MIGRAINE IS A NEURONAL DISORDER

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Migraine attack is generated by the complex interaction of various players such as genetic predisposition, environmental and intrinsic factors. Neuronal contribution, particularly cerebral cortex has long been of interest and in my talk I will provide research data that demonstrates the neuronal involvement in migraine headache.

Headache phase of migraine is associated with activation of trigeminal nerve that leads to CGRP and other neuropeptide release onto cerebral vessels and secondary vascular changes take place in meninges such as vasodilation, blood flow increase and edema. Other accompanied symptoms such as photophobia, phonophobia, osmophobia results from neuronal dysfunction in cerebral cortex or subcortical structures. Electrophysiological and clinical studies are essentially in favour of neuronal dysfunction and disclose increased response of migraineur brain to various external stimuli that is compatible with cortical hyperexcitability or hyperresponsivity.
Migraine aura originates clearly from cerebral cortex. Cortical spreading depression (CSD), a pathophysiological event underlying migraine aura triggers various neuronal and vascular changes in brain parenchyma as well as in the meningeal membranes called pia, arachnoid and dura mater. During CSD, a brief hyperperfusion followed by a prolonged oligemia is associated with DC shift and propagates over cerebral cortex (without necessarily matching any vascular territory). CSD is also able to induce trigeminovascular activation that is a characteristic feature of headache phase.

Recent genetic and pharmacological findings are also supportive of important role of CSD in migraine. Otosomal dominantly inherited form hemiplegic migraine is caused by mutation of ion channels or transporters such as CACNA1A and SCNA1 or Na+-K+ ATPase, in a way that results in release of excessive glutamate from neurons, reduced uptake of glutamate from the synaptic cleft into glia, and/or reduced buffering capacity to potassium ions. The common result of all three identified mutations is the hyperexcitability and reduced threshold for CSD induction, which all probably contribute to the vulnerability of the brain to migraine attacks. From the therapeutic perspective, the efficacy of certain anti-epileptic drugs in migraine patients and their action on excitability or even on CSD is noteworthy.