

PERSPECTIVE

Changes in body composition and homeostatic control of resting energy expenditure during dietary weight loss

Manfred J. Müller¹  | Steven B. Heymsfield²  | Anja Bösy-Westphal³ 

¹Institute of Human Nutrition and Food Science, Christian-Albrechts-Universität zu Kiel, Kiel, Germany

²Pennington Biomedical Research Center, LSU System, Baton Rouge, Louisiana, USA

³Department of Human Nutrition, Kiel University, Kiel, Germany

Correspondence

Manfred J. Müller, Institute of Human Nutrition and Food Science, Christian-Albrechts-Universität zu Kiel, Düsternbrooker Weg 17-19, D 24105, Kiel, Germany.
Email: mmueller@nutrfoodsc.unikiel.de

Anja Bösy-Westphal, Department of Human Nutrition, Kiel University, Kiel, Germany.
Email: abosyw@nutrition.uni-kiel.de

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Abstract

Adaptive thermogenesis (AT) is the mass-independent decrease in energy expenditure (EE) in response to caloric restriction and weight loss. AT becomes manifest throughout all periods of weight loss and persists during subsequent weight maintenance. AT occurs in resting and nonresting energy expenditure as AT_{REE} and AT_{NREE} , respectively. AT_{REE} appears in different phases of weight loss, each with likely different mechanisms. By contrast, during weight maintenance after weight loss, AT_{NREE} exceeds AT_{REE} . Some of the mechanisms of AT are known now and others are not. Future studies on AT will need an appropriate conceptual framework within which to design experiments and interpret results.

INTRODUCTION

Adaptations to voluntary caloric restriction (CR) are manifest as coordinated physiological and endocrine responses: decreases in energy expenditure (EE) and urinary nitrogen excretion; glycogen and lipid mobilization; changes in body composition (BC), notably decreases in fat-free mass (FFM) and fat mass (FM); decreases in plasma levels of insulin, leptin, thyroid hormones, insulinlike growth factor I, sex hormones and sympathetic nervous system activity; and decreases in body temperature, heart rate, blood pressure, rate of respiration, reproductive processes, and glomerular filtration rate [1]. Adaptive thermogenesis (AT) refers to the mass-independent change in EE with CR. AT occurs in resting and nonresting EE as AT_{REE} and AT_{NREE} , respectively, which show relationships to each other at different times during periods of negative energy balance and during weight maintenance [2]. On a physiological level, AT may impede weight loss, predispose to

weight (FM) regain and thus characterize a thrifty phenotype [3], and reflect a mechanism of energy conservation impacting longevity [4]. Recent findings from our group [5–7] provide some further insights that may add to an improved conceptualization of AT.

USE OF A MULTICOMPONENT VERSUS A TWO-COMPONENT MODEL OF BC TO CALCULATE AT

AT_{REE} can be partially accounted for by comprehensive analysis of BC changes. Weight loss affects masses of organs and tissues as well as the relationships between individual body components (e.g., the partitioning between FM and FFM). In addition, losses in FFM and FM are associated with comprehensive changes in their anatomical as well as the molecular compositions [5, 7]. AT can be calculated from changes

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of REE adjusted for BC (FFM, organ and tissues masses, molecular components of the body) based on multiple regression analyses. In addition, REE can be predicted as REE_p according to EE calculated from individual organ and tissue masses times their specific metabolic rates. Then the difference between REE_p and measured REE reflects organ and tissue mass-independent changes in REE.

Adjusting the absolute decrease in REE for the CR-associated changes in BC, changes in FFM reduced the absolute REE changes by 33% while adjusting for changes in FFM plus changes in the anatomical composition of FFM (i.e., changes in skeletal muscle, liver, kidney, and brain mass), leaving 48% of the decrease in REE (i.e., 80–100 kcal/d) unexplained that then constitutes AT_{REE} [7]. Obviously, using a two-component model (i.e., FM and FFM) to calculate AT_{REE} is a simplification.

ORGAN/TISSUE MASSES AND THEIR SPECIFIC METABOLIC RATES CAN BE USED TO PREDICT AT DURING WEIGHT LOSS

Assuming a constant specific metabolic rate of individual organs and tissues [8], “mass-dependent” decreases add up to 94 kcal/d, with

65% explained by decreases in liver and skeletal muscle masses. In addition, mass-independent decreases (i.e., decreases in specific metabolic rates of organs and tissues) as calculated from decreases in urea production (–2.8%), glomerular filtration rate (–12%), heart rate (–9%), and body temperature (–0.12°C) result in a further decrease of 40 to 60 kcal/d. Then “mass-dependent” plus “mass-independent” decreases in REE reach 130 to 150 kcal/d, which is close to the observed decrease in REE of 173 kcal/d.

