

**P004** The regulation of acetyl CoA carboxylase in models of hyperlipidemia

Stephen St.George-Smith, Xiaolu Yu, Peter J. Stanley,

Simon M. Luckman

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Hyperlipidemia is a hallmark of obesity and it is instrumental to the onset of metabolic syndrome with concomitant pancreatic cell dysfunction and peripheral organ insulin resistance (Haber *et al.*, 2002). Hyperlipidemia may accentuate the onset of obesity by compromising homeostatic brain functions, including nutrient sensing. Corroborative evidence indicates that hypothalamic neurones can sense changes in plasma fatty acid concentration with measurable outcomes (Kasser *et al.*, 1985; Wang *et al.*; 1994; Obici *et al.*, 2003). We propose that fat 'sensing' neurones within the hypothalamus respond to acute hyperlipidemia by increased phosphorylation of the enzyme acetyl CoA carboxylase (ACC), effectively favouring fatty-acid oxidation over synthesis. We report that saturated fatty acids cause an increase in ACC phosphorylation in pancreatic cell lines and in two novel hypothalamic cell lines (Belsham *et al.*, 2004) that express neuropeptide Y and pro-opiomelanocortin. Changes in fat oxidation are probably linked with mechanisms to maintain energy homeostasis.