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PUFA *N*-acylethanolamines increase intracellular calcium through cannabinoid and TRPV1 receptors

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Background: Both CB_1 and CB_2 cannabinoid receptors are described to inhibit adenylyl cyclase and activate extracellular signal-regulated kinase, although only CB_1 receptors are described to regulate ion channel function[1]. Anandamide (*N*-arachidonoylethanolamine) acts at both these receptors and also through activation of TRPV1 receptors, which are non-selective cation channels. In this study, we have compared polyunsaturated (PUFA) N-acylethanolamines (NAEs) for the ability to elevate intracellular calcium ions in cells expressing CB_1, CB_2 and TRPV1 receptors.

Methods: Intracellular calcium levels were monitored in CHO-hCB_1 and CHO-hCB_2 cells using a FlexStation, while rat dorsal root ganglion (DRG) neurones were used to assay TRPV1 in a calcium imaging apparatus[2]. Data were collected from at least four separate preparations and were expressed relative to positive controls (ATP for CHO cells, and capsaicin for DRG cells).

Results: Anandamide evoked an elevation of intracellular calcium levels in CHO-hCB_1, CHO-hCB_2 and rat DRG neurones (Table). In CHO-hCB_2 cells, there appeared to be little variation in responses evoked by any of a series of polyunsaturated NAEs. For DRGs with endogenous TRPV1 receptors, there was also little variation in the level of responses, with the exception of N-eicosapentaenoylethanolamine, which appeared less effective. For CB_1 cannabinoid receptors, however, ω-6 NAEs appeared to evoke consistent responses, while responses to ω-3 NAEs were difficult to distinguish from baseline responses.

Conclusions: We conclude that there is heterogeneity of responses to polyunsaturated NAEs for CB_1 receptors in comparison to CB_2 and TRPV1 receptors, at least in terms of coupling to intracellular calcium ion levels.

References

1. Pertwee et al. (2010). Pharmacol Rev PMID:21079038

2. Sagar et al. (2005). Eur J Neurosci PMID:16045490

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