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## Basic Science

# Imposed rate and extent of weight loss in obese men and adaptive changes in resting and total energy expenditure☆☆☆



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## ARTICLE INFO

### Article history:

Received 3 October 2014

Accepted 17 March 2015

### Keywords:

Obesity

Weight loss

Energy expenditure

Metabolic adaptation

## ABSTRACT

**Objectives.** Weight loss (WL) is associated with a decrease in total and resting energy expenditure (EE). We aimed to investigate whether (1) diets with different rate and extent of WL determined different changes in total and resting EE and if (2) they influenced the level of adaptive thermogenesis, defined as the decline in total or resting EE not accounted by changes in body composition.

**Methods.** Three groups of six, obese men participated in a total fast for 6 days to achieve a 5% WL and a very low calorie (VLCD, 2.5 MJ/day) for 3 weeks or a low calorie (LCD, 5.2 MJ/day) diet for 6 weeks to achieve a 10% WL. A four-component model was used to measure body composition. Indirect calorimetry was used to measure resting EE. Total EE was measured by doubly labelled water (VLCD, LCD) and 24-hour whole-body calorimetry (fasting).

**Results.** VLCD and LCD showed a similar degree of metabolic adaptation for total EE (VLCD = −6.2%; LCD = −6.8%). Metabolic adaptation for resting EE was greater in the LCD (−0.4 MJ/day, −5.3%) compared to the VLCD (−0.1 MJ/day, −1.4%) group. Resting EE did not decrease after short-term fasting and no evidence of adaptive thermogenesis (+0.4 MJ/day) was found after 5% WL. The rate of WL was inversely associated with changes in resting EE ( $n = 30$ ,  $r = 0.42$ ,  $p = 0.01$ ).

**Conclusions.** The rate of WL did not appear to influence the decline in total EE in obese men after 10% WL. Approximately 6% of this decline in total EE was explained by mechanisms of adaptive thermogenesis.

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**Abbreviations:** WL, weight loss; EE, energy expenditure; VLCD, very low calorie diet; LCD, low calorie diet; fat mass, fat mass; FFM, fat free mass; DIT, dietary induced thermogenesis; RINH, Rowett Institute of Nutrition and Health; DLW, doubly labelled water; CR, caloric restriction.

☆ The material presented in this manuscript is original and it has not been submitted for publication elsewhere whilst under consideration for Metabolism — Clinical and Experimental.

☆☆ The authors have no conflicts of interest to declare.

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<http://dx.doi.org/10.1016/j.metabol.2015.03.011>

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## 1. Introduction

Weight loss (WL) is associated with modifications of fuel oxidation and resting and total energy expenditure (EE) [1,2]. Changes in body composition [i.e., fat mass (FM) and fat free mass (FFM)] explain a large proportion of the decrease in EE, which may be linked to the loss of metabolically active cellular mass, lower dietary induced thermogenesis (DIT) and energy cost of physical activity [1,2]. The residual EE not accounted for by the observed body composition and metabolic changes could derive from modifications of the efficiency and activity of metabolic, endocrine and autonomic pathways (i.e., adaptive thermogenesis) [1,2].

However, the occurrence of adaptive metabolic changes during WL is not a consistent finding across WL studies [3–8]. These differences could be explained by the different approaches used to quantify metabolic adaptation, such as application of different methods for the measurement of body composition and/or energy expenditure, as well as to the characteristics of the study population (adiposity, age, health status), degree of negative energy balance and duration of the WL interventions [1]. Specifically, the level of the negative energy balance (i.e., very low calorie diet (VLCD), low calorie diet (LCD)), the macronutrient composition of the hypocaloric diets (i.e., high protein, low fat) and the type (i.e., resistance, aerobic) and intensity (i.e., workload and frequency) of physical activity can influence the rate of weight change (how quickly you lose weight over time, kg/day), and amount of WL (total loss in kg, or relative loss %) [1,5,9–12].

