

## Metabolic adaptations to over-and underfeeding-still a matter of debate?

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# **REVIEW** Metabolic adaptations to over—and underfeeding—still a matter of debate?

## **KR Westerterp**

Weight changes in response to a change in energy intake are smaller than calculated from the excess or deficit of energy intake. Digestion efficiency is not affected by intake level when consuming the same diet. Over- or underfeeding induces an increase or decrease in energy expenditure. Intake-induced expenditure changes are largely explained by proportional changes in diet-induced energy expenditure, in activity-induced energy expenditure and in maintenance expenditure as a function of changes in body weight and body composition. Additionally, underfeeding causes a metabolic adaptation as reflected in a reduction of maintenance expenditure below predicted values and defined as adaptive thermogenesis. Thus, alternating overfeeding and underfeeding with an iso-energetic amount results in a positive energy balance. The latter might be one of the explanations for the increasing incidence of obesity in our current society with an ample food supply.

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**Keywords:** energy balance; digestion efficiency; diet-induced energy expenditure; activity-induced energy expenditure; resting energy expenditure

#### INTRODUCTION

Humans perfectly maintain energy balance as shown by a constant body weight in adult life. On a yearly basis, body weight might change with 1 kg but such a change is relatively small compared with the energy turnover in 1 year. An average individual has an energy turnover of 10–15 MJ/d or 3650–5475 MJ/year. A weight change of 1 kg, equivalent to 30 MJ, denotes a discrepancy between intake and expenditure of only 0.6–0.8%. On the other hand, nowadays many people gain weight because even a small but systematically positive energy balance over subsequent years adds up to getting overweight or obese. One explanation is a difference in metabolic adaptations to overand underfeeding. It is easier to gain weight than to lose weight as illustrated by intervention studies on over- and underfeeding.

Energy balance is a function of energy intake and energy expenditure, where energy intake seems to be the overriding factor. Humans can easily double daily energy intake, as will be shown by one of the overfeeding studies.<sup>1</sup> Doubling energy expenditure implies in practice getting more physically active. However, activity energy expenditure is only a fraction of daily energy expenditure, about one-third for a moderately active subject. A moderately active subject, with a total energy expenditure (TEE) of 12 MJ/d and an activity energy expenditure from 4 to 16 MJ/d, has to increase activity energy expenditure from 12 to 24 MJ/d. An activity energy expenditure of 16 MJ/d is only feasible for endurance athletes.<sup>2</sup>

Changing energy intake by over- or underfeeding does not induce an iso-energetic change in energy balance. Many mechanisms are involved, including a change in digestion efficiency and a change in one of the three components of TEE: expenditure for food processing or diet-induced energy expenditure (DEE); activity-induced energy expenditure (AEE); and expenditure for body maintenance or basal metabolic rate (BMR). Metabolic adaptations to over- and underfeeding are presented by reviewing separately reported effects on digestion efficiency and on the three components of (TEE), followed by an integrative discussion.

#### **DIGESTION EFFICIENCY**

The digestibility of mixed diets is mainly determined by the amount of fibre or roughage in the diet. If the roughage in the diet remains constant, there does not seem to be a difference in digestibility between various levels of energy intake. Van Es et al.<sup>3</sup> observed faecal energy losses of 7, 6, and 6%, respectively, at intake levels of 50% below maintenance requirement, equivalent to maintenance requirement and 50% above maintenance requirement. Webb and Annis<sup>4</sup> measured faecal energy losses of 8% at a weight maintenance diet and 7% during a 30-day interval where subject consumed 4.2 MJ more than maintenance requirement. Digestibility is not affected by intake level and is also similar for subjects with and without overweight. In the study by Webb and Annis<sup>4</sup>, lean and overweight subjects did not differ in loss of energy in faeces. The latter might be surprising with the recent evidence for differences in intestinal microbiota between lean and obese subjects.<sup>5</sup> However, so far there is no evidence indicating that the composition of a gut's micro biome affects the ability of the intestines to extract energy from food.<sup>6</sup>

In conclusion, digestion efficiency of the refined Western diet seems to be >90%, not affected by intake level and similar between subjects when consuming the same diet.

