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Energy Constraint and Compensation:
Insights from Endurance Athletes

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ABSTRACT

The *Constrained Model of Total Energy Expenditure* predicts that increased physical activity may not influence total energy expenditure, but instead, induce compensatory energetic savings in other processes. Much remains unknown, however, about concepts of energy regulation, constraint and compensation in different populations, and it is unclear whether this model applies to endurance athletes, who expend very large amounts of energy during training and competition. Furthermore, it is well-established that some endurance athletes consciously or unconsciously fail to meet their energetic requirements via adequate food intake, thus exacerbating the extent of energetic stress that they experience. Within this review we A) Describe unique characteristics of endurance athletes that render them a useful model to investigate energy constraints and compensations, B) Consider the factors that may combine to constrain activity and total energy expenditure, and C) Describe compensations that occur when activity energy expenditure is high and unmet by adequate energy intake. Our main conclusions are as follows: A) Higher activity levels, as observed in endurance athletes, may exceed the capacity of the body to compensate for, and thus increase TEE; B) That while a range of factors may combine to constrain sustained high activity levels, the ability to ingest, digest, absorb and deliver sufficient calories from food to the working muscle is likely the primary determinant in most situations and C) That energetic compensation that occurs in the face of high activity expenditure may be primarily driven by low energy availability *i.e.,* the amount of energy available for all biological processes after the demands of exercise have been met, and not by activity expenditure *per se.*

Keywords

Energy regulation; constrained energy; compensation; trade-offs; athletes; exercise, endurance; training.

Table 1: Operational Definition of Terms

Note: Many of the terms used throughout this piece lack a universally agreed definition and may be open to interpretation, or used differently in different fields. The purpose of the definitions provided herein is to add clarity to our commentary, but not to imply a definitive interpretation. Relevant terms are italicized on first use within the main text.

Adaptation	The process of adjusting or changing to become more suited to an environment. This process can occur on a range of time-scales, with evolutionary biologists generally concerned with natural selection for genetic, heritable, traits that occur across generations and favor fitness in a given environment. Exercise physiologists generally investigate adaptations that occur within a lifetime, whereby morphological, physiological and behavioral traits vary in response to changing environmental circumstances and stressors without alterations to the genetic code (otherwise known as phenotypic plasticity).
Constrained Model of Total Energy Expenditure	A model that predicts that total energy expenditure is constrained, and that an excess of energy spent in one process, such as habitual physical activity, will induce energetic savings elsewhere [1].
Energetic trade-offs	A reduction in energy allocation to one function, as a result of energy allocation to another (considering that energy is finite and that energy used for one purpose cannot be used for others) [2].
Metabolic energy availability	Within exercise science, metabolic energy availability is defined as the amount of energy that is available to support biological processes after the demands of exercise training have been met [3].
Energy compensation	A form of energetic trade-off that occurs in an attempt to restore energy balance in the face of changes to either intake or expenditure.
Exercise	A specific type of physical activity that is planned, structured and repeatedly performed to improve or maintain physical fitness or health [4]. Humans evolved to be active for either necessity or play [5], but the concept of undertaking physical activity with the express purpose of improving health or performance (‘exercise’) is a relatively new concept.
Exercise Hypogonadal Male Condition	A significant and persistent reduction in testosterone levels in men who participate in chronic endurance exercise training [6].
Overtraining Syndrome	A condition of prolonged maladapted physiology when large training volumes with excessive overload are undertaken without adequate rest and recovery [7].
Physical activity	Any bodily movement produced by the skeletal muscles that results in energy expenditure [4].
Physical activity level (PAL)	Total energy expenditure, expressed as a multiple of basal metabolic rate. PALs typically range from approximately 1.3/1.4 for sedentary individuals, to >2.5 for highly active individuals (*e.g.,* endurance athletes).
Relative Energy Deficiency in Sport (REDS)	A syndrome of impaired physiological functioning caused by low energy availability that includes impairments of a variety of health- and performance-related factors, including , but not limited to menstrual function, bone health, metabolism, immunity, recovery, strength and endurance [8].
The Female and Male Athlete Triad	A syndrome of three interrelated conditions that exist on a continuum of severity, including low energy availability (with or without disordered eating), reproductive suppression and impaired bone health [9,10].

Total energy expenditure	The absolute amount of energy expended by an individual within a given period of time (usually reported as kcal·day^{-1}). Total energy expenditure will comprise basal metabolism, the thermic effect of food, physical activity, and when required, the costs of reproduction, growth and immune defense.

1. INTRODUCTION

All biological processes require energy, and this energy is obtained from ingested foods. Imbalance between energy expended and consumed, be it a surplus or deficit, poses substantial risks to human health and performance. This problem is substantial, with World Health Organisation estimates indicating that energy imbalance affects approximately 2.4 billion adults worldwide, with 1.9 billion estimated to be overweight and 462 million to be underweight [11]. As such, a better understanding of how the body regulates energy intake and expenditure, and the causes and consequences of imbalance, have enormous potential to influence individual and societal well-being.

