ARTICLE

Constrained Total Energy Expenditure and the Evolutionary Biology of Energy Balance

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PONTZER, H. Constrained total energy expenditure and the evolutionary biology of energy balance. *Exerc. Sport Sci. Rev.*, Vol. 43, No. 3, pp. 110–116, 2015. *The human body adapts dynamically to maintain total energy expenditure (TEE) within a narrow physiological range. Rather than increasing with physical activity in a dose-dependent manner, experimental and ecological evidence suggests the hypothesis that TEE is a relatively constrained product of our evolved physiology.* **Key Words:** total energy expenditure, homeostasis, evolutionary medicine, factorial model, metabolism

INTRODUCTION

"Nothing in biology makes sense except in the light of evolution," the geneticist Theodosius Dobzhansky famously wrote (8). This evolutionary mantel has been taken up with zeal by many in public health (26), shedding critical light on the etiology of obesity, Type II diabetes, cardiovascular disease, and other "diseases of affluence" plaguing developed countries. The evolutionary perspective is powerful yet straightforward: the human body has been shaped through natural selection to meet a particular set of ecological conditions and challenges, and recent changes to our environment can lead to harmful, yet evolutionarily predictable, physiological responses.

Models of energy balance, and particularly of energy expenditure, have been a notable exception to the embrace of evolutionary biology in public health and nutrition. Additive models of energy expenditure (also called "factorial" models) that currently predominate (13) treat total energy expenditure (TEE) simply as a product of body size and physical activity (PA) without regard for potential changes in energy allocation in response to variation in activity levels. In this review, I propose the hypothesis that TEE is a relatively stable homeostatically controlled trait that is more a reflection of our evolutionary past than our current lifestyle.

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In developing this Constrained TEE model of energy expenditure and balance, I begin by considering TEE as an evolved metabolic strategy and outline a Constrained TEE model for energy metabolism. I then examine empirical evidence from experimental studies of TEE, manipulating PA levels in humans and other species, and show that the observed relationship between habitual PA and TEE is consistent with a Constrained TEE model but not with current, commonly used, Additive TEE models. Afterward, I review ecological studies of habitual TEE using doubly labeled water to measure TEE across populations and species, which suggest that PA and food availability may work in concert to determine a set point (or narrow range) for TEE that the body works to maintain. Finally, I discuss the implications of a Constrained TEE model for the etiology of obesity and metabolic disease, the health effects of exercise, and the role of physical activity in models of energy balance.

TEE AS AN EVOLVED STRATEGY

TEE represents the summed daily metabolic activity of all organ systems (*e.g.*, immune, reproduction, digestive, musculoskeletal), including homeostatic activity, somatic maintenance, and growth. For humans and many other animals, PA (*i.e.*, musculoskeletal activity) is the most variable component of TEE, and it also can be the largest. During a day spent at rest, PA might account for a small fraction of TEE. However, during periods of intense activity, PA can exceed the energy cost of all other physiological activities combined (5). In the wild, and for humans in traditional hunting and gathering or subsistence farming populations, variation in PA will be driven in large part by food availability; depending on the species and the local ecology, individuals might travel farther and work harder when food is scarce or they might work hardest when food is plentiful to maximize intake or storage.

Consider two metabolic strategies in this context (Fig. 1). In an Additive TEE strategy (13), the energy spent each day on non-PA physiological activity (*i.e.*, on organ systems other than the musculoskeletal) is fixed and does not change, regardless of variation in PA (Fig. 1). By contrast, in a Constrained TEE strategy, non-PA energy expenditure adapts dynamically to variation in PA to maintain TEE within some narrow physiological range (Fig. 1). In both cases, during the long-term, mean TEE must equal mean food energy intake (accounting for digestive efficiency) for organisms to maintain weight stability and viability.