KINETICS OF WEIGHT LOSS SUGGEST DIFFERENT FORMS OF AT

AT appears in different phases: during *early* (i.e., from a few days to a week) and *late* weight loss (i.e., during subsequent few weeks), weight maintenance, and possibly with weight regain (Figure 1). Each phase likely has different mechanisms. Some of these mechanisms are known now and others are not. Within the first days of CR, early AT_{REE} is related to negative carbohydrate balance and decreases in intracellular water content resulting from the fall in plasma insulin levels with a concomitant rise in glucagon secretion

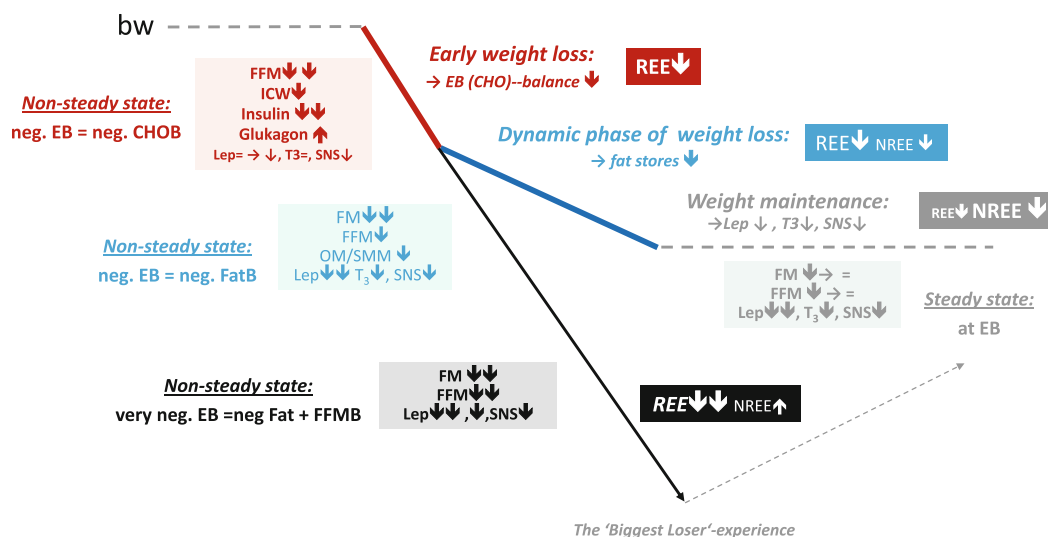


FIGURE 1 During a controlled 3-week semistarvation protocol [5], AT_{REE} is of comparable size throughout different weight loss periods (i.e., *early* weight loss from a few days to a week and *late* weight loss during the subsequent 2 weeks), and during weight maintenance, AT_{REE} has a different metabolic basis in which different systems function together to execute homeostatic control mechanisms. Considering changes in FFM and its anatomical composition (i.e., changes in organ and tissues masses within FFM), metabolic adaptation to caloric restriction and weight loss is about 100 kcal/d. Early weight loss is characterized by a negative carbohydrate balance and decreases in intracellular water, resulting from the fall in plasma insulin levels with a concomitant rise in glucagon secretion. After depletion of glycogen stores, late weight loss is mainly characterized by lipid mobilization. After weight loss and during weight maintenance, body mass and body composition are stable. Although weight loss is associated with mass-dependent and mass-independent decreases in REE (and, thus, AT_{REE}), metabolic adaptation in nonresting energy expenditure (i.e., AT_{NREE}) exceeds AT_{REE} during weight maintenance after weight loss. AT_{NREE} is related to reduced plasma levels of Lep and T3 at low activity of the SNS. Today, different authors have addressed AT during different phases of weight loss and weight maintenance. For example, early AT has been assessed by Heinitz et al. [3] and ourselves [5, 7] and late AT again in our study [5, 7]. In addition, AT during weight maintenance has been investigated by Leibel and Rosenbaum [9, 10], as well as the authors of the CALERIE study [1]. Finally, the “Biggest Loser” experience [11] was about a disproportionate decrease in REE in response to massive weight loss in patients with severe obesity undergoing drastic dietary restrictions plus an intensive exercise program. It is obvious that during the different phases, steady-state and non-steady-state conditions exist, which limit the meaningfulness of the investigations of the determinants of AT. AT, adaptive thermogenesis; bw, body weight; CHO B, carbohydrate balance; EB, energy balance; FAT B, fat balance; FFM, fat-free mass; FFMB, FFM balance; FM, fat mass; ICW, intracellular water; Lep, leptin; SMM, skeletal muscle mass; NREE, nonresting energy expenditure; OM, organ masses (i.e., masses of brain + heart + liver + kidneys); REE, resting energy expenditure; SNS, sympathetic nervous system; T3, triiodothyronine [Color figure can be viewed at wileyonlinelibrary.com]