Several studies have investigated the effects of fasting or energy-restricted diets on body composition and EE in obese subjects [6,13–18]. These studies aimed primarily at testing the effects of the extent of WL on EE; however, none of them has so far compared the effects of diets inducing different rates of WL on resting and total EE in controlled, experimental settings. The majority of these studies have been conducted in free-living conditions, which may have contributed to the inconsistent results and, consequently, fuelled the debate on the existence and physiological relevance of adaptive thermogenesis associated with WL [19,20].

We hypothesised that the rate of WL may represent the primary determinant of the decline in resting and total EE in obese subjects losing a similar amount of body weight. We predicted that a greater level of negative energy balance could be associated with a greater loss of FFM, which may result in greater adaptive changes in both resting and total EE.

This analysis aimed to investigate whether three groups of obese men, exposed to different levels of negative energy balance (fasting, very low calorie diet (VLCD, 2.5 MJ/day) and low-calorie diet (LCD, 5.2 MJ/day)) in experimental controlled conditions, were characterised by distinct changes in resting and total EE after losing a similar amount of body weight (5% and 10% WL). The study also provided the opportunity to test if the rate of WL and weight lost as FFM were associated with the level of adaptive thermogenesis.

## 2. Materials and methods

### 2.1. Subject characteristics

Eighteen ( $n = 6$  in each group), healthy, non-smoking, obese (body mass index (BMI) = 33–40 kg/m<sup>2</sup>) male subjects, aged

between 19 and 55 years, were recruited. Subjects were not following any special diet and were not prescribed any regular medication. A description of the inclusion and exclusion criteria is reported in the online supplementary material. The study was approved by the Grampian Research Ethics Committee. Written informed consent was obtained.

### 2.2. Experimental design

Subjects were non-randomly allocated to three WL interventions (fasting, VLCD, LCD) with a similar study design as previously described [21]. A description of the study protocol for each WL intervention is provided in the online supplementary material (Figs. S1–S3). Briefly, during the 6-day baseline period subjects consumed a fixed maintenance diet (13% protein, 30% fat and 57% carbohydrate). After the 7-day baseline period, each group followed the specific diet to lose 5% and 10% of their baseline body weight. However, the duration of the fasting was of 6 days as ethical constraint allowed to fast subjects to lose 5% of their baseline body weight. The duration of the WL phases to achieve a 10% WL was of 3 and 6 weeks for the VLCD and LCD groups, respectively. Throughout the study, participants were residential in the Human Nutrition Unit at the Rowett Institute of Nutrition and Health (RINH), Aberdeen, UK. All food and drinks consumed by each participant during the study were supplied by the dietetics staff in the Unit. The participants were requested not to undertake any other strenuous physical activity during the study and they were asked to record their individual exercise sessions.

### 2.3. Energy and dietary intake

Energy intake (EI) was measured daily, based on the recorded weighed intakes of food and drink and using values from McCance and Widdowson, 'The composition of foods' [22]. During starvation, the participants had access to water only. The VLCD comprised: daily weight 642 g, energy 2.55 kJ/g, protein 49.4 g (32%), carbohydrate 52.8 g (35%), and fat 23.1 g (33%). The LCD comprised: daily weight 1260 g, energy 5.2 kJ/g, protein 50.3 g (17%), carbohydrate 155.7 g (50%), and fat 45.4 g (33%). Further details are provided in Table S1 of the online supplementary material. Diets and recipes are available upon request. The Department of Health and Social Security (1987) guidelines were adopted for the design of the WL diets and ensure a balanced intake of protein, minerals and vitamins [23].

### 2.4. Resting energy expenditure

REE was measured at baseline and at the end of each WL phase (5% and 10% WL) by indirect calorimetry over 30–40 min using a ventilated hood system (Deltatrac II, MBM-200, Datex Instrumentarium, Finland). During the measurement, subjects lay on a bed in a thermo-neutral room and were instructed to lie still but not to fall asleep. Resting EE was calculated from minute-by-minute data using the mean of 15 min of stable measurements, with the first and last 5 min excluded. The equations of Elia and Livesey [24] were used to derive resting EE. Details of calibration burns and repeatability testing have been described previously [25].

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