Current factorial models of TEE, common in public health and nutrition (13), implicitly assume that humans follow an Additive TEE strategy (Fig. 1). However, in nearly every conceivable ecological scenario relevant to humans, a Constrained TEE strategy would be favored by natural selection. For organisms with high PA during food-poor periods, an Additive TEE strategy would maximize energy requirements precisely when the risk of starvation was most severe, whereas a Constrained TEE strategy would reduce energy requirements and mortality risk. For organisms that work hardest when stockpiling food energy during food-rich periods, a Constrained TEE strategy would lower energy requirements and thereby maximize surplus energy gain. A Constrained TEE also could reduce the risk of predation while foraging by reducing the amount of time needed to obtain food during high-PA periods.

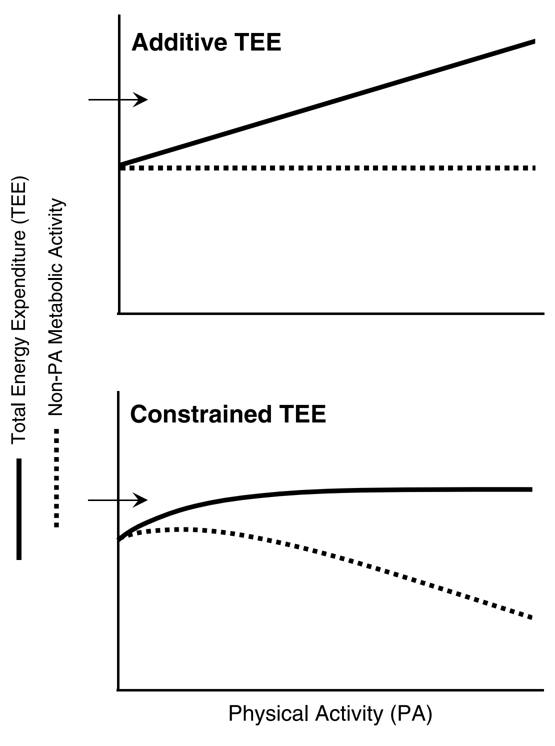

Figure 1. The relationship between total energy expenditure (TEE), physical activity (PA), and non-PA metabolic activity following an Additive TEE model (*top*) and a Constrained TEE model (*bottom*). In the Additive TEE model, TEE increases with PA in a linear dose-dependent manner. Non-PA metabolic activity (which includes basal metabolic rate) is not affected by variation in PA. In the Constrained TEE model, TEE is homeostatically maintained within a narrow range. Increasing PA has a limited effect on TEE and instead leads to a reduction in non-PA metabolic activity to keep TEE near its set point. In either model, mean TEE must equal mean food energy intake (indicated with an arrow on the y-axis) to maintain a stable weight.

The evolutionary cost of a Constrained TEE strategy is the reduction in energy allocation to non-PA activity, particularly reproduction, during periods of high PA. However, reproduction during periods of food scarcity or energy storage would be risky, with an increased probability of starvation for the mother and decreased probability of offspring survival. For relatively long-lived iteroparous species like mammals and birds, the opportunity cost of foregoing these low-quality reproductive opportunities likely will be outweighed by the benefit of improved survival and future reproduction. A Constrained TEE strategy keeps energy requirements in check while allowing the organism to prioritize and allocate energy among various organ systems in a dynamic manner that is responsive to current conditions and maximizes lifetime reproductive fitness. Evolutionarily informed models of energy expenditure and balance should therefore expect an adaptive Constrained TEE metabolic strategy.

TEE AND PA IN THE LABORATORY AND IN THE FIELD

Empirical measures of TEE across varying levels of PA provide a useful test and comparison of the Constrained TEE model. Perrigo (19,20) began a series of classic laboratory studies in the 1980s, measuring TEE and other metabolic function while manipulating PA, and this approach continues to shed light on adaptive metabolic response to changes in workload. More recently, the adoption of the doubly labeled water method in human ecology has provided data on TEE across diverse lifestyles with wide variation in PA. Both lines of evidence support a Constrained TEE model.

