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Pathophysiology of migraine: What does calcitonin gene-related peptide do in early stage of migraine?

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Migraine is a severe, episodic, unilateral headache lasting hours to days and affects an estimated 16% of the population worldwide. Cortical Spreading Depression (CSD) is known to be the substrate of migraine with aura and may also lead to migraine like behavior by potentiation of inflammatory responses. Calcitonin-gene related peptide (CGRP) receptors play a crucial role in mediating the magnitude of CSD in rat cortical slice. However, how central CGRP is involved in early stage of migraine remains far from clear. This study aimed to examine if central CGRP could be induced by CSD and if CGRP and its receptors contribute to CSD genesis and propagation. CSD was induced and monitored both in vitro using intrinsic optical signal and in vivo using electrophysiology approach. Quantitative PCR and ELISA were used to quantify CGRP mRNA and peptide levels. The data demonstrated multiple but not single CSD, significantly increase CGRP mRNA and peptide in discrete regions of ipsilateral cortices and subcortical region. In addition, inhibition of both CGRP and CGRP receptors markedly prolonged CSD latency and reduced CSD magnitude in chick retina and mouse cortical slice, which actions on CSD were blocked by exogenous CGRP. Furthermore, reduction of CSD by CGRP receptor inhibition was also observed in vivo. These findings uncover a previously unknown role of cortical CGRP in mediating CSD, suggesting CGRP contributes to migraine pathophysiology and other CSD associated diseases.

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