Total energy expenditure (TEE) comprises all biological processes, including basal metabolism, the energy required to digest and process ingested foods, *physical activity* and – when required - the costs of reproduction, growth and immune defense. Previous assumptions that expenditure between these processes was additive, and that TEE could be estimated by combining the amount of energy expended in each, has been challenged, and the *Constrained Model of Total Energy Expenditure* (CMEE) predicts that TEE is constrained within physiological limits. This means that increased expenditure in one process, such as physical activity, may not increase TEE, but instead induces *compensations* that will save energy elsewhere [1,12,13], *e.g.,* through reducing basal metabolism or non-*exercise* activity expenditure, or through increasing biomechanical or metabolic efficiency [14,15]. This evolved constraint on TEE is purported to allow for a maintenance of total energy requirements when high levels of physical activity were required to procure food during times of scarcity, or to optimize energy storage when stockpiling energy during times of abundance [12].

The CMEE was initially conceived following observations that different populations (such as hunter-gatherers versus individuals living in industrialized societies) have strikingly similar levels of TEE, despite very different physical activity patterns [16,17]. For example, Pontzer et al. [16] compared TEE of the Hadza hunter-gatherer tribe in northern Tanzania with industrialized populations. Hunter gatherers lead substantially more active lives than their comparatively sedentary Western counterparts, and so the *a-priori* assumption of this study was that they would have higher TEE. This was not the case, however, with comparable body size-adjusted TEE reported between both populations. This finding of similar TEE between active and less active populations has been reproduced in other studies [18–21]. These data, along with a range of other theoretical and empirical lines of evidence (detailed description of which is beyond the scope of this article but is available elsewhere [1,12,13]), led to the development of the CMEE. This model has broad public health implications, not least in that it challenges the notion that declining physical activity levels, and an associated reduction in total energy expenditure, may be causative in the ever-increasing obesity levels apparent in industrialized societies. [22], which in turn questions the role of increased physical activity to induce weight loss. Yet much remains unknown about the underlying factors that constrain TEE, nor of the compensations that may occur when activity energy expenditure is high, and substantial further investigation is required.

Endurance athletes, such as runners, cyclists, triathletes and rowers are a particularly interesting group on which to explore these concepts. These athletes habitually undertake very high training volumes, which have a very substantial energetic cost [23–26], opening the question of whether it is really possible to compensate for this, and if so, through via which mechanisms this takes place. Importantly, high levels of activity expenditure in endurance athletes are often unmatched by adequate energy intake, which may occur due to conscious restriction to meet a desired body mass, inadvertent undereating or alimentary limits to the amount of food that can be ingested or absorbed [8,9,27,28]. This combination of stressors to both the expenditure and intake sides of the energy balance equation render endurance athletes particularly susceptible to energy deficiency, and within this review we argue that it is energy deficiency, rather than exercise energy expenditure *per se*, that may underpin compensatory responses. Accordingly, the aim of the current perspective is to A) Describe the characteristics of endurance athletes that render them a useful model to explore concepts related to energy constraints and compensation (section 2), B) Consider constraints to activity energy expenditure (section 3.1) and C) Describe compensations that may occur when activity energy expenditure is high and unmet by adequate energy intake (section 3.2).

1. ENDURANCE EVENTS AND ATHLETES

Endurance sports, such as distance cycling, running, rowing, swimming and cross-country skiing, involve repeated contraction of large muscle groups over prolonged periods of time, the aim of which is usually to complete a set distance within the shortest time possible. Distances covered, and event durations, vary widely, with events such as the marathon (42 km) or the Olympic distance triathlon (1.5 km swim, 40km cycle and 10km run) typically taking on average about 4.5 and 3 hours to complete (although elite performers are capable of completing these distances much faster, *e.g.,* the current marathon world record, set by Eliud Kipchoge at the 2022 Berlin Marathon was 2:01:09). Ultra-endurance and multi-stage events are a more extreme type of endurance event, which are ever-increasing in popularity [29], and can last anywhere from about 4 hours to several weeks or even months [30]. Popular examples include the Ironman (3.8km swim, 180km cycle and 42.2 km run), or multi-stage events such as the European cycling grand tours (Tour de France, Giro d'Italia and La Vuelta a Espana) which cover distances of approximately 3500km and last about 3 weeks; The 5100km Self-Transcendence race which is the world's longest certified footrace and takes approximately 6 – 7 weeks or the Talisker Whisky Atlantic Challenge, which involves rowing across the Atlantic Ocean (4800km) and takes approximately 4 – 6 weeks.

TEE during endurance events such as these have been measured using the doubly labelled water technique, and evidence syntheses indicate that well-trained humans are capable of achieving *physical activity levels* (PALS; *i.e.,* total expenditure expressed as a multiple of basal metabolic rate (BMR)) of >5 [25,31,32], which is comparable to TEE of other highly active species who undertake large amounts of endurance activity, *e.g.,* migratory birds [14]. These very high expenditures can be sustained for days, weeks, or even months, as evidenced by estimates provided from the assessment of doubly labelled water during cycling grand tours [33,34] and a 95 day artic trek [35]. Participation in events such as these requires arduous, all-consuming and sustained preparatory programs. For example, elite rowers habitually train for around 30 hours per week, with this training predominantly rowing specific, complemented by non-specific endurance (*e.g.,* running, swimming or cycling), resistance and mobility training [23,36,37]. Similarly high training volumes have been reported for other endurance athletes, including cyclists, runners and triathletes [26,38–41]. The energetic costs of endurance activities are usually reported in metabolic equivalents (METS), which represent the proportion to which any given activity increases metabolism above basal requirements. For example, the energetic costs of cycling at 22.5km$\cdot$hr^{-1}, or running at 11.2 km$\cdot$hr^{-1} are approximately 10 and 11 METS. An athlete that trains for 2 – 4 hours at an average MET of 10 may burn approximately 1575 – 3150 kcal in that training session alone. Considering that the same athlete may have a basal metabolic rate of approximately 1750 kcal$\cdot$day^{-1} this is clearly beyond the capacity of the body to compensate for.

