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Response of appetite and potential appetite regulators following intake of high energy nutritional supplements

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ABSTRACT

Background: The net clinical benefit of high-energy nutritional supplements (HENSDs) consumption is lower than expected.
Objectives: To investigate the extent to which consumption of oral HENSD in the fasted state reduces energy intake in slim females during consecutive breakfast and lunch, and whether this relates to changes in appetite and metabolic appetite regulators.
Design: Twenty three females of 24.4 ± 2.8 years with BMI of 18.2 ± 0.8 kg/m^2 consumed HENSD (2.5 MJ) or PLACEBO (0.4 MJ) in fasted state in a single blind randomized cross-over study. Appetite and metabolic rate measurements and blood collection were conducted prior to and during 240 min after the intake of the supplements. Energy intake was recorded during *ad libitum* buffet breakfast and lunch served 60 min and 240 min post supplementation respectively.
Results: Energy intake during breakfast was significantly ($P < 0.01$) lower in the HENSD trial but the net cumulative effect on energy intake was 1.07 ± 0.34 MJ higher in the HENSD compared to PLACEBO. Plasma concentration of CCK and PYY and insulin and were significantly ($P < 0.05$) higher in the HENSD trial while appetite measures were not significantly different between HENSD and PLACEBO trials. Correlations for the within participant relations between the responses of plasma hormones and appetite scores were significant ($P < 0.05$) for PYY and insulin but not CCK. The energy expended above resting metabolic rate was significantly ($P < 0.05$) higher in the HENDS trial but relative increase in energy expenditure was not significantly different between the two trials.
Conclusion: Oral high-energy nutritional supplements have a partial and relatively short lived suppressive action on energy intake and can be expected to increase net energy intake by approximately half the energy value of the supplement consumed.

1. Introduction

Systematic reviews and meta-analyses consistently suggest that oral, ready to drink high energy liquid supplements (HENSD) improve body weight and energy and nutritional intake, and thus may have various clinical and functional benefits in patients with an increased risk of becoming malnourished (Cawood, Elia, & Stratton, 2012; Stratton & Elia, 2010; Stratton, Hébuterne, & Elia, 2013). HENSD typically contain a mixture of macro and micronutrients, providing between 6·3 kJ/ml to 10·1 kJ/ml per typical serving of 125–220 ml (Stratton & Elia, 2010). Although HENSD should increase daily energy intake by an average of 1569 kJ/d, their net benefit is lower than anticipated (Milne, Avenell, & Potter, 2005; Poustie, Russell, Watling, Ashby, & Smyth, 2006), implying that HENSD consumption partially displaces food and energy intake during habitual meals. As another determinant of energy balance, energy expended during physical activity, may also play an important role. Indeed, a study investigating the impact of oral nutritional supplementation in depleted ambulatory patients with chronic obstructive pulmonary disease suggests that absence of body weight gain during three months of supplementation may be

Abbreviations: HENSDs, High energy nutritional supplement drinks; PYY, Peptide YY; CCK, Cholecystokinin; AUCs, areas under response vs. time curves.

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explained by enhanced energy expenditure via physical activity (Goris, Vermeeren, Wouters, Schols, & Westerterp, 2003).

So far, the mechanisms mediating compensation of habitual energy intake in relation to malnutrition treatment have been investigated primarily in tube feeding studies and only considered the role of metabolic and hormonal appetite regulators (Stratton & Elia, 1999; Stratton, Stubbs, & Elia, 2008). Oral intake compensation for energy provided by 3 days of bolus tube feeding has been reported to be equivalent to 40% of the bolus feed energy content, with plasma concentration of ghrelin, leptin, insulin, and glucose being modified in the direction expected to reduce hunger and increase satiety (Stratton et al., 2008). It is important to note that tube feeding delivers nutrients directly into the stomach and thus bypasses the sensory aspects of oral consumption and the cephalic phase response (Stratton & Elia, 1999; Stratton et al., 2008). Thus, the interaction between appetite, food intake, and the wider spectrum of hormonal appetite and satiety regulators following oral supplementation remains to be investigated.

Appetite and energy intake following food or supplement consumption can also relate to their impact on gastric emptying and diet induced thermogenesis as reduced hunger and enhanced satiety were reported to be linked with delayed gastric emptying (Wang et al., 2008) and with higher diet induced thermogenesis (Crovetti, Porrini, Santangelo, & Testolin, 1998; Mansour et al., 2012). Therefore, the aim of this study was to investigate the level of energy intake compensation in lean adult women following HENSD consumption and find out how it relates to responses of a range of hormonal and metabolic appetite regulators as well as a measure of gastric emptying and diet induced thermogenesis.

