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Effect of menstrual cycle phase and oral contraceptive use on dietary protein-induced thermogenesis

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Globally, obesity is more prevalent in women than in men, and of particular concern is the rising prevalence amongst young women of childbearing age. Whilst the underlying mechanism for this gender disparity is largely unknown, oral contraceptive pill (OCP) use may be a factor that contributes to the alteration in energy balance in young women**.** Given the considerable interest in the use of dietary protein for body weight maintenance, the primary objective of this project was to examine in healthy young adults, the influence of *sex, menstrual cycle phase* and *oral contraceptive use* on resting energy expenditure, substrate oxidation, and heart rate as well as appetite and satiety ratings in response to isoenergetic meals varying in protein content.

Four studies were conducted, each involving the measurement of the thermic effect of standardized meals by ventilated-hood indirect calorimetry, coupled with techniques of substrate oxidation and heart rate monitoring, body composition analysis, assessment of appetite and satiety ratings, blood and urine biochemistry. These studies measured: *i)* the acute response to a standardized high protein meal (24% of total energy from protein) versus a normal protein meal (11% of total energy from protein), both without (*Chapters 3 and 6*), and with (*Chapter 4*) manipulation of habitual protein intake; and, *ii)* the dose-response relationship between acute protein intake, resting energy expenditure, substrate oxidation and satiety using three levels of meal protein content (11%, 23%, and 31% of total energy from protein; *Chapter 5*). In all studies the ratio of the non-protein macronutrients (carbohydrates, fats) was kept constant, and the levels of meal protein used represented the range of protein intake observed in the general population.

The menstrual cycle was not found to alter protein-induced thermogenesis. However, in contrast to men and women not taking oral contraception, the use of OCP in women blunted the thermic response to increasing protein intake, with no difference in protein-induced thermogenesis observed across the three-fold range of meal protein content, from normal (11%) to high (up to 31% of total energy). This effect persisted even when the habitual protein intake was matched to meal protein content. Urea urinary nitrogen excretion was also blunted in OCP users, along with an increase in circulating cortisol and indications of decreased insulin sensitivity, as well as a negative lipid profile (low plasma HDL-cholesterol and high plasma triglyceride). The use of OCP was also found to be associated with decreased physical activity and a reduction in protein-induced satiety.

This study shows a blunting of the greater thermic effect of a high protein meal versus normal protein meal in women taking the oral contraceptive pill. Although the mechanisms remain to be determined, this finding has important implications for the effective use of high protein meals for body weight regulation in women taking oral contraception. With current obesity prevention and management strategies largely ineffective in women, understanding the relationship between sex hormone status and the metabolic response to dietary factors, such as protein intake, is key to refining existing diet/lifestyle recommendations to optimise health outcomes in women.

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