

Further evidence that the hypophagia elicited by intraperitoneal administration of cholecystokinin (CCK) is partially mediated a prostaglandin mechanism

Katherine N Romans, Ivor S Ebenezer. School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, PO1 2DT, United Kingdom.

Systemic administration of CCK, at doses that inhibit food intake, also produce increases in plasma levels of stress hormones (see Baldwin *et al.*, 1998). Exposure of animals to various stressors causes the *de novo* synthesis and release of prostaglandins (PGs) into the circulation (Morimoto *et al.*, 1991). We have shown that i.p. administration of CCK produces an increase in plasma levels of PGE₂ in rat and that the cyclooxygenase (COX) inhibitors can attenuate the suppressant effects of CCK on feeding (Ebenezer *et al.*, 2000). The present study was carried out to extend these observations. **Expt 1:** The effects of the PGE₂/3 agonist misoprostol (Miso) was investigated on food intake in male Wistar rats (n = 7, b. wt: 350 – 380 g) that were fasted for 22 h. The rats were injected i.p. with either saline (Sal) or Miso (10, 50 or 100 mg kg⁻¹) in a repeated measures design and placed singly in experimental cages with free access to food and water and food intake was recorded. **Expt. 2.** The effects of pre-treatment with the COX-inhibitor ibuprofen (Ibu) was investigated in 22 h-fasted male Wistar rats (n = 8, b. wt: 310 – 350 g). Each rat received the following treatments i.p. in a repeated measures design: vehicle (Veh; 2%w/v sodium carbonate) followed by saline (Sal), Veh followed by CCK (5 µg kg⁻¹), Ibu (20 mg kg⁻¹) followed by Sal, or Ibu followed by CCK. Thirty min separated the 2 injections. The rats were placed in separate experimental cages immediately after the 2nd injection with free access to food and water and food intake measured. The data was analysed by ANOVA and *post-hoc* Tukey test. The results from Expt. 1 showed that Miso (10 – 100 mg kg⁻¹) produces a dose-related decrease in food intake. Thus, for example, cumulative food intake (g) at 15 min ± s.e. mean was as follows: Sal 5.9 ± 0.4 g, Miso (10 mg kg⁻¹) 3.4 ± 0.4 g (P<0.02), Miso (50 mg kg⁻¹) 1.7 ± 0.3 g (P<0.01), Miso (100 mg kg⁻¹) 0.9 ± 0.2 g (P<0.01). The cumulative food intake data obtained at 15 min for Expt 2 are illustrated in Fig. 1. ANOVA revealed that there was a significant interaction between the treatments ($F_{(1,7)} = 5.5719$, P<0.05) and *post-hoc* tests show that the hyperphagic effect of CCK was significantly (P<0.05) reversed by pre-treatment with Ibu. The results show that (i) administration of a PGE₂/3 agonist suppresses food intake in fasted rats, and (ii) the COX inhibitor Ibu attenuates the hypophagic effects of CCK. These data extend previous results and lend further support for the hypothesis that the inhibitory effects of exogenous peripheral CCK on food intake in rats is partially mediated by a prostaglandin mechanism.

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