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Current Evidence of Cannabinoid-Based Analgesia Obtained in Preclinical and Human Experimental Settings

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Abstract

Cannabinoids have a long record of recreational and medical use and become increasingly approved for pain therapy. This development is based on preclinical and human experimental research summarized in this review. Cannabinoid CB_1 receptors are widely expressed throughout the nociceptive system. Their activation by endogenous or exogenous cannabinoids modulates the release of neurotransmitters. This is reflected in antinociceptive effects of cannabinoids in preclinical models of inflammatory, cancer and neuropathic pain, and by nociceptive hypersensitivity of cannabinoid receptor-deficient mice. Cannabis-based medications available for humans mainly comprise Δ^9 -tetrahydrocannabinol (THC), cannabidiol (CBD) and nabilone. During the last 10 years, six controlled studies assessing analgesic effects of cannabinoid-based drugs in human experimental settings were reported. An effect on nociceptive processing could be translated to the human setting in functional magnetic resonance imaging studies that pointed at a reduced connectivity within the pain matrix of the brain. However, cannabinoid-based drugs heterogeneously influenced the perception of experimentally induced pain including a reduction in only the affective but not the sensory perception of pain, only moderate analgesic effects, or occasional hyperalgesic effects. This extends to the clinical setting. While controlled studies showed a lack of robust analgesic effects, cannabis was nearly always associated with analgesia in open-label or retrospective reports, possibly indicating an effect on well-being or mood, rather than on sensory pain. Thus, while preclinical evidence supports cannabinoid-based analgesics, human evidence presently provides only reluctant support for a broad clinical use of cannabinoid-based medications in pain therapy.

Significance: Cannabinoids consistently produced antinociceptive effects in preclinical models, whereas they heterogeneously influenced the perception of experimentally induced pain in humans and did not provide robust clinical analgesia, which jeopardizes the translation of preclinical research on cannabinoid-mediated antinociception into the human setting.

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