CGRP RECEPTOR BLOCKADE IS THE MOST EFFECTIVE TREATMENT FOR MIGRAINE Lars Edvinsson

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Calcitonin gene-related peptide (CGRP) is localized in primary spinal afferent C and Að fibers of sensory ganglia and in the CNS, e.g. colliculi and cerebellum. Trigeminal nerve activation results in antidromic release of CGRP that result in vasodilatation via a CGRP receptor complex (calcitonin-like receptor, CLR, and receptor activity modifying protein 1, RAMP1). At central synapses in the trigeminal nucleus caudalis, CGRP acts on second-order neurons to transmit pain signals centrally. CLR and RAMP1 are widely expressed throughout the brain, and in intracranial arteries and the trigeminal system. CGRP does not induce neurogenic inflammation or sensitization at peripheral meningeal sites but relays nociceptive information to the second-order neurons in the brainstem. Recently, developed CGRP receptor antagonists have excellent antimigraine effects and a low side-effect profile. The CGRP receptor antagonists reduce signaling in the trigeminovascular pathway at multiple sites and at central sites, however, the exact site of antimigraine effect is still discussed.