Experimental Studies of PA and TEE

Several laboratory studies in nonhuman animals have measured TEE under different exercise workloads by manipulating the amount of PA needed to acquire food (1,7,19, 20,28,29,32,33; Fig. 2C–K). For example, in rodent studies (19,20,29), an exercise wheel placed in the cage is connected to a food dispenser, and the number of revolutions needed to dispense one food pellet is then varied to create different PA conditions. There is no limit to the amount of food available, and the food energy gained per unit of PA (*e.g.*, per wheel revolution) far exceeds the energy cost per unit of PA. Thus, in principle, animals could increase PA directly in response to changes in the ratio of PA:food in each condition, with TEE increasing linearly in response to PA and basal metabolic rate (BMR) maintained at a constant level across conditions, as expected by Additive TEE models. Each condition is maintained for several days or weeks, such that animals within each condition are weight stable and, thus, in energy balance during metabolic measurements (although body weight may vary across conditions).

As shown in Figure 2, the observed pattern of PA and TEE in these studies is consistent with a Constrained TEE model. Across several species of birds and mammals, these studies show that increasing PA has a diminishing effect on TEE, with daily energy throughput constrained within some physiological window. In

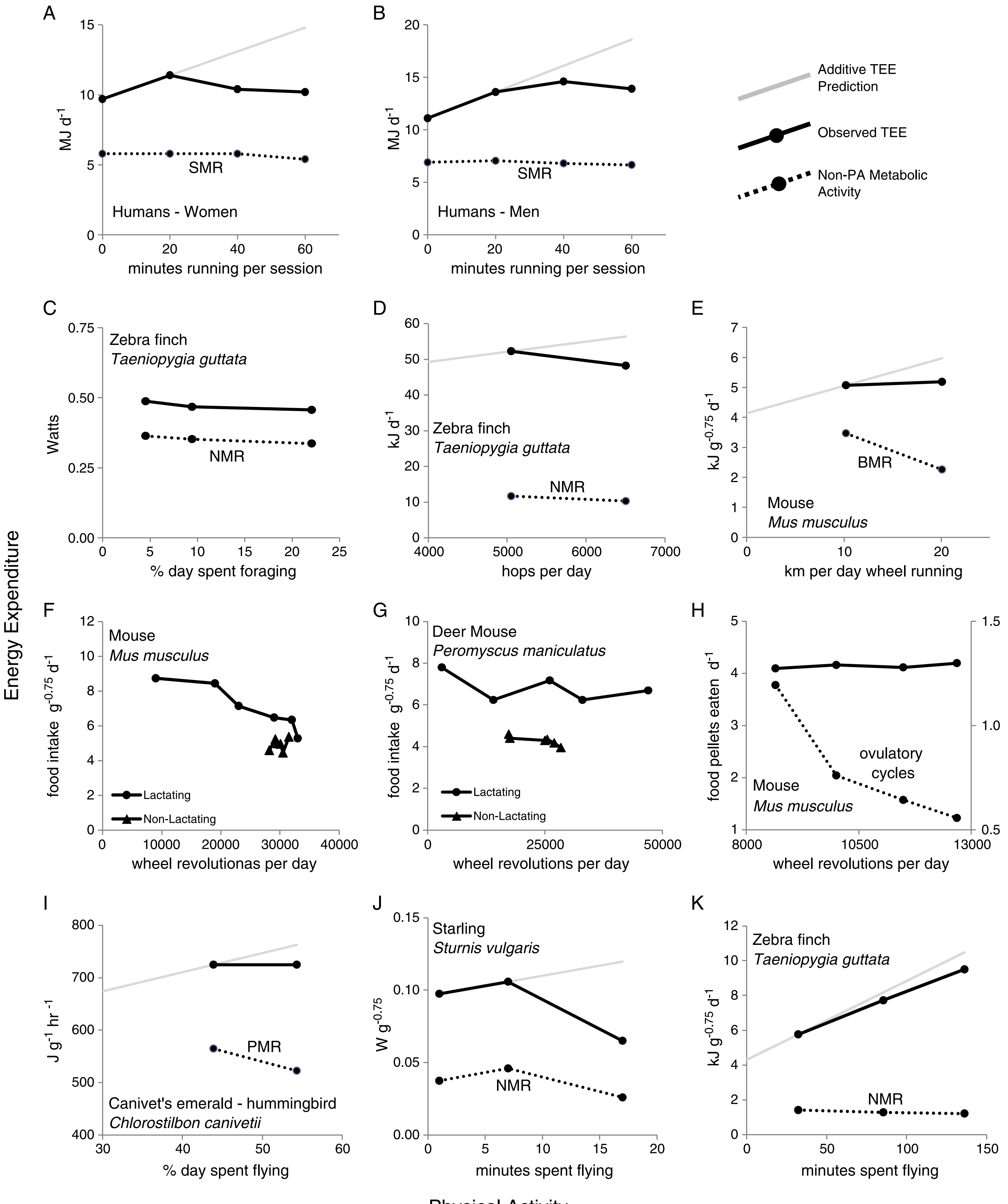

Figure 2. Experimental studies of total energy expenditure (TEE) and non–physical activity (PA) metabolic activity in response to manipulations in PA. In A to E, TEE was measured via indirect calorimetry (doubly labeled water or respirometry). In F to K, TEE was measured from food energy intake, accounting for any changes in body weight. In studies where body mass changed more than 10% across conditions (E, F, G, J, K), energy expenditure was scaled to (body mass)$^{0.75}$. Non-PA metabolic activity was measured via respirometry unless noted otherwise (SMR, sleeping metabolic rate; NMR, nighttime metabolic rate; PMR, perching metabolic rate). Additive TEE prediction was calculated from measured PA costs (D, E, K) by extrapolating the effect of PA on TEE between the sedentary and low-PA conditions (A, B, I, J). In I, sedentary TEE was estimated assuming TEE = PMR when PA = 0. Sources: A (30), B (30), C (33), D (7), E (29), F (19), G (19), H (20), I (28), J (1), K (32). BMR, basal metabolic rate.

