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Cannabinoid receptors and pain

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Abstract

Mammalian tissues contain at least two types of cannabinoid receptor, CB_1 and CB_2, both coupled to G proteins. CB_1 receptors are expressed mainly by neurones of the central and peripheral nervous system whereas CB_2 receptors occur centrally and peripherally in certain non-neuronal tissues, particularly in immune cells. The existence of endogenous ligands for cannabinoid receptors has also been demonstrated. The discovery of this 'endocannabinoid system' has prompted the development of a range of novel cannabinoid receptor agonists and antagonists, including several that show marked selectivity for CB_1 or CB_2 receptors. It has also been paralleled by a renewed interest in cannabinoid-induced antinociception. This review summarizes current knowledge about the ability of cannabinoids to produce antinociception in animal models of acute pain as well as about the ability of these drugs to suppress signs of tonic pain induced in animals by nerve damage or by the injection of an inflammatory agent. Particular attention is paid to the types of pain against which cannabinoids may be effective, the distribution pattern of cannabinoid receptors in central and peripheral pain pathways and the part that these receptors play in cannabinoid-induced antinociception. The possibility that antinociception can be mediated by cannabinoid receptors other than CB_1 and CB_2 receptors, for example CB_2-like receptors, is also discussed as is the evidence firstly that one endogenous cannabinoid, anandamide, produces antinociception through mechanisms that differ from those of other types of cannabinoid, for example by acting on vanilloid receptors, and secondly that the endocannabinoid system has physiological and/or pathophysiological roles in the modulation of pain.

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