Activation of CB1 receptor inhibits fasting-induced increase in growth hormone (GH) secretion in mice

J.W. Leong, F.J. Steyn, L. Huang and C. Chen, School of Biomedical Sciences (SBMS), University of Queensland, St Lucia, QLD 4067, Australia.

The endocannabinoid system is one of the main regulators of energy homeostasis. While the mechanisms by which endocannabinoids regulate food intake are still under investigation, growing evidence supports a potential interaction with endocrine factors. Initial observations suggest that activation of cannabinoid receptor type 1 (CB1) by the cannabinoid Δ-9-tetrahydrocannabinol (Δ9THC) results in suppression of the potent anabolic hormone growth hormone (GH). To address the impact of cannabinoids on GH secretion, we measured the effects of Δ9THC (1.0mg/kg, IP) treatment on the activation of the GH axis following fasting. We isolated measures of peripheral hormones involved in the regulation of food intake and GH secretion, and correlated these to hypothalamic and pituitary gene expression of factors involved in the regulation of GH secretion. To characterise GH secretion we incorporated a newly developed and sensitive GH ELISA with repeated tail tip blood samples in 7-9 week old male C57 mice. Results confirm that fasting results in an initial increase and an eventual decrease in GH secretion. Addition of Δ9THC treatment inhibits the fasting-induced increase in GH secretion. Immunofluorescent staining in GH-GFP transgenic mice confirms that somatotrophs do not express CB-1 receptors. Δ9THC treatment does not change pituitary GH mRNA expression. Within the arcuate nucleus we observed an increase in growth hormone releasing hormone (GHRH) and somatotropin releasing inhibiting factor (SRIF) mRNA expression after fasting. This does not occur following Δ9THC treatment. These changes appear to be independent of orexigenic and anorexigenic pathways as Δ9THC does not impact fasting induced changes in NPY, AgRP, POMC or CART mRNA expression. We observed no changes in circulating levels of plasma leptin or active ghrelin in response to Δ9THC treatment. Based on these results, the consequence of Δ9THC treatment on fasting GH secretion is most likely mediated by hypothalamic mechanisms. This is consistent with prior reports confirming the expression of CB1 in the arcuate nucleus. Specifically, results suggest that CB1 activation inhibits the initial rise in GH secretion during fasting through an interaction with GHRH and SRIF neurons.