cases where the expected TEE for an Additive TEE model can be estimated, the observed TEE response to increased PA is consistently lower (Fig. 2). In only one study (32), in starlings, did observed TEE approach the expectations of an Additive TEE model (Fig. 2K). However, these starlings lost approximately 20% of their body mass, including flight muscle, in the high-PA conditions, indicating that these birds compensated for increased PA in part by losing valuable somatic capital rather than simply increasing TEE (32). Indeed, in many of these studies (but not all), animals in the high PA condition lost substantial body mass, which may be one strategy for keeping TEE in check in high PA environments.

Measurements of BMR, nighttime metabolic rate, or resting (*e.g.,* perching) metabolic rate show reductions in non-PA physiological activity in high-PA conditions in these studies, consistent with the Constrained TEE model (Fig. 2). Several of these studies measured reproductive activity or somatic repair, allowing these reductions in non-PA physiological activity to be linked to specific organ systems. Zebra finches in high-PA environments delayed the onset of reproduction (6) and increased the interval between reproductive events (33), indicating a reduction in reproductive system metabolic activity. Increasing PA also led to slower somatic repair, measured as the rate of new feather growth (33). Juvenile female mice delayed growth and reduced or delayed ovulatory cycling, and mothers cannibalized pups, in high-PA conditions (19,20). Deer mouse mothers reduced lactation in high-PA conditions (19). The work by Perrigo (19) examining PA and TEE in lactating female rodents is particularly illuminating. TEE was greater in nursing mothers than in other females but, in both conditions, PA had essentially no effect on TEE (Fig. 2F, G). These observations indicate that TEE is somewhat labile but is under endocrine control rather than simply responding to PA.

