

## Headache pathophysiology - Central mechanisms

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A wide variety of evidence indicates that migraine and other primary headache disorders are generated primarily by brain mechanisms. Although changes in vascular function clearly occur with migraine, there is growing evidence that these vascular changes are neither necessary nor sufficient to cause headache. The clinical features of a migraine attack including premonitory symptoms, aura, headache, and postdrome are consistent with changes in the activity of brainstem, hypothalamus, thalamus, and cortex during an attack. These changes in brain activity are verified by functional imaging studies using PET and fMRI. Clinical electrophysiology studies also show characteristic alterations in brain activity during and between migraine attacks. Cortical spreading depression (CSD) in animals has been used as a model of changes in cortical excitability that occur during a migraine. CSD is a complex wave of brain activity that involves dramatic changes in the function of neurons, glial cells, and vascular cells. Although it is not known whether CSD causes headache, there is good evidence that CSD in rodents is a translational model for basic mechanisms of migraine. Most migraine preventive therapies likely have central mechanisms of action, and there is growing evidence that acute medications such as triptans may also work by targeting brain receptors. It is important to recognize that although migraine may be fundamentally a brain disorder, peripheral mechanisms may still be important, and may represent therapeutic targets through their modulation of central nervous system function.

Andrew Charles, MD, is Professor and Director of the Headache Research and Treatment Program in the Department of Neurology at the David Geffen School of Medicine at University of California, Los Angeles (UCLA). He has recently been named the Meyer and Renee Luskin Chair in Migraine and Headache Studies at UCLA.

Dr. Charles received his medical degree from UCLA in 1986 and completed a residency and a research fellowship in neurology before becoming a professor at this institution. Now, as Director of the Headache Research and Treatment Program, Dr. Charles oversees a comprehensive effort toward advancing headache medicine that includes basic and clinical research, education, and patient care. His laboratory uses advanced imaging and electrophysiological techniques to investigate basic mechanisms of neuronal, glial, and vascular signaling related to migraine and other brain disorders.

Dr. Charles has been an associate editor of the journal *Cephalalgia* since 2009. He also serves on the board of directors of the American Headache Society, and the board of trustees of the International Headache Society. He is Co-Chair of the NINDS Common Data Elements Project Group for Headache.