

**Predictors of Progression**
Ann J. Scher, PhD

**Mechanisms of Progression**
K. Michael Welch, MD, CB, FRCP

**Therapeutic Approaches to Progression**
Frederic G. Freitag, DO

**3:15pm to 3:30pm**
**REFRESHMENT BREAK**

**VIEWING OF POSTERS**

**3:30pm to 6:30pm**

**Issues in Clinical Trial Design/Interpretation**
Jalil M. Ramadan, MD, MBA, FANZ, FAHS, Chair

**Surgical and Device Trials**
Jalil M. Ramadan, MD, MBA, FANZ, FAHS

**Future Headache Therapeutics: Beyond Traditional Clinical Trials**
Melissa Atkinson, MD, PhD, Dr Med Sci

**Pediatric Clinical Trials**
Andrew D. Hurwitz, MD, PhD

**The Placebo Response**
Dawn Marcus, MD

Dr. Michael Moskowitz, professor of neurology, Harvard Medical School and member of the faculty of the Harvard-MIT Division of Health Sciences and Technology, launched the Summit on Wednesday evening with a keynote address that focused on the translational research of migraine pathophysiology. His presentation included a retrospective on migraine research and demonstrated how advancements in genetics, epigenetics, and novel medical imaging modalities have helped to expedite solutions posed by complex hypotheses.

Thursday’s full-day symposium featured 20 presenters. The first five speakers focused on research findings derived from various types of functional medical imaging, such as nuclear-based single photon emission computed tomography (SPECT) and positron emission tomography (PET); magnetic-radiofrequency based blood oxygen level dependent (BOLD)-functional magnetic resonance imaging (fMRI) and diffusion weighted MRI; in addition to novel methods of neuroimaging, such as diffusion tensor imaging and magnetoencephalography. These technologies have been used to demonstrate information about one or more of the following neuronal activities now associated with migraine: cortical spreading depression, receptor expressions, ion channel disturbances, white matter lesions, gastric emptying, and supraspinal foci attributed to the development and continuation of pain.
The second set of five presentations centered on genetics and its role in migraine research and in the development of personalized medicine. Scientists observe people with familial hemiplegic migraine (FHM) to determine exact locations of dysfunctional mutations and the receptor or ion channel activities affected, eg, serotonin receptors, calcium channels, calcitonin gene-related peptide (CGRP) receptors, glutamate receptors and transporters. Knock-in and knock-out mice are also used to confirm assumptions. Information obtained from genetic research will ultimately aid bench scientists in the development of new targeted therapies for migraine and help to personalize medical interventions. As the integrated pathway of migraine becomes clearer, therapies can be targeted upstream in the migraine cascade to prevent migraine at an earlier point in time, minimizing symptoms and neuronal dysfunctions that may eventually lead to neural plasticity and chronification of migraine.

The third set of five topics addressed the epidemiology of migraine, mechanisms attributed to its anatomic and clinical progression and therapeutic approaches designed to delay the advancement of migraine pathophysiology. Many factors were mentioned that may contribute to neuronal hyperexcitability, a predominant feature of migraine, and allostatic load, a chronic stress condition implicated in activating a cellular environment of stress-induced inflammation. Both of these mechanisms are felt to be partially responsible for the maladaptive cycle that contributes to the progressive nature of migraine and its chronification, sometimes referred to as ‘transformed migraine.’ Similarities between migraine and stroke (ie, white matter lesions and peripheral nervous system dysmyelination) and migraine and chronic pain (ie, central sensitization) were also discussed. Discovery of an effective and safe therapy to preempt these conditions is considered the ‘Holy Grail’ in the medical management of migraine disorder.

The closing set of presentations focused on research trial design, including the necessity of sham controls (including their use in device trials); human research design meant to decrease reliance on rodent studies and speed the drug discovery process; improved study designs and dedicated tools for use in pediatric populations; and consideration during study protocol design regarding the paradox of placebo effect (parallel, rather than crossover, design is best to account for and balance placebo effects).

Although many advancements in migraine research have been made, researchers believe that it is in its infancy, equating it qualitatively to where cardiology or chronic pain research was a decade ago. In spite of the many new discoveries, many migraineurs must still contend with a loss of function and debilitated quality of life. Research needs to be funded and continued in order to broaden understanding of the migraine process; assert that ‘migraine’ may not actually be one disorder, and; discover targeted upstream therapies for personalized, safe and effective migraine prevention. Adjuvant and alternative therapies must also be explored.

The 2009 National Headache Foundation’s 7th Headache Research Summit will be held in Chicago, Illinois.