Westerterp and colleagues (30) conducted an exercise intervention study in humans that mimics some important aspects of these PA manipulation studies. Sedentary men and women participated in a 40-wk training regimen designed to prepare them for a half-marathon (21 km) running race. TEE and sleeping metabolic rate were measured at 8, 20, and 40 wk into the study, as the amount of prescribed running per week was increased incrementally. Food energy intake was not manipulated; subjects were free to eat as they wanted. At 8 wk, subjects exhibited clear increases in TEE. However, in wk 20 and 40, despite increasing exercise workloads, TEE leveled off in both men and women (Fig. 2A, B). By contrast, sleeping metabolic rate was lower at wk 40 than at baseline ($P < 0.01$, paired *t*-test, n = 23 subjects). The plateau in TEE and reduction in sleeping metabolic rate developed despite an increase in fat-free mass. These metabolic adaptations to increased PA are similar to those observed in other species (Fig. 2) and support a Constrained TEE model for human metabolic physiology.

Ecological Studies of TEE and PA

Ecological studies of habitual TEE and BMR in populations with different varying degrees of PA in their normal daily lives inherently lack the experimental control of laboratory or exercise intervention studies but provide invaluable insight on the nature of long-term and ontogenetic adaptation to PA in humans and other species. TEE comparisons across human populations generally are consistent with a Constrained TEE model. Dugas and colleagues (9) conducted a meta-analysis of TEE, measured using doubly labeled water in 183 same-sex cohorts representing a global sample of 98 populations. They found no effect of Human Development Index, a measure of industrialization and thus habitual PA, on energy expenditure after controlling for body weight. Pontzer and colleagues (22) measured TEE using doubly labeled water in an adult sample (n = 30) of traditional hunter-gatherers. Despite high levels of PA in this population, Pontzer and colleagues (22) found no difference in TEE between hunter-gatherers and a comparative sample of European and American adults after controlling for fat-free mass. Some populations of subsistence farmers do appear to have marginally greater TEE after controlling for body size (22), which may indicate some ontogenetic flexibility in establishing the TEE window, as discussed later. However, the similarity in TEE across a broad range of populations, including those with habitually high levels of PA, suggests that TEE in humans is constrained physiologically.

Measurements of BMR and non-PA physiological activity in physically active traditional populations suggest compensation to high levels of PA, consistent with the Constrained TEE model. Pregnant and nursing mothers in traditional farming populations with high PA have been shown to decrease BMR, reducing the effects of pregnancy and lactation on TEE (16). Seasonal increases in PA also have been associated with decreases in ovarian hormone levels, a measure of reproductive system activity (11). Men in physically active traditional populations have lower testosterone levels, a measure of both reproductive activity and systemic anabolic activity, than age-matched men in comparatively sedentary industrialized populations (10). Together, these studies indicate that humans in high-PA environments reduce non-PA metabolic activity, reducing TEE as predicted by a Constrained TEE model.

Comparatively few studies have compared TEE in nonhuman animals across markedly different lifestyles, but the available data are consistent with those in humans. In a recent study of energy expenditure in 17 primate species, Pontzer and colleagues (21) found no difference in TEE between populations living in the wild versus those in captivity. Other studies have found similar TEE in red kangaroos living in pastures versus the wild and in wild and captive populations of tenrecs (see 21).

A pattern of TEE, PA, and body size emerges from ecological studies in humans and other species (Fig. 3). Populations in low-PA high-food availability environments (zoos, industrialized populations) achieve larger adult body mass than populations in high-PA environments where food energy is comparatively difficult to obtain (hunter-gatherer human populations; animals in the wild). Low-PA high–food availability populations also have greater TEE, but this difference disappears after correction for their larger body size. This pattern of covariance in PA, TEE, and body size suggests that the body may respond ontogenetically to levels of PA and food availability, growing larger and establishing a correspondingly higher TEE set point when food energy is readily available and PA demands are low. In this context, the elevated TEE seen in some subsistence farming populations (22) may reflect a combination of high-PA and high food availability during development. Developing individuals in these high-PA high–food availability environments might target a

