ENDOCANNABINOIDS AS PHYSIOLOGICAL REGULATORS OF COLONIC MOTILITY IN MICE

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Background & Aim
Activation of enteric cannabinoid CB_1 receptors inhibits motility in the small intestine; however, it is not known if endogenous cannabinoids (anandamide and 2-arachidonyl-glycerol) play a physiological role in regulating intestinal motility. In the present study we have studied the possible involvement of endocannabinoids in regulating colonic propulsion in mice *in vivo*.
Methods
Intestinal motility was studied measuring the expulsion of a glass bead inserted into the distal colon; endocannabinoid levels were measured by isotope-dilution gas chromatography-mass spectrometry; anandamide amidohydrolase activity was measured by specific enzyme assays. CB_1 receptors were localised by immunohistochemistry.
Results
Intraperitoneal administration (ip) of the non-selective cannabinoid receptor agonists WIN 55,212-2 (0.1-3 mg kg^{-1}), anandamide (2.5-20 mg kg^{-1}) and cannabinol (3.75-30 mg kg^{-1}) and of the selective CB_1 receptor agonist ACEA (0.1-3 mg kg^{-1}) significantly inhibited colonic propulsion in mice. The selective CB_2-receptor agonist JWH-015 (1-10 mg kg^{-1}) was without effect.
The inhibitory effect of cannabinoid agonists on colonic propulsion was counteracted by the CB_1 receptor antagonist SR141716A (1 mg kg^{-1}, ip). Administered alone SR141716A (10 mg kg^{-1}, ip) increased, while the inhibitor of anandamide cellular re-uptake, VDM11, decreased motility.
High amounts of 2-arachidonyl-glycerol and particularly, anandamide were found in the colon, together with a high activity of anadamide amidohydrolase. CB_1 receptor immunoreactivity was colocalised to a subpopulation of choline acetyltransferase-immunoreactive neurones and fiber bundles in the myenteric plexus.
Conclusions
It is concluded that endocannabinoids acting on myenteric CB_1 receptors tonically inhibit colonic propulsion in mice.