



Highlights from the 14th Congress of the International Headache Society

A brief summary of key findings from three sessions held at this important meeting

Frontiers in Imaging Pain and Migraine, a scientific plenary session presented by Peter Goadsby, MD, PhD; David Borsook, MD; A. Vania Apkarian, PhD; and Robert C. Coghill, PhD, included some interesting findings related to chronic pain. Functional brain imaging of patients with various types of chronic pain conditions (eg, low back pain, osteoarthritis, fibromyalgia, etc.) demonstrated distinct and unique areas of the brain perfusion activated in each chronic pain state, with some perfusion hyperactivity correlated to duration of pain. Pain intensity-related perfusion patterns have been identified in a global, bilateral brain system including parietal, insular, cingulate, and frontal cortical areas, as well as thalamus, amygdala, and midbrain. In humans, the prefrontal cortex is known to be important in higher-order cognitive and emotional functions, while the medial prefrontal cortex has been correlated with chronic pain, suggesting a pathological reorganization of this brain region. The area of the cortex used primarily in executive decision making reduces in volume, while the area tied to emotion demonstrates hyperactivity. All of the chronic pain conditions were associated with gray matter atrophy and reduction in cortical volume.

Research findings have also led investigators to believe that the insular cortex may function as a filter for perception of sensitivity to pain. Further research studies using tractography* continue in the hope of discovering the connectivity relationship between gray and white matter at the interface of both regions in patients with chronic pain and documented brain atrophy. It is understood that central nervous system (CNS) plasticity evokes global reorganization of brain activity in patients with chronic pain. Both pain memory and individual stress response elicit changes in brain activity and impact pain response. The ultimate goal of imaging research is to classify global brain reorganization for each chronic pain condition in order to improve targeted treatment options and therapeutic outcomes. Research designed to determine exactly how these observations in the chronic pain population correlate to conditions of migraine is needed.

*Magnetic resonance diffusion tensor imaging method (ie, Bootstrap, q-ball) used to explore neural connectivity between brain regions and reconstructs white matter fiber structure and neural segmentation *in vivo*.

Migraine and Epilepsy, a presentation given by Michael A. Rogawski, MD, focused on the pathophysiologic mechanisms common to both epilepsy and migraine. It was reported that 6% of patients with migraine also have epilepsy. A migraine can trigger an epileptic seizure and alternately, a seizure can trigger a post-attack migraine. Patients who experience dual conditions are sometimes said to have 'migralepsy.'



Cortical hyperexcitability, ion channel dysfunction, and the glutamatergic system are all common to both conditions. Glutamate plays a role in cortical spreading depression, trigeminovascular activation, and peripheral and central sensitization. These commonalities may partially explain why antiseizure drugs are effective in the prophylactic treatment of both conditions. N-methyl-D-aspartic acid (NMDA), alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionate (AMPA), and kainate receptors (KARS), especially KARS GluK1 (GluR5) subunits present in the trigeminal ganglion, all act as mediators of neural hyperexcitability. Antagonists for GluK1 have shown positive activity in animal models of pain, migraine, epilepsy, stroke and anxiety, while magnesium and memantine have been shown to interfere with cortical spreading depression and block progression at the NMDA receptor and ion channel. Calcium 2+ channel alpha 2 delta subunits are the therapeutic target for gabapentin and pre-gabalin. Both of these prophylactic medications have been shown to be effective in the treatment of migraine. The mechanism of action of topiramate is not fully understood, but has also demonstrated efficacy in the treatment of both epilepsy and migraine. Research continues in rodents to better understand the connection and difference between these two conditions and improve prevention of attacks. To date, rat model data in epilepsy and migraine studies have proven to be predictive of human response.

The International Headache Society Special Lecture entitled: *The Cerebral Abnormalities in Migraine, an Epidemiologic Risk Analysis-CAMERA-II Study (1999-2008)* was chaired by Michael A. Moskowitz, MD, and presented by Michel Ferrari, MD. People who have migraine with aura have a significant and increased risk of developing deep matter white lesions and subclinical ischemic brain infarcts in the posterior circulation (vascular border zone/cerebellum) compared to a control population. Evidence from the CAMERA studies of this population also supports an increase in risk of stroke, which is again significantly increased in migraineurs who smoke as well as in those who are prescribed oral contraceptives. An increase in migraine attack frequency correlates with a likelihood of increased posterior circulation infarcts and white matter lesions (23% migraine with aura vs. 7% control). A frequency of one migraine attack of at least once a month was sufficient to increase the number of white matter lesions. Iron deposition associated with oxidative stress was also noted on the MR images and may reflect progressive neuronal damage related to recurrent migraine attacks. How the amount of iron correlates with duration of the condition and with migraine versus chronic daily headache needs to be determined. An increase in new posterior circulation infarcts, in addition to previously visualized lesions, was noted in the migraine population. Study participants with migraine and infarcts possessed a higher risk for cardiovascular disease and further in-depth analysis of these data is necessary to determine if the presence of the infarcts are independent of Framingham risk factors. These data are preliminary and no formal publication of the study's outcomes has yet to be published.