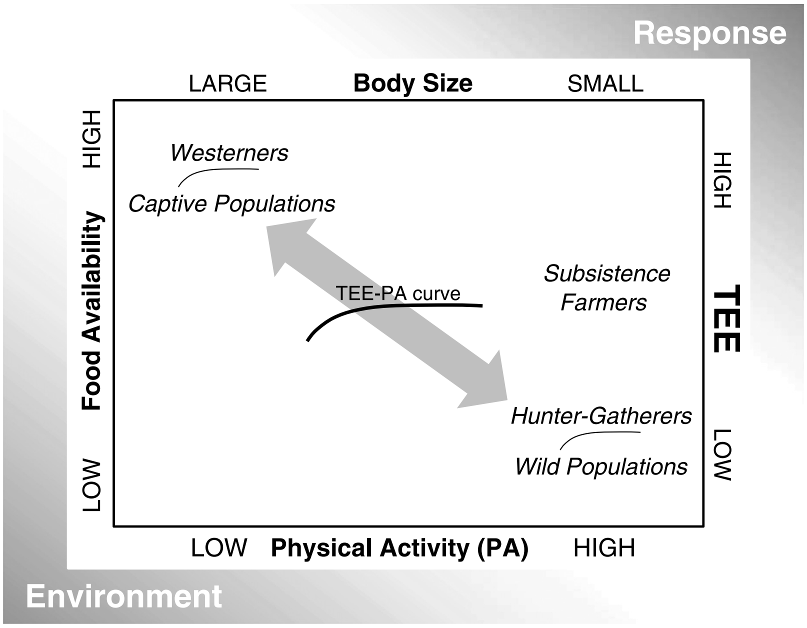

Figure 3. Hypothesized ontogenetic responses in body size and total energy expenditure (TEE) to environmental signals of food availability and physical activity (PA). Beginning in the center, a developing individual responds to its environment by targeting a higher or lower TEE. Because PA and food availability tend to be correlated inversely among human populations, individuals will tend to vary along the axis indicated by the *gray double arrow*. In populations where PA and food availability are both high, developing individuals may target a higher TEE and smaller body size, reducing non-PA metabolic requirements while maintaining a higher TEE ceiling.

higher TEE while maintaining a smaller body size. Smaller body size would in turn reduce non-PA energy demands, particularly if the size of metabolically expensive organs (*e.g.*, liver, kidneys, gastrointestinal tract) were reduced (14). This developmental strategy would keep non-PA metabolic requirements low while maintaining a higher TEE range to accommodate high PA demands; it also would result in relatively high TEE for their body mass, as reported previously in farming populations (22). Similarly, the remarkably high TEE reported for some elite athletes during training (5) may reflect the exceptionally high workloads and food availability during their adolescence. Investigating the ontogenetic responses to variation in PA and food availability, and the limits of developmental plasticity in body size and TEE, would be a fruitful direction for future research.

EXERCISE, OBESITY, AND HEALTH

The Constrained TEE model provides a useful framework for investigating and interpreting the role of exercise in weight management and overall health. The health benefits of exercise are well established and beyond debate. However, the effect of exercise intervention in generating and sustaining weight loss is much less clear (3,4,24). The adaptive nature of TEE in response to increased PA envisioned in the Constrained TEE model (Fig. 1) may provide insight into both the utility of exercise in preventing chronic disease and the futility of many exercise-based strategies for weight loss.

Strategies for using exercise as a tool to lose weight typically assume an Additive TEE model, whereby increases in PA lead to corresponding increases in TEE and result in negative energy balance (3,4,24). The Constrained TEE model suggests that these strategies may have some effect for sedentary individuals, as TEE increases somewhat with PA in the very low range of PA (Fig. 1). Indeed, low-intensity exercise interventions in sedentary subjects have been shown to induce weight loss (4). However, as the body adapts to higher levels of PA to maintain TEE within a homeostatically constrained range, the effects of increased PA will diminish. Specifically, the Constrained TEE model expects the effects of exercise interventions to diminish at higher levels of PA and across longer periods of measurement. Consistent with these expectations, Church and colleagues (4) reported less-than-expected weight change in an exercise-only intervention among high-PA subjects. Ross and Janssen (24), in a meta-analysis of exercise intervention studies, found that long-term weight loss (>20 wk) was invariably less than expected from exercise energy expenditures, and that the amount of exercise energy expenditure had no correlation with weight loss in these longer studies. Byrne and colleagues (3), using a combined exercise and diet restriction design, reported a reduction in resting metabolic rate among subjects that accounted largely for the discrepancy between expected and observed weight loss.