These examples indicate that activity energy expenditure does have the capacity to increase TEE, and it seems likely that there is a threshold of activity energy expenditure beyond which the body can compensate for (see Figure 1). Indeed approximately 600 kcal$\cdot$day^{-1} has been suggested as human's maximum capacity for metabolic compensation [31] although this number is likely to depend on a range of factors, including the individual’s training status and energy availability (discussed in Section 3.2 of this review). It is also important to consider that athletes are a unique and specific population, with highly trained, elite and world-class athletes considered to represent 0.014%, 0.0025% and 0.0006% of the global population, respectively [42]. Adherence to the training and nutritional programs required to compete in endurance and ultra-endurance events, may frequently require a conscious, planned and supported over-riding of evolved biological signals relating to energy balance. Throughout *Homo sapien*’s evolutionary journey, energy scarcity was a common occurrence and populations often lived at the lower margins of energy balance. Powerful selective forces therefore drove adaptations for energetic efficiency both in terms of maximizing energy input (via increasing food intake), and in minimizing energy output (via reducing activity) [5,43]. In other words, our ancestors undertook only enough activity as was required to procure sufficient food, and minimized any excess or unnecessary activity to ensure precious energy stores were not wasted. Contemporary endurance athletes do not experience the same relationship between physical activity energy expenditure and energy intake. In fact, this relationship is flipped, whereby many times nutritional intake is planned and manipulated to support exercise training, as opposed to undertaking exercise for the primary purpose of meeting nutritional needs. What drives endurance athletes to overcome these evolutionary drivers, and to strive to meet, and extend, the limits of human endurance likely represents a mix of biological, psychological and sociological factors [44], and elucidation of these represent a fascinating and highly warranted avenue for ongoing investigation.

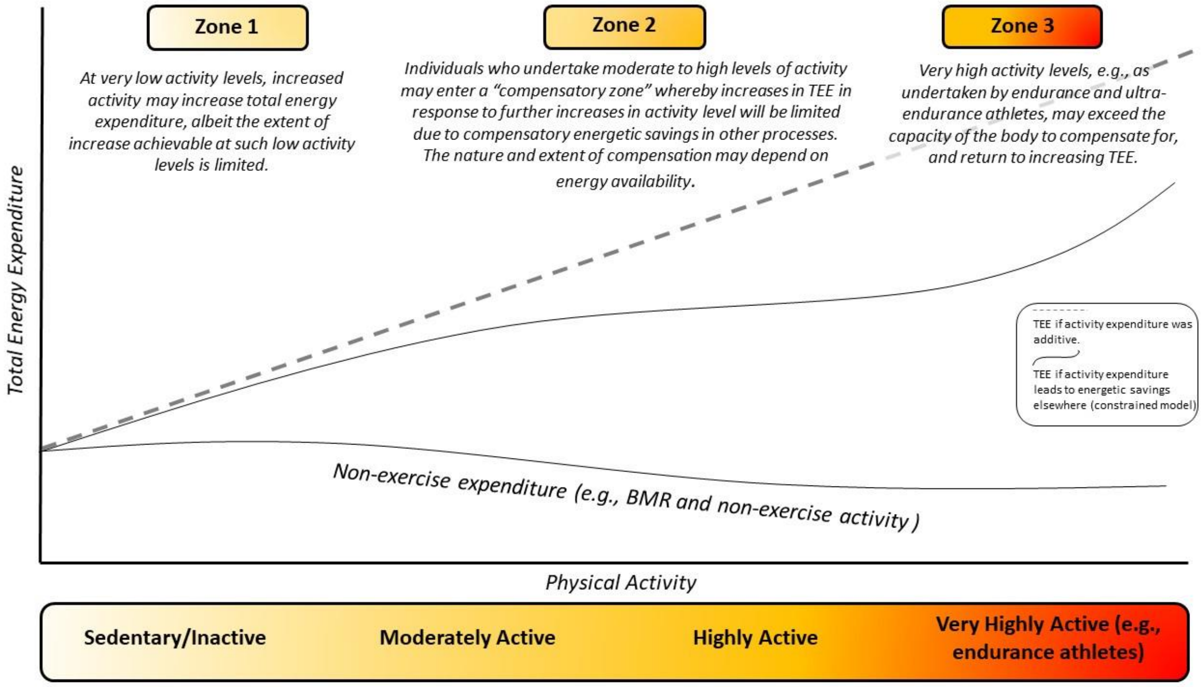

Figure 1: The influence of activity energy expenditure on total energy expenditure.

Legend: *The extent of compensation that occurs, and thus the extent to which activity energy expenditure increases total energy expenditure may depend on the absolute amount of activity undertaken. At very low activity levels (Zone 1), increases are likely to be largely additive, although the extent of contribution to TEE at such low activity levels will be small. Moderate to high activity levels are likely to induce relatively smaller increases to TEE, as energy costs of increased activity may be off-*

set by energetic savings elsewhere (Zone 2 – The "compensatory" zone). The nature and extent of these compensations is likely to be determined by energy availability, with lower energy availabilities inducing greater compensation. The amount of energy required to support the very large amounts of activity undertaken by endurance athletes is likely to exceed the capacity of the body to compensate, and can lead to further increases in TEE (Zone 3). These increases are still likely to be less than predicted by an entirely additive model, as some compensation is likely to occur.

