

&lt;招待講演&gt;

## Molecular Mechanism of Migraine

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The molecular and cellular origins of migraine headache are among the most complex problems in contemporary neurology. To meet these challenges, researchers have successfully applied the tools of neuroimaging, neurogenetics, neuropharmacology and neurophysiology. With recent advances, we now have a clearer description of cellular events that characterize the migraine visual aura such as cortical spreading depression.

This presentation will review translational advances with special emphasis on the evidence implicating genes regulating ion channels and pumps, sex hormones and migraine prophylactic drugs as modulators of cortical spreading depression (CSD). Cortical spreading depression, a slowly propagating wave of neuronal and glial depolarization, was first linked to visual aura in the 1940's based on the close correspondence between CSDs known neurophysiological characteristics and the evolving visual percept of migraine. High field

strength, near-continuous BOLD imaging recordings during visual aura substantiate this association and implicate CSD as a noxious event capable of triggering headache. In knock-in mice expressing the Familial Hemiplegic Migraine-1 missense mutation in a gene encoding a subunit of Cav 2.1 (P/Q calcium channel), susceptibility to evoked CSDs is enhanced, but especially in female mice. In addition to sex hormones and genes regulating ion translocation, CSD is modulated in normal rats by chronic administration of migraine prophylactic drugs. These and other experimental data are consistent with the notion that headaches developing after migraine aura are caused by CSD-induced release and extracellular build-up of noxious molecules normally sequestered in neuronal and non-neuronal cellular compartments. The translational relevance and congruence of this body of work to the phenotype of common forms of migraine will be discussed.