The Constrained TEE model also may prove useful in understanding the etiology of unhealthy weight gain and the recent global rise in obesity. Whatever societal or dietary variables promote the development of obesity, its fundamental underlying cause must be an imbalance of energy intake and energy expenditure. Individuals growing up in low-PA high–food availability settings typical of economically developed countries would be expected to develop a high TEE set point in part by achieving a larger body size (Fig. 3). Nonetheless, as with any ontogenetic response, there will be an evolved upper limit to attainable TEE and, in economically developed countries where food energy is essentially unlimited and packaged in very energy-dense forms (*e.g.*, sugary drinks), it still would be relatively easy for energy intake to exceed TEE. Indeed, just as TEE appears to be nonresponsive to increased PA in humans and other species (Fig. 2), studies manipulating food intake in humans generally find no effect of increased energy intake on TEE (31). If TEE does not increase in response to overconsumption, as suggested by the Constrained TEE model, the additional energy intake will be stored, much of it as fat. When these same individuals increase their exercise workload (with no change in food energy intake) in an effort to combat this weight gain, the Constrained TEE model suggests that the body will respond by reducing non-PA activity rather than increasing TEE (Fig. 1). Over the long-term, these individuals will find it difficult to achieve weight loss through increased exercise alone as the body defends its mass by maintaining TEE within a narrow range. From this perspective, the obesity pandemic is fundamentally a problem of chronically high–food energy availability and intake combined with a limited ability to increase TEE.

Although metabolic responses to increased PA may frustrate exercise-based weight loss programs, the reduction in non-PA metabolic activity in response to increased PA appears to be a critical mechanism by which exercise protects against chronic disease (23,25). In a Constrained TEE model, increased exercise is expected to reduce non-PA metabolic activity, which may in turn reduce inflammatory or endocrine response to pathogens and other physical or psychological stressors. Indeed, the anti-inflammatory benefits of exercise are well documented (25), and exercise has been shown to reduce inflammation related to cardiovascular disease risk (*e.g.*, C-reactive protein; 17) and rheumatic disease (2). By decreasing non-PA metabolic activity, increased exercise also may dampen stress reactivity and reduce or normalize the endocrine response to psychological stressors, providing benefits for psychological health (23,25).

At much higher exercise workloads, the Constrained TEE model predicts that exercise can have detrimental health effects, as the energy available for critical non-PA metabolic activity is reduced below adequate levels. As discussed previously, experimental studies manipulating PA levels in nonhuman animals have shown reductions and delays in growth, reproduction, and somatic repair at higher workloads (19,20,33; Fig. 2H). Similarly, an exercise-induced reduction in non-PA metabolic activity may underlie many of the symptoms (*e.g.*, fatigue, immunosuppression, increased recovery times) associated with overtraining in elite athletes (15,34), including the disruption of menstrual cycling in female athletes. Indeed, exercise-induced suppression of ovarian activity is well documented and is found even in women who are weight stable (12). Ellison and others (12) have found that less severe suppression can be seen even with moderate exercise, suggesting that ovarian activity responds in a dose-dependent manner to increasing PA, which is consistent with the Constrained TEE model.