2. Energy constraint and compensation: Insights from endurance athletes

The CMEE is based on the premise that in the long-term, increases in activity energy expenditure will not increase TEE, due to compensatory energetic savings elsewhere [12]. But the aforementioned examples from endurance athletes indicate that in certain situations, the volume of training habitually undertaken may exceed the capacity of the body to compensate. As depicted in Figure 1, compensations that occur in the face of increased activity energy expenditure are likely to be partial, and the high training loads undertaken by endurance athletes can increase TEE, albeit to a lesser degree than may be predicted by an additive model. This in turn opens further questions, including what constrains the absolute amount of activity that can be undertaken, how much energy can feasibly be saved via compensation, and through what mechanisms this occurs. Within the following sections, two particularly pertinent issues relevant to understanding the relationship between endurance exercise and TEE will be considered through A) Exploring what constrains the absolute amount of endurance exercise that can be undertaken, and B) Considering compensations that may occur in the face of high activity energy expenditure when unmet by adequate energy intake.

3.1. Constraints to activity energy expenditure

A number of factors may constrain human's capacity to sustain high activity levels, otherwise known as the "metabolic ceiling" [32,45]. Potential limiting factors include food availability, capacity to digest, absorb, process and deliver said fuel to the working muscles, capacity to oxidize available fuels, waste removal, time required for recovery and repair, or thermoregulatory limits [31,32,45], with the relative contribution of each of these factors likely to depend on both the intensity and duration of activity undertaken. As described above, PALs > 5 are achievable during prolonged endurance events, however such high activity levels are generally accompanied by substantial tissue loss, indicating that at least a portion of the energy required to support them may came from body stores, rendering them unsustainable in the long-term [25,31]. Importantly, the extent of tissue loss during prolonged endurance events relates to energy intake [25], indicating that the capacity to sustain high activity levels may largely depend on capacity to fuel it. This perspective is also supported by data from other populations with lower activity levels. Willis et al. [46] investigated the relationship between physical activity (using accelerometry) and TEE (assessed using doubly labelled water) in a group of 584 older adults and observed that the relationship between physical activity and TEE was additive in those defined as weight stable or positive, but was consistent with the constrained model for those categorized as being in negative energy balance [46], again emphasizing the importance of fueling to sustain higher activity levels. Finally, Thurber et al. [31] recently synthesized available evidence related to TEE during endurance events, and reported that although PALs > 5 were achievable, those in excess of approximately 2.5 generally induced tissue loss, and as such were considered unsustainable. Interestingly, the authors also synthesized evidence from over-feeding studies, which suggests that approximately 2.5 times the BMR is the maximum amount of food that can be ingested/absorbed, reinforcing the perspective that alimentary limits may act as the primary constraint to a human's metabolic ceiling.

Although energy intake is undoubtedly an important factor to consider, and in many situations may be the primary determinant of human's metabolic ceiling, it is important to consider that other factors are also likely to play a role. Fueling high activity levels is not just about consuming sufficient calories. These calories must be digested in the mouth, stomach and intestine, absorbed into the bloodstream, taken up by the working muscles, and then to enter one of the available bioenergetics pathways that use energy from food to regenerate ATP at a rate commensurate to the demands of the activity [47]. Macronutrients not used immediately may also be stored in the liver or muscle, which may further delay their delivery when required. Bioenergetic pathway efficiency also depends on capacity to deliver oxygen to the working muscle, to remove metabolic by-products, and to regulate body temperature, thus the capacity of the cardiorespiratory, circulatory and thermoregulatory systems are also integral to support high activity levels. Constraints to any of these systems and processes can influence the metabolic ceiling, and their relative contribution may vary due to individual (*e.g.,* age, sex, body composition, health, nutrition and training status) and environmental (*e.g.,* temperature, humidity and altitude) factors. For example, thermoregulatory limits may have a more important role to play in constraining activity undertaken in a hot and humid environment, than the same activity undertaken under ambient conditions [48]. An untrained individual may have a relatively low metabolic ceiling that is rapidly reached due to cardiorespiratory or metabolic constraints, with other factors such as food availability or thermoregulatory limits unlikely to meaningfully influence the amount of activity undertaken. In contrast, constraints to the amount of activity undertaken by endurance and ultra-endurance athletes is likely to be multi-factorial, with each of the aforementioned constraints, along with the time required to sleep and recover between exercise bouts, likely combining to prevent further increases. Take, for example, the Talisker Whiskey Atlantic Challenge, which is a 4800km rowing race across the Atlantic Ocean, undertaken by individuals, or small teams of 2 - 5 rowers. The race lasts approximately 4 – 8 weeks, and a typical strategy employed by a small team is for half of the team to row while the other half eats and rests, in a 2-hour-on-2-hour-off shift pattern. Individual rowers adopt a more variable shift pattern, and may row more than 12-hours per 24-hour cycle. Participation in extreme events such as these requires extensive training and preparation programs, and it is unlikely that any one factor will constrain the absolute amount of activity undertaken during the event itself, but instead that these athletes may reach the limits of most, if not all, potential physiological and psychological constraints.