[3, 5]. There is late AT_{REE} with ongoing (linear) weight loss. It is explained by decreases in FFM and changes in its anatomical composition together with a reduction in specific metabolic rate of organs and tissues. AT_{REE} can be partially accounted for by functional and metabolic changes such as decreases in core temperature, heart rate, and glomerular filtration rate. In addition, there is AT_{NREE} as reflected by improved skeletal muscle work efficiency as assessed by indirect calorimetry walking at low intensity on a treadmill ergometer [5]. Remaining changes in REE after accounting for these determinants are roughly ~ 100 kcal/d. Late AT_{REE} is related to lipid mobilization [5,7]. After weight loss and during weight maintenance, AT_{NREE} has been shown to exceed AT_{REE} , which is associated with improved skeletal muscle work efficiency that is preserved from the previous period [9, 10]. During this steady-state condition, AT_{NREE} is related to reduced plasma levels of leptin and triiodothyronine and low activity of the sympathetic nervous system [10]. Taken together, different systems execute homeostatic control on early and late AT_{REE} (Figure 1).

AT_{REE} IS ONLY ONE PART OF METABOLIC ADAPTATION TO WEIGHT LOSS; IT DEPENDS ON MOBILIZATION OF BODY ENERGY STORES

With weight loss, AT_{REE} is only part of metabolic adaptation and it is related to carbohydrate and lipid mobilization. Faced with the small energy store as glycogen, energy reserves as lipids are the primary source of fuel during CR in the long term, and thus, lipid mobilization has an important part in metabolic adaptation to CR. During CR, both lipid mobilization and food intake serve to maintain ATP production. In our semistarvation study [5, 7], energy intake was reduced to 1,353 kcal/d. Concomitantly lipid mobilization was 819 kcal/d with AT_{REE} of 104 kcal/d. Thus, lipid mobilization and AT_{REE} met 71% and 8% of the energy deficit, respectively, while there were further adaptations in NREE spent for physical activities, muscle work efficiency, and diet-induced thermogenesis [5, 10]. Obviously, AT_{REE} is just one part of metabolic adaptation. Because there was a negative association between late AT_{REE} and fat mobilization, it is tempting to speculate that the degree of lipolysis determines AT_{REE} , i.e., the greater the lipid mobilization, the smaller the AT_{REE} .

CONCLUSION

Different systems execute homeostatic control on early and late AT_{REE} . Early AT_{REE} is associated with carbohydrate mobilization and negative fluid balance directed by its endocrine determinants, whereas late AT_{REE} is related to fat mobilization. Up to now, different authors have addressed AT during different phases of dietary weight loss and during weight maintenance. Although AT may have a similar magnitude, it may differ in its metabolic basis. Thus, a future conceptual framework must go beyond the mere description of the phenomenon. AT_{REE} and

AT_{NREE} are part of a greater picture, i.e., adaptations of carbohydrate and lipid metabolism. In addition, steady-state (during weight maintenance) and non-steady-state conditions (during weight loss) affect insights in the determinants of AT (Figure 1).

AUTHOR CONTRIBUTIONS

The authors' responsibilities were as follows: MJM had the idea and the concept and wrote the first version of the manuscript; MJM, SBH, and ABW contributed to the discussion of the results and writing of the manuscript; all authors have read and approved the final manuscript.

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CONFLICT OF INTEREST

MJM and ABW declared no conflict of interest; SBH is on the Medical Advisory Board of Medifast and Tanita.

ORCID

Manfred J. Müller  <https://orcid.org/0000-0002-7280-2411>

Steven B. Heymsfield  <https://orcid.org/0000-0003-1127-9425>

Anja Bosy-Westphal  <https://orcid.org/0000-0002-8318-9448>

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