

CORTICAL SPREADING DEPRESSION IS NECESSARY TO START A MIGRAINE ATTACK: YES **Hayrunnisa Bolay**

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Investigating the origin of a migraine attack is a challenging task and the scientific evidences so far indicate the contribution of cerebral cortex and particularly cortical spreading depression (CSD), as the most likely initiating event.

Migraine aura, a transient neurological deficit anticipating headache, originates from cerebral cortex and caused by CSD. CSD is confined to the cerebral cortex, leading to various neuronal and vascular changes in brain parenchyma as well as in the meningeal membranes called pia, arachnoid and dura mater, also able to induce trigeminovascular activation and neurogenic edema that is a characteristic feature of headache phase. Imaging techniques demonstrated the altered activation of occipital cortex at the beginning of an attack regardless of aura. CSD was able to propagate to other brain structures such as basal ganglia, hippocampus, amygdala, thalamus and brain stem.

Recent genetic and pharmacological findings are also supportive of important role of CSD in migraine. Autosomal dominantly inherited form hemiplegic migraine is caused by mutation of ion channels or transporters such as CACNA1A and SCN1A 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 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. Electrophysiological and clinical studies are essentially in favor of cortical dysfunction and disclose increased response of migraineur brain to various external stimuli that is compatible with cortical hyperexcitability or hyperresponsivity. In that sense the demonstration of hyperexcitability and sustained increase in the efficacy of synaptic transmission in the affected neocortex as a longterm complication of CSD in human brain tissue is remarkable. Impaired neurovascular coupling associated with CSD was reported. Osmophobia in migraine is worth of mentioning since the perception of scent does not require any subcortical connection. Osmophobia seems to be specific to migraine and obviously associated with cortical excitability change.

Despite clear demonstration of spreading depression in cerebral cortex in migraine, the involvement of other subcortical brain structures remain unclear.