3.2. Compensatory responses to high activity energy expenditure unmet by adequate intake.

As described in Section 3.1, sustaining high activity levels for prolonged periods of time largely depends on the capacity to fuel said activity. The challenges of adequate fueling for the amount of training typically undertaken by endurance athletes is well-documented [23,26,49], as are the health and performance consequences of low *energy availability (LEA)* [3,8,9,28], which is defined as the amount of energy available to support bodily processes after the demands of exercise have been met [3,28]. This is a topical area of investigation within sport and exercise science, with current understanding summarized in models including the *Female and Male Athlete Triads* [9,10], *Relative Energy Deficiency in Sport Syndrome (REDS)* [8] and related conditions including the *Exercise Hypogonadal Male Condition* [6] and *Overtraining Syndrome* [7]. The consequences of these conditions are all likely to stem from a cascade of metabolic compensations that occur in the face of increased training energy expenditure unmet by adequate energy intake (or alimentary limits), and as such, considering them from this perspective may facilitate development of prediction, management and treatment strategies.

Recently, our group described the consequences of low energy availability in athletes from a life history perspective [2], and in relation to the *energetic trade-offs* that may occur when insufficient energy is available to simultaneously sustain all biological processes, along with the demands of training [50,51]. Briefly, energy is a finite resource, which must be distributed throughout the body to fuel all biological processes. Energy that is used for one function cannot be used for others, and so "trade-offs" between biological processes or tissues may occur. Competition between internal biological processes will be heightened when energy availability is low, and those considered most immediately essential to survival will be protected, even if this requires the diversion of energy away from, and potential downregulation of, others [13,52,53]. Compensation in the face of high activity expenditure unmet by adequate energy intake represents a form of energetic trade-off, the aim of which is to restore energy balance.

The compensatory energetic savings that may occur in the face of high activity expenditure, unmet by adequate intake, can be broadly categorized as behavioral and metabolic [14]. Behavioral compensations in response to increased activity expenditure could include increased food intake, or a reduction in non-exercise activity (*e.g.,* leisure and household activities, fidgeting or pottering; also known as "non-exercise activity thermogenesis" or NEAT [54]). In relation to food intake, the balance between energy intake and expenditure is poorly regulated, particularly in less active populations, with intake often exceeding expenditure [55,56]. In contrast, many endurance athletes do not eat enough even when food is abundant [57]. This may occur due to a number of factors, including intentional dietary restriction to reduce body weight or to achieve leanness, inadvertently due to poor nutritional knowledge, lack of time or resources, or to gastrointestinal limits to the amount of food that can be tolerated or absorbed [27]. Considering NEAT, reduced energy expenditure in non-exercise activities is apparent in many athletes, with meta-analytic data indicating that outside of training, athletes spend substantially more time in sedentary activities (+80 minutes·day^{-1}) than the general population, rendering them simultaneously "highly active and highly sedentary" [58]. Despite this, the capacity of reduced NEAT to compensate for the amount of energy required to support habitual endurance training programs is limited, considering that exercise expenditure often exceeds BMR (see examples in Section 3.1), whereas NEAT typically comprises approximately 0.2*BMR. As such, metabolic compensations to conserve energy may be necessary when energy availability is low. For example, reduced resting metabolic rate (RMR) has been reported in observational studies of exercising women with symptoms of low energy availability, such as functional hypothalamic amenorrhea [59–61], or in rowers and cyclists after a period of intensified training [62,63]. The factors that contribute to reduced BMR are unknown, but may include, for example, increased mitochondrial efficiency [14,64], or a downregulation of reproductive and metabolic hormones [65], such as oestrogen, testosterone, leptin and T3. Many of these hormones act systemically and may subsequently influence other tissues, such as bone, which is known to be particularly vulnerable to chronically low energy availability [66]. It is important to highlight, however, that reduced BMR is not universally observed in situations of metabolic compensation and much remains unknown about the means through which energetic savings are made (see [14] for a detailed review on this topic). It is possible that a lack of sensitivity in available measures of BMR (or its proxy RMR) may preclude detection of the relatively small expected effects and substantial ongoing research is required to explore mechanisms through which compensation to increased exercise energy expenditure may occur.

The order in which different biological processes may be protected or downregulated during times of acute or chronic LEA has been described as the “hierarchy of functional preservation” and processes deemed more immediately essential to survival, are predicted to be protected, even if this comes at the expense of others [67–69]. This hierarchy is likely to be impacted by a wide range of parameters, including the extent and duration of low energy availability along with individual (*e.g.,* sex, age, body composition, training, nutrition and health status) and environmental (*e.g.,* temperature and altitude) factors. The ultimate consequences of compensation for health, or athletic performance, may range from positive, benign, or harmful, depending on the extent of the deficit, the environment within which it occurs and the specific outcome of interest [2]. For example, energy restriction throughout the lifespan has been reported to improve longevity and health-span [70], which may occur due to a range of mechanisms which are beyond the scope of this piece, but have been described in detail elsewhere [71–73]. Within the sport and exercise science field, brief exposure to LEA as part of a structured, periodized, training and nutrition program can bring about positive outcomes, such as favoring metabolic responses that increase exercise efficiency, or facilitating optimization of the power-mass ratio through reducing body fat levels [74,75]. But as with many things “*the dose makes the poison*” and while moderate energy restriction can bring about certain benefits, longer-term exposure to more severe deficits may induce energetic trade-offs with potentially harmful consequences.

