DOES THE FIRST PHASE OF MIGRAINE ATTACK ORIGINATE IN THE CEREBRAL CORTEX AS OPPOSED TO THE BRAINSTEM? BRAINSTEM

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Several studies have suggested the crucial role of the brainstem in migraine resulting in primary dysfunction of the endogenous antinociceptive systems. The most important brain areas are the dorsal raphe nuclues (DRN), the periaqueductal grey matter (PGM) and locus coeruleus (LC). LC, the major noradrenergic nuclus, has a critical role in the regulation of cortical function. In positron emission tomography (PET) studies investigating acute migraine attacks, activation of an area of the dorsolateral brainstem that included the LC has been published. Dysfunction of the brainstem sturctures (and networks) could not only account for the somatosensory component of migraine but also for the auditory, olfactory, visual components and anxiety of patients. Furthermore, one of the key molecules involved in migraine is glutamate, whose receptors is found on the first-, second- and third-order trigeminal neurones and is also present in migraine generators (DRN, nucleus raphe magnus (NRM), LC and PGM). The kynurenine metabolite kynurenic acid (KYNA) exerts a blocking effect on ionotropic glutamate and alpha7-nicotinc acetylcholine receptors. Thus, KYNA and its derivatives may act as modulators various levels of the pathomechanism of migraine. They can give rise to antinociceptive effects at the periphery, in the trigeminal nucleus caudalis, and may also act on migraine generators. Indeed, KYNA reduced the responses of serotoninergic neurones of the DRN that were evoked by phasic auditory stimuli, by stimulation of the lateral habenula, by local electrical stimulation of afferent terminals and by substance P microinfusion. KYNA can also abolish the activation of neurones in the NRM excited by glutamate administration and by low-intensity electrical stimulation of the mesencephalic nuclues cuneiformis. KYNA injection into the PAG can modulate the excitatory and inhibitory effects of electrical and chemical stimulation of the medial preoptic nucleus of the hypothalamus on the NRM. The experimental data suggest that [UTF-8?]KYNAďž˝s derivatives might offer novel approach to migraine therapy.

References

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