MECHANISMS AND LIMITS IN ESTABLISHING AND MAINTAINING TEE

A Constrained TEE model is consistent with much of the available data from experimental and ecological studies of PA and TEE, but a number of issues remain unresolved. Perhaps most fundamentally, if TEE is a homeostatically controlled physiological trait, how does the body establish and maintain its target range of energy throughput? Energy balance requires that, across the long-term, mean TEE equal mean energy intake (Fig. 1), suggesting that the TEE set point may be developed at least partly in response to environmental cues of food availability. Experimental manipulations of food availability in adults have shown that humans can respond to reductions in energy intake with corresponding changes in TEE (31), but ontogenetic responses to food availability are less well studied. Data from ecological studies of TEE (Fig. 3) as well as a wealth of data on human growth and development (27) suggest that body size and TEE do indeed respond developmentally to PA and food availability, but the underlying mechanisms warrant further study. As noted previously, varying adult body size and proportion, and in turn the size of metabolically expensive organs, could be one developmental strategy for reducing non-PA metabolic activity (14) and hence TEE. Individuals also may respond to food availability through changes in the metabolic cost of activity, as shown recently by Yamada and colleagues (35). Comparative studies of TEE across species (21) indicate that TEE set points can change dramatically across evolutionary time, adding an additional layer of analysis.

Once the TEE target is established, the Constrained TEE model posits that the body defends it by regulating non-PA metabolic activity (Fig. 1), requiring signaling mechanisms between the musculoskeletal system and others that relay the intensity of PA and suppress or promote non-PA metabolism appropriately. The time course for responding to changes in PA may shed some light on the mechanisms involved; exercise intervention studies (24,30) suggest that the period of adjustment is approximately 20 wk in humans. Recent work has brought the secretory role of muscle and the endocrine and paracrine effects of myokines into increasingly better focus (2,18), revealing a broad array of potential pathways for regulating non-PA activity in response to exercise, but more work is needed. Such work might reveal the prioritization of energy resources as PA increases. For example, work in zebra finches suggests that they sacrifice somatic repair and delay reproduction, but maintain offspring size, when exercise loads reduce non-PA resources (6,32), but prioritization may well differ across species.

Finally, the limits of adaptation to increased PA are unclear. Under a Constrained TEE model, non-PA metabolic activity decreases as exercise workload increases, but once some lower limit to non-PA expenditure is reached, any further increase in PA must, by necessity, increase TEE. Extreme endurance events (*e.g.*, arctic treks, multistage cycling races) raise TEE to levels well above any feasible TEE set point (5), but the substantial weight loss and protracted recovery times for these events suggest that this level of throughput does not represent truly sustainable TEE. Nonetheless, elevated TEE levels are evident in elite athletes outside of competition (5), and to the extent that these levels are maintained across the course of months or years, they present an interesting challenge to the Constrained TEE model. As discussed previously, one hypothesis is that, by training intensively from a young age, and with good nutritional support, these athletes have developed a higher TEE set point than nonathletes. Alternatively, these athletes may be self-selected, such that individuals with inherently high TEE set points are better able to maintain the high levels of sustained exercise needed to succeed at the elite level. It also is notable in this context that many of the performance-enhancing drugs commonly implicated in professional sports (*e.g.*, human growth hormone, testosterone) are those that promote non-PA metabolic activity, in effect circumventing the downregulation of non-PA activity at high workloads. The Constrained TEE model may provide a useful framework for understanding the physiological limits and consequences of sustained endurance training.

SUMMARY

The relationship between PA and TEE is more complex than current Additive TEE models in widespread use (13) allow. Rather than increasing with PA in a linear dose-response relationship, ecological and experimental data from several species suggest that TEE is constrained with respect to PA. In this review, I have proposed a Constrained TEE model for metabolic physiology, in which TEE is maintained homeostatically within a narrow range, and the body adapts to long-term increases in PA by reducing energy expenditure in other systems (Fig. 1). The Constrained TEE model is consistent with evolutionary predictions for metabolic physiology and with empirical evidence on energy expenditure and exercise (Fig. 2). Additional work is needed to clarify the mechanisms by which an individual's target TEE range is determined and defended, and the limits to long-term adaptation to changes in PA. The Constrained TEE model provides an integrative framework for investigating the protective health effects of exercise, the potential negative effects of overtraining, and the difficulty in achieving long-term weight loss though increased exercise.

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