#### DIET-INDUCED ENERGY EXPENDITURE

Ingestion of food stimulates energy-requiring processes, including intestinal absorption of nutrients, the initial steps of their

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metabolism and the storage of the absorbed, but not immediately oxidized nutrients. DEE is measured as the increase in energy expenditure above BMR after a test meal. Then, measured DEE values for separate nutrients are 0–3% of the energy content for fat, 5–10% for carbohydrate, and 20–30% for protein.<sup>7</sup> Thus, the main determinants of DEE are composition and energy content of the diet. A mixed diet consumed at energy balance results in a DEE of 5–15% of TEE.<sup>8</sup>

So far, there are no indications that DEE is different during overand underfeeding. Models on metabolic adaptations and energy regulation in humans, based on the current literature, assume that DEE is a fixed proportion of energy intake as also mentioned above.<sup>9,10</sup> Thus, over- or underfeeding with 50%, while consuming a mixed diet, is assumed to induce, respectively, a 5 (10 of the 50% change in energy intake) increase or decrease of TEE due to the change in DEE. However, overfeeding will result in an additional increase in energy expenditure when excess energy is converted into new tissue. Flatt calculated the cost of storage for separate nutrients, ranging from 3% for carbohydrate storage as muscle glycogen, 7% for fat storage in adipose tissue, to 24% for protein storage as protein.<sup>11</sup> Assuming that excess energy during overfeeding is stored as fat mass and fat free mass in a mass ratio of 75:25 or in an energy ratio of 95:5, the conversion cost is estimated at a value around 10% of the energy surplus.<sup>1</sup>

Differences in DEE between individuals, more specifically between lean and obese subjects, have been ascribed to methodological issues. De Jonge and Bray concluded that of 29 studies measuring DEE in subjects that were age matched and sufficiently obese, 22 reported reduced DEE in obesity.<sup>13</sup> The lower DEE in obese individuals was ascribed to a reduced sympathetic response to feeding resulting from hyperinsulinemia. A later review ascribed a reduced DEE in obesity to methodological variations including factors affecting measurement of resting energy expenditure, postprandial energy expenditure, and subsequent calculations of DEE.<sup>14</sup>

In conclusion, DEE is around 10% of energy intake for a typical Western diet, not affected by intake level, and similar between subjects when consuming the same diet. Overfeeding results in an additional energy cost, around 10% of the energy surplus, for the energy surplus to be stored as fat mass and fat free mass.

#### ACTIVITY-INDUCED ENERGY EXPENDITURE

AEE is the most variable component of TEE. Activity energy expenditure can be calculated from measured TEE and BMR:  $AEE = 0.9 \times TEE - BMR$ . The calculation assumes that the third component of TEE, DEE, is a constant fraction of 10% of TEE in subjects consuming an average mixed diet that meets energy requirements as explained in the foregoing section on DEE. TEE is ideally measured under unrestrained conditions, over a time interval of  $\ge 1$  weeks, using doubly labelled water as the most reliable method.<sup>15</sup> The main determinants of AEE are body weight and body movement. To compare body movement between differently sized subjects or detect changes in body movement within subjects changing weight, physical activity is calculated

as the physical activity level (PAL = TEE/BMR). An alternative is the assessment of PAL with a doubly labelled water-validated accelerometer (Philips Consumer Lifestyle, Amsterdam, The Netherlands) for movement registration.<sup>16</sup>

There are six overfeeding studies in which TEE was measured with doubly labelled water.<sup>17</sup> The effect of overfeeding on PAL was non-significant in four studies. One study showed an overfeeding-induced increase in PAL. Here, baseline PAL was calculated from energy intake for weight maintenance, and physical activity based on accelerometers, as measured at baseline and during overfeeding, was not changed. One study, doubling intake for 9 weeks resulting in a body weight gain of  $17 \pm 4$  kg, reported a decrease in PAL from 1.87 to 1.45. Thus, there was no effect of overfeeding on physical activity when intake during overfeeding was lower than twice the requirements for maintaining body weight.

Underfeeding studies in which TEE was measured with doubly labelled water were not reviewed before. A literature search provided five studies on energy restriction without an exercise intervention reporting PAL or allowing calculating PAL from reported TEE and BMR (Table 1). Two studies induced energy restriction with surgical treatment in morbidly obese subjects, resulting after 1 year in an average weight loss of around 50 kg. None of the five studies reported a significant change in PAL. Recently, results were published on the effect of underfeeding on doubly labelled water assessed magnitudes of PAL in >100 overweight women and men, distributed over three study sites in the United States.<sup>23</sup> Subjects were underfed for 12 months and measurements were performed with 3-month intervals. There was a significant decrease in PAL in subjects underfed with 20% for 6 months in one of the study sites. All other comparisons were nonsignificant. Thus, underfeeding does not seem to affect PAL though there are indications for a reduction, not persisting in time.

