EFFECTS OF CANNABINOIDS ON FOOD INTAKE AND VENTROMEDIAL HYPOTHALAMIC SEROTONIN RELEASE

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The use of cannabis derivatives as recreational and therapeutic drugs can be traced back to the earliest civilization and today, extracts of cannabis are among the most commonly used drugs for psychotropic effects. Cannabinoid receptors (mainly CB1) are expressed at high levels in many brain regions and the anatomical distribution is consistent with behavioural effects of cannabinoids, including: euphoria, decreased motor activity, impairment of memory, antinociception and modulation of food intake. The regulatory effect of cannabinoids on feeding behaviour is believed to be mediated through significant interactions between hypothalamic endocannabinoid system and anorexigenic/orexigenic pathways.

On other hand, there is extensive evidence to indicate that serotonin (5HT) innervation of the medial hypothalamus is involved in the control of the daily food intake. For example direct hypothalamic injections of 5HT and its agonists inhibit food intake.

In light of this we are investigating the relationship between cannabinoids and the serotonin innervation of the ventromedial hypothalamus by evaluating the effects of central and peripheral administration of cannabinoids agonists and inverse agonists on food intake and hypothalamic 5HT levels using HPLC and microdialysis techniques.

Our results indicate that central or peripheral administration of the synthetic cannabinoid agonist, WIN 55,212-2, to partially satiated rats had a significant and prolonged hyperphagic effect. In contrast, central or peripheral injections of the selective CB1 receptor inverse agonist, AM251, produce a strong anorexic effect. Taken together, the results suggest that the hyperphagia evoked by cannabinoid receptor agonists, as well as the anorexia elicited by the CB1 inverse agonists, my depend on the interaction of these agents with central and peripheral cannabinoid receptors. Study of the hypothalamic 5HT release shows a progressive increase in extracellular 5HT and 5HIAA (the major metabolite of 5HT) levels just after the initiation of food intake. Central administration of WIN 55,212-2 attenuate these changes while central administration of AM251 increase the stimulated effect of food intake on serotonin release. As, an enhanced release of 5HT in the medial hypothalamic nuclei is believed to be associated with inhibition of food intake, we can suggest that one of the possible mechanisms allowing the stimulation of food intake by CB1 receptor agonists is through an inhibition (or delaying) of the VMH 5HT neurotransmission implicated in the regulation of the satiety processes.

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