Summary and Future Perspectives

The *Constrained Model of Total Energy Expenditure (CMEE)* holds that energy expended in increased physical activity will not add to total energy expenditure, but instead to induce compensatory energetic savings elsewhere. Herein, we discuss this theory from the perspective of endurance athletes, and key-points from this review can be summarized as follows: A) Higher activity levels, as observed in endurance athletes, may exceed the capacity of the body to compensate for, and thus increase TEE; B) A range of factors may combine to constrain activity energy expenditure, with the ability to ingest, digest, absorb and deliver sufficient calories from food to the working muscle likely to be the primary determinant to sustaining the high activity levels that endurance athletes habitually undertake and C) That compensations in the face of high activity expenditure may be primarily driven by low energy availability *i.e.,* the amount of energy available for all biological processes after the demands of exercise have been met, and not by activity expenditure *per se.*

Looking forward, endurance athletes may represent a useful model to investigate more nuanced questions related to these concepts, such as the upper limit of the human metabolic ceiling, along with the factors that determine this; the extent to which physical activity can influence TEE, and the underlying mechanisms through which the body conserves energy when availability is low. Of particular interest is a better understanding of what systems may be protected or sacrificed when insufficient energy is available to simultaneously support the demands of activity alongside all other biological processes, and how individual and environmental factors may influence this. The answers to these questions may be of considerable interest to sport and exercise scientists striving to support their athletes to reach and extend the limits of human performance; medical and public health researchers interested in reducing the individual and societal burdens imposed by conditions caused by physical inactivity and/or food over-consumption; and evolutionary biologists seeking to better understand how evolutionary drivers related to energy expenditure and intake have shaped the development of our species.

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REFERENCES:

1. Pontzer H, Durazo-Arvizu R, Dugas LR, Plange-Rhule J, Bovet P, Forrester TE, et al. Constrained total energy expenditure and metabolic adaptation to physical activity in adult humans. Curr Biol [Internet]. Elsevier Ltd; 2016;26:410–7. Available from: http://dx.doi.org/10.1016/j.cub.2015.12.046

2. Shirley M, Longman D, Elliott-Sale K, Hackney A, Sale C, Dolan E. A life history perspective on athletes with low energy availability. Sport Med. 2022;52:1223–34.

3. Loucks AB, Kiens B, Wright HH. Energy availability in athletes. J Sports Sci. 2011;29:37–41.

4. Caspersen C, Powell K, Christenson G. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep. 1985;100.

5. Lieberman D. Is exercise really medicine? An evolutionary perspective. Curr Sports Med Rep. 2015;14:313–9.

6. Hackney A. Hypogonadism in exercising males: Dysfunction or adaptive-regulatory adjustment? Front Endocrinol (Lausanne). 2020;11:11.

7. Meeusen R, Duclos M, Foster C, Fry A, Gleeson M, Nieman D, et al. Prevention, diagnosis, and treatment of the overtraining syndrome: joint consensus statement of the European College of Sport Science and the American College of Sports Medicine. Med Sci Sport Exerc. 2013;45:186–205.

8. Mountjoy M, Burke L, Ackerman KE, Blauwet C, Lebrun C, Melin A, et al. International Olympic Committee (IOC) consensus statement on relative energy deficiency in sport (RED-S): 2018 Update. Int J Sport Nutr Exerc Metab. 2018;28:316–31.

9. Nattiv A, Loucks AB, Manore MM, Sanborn CF, Sundgot-Borgen J, Warren MP. The female athlete triad. Med Sci Sports Exerc. 2007;39:1867–82.

10. Nattiv A, De Souza M, Koltun K, Misra M, Kussman A, Williams N, et al. The male athlete triad - A consensus statement from the female and male athlete triad coalition part 1: Definition and scientific basis. Clin J Sport Med. 2021;31:345–53.

11. WHO. WHO Fact Sheet on Malnutrition [Internet]. 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/malnutrition

12. Pontzer H. Constrained total energy expenditure and the evolutionary biology of energy balance. Exerc Sport Sci Rev. 2015;43:110–6.

13. Pontzer H. Energy constraint as a novel mechanism linking exercise and health. Physiol. 2018;33:384–93.

14. Halsey L. The mystery of energy compensation. Physiol Biochem Zool. 2021;94:380–93.

15. Goldsmith R, Joanisse D, Gallagher D, Pavlovich K, Shamoon E, Leiber R, et al. Effects of experimental weight perturbation on skeletal muscle work efficiency, fuel utilization, and

biochemistry in human subjects. Am J Physiol Regul Integr Comp Physiol. 2010;298:R79-88.

16. Pontzer H, Raichlen D, Wood B, Mabulla A, Racette S, Marlowe F. Hunter-gatherer energetics and human obesity. PLoS One. 2012;7:40503.

17. Dugas L, Harders R, Merrill S, Ebersole K, Shoham D, Rush E, et al. Energy expenditure in adults living in developing compared with industrialized countries: a meta-analysis of doubly labeled water studies. Am J Clin Nutr. 2011;93:427–41.

18. Dugas L, Harders R, Merrill S, Ebersole K, Shoham D, Rush E, et al. Energy expenditure in adults living in developing compared with industrialized countries. A meta-analysis of double labeled water studies. Int J Obes. 2008;32:1256–63.

