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Acute and chronic effects of the *n*-3 fatty acid DHA on cholecystokinin (CCK) secretion, storage and metabolism

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Rates of obesity have risen dramatically worldwide over the past 30 years[1]. There are various factors implicated in the determination of the regulation of body weight, including biological and environmental factors. Recent evidence has suggested that hormones that are secreted in the gut may play a role in the regulation of body weight[2] and as a result may be pursued as nutrient-related targets for reducing BMI.

CCK is a hormone produced and secreted by I cells, which are located in the duodenal and jejunal mucosa of the intestine[3]. This secretion occurs following the ingestion of a meal. CCK has been implicated to have various actions within the body, including the inhibition of gastric emptying and contraction of the gallbladder. A major action of CCK relates to its role as a satiety signal. Studies have shown that the infusion of CCK leads to a reduction in food intake and initiates meal termination in human subjects[4]. Various nutrients have been implicated to induce the secretion of CCK, including fatty acids with a chain length of ≥ 12[5]. DHA (22: 6 Δ4,7,10,13,16,19) is an *n*-3 PUFA present at high levels in fish oils. The present study involved the use of an enteroendocrine cell line (STC-1) to evaluate the effects of DHA on acute CCK secretion, chronic effects on CCK biosynthesis and storage, and chronic affects of DHA on cellular metabolism.

An ELISA (concentration producing 50% maximum inhibitory response 2.6×10^{-10} M) was established to assay sulfated CCK-8 in picomolar quantities. STC-1 cells (2×10^{6}) were seeded into twelve-well plates and incubated overnight (5% (v/v) CO_2; 37°C) to allow attachment. The following morning media was discarded, cells were washed with HEPES buffer and test incubations (*n* 8) containing DHA (100 μM) or vehicle control were added. After 30 min test incubations were removed and stored at −20°C before ELISA. For chronic studies 1.5×10^{6} cells were seeded into six-well plates and similar incubations were carried out for a 72 h period (*n* 4). After the test period buffer was discarded and acid–ethanol extractions performed to remove cellular CCK. To examine effects of DHA on cellular metabolism a BrdU labelling kit (measuring DNA synthesis; *n* 8; Roche Diagnostics, Mannheim, Germany), Alamar Blue dye (measuring cell viability; *n* 8; Invitrogen, Paisley, UK) and a Lactate Dehydrogenase assay (measuring cytotoxicity; *n* 8; Roche Diagnostics, Mannheim, Germany) were employed. Unpaired student's t-tests were used for all tests, with $P < 0.05$ deemed to be significant. Acute incubation of DHA significantly increased CCK secretion, with a 5.1-fold increase compared with vehicle control ($P < 0.001$). Chronic incubations with DHA caused a 9.1-fold decrease in cellular CCK content compared with control ($P < 0.001$). Cellular metabolism (as indicated by DNA synthesis, cell viability and cytotoxicity) was unaffected by chronic exposure of STC-1 cells to DHA.

In conclusion these data indicate that DHA is a potent stimulator of CCK secretion from STC-1 cells and it does not detrimentally affect cellular metabolism. However, prolonged stimulation of cells with this *n*-3 fatty acid leads to a considerable depletion in intracellular pools of CCK.

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