2. Material and methods

2.1. Participants

Eligible participants of this study were slim (BMI < 20 kg/m^2), healthy, young women recruited by means of advertisement and word of mouth in the campus of the University of Glasgow and in other public places. Participants were non-smokers, with stable weight for one month prior to the study, not pregnant, had regular menstrual cycle, and were not on any medication, nutritional supplement or following a special diet. Before enrolling in the study, participants underwent a detailed health screen regarding participant's health to exclude chronic illness, eating disorders and past history of gastrointestinal operations which could interfere with the results of the study. All participants gave written informed consent. The study was approved by College of Medical, Veterinary and Life Sciences Ethics Committee of Glasgow University.

2.2. Study design

This study used a single blind crossover design with two randomly sequenced experimental trials, separated by four weeks. On the morning of the experiment trial, participants reported to the metabolic investigation room between 0800 and 0900 after 12 h fast. Height (Seca, Leicester, UK) body mass and body fat (TBF-300, TANITA, Cranlea, UK), and resting metabolic rate (RMR) were measured. A venous cannula was then inserted and, after an interval of 10 min, baseline blood sample was obtained. Subsequently, an appetite questionnaire was completed. Within 10 min, participants were then asked to consume 240 ml of either a HENSD (Scandishake, Chocolate, Nutricia) prepared with full fat milk (HENSD trial), supplying 2.5 MJ, or a low calorie drink made up with skimmed milk, cocoa and artificial sweeteners (PLACEBO trial), supplying 0.4 MJ (Table 1). Participants were blinded of the preload drink and they were not told which drink they would consume and the order in which drinks were provided was randomly allocated. HENSD and PLACEBO drinks had the same colour, volume, flavour and texture and were not distinguishable, as reported in an independent pilot trial. Following supplement intake, 1000 mg of paracetamol with 100 ml of water were given to participants to measure a proxy of gastric emptying (Clements, Heading, Nimmo, & Prescott, 1978). Participants completed further appetite questionnaires and blood samples were collected at 30 and 60 min post supplement whilst metabolic rate was measured every minute for the duration of 20 min after each blood sample. One hour after supplement consumption, an *ad libitum* buffet style breakfast was served. Appetite questionnaires and blood samples were collected at 120, 150, 180, 210, and 240 min. An *ad libitum* buffet lunch was presented 240 min after the baseline measurements.

Table 1
Energy, carbohydrate (CHO), fat and protein provided by HENSD and PLACEBO drinks.

	HENSD	PLACEBO
Energy (MJ)	2.49	0.38
CHO (g)	68.8 g	11.3 g
Fat (g)	30.4 g	1.3 g
Protein (g)	11.9 g	9 g
Energy from CHO (%)	46	48
Energy from Fat (%)	46	13
Energy from Protein (%)	8	39

2.3. Ad libitum buffet meals

Ad libitum buffet meals consisted of a variety of standardised foods with total energy about three times what participants were expected to consume. They were served in the same setting, serving the same type of food in the same coloured dishes scheduling meals at the same time, and in the same table in order to avoid any bias in eating behaviour. The participants were given 30 min to consume their meal and were advised to eat according to their appetite until satisfied and comfortably full. Breakfast comprised of a variety of breakfast cereals, milk (semi-skimmed, skimmed and whole cream), croissants, jam, butter, banana and apples, apple and orange juice. Lunch comprised of two filled white bread sandwiches, two filled whole meal bread sandwiches, mixed leaf salad, yoghurt, apple, banana, grapes, and apple or orange juice. The food was cut into smaller pieces to eliminate portion related cues. All food offered and remaining after the intake was weighed by the researcher using an electronic kitchen scale (Salter Housewares Ltd., Tonbridge, U.K.). Water was available throughout the trial. Participants were given 30 min to consume their meal and were advised to eat according to their appetite until satisfied and comfortably full. The researchers were not present when the participants ate their meals to avoid any potential effect of the researcher on feeding behaviour. The participants were blinded to the actual purpose of buffet meals i.e. measurement of food intake.

3. Measurement of food and energy intake

The macronutrient and energy intake was calculated by dietary software Windiets 2005 (The Robert Gordon University, Aberdeen, Scotland, UK). The calculations on energy and macronutrient intake were independently conducted by two researchers and mean values of two calculations were used.

3.1. Appetite measurements

Participants were asked to mark their feeling of hunger, satiety, fullness, prospective food consumption and desire to eat on Visual