19. Urlacher S, Snodgrass J, Dugas L, Madimenos F, Sugiyama L, Liebert M, et al. Childhood daily energy expenditure does not decrease with market integration and is not related to adiposity in Amazonia. J Nutr. 2021;151:695–704.

20. Ebersole K, Dugas L, Durzo-Arvizu R, Adeyemo A, Tayo B, Omatade O, et al. Energy expenditure and adiposity in Nigerian and African American Women. Obesity. 2008;16:2148–54.

21. Pontzer H, Wood B, Raichlen D. Hunter-gatherers as models in public health. Obes Rev. 2018;S1:24–35.

22. Jebb S, Moore M. Contribution of a sedentary lifestyle and inactivity to the etiology of overweight and obesity: Current evidence and research issues. Med Sci Sports Exerc. 1999;31:534–41.

23. Winkert K, Steinacker J, Koehler K, Treff G. High energetic demand of elite rowing - Implications for training and nutrition. Front Physiol. 2022;13:829757.

24. Sjodin A, Andersson A, Hogberg J, Westerterp K. Energy balance in cross-country skiers: a study using doubly labeled water. Med Sci Sport Exerc. 1994;26:720–4.

25. Cooper J, Nguyen D, Ruby B, Schoeller D. Maximal sustained levels of energy expenditure in humans during exercise. Med Sci Sport Exerc. 2011;43:2359–67.

26. Etxebarria N, Mujika I, Pyne D. Training and competition readiness in triathlon. Sports. 2019;7:101.

27. Wasserfurth P, Palmowski J, Hahn A, Kruger K. Reasons for and consequences of low energy availability in female and male athletes: Social environment, adaptations, and prevention. Sport Med - Open. 2020;6:44.

28. Areta J, Taylor H, Koehler K. Low energy availability: history, definition and evidence of its endocrine, metabolic and physiological effects in prospective studies in females and males. Eur J Appl Physiol. 2021;121:1–21.

29. Scheer V. Participation trends of ultra endurance events. Sport Med Arthropscopy Rev. 2019;27:3–7.

30. Koehler K, Geesman B. Nutrition for Ultraendurance Exercise. Nutr Enhanc Sport Perform. 2nd ed. Academic Press; 2019. p. 521–31.

31. Thurber C, Dugas L, Ocobock C, Carlson B, Speakman J, Pontzer H. Extreme events reveal an alimentary limit on sustained maximal human energy expenditure. Sci Adv. 2019;5:eaaw0341.

32. Hammond K, Diamond J. Maximal sustained energy budgets in humans and animals. Nature. 1997;386:457–62.

33. Westerterp K, Saris W, Van Es M, ten Hoor F. Use of the doubly labeled water technique in humans during heavy sustained exercise. Journaly Appl Physiol. 1986;61:2162–7.

34. Van Hooren B, Cox M, Rietjens G, Plasqui G. Determination of energy expenditure in professional cyclists using power data: Validation against doubly labeled water. Scand J Med Sci Sport. 2022;

35. Stroud M, Ritz P, Coward W, Sawyer M, Constantin-Teodosiu D, Greenhaff P, et al. Energy expenditure using isotope-labelled water (2H218O), exercise performance, skeletal muscle enzyme activities and plasma biochemical parameters in humans during 95 days of endurance exercise with inadequate energy intake. Eur J Appl Physiol Occup Physiol. 1997;76:243–52.

36. Fiskerstrand A, Seiler K. Training and performance characteristics among Norwegian international rowers 1970 - 2001. Scand J Med Sci Sport. 2004;14:303–10.

37. Tran J, Rice A, Main L, Gastin P. Profiling the training practices and performances of elite rowers. Int J Sports Physiol Perform. 2015;10:572–80.

38. Van Erp T, Sanders D, de Koning J. Training characteristics of male and female professional road cyclists: A 4-year retrospective analysis. Int J Sports Physiol Perform. 2019;1–7.

39. Haugen T, Sandbakk O, Seiler S, Tonnessen E. The training characteristics of world-class distance runners: An integration of scientific literature and results-proven practice. Sport Med - Open. 2022;8:46.

40. Solli G, Tonnessen E, Sandbakk O. The training characteristics of the world’s most successful female cross-country skier. Front Physiol. 2017;8:1069.

41. Areta J. Case study: Resumption of eumenorrhea in parallel with high training load after 4 years of menstrual dysfunction: A 5-year follow-up of an elite female cyclist. Int J Sport Nutr Exerc Metab. 2020;1–6.

42. McKay A, Stellingwerff T, Smith E, Martin D, Mujika I, Goosey-Tolfrey V, et al. Defining training and performance caliber: A participant classification framework. Int J Sports Physiol Perform. 2022;17:317–31.

43. Speakman J. An evolutionary perspective on sedentary behavior. Bioessays. 2020;42:e1900156.

44. Foster C, Barroso R, Beneke R, Bok D, Boulloso D, Casado A, et al. How to succeed as an athlete: What we know, what we need to know. Int J Sports Physiol Perform. 2022;17:333–4.

45. Peterson C, Nagy K, Diamond J. Sustained metabolic scope. Proc Natl Acad Sci USA. 1990;87:2324–8.

46. Willis E, Creasy S, Saint-Maurice P, Kozey Keadle S, Pontzer H, Schoeller D, et al. Physical activity and total daily energy expenditure in older US adults: Constrained versus additive models. Med Sci Sport Exerc. 2022;54:98–105.