#### EXPENDITURE FOR BODY MAINTENANCE

Energy expenditure for body maintenance or BMR is usually the main component of TEE. It is the energy expenditure in the fasted state, at rest, while awake and in a thermoneutral environment. The BMR of a subject can be measured or can be calculated with a prediction equation. Then, it appears that prediction equations, including body composition parameters like fat-free mass and fat mass are superior to prediction equations, including only height, weight, age and gender of a subject, especially when comparing subjects with different ethnicity.<sup>24</sup> Overfeeding and underfeeding result in changes in BMR through changes in body composition. Thus, BMR is the main determinant of a higher TEE in obese than in normal-weight subjects.<sup>25</sup>

Underfeeding induces a reduction of BMR below predicted values, as based on the new body composition reached after underfeeding-induced weight loss.<sup>26–28</sup> The BMR reduction, adjusted for changes in body composition, ranges between 5% and slightly more than 10% of the initial value, depending on time interval after the intervention. Van Gemert *et al.*<sup>29</sup> observed an

Table 1.     Underfeeding studies without exercise in which total energy expenditure was measured with doubly labelled water				
Reference	Subjects	Underfeeding	PAL <sub>baseline</sub> a	PALunderfeeding
18	1 Female, 4 males	Gastric surgery	1.52±0.24	1.63 ± 0.20 <sup>ns</sup>
19	10 Females	8 Weeks 2–3.5 MJ/d	$1.75 \pm 0.20$	$1.74 \pm 0.24^{ns}$
20	8 Males	10 Weeks 80% baseline	$1.85 \pm 0.37$	1.65 ± 0.29 <sup>ns</sup>
21	7 Females, 1 male	Gastric surgery	$1.63 \pm 0.08$	1.62 ± 0.19 <sup>ns</sup>
22	32 Females	3.4 MJ/d <sup>b</sup>	1.50	1.58 <sup>ns</sup>

Abbreviations: PAL, physical activity level; ns, not statistically significant difference with baseline. <sup>a</sup>Physical activity level, doubly labelled water-assessed total energy expenditure as a multiple of resting energy expenditure. <sup>b</sup>Energy-restricted diet until subjects lost 10 kg weight.

1.1.1

average reduction of 12% at 3 months after the start of weight loss and of 6% when weight loss was maintained for >3 years.

There is not yet a mechanistic explanation for the underfeedinginduced reduction of BMR below predicted values. Relative preservation of fat-free mass, by combination of underfeeding with vigorous exercise, did not prevent the BMR reduction.<sup>30</sup> A disproportionate loss in high metabolic activity components of fat-free mass, like brain, heart, kidney and liver, can only explain a minor part of the underfeeding-induced reduction of BMR below predicted values.<sup>31</sup> An alternative explanation could be a reduction of metabolic activity of tissues like an underfeeding-induced reduction of protein turnover and substrate cycling.

## DISCUSSION

Metabolic adaptations to over- or underfeeding were shown to be limited to an underfeeding-induced reduction of BMR below predicted values. Digestion efficiency and DEE are mainly a function of diet composition and are not affected by changes in intake level at the same diet. So far, there is little evidence for a change in PAL when subjects are overfed or underfed.

The limited metabolic adaptations to underfeeding have an important implication. It may be one of the explanations for the increasing incidence of obesity in our current society with an ample food supply. Overfeeding  $\geq 1$  days and subsequently underfeeding with an equivalent amount over the same time interval results in a positive energy balance. Overfeeding requires more underfeeding to re-establish energy balance. There is additional evidence for a prolongation of the underfeeding-induced reduction of BMR during re-feeding.<sup>32</sup> The implication is that dieting increases the risk of the yo-yo effect, resulting in becoming fatter.

Over- or underfeeding has larger effects when getting to extremes. Massive overfeeding or chronic underfeeding does seem to affect physical activity as well. Doubling intake for 9 weeks did not change doubly labelled water-assessed TEE, while accelerometer-assessed body movement showed a decrease.<sup>1</sup> Activity-induced energy expenditure decreased, whereas the cost of DEE and the cost of storage of excess nutrients increased. Chronic underfeeding, as in subjects with anorexia nervosa reaching a body mass index far below 18.5 kg/m<sup>2</sup>, reduces AEE through reduced physical work capacity.<sup>33</sup>

Taken together, over- and underfeeding do not affect digestion efficiency. Changes in energy expenditure are largely explained by proportional changes in DEE, in AEE and in maintenance expenditure as a function of changes in body weight and body composition. Additionally, underfeeding causes a metabolic adaptation generally referred to as adaptive thermogenesis, reflected in a reduction of maintenance expenditure below predicted values.

In conclusion, adaptive thermogenesis takes place due to underfeeding but not with overfeeding.

## CONFLICT OF INTEREST

The author declares no conflict of interest.

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