47. Neufer D. The bioenergetics of exercise. Cold Springs Harb Perspect Med. 2018;8:a029678.

48. Hargreaves M. Physiological limits to exercise performance in the heat. J Sci Med Sport. 2008;11:66–71.

49. Burke L, Jeukendrup A, Jones A, Mooses M. Contemporary nutrition strategies to optimize performance in distance runners and race walkers. Int J Sport Nutr Exerc Metab. 2019;29:117–29.

50. Oliveira-Junior G, Pinto R, Shirley M, Longman D, Koehler K, Saunders B, et al. The skeletal muscle response to energy deficiency: A life history perspective. Adapt Hum Behav Physiol. 2021;in press.

51. Pontzer H, McGrosky A. Balancing growth, reproduction, maintenance and activity in evolved

energy economies. Curr Biol. 2022;32:R709–19.

52. Stearns SC. Trade-offs in life-history evolution. Funct Ecol. 1989;3:259.

53. Hill K. Life history theory and evolutionary anthropology. Evol Anthropol Issues, News, Rev. 1993;2:78–88.

54. Garland JR T, Schutz H, Chappell M, Keeney B, Meek T, Copes L, et al. The biological control of voluntary exercise, spontaneous physical activity and daily energy expenditure in relation to obesity: human and rodent perspectives. J Exp Biol. 2011;214:206–29.

55. Höchsmann C, Koehler K. Why exercise is often ineffective for weight loss but crucial for weight management. Sport Exerc Med Switz. 2022;10.34045/SEMS/2022/21.

56. Bosy-Westphal A, Hagele F, Muller M. Impact of energy turnover on the regulation of energy and macronutrient balance. Obesity. 2021;29:1114–9.

57. Gibbs JC, Williams NI, De Souza MJ. Prevalence of individual and combined components of the female athlete triad. Med Sci Sports Exerc. 2013;45:985–96.

58. Franssen W, Vanbrabant E, Cuveele E, Ivanova A, Franssen G, Eijnde B. Sedentary behaviour, physical activity and cardiometabolic health in highly trained athletes: A systematic review and meta-analysis. Eur J Sport Sci. 2022;22:1605–17.

59. Strock N, Koltun K, Southmayd E, Williams N, De Souza M. Indices of resting metabolic rate accurately reflect energy deficiency in exercising women. Int J Sport Nutr Exerc Metab. 2020;1–11.

60. De Souza MJ, West SL, Jamal SA, Hawker GA, Gundberg CM, Williams NI. The presence of both an energy deficiency and estrogen deficiency exacerbate alterations of bone metabolism in exercising women. Bone. 2008;43:140–8.

61. De Souza M, Lee D, VanHeest J, Scheid J, West S, Williams N. Severity of energy-related menstrual disturbances increases in proportion to indices of energy conservation in exercising women. Fertil Steril. 2007;88:971–5.

62. Stenqvist T, Torstveit M, Faber J, Melin A. Impact of a 4-week intensified endurance training intervention on markers of relative energy deficiency in sport (RED-S) and performance among well-trained male cyclists. Front Endocrinol (Lausanne). 2020;11:512365.

63. Woods A, Rice A, Garvican-Lewis L, Wallett A, Lundy B, Rogers M, et al. The effects of intensified training on resting metabolic rate (RMR), body composition and performance in trained cyclists. PLoS One. 2018;14:e0191644.

64. Koch R, Buchanan K, Casagrande S, Crino O, Dowling D, Hill G, et al. Integrating mitochondrial aerobic metabolism into ecology and evolution. Trends Ecol Evol. 2021;36:321–32.

65. Dipla K, Kraemer R, Constantini N, Hackney A. Relative energy deficiency in sports (RED-S): elucidation of endocrine changes affecting the health of males and females. Hormones. 2021;20:35–47.

66. Papageorgiou M, Dolan E, Elliott KJ, Craig S. Reduced energy availability: Implications for bone health in physically active populations. Eur J Nutr. 2018;57:847–59.

67. Longman DP, Prall SP, Shattuck EC, Stephen ID, Stock JT, Wells JCK, et al. Short-term resource allocation during extensive athletic competition. Am J Hum Biol. 2018;30:1–11.

68. Longman D, Stock JT, Wells JCK. A trade-off between cognitive and physical performance, with relative preservation of brain function. Sci Rep. Springer US; 2017;7:1–6.

69. Longman D, Dolan E, Wells J, Stock J. Patterns of energy allocation during energetic scarcity: evolutionary insights from ultra-endurance events. Comp Biochem Physiol Part A Mol Integr Physiol. 2023;281:111422.

70. Speakman J, Mitchell S. Caloric restriction. Mol Aspects Med. 2011;32:159–221.

71. Merry B. Molecular mechanisms linking calorie restriction and longevity. Int J Biochem Cell Biol. 2002;34:1340–54.

72. Speakman J. Why does caloric restriction increase life and healthspan? The “clean cupboards” hypothesis. Natl Sci Rev. 2020;7:1153–6.

73. Sinclair D. Toward a unified theory of caloric restriction and longevity regulation. Mech Ageing Dev. 2005;126:987–1002.

74. Stellingwerff T, Morton J, Burke L. A framework for periodized nutrition for athletes. Int J Sport Nutr Exerc Metab. 2019;29:141–51.

75. Burke L, Hawley J. Swifter, higher, stronger: What’s on the menu? Science